Dietary indiscretion contributes to the severity of many diseases such as inherited metabolic disorders like phenylketonuria in which excess dietary protein causes symptoms. But, dietary indiscretion also causes symptoms in more common diseases. For example, excessive carbohydrate intake will aggravate diabetes, excess fatty foods will accelerate atherosclerosis, too much salt will accentuate hypertension or edema, and a diet rich in protein will cause neurologic problems for liver disease patients. The “protein intolerance” of CKI is another example of the relationship between dietary indiscretion and symptoms (1): foods rich in protein lead to metabolic acidosis and accumulation of uremic toxins, while an excess of salt will aggravate hypertension and phosphate-rich foods will accelerate secondary hyperparathyroidism.

Recent publications detailing the benefits of aggressively treating patients with CKI underline why a comprehensive diagnostic and therapeutic plan is needed (2–5). The plan must be comprehensive because the benefits of lowering BP, reducing proteinuria, or even slowing the loss of kidney function (i.e., slowing progression) will be lost if other complications of CKI such as neuropathy and muscle or bone disorders develop. Many of these complications can be prevented by manipulating the diet (6). It is not surprising, therefore, that Beale (7) concluded over 130 yr ago that a dietary plan should be a standard therapeutic approach for CKI patients.

The influence of the diet on blood chemistry abnormalities found in CKI patients can be detected in results from the Modification of Diet in Renal Disease (MDRD) Study (T. Greene, Cleveland Clinic Foundation, personal communication). In patients with moderately severe CKI, average baseline values of serum bicarbonate (23 mM), phosphorus (3.6 mg/dl), and urea nitrogen (30 mg/dl) were significantly lower in those who successfully reduced their protein intake by 0.2 g of protein/kg per d for 1 yr (Figure 1). Similar benefits occurred in those with more severe CKI and average baseline values of serum bicarbonate (22 mM), phosphorus (4.2 mg/dl), and urea nitrogen (46 mg/dl). Thus, a comprehensive treatment strategy for CKI patients that includes a dietary plan can yield benefits. The benefits will be realized if enough essential and nonessential amino acids are provided to synthesize protein while avoiding the accumulation of unexcreted, potentially toxic ions and compounds arising from the breakdown of foods rich in protein (8–10). Fortunately, the majority of CKI patients will accept dietary changes (11).

A severely deficient diet can lead to loss of muscle mass, although more commonly, complications of CKI such as acidosis or inflammation activate the enzymes that breakdown protein to cause loss of protein stores (12–14). Notably, catabolism will not be halted by prescribing an excess of protein-rich foods, nor will such diets result in muscle growth. Instead, raising dietary protein will lead to the accumulation of unexcreted inorganic ions (i.e., phosphates, potassium, etc.) and products of amino acid metabolism that are potential uremic toxins (e.g., phenols, middle molecules, etc.) (1.6). The outcome is predictable, an increasing risk of developing acidosis, hyperkalemia, hyperphosphatemia, edema, a high serum urea nitrogen, and the symptoms of uremia, but no increase in muscle mass until the catabolic stimulus is removed (12, 13).

Besides reducing waste products, benefits of a protein-restricted diet include suppressing proteinuria (4,15–17) and amelioration of glucose intolerance and other metabolic complications of CKI (6). Why then is dietary counseling used irregularly (18)? We believe there are four major reasons: (1) designing these diets requires a skilled dietitian, and this can be costly (in the US, this cost is paid for Medicare recipients); (2) changing the diet is difficult for some patients; (3) there is concern that a low-protein diet could cause loss of protein stores; and (4) the initial MDRD report concluded that a low-protein diet did not significantly slow progression of CKI in nondiabetic patients (19). We believe none of these are sufficiently persuasive to avoid using this time-tested therapy to prevent complications of CKI (7). A skilled dietitian will incorporate a patient’s food preferences, adequate calories, and a proper distribution of foods while encouraging compliance and avoiding inappropriate dietary fads. Specific dietary requirements for CKI patients (1,20) are summarized in Table 1. The minimal amount of dietary protein and calories required by normal adults or those with uncomplicated CKI is 0.6 g of protein/kg per d and 30 to 35 kcal/kg per d (20, 21). With such a regimen, there is neutral protein balance and stability of lean body mass during long-
term therapy (9, 10, 20). If there has been loss of muscle mass but no reason that protein breakdown is accelerated by other illnesses, then 0.8 g/kg per d of dietary protein will be sufficient (20). With proteinuria, the diet should contain no more than 0.8 g of protein/kg per d plus 1 g of protein per gram of proteinuria; even less dietary protein may be sufficient (20, 22).

What about the concerns centering around CKI patients developing malnutrition? Malnutrition is defined as abnormalities caused by an inadequate diet, but the word is commonly used to describe abnormalities found in CKI patients developing from causes not linked to the diet. Despite reports that some patients spontaneously reduce their dietary protein with progressive CKI, malnutrition is rare when a properly monitored diet is used to treat patients, even when GFR is below 10 ml/min (9–11). This point is emphasized because of the suggestion that a decrease in protein in the diet of a CKI patient is a signal to start dialysis (23–25). When little or no attention is given to the diet, there will be severe metabolic disturbances, including metabolic acidosis, hyperphosphatemia, low values of serum proteins, etc (26). With proper attention, these problems do not occur: CKI patients (average GFR 18 ml/min) were given a restrictive diet plus a supplement of essential amino acid analogues and followed for 1 yr (27). The patients were found to be in neutral nitrogen balance, and they had no acidosis and normal values of serum phosphorus and albumin. Walser and Hill (9) evaluated 76 patients with GFR values < 15 ml/min and followed them for a median of 1 yr while they ate a low-protein diet. Weight did not decline, and average serum biochemistry values were: $\text{HCO}_3^-$, 22 mM; phosphorus, 5.6 mg/dl; and albumin, 4.1 g/dl (9). Aparicio et al. (10) reported similar outcomes in 239 CKI patients followed for an average of 29.6 mo. There was no decline in weight or body mass index, and average values of serum $\text{HCO}_3^-$ and albumin were 24 mM and 3.9 g/dl, respectively. A few reports indicate that prolonged use of low-protein diets by CKI patients does not impair their survival after beginning dialysis (28, 29). Finally, MDRD patients assigned to different diets were examined repeatedly over an average of 2.2 yr (8). The average values of “nutritional indices” (including weight and serum proteins) of those given low-protein diets remained within the normal range. There were small, statistically significant decreases in certain parameters in each of the groups eating protein-restricted diets, but only two patients had to withdraw from the MDRD because of abnormalities in nutritional status values. We emphasize these results because they document the nutritional safety of dietary therapy. They also underscore the need to use strategies to delay the need for dialysis (2–5) because dialysis is not possible for all of the patients who will develop kidney failure throughout the world. Moreover, survival of CRF patients is not improved by beginning chronic dialysis at higher levels of renal function (30, 31). This points out why strategies must be developed to avoid or delay the development of ESRD.

What about progression of CKI? The conclusion from the MDRD Study was that assignment to a low-protein diet did not significantly slow the loss of GFR (19). This outcome understandably cooled enthusiasm for dietary manipulation. However, the hypothesis was that eating a low-protein diet would

### Table 1. Specific dietary requirements for CKI patients

<table>
<thead>
<tr>
<th>Patients</th>
<th>Protein Requirement</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal adults or those with uncomplicated CKI&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Minimum: 0.6 g of protein/kg per day</td>
<td>• 30 to 35 kcal/kg per day needed to utilize dietary protein efficiently</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Adjustments for specific problems (diabetes, hyperphosphatemia)</td>
</tr>
<tr>
<td>CKI patients with muscle mass loss</td>
<td>0.8 g of protein/kg per day</td>
<td>• This is the maximum needed</td>
</tr>
<tr>
<td>CKI patients with proteinuria</td>
<td>≤0.8 g of protein/kg per day plus 1 g protein per gram of proteinuria</td>
<td>• Even less dietary protein may be sufficient</td>
</tr>
</tbody>
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<sup>a</sup> CKI, chronic insufficiency of kidney function.
slow progression, and it was subsequently concluded that those who did lower their dietary protein by 0.2 g/kg per d had a reduced loss of GFR of 29% and a 41% increase in the time to dialysis or death ($P < 0.01$) (32). Why this benefit occurs is unknown, but a low-protein diet can reduce proteinuria, which has been proposed as a major factor in progressive loss of function and responds to angiotensin-converting enzyme inhibitors (ACEI) therapy (4.15–17). Because a low-protein diet can act synergistically with ACEI to suppress proteinuria (33), dietary manipulation should be used to decrease the risk of hyperkalemia from ACEI therapy (33).

Our conclusion is that the many benefits of dietary therapy for CKI patients should not be supplanted by concerns about the influence of low-protein diets on progression of CKI. Integrating dietary manipulations into a comprehensive strategy will help prevent or ameliorate complications of CKI, including acidosis, hyperkalemia, hyperphosphatemia, and uremic symptoms, and this strategy is nutritionally sound (6,20). Treatment of CKI patients should include documentation of components of the diet and instruction and monitoring, just as in the treatment plan for patients with inherited metabolic defects, cirrhosis, diabetes, etc.

References

7. Beale LS: Kidney Diseases, Urinary Deposits and Calculous Disorders; their Nature and Treatment. Philadelphia, Lindsay and Blakiston, 1869
29. Chauveau P, Barthe N, Rigalleau V, Ozanne S, Castaing F, Delclaux C, de Precigout V, Combe C, Aparicio M: Outcome of


