

# Conservative Management of Chronic Renal Failure\*

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The successful application of chronic dialysis and/or renal transplantation to patients with chronic uremia has sometimes obscured the fact that significant progress has also been made in our understanding of other therapeutic approaches to chronic renal failure. These less dramatic advances are commonly labeled "conservative" in nature, yet they have contributed decisively to the welfare of many uremic patients by improving their sense of well-being and delaying their need for such types of therapy as regularly repetitive dialysis. I shall comment first on certain general principles of management and then review some of the scientific therapeutic maneuvers and concepts that comprise the main foundation for the so-called conservative management of chronic uremia. Although my remarks are directed primarily toward patients with progressive primary renal disease, they are of equal pertinence to patients with renal failure of several types or etiologies.

## General Principles of Management

The progressive destruction of renal tissue effects an ever changing clinical pattern in which new and different signs and symptoms ap-

pear at differing rates in individual patients. All would agree that conservative therapy should be initiated prior to the appearance of terminal renal failure, but general agreement has not yet been reached on the exact time at which certain dietary programs should be started during the earlier phases of disease. Nevertheless, once therapy has been initiated, additional conservative measures must be added until the entire conservative armamentarium, including an occasional dialysis, becomes insufficient to sustain useful life. Chronic dialysis and/or renal transplantation must then be considered. It is important to realize that conservative therapy, dialysis, and transplantation must be combined carefully for best results. One of these therapeutic approaches cannot be used to the exclusion of the others. Certainly the institution of chronic dialysis does not eliminate the need for conservative therapy. Optimal treatment reflects a continuum of effort utilizing several therapeutic concepts and modalities.

If I can assume today that we are dealing with an azotemic patient whose underlying renal disease is irreversible, our first management responsibility should be the exclusion of factors that may have reversibly intensified the degree of azotemia. In order to appreciate the unique importance of reversible factors in the treatment

of chronic uremia, we must also understand the well-established relationship between changes of the blood-urea-nitrogen (BUN) concentration and the creatinine clearance or any other index of filtration rate. From an analysis of Figure 1 it is evident that the BUN concentration varies inversely with associated changes of filtration rate. Although the BUN concentration rises with the earliest reduction of filtration rate, it ordinarily does not exceed the upper limits of normal until the filtration rate has been reduced to between 25% and 50% of normal. Furthermore, from any point of departure, a 50% reduction of the filtration rate can be expected to effect a corresponding twofold increase of the BUN concentration. Obviously the patient whose filtration rate is only 10 ml/min, or approximately 10% of a hypothetically normal value, cannot afford to sustain a further 50% reduction of filtration rate, even transiently. All other factors being constant, a transient reduction of filtration rate from 10 to 5 ml per minute might be accompanied by an increase of the BUN concentration from, perhaps, 75 to 150 mg per 100 ml.

The relationship between functioning renal mass and the signs and symptoms of renal failure can be described similarly (Fig. 1). When the limits of renal reserve have been exceeded, uremic symp-

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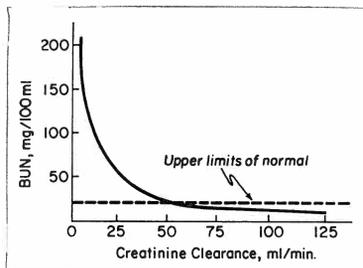


Fig. 1—Relationship between creatinine clearance and the blood-urea-nitrogen concentration.

toms appear rapidly in association with further and much smaller reductions in renal mass, and the condition of the patient deteriorates alarmingly. This disproportionate progression of clinical symptomatology may be associated with little change in the actual rate of histologic progression of the disease. Obviously, at this point, a small absolute reduction in function is of great importance to the patient. Thus, the correction of reversible factors that transiently reduce renal function is a primary and urgent responsibility of the physician.

Table 1 lists a few of the many factors that may contribute to a transient and potentially reversible reduction of filtration rate in patients with severe renal disease.

Congestive heart failure is certainly one of the most common clinical occurrences that may intensify renal failure reversibly; its appearance is almost always associated with some degree of filtration rate depression. Its correction may make the difference between clinical compensation and progressive uremia. Cautious digitalization and/or diuretic therapy, or even dialysis, may be required for the removal of excess water and electrolytes. If digitalization is necessary, both the initial and maintenance doses must be reduced, since digitalis is normally excreted by the kidneys.

Next, one must realize that active bacterial pyelonephritis can exist in the absence of fever, chills, or C.V.A. tenderness, and that a urine

culture should be mandatory in every patient with chronic renal disease. The presence of a systemic infection with fever and tissue injury can markedly accelerate the development of azotemia by increasing protein catabolism and the subsequent presentation of nitrogenous products to the organ for excretion. Correctable causes of urinary tract obstruction must also be sought. Intravenous urography is the safest technique for such a diagnostic search, but special roentgenographic techniques utilizing large doses of contrast media may be required in patients with severe renal failure.

Lastly, the presence of salt and/or water depletion, when viewed collectively, represents an extremely common event leading to a reversible intensification of renal failure. Gastrointestinal losses from nausea and vomiting or even overnight water restriction for a concentration test or an intravenous urogram may initiate a serious chain of events. A decrease in extracellular volume leads to a reduction in filtration rate and a decrease in urine flow, thereby compromising still further the excretory efficiency of an already damaged kidney.

Factors such as those in Table 1, if present, must be identified promptly and corrected judiciously. Once this is accomplished, the efforts of the physician can then be directed toward the specific management of other uremic signs and symptoms.

In simplified fashion, Figure 2 depicts an essential characteristic of the functional response of the diseased kidney to variations in the excretory load of water, nitrogenous products, or electrolytes. Although the functional response of the residual nephron population may be perfectly normal in a qualitative sense, it may be lacking in another important respect—namely, in the flexibility of its response. The diseased kidney is unable to compensate rapidly and efficiently

for associated changes in the volume or composition of the body fluids. As illustrated by the solid arrows, the normal kidney can rapidly and effectively adjust its rate of excretion to dispose of a wide range of excretory loads, so that excretion can equal intake plus production minus internal degradation. If the excretory load is large, the healthy kidney quickly increases excretion to equal the load; if the excretory load is reduced, renal excretion is reduced efficiently and appropriately. In contrast, as shown by the dashed-line arrows, the range of excretory adjustments by the diseased kidney to similar loads is restricted severely. When the load is large, the excretory capacity may be insufficient to effect complete disposal; when the load is reduced sharply, the capacity to reduce excretion (conservation) may be insufficient to prevent the appearance of a body deficit. Excretory adjustments cannot be increased to the usual maximum or decreased to the usual minimum. As a consequence, both excess and deprivation are tolerated poorly. It then becomes the responsibility of the physician to adjust the intake to equal the excretory capacity instead of depending on the functional response of a damaged organ to make the necessary excretory adjustments.

### Specific Management Problems

An incomplete list of specific management problems or considerations that must be entertained is given in Table 2. Those items followed by an asterisk can be approached at least partially by appropriate adjustment of dietary intake. Their very number offers mute testimony to the fact that dietary therapy affords a major foundation for the management of chronic uremia.

First, let us consider the adjustment of *water intake* in nonoliguric patients with severe chronic uremia. In such patients, water excess with dilutional hyponatremia is

**TABLE 1**  
Reversible Causes of Filtration Rate Depression in Patients with Underlying Renal Disease

1. Congestive heart failure
2. Infection
  - a. Genitourinary
  - b. Systemic
3. Urinary tract obstruction
4. Salt and water depletion

**TABLE 2**  
Management Considerations

1. Salt and water requirements\*
2. Control of azotemia and maintenance of nitrogen balance\*
3. Hyperkalemia\*
4. Acidosis\*
5. Anemia
6. Infection
7. Other:
  - a. Hypertension
  - b. Edema and/or heart failure\*
  - c. Bone disease
  - d. Uremic syndrome: nausea, vomiting, pruritus, malaise, CNS irritability, etc.\*

a frequent consequence of aggressive fluid therapy. This phenomenon may be seen when a conscious patient with chronic uremia is asked to force fluids for the performance of an ill-advised P.S.P. test. Occasionally, excessive fluid intake is prescribed because of the mistaken impression that renal function can be improved. The modest reduction in azotemia that may occur as a consequence of such a maneuver may be viewed as the net effect of hemodilution and a modest increase in urine flow; it does not reflect an improvement of glomerular filtration. Dilutional hyponatremia may also appear, simply because the intake of water has been increased above the excretory capacity of the damaged kidneys. In many patients, a suitable intake of water is that which is dictated by thirst. In other patients whose filtration rate may be reduced more severely, certainly below 5 ml/min, the intake of water may have to be adjusted so that it exceeds an already near-maximal urine output by no more than 300 to 400 ml per day. In such patients, water retention may occur if the total daily fluid intake, perhaps even including dietary water, is increased to a value no higher than 1500 ml. Consequently, an arbitrary and ideal fluid intake that is suitable for all patients cannot be identified. Rather, maximal fluid intakes can be ascertained only by serial observations of body weight, urine output, and fluid intake. Conversely, despite the fact that gross water wasting is rare in chronic renal failure, one may find patients with obligatory minimal urine volumes consequent to an endogenous solute diuresis which may be as high as 2 liters/day. Such patients may rapidly become water-depleted if intake is restricted for any ill-advised reason. Drugs that cause nausea must be used with caution, and hospital procedures that promote dehydration should not be employed. Obviously, a water deficit, if present, should be treated appropriately.

The existence of chronic renal disease should not be equated with a necessity for *sodium restriction*. In fact, in the absence of edema and, perhaps, severe hypertension, rigid dietary sodium restriction is contraindicated. As renal failure progresses, the diseased kidney loses its normal capacity to alter sodium excretion over a wide range. In contrast to the usual sequence during good health when renal sodium conservation is extremely efficient (Fig. 3), the diseased kidney cannot reduce urine sodium excretion maximally, even after a relatively long period of dietary deprivation. Although the daily quantitative deficit is small, a larger and significant cumulative deficit may occur over a more protracted period. Sodium may be lost in the urine in small amounts even in the presence of a falling concentration of serum sodium. Hyponatremia will occur if the patient drinks excess electrolyte-free water or loses sodium in excess of water via other routes. The loss of GI secretions by vomiting or diarrhea represents another important cause of sodium depletion. Replacement of fluids with salt-free solutions such as 5% dextrose in water may restore extracellular volume at the cost of hyponatremia. Sodium depletion may be facilitated further by the injudicious use of potent diuretics in patients whose dietary sodium has been rigidly restricted. It is important to remember that the residual nephron population can effect a significant increase in fractional sodium excretion in response to the use of potent diuretics such as furosemide, even when the filtration rate is as low as 1 ml/min. Once again, the quantitative daily deficit may be small, but long-term diuretic therapy may contribute to the appearance of a significant sodium deficit.

Conversely, when the dietary salt intake is increased, the patient with renal disease may be unable to excrete the same sodium load that could have been handled with ease

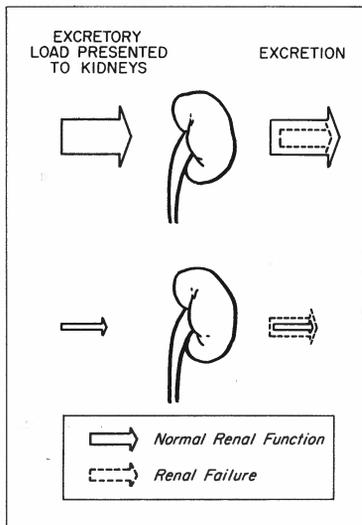


Fig. 2—Renal response to complete dietary sodium restriction in health and renal disease.

by a patient with normal renal function. Sodium intake must be kept sufficiently low to avoid sodium excess. Ideally, one would prefer to maintain the sodium intake at a level that is somewhat below that amount which is capable of inducing sodium excess. In practice, the upper limits must be defined individually for each patient, since they are not predictable with confidence. Most importantly, one must also realize that both the upper and lower limits of sodium excretory adjustments may change with the passage of time and the progression of disease. In the absence of edema or congestive heart failure, it is our own practice to initiate therapy with a 5 gm or 85 millimol salt (NaCl) diet. If sodium bicarbonate is required for the treatment of systemic acidosis, the dietary intake of sodium chloride may have to be reduced equivalently. In other patients, even greater amounts of sodium chloride may be tolerated safely. On admission, some patients may exhibit unrecognized salt depletion with plasma volume contraction and filtration rate reduction. The judicious administration of salt and water, with subsequent stabilization of the body weight somewhat above the admission weight, as well as a measurable increase of creatinine clearance strongly suggest that salt depletion was present. After replacement, the maintenance salt intake is prescribed at a level somewhat below the defined upper limits of excretory capacity.

Important complications of, or contraindications to, an excessive salt intake are hypertension or the appearance of a congestive state. With certain exceptions, there is general agreement that the treatment of hypertension can be accomplished satisfactorily with drugs in the usual nonoliguric patient. In such patients, the hazards of rigid dietary sodium restriction would seem to weigh the small contribution of dietary sodium restriction to the control of diastolic hy-

pertension. Of course, in patients whose renal function is so reduced that repetitive dialysis is required, rigid limitation of the dietary intake of salt and water may well be necessary to control hypertension and prevent salt and water excess. The choice of anti-hypertensive drugs rests largely on the experience of the physician. Apresoline, alpha-methyldopa, and guanethidine have all been used successfully.

The data in Table 3 reflect an average expression of the traditional views of most physicians regarding *dietary protein restriction*. Theoretically, dietary protein restriction might be expected to minimize the intensity of systemic acidosis, and there is good evidence to support the notion that the reduction of azotemia may restore a sense of well-being to patients who complain of malaise, anorexia, nausea, and vomiting. There is somewhat less agreement as to just when dietary protein should be restricted in patients with early renal failure. Certainly, there is little evidence that azotemia, itself, is harmful to the asymptomatic patient with mild and uncomplicated renal failure, and in such a patient there may be little basis for rigid dietary protein restriction. The indications for dietary protein restriction in Table 3 admittedly are arbitrary, but they are in agreement with common practice at many institutions. The usual low-protein hospital diet necessitates a protein intake at the indicated level, if negative nitrogen balance is to be avoided. Overall, the goal of protein restriction is to reduce protein catabolism while simultaneously avoiding the hazards of nitrogen depletion. To this end, dietary protein restriction should be coupled with the provision of adequate protein-sparing calories such as carbohydrate and fat, the prevention and treatment of infection, the encouragement of maximal tolerable ambulation, the avoidance of unnecessary surgery and manipulation, the provision of anabolic steroids, and the avoidance of inhi-

bitors of protein anabolism such as tetracycline and adrenal glucocorticoids.

Recently, two European investigators, Giordano (1967) and Giovannetti (1967), have been associated with an increased interest in the control of uremic symptoms by dietary management. Their own clinical results have been impressive, and most would agree that the morbidity of chronic uremia appears to have been lessened significantly by their dietary efforts. Basically, these investigators have demonstrated that nitrogen balance can be maintained and that protein depletion can be avoided by the provision of remarkably low nitrogen diets if the dietary protein is comprised of proteins of high biological value. Nitrogen balance has been maintained in patients with chronic uremia on a dietary protein intake as low as 15 to 20 gm per day. Marked clinical improvement has been observed simultaneously. Anorexia, nausea, vomiting, fatigue, twitching, and mental changes have disappeared completely or decreased significantly. The severity of anemia has been ameliorated in a few patients. Fundamentally, low-protein diets are directed toward control of the

TABLE 3  
Dietary Protein Restriction in  
Renal Failure

Rationale:	1) Diminished accumulation of metabolic acid, urea, and other nitrogenous products
Indications:	1) Azotemia (BUN > 50 mg/100 ml) 2) Hyperphosphatemia 3) Acidosis
Amount:	1) 0.5 to 0.6 gm per kg plus urinary losses

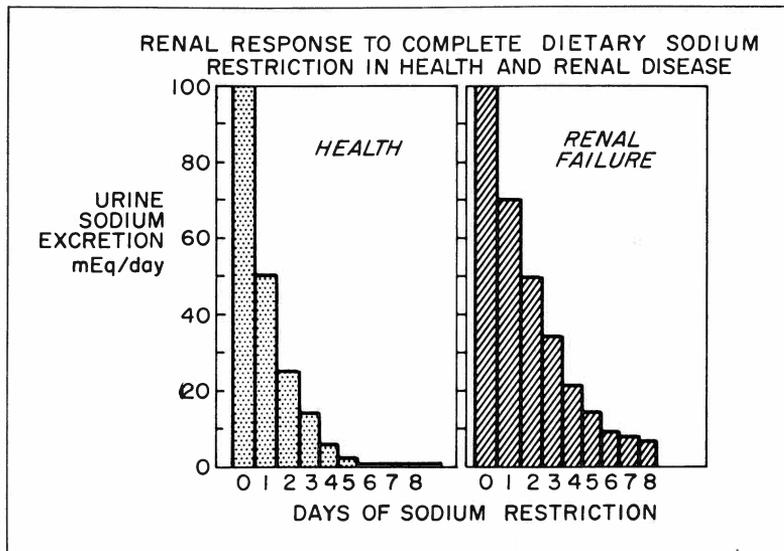


Fig. 3—Efficiency of renal sodium conservation by the normal and diseased kidneys.

serious nutritional defects that are characterized by weight loss, profound weakness, and gross evidence of decreased muscle mass. In the past, concern over the nutritional status of the uremic patient was often considered futile, because the presence of severe nausea and vomiting appeared to prevent adherence to an effective nutritional regimen. Obviously, if malnutrition is to be avoided, a diet for uremic patients should contain sufficient calories to exert a maximal protein-sparing action and sufficient amino acids of appropriate quality and quantity to promote optimal protein synthesis without increasing the degree of azotemia.

In patients whose creatinine clearances were as low as 5 ml/min, Giovannetti has shown that the institution of a basal diet containing small amounts (12 gm) of high biological protein can be associated with a simultaneous decrease in both azotemia and the negativity of overall nitrogen balance. The further addition of essential amino acids in amounts sufficient to increase the total protein intake to between 15 and 20 gm was followed by the appearance of slightly posi-

tive nitrogen balance without an attendant increase in azotemia. Similar results were achieved when egg protein was utilized instead of individual essential amino acids. For practical purposes, the additional nitrogen, as essential amino acids, appeared to be utilized completely without inducing a measurable increase in overall protein catabolism. Furthermore, the urease-induced elaboration of ammonia nitrogen in the gut provided a pathway for the re-utilization of endogenous urea nitrogen for protein synthesis. One important fact that emerges from these studies is the realization that it is possible to improve the nutrition of the uremic patient via the provision of extremely low-protein diets of high biologic value, and that their use may be associated with striking clinical improvement, even in individuals with severe filtration reduction.

Unfortunately, the diets of Giordano and Giovannetti are much better suited to Italian than American tastes. Recently, however, a variety of similar low-protein diets have appeared in this country and seem to offer great promise. Monotony, rather than palatability,

constitutes the major barrier to their acceptance by the patient. Basically, these diets consist of appropriate fruits and vegetables, other sources of carbohydrate and fat, and egg protein. Recently, lactalbumin from electro-dialyzed whey has been utilized as a protein source of high biologic value. It can be offered to the patient as a reasonably palatable, albeit monotonous, milkshake-like drink. These diets prohibit the use of flour in any form, and special baking recipes have proliferated, each of which utilizes pure wheat starch. Low-protein bakery products of wheat starch can be quite satisfactory, although baking with wheat starch does pose many culinary problems for the housewife. These products are fast-rising, and housewives must learn to initiate the baking process in a cold oven rather than one that has been prewarmed, if they are to avoid a product that has a consistency resembling castiron. At present, at least one commercial company with national distribution is experimenting with a ready-mix baking product of wheat starch that may prove to be satisfactory and originative. As long as facilities are so limited that the patient's admittance to repetitive dialysis must be delayed, the extra effort involved in these dietary manipulations would appear to justify their time and expense.

*Acidosis* (Table 3) is a constant feature of chronic uremia that should be controlled, because it may lead to such adverse events as an extracellular shift of potassium and the appearance of hyperkalemia, increased respiratory effort, anorexia, somnolence, bony demineralization, and even, perhaps, reduction in the effectiveness of endogenous insulin. Efforts directed toward minimizing protein catabolism also decrease the endogenous production of fixed acid, and the provision of an additional buffer such as sodium bicarbonate helps to neutralize the effects of excess metabolic acid. We prefer to utilize sodium bicarbo-

nate, rather than sodium lactate, in a daily dose sufficient to maintain the plasma bicarbonate concentration between 18 and 20 mmole per liter. The lactate anion, as you are aware, must first be metabolized, and there is some evidence that the hepatic degradation of lactate may be significantly impaired in uremia. If edema is present and sodium bicarbonate therapy is required, it is obvious that the dietary intake of sodium chloride may have to be reduced in order to keep the total dietary sodium intake within the desired range. Unfortunately, in some patients, one may have to accept an incomplete control of acidosis if aggravation of congestive heart failure by sodium salt administration is to be avoided. Peritoneal dialysis provides a convenient way of correcting severe acidosis without an associated net addition of sodium to the body.

Several therapeutic maneuvers may be utilized in the management of acute *hyperkalemia* (Table 3). It is true that serious hyperkalemia is uncommon in the usual nonoliguric patient with chronic renal failure. On the other hand, a marginal and persistent elevation of the serum potassium concentration is rather frequent in our experience. The correction of acidosis alone will often facilitate the control of this type of hyperkalemia. An adjustment of sodium intake may also be of importance. We have seen patients on rigid dietary sodium restriction in whom the provision of increased dietary sodium was accompanied by a reduction in modest hyperkalemia, perhaps as a consequence of the increased availability of sodium within those portions of the nephron where sodium-potassium-hydrogen exchange occurs. Sodium-cycle cation exchange resins may be used effectively in small daily maintenance doses. Since their use contributes to the dietary intake of sodium, an appropriate reduction of dietary sodium may be necessary if the control of

sodium balance is important. Lastly, the appearance of hyperkalemia can be minimized greatly by moderate dietary restriction, an avoidance of potassium-containing drugs, and prompt control of increased catabolism due to fever, etc.

Anemia is probably best untreated, unless it is symptomatic (undue fatigue, angina, etc.) or unusually severe and complicated by bleeding or excessive hemolysis. The etiology of the anemia of chronic renal failure, in the most general terms, can be related to the net effect of bone marrow suppression, increased hemolysis (perhaps as a consequence of an extracellular hemolysin), defective erythropoietin production by the kidney, and bleeding. Transfusion is the treatment of choice, and maintenance of the hematocrit between 18 and 25 vol% is generally adequate for the relief of symptoms. A further increase serves little purpose, and the short-lived survival time of even fresh red cells in uremic patients often means that repeated transfusions will be necessary. Since the restoration of volume is not a consideration, the use of fresh-packed red cells is preferable. Other types of therapy have been tried (vitamin B<sub>12</sub>, cobalt salts, etc.), but their use is often impractical, and predictable benefits have not been observed.

Time does not permit detailed discussion of all the items listed in Table 3. However, in closing, I would like to comment briefly on just a few *additional therapeutic approaches*. The use of anabolic agents has some degree of merit, in my opinion. It is difficult to establish proof in a given individual that agents such as norethandrolone or oxandrolone really contribute to the management of uremia, although, in perhaps a third of the patients, some decrease in protein catabolism and azotemia may be observed. If an anabolic agent is utilized, one with minimal virilizing effects should be chosen. Pruritus can be controlled in some patients by the use of selected antihistamines; symptomatic

relief of nausea can be provided by many members of the phenothiazine family. Finally, the control of hyperuricemia is deserving of comment. Whether or not hyperuricemia should be controlled at all is, perhaps, problematic. There is little factual evidence as to whether hyperuricemia *per se* contributes either to progression of the underlying disease or to uremic symptomatology. Hypothetically, either circumstance is possible. Empirically, we have treated several patients with allopurinol, a potent inhibitor of xanthine oxidase. Therapy has been restricted to patients with marked hyperuricemia (> 12 mg/100 ml), and impressive reductions of the plasma uric acid concentration have been observed. Nevertheless, further investigation is required to establish the real benefits of such therapy.

In closing, I would emphasize that I have failed to discuss many equally important aspects of conservative management. Uremia is a strange disease; it is a difficult illness for the patient, and it is one that requires careful preparation of the family for long-term involvement. If dialysis or transplantation cannot be performed, our minimal objective should be the provision of life that is at least as comfortable as possible. For the most part, this objective can be achieved with proper attention to the selection of tools from our conservative armamentarium.

## References

- GIORDANO, C., R. ESPOSITO, C. DE PASCALE AND N. G. DE SANTO. Dietary treatment in renal failure. In *Proceedings of the Third International Congress of Nephrology*. G. E. Schreiner (ed.). Vol. 3. Basel (Switzerland)/New York: Karger, 1967, pp. 214-229.
- GIOVANNETTI, S. Diet in chronic uremia. In *Proceedings of the Third International Congress of Nephrology*. G. E. Schreiner (ed.). Vol. 3. Basel (Switzerland)/New York: Karger, 1967, pp. 230-236.