Bone Marrow Transplant Nephropathy: A Case Report and Review of the Literature

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Abstract. Bone marrow transplantation can be complicated by renal failure resulting from a variety of causes. Early renal injury most often results from infection and its subsequent treatment with nephrotoxic medications. Late renal injury after bone marrow transplantation is characterized by a syndrome similar to the hemolytic uremic syndrome. This renal syndrome, called “bone marrow transplant nephropathy,” is thought to evolve from the late effects of radiation therapy and cytotoxic chemotherapy on the kidney. In this article, a case of bone marrow transplant nephropathy and a review of the clinical and pathologic features are presented. (J Am Soc Nephrol 8: 166–173, 1997)

Transplantation of either allogenic or autologous bone marrow has become an increasingly applied and successful therapy for patients with hematologic malignancies and certain solid tumors. Pretransplant treatment of the recipient now includes ablative chemotherapy and total body irradiation (TBI). Post-transplant treatment typically includes cyclosporin A and possibly other chemotherapies to either prevent or treat graft-versus-host disease (GVHD).

A variety of renal injury syndromes occurring after bone marrow transplantation (BMT) have been recognized. Renal injury may result in the first days and weeks after BMT from infection and its subsequent treatment with nephrotoxic medications, GVHD, and veno-occlusive disease (1). Early or late renal toxicity after BMT can occur because of treatment with cyclosporin A. Distinct from these injuries, a syndrome of delayed chronic renal insufficiency, anemia, and hypertension is now recognized in a subset of BMT patients. Termed “bone marrow transplant nephropathy,” this syndrome is thought to develop from pretransplant radiation therapy potentiated by certain components of the cytotoxic chemotherapy program (2).

Case Report
A 27-yr-old Caucasian man was diagnosed with acute myelogenous leukemia in 1993, and was treated with vincristine, asparaginase, prednisone, adriamycin, cytarabine, and intrathecal methotrexate, with induction of remission. He subsequently underwent BMT from a matched unrelated bone marrow donor. Pretransplant treatment consisted of cyclophosphamide (1880 mg/M²) and cytarabine (3 g/M² twice daily) for 3 days, plus fractionated total body irradiation (1400 rads) over 4 days. Post-transplant therapy included antithymocyte globulin and cyclosporine. Within the first month of BMT, the patient developed a capillary leak syndrome from cyclosporine, which required its discontinuation. He also developed multiple infections requiring treatment with amikacin, imipenem, vancomycin, and amphotericin B. Cytomegalovirus antigenemia was treated with Ganciclovir; foscarnet was substituted when leukopenia developed. Trimethoprim-sulfamethoxazole for Pneumocystis carinii pneumonia prophylaxis was initiated but subsequently discontinued when the patient developed renal insufficiency (peak serum creatinine [Cr] level of 1.8 mg/dL). GVHD also developed and was treated with prednisone. The patient was discharged 2 months after BMT, and his renal function had stabilized with a serum Cr value of 1.2 mg/dL.

One month later, the patient was admitted with Enterobacter sepsis. Treatment with ceftazidime and ciprofloxacin cleared the infection, while foscarnet was discontinued. Discharge BUN and Cr levels were 30 mg/dL and 1.5 mg/dL, respectively.

Readmission 2 months later for bronchiolitis obliterans with obstructing pneumonia and Klebsiella bacteremia was notable for a BUN value of 42 mg/dL and Cr level of 3.2 mg/dL. Aztreonam, cefoperazone, and ciprofloxacin successfully treated the infection. The patient’s BUN value was 46 mg/dL and Cr level was 1.9 mg/dL at discharge.

A parapneumonic pleural effusion developed the following month. This resolved with a course of vancomycin, ampicillin-sulbactam, and ciprofloxacin. Hypertension, pedal edema, anemia (hematocrit value, 29%), thrombocytopenia (40,000/μL), and worsened renal function (BUN value, 44 mg/dL; Cr level, 2.2 mg/dL) were noted. A 24-h urine sample revealed 1.26 g of protein, with a Cr clearance rate of 58 mL/min. Nifedipine was started for treatment of hypertension.

Eight months after BMT, the patient’s serum Cr concentration was 2.6 mg/dL. Urine sediment contained leukocytes and red blood cells. A 24-h urine sample showed 2.83 g of protein. Creatinine clearance rate was 62 mL/min. Further evaluation...
revealed normal serum complements and normal serum protein electrophoresis. Hepatitis serologic testing was positive only for HBsAb. Renal biopsy was recommended to the patient, but refused.

Over the next several months, the patient was admitted an additional three times for infectious complications requiring multiple antibiotics. Renal function continued to deteriorate, whereas proteinuria increased. Anemia and thrombocytopenia remained prominent, and the patient’s lactate dehydrogenase (LDH) level was elevated. Urine sediment examinations revealed persistent proteinuria with microscopic hematuria and rare granular casts. Peripheral blood smear showed occasional schistocytes and ovalocytes. Table 1 shows the pertinent laboratory studies and blood pressure measurements during the period from pretransplant to the time of biopsy. The physical examination on the latest admission was remarkable for mild hypertension (blood pressure, 150/90) and a Hickman venous catheter exiting over the right anterior chest. The patient had no skin rash or arthropathy.

A percutaneous renal biopsy under ultrasound guidance was performed 11 months after BMT. All glomeruli demonstrated extensive mesangiolysis and focal aneurysmal capillary dilatation (Figure 1). Focal fibrin thrombi were identified within the capillary loops. One glomerulus appeared globally thrombosed. Mild to moderate diffuse interstitial scarring and tubular dropout was present. There was a patchy interstitial infiltrate that was predominantly plasmalymphocytic. The arterioles demonstrated mild vascular thickening and narrowing of the lumen. There was no specific immunofluorescence pattern identified for immunoglobulin (Ig)A, IgE, IgG, IgM, complements C3 and C4, and albumin. There was only focal fibrinogen within glomeruli. On electron microscopy, the glomerular architecture was distorted by diffuse and severe mesangiolysis, with extensive separation of the glomerular capillary endothelial lining from the basement membrane. Electron lucent material consistent with fibrin or mesangialytic material filled the space between the basement membrane and endothelial lining (Figure 2). Other areas demonstrated marked aneurysmal dilatation of capillary loops secondary to the dissolution of the mesangial matrix stalk.

Enalapril was prescribed for blood pressure control, and nifedipine was discontinued. However, the patient developed acute renal failure (BUN value, 71 mg/dL; Cr level, 8.1 mg/dL) on enalapril. Renal function improved after this medication was discontinued. Sustained-release nifedipine was restarted for treatment of his hypertension. Because his anemia was in part related to his chronic renal failure, subcutaneous recombinant erythropoietin was prescribed. There was an improvement in his hematocrit value, and this has remained at values greater than or equal to 30%. Laboratory parameters presently show no clinically significant evidence of hemolysis, and peripheral blood smears now show normal erythrocyte morphology. Twenty months after BMT, he continues to have stable moderate renal insufficiency and proteinuria.

**Discussion**

**Background**

Bone marrow transplantation is an effective treatment for a variety of hematologic neoplasms, refractory lymphomas, and some solid tumors. An increasing number of bone marrow transplants are performed every year. A variety of renal lesions may occur in the setting of BMT. Early in the course of BMT,

**Table 1. Laboratory data for case presentation**

<table>
<thead>
<tr>
<th>Date</th>
<th>BP (mm Hg)</th>
<th>BUN (mg/dL)</th>
<th>Cr (mg/dL)</th>
<th>CrCl (mL/min)</th>
<th>24-Hour Urine Protein (g)</th>
<th>Hct (%)</th>
<th>Plt (X10^9/μL)</th>
<th>LDH (U/L)</th>
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<td>Pre-BMT</td>
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<td>11</td>
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<td></td>
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<td>1.26</td>
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<td>2.93</td>
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<td>287</td>
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<td>8.1^b</td>
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<td>31</td>
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<td>31^c</td>
<td>114</td>
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<td></td>
<td></td>
<td>33^c</td>
<td>143</td>
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</table>

*a BMT, bone marrow transplant; Cr, creatinine; CrCl, creatinine clearance rate; Hct, hematocrit; Plt, platelets; LDH, lactate dehydrogenase.

^b While on enalapril.

^c While on subcutaneous recombinant human erythropoietin.
An incidence between 0.6 and 1.3% has been noted in adult patients undergoing BMT (2–6). Children appear to develop this lesion slightly more commonly, with a reported incidence as high as 45% (7–10). The higher incidence in pediatric patients may be a result of a lower radiation tolerance in the developing kidney, as animal studies suggest a greater susceptibility of young dogs to renal damage from TBI (11). The occurrence of BMT nephropathy appears unrelated to the disease for which BMT is performed, and it has been reported after both allogenic and autologous BMT. It is unrelated to any acute renal failure syndromes that may develop early after BMT and does not occur more frequently in those patients (9). The condition is characterized by anemia, hypertension, and decreased GFR, with distinct histopathologic features. Table 3 compares the incidence of BMT nephropathy, delay of onset from the time of BMT, and types of BMT, conditioning, and immunosuppressive regimens in adult and pediatric populations.

**Clinical Manifestations**

Cohen et al. observed two clinical patterns of BMT nephropathy in their series of adult patients (3). They called these patterns “acute” and “chronic” BMT nephropathy (Table 4), although it has been argued that this division is somewhat arbitrary. Acute BMT nephropathy characteristically presents with an HUS-like picture. Features include severe hypertension with or without congestive heart failure, peripheral edema, microangiopathic hemolytic anemia with red blood cell fragmentation, thrombocytopenia, and an elevated LDH level. Renal manifestations include a rapid progressive decline in renal function, significant proteinuria, and microscopic hematuria with or without cellular casts (2,4,7,8). Recovery of renal function is unusual, and mortality is high, ranging from 50 to 75% (2,3,7).

A less acute presentation of BMT nephropathy with features that differ from that of the acute syndrome is seen in some patients (termed “chronic BMT nephropathy”). Hypertension is only mild to moderate. Hemolytic anemia is typically less severe and may be transient. All patients, however, tend to have anemia that is out of proportion to the level of azotemia. A slower decline in renal function, as gauged by the slope of 100/Cr versus time, is characteristic (2,3). In most of these patients, a biphasic pattern in the deterioration of renal function is seen. In the first 12 to 24 months after BMT, renal function deteriorates steadily. After this phase, there appears to be a stabilization of renal function over time, but no recovery. Although most patients with chronic BMT nephropathy seem to follow this pattern, there have been a few reports of continued progressive loss of renal function without stabilization, as well as isolated reports of recovery (3,7,8). Proteinuria, usually greater than 1 g/24 h, and microscopic hematuria with or without casts are also present. Other reported laboratory features include hyperkalemia, metabolic acidosis, and low erythropoietin levels (2). Infection has been noted to precipitate acute exacerbations of the syndrome (4).

Our patient demonstrated most of these findings. He developed hypertension and peripheral edema approximately 6 months after BMT. Proteinuria, an active urine sediment, and renal complications often result from infection and its treatment. Acute tubular necrosis may arise as a direct consequence of sepsis with or without hypotension, or from therapy with a variety of nephrotoxic drugs (1). Allergic interstitial nephritis may evolve from antibiotics or allopurinol. Cyclosporine, used in the early post-transplant period to prevent GVHD, is another agent capable of producing either acute or chronic nephrotoxicity. Hepatic veno-occlusive disease may lead to a hemodynamic form of acute renal failure. Table 2 lists the potential etiologies of renal failure after BMT, both in the early and late post-transplant period. An in-depth review of acute renal failure occurring early after BMT is available (1); however, the renal complications occurring more than 3 to 4 months after BMT will be the subject of this review.

A distinct syndrome of late renal toxicity, defined as nephrotoxicity developing more than 3 months after BMT, has been reported by multiple centers that perform BMT with pre-transplant TBI. Initial reports of this syndrome described clinical and pathologic features similar to hemolytic uremic syndrome (HUS). The term “BMT nephropathy” was used by Cohen et al. to describe this characteristic renal syndrome (2). An incidence between 0.6 and 13% has been noted in adult patients undergoing BMT (2–6).
Figure 2. Electron microscopy from renal biopsy. The endothelium (arrow) is completely stripped from the basement membrane (double arrows). Electron lucent material fills the space between the basement membrane and the endothelial lining. The capillary lumen is decreased in caliber. Red blood cell fragments are seen within the mesangial area. (Original magnification, X4250).

azotemia became persistent. He had persistent anemia, thrombocytopenia, and an elevated LDH level. In addition, transient rises in Cr level occurred in association with intercurrent episodes of infection. Finally, his biopsy revealed the characteristic changes of BMT nephropathy.

Pathology and Pathogenesis

In both the acute and chronic form of BMT nephropathy, light microscopy of renal tissue demonstrates ballooning of the lobules of glomerular tufts, which are enlarged and hypercellular. The lobules are filled with fine strands of mesangial matrix arranged in a trabecular pattern. There are intraluminal fibrin thrombi in glomerular capillaries and renal arterioles. The subendothelial space is considerably widened, giving a double contour appearance to the capillary loops. RBC are trapped in the mesangial areas, with scattered fusiform mesangial cells and cellular debris. Disintegration of the mesangial matrix, termed "mesangiolysis," is a prominent finding. Arteriolar hyalinization, interstitial edema, and tubular atrophy with interstitial fibrosis are sometimes seen. Immunofluorescence
may show deposits of fibrin and IgM in some glomeruli. Electron microscopy reveals endothelial cell injury and accumulation of clear heterogenous material in the subendothelial zone and mesangial areas. Podocytes are normal, with only focal effacement of the foot processes (2,6-8).

Interestingly, these histologic changes are very similar to those of radiation nephritis (8). This type of lesion is also similar but not identical to that seen in classical HUS, in which there may be subendothelial widening of the glomerular basement membrane with amorphous material and scattered small dense granules. Chappell et al. noted that patients with a rapidly progressive course had prominent vascular disease on biopsy (5). In contrast, patients with a more chronic course had less thrombosis and fewer vascular changes, but extensive endothelial detachment in glomeruli.

Because TBI precedes BMT to “condition” immune cells, the renal lesion is thought to result from the radiation treatment. The mechanism by which radiation injury causes the HUS-like lesion of BMT nephropathy is not completely understood. Within the kidney, the endothelial cell is believed to be the cell most susceptible to radiation injury, and even low doses of radiation can result in single-stranded DNA breaks. With high doses of radiation, or in the presence of radiomimetic chemotherapeutic drugs, double-stranded DNA breaks can occur. In addition, the hydroxy radical, a by-product of radiation’s interaction with cell water, triggers a cascade of oxidative reactions. This results in critical cellular damage, ranging from sublethal injury to cell death. Presumably, the damaged endothelium is predisposed to microthrombus formation, and this process culminates in HUS (1).

However, the amount of radiation given is lower than 2000 rads, the typically accepted limit of renal radiation tolerance (2-4,7,8). It has been argued that potentiation of radiation injury by cytotoxic chemotherapy may occur (12). This phenomenon has been noted in other tissues such as skin, esophagus, intestine, and lung. In fact, some studies have evaluated the effect of a variety of drugs on the development of radiation nephropathy in a rat syngeneic BMT model. However, only busulfan, cisplatinum, and BCNU (carmustine) appear to enhance renal radiation damage (13,14). Cyclosporine does not exacerbate renal dysfunction in this model, and reports of BMT nephropathy in patients not treated with cyclosporine have been described (4-8,15-19). Although cyclophosphamide therapy has been frequently reported with BMT nephropathy (2,4-8,10,15,17-22), it does not enhance radiation-induced nephrotoxicity in the rat syngeneic BMT model (13). Thus, the mechanism and contribution of chemotherapeutic potentiation of renal radiation injury in the development of BMT nephropathy remain unclear.

Although radiation-induced renal injury is the most commonly implicated factor in the pathogenesis of BMT nephropathy, this entity has been recently described in the absence of TBI (6,16). This suggests that TBI is not necessarily the sole causative factor.

The disproportionate anemia associated with BMT nephropathy is potentially explained by radiation damage to the interstitial capillary endothelium, the likely site of erythropoietin production in the kidney (2). The favorable response to exogenous erythropoietin is compatible with this interpretation. It has also been suggested that the anemia associated with radiation nephritis may be compounded by intravascular hemolysis. Radiation-induced injury to the endothelial cells in the kidney could precipitate local platelet adherence with subsequent development of hemolysis and thrombocytopenia. The presence of schistocytes on peripheral blood smear supports this notion.

**Prevention**

Theoretically, a number of strategies can be utilized to decrease the risk of development of BMT nephropathy (Table 5). These include partial renal shielding during TBI, hyperfractionation of the total radiation dosage, slow radiation administration, and the use of exogenous free radical scavengers (1). The latter strategy is based on the presumption that the hydroxy radical, a byproduct of radiation’s interaction with cell water, is the prime mediator of radiation injury. However, all of these interventions present a potential risk for either decreased tumor killing or impairment of marrow engraftment and subsequent proliferation.

**Treatment**

BMT nephropathy, once established, is largely unresponsive to all treatment, except supportive therapy. Because the acute form of BMT nephropathy has some features of HUS, plasmapheresis has been utilized in its treatment (Table 5). However, the reported results are generally disappointing (2,4,23). A prospective uncontrolled trial using plasmapheresis in eight patients has been reported (23). Four patients did not respond, whereas the rest showed some hematologic improvement. Of these patients, however, seven died within 3 months of the onset of disease. Hence, the role of plasmapheresis remains controversial. Some centers, however, use a trial of five to ten treatments in the hope of achieving a clinical response (1).

Many physicians have traditionally reduced the cyclosporine dose in patients who develop BMT nephropathy, whereas others choose to discontinue the drug completely (1). The vascular toxicity of cyclosporine has been thought to play a role in the progression of the disease, although it is unlikely to
**Table 3. Data from cases of bone marrow transplant (BMT) nephropathy**

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</th>
<th>Onset&lt;sup&gt;a&lt;/sup&gt; (months)</th>
<th>Allogenic BMT (%)</th>
<th>Autologous BMT (%)</th>
<th>Chemotherapy Agents&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Use of CY (%)</th>
<th>Use of TBI (%)</th>
<th>Use of CS (%)</th>
<th>GVHD Present (%)</th>
<th>Infection Present (%)</th>
<th>Outcome (%)</th>
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<tr>
<td>Adult</td>
<td>4</td>
<td>16 (9.5)</td>
<td>3-11</td>
<td>31</td>
<td>69 CY Ara-C</td>
<td>100</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>100 CRI</td>
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<tr>
<td></td>
<td>6</td>
<td>8 (0.6)</td>
<td>4-29</td>
<td>38</td>
<td>62 CY Ara-C</td>
<td>88</td>
<td>62</td>
<td>25</td>
<td>38</td>
<td>62</td>
<td>88 Died</td>
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<tr>
<td></td>
<td>5</td>
<td>7 (3)</td>
<td>9-22</td>
<td>71</td>
<td>29 CY Ara-C</td>
<td>100</td>
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<td>14</td>
<td>71</td>
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<td>6-11</td>
<td>100</td>
<td>0 CY Ara-C</td>
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<td>16, 19, 22, 25&lt;sup&gt;d&lt;/sup&gt;</td>
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<td>5-8</td>
<td>75</td>
<td>25 CY Ara-C Melphalan BCNU</td>
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<td>67</td>
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<td>0</td>
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<tr>
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<td>8</td>
<td>14 (45)</td>
<td>3-7</td>
<td>21</td>
<td>79 CY Ara-C VM-26 Melphalan Cis-plat</td>
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<sup>a</sup> Only cases with onset of clinical syndrome >3 months after BMT are included in the table. CY, cyclophosphamide; TBI, total body irradiation; CS, cyclosporine; GVHD, graft-versus-host disease; Ara-C, cytarabine; VP-16, etoposide; VM-26, teniposide; cis-plat, cis-platinum; CRI, chronic renal insufficiency; NS, not stated in article; NA, not applicable.

<sup>b</sup> Delay in onset of clinical syndrome after BMT.

<sup>c</sup> Conditioning chemotherapy prior to BMT.

<sup>d</sup> Compiled data from case reports.

be the causative agent. However, no proof exists that discontinuation of cyclosporine is absolutely necessary or specifically beneficial.

Blood pressure control to diastolic values less than 90 mm Hg is probably important. This appeared to slow the progression of renal insufficiency in five cases of chronic BMT nephropathy (2). However, the lack of controls and small number of patients does not permit a definite conclusion. Experimentally, angiotensin-converting enzyme inhibitors have been effective in prevention and treatment of renal radiation injury (1). The effectiveness of these inhibitors in BMT nephropathy remains to be shown.

Finally, a small number of these patients progress to ESRD requiring maintenance dialysis (2). Transplantation of a kidney from the bone marrow donor to the patient with BMT nephropathy and ESRD is an interesting possibility. Because the donor marrow presumably has reconstituted the patient's immune system, the kidney theoretically should be well tolerated. Successful kidney transplantation using this technique has been reported in two patients (24).
our patient, the histopathology is characterized by mesangioly-
interpretation of

Acknowledgments

References

1. Zager R: Acute renal failure in the setting of bone marrow

Summary

BMT nephropathy can be a late complication of bone mar-
row transplantation. It differs from the acute renal failure that
develops in the early posttransplant period for a number of
reasons. First, the syndrome occurs later (3 to 4 months) and
the etiology is unrelated to infection, hypotension, or drug
toxicity. Second, the clinical syndrome may at times mimic the
hemolytic uremic syndrome with microangiopathic hemolytic
anemia, thrombocytopenia, and renal failure. Third, as seen in
our patient, the histopathology is characterized by mesangioly-
sis with focal aneurysmal dilatation, fibrin thrombi in capillary
loops, and marked widening of the subendothelial space result-
ing from deposition of amorphous material, similar to the
appearance of radiation nephritis. Finally, no definitive treat-
ment is currently available for BMT nephropathy, except for
supportive therapy.

Acknowledgments

We thank Drs. Hugh Carey and Michael Kashgarian for the prepa-
ration and interpretation of the histopathological specimens.

Table 4. Clinical features of acute and chronic bone marrow
transplant (BMT) nephropathy

<table>
<thead>
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<th>Chronic BMT Nephropathy</th>
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<tbody>
<tr>
<td>Severe hypertension +/− hypertensive crisis</td>
<td>Mild to moderate hypertension</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Mild or transient hemolytic anemia</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Severe hemolytic anemia</td>
<td>Elevated lactate dehydrogenase level</td>
</tr>
<tr>
<td>Fragmentation of red blood cells</td>
<td>Low erythropoietin levelsb</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Renal insufficiency (biphasic pattern of decline in renal function)</td>
</tr>
<tr>
<td>Elevated lactate dehydrogenase level</td>
<td>Hyperkalemiab</td>
</tr>
<tr>
<td>Renal failure (rapid decline in renal function)</td>
<td>Metabolic acidosisb</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>Proteinuria</td>
</tr>
<tr>
<td>Microscopic hematuria</td>
<td>Microscopic hematuria</td>
</tr>
<tr>
<td>Cellular and/or granular castsa</td>
<td></td>
</tr>
</tbody>
</table>

* May or may not be present.

In patients in whom this was measured.

Table 5. Preventive and therapeutic strategies for bone
marrow transplant nephropathy

<table>
<thead>
<tr>
<th>Prevention</th>
<th>Treatment</th>
<th>Supportive Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial renal shielding</td>
<td>Plasma exchange +/− vincristine</td>
<td>Transfusion of blood products (platelets, packed red blood cells)</td>
</tr>
<tr>
<td>Hyperfractionation of radiation dose</td>
<td>Withdrawal of cyclosporine</td>
<td>Diuretics</td>
</tr>
<tr>
<td>Slow administration of radiation</td>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>Blood pressure control</td>
</tr>
<tr>
<td>Antioxidants</td>
<td>Blood pressure control</td>
<td>Recombinant erythropoietin for anemia</td>
</tr>
<tr>
<td>Renal replacement therapy (dialysis, renal transplantation)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

course of late-onset bone marrow transplant nephropathy. Nephron 64: 626–634, 1993
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The Training Program in Nephrology at the Yale University School of Medicine

Postdoctoral training in nephrology at Yale University had its origins in the 1940s within the Section of Metabolism created by Dr. John Peters. Since 1972, a distinct nephrology program has existed, which is currently directed by Dr. Peter Aronson. The goal of the program is the training of academic nephrologists, and 70% of our graduates hold full-time faculty appointments.

We offer a combined clinical/research fellowship that is 3 (or more) yr in duration and includes 1 yr of full-time clinical training and 2 (or more) yr devoted to clinical or laboratory research. Clinical-only and research-only fellowships are also available. There are currently 24 nephrology fellows. Clinical training is based at the Yale-New Haven Hospital, the West Haven VA Medical Center, and the Yale-REN Dialysis Center. Clinical fellows gain expertise in the diagnosis and management of patients with a broad array of nephrologic disorders, including fluid and electrolyte disturbances, glomerulonephritis, interstitial nephritis, hypertension, acute and chronic renal failure, and intoxications. Fellows also receive intensive training in the care of patients receiving renal homografts. Training in the outpatient practice of nephrology includes firsthand experience with maintenance hemodialysis and home peritoneal dialysis, and emphasizes continuity of care.

The 19 full-time faculty members of the Section of Nephrology have scientific interests in the areas of epithelial transport, hypertension, hereditary renal disease, gene regulation, immunobiology, acute renal failure, nutritional balance in chronic renal failure, and clinical pathologic correlations in glomerular disease. Clinical investigation emphasizes renal transplantation, disorders of potassium homeostasis, natural history of glomerular disease, outcomes in dialysis management, and anemia of renal insufficiency. Research training is supported by a training grant from the National Institutes of Health. The Yale University School of Medicine is unique in having a large group of distinguished faculty outside of the Section of Nephrology whose research interests include the study of the kidney and who also serve as research mentors for nephrology trainees. This provides fellows with access to a broad range of research projects within the fields of biostatistics, genetics, transplantation biology, physiology, and cell biology.