Wegener's Granulomatosis

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by Roxana Ursea, MD, Robert B. Nussenblatt, MD, and Ronald R. Buggage, MD
Laboratory of Immunology
National Eye Institute, National Institutes of Health
Bethesda, MD, USA

Introduction
Wegener's granulomatosis is an uncommon disease defined by inflammation of the blood vessels (vasculitis), kidneys (glomerulonephritis) and the upper and lower respiratory tract (sinuses, nose, trachea, and lungs). A characteristic feature of the inflammation in Wegener's granulomatosis is the presence of discrete groups of inflammatory cells called granulomas. Wegener's granulomatosis most commonly affects individuals in the 4^{th} or 5^{th} decade of life. The disease can, however, affect people at any age (age range: 5-91 years), with approximately 15% of cases beginning before 20 years of age. Wegener's granulomatosis strikes both men and women. It is most common in Caucasians (97%) and is rare in African Americans (2%).

History
In 1931, Heinz Klinger of the University of Berlin first reported two patients who died of inflammation of blood vessels (vasculitis) scattered throughout the body. Five years later, Friederic Wegener, a German pathologist from Breslau described three patients with necrotizing (a description of the microscopic appearance of dying tissue) granulomas involving both upper and lower respiratory tract. He was the first one to recognize this disorder as a distinct form of vasculitis. Other names used for Wegener's granulomatosis are Wegener's arteritis, Wegener's disease, or midline granulomatosis.

Course of Disease
Although Wegener's granulomatosis may involve other body systems, the classic features are vasculitis, glomerulonephritis and granulomas of the upper and lower respiratory tract. Ninety to 95% of patients have lung or sinus disease and involvement of the respiratory tract (sinuses, nose, trachea, and lungs) is the first sign of the disease in 90% of patients. Symptoms may include cough, sinus pain, coughing up blood (hemoptysis), chest discomfort, and pain on breathing. A common sign of the disease is an almost constant "runny nose" (rhinorrhea) or other cold symptoms that are not responsive to cold medicines. Rarely, a perforation (hole) may develop in the cartilage of the nose, which may lead to collapse or flattening of the nasal bridge (called a saddle-nose deformity). Eighty-five percent of patients with Wegener's granulomatosis suffer from kidney disease. Glomerulonephritis causes

blood (hematuria) and increased protein (proteinuria) in the urine which may change its color. Almost 50% of patients with Wegener's granulomatosis develop skin lesions that appear as small red or purple raised areas (rash), ulcers (sores) or bumps (nodules). Inadequate blood flow can lead to extreme cold sensitivity in the fingers and toes (Raynaud's phenomenon).

In some patients, the initial symptoms of Wegener's granulomatosis may include fever, fatigue, ill-feeling (malaise), loss of appetite (anorexia), weight loss, joint pain, and night sweats. Not all Wegener's patients experience all symptoms and the severity of the disease is different with each patient.

Eye symptoms may be the first manifestation in 16% of patients with Wegener's granulomatosis, while overall approximately half of patients will eventually develop eye involvement. A common eye problem in Wegener's granulomatosis is tearing due to closure of the passage between the eye and nose (nasolacrimal duct obstruction). Inflammation in the eye socket (orbit) can cause loss of vision, pain behind the eyes, double vision, bulging or protrusion of the eyes, or orbital bone erosion. Orbital involvement has been reported in 45-70% of patients. The cornea and sclera compose the outer wall of the eye and vision loss in patients with Wegener's granulomatosis may result from inflammation affecting the cornea (peripheral ulcerative keratitis) or sclera (scleritis). Other less common eye findings in Wegener's granulomatosis include uveitis, retinal vasculitis, optic neuropathy, restricted movement of the eye muscles and conjunctival scarring. Proptosis (a prominent or bulging eye) in the setting of upper and lower respiratory disease is highly suggestive of Wegener's.

Diagnosis and Testing

The diagnosis of Wegener's granulomatosis requires evidence of inflammation affecting the blood vessels, kidneys or respiratory tract. Because of its variable presentation, there is often a delay in the diagnosis of 1-2 years. Wegener's granulomatosis must be distinguished from other causes of vasculitis. A positive biopsy of an involved organ (for example sinus, kidney or lung) confirms the diagnosis of Wegner's granulomatosis. Lung tissue provides the highest likelihood of making the diagnosis, however, biopsy may not be practical in all patients because of the associated risks.

Laboratory tests can be helpful in making the diagnosis of Wegner's granulomatosis. The presence of anti-neutrophil cytoplasmic antibodies in a classic or cytoplasmic pattern (c-ANCA) is highly specific (90%) and sensitive (50% to 100%, depending on disease extent) for Wegener's granulomatosis. Urinalysis is often used as a screening test and to assess kidney function. A chest X-ray is important since the lungs are frequently involved. Definitive diagnosis requires a biopsy.

Treatment

The goal of therapy in patients with Wegener's granulomatosis is control of the inflammation in the affected part of the body. In most cases, treatment consists of a combination of corticosteroids (for example, prednisone) and another immunosuppressant medication such as cyclophosphamide, methotrexate or azathioprine. Using a regimen of high dose prednisone along with cyclophosphamide, more than 90% of patients improve and 75% achieve long-term remissions. Unfortunately, 50% of these patients subsequently relapse. Recurrences of Wegener's are usually responsive to the same treatment that induced remission, but sometimes additional medications are required.

Cause of Condition
The cause of Wegener's granulomatosis is unknown. Although the exact mechanism of the disease is unclear, the high occurrence of respiratory tract involvement suggests affected patients may have an abnormal immune response to inhaled substances.

Prognosis
Until the 1970's, Wegener's granulomatosis was nearly always fatal. Untreated, the prognosis is very poor, with a mean survival of only 5 months. With appropriate treatment, the outlook for patients with Wegener's granulomatosis is generally good. Treatment with prednisone and cyclophosphamide leads to improvement in 90% of patients, though even with treatment, up to 13% of patients may die.

Research and Future Outlook
Since the 1970's, physicians at National Institute of Health have been testing novel therapies for Wegener's granulomatosis. Use of the combination of steroids with cyclophosphamide for treatment was recommended based on this work. Despite the success of these medicines, all have potentially serious side effects and cannot be tolerated by everybody.

Significant advances in understanding Wegener's disease have occurred recently. In the next few years scientific breakthroughs may lead to the design of more specific ways to treat patients with this disease.

The National Institute of Allergy and Infectious Diseases (NIAID) is currently conducting several studies to investigate new treatments for Wegner's granulomatosis. Although there are specific inclusion criteria, these studies are open to patients with definitive diagnosis of Wegener's granulomatosis and those with active disease. The following studies are currently available:

1. Daclizumab to Treat Wegener's Granulomatosis
2. Etanercept for Wegener's Granulomatosis
3. Autologous Peripheral Blood Stem Cell Transplantation in Patients With Life Threatening Autoimmune Diseases
4. Analysis of Bronchial Tissue and Fluid in Patients with Wegener's Granulomatosis
5. Comparison of Treatments to Maintain Disease Remission in Patients with Wegener's Granulomatosis and Related Vasculitis Syndromes

Further information about these studies may be found at
http://www.niaid.nih.gov/dir/labs/lir/sneller.htm

For information on patient support groups contact:
Wegener's Granulomatosis Association International
P.O. Box 28660
Kansas City, MO 64188-8660
1-800-277-WGSG (1-800-277-9474)
http://www.wgassociation.org