The microangiopathic hemolysis of recurrent hemolytic uremic syndrome (HUS) is identical to the original disease, with extensive erythrocyte fragmentation and thrombocytopenia. The incidence of HUS recurrence is difficult to assess. At one extreme, five of 11 children suffered graft loss because of recurrent disease. However, most series have reported substantially lower recurrence rates: no recurrences in 16 adults and children, one of 34 grafts in 28 children, and two probable recurrences of 24 grafts in 20 children [4,45,46]. Graft loss occurs in 10% to 50% of patients with recurrence. HUS has been diagnosed 1 day to 15 months after transplantation (usually in less than 2 months), and the incidence of recurrence is increased in patients receiving grafts less than 3 months after their initial disease. Treatment of recurrent disease is plasma exchange for plasma or cryosupernatant, or plasma infusions, and dose reduction of cyclosporine. Recurrence may be prevented by aspirin and dipyridamole.

**DIFFERENTIAL DIAGNOSIS OF RECURRENT HEMOLYTIC UREMIC SYNDROME**

<table>
<thead>
<tr>
<th>Differential Diagnosis</th>
<th>Recurrence Rate</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombotic microangiopathy associated with cyclosporine</td>
<td></td>
<td></td>
<td>Differentiation from acute and chronic vascular rejection can be difficult</td>
</tr>
<tr>
<td>Acute vascular rejection</td>
<td></td>
<td></td>
<td>Renal transplantation does not halt the progress of Fabry’s disease because the new kidney is not an adequate source of α-galactosidase; patients have frequent systemic complications</td>
</tr>
<tr>
<td>Accelerated phase hypertension</td>
<td></td>
<td></td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Tacrolimus- (FK-506) associated thrombotic microangiopathy</td>
<td></td>
<td></td>
<td>Recurrence associated with extrarenal features including arthralgias and purpura</td>
</tr>
</tbody>
</table>

**OTHER CONDITIONS THAT RECUR IN RENAL ALLOGRAFTS**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Recurrence Rate</th>
<th>Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic sclerosis</td>
<td>20%</td>
<td>Usually graft failure</td>
<td>Differentiation from acute and chronic vascular rejection can be difficult</td>
</tr>
<tr>
<td>Fabry’s disease</td>
<td>Rare recurrence of ceramide in the graft</td>
<td>Poor</td>
<td>Renal transplantation does not halt the progress of Fabry’s disease because the new kidney is not an adequate source of α-galactosidase; patients have frequent systemic complications</td>
</tr>
<tr>
<td>Immunotactoid glomerulopathy</td>
<td>50%</td>
<td>Nephrotic syndrome</td>
<td>Nephrosis reported between 21 and 60 mo</td>
</tr>
<tr>
<td>Mixed essential cryoglobulinemia</td>
<td>50%</td>
<td>Poor</td>
<td>Recurrence associated with extrarenal features including arthralgias and purpura</td>
</tr>
<tr>
<td>Cystinosis</td>
<td>0%</td>
<td>Good</td>
<td>Cystinosis does not recur; however, the allograft can become infiltrated by macrophages containing cysteine, with no pathologic or clinical effect</td>
</tr>
</tbody>
</table>

**FIGURE 17-36**

Blood film abnormalities, microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure occur in accelerated hypertension and acute vascular rejection. A renal biopsy usually distinguishes acute vascular rejection, and malignant hypertension should be obvious clinically. The microangiopathy of cyclosporine can be difficult to differentiate from hemolytic uremic syndrome; however, glomerular pathology usually is less marked and vascular changes more obvious with cyclosporine toxicity. De novo hemolytic uremic syndrome also has been reported in patients treated with tacrolimus (FK-506) [27].

**FIGURE 17-37**

A number of other conditions have been reported to recur in allografts. Very few patients with systemic sclerosis have received transplantation, and the incidence of acute renal failure caused by systemic sclerosis has declined with the widespread use of angiotensin-converting enzyme (ACE) inhibitors. About 20% of patients with a malignant course of scleroderma receiving a transplantation develop recurrence, which usually causes graft loss. The value of ACE inhibitors after transplantation is unknown. Two of four patients with immunotactoid glomerulopathy developed recurrent disease heralded by massive proteinuria. Transplantation in Fabry’s disease rarely leads to graft-related problems; however, patients die from systemic complications of ceramide deposition.
MANAGEMENT OF RECURRENT DISEASE AFTER KIDNEY TRANSPLANTATION

<table>
<thead>
<tr>
<th>Disease</th>
<th>Treatment of recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>Plasma exchange, immunoadsorption, steroids, angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Immunoglobulin A nephropathy</td>
<td>With crescents: plasma exchange, cytotoxins</td>
</tr>
<tr>
<td>Henoch-Schonlein purpura</td>
<td>Steroids</td>
</tr>
<tr>
<td>Mesangiocapillary glomerulonephritis type I</td>
<td>Aspirin, dipyridamole</td>
</tr>
<tr>
<td>Mesangiocapillary glomerulonephritis type II</td>
<td>Plasma exchange</td>
</tr>
<tr>
<td>Membranous nephropathy</td>
<td>Plasma exchange, cyclophosphamide</td>
</tr>
<tr>
<td>Anti-glomerular basement membrane disease</td>
<td>Plasma exchange, plasma infusion</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome</td>
<td>Cyclophosphamide and steroids</td>
</tr>
<tr>
<td>Antineutrophil cytoplasm antibody-associated vasculitis</td>
<td>Glycemic control</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Aggressive perioperative dialysis, hydration, low oxalate diet, low ascorbic acid diet, phosphate supplements, magnesium glycerophosphate, pyridoxine</td>
</tr>
<tr>
<td>Oxalosis</td>
<td></td>
</tr>
</tbody>
</table>

WHEN TO AVOID USING LIVING RELATED DONORS IN KIDNEY TRANSPLANTATION

Focal segmental glomerulosclerosis with risk factors for early recurrence
Henoch-Schonlein purpura
Mesangiocapillary glomerulonephritis type I
Mesangiocapillary glomerulonephritis type II with risk factors
(familial immunoglobulin A nephropathy and hemolytic uremic syndrome)

References


FIGURE 17-38
No controlled data exist on the management of recurrent disease after transplantation. For patients with primary hyperoxaluria, measures to prevent further deposition of oxalate have proved successful in controlling recurrent renal oxalosis [9]. In diabetes mellitus, the pathophysiology of recurrent nephropathy undoubtedly reflects the same insults as those causing the initial renal failure, and good evidence exists that glycemic control can slow the development of end-organ damage. Plasma exchange and immunoadsorption are promising therapies for patients with nephrosis who have recurrent focal segmental glomerulosclerosis; however, these therapies do not provide sustained remission [6,7]. In all these cases, establishing a diagnosis of recurrent disease is critical in identifying a possible treatment modality.

FIGURE 17-39
In these diseases, rapid recurrence leading to graft failure is frequent enough to warrant extreme caution in using living related donors. Even excluding these conditions, the overall rate of recurrence of glomerulonephritis is substantially increased in living related donors, and patients should be made aware of this risk [4]. For familial diseases, the risk of recurrence is even higher (e.g., some families with immunoglobulin A disease and hemolytic uremic syndrome). Finally, recurrent glomerulonephritis has been reported in up to 30% of renal isografts, with disease onset between 2 weeks and 16 years after grafting.