Goodpasture syndrome, also known as anti–glomerular basement membrane disease, is a rare autoimmune disease. Patients with the syndrome experience a rapid progression to renal failure and death if the disease is not recognized and treated early. First described by Ernest Goodpasture during the influenza pandemic of 1919, the syndrome has been extensively studied and has led to a better understanding of autoimmunity. In this article, I review the pathophysiology, diagnosis, and treatment of the acute phase of Goodpasture syndrome and describe the nursing interventions. A case study illustrates the multisystem failure encountered by patients with the syndrome.

Definition

Goodpasture syndrome, a disease of the glomerular and alveolar basement membranes, is characterized by pulmonary hemorrhage and crescentic glomerulonephritis. It is associated with serum antibodies to glomerular basement membrane and linear deposits of antibodies along the glomerular and alveolar basement membrane and may result in rapidly progressive glomerulonephritis. However, some confusion exists between the terms Goodpasture syndrome and Goodpasture disease. Reisli et al note that Goodpasture disease is characterized by the presence of antibodies to glomerular basement membrane, whereas the syndrome is the rapidly progressive glomerulonephritis and pulmonary hemorrhage alone. According to Bolton, patients who have antibodies to glomerular basement membrane deposited in tissue have Goodpasture disease and patients who have Goodpasture disease along with glomerulonephritis and/or hemoptysis have Goodpasture syndrome. Salama et al note that the term Goodpasture syndrome is rarely used in Europe; there the disorder is known as Goodpasture disease.

Epidemiology

Goodpasture syndrome is diagnosed in 1 in 1 million persons each year. Whites are affected more than any other race, and the incidence is slightly higher in men than in women. The syndrome affects 2 different age groups: persons in their mid 30s and persons in their late 50s. With current therapy, survival through the acute phase is more than 90%. However, 2-year survival is less than 50%, and the mortality rate in patients with chronic renal failure is even worse. End-stage renal disease develops in 40% to 70% of patients who have nephritis mediated by antibodies to glomerular basement membrane. Glomerulonephritis, a potential consequence of Goodpasture syndrome, is responsible for 10% to 15% of all patients with end-stage renal disease in the United States. The syndrome has a genetic component and has been linked to the HLA DRBI 1501 region. Recurrence of the syndrome is infrequent, and pulmonary hemorrhage seldom occurs in patients who do not smoke tobacco.

Pathophysiology

Patients with Goodpasture syndrome have a type II hypersensitivity reaction (Figure 1). A type II hyper-
A sensitivity reaction occurs when antibodies are directed against specific antigens on cell surfaces or connective tissues. In Goodpasture syndrome, the antibodies attack the NC1 domain of the α3 chain of type IV collagen located in the basement membranes of the kidneys and alveoli. Basement membranes are thin structures that form a barrier between epithelial cells and connective tissue. These membranes, consisting of type IV collagen, laminin, proteoglycans, entactin, and other proteins, assist in the maintenance of tissue differentiation and function. Although the hypersensitivity reaction affects all collagen contained within the body, organs containing alveolar and glomerular basement membranes are affected more than are other organs containing type IV collagen. This difference occurs because an increase in the accessibility of epitopes (antigen molecules that permit attachment of a matching antibody) associated with an increase in the expression of α3 collagen chains in these basement membranes allows access and formation of antibodies.

In the kidney, the basement membrane is the principal selective barrier of the glomerulus, preventing plasma proteins, erythrocytes, leukocytes, and platelets from passing through into the nephron. Deposits of IgG, IgA, and sometimes IgM antibodies in the basement membrane break down collagen and interrupt membrane integrity. A loss of membrane integrity causes leakage of blood and a rapid inflammatory response, leading to proteinuria, hematuria, oliguria, and alveolar damage with subsequent pulmonary hemorrhage. Activated monocytes cause new moon–shaped formations known as crescents within the kidney; the formation is enhanced by the attraction of interleukin-1 by fibroblasts in the renal interstitium.

Clinical Manifestations

The clinical manifestations of Goodpasture syndrome vary. In some patients, pulmonary signs and symptoms occur weeks to months before renal manifestations are evident. Commonly, signs and symptoms of Goodpasture syndrome are associated with a history of smoking or exposure to other hydrocarbons, including trichloroethane, carbon tetrachloride, xylene, and ethyl ether. This exposure is thought to damage the basement membrane and expose antigenic sites within the lung, causing alveolar damage and subsequent pulmonary hemorrhage.

The initial signs and symptoms consist of a flulike malaise followed by a rapid onset of microscopic hematuria and proteinuria. More than half of patients with Goodpasture syndrome have pulmonary signs and symptoms, including cough, mild shortness of breath, and hemoptysis. The skin appears pale because of iron deficiency anemia. Renal manifestations can also include edema and hypertension, which can rapidly progress to acute renal failure. Acute renal failure may progress to chronic renal failure, and the need for lifetime hemodialysis or a kidney transplant can be a manifestation of Goodpasture syndrome. Rarely, patients also have arthritis, peripheral neuropathy, uveitis, or leukocytoclastic vasculitis of the skin.

Differential Diagnosis

Goodpasture syndrome mimics many other conditions, including systemic vasculitis, Wegener granulomatosis, polyarteritis nodosa, systemic lupus erythematosus, infection, and any cause of pulmonary hemorrhage with decreased renal function known as pulmonary-renal syndrome. The occurrence of hemoptysis may be caused by other disease states, including atrioventricular fistula, left ventricular failure, pulmonary embolism, pulmonary hypertension, thrombocytopenia, bronchitis, cystic fibrosis, lung can-
cer, systemic lupus erythematosus, trauma, aortic aneurysm, and multiple other causes. The most probable cause of hemoptysis is bronchitis and primary lung disease. A complete analysis of the patient’s history, laboratory tests, and physical examination aids in the differential diagnosis (Table 1).

### Diagnostic Studies

Table 2 gives typical laboratory values for patients with Goodpasture syndrome.

### Pulmonary Tests

Initial evaluation of the pH of the expectorated blood assists in determining if the blood is gastric or pulmonary. An acidic pH (<7.4) indicates a gastric source. The values on the diffusing capacity of carbon monoxide test, used to determine carbon monoxide uptake, are elevated if pulmonary hemorrhage is present. Patients with Goodpasture syndrome have decreased alveolar gas volumes, total lung capacity, and vital capacity. (On pulmonary function tests, total lung capacity is equal to the tidal volume plus expiratory reserve volume plus residual volume plus inspiratory reserve volume. Vital capacity is equal to the total volume exhaled after maximum inspiration.)

Chest radiographs show bilateral infiltrates with apical sparing. If the findings on chest radiographs are normal, a computed tomography scan may show minor parenchymal involvement. Bronchoscopy may be performed to rule out other causes of bleeding and determine the extent of lung involvement. Blood is often visualized in the tracheobronchial tree. Examination and culturing of bronchial washings are used to rule out infectious causes of hemoptysis. Immunofluorescence of lung tissue reveals linear IgG staining of the basement membrane of the alveolar wall. On electron micrographs, lung tissue has a thick basement mem-

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Table 1 Differential diagnosis in Goodpasture syndrome

<table>
<thead>
<tr>
<th>Diagnosis and definition</th>
<th>History</th>
<th>Findings on physical examination</th>
<th>Laboratory data</th>
<th>Findings on renal biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodpasture syndrome</td>
<td>Smoker or exposure to hydrocarbons Age in 30s or 50s White</td>
<td>Weight loss Malaise Hemoptysis Periorbital edema</td>
<td>Antibodies to GBM Iron deficiency anemia Proteinuria Hematuria</td>
<td>Linear deposits of IgG antibodies in the GBM on immunofluorescence Crescents present</td>
</tr>
<tr>
<td>Diabetic nephropathy</td>
<td>Dependence on insulin or oral hypoglycemic agents Hypertension Cardiovascular disease</td>
<td>Weight gain Oliguria Peripheral edema Diminished peripheral pulses</td>
<td>Proteinuria Decreased glomerular filtration rate Increased level of serum urea nitrogen Increased creatinine level</td>
<td>May have greater incidence of bleeding and complications after biopsy</td>
</tr>
<tr>
<td>Alport syndrome</td>
<td>Sensononeural hearing loss starting in childhood Cataracts Chronic renal failure beginning in second or third decade Childhood disease</td>
<td>Bloody urine Hearing loss Visual disturbances</td>
<td>Hematuria Anemia Proteinuria</td>
<td>Mixed nephritis with foam cells on immunofluorescence Thickening and splitting of GBM with no immune deposits</td>
</tr>
<tr>
<td>Lupus nephritis</td>
<td>Diagnosis of systemic lupus erythematosus within previous year Fever Joint pain Malaise More frequent in young women than in other groups</td>
<td>Butterfly rash Photosensitivity Oral ulcers Arthritis of 2 or more digits Skin rash from sunlight</td>
<td>Antibodies to double-stranded DNA Antibodies to smooth muscle Proteinuria Decreased levels of C3 and C4 components of complement Antibodies to nuclear antigens</td>
<td>Mesangial and subepithelial immune deposits</td>
</tr>
</tbody>
</table>

Abbreviation: GBM, glomerular basement membrane.
brane with hyperplasia of type I and II pneumocytes.3,6

Renal Studies
A urinalysis is necessary to determine if albumin is present in the urine and to obtain the urinary concentration of creatinine. In Goodpasture syndrome, albumin is present in the urine because of the damage to the glomerular basement membrane, and the 24-hour urine creatinine concentration is decreased, indicating decreased glomerular filtration rates.17 The urine sediment contains dysmorphic red cells and casts.8 Measurements of the serum levels of urea nitrogen and creatinine are used to determine the extent of renal function. The levels of both are elevated in patients who have rapidly progressive glomerulonephritis.

Table 2 Laboratory values in Goodpasture syndrome

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Normal value</th>
<th>Value in Goodpasture syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon monoxide uptake</td>
<td>25 mg/min per m²</td>
<td>Increased</td>
</tr>
<tr>
<td>Total lung capacity</td>
<td>5500 mL</td>
<td>Decreased</td>
</tr>
<tr>
<td>Vital capacity</td>
<td>4000 mL</td>
<td>Decreased</td>
</tr>
<tr>
<td>24-hour urine creatinine</td>
<td>8.8-17.7 mmol/d (1-2 g/24 h)</td>
<td>Decreased</td>
</tr>
<tr>
<td>Serum urea nitrogen</td>
<td>1.8-7.1 mmol/L (5-20 mg/dL)</td>
<td>Elevated</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>Male 53-90 µmol/L (0.6-1.02 mg/dL) Female 44-97 µmol/L (0.5-1.1 mg/dL)</td>
<td>Elevated</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>Male 136-172 g/L Female 120-150 g/L</td>
<td>Normal or decreased</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Male 0.42-0.52 Female 0.35-0.47</td>
<td>Normal or decreased</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>5 × 10⁴/L to 10 × 10⁹/L</td>
<td>Normal or increased</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>10-15 seconds</td>
<td>Normal or increased</td>
</tr>
<tr>
<td>Partial thromboplastin time</td>
<td>Depends on laboratory Standard &lt;35 seconds</td>
<td>Normal or increased</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
<td>Age &lt;50 years          Male 15 mm/h Female 20 mm/h Age 50-85 years Male 20 mm/h Female 30 mm/h</td>
<td>Normal or increased</td>
</tr>
<tr>
<td>Antibodies to glomerular basement membrane</td>
<td>Negative</td>
<td>Yes in 87% of cases</td>
</tr>
</tbody>
</table>

Patients without Goodpasture syndrome are negative for these antibodies. All patients must fast 8 hours before a blood sample for the test is obtained.20

Sonography and Renal Biopsy
Sonograms of patients with Goodpasture syndrome reveal normalized kidneys.9 Renal biopsy specimens have linear deposits of IgG and fibrin along the glomerular basement membrane in a crescent shape. A definitive diagnosis of Goodpasture syndrome is made if a patient has circulating antibodies to glomerular basement membrane and examination of renal biopsy specimens reveals linear deposits of IgG with crescent formation.11

Other Baseline Tests
A complete blood cell count with a manual differential is used to detect anemia and the white blood cell count. In Goodpasture syndrome, the results may or may not be normal (Table 2). Other tests may include prothrombin time, partial thromboplastin time, erythrocyte sedimentation rate, complete chemistry panel, blood cultures, complement panel, enzyme-linked immunosorbent assay, and anti-neutrophil cytoplasmic antibody test.3 The transferrin level may be assessed to detect iron deficiency anemia.

Treatment and Nursing Considerations
Table 3 is a potential care plan for patients with Goodpasture syndrome.

Pulmonary Measures
In Goodpasture syndrome, pulmonary hemorrhage can be severe and iron deficiency anemia develops.4 A blood loss of 600 mL/d increases mortality from 7% to 85%.10 This
blood loss leads to anemia; therefore, blood transfusions are necessary to support proper hemoglobin levels, reduce hypoxia, and prevent further circulatory collapse. Maintaining hemodynamic stability and adequate oxygen delivery is paramount. Supportive airway management is necessary for adequate tissue oxygenation. In acute hemoptysis (blood loss of 600 mL/d), asphyxiation is the usual cause of death and airway clearance is essential to prevent further hypoxia.16 Bronchoscopy is used to detect the site of bleeding, and if possible the lung involved should be isolated from healthy lung tissue by intubation of the contralateral lung or by separating the lungs with a double-lumen endotracheal tube.16 Ventilator management in the acute respiratory phase is necessary to preserve optimal airway function and prevent further airway decline. Hemoptysis may not always be alleviated.

Therapeutic Plasma Exchange

Therapeutic plasma exchange, used to decrease the level of circulating antibodies to glomerular basement membrane, along with administration of pulse methylprednisolone, is used to alleviate hemoptysis.8,16,21 Patients have plasmapheresis daily for a total of 14 days or until antibodies to glomerular basement membrane are no longer detected.13 Therapeutic plasma exchange requires a large-bore dual-lumen catheter, and fluid replacement must be carefully monitored to prevent fluid overload and/or protein depletion. Hemodynamic monitoring is necessary to help determine and prevent decreased levels of circulating fluid.

Isotonic sodium chloride solution may be administered if signs or symptoms of rapid volume depletion occur during plasmapheresis.23 The amount of plasma exchanged is 50 mL/kg for a maximum exchange of 4 L/d.4 The plasma removed is replaced with a solution of 4% to 5% albumin, and fresh-frozen plasma may be given at the end of the exchange if active bleeding is present or the patient has undergone a recent biopsy.4 Once the hemoptysis stabilizes, renal dysfunction may progress and become the next challenge.

Immunosuppression and Pulse Methylprednisolone

Patients with rapidly progressive glomerulonephritis leading to acute renal failure are treated with therapeutic plasma exchange and immunosuppression, which are effective in 80% of cases.5,7 For immunosuppression, cyclophosphamide 40 to 50 mg/kg or 60 to 250 mg/m² is given intravenously in divided doses over 2 to 5 days and then orally in doses of 2 to 4 mg/kg per day.22,23 Cyclophosphamide is always given concurrently with therapeutic plasma exchange to prevent immunoglobulin rebound suppression.8 Other clinicians prefer to use pulse methylprednisolone. Controversy exists regarding the effectiveness of pulse methylprednisolone. Most clinicians agree that therapeutic plasma exchange stops pulmonary hemorrhage, although documentation is lacking.24 According to Salama et al,4 pulsed methylprednisolone is ineffective and is complicated by severe infections. However, Couser11 has determined that pulmonary hemorrhage responds to pulse methylprednisolone therapy. Couser11 prefers to use therapeutic plasma exchange in patients who have renal involvement.

Pulse methylprednisolone is usually given intravenously at a dose of 30 mg/kg every other day for a total of 3 doses.8,11 None of the 3 doses should exceed 3 g. and no diuretics may be given 3 hours before any dose.8 Once treatment with pulse methylprednisolone is complete, patients are started on oral doses of the drug of 1 mg/kg per day.11 Whether pulse or regular-dose methylprednisolone is used, corticosteroid therapy is beneficial for patients with Goodpasture syndrome. Immunosuppression therapy is adjusted according to the white blood cell count and is continued for 12 to 18 months after recovery from Goodpasture syndrome.16,20

For patients with severe renal impairment with a serum level of creatinine greater than 530 μmol/L (6 mg/dL.), long-term hemodialysis and kidney transplantation are indicated.4 Chronic renal failure is common in patients with Goodpasture syndrome who have a moderate reduction in glomerular filtration rate at the start of treatment.4

Conclusion

Caring for patients with Goodpasture syndrome is stressful because of the high rate of complications associated with the disease (Table 4).
Use of therapeutic plasma exchange, methylprednisolone, and cyclophosphamide and excellent critical care nursing can improve outcomes in patients who have the syndrome. Open communication between all members of the healthcare team and collaborative team management in the treatment regimen, along with careful consideration for the concerns of patients’ families, may alleviate some of the stressors associated with Goodpasture syndrome. Preparation for lifetime hemodialysis may be necessary, and associated lifestyle changes must be considered.

The prognosis for patients with Goodpasture syndrome has improved.
with the advent of plasmapheresis, but the possibility of infection related to the many invasive catheters and procedures and the use of immunosuppressive agents can cause adverse events. The benefits of these treatments certainly outweigh the associated risks. Careful monitoring and expert collaborative care is essential for the survival of these patients.

Case Study

A 55-year-old woman came to the emergency department because she had shortness of breath with hemoptysis. The hemoptysis had started 2 days earlier and was increasing in intensity. The patient did not smoke tobacco but was exposed to secondary smoke from her husband. She had allergies to ragweed and penicillin. While she was in the emergency department, severe hemoptysis with acute respiratory failure developed. She was intubated, treated with mechanical ventilation, typed and cross-matched for 2 units of blood, and transferred to the critical care unit. Results of arterial blood gas analysis were pH 7.33, PaO₂ 60 mm Hg, PaCO₂ 40 mm Hg, and bicarbonate 33 mmol/L, indicating partially compensated respiratory acidosis. The hematocrit was 0.21, and the hemoglobin level was 60 g/L. The platelet count was low at 100 × 10⁹/L. Prothrombin and partial thromboplastin times were normal. A chest radiograph showed right-sided alveolar shadowing. The serum concentration of potassium was 5.5 mmol/L, indicating slight hyperkalemia, and the total carbon dioxide content was 35 mmol/L. The serum level of urea nitrogen was elevated at 11.8 mmol/L (33 mg/dL), and the serum level of creatinine was 194 μmol/L (2.2 mg/dL).

Two large-bore 14-gauge intravenous catheters were inserted, one in each antecubital space, and 5 mg of midazolam (Versed) was administered as an intravenous bolus. Another 2 units of blood was transfused to alleviate the anemia. Frequent clearing of bloody secretions from the endotracheal tube was required. Ventilator settings included fraction of inspired oxygen 0.60, positive end-expiratory pressure 5 mm Hg, and respirations 16/min. An electrocardiogram revealed sinus tachycardia, and a noninvasive automatic cuff monitor indicated a blood pressure of 90/60 mm Hg. An arterial catheter was inserted to monitor blood pressure and to obtain samples for serial arterial blood gas analyses. The patient was typed and cross-matched for 2 more units of blood, and samples for arterial blood gas analysis were obtained.

Consent was obtained for bronchoscopy to determine the source of bleeding, and bronchial washings were sent to the laboratory for evaluation. The bronchial sample contained alveolar blood, numerous hemosiderin-laden macrophages, and a mild inflammatory infiltrate. Blood serum was sent for assay for antibodies to glomerular basement membrane, and treatment with levofloxacin 250 mg intravenously every 6 hours was started.

The pulmonologist suspected Goodpasture syndrome and consulted with the nephrologist. They agreed to perform a renal biopsy to confirm their suspicions. The renal biopsy revealed linear IgG deposits with crescent formation (Figure 2). The patient was started on daily plasmapheresis for an exchange of 1 L/d. In addition, methylprednisolone was given intravenously on odd days at a dose of 300 mg for 3 doses and then daily at a dose of 100 mg/d. Cyclophosphamide was given intravenously at a dose of 400 mg/d. The hemoptysis stopped on the patient’s second day in the critical care unit. The serum level of antibodies to glomerular basement membrane was 35 mg/dL.

On the third day in the critical care unit, the patients was weaned to

![Figure 2](http://ccn.aacnjournals.org/)

Figure 2 Renal biopsy specimens. Left, High-power view of a glomerulus shows a cellular crescent compressing the glomerular tuft and a small area of fibrinoid necrosis. Right, Strong linear staining is evident along the glomerular basement membrane.

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Immunology

a T-tube and a fraction of inspired oxygen of 0.45. During the plasmapheresis, severe hypotension developed, necessitating discontinuation of the treatment. The patient was given 2 L of isotonic sodium chloride solution. Her body temperature increased to 38.9°C rectally, and blood cultures were positive for Staphylococcus aureus. Treatment with intravenous vancomycin was at a dose of 1 g/12 h for 7 days was started.

Plasmapheresis was continued daily for a total exchange of 3 L. On day 6, the patient’s renal status deteriorated; the serum level of urea nitrogen was 23.2 mmol/L (65 mg/dL) and the serum level of creatinine was 389 μmol/L (4.4 mg/dL). Urinary output diminished to 60 mL in 8 hours. Central venous pressure was 16 mm Hg and pulmonary capillary wedge pressure was 8 mm Hg. Hemodialysis was started, and 1 L of fluid was removed during the first dialysis treatment. Central venous pressure after dialysis was 10 mm Hg with a pulmonary capillary wedge pressure of 6 mm Hg. The patient continued to require hemodialysis 3 d/wk in 4-hour increments, and her condition continued to improve. On day 10, her test for antibodies to glomerular basement membrane was negative, and her urea nitrogen and creatinine was 23.2 mmol/L (65 mg/dL), and she was transferred with dialysis, and she was started on a full liquid diet on day 11. On that time, her urine output was 2 L/d, her serum urea nitrogen was 6.1 mmol/L (17 mg/dL), and her serum creatinine was 80 μmol/L (0.9 mg/dL). At the time of discharge, she was taking oral methylprednisolone at 10 mg/d and oral cyclophosphamide at 100 mg twice daily. She did not require long-term hemodialysis and was to follow up with her primary care physician.

Acknowledgments

The insignificant characteristics of the case study have been changed for confidential reasons, and any resemblance to a real person is coincidental.

References

Goodpasture Syndrome
Laura Bergs

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