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MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

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CONSERVATIVE MANAGEMENT OF CHRONIC RENAL FAILURE

INDEX

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Acute Renal Failure during the Progression of Renal Disease:

Late (severe) Renal Failure

Hemodialysis:

- Center
- Home
- Limited Care

Transplantation:

- Related Living Donor
- Cadaveric

Death

DEFINITIONS:

Conservative Management

Therapy required to relieve symptoms or retard the development of problems associated with renal disease. Peritoneal dialysis, for example, should be considered as conservative management. This technique can relieve symptoms and severe problems acutely, but it has little if any place in long-term therapy.

Renal Failure - Acute

Any reversible form of renal disease. This may even require more than conservative management. By definition the kidney recovers life-supporting function.

Renal Failure - Early (asymptomatic)

The period during which the serum creatinine rises to between 4 and 5 mgm%, or a decrease in creatinine clearance down to 25 cc/min. Such patients may have findings associated with renal disease, e.g., hypertension, but they usually have few signs and no symptoms. HOWEVER, TREATMENT MAY BE MOST IMPORTANT AT THIS STAGE and perhaps only here can disease progression be retarded.

Renal Failure - Moderate (symptomatic ?)

As the clearance falls from 25 to 10 cc/min or the serum creatinine rises from 4 to 10 mgm%, signs and symptoms begin to appear in most but not all cases. This period of years and later months is important because this end-point, a serum creatinine of 10 mgm% or a creatinine of 10 cc/min, marks where a decision should be made regarding future management. From this stage forward time may be short and unpredictable.

Renal Failure - Late (severe)

While some patients can work with a serum creatinine of 20, a careful history will show that such patients are true stoics. This period should be managed with definitive treatment or no treatment, especially if neuropathy has appeared.

Azotemia

Elevation of the blood urea nitrogen (BUN) due to retention of nitrogenous end-products of protein catabolism.

Uremia - A Syndrome

"Urine in the blood." A retention of metabolic waste products normally excreted in the urine causing nausea, vomiting, vertigo, weakness, dimness of vision and twitching ending in convulsions and coma.

THE FAILING KIDNEY-MASS vs ENVIRONMENT:

The question arises as the kidney function decreases as to what is the etiology of the varied symptomatology that results. Is it merely a function of the number of diseased, damaged or distorted nephrons produced over time? Or could it perhaps be related to the uremic environment that this gradual loss of nephrons produces?

In a series of brilliant experiments summarized in the protocol below (1,2,3) Bricker has attacked this question. Using a split-bladder preparation in order to study function from each kidney, he produced damage by various maneuvers to cover a loss of functional and/or actual nephron mass. This model allowed him to study the function of diseased or damaged nephrons in an environment that was kept normal by the presence of the unaffected kidney. His next step was to remove

the undamaged kidney and study the function of the same previously damaged kidney, as the environment changed to that of the azotemic or even uremic state.

In the presence of a normal environment the damaged kidney performed proportionately as well as its undamaged partner in most areas studied. In a few functions, however, the diseased kidney did not perform as well; for example, it was not able to concentrate or dilute to quite the extent of the normal kidney. These slight differences were attributed by Bricker to an increased GFR per nephron. In other words, the remaining nephrons, due to environmental affects, would always be undergoing an osmotic diuresis and indeed when solute load was reduced, concentrating ability was improved.

Bricker's data and interpretation has recently been challenged by Gottschalk's group (4), but I will not go into that because I think the points raised although pertinent, are not a major objection to Bricker's work.

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2. Bricker, N.S., P.A.E. Morrin, and S.W. Kime, Jr.: The pathological physiology of chronic Bright's Disease. Am. J. Med. 28:77, 1960.
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4. Biber, T.U.L., M. Mylle, A.D. Baines, C.W. Gottschalk, J.R. Oliver, and M.C. McDowell: A study of micropuncture and microdissection of acute renal damage in rats. Am. J. Med. 44:664, 1968.

MEASUREMENT OF RENAL FUNCTION:

In most hospitals the BUN is the primary means of evaluating renal function. This is unfortunate because it does not detect early changes and worse it is affected by many other things.

FACTORS CAUSING VARIATIONS IN BUN

1. URINE FLOW
2. PROTEIN INTAKE
3. BLEEDING
4. DRUGS - STEROIDS
   - TETRACYCLINE
5. INFECTION

Creatinine

This is a much better way to measure renal function using a less labile endogenous product. While there are variations in creatinine production and secretion as renal failure progresses, it is not affected by most of the things listed above. Still, there are 2 points to note using serum creatinine or creatinine clearance.

1. Patients with marked loss of muscle mass may give falsely low valuse for serum creatinine
2. The early changes around the normal range do not really disclose the marked changes occurring in function.

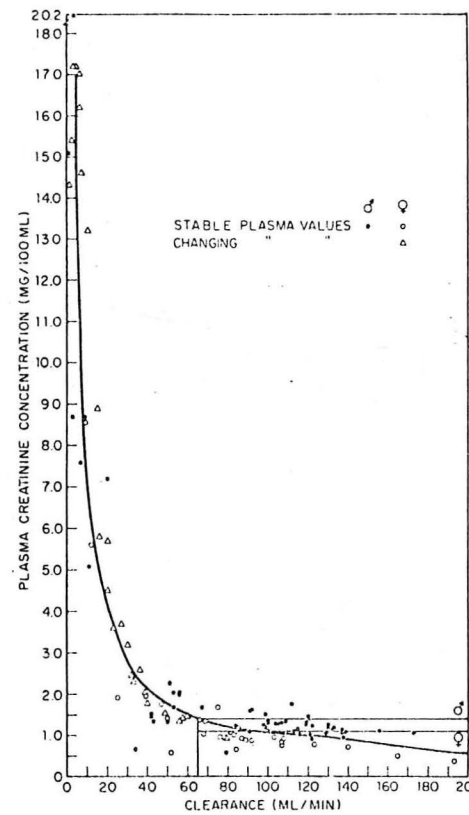

FIG. 1. The relationship between the plasma concentration and endogenous clearance of creatinine.

Doolan et al., Am. J. Med. 32:65, 1962

5. Berlyne, G.M., H. Varley, S. Melwarangkur and M. Hoerni: Endogenous creatinine clearances and glomerular filtration rate. Lancet 874, October 24, 1964.

6. Doolan, P.D., E.L. Alpen, and G.B. Theil: A clinical appraisal of the plasma concentration and endogenous clearance of creatinine. Am. J. Med. 32:65, 1962.

PROBLEMS & TREATMENT:

As defined before, renal failure can be divided easily into 3 major periods. In these periods the function, signs, symptoms and progression are variable and require different modes of treatment.

Early (asymptomatic) Renal Failure

This stage, which usually extends over a period of years, is marked by no symptoms directly related to renal function. However, changes occur during this period that may play a more important part in the progression of the disease than at either of the 2 later stages. The decision of what to do about these events is the major contribution of anyone seeing such patients.

Hyperuricemia: Very early in renal disease, often before changes are seen in renal function, the serum uric acid rises. This initial rise is not continuous and does not, like creatinine or BUN, become a more accurate marker of function as failure increases. However, McPhaul has shown that it may be a very early change in renal disease.

URIC ACID ELEVATION WITH EARLY RENAL FAILURE

	Normals	Kidney Disease	
		Normal GFR	Low GFR
C_{INULIN}	120	113	52
C_{PAA}	577	503	326
S_{UA}	4.3	5.05	5.41
C_{UA}	12.9	9.05	7.37

To test this we looked at a large number of our clearance studies and found a similar relationship.

It is very important to realize that an elevated uric acid can be associated with many other things. However, there is a tendency in medicine to treat any elevation in uric acid. In studies of large numbers of people (males) with hyperuricemia, the number that developed gout was 36% of those with uric acids over 8 mgm% (7). It is my impression that the incidence is much lower in chronic renal failure.

In renal failure patients, that is anyone with a demonstratable increase in BUN or creatinine, treatment is probably not indicated unless the uric acid rises above 9 or 10. Those that develop stones or one gouty attack should then be treated. However, one should remember that one U.A. stone in this area is very common in normal patients. The number of renal failure patients with gout is small and may indicate those who have latent gout. Treatment when required in renal failure is essentially the same as in gout.

7. McPhaul, J.J.,Jr.: Hyperuricemia and urate excretion in chronic renal disease. Metabolism 17:430, 1968.

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Proteinuria:

Hamburger (9) defines proteinuria as:

Primary - due to kidney disease per se, and

Secondary - that arising from systemic diseases affecting the kidney.

Approximately 75% of proteinuria is primary by this definition.

NEPHROTIC SYNDROME: CLASSICALLY, IN MOST TEXTBOOKS THIS IS DEFINED AS:

1. EDEMA
2. PROTEINURIA >2.5 GM/24 HOURS
3. HYPOALBUMINEMIA -- TOTAL SERUM PROTEIN <6 GMS% OR ALBUMIN <3 GM%
4. HYPERCHOLESTEROLEMIA

Hamburger has pointed out that #2 and #3 are really the most important points. I would like to go further and say PROTEINURIA is the most important point. Using 3% sulfasalcylic acid a "trace" reading is important and requires a follow up accurate 24/hour urine collection. If two collections both contain more than 200 mgm/24 hours, it is significant. Such a finding requires one to rule out benign causes of proteinuria.

PROTEINURIA NOT ASSOCIATED WITH DISEASE

1. Orthostatic
2. Lordotic
3. Effort
4. Associated with meals
5. Hyperpyrexia
6. Isolated Proteinuria ?

The most important is orthostatic and this must be looked for carefully, particularly in young males. The patient is asked to lie down and one hour after assuming this position he voids while lying. Urine is then collected over a time period with the subject voiding, while still lying. The urine collected to confirm the diagnosis must be:

1. Free of cellular components
2. Negative with 3% sulfosalcylic acid or
3. Contain <.03 mgm/min of protein

Note: A DECREASE in protein is NOT satisfactory. Therefore, proteinuria > 200 mgm/24 hours that cannot be shown to be due to the benign forms above should be investigated and requires in our center a renal biopsy and clearance studies.

Treatment of Proteinuria:

There are no satisfactory controlled studies for the treatment of adult proteinuria in the literature. The main reason for this is that no one sees enough of any one type of lesion to do controlled studies. Any study of significant size is a combined one with all the problems that involves.

Problems in Evaluating Treatment of Proteinuria:

1. Different drug dosages
2. Difficulty in pathological interpretation of the biopsy
3. Basic pathological type not defined
4. Drug combinations, e.g., cytoxan + a small steroid dose
5. Duration and degree of disease when treatment started
6. Age of patient
7. No controls

The best controlled study in the literature is the combined English experience (10). They studied 125 adult patients (64 controls) for two years with three groups divided on the basis of biopsy:

A. Minimal change

B. Membraneous

C. Proliferative

The only major flaw in this study was that the steroid dose was too low (30 mgm Prednisone/day). However, the results even at this low dose are worth looking at.

COMPARISON OF 125 ADULT NEPHROTICS TREATED OVER TWO YEARS WITH STEROIDS

NUMBER	DEATHS	NON-RENAL DEATHS	RENAL FAILURE	SERIOUS COMPLICATIONS
CONTROL 64	11	1	7	0
STEROIDS 61	16	11*	5	15

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* ONLY 1 UNDER 45 YEARS

C.V. - 7
INF. - 2
G.I. - 1
CAN. - 1

COMPLICATIONS:

ULCER - 6 (3)
PSYCHOSES - 4
INF. - 4
C.V.A. - 1

Proteinuria in the control group (A) Minimal Change all progressed toward normal. Renal function showed no significant change, but tended to favor the steroid group. Blood pressure was not affected. Finally, repeat biopsy showed progression in the membraneous and the proliferative group, regardless of the treatment. The minimal change patients showed progression in a few, but most were stable. There was no relationship between progression and treatment.

In summary:

1) Minimal change or adult lipoid nephrosis responded faster with treatment, but the complications were higher.
2) Membraneous and proliferative lesions showed no response to steroids, but again a higher complication rate.

Azothiaprine (Imuran): Some authors (12) suggest its use with steroids. It may increase remissions, but this seems to be merely an effect of dose. In our experience and that of others, steroid responders can go into remission with each of the immunosuppressive agents. Non-responders are not affected by any of the agents.

Cyclophosphamide (Cytoxan): Appears to be effective in children (16). In other studies again used with steroids, Cytoxan prolonged remissions (14). Again, the combined effect may be like an increased dose of steroids. Our experience is zero response in 6 adult steroid non-responders.

Recommended Treatment of Proteinuria:

1. Biopsy if possible
2. All minimal change lesions. Steroids 1-1/2 mgm/kgm for two weeks, then 3 mgm/kgm every other day for 2 weeks, then begin to decrease.
3. Low-salt diet and diuretics
4. If no response at 1 month, decrease and stop drug over another month
5. If response, treat for 1 year but get dose as low as possible on alternate-day therapy
6. Exacerbations increase the dose to induce remission and then come down again slowly.

9. Hamburger, J.: Nephrology - W.B. Saunders Company, 1968.
10. Black, D.A.K., G. Rose and D.B. Brewer: Controlled trial of prednisone in adult patients with the nephrotic syndrome. B.M.J. 421:August 22, 1970.

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13. Miller, R.B., J.T. Harrington, W. Schwartz and A. Relman: Long-term results of steroid therapy in adults with idiopathic nephrotic syndrome. Am. J. Med. 46:919, 1969.

14. Barratt, T.M. and J.F. Soothill: Controlled trial of cyclophosphamide in steroid sensitive relapsing enphrotic syndrome of childhood. Lancet II, 479, Sept. 1970.

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16. Drummond, K.N., D.A. Hillman, J.H.V. Marchessault and W. Feldman: Cyclophosphamide in the nephrotic syndrome of childhood. Can. Med. Assn. J. 98:524, 1968.

Hypertension:

Recent studies have confirmed what has been suspected for some time. THE COMPLICATIONS OF HYPERTENSION ARE PREVENTABLE.

In a series of two papers (18,19) the combined V.A. study group have shown that treatment reduces morbidity and mortality.

COMPLICATIONS IN A HYPERTENSIVE POPULATION

Initial Diastolic Pressure	115-129	105-114	90-104
Time (Months)	15.7	38	?
Control	27/70	35/110	21/84
Treated	2/73	8/100	14/86

While this was an all-male group, there is supporting evidence in a mixed population (17).

Renal failure may be transiently produced by antihypertensive agents or, more important,when present may progress significantly to even anuria. The importance and necessity of treatment has been best shown by Finnerty's group (20).

HYPERTENSIVE TREATMENT & CONTROL IN RENAL FAILURE

Number	Bun Adm.	Creatinine mgm% Adm.	Creatinine mgm% 7-10 Days	Creatinine mgm% 2 Years
12/12	35-60	4.6	5.0	1.3
10/13	60	9.7	11.0	3.4

Recommended Treatment:

1. Labile hypertension -- observe carefully
2. Fixed distolic above 90 should be controlled in all males and all females below 55 years of age
3. Therapy should be the least amount of drug to produce diastolic pressures of 90 or less after being in the upright position for 2 minutes.

Mild - Thiazide

Moderate - Thiazide, reserpine, apresoline

Severe - Thiazide, aldomet, ismelin

Malignant - Diazoxide, nitro prusside, arfonad

17. Pomerantz, H.Z.: Hypotensive drug therapy in the management of hypertension. Am. Heart J. 78:433, Oct. 1969.

18. V.A. combined study: Effects of treatment on hypertension. JAMA 202: 116, 1967.

19. V.A. combined study: Effects of treatment on morbidity in hypertension. JAMA 213:1143, 1970.

20. Mroczek, W.J., M. Davidov, L. Gavrilovich, F.A. Finnerty, Jr.: The value of agressive therapy in the hypertensive patient with azotemia. Circulation 40:893, 1969.

Moderate (symptomatic ?) Renal Failure

Acidosis:

The metabolic acidosis that develops is usually progressive until a serum bicarbonate of approximately 15 mEq/L is reached. At this point most patients stabilize, probably due to an increase in titratable acids. The rationale for treatment with alkali therapy (Shohl's solution) is as follows:

1. Hyperkalemia is exaggerated (26)
2. May leach from bone and increase renal osteodystrophy (25)
3. Circulatory influence
    a) Veno-constriction (24)
    b) Decreased myocardial contractility (23)
4. May increase anorexia and nausea
5. May increase lethargy and dyspnea
6. Less reserve in any acute stress, e.g., diarrhea, or lactic acidosis
7. Patient's testimony

    Note: A common side effect of Shohl's solution is diarrhea that resolves with decreasing the daily dosage.

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22. Ad. Hoc Committee: Statement of acid-base terminology. Ann. Int. Med. 63: 885, 1965.

23. Wildenthal, K., D.S. Mierzwiak, R.M. Myers, and J.H. Mitchell: Effects of acute lactic acidosis on left ventricular performance. Am. J. Physiol. 214:1352, 1968.

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25. Litzow, J.R., J. Lemann , Jr., and E.J. Lennon: The effect of treatment of acidosis on calcium balance in patients with chronic azotemic renal disease. JCI 46:280, 1967.

26. Burnell, J.M., M.F. Villamil, B.T. Unyeo and B.H. Scribner: Effects in humors of extracellular pH changes on the relationship between serum potassium concentration and intracellular potassium. JCI 35:935, 1956.

Edema:

The presence of edema in renal failure with a normal albumin is a warning marker. It is most frequently due to intake being greater than failing function can handle and/or heart failure. In either situation, treatment is required as this can strain marginal reserve of the patient. It also can make hypertension refractory to treatment.

Treatment:

1. Diet
2. Diuretics
   A. Edecrin (29)
   B. Lasix (28)
3. Digitalis (27)

Note: The excessive use of diuretics probably initiates more problems in renal failure than any other single cause.

27. Jelliffe, R.W.: An improved method for replacing one digitalis glycoside with another. Med. Times 98:105, 1970.

28. Schwartz, G.H., D.S. David, R.R. Riggio, K.H. Stenzel, and A.L. Rubin: Ototoxicity induced by Furosemide. N.E.J.M. 282:1413, 1970.

29. Schwartz, F.D., V.K.G. Pillagy, R.M. Kark: Ethracrynic acid: Its usefullness and untoward effects. Am. Heart. J. 79:427, 1970.

Sodium:

The diseased kidney still retains the ability to handle sodium, but the range of control is reduced. In balance studies all patients with moderate renal failure lose salt, i.e., they cannot reduce their urinary sodium as low as a normal (31). This is probably due to the fact they are always under the stress of an increased osmotic load. However, this problem is not seen on a diet above 2 gm of NaCl. There is another group by contrast that can get into trouble with a 2 to 5 gm NaCl diet. There are the rare salt wasters, usually patients with diseases that destroy medullary tissue preferentially, e.g., polycystic disease, hydronephrosis, medullary cystic disease, analgesic nephritis or pyelonephritis (30). The amount of salt wasting is variable from case to case, but should be watched for. Usually, these patients can balance themselves by long experience if left alone.

Note: The salt wasting patient can for various reasons become a salt retainer, particularly as function continues to decrease.

Hyponatremia:

The major cause of salt loss, beside diuretics, is extra renal through vomiting or diarrhea. Often this is compounded by water intake. Treatment here can include salt replacement and/or water restriction, depending on the etiology and whether renal function is adequate. In many cases of advanced renal failure with hyponatremia, water overload and acidosis, peritoneal dialysis can correct things faster and get the patient out of danger.

30. Franklin, S.S., and J.P. Merrill: The kidney in health, the nephron in disease. Am. J. Med. 28:1, 1960.

31. Coleman, A.J., M. Arias, N.W. Carter, F.C. Rector, Jr., and D.W. Seldin: The mechanism of salt wastage in chronic renal disease. JCI 45:1116, 1966.

Potassium:

Patients are usually able to handle potassium on whatever diet they tolerate until function is very low. The excretion of potassium is a distal tubular mechanism and requires the presence of sodium for exchange. In keeping serum potassium from climbing above the high normal range, the diseased kidney is probably working at a close-to-peak capacity. Therefore, any changes can produce hyperkalemia very quickly (33).

1. Acidosis (32)
2. Tissue catabolism
3. Exogenous K loads, e.g., salt substitutes
4. Decreases distal sodium delivery
5. K-retaining diuretics

A few patients with mild renal failure can become potassium-depleted due to increased renal loss, probably by aldosterone secretion. However, as renal failure progresses, depletion via the kidney is usually not a problem. Although extra renal losses can deplete any patient if severe, e.g., prolonged diarrhea.

Treatment:

1. Alkali: $NaHCO_3$ push with EKG monitoring
2. Kayexalate - orally with sorbitol or by enema (34)
3. Glucose and insulin
4. Calcium
5. Dialysis -peritoneal or hemodialysis

   Note: During peritoneal dialysis most patients DO NOT require K added to fluid unless they are on digitalis.

32. Berliner, R.W., T.J. Kennedy,Jr., and J. Orloff: Relationship between acidification of the urine and potassium metabolism. Am. J. Med. 11:274, 1957.

33. Steinmelz, P.R., and J.E. Kiley: Hyperkalemia in renal failure. JAMA 175:689, 1961.

34. Scherr, L., D.A. Ogden, A.W. Mead, N. Spritz and A.L. Rubin: Management of hyperkalemia with a cation exchange resin. N.E.J.M. 264:1961.

Calcium and Phosphorous:

Sometimes during this symptomatic period hypocalcemia begins to appear. This may be, but is often not associated with hypoalbuminemia. In late failure the serum calcium may be as low as 4-5 mgm%, yet in most cases tetany does not

occur. It has been proposed that most of the calcium is ionized, but measurements do not support this belief (36). The reason why chronic renal patients are not subject to tetany is not known. But unless a positive Trousseau sign is present calcium ingestion is NOT indicated (37).

Hyperphosphatemia does not appear until the clearance falls to <25 cc/min (38). This must mean tubular reabsorption is decreased,probably secondary to increased parathormone levels. When the phosphate begins to rise parathormone has exerted its maximal effect, yet the hormone probably continues to rise causing bone mobilization.

There are two major types of bone disease:

1) Osteomalacia -- with bone pain and pathological fracture. While treatment with Vitamin D and calcium can be undertaken, the complications are such that it should be done only if transplantation is not available.
2) Ostetitis Fibrosa -- treatment here is simpler and the results are better. Sub-total parathyroidectomy if to be transplanted. Total removal if no transplant is planned in the future (39).

Itching is a common problem with renal disease and, short of parathyroidectomy, which is a questionable cure, we have used phosphate binders. In many of our cases this controls the itching. The literature always states aluminum hydroxide as the binder of choice. This is almost as difficult for the patient to tolerate as a low phosphate diet, and recently we have used magnesium containing antacids with a better patient response and much lower serum phosphates.

35. Reiss, E., J.M. Canterbury and R.H. Egdahl: Experience with a radioimmunoassay of parathyroid hormone in human sera. Trans. Am. Assn. of Phys. 21: 104, 1968.

36. Fanconi, A. and G.A. Rose: The ionized complexed and protein-bound fractions of calcium in plasma. Quart. J. Med. 27:463, 1958.

37. Terman, D.S., A.C. Alfrey, W.S. Hammond, T. Donndelinger, D. Ogden and J.H. Holmes: Cardiac calcification in uremia. Am. J. Med. 50:744, 1971.

38. Goldman, R. and S.H. Bassett: Phosphate excretion in renal failure. JCI 33:1623, 1954.

39. Bricker, N.S., E. Slotopolsky, E. Reiss and L. V. Avioli: Calcium, phosphorous and bone in renal disease and transplantation. Arch. Int. Med. 123:543, 1969.

Magnesium:

Normal values for serum magnesium are 1.5 to 2 mEq/L (41). Symptoms occur around 10 mEq/L or above (40). Our studies and those of others (42) both on dialysed and undialyzed patients show magnesium to 3 or 4 mEq/L and no higher. Whether there is a G.I. protective mechanism or not is unknown, but the patients tolerate these levels very well. It is not known if elevated magnesium in this range has any side effects. However, higher levels and symptoms can be obtained with I.V. use and,regardless, serum levels should be checked with even oral treatment.

40. Smith, W.O. and J.F. Hammarsten: Serum magnesium in renal disease. Arch. Int. Med. 102:5, 1958.

41. Alfrey, A.C.: Magnesium -- Grand Rounds, Univ. of Texas Southwestern Medical School, 1969.

42. Hampers, C.L.: Personal communication.

Carbohydrate Intolerance:

Abnormal glucose tolerance tests and glucosuria are common in renal failure. Some patients show high fasting glucose levels as well (45). Studies by Bricker's group (46) show that at least the glycosuria is not present if the contralateral normal kidney is present to keep the environment normal. In the abnormal state of renal failure insulin secretion is slow, but at least normal and insulin antagonists are present (43,44).

All these features are reversible with frequent chronic hemodialysis (43, 44).

Treatment:

There are four points to be aware of:

1) Treatment of the elevated fasting sugar is usually not indicated
2) Some patients, particularly on peritoneal dialysis, get elevated blood sugars
3) A diabetic glucose tolerance curve in a uremic is not a contraindication to transplantation
4) As renal failure becomes severe, less insulin may be needed in diabetic patients

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44. Hampers, C.L., J.S. Soeldner, P.E. Doak and J.P. Merrill: Effect of chronic renal failure and hemodialysis on carbohydrate metabolism. JCI 45:1719, 1966.

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PROTEIN

~~Potassium~~ Intolerance:

While urea itself is not the agent that causes changes in renal failure, another substance associated with nitrogenous waste products may be. Giordano (47), applying the basic work of Rose (50) produced a low-protein diet (7-8 gms) that lowered the BUN and reduced the symptoms of renal failure and uremia. Essential amino acids can be utilized by the body with urea and nitrogenous breakdown products to produce protein. Berlyne's modification of this diet to the English palate utilized 15 gm of protein.

Subsequent work by Ginn (52) and Rubini (51) has demonstrated that there is very little elevation of BUN when a 40 gm high biological value diet is utilized in place of a 20 gm diet. Essentially, protein is restricted to eggs, first-class meat, and milk with 2000 calories of carbohydrates and unlimited fat.

Treatment:

1. Dietary consult as the creatinine approaches 10, or earlier if symptoms develope
2. No anabolic steroids
3. No added methionine
4. Less than a 40 gm high biological value protein has no place in adults awaiting dialysis and transplantation

47. Giordano, C.: Use of exogenous and endogenous urea for protein synthesis in normal and uremic subjects. J. Lab and Clin. Med. 62:231, 1963.

48. Giovannetti, S., and Q. Maggiore: A low-nitrogen diet with proteins of high biological value for severe chronic uremia. Lancet 1:1000, 1964.

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Anemia:

Almost all patients develop a normocytic-normochronic type anemia as renal failure progresses. This seems in our experience, and that of others (57), to be less marked in polycystic kidney disease. The etiology would appear to be:

1. Decreased production of erythropoietin (58)
2. Decreased life span (particularly late in renal failure) (59)
3. Blood loss (56)

A platelet dysfunction is associated with renal failure and probably plays a major role in terminal bleeding (53).

Treatment:

1. Rule out any other possible causes, e.g., Fe
2. Testosterone is probably ineffective without dialysis
3. Cobalt is of limited use because of G.I. irritation
4. If a transplant candidate, NEVER transfuse unless an emergency and then with WBC poor blood
5. On dialysis most patients will not require transfusions

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Superimposed Acute Renal Failure:

At any point during the course of renal disease acute reversible renal failure can occur. The incidence probably increases as function and reserve become less. Problems such as (1) volume depletion, (2) cardiac failure, (3) obstruction and (4) infection can be treated and allow the patient months or years of satisfactory function before more definitive treatment is undertaken. The history is probably one of the best means of determining duration.

Treatment:

1. Rule out other causes (especially in a new patient who presents with renal failure and an unknown history)
   a) Replace volume
   b) KUB , tomogram or infusion IVP for kidney size
   c) Rule out obstruction -- one-sided retrograde if anuric
   d) Biopsy if kidneys normal in size
2. Peritoneal dialysis - "once" is a reasonable approach in most cases of failure where the diagnosis is not certain

Late (severe) Renal Failure:

A decision regarding definitive treatment should be made before this stage begins. The early evaluation allows preparation for training or transplanting to be done on a stable patient vs. a debilitated one if uremia has developed.

Hemodialysis:

Coils with an arterio-venous fistula are now the method of choice.

Center Dialysis: Only for acute problems or pre- and post-op transplant patients.

Home Dialysis: For motivated, basically intelligent, strongly-motivated people with good family support. Two groups should be considered:

a) Older patients over 55-60 who have no possibility of transplantation

b) Patients awaiting cadaveric transplantation (method of choice)

Limited Care: For patients unable to go home. This probably will allow more people to be transplanted than all other methods combined.

Transplantation:

Undoubtedly the eventual solution to most, if not all, renal failure.

Related Living Donor: A near relative with a compatible blood group and 2 out of 4 H.L.A. antigens matching the recipient.

Cadaveric: In most cases restricted to a compatible blood group with 3 out of 4 H.L.A. antigens matching the recipient.

Death:

In all cases we must decide if we are prolonging life or death. This can only be a decision of the individual doctor with regard to his patient.