

# Report

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## Your Question

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My daughter has had Wegeners Granulomatosis (Wegeners Disease) for 12 years and never has gone into remission. She takes Cytoxan and steroid to maintain the symptoms, but has had to have surgery on her sinuses, throat, nose and both eyes.

Can you tell me if there is any new research being done on new treatments or research going on for people who have not gone into remission with this disease. It is listed as a 'rare immune system disease' with NIH.

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## Lay Summary

Wegener's Granulomatosis is an autoimmune disease which is a large group of diseases thought to be caused by malfunction of the body's immune system. Its symptoms are similar to a number of diseases that are equally illusive in term of the cause and the development. The cause of Wegener' granulomatosis is still unknown. It mainly affects the blood vessels throughout the body particularly in the upper respiratory tract, the lung and the kidney. The current treatment strategy is to manipulate the immune system and to suppress the inflammation. Cytoxan is a drug normally used to treat cancer. It kills cancer cells but with many side effects. Cytoxan has also been used to treat Wegener's granulomatosis. Details of the possible side-effects are presented in the content of this report. This drug may also interact with a list of other medications that should be carefully watched when taken, or avoided. After an extensive search in the literature, no report of new treatment for this disease was found. In a research article, 11 Wegener's granulomatosis were found to improve in overall conditions when treated with antimicrobial treatment and this suggests the possibility of a microbial infection as the inciting cause of Wegener's granulomatosis in some patients.

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## Comprehensive report

Wegener's granulomatosis

Alternative names

Midline granulomatosis

## Definition

A rare disorder which causes inflammation of blood vessels (vasculitis) in the upper respiratory tract (nose, sinuses, ears), lungs, and kidneys. Many other areas of the body may also be affected, with arthritis (joint inflammation) occurring in almost half of all cases. The eyes and skin may also be affected.

## Causes and risks

The cause is unknown, but Wegener's Granulomatosis is thought to be an autoimmune disorder and is often classified as one of the rheumatic diseases. Destructive lesions develop in the upper and lower respiratory tract and the kidney. In the kidney, these lesions cause glomerulonephritis that may result in hematuria (blood in the urine) and kidney failure. It occurs most often between the ages of 30 to 50, and men are affected twice as often as women. It is rare in children, but has been seen in infants as young as 3 months old.

The kidney disease can progress rapidly, with kidney failure occurring within months of the initial diagnosis. If untreated, kidney failure and death occur in more than 90% of all patients with Wegener's granulomatosis.

## Prevention

No preventive measures are known.

## Symptoms

Early symptoms are often systemic and may include fatigue, malaise (an ill feeling), fever, and a sense of discomfort around the nose and sinuses. Upper respiratory infections such as sinusitis or ear infections frequently precede the diagnosis of Wegener's Granulomatosis. Other upper respiratory symptoms include nose bleeds, pain, and ulcers or sores around the opening of the nose.

Persistent fever without an obvious cause (fever of undetermined origin -- FUO) may be an initial symptom. Night sweats may accompany the fever. Anorexia and weight loss are common. Skin lesions are common, but there is no one characteristic lesion associated with the disease.

Kidney disease is necessary to make the definitive diagnosis of Wegener's Granulomatosis. The urine may be bloody, which often first appears as red or smoky urine. It may have no symptoms, however, it is readily diagnosed with laboratory studies. Eye problems develop in a significant number of patients and may range from a mild conjunctivitis to severe inflammation of the eyeball and the tissues around the eyeball. Additional symptoms include:

- weakness

- loss of appetite
- weight loss
- bloody discharge from the nose
- pain over the sinuses
- sinusitis
- lesions (ulcers, sores, and crusting) in and around opening of the nose
- cough
- coughing up blood
- bloody sputum
- shortness of breath
- wheezing
- chest pain
- blood in the urine
- rashes
- joint pains

### Signs and tests

- biopsy of abnormal tissue, which may include:
  - open lung biopsy
  - upper airway biopsy
  - nasal mucosal biopsy
  - bronchoscopy with transtracheal biopsy
- urinalysis, protein and blood in the urine (proteinuria and hematuria)
- chest X-ray (cavity formation, pulmonary infiltrates)
- bone marrow aspiration (may be done)
- blood tests to look for the presence of autoantibodies (antibodies that the body makes against its own tissue)

### Treatment

Treatment with corticosteroids, cyclophosphamide, methotrexate, or azathioprine produces long-term remission in over 90% of affected people.

### Support groups

Support groups with others who suffer from similar diseases may help patients and their families learn about their diseases and adjust to the changes associated with the treatment.

### Prognosis

With treatment, most people recover within months, although chronic renal failure may develop. Without treatment, the disease is usually fatal within a few months of diagnosis.

### Complications

- chronic renal failure
- hemoptysis (coughing up blood)
- respiratory failure
- inflammation of the eyes
- nasal septum perforation (hole)
- rash
- side effects of medications used to treat the disease

Note: Complications usually result from lack of treatment.

Call your health care provider if

Call your health care provider if chest pain, coughing up blood, blood in the urine, or other symptoms of this disorder are present.

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## More Detailed Information

Wegener granulomatosis is a necrotizing vasculitis characterized by the triad of (1) *acute necrotizing granulomas* of the upper respiratory tract (ear, nose, sinuses, throat), the lower respiratory tract (lung), or both; (2) *focal necrotizing or granulomatous vasculitis* affecting small to medium-sized vessels (e.g., capillaries, venules, arterioles, and arteries), most prominent in the lungs and upper airways but affecting other sites as well; and (3) renal disease in the form of focal or necrotizing, often crescentic, glomerulitis.<sup>[67]</sup> Some patients who do not manifest the full triad are said to have *limited* Wegener granulomatosis, in which the kidneys are unaffected and the involvement is restricted to the respiratory tract. Men are affected somewhat more often than women, at an average age of about 40 years.

Pathogenesis.

The striking resemblance to polyarteritis nodosa and serum sickness suggests that Wegener granulomatosis may represent some form of hypersensitivity, possibly to an inhaled infectious or other environmental agent, but this is unproved. Immune complexes have been seen in the glomeruli and vessel walls in occasional patients. The presence of granulomas and dramatic response to immunosuppressive therapy also strongly suggest an immunologic mechanism, perhaps of the cell-mediated type. c-ANCA are present in the serum in 90% of patients with active generalized disease, and this appears to be a good marker for disease activity. During treatment, a rising titer of c-ANCA suggests a relapse; most patients in remission have a negative test, or the titer falls significantly.

MORPHOLOGY.

Morphologically the upper respiratory tract lesions range from inflammatory sinusitis resulting from the development of mucosal granulomas to ulcerative lesions of the nose, palate, or pharynx, rimmed by necrotizing granulomas and accompanying vasculitis. In the lungs, dispersed focal necrotizing granulomas may coalesce to produce nodules that may undergo cavitation. Microscopically the granulomas reveal a geographic pattern of necrosis rimmed by lymphocytes, plasma cells, macrophages, and variable numbers of giant cells. In association with such lesions, there is a necrotizing or granulomatous vasculitis of small and sometimes larger arteries and veins. Almost identical with those of the acute phase of PAN, these lesions often contain granulomas, which may be within, adjacent to, or clearly separated from the vessel wall. These areas are generally surrounded by a zone of fibroblastic proliferation with giant cells and leukocytic infiltrate and may become cavitory creating a more than superficial resemblance to a tubercle. Thus, the major pathologic differential is mycobacterial or fungal infection. Lesions may ultimately undergo progressive fibrosis and organization.

The renal lesions are of two types.. In milder forms or early in the disease, there is acute focal proliferation and necrosis in the glomeruli, with thrombosis of isolated glomerular capillary loops (focal necrotizing glomerulonephritis). More advanced glomerular lesions are characterized by diffuse necrosis, proliferation, and crescent formation (crescentic glomerulonephritis). Patients with focal lesions may have only hematuria and proteinuria responsive to therapy, whereas those with diffuse disease can develop rapidly progressive renal failure.

#### Clinical Features.

The peak incidence is in the forties. Typical clinical features include persistent pneumonitis with bilateral nodular and cavitory infiltrates (95%), chronic sinusitis (90%), mucosal ulcerations of the nasopharynx (75%), and evidence of renal disease (80%). Other features include skin rashes, muscle pains, articular involvement, mononeuritis or polyneuritis, and fever. Untreated, the course of the disease is malignant; 80% of patients die within 1 year. When the diagnosis is established, appropriate therapy (i.e., immunosuppressive drugs, cyclophosphamide, possibly prednisone, and sometimes antibacterial drugs) produces a gratifying response in most patients, with only occasional relapses.

Sometimes difficult to differentiate from Wegener granulomatosis is a condition called *lymphomatoid granulomatosis*, characterized by pulmonary infiltration by nodules of lymphoid and plasmacytoid cells, often with cellular atypia. Although these infiltrates invade vessels, giving the histologic appearance of a vasculitis, they do not constitute a true vasculitis. About one third of patients eventually show similar lesions in the kidneys, liver, brain, and other organs. Lymphomatoid granulomatosis probably represents an evolving lymphoproliferative disorder because up to 50% develop a lymphoid malignancy, most commonly non-Hodgkin lymphoma.

*Goodpasture syndrome, microscopic polyarteritis and Wegener granulomatosis* are commonly associated with glomerular lesions, as described in the discussion of these diseases. Suffice it to say here that the glomerular lesions in these three conditions can be similar. In the early or mild forms of involvement, there is focal and segmental, sometimes necrotizing, glomerulonephritis, and most of these patients will have hematuria with mild decline in GFR. In the more severe cases associated with RPGN, there is also extensive necrosis, fibrin deposition, and the formation of epithelial crescents.

The above information is provided by: David A. Kaufman, M.D., Pulmonary & Critical Care Medicine, University of Pennsylvania Medical Center, Philadelphia, PA. Review provided by VeriMed Healthcare Network.

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## About Cytoxan

Other Names: Cyclophosphamide

Purpose:

Cytoxan is a drug used in the treatment of cancer. It interferes with the multiplication of cancer cells and slows or stops their growth and spread in the body.

Side Effects:

**Nausea & Vomiting:** You will be offered medication to help prevent these side effects. If this medication is not effective, notify the doctor or nurse. *See the handout on Nausea and Vomiting.*

**Decreased blood counts (Bone Marrow Depression):** Your bone marrow produces your blood cells. Cytoxan can lower the number of white blood cells which guard against infections and platelets which prevent bleeding. *See the handout on Bone Marrow Depression.*

**Hair Loss (Alopecia):** Temporary thinning or hair loss may occur. The hair will grow back.

**Irritation of the bladder:** Irritation of the bladder wall can be prevented by drinking large amounts of fluids after taking this drug (about three quarts a day for three days) and emptying your bladder about every three hours while taking the drug or for 24 hours after IV administration. If you notice any irritation or blood in your urine, report it to your

doctor or nurse.

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## Detailed Information About Cytosan (Cyclophosphamide)

### Cyclophosphamide (Systemic)

#### Brand Names

Some commonly used brand names are:

In the U.S.--

- Cytosan
- Neosar

In Canada--

- Cytosan
- Procytox

Generic name product may be available in the U.S.

#### Category

- Antineoplastic
- immunosuppressant

#### Description

Cyclophosphamide (syeh-kloeh-FOSS-fah-mide) belongs to the group of medicines called alkylating agents. It is used to treat cancer of the ovaries, breast, blood and lymph system, nerves (found primarily in children), retinoblastoma (a cancer of the eye found primarily in children), multiple myeloma (cancer in the bone marrow), and mycosis fungoides (tumors on the skin).

Cyclophosphamide is also used for treatment of some kinds of kidney disease.

Cyclophosphamide may also be used for other conditions as determined by your doctor.

Cyclophosphamide interferes with the growth of cancer cells, which are eventually destroyed. Since the growth of normal body cells may also be affected by cyclophosphamide, other effects will also occur. Some of these may be serious and must be reported to your doctor. Other effects, like hair loss, may not be serious but may cause concern. Some effects may not occur for months or years after the medicine is used.

Before you begin treatment with cyclophosphamide, you and your doctor should talk about the good this medicine will do as well as the risks of using it.

Cyclophosphamide is available only with your doctor's prescription, in the following dosage forms:

*Oral*

- Oral solution (U.S. and Canada)
- Tablets (U.S. and Canada)

*Parenteral*

- Injection (U.S. and Canada)

## Before Using This Medicine

In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For cyclophosphamide, the following should be considered:

**Allergies**--Tell your doctor if you have ever had any unusual or allergic reaction to cyclophosphamide.

**Pregnancy**--This medicine may cause several different birth defects if either the male or female is taking it at the time of conception or if it is taken during pregnancy. In addition, many cancer medicines may cause sterility. Although sterility occurs commonly with cyclophosphamide, it is usually only temporary.

Be sure that you have discussed this with your doctor before taking this medicine. It is best to use some kind of birth control while you are taking cyclophosphamide. Tell your doctor right away if you think you have become pregnant while taking cyclophosphamide.

**Breast-feeding**--Cyclophosphamide passes into the breast milk. Because this medicine may cause serious side effects, breast-feeding is generally not recommended while you are taking it.

Children--This medicine has been tested in children and has not been shown to cause different side effects or problems than it does in adults.

Older adults--Many medicines have not been studied specifically in older people. Therefore, it may not be known whether they work exactly the same way they do in younger adults. Although there is no specific information comparing use of cyclophosphamide in the elderly with use in other age groups, it is not expected to cause different side effects or problems in older people than it does in younger adults.

Other medicines--Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When you are taking or receiving cyclophosphamide, it is especially important that your health care professional know if you are taking any of the following:

- Amphotericin B by injection (e.g., Fungizone) or
- Antithyroid agents (medicine for overactive thyroid) or
- Chloramphenicol (e.g., Chloromycetin) or
- Colchicine or
- Flucytosine (e.g., Ancobon) or
- Ganciclovir (e.g., Cytovene) or
- Interferon (e.g., Intron A, Roferon-A) or
- Methotrexate or
- Plicamycin (e.g., Mithracin) or
- Zidovudine (e.g., AZT, Retrovir) or
- If you have ever been treated with radiation or cancer medicines--  
Cyclophosphamide may increase the effects of these medicines or radiation therapy on the blood
  
- Cocaine--Cyclophosphamide may increase the effects and toxicity of this medicine
  
- Cytarabine--Cyclophosphamide may increase the effects of this medicine on the heart and blood
  
- Azathioprine (e.g., Imuran) or
- Chlorambucil (e.g., Leukeran) or
- Corticosteroids (cortisone-like medicine) or
- Cyclosporine (e.g., Sandimmune) or
- Mercaptopurine (e.g., Purinethol) or
- Muromonab-CD3 (monoclonal antibody) (e.g., Orthoclone OKT3)--There may be an increased risk of infection and development of cancer because cyclophosphamide reduces the body's ability to fight them
  
- Probenecid (e.g., Benemid) or

- Sulfinpyrazone (e.g., Anturane)--Cyclophosphamide may increase the amount of uric acid in the blood. Since these medicines are used to lower uric acid levels, they may not work as well in patients taking cyclophosphamide

Other medical problems--The presence of other medical problems may affect the use of cyclophosphamide. Make sure you tell your doctor if you have any other medical problems, especially:

- Chickenpox (including recent exposure) or
- Herpes zoster (shingles)--Risk of severe disease affecting other parts of the body
- Gout (history of) or
- Kidney stones (history of)--Cyclophosphamide may increase levels of uric acid in the body, which can cause gout or kidney stones
- Infection--Cyclophosphamide can decrease your body's ability to fight infection
- Kidney disease--Effects of cyclophosphamide may be increased because of slower removal from the body
- Liver disease--The effect of cyclophosphamide may be decreased
- Prior removal of adrenal gland(s)--Toxic effects of cyclophosphamide may be increased, dosage adjustment may be necessary
- Tumor cell accumulation--Increased risk of tumor cells entering the bone marrow, due to bone marrow depression from high doses of cyclophosphamide

## Proper Use of This Medicine

*Take this medicine only as directed by your doctor.* Do not take more or less of it, and do not take it more often than your doctor ordered. The exact amount of medicine you need has been carefully worked out. Taking too much may increase the chance of side effects, while taking too little may not improve your condition.

Cyclophosphamide is sometimes given together with certain other medicines. If you are using a combination of medicines, make sure that you take each one at the proper time and do not mix them. Ask your health care professional to help you plan a way to remember to take your medicines at the right times.

*While you are using cyclophosphamide, it is important that you drink extra fluids so that you will pass more urine.* Also, empty your bladder frequently, including at least once during the night. This will help prevent kidney and bladder problems and keep your kidneys working well. Cyclophosphamide passes from the body in the urine. If too much

of it appears in the urine or if the urine stays in the bladder too long, it can cause dangerous irritation. *Follow your doctor's instructions carefully about how much fluid to drink every day* . Some patients may have to drink up to 7 to 12 cups (3 quarts) of fluid a day.

Usually it is best to take cyclophosphamide first thing in the morning, to reduce the risk of bladder problems. However, your doctor may want you to take it with food in smaller doses over the day, to lessen stomach upset or help the medicine work better. Follow your doctor's instructions carefully about when to take cyclophosphamide.

Cyclophosphamide often causes nausea, vomiting, and loss of appetite. However, it is very important that you continue to use the medicine even if you begin to feel ill. *Do not stop taking this medicine without first checking with your doctor* . Ask your health care professional for ways to lessen these effects.

If you vomit shortly after taking a dose of cyclophosphamide, check with your doctor. You will be told whether to take the dose again or to wait until the next scheduled dose.

Dosing--The dose of cyclophosphamide will be different for different patients. The dose that is used may depend on a number of things, including what the medicine is being used for, the patient's weight, whether the medicine is being given by mouth or by injection, and whether or not other medicines are also being taken. *If you are taking or receiving cyclophosphamide at home, follow your doctor's orders or the directions on the label* . If you have any questions about the proper dose of cyclophosphamide, ask your doctor.

Missed dose--If you miss a dose of this medicine, do not take the missed dose at all and do not double the next one. Instead, go back to your regular dosing schedule and check with your doctor.

Storage--To store this medicine:

- Keep out of the reach of children.
- Store away from heat and direct light.
- Do not store in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down.
- Store the oral solution form of this medicine in the refrigerator. Keep it from freezing.
- Do not keep outdated medicine or medicine no longer needed. Be sure that any discarded medicine is out of the reach of children.

## Precautions While Using This Medicine

*It is very important that your doctor check your progress at regular visits to make sure that this medicine is working properly and to check for unwanted effects.*

While you are being treated with cyclophosphamide, and after you stop treatment with it, *do not have any immunizations (vaccinations) without your doctor's approval* . Cyclophosphamide may lower your body's resistance and there is a chance you might get the infection the immunization is meant to prevent. In addition, other persons living in your house should not take oral polio vaccine since there is a chance they could pass the polio virus on to you. Also, avoid persons who have recently taken oral polio vaccine within the last several months. Do not get close to them, and do not stay in the same room with them for very long. If you cannot take these precautions, you should consider wearing a protective face mask that covers the nose and mouth.

Before having any kind of surgery, including dental surgery, or emergency treatment, make sure the medical doctor or dentist in charge knows that you are taking this medicine, especially if you have taken it within the last 10 days.

Cyclophosphamide can temporarily lower the number of white blood cells in your blood, increasing the chance of getting an infection. It can also lower the number of platelets, which are necessary for proper blood clotting. If this occurs, there are certain precautions you can take, especially when your blood count is low, to reduce the risk of infection or bleeding:

- If you can, avoid people with infections. *Check with your doctor immediately* if you think you are getting an infection or if you get a fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination.
- *Check with your doctor immediately* if you notice any unusual bleeding or bruising; black, tarry stools; blood in urine or stools; or pinpoint red spots on your skin.
- Be careful when using a regular toothbrush, dental floss, or toothpick. Your medical doctor, dentist, or nurse may recommend other ways to clean your teeth and gums. Check with your medical doctor before having any dental work done.
- Do not touch your eyes or the inside of your nose unless you have just washed your hands and have not touched anything else in the meantime.
- Be careful not to cut yourself when you are using sharp objects such as a safety razor or fingernail or toenail cutters.
- Avoid contact sports or other situations where bruising or injury could occur.

Before you have any medical tests, tell the medical doctor in charge that you are taking this medicine. The results of some tests may be affected by this medicine.

## Side Effects of This Medicine

Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

Also, because of the way these medicines act on the body, there is a chance that they might cause other unwanted effects that may not occur until months or years after the medicine is used. These may include certain types of cancer, such as leukemia or bladder cancer. Discuss these possible effects with your doctor.

*Check with your doctor or nurse immediately* if any of the following side effects occur:

*More common*

Cough or hoarseness; fever or chills; lower back or side pain; missing menstrual periods; painful or difficult urination

*With high doses and/or long-term treatment*

Blood in urine; dizziness, confusion, or agitation; fast heartbeat; joint pain; shortness of breath; swelling of feet or lower legs; unusual tiredness or weakness

*Less common*

Black, tarry stools or blood in stools; pinpoint red spots on skin; unusual bleeding or bruising

*Rare*

Frequent urination; redness, swelling, or pain at site of injection; sores in mouth and on lips; sudden shortness of breath; unusual thirst; yellow eyes or skin

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. Also, your health care professional may be able to tell you about ways to prevent or reduce some of these side effects. Check with your health care professional if any of the following side effects continue or are bothersome or if you have any questions about them:

*More common*

Darkening of skin and fingernails; loss of appetite; nausea or vomiting

*Less common*

Diarrhea or stomach pain; flushing or redness of face; headache; increased sweating; skin rash, hives, or itching; swollen lips

Cyclophosphamide may cause a temporary loss of hair in some people. After treatment has ended, normal hair growth should return, although the new hair may be a slightly different color or texture.

After you stop using cyclophosphamide, it may still produce some side effects that need attention. During this period of time, *check with your doctor immediately* if you notice the following side effect:

Blood in urine

Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

## Additional Information

Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. Although these uses are not included in product labeling, cyclophosphamide is used in certain patients with the following medical conditions:

- Cancer of the bladder
- Cancer in the bones
- Cancer of the cervix
- Cancer of the endometrium
- Cancers of the lungs
- Cancer of the prostate
- Cancer of the testicles
- Cancer of the adrenal cortex (the outside layer of the adrenal gland)
- Ewing's sarcoma (a certain type of bone cancer)
- Germ cell tumors in the ovaries (a cancer in the egg-making cells in the ovary)
- Gestational trophoblastic tumors (a certain type of tumor in the uterus/womb)
- Soft tissue sarcomas (a cancer of the muscles, tendons, vessels that carry blood or lymph, joints, and fat)
- Thymoma (a cancer in the thymus, a small organ beneath the breastbone)
- Tumors in the brain
- Waldenström's macroglobulinemia (a certain type of cancer of the blood)
- Wilms' tumor (a cancer of the kidney found primarily in children)
- Histiocytosis X (a certain type of cancer found primarily in children)
- Organ transplant rejection (prevention)
- Rheumatoid arthritis
- Wegener's granulomatosis
- Systemic lupus erythematosus
- Systemic dermatomyositis or
- Multiple sclerosis (a disease of the nervous system)

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## Research data related to your question

Nasal cavity squamous cell carcinoma in Wegener's granulomatosis.

Stein J, Sridharan ST, Eliachar I, Niv A, Wood B, Hoffman GS.

Department of Otolaryngology and Communicative Disorders, Desk A71, The Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195, USA.

Wegener's granulomatosis is a chronic debilitating disease with multiple organ system involvement, variable course, and myriad complications that cause morbidity and mortality. We report 2 cases of nasal cavity squamous cell carcinoma occurring in long-standing Wegener's granulomatosis.

Squamous cell carcinoma of the nasal septum with Wegener's granulomatosis treated with cyclophosphamide and corticosteroids.

Wakisaka N, Tanaka S, Nagayama I, Furukawa M.

Department of Otolaryngology, School of Medicine, Kanazawa University, Japan.

Well differentiated squamous cell carcinoma of the nasal septum developed in a 55-year old man with Wegener's granulomatosis. It is suggested that the malignancy was induced by immunosuppressive state from an increased and prolonged use of cyclophosphamide and corticosteroids. Although the efficacy of the therapeutic concept using cyclophosphamide and corticosteroids is well established, there have been some few reports that cyclophosphamide could be implicated in the genesis of malignancies. The pathophysiology of Wegener's granulomatosis should be better understood, and effective and less toxic alternative protocol should be established.

J Pediatr 1993 Jan;122(1):26-31

Wegener granulomatosis in children and adolescents: clinical presentation and outcome.

Rottem M, Fauci AS, Hallahan CW, Kerr GS, Lebovics R, Leavitt RY, Hoffman GS.

Laboratory of Clinical Investigation, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland 20892.

We prospectively studied and compared clinical features, treatment, course of illness, and long-term morbidity and mortality rates for Wegener granulomatosis in 23 childhood-

onset patients with those of 135 adult-onset patients who were studied concurrently. Treatment was usually provided with glucocorticoids and cyclophosphamide. The mean follow-up period was 8.7 years for childhood-onset and 7.6 years for adult-onset Wegener granulomatosis. Most aspects of Wegener granulomatosis were similar in childhood-onset and adult-onset patients. Permanent morbidity from disease occurred in 86% of both groups. However, some features were significantly different. Wegener granulomatosis in childhood-onset patients was complicated five times more often by subglottic stenosis and twice as often by nasal deformity. Treatment-related permanent morbidity occurred in 22% of childhood-onset patients and 45% of adult-onset patients. After similar periods of cyclophosphamide therapy and follow-up, cyclophosphamide-related malignancies were less likely (0% vs 11%) to have developed in childhood-onset patients. Although 89% of patients treated with glucocorticoids and cyclophosphamide had remission, prolonged delay in achieving remission and relapses led in both patient groups to freedom from active disease for approximately 50% of the total patient-years. As a result, morbidity was substantial and has led to comparative studies of alternative therapies.

J Reprod Med 1991 Jun;36(6):463-6

Wegener's granulomatosis complicated by pregnancy. A case report.

Fields CL, Ossorio MA, Roy TM, Bunke CM.

Division of Respiratory and Environmental Medicine, University of Louisville School of Medicine, Kentucky 40292.

A 23-year-old woman who presented in the 17th week of her third intrauterine pregnancy was diagnosed as having active Wegener's granulomatosis. Therapy, consisting of corticosteroids, cyclophosphamide and hemodialysis, was instituted and maintained until delivery. Although Wegener's granulomatosis complicated by pregnancy has been reported previously, this is the first reported patient to be treated successfully with the above agents during the second and third trimesters without apparent harm to her or her infant

Mayo Clin Proc 1985 Jan;60(1):27-32

Wegener's granulomatosis: observations on treatment with antimicrobial agents.

DeRemee RA, McDonald TJ, Weiland LH.

Twelve patients with Wegener's granulomatosis were treated with antimicrobial agents, chiefly trimethoprim-sulfamethoxazole. The clinical course improved in 11 of the 12 patients who received this treatment. The success of antimicrobial treatment suggests the possibility of a microbial infection as the inciting cause of Wegener's granulomatosis in

some patients. Alternatively, these agents--in particular, trimethoprim-sulfamethoxazole--may possess immunosuppressant activity.

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