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Pemphigus & Pemphigoid Patient Guide

Discovering you have a disease of any kind can be devastating to say the least. The news alone may spur more problems than the disease itself, like depression, stress, and restlessness. Being diagnosed with pemphigus or pemphigoid may also cause anger, confusion, and fear with some patients. The process of understanding the diseases and treatments; changing how you eat, live, and sleep; and incorporating change and acceptance into your personal and professional life may be overwhelming. This is more difficult when you feel fine one day, then hopeless the next. Added to the emotional distress is a fear of taking medication you have never heard of, and being observed by family, friends, and physicians for any changes can be frightening.

As a newly diagnosed patient, you are probably asking questions like, “What is Pemphigus or Pemphigoid?”, “What did I do to cause this?”, or “What can I do to cure it?”

The International Pemphigus & Pemphigoid Foundation can help you address these questions with the help of this Patient Guide. This guide will help you understand the illness, treatments available and important information that can make living with the disease a little more bearable. Coupled with the experience and compassion of our Peer Health Coaches and Caregivers, patients eventually realize these diseases may be rare, but they are never alone.

If you have any questions or comments, please contact me at (855) 4PEMPHIGUS.

Marc Yale
Executive Director
International Pemphigus & Pemphigoid Foundation

DISCLAIMER: The IPPF does not endorse any drugs, treatments, or products in this guide. Information is provided for informational purposes only. Because the symptoms and severity of pemphigus and pemphigoid vary among individuals, we recommend all drugs and treatments be discussed with the reader’s physician(s) for proper evaluation, treatment, and care.

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Basic Information

Pemphigus and Pemhigoid are rare autoimmune blistering diseases of the skin and/or mucous membranes. There is currently no cure for pemphigus or pemphigoid, only remission.

“Pemphigus” is used in a very specific way to describe blistering disorders caused by autoantibodies against some part of the epidermis, which lead to disruption of the intercellular junctions (and hence bullae).

Men and women are equally affected.

The patient’s immune system makes antibodies, which attack viruses and harmful bacteria. With pemphigus, antibodies instead attack healthy cells in the skin or mucous membranes. As a result,

- Skin cells separate from each other
- Fluid collects between skin layers
- Blisters form and may cover a large area of skin

It is known to affect people across racial and cultural lines. However, there are certain groups of people (Ashkenazi Jews, people of Mediterranean, North Indian and Persian decent) who have a higher incidence of the disease. Pemphigus and pemphigoid are not genetic though there can be a genetic predisposition to develop pemphigus, there is no indication that the disease is hereditary so it's not possible to predict who may get pemphigus.

The disease is now rarely fatal, and the majority of deaths occur from infections.

For most patients with pemphigus, the disease can be controlled with corticosteroids and other medications, these medications can eventually be completely discontinued. High-dose oral corticosteroids, such as prednisone or prednisolone, are the main treatment for pemphigus.

All forms of pemphigus are characterized by the development of blistering eruptions on the outer layer of the skin (epidermis). Mucous membranes are the thin, moist coverings of many of the body's internal surfaces. If left untreated, pemphigus will usually be fatal.

Pemphigus and pemphigoid are NOT contagious.
Not by blood.
Not by fluids.
Not by anything.

Pemphigus Types

Pemphigus Vulgaris (PV)

Most common of types. Blisters are soft and fragile and may form at the mouth first and then spread to the skin and even the genitals. Blisters are frequently painful but not itchy, and in the mouth make chewing and swallowing difficult. PV does not cause permanent scarring unless there is an infection associated with the sore.

Pemphigus Foliaceus (PF)

Less severe type. Blisters may form on the scalp and face first and then spread to the

chest and back. Blisters do not occur in the mouth. Blisters are not usually painful and are superficial and form crusts.

Pemphigus Vegetans

Thicker sores mainly in groin and under arms.

IgA Pemphigus

Caused by the IgA (an antibody) binding to the epidermal cells. May resemble pemphigus foliaceus or may appear as small pustules.

Paraneoplastic Pemphigus (PNP)

Associated with certain forms of cancer. Blisters form inside the mouth and may affect the lungs, leading to a fatal outcome. Sores of the mouth, lips and esophagus are almost always present; and skin lesions of different types occur. PNP can affect the lungs. In some cases, the diagnosis of the disease will prompt doctors to search for a hidden tumor. In some cases the tumor will be benign and the disease will improve if the tumor is surgically removed.

Benign familial pemphigus, also known as Hailey-Hailey disease is NOT an autoimmune disease. Hailey-Hailey is a genetic form of pemphigus.

Pemphigoid Types

Mucous Membrane Pemphigoid (MMP)

Affects the eyes, mouth, and throat. A clinical form called ocular cicatricial pemphigoid (OCP) can result in blindness if it involves the eyes and respiratory compromise if it involves the deeper parts of the throat.

Bullous Pemphigoid (BP)

Limited to the skin with blisters presenting predominantly on the abdomen, groin, back, arms and legs. The blisters may itch and be painful.

Gestational Pemphigoid (GP)

Blistering rash starting around the naval and spreading to the entire body, typically in the second trimester.

Epidermolysis Bullosa Acquisita

Blistering rash on the skin without involvement of mucosal surfaces. Blisters are usually smaller than in pemphigoid.

Pemphigoid vs. Pemphigus

Pemphigoid affects a lower layer of the skin, between the epidermis and the dermis, creating tense blisters that do not break easily while Pemphigus affects the upper layer within the epidermis and causes lesions and blisters that are easily ruptured. Sometimes pemphigoid may look like hives or eczema and not have blisters.

Diagnosis

Pemphigus and pemphigoid are diagnosed through special testing.

Clinical Presentation — visual examination of skin lesions

Lesion Biopsy — a sample of the blistered skin is removed and examined under the microscope. Additionally, the layer of skin in which cell-to-cell separation occurs can be determined.

Direct Immunofluorescence — the skin sample is treated to detect desmoglein antibodies in the skin. The presence of these antibodies indicates pemphigus.

Indirect Immunofluorescence or Antibody Titer Test — this measures desmoglein autoantibodies in the blood serum. It may be used to obtain a more complete understanding of the course of the disease.

ELISA — a serum assay for desmoglein antibodies, known as ELISA, is also available. Although in many cases there is a correlation between ELISA and disease activity it is not so in every case.

Treatments

Corticosteroids

Prompt and sufficient doses of corticosteroids, usually prednisone or prednisolone, are required to bring pemphigus under control. Once controlled, the steroid is reduced slowly to minimize side effects. Some patients then go into remission; however, many need a small maintenance dose to keep the disease under control.

Topical steroids can be used for the treatment of pemphigus. In mild cases, a single application of potent topical steroid can control the lesion. Regarding oral erosion, steroid mouthwash, paste, ointment or aerosol is used. Topical cyclosporine can also be used for the treatment of oral pemphigus lesions.

Anti-inflammatory agents

Anti-inflammatory agents such as dapsone and tetracyclines are used as they also may have a steroid sparing effect in mild to moderate disease (e), often in patients who are in maintenance phase but corticosteroid-dependent. Dapsone is a first-line treatment in dermatitis herpetiformis, linear IgA disease, and milder cases of pemphigus foliaceus:

Dapsone

Dapsone must be started after glucose-6-P-dehydrogenase screening and is administered as 7.5mg/kg/day, up to 200mg/day.

- Topical corticosteroids (high potency) are commonly used for management of lesions.
- Coping with erosions and the pain of the erosions.
- In an open prospective study of 18 cases, low-dose methotrexate was shown to be effective for maintenance of clinical remission induced by initial short-term use of potent topical steroids;

- Considering that the prognosis of untreated BP is better than that of pemphigus, side effects of treatmentare of greater concern.
- Two small studies of severe ocular mucous membrane pemphigoid suggest that this condition responds more favorably to treatment with cyclophosphamide combined with prednisone, whereas dapsone suppresses some cases of mild to moderate disease.

Tetracycline antibiotics

Tetracycline, doxycycline and minocycline have been used by some in glucocorticoid-dependent patients in the maintenance phase of therapy, often with niacinamide (nicotinamide). It is administered as tetracycline 2g/day and niacinamide 1.5g/day (in divided doses, or minocycline 100mg twice daily) and niacinamide 1.5g/day (in divided doses.

Oral

For multiple oral erosions, 'corticosteroid mouthwashes are practical, for example, soluble betamethasone sodium phosphate 0.5 mg tablet dissolved in 10 mL water may be used up to four times daily, holding the solution in the mouth for about 5 min. Isolated oral erosions could be treated with application of triamcinolone acetonide 0.1% in adhesive paste or clobetasol 0.05% gel. Topical cyclosporine (100 mg/ m1) in oral pemphigus has been described and may be of some benefit but is expensive (qq).

Immunosuppressants – these work by suppressing the immune system.

Azathioprine (Imuran®, Azasan®)

Mycophenolate (CellCept®, Myfortic®)

Cyclophosphamide (Cytoxan®)

Cyclosporine (Gengraf®, Neoral®, Sandimmune® Capsules, Sandimmune® Oral Solution)

For more information, visit the manufacturer website or contact the office.

Additional Treatments

Rituximab (Rituxan®) - Rituximab is an immunosuppressant since it destroys B-cells that have CD20 on their surfaces, so it has been used to treat diseases in which the B-cells of the immune system have gone awry, as in several autoimmune diseases. CD20 is a B-lymphocyte antigen and it dictates how the antibodies respond to T-independent antigen.

IVIG

Intravenous Immunoglobulin (IVIG) therapy is prepared from extracting the plasma in human blood. IVIG is given intravenously, directly into the veins. The dose depends on

what the IVIG is being given for and is also based on body weight. To treat pemphigus, the doses are as high as 2000mg/kg. Because the doses are higher, they are divided into infusions that are given over the course of up to five days, and they can be consecutive or nonconsecutive days. IVIG has a half-life that is on average 30 days, depending on the brand and the person. Many times this regimen is indefinite or even life time. In other cases, the condition resolves and the IVIG can be discontinued.

Side Effects & Precautions

It is very important to make certain that all physicians, doctors, and specialists involved with a treatment regimen are in contact with one another to avoid conflicting medications and to be sure that each doctor's treatments are working in harmony with the others. Also, all lab test results should automatically be given to all physicians on a particular case.

Prednisone

Potential side effects may include:

- Headaches
- Nausea
- Stomach aches
- High blood pressure
- Stroke
- Emotional difficulties or mood swings
- Weight gain

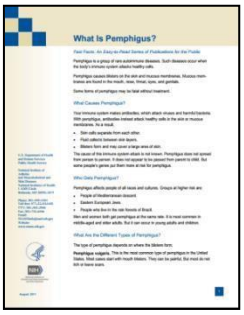
Type 2 Diabetes (steroid-induced diabetes) is a common side effect of prednisone and creates a need for a modified diet. Generally, this type of diabetes will diminish as the dosage of prednisone is reduced and goes away when prednisone is stopped.

Another commonly reported side effect of prednisone is weight gain. A high protein, low carbohydrate, low fat diet, as well as a regular exercise program is recommended for those taking prednisone.

Osteoporosis, glaucoma, and cataracts are also known side effects of prednisone. Regular checkups with your health care providers will enable most patients on prednisone to effectively counter these side effects with appropriate therapies and attention.

TIP!

It is recommended that everyone get a bone density test when they first start taking prednisone as a baseline for bone density loss. *See Bone Mass Measurement: What the Numbers Mean included in the toolkit. (http://www.niams.nih.gov/Health_Info/Bone/Bone_Health/bone_mass_measure.asp)*



IVIG

Side effects are manageable and may include:

- Headache
- Fever
- Fatigue
- Chills
- Flushing
- Dizziness
- Urticaria
- Chest Tightness
- Nausea and Vomiting
- Muscle cramping
- Blood pressure changes

In general, IVIG is considered to be safe, and the majority of people tolerate it without problems. The adverse reactions occur only in less than 1% of patients. Patients with pemphigus and pemphigoid who suffer from side effects of steroid therapy have a higher risk. Most of the side effects occur because it's administered too quickly. Because of this, it is gradually infused, starting at a very low rate and increased at intervals until the maximum rate is reached.

Rituximab

Rituximab is increasingly used in patients with pemphigus vulgaris (PV) who are non-responders to conventional therapy.

Side effects include feeling:

- Dizzy
- Weak
- Nauseated
- Light-headed
- Itchy

Or if you have a fever:

- Chills
- Muscle pain
- Sneezing
- Sore throat
- Trouble breathing
- Pain in chest or shoulders

Infusion reactions often occur within the first 24 hours after first rituximab infusion.

Other Complications

Before the disease is controlled, you might experience difficulty in:

- Getting information that you want.
- Coping with the high drug doses that you will need in the initial stages of treatment.
- Coping with frequent outpatient visits
- Coping with the erosions themselves and the pain of the erosions.

The exact cause of pemphigus is unknown.

You might also find that you are misdiagnosed in the early stages because PV is a rare disease.

Once the disease is controlled, you might encounter difficulty in:

- Coping with relapses and flare-ups.
- Living with pain and minor lesion activity.
- Itching and burning of skin erosions.
- Coping with the side effects of drug treatments, especially prednisolone and other immunosuppressive drugs. This can range from feeling mildly ill a lot of the time to high levels of disability.
- Coping with other reported effects like muscle pain, insomnia, exhaustion or nausea.

Some patients find that once PV is controlled, their lives are not changed too much. Others find the disease impacts their lives in many different ways, for example:

- Financial problems at a time of increased financial needs (for prescriptions, special dressings and creams, special liquidized food etc.) These problems can be caused by:
    - Having to stop work, sometimes permanently, or move into part-time work.
    - Difficulties in obtaining Incapacity Benefit and/or Disability Living Allowance.
- Slowing down, limiting what they do, and keeping 'low-key' to conserve limited energy.
- Managing the social effects of PV's unpredictability (flare-ups and 'bad' days), for example having to cancel a prearranged social event at the last minute.
- The disfiguring effects of the disease: weight gain (from steroids); visible erosions on the skin that may leave discolored marks that patients often think of as scars.

Nutrition

Many nutrition concerns arise from prednisone. In order to control an outbreak of pemphigus, a prompt response with a large dose of prednisone is generally prescribed.

Use of this drug requires a diet high in protein, low in carbohydrates, low in salt, low in fat, with special attention paid to calcium and potassium levels.

Calcium with vitamin D supplements is routinely ordered.

Acidophilus, beneficial bacteria found in yogurt, as well as in dietary supplements, is recommended for those who frequently use antibiotics. It also may help prevent yeast infections.

It has been documented that some patients have sensitivity to garlic, onions and leeks (the Allium food group). These foods and possibly others may trigger or worsen flair-ups.

If you suspect that eating certain foods causes blisters, then try it a second time, and if it happens again, eliminate that food from your diet. Be sure to discuss your present diet, medications, and lifestyle with your physician and/or dietician before making changes to your diet.

Nobody should avoid these foods, but consideration can be given on a case by case basis, as some patients report exacerbation of disease by certain food groups containing one or more of four ingredients: thiol, isothiocyanates, phenols or tannins.

- **Thiols:** garlic and other members of the Allium group that contain plants such as onion, shallot, chive and leek.
- **Isothiocyanates** (mustard oils): are found in 3,200 species of plants including mustard, horseradish, winter cress, turnip, broccoli, radish, cabbage, brussel sprouts and cauliflower.
- **Phenols**: Urushiol can cause contact dermatitis and is most notably found in poison ivy, poison oak and poison sumac that are related to mango, pistachio and cashew. The artificial sweetener aspartame is phenolic and common in many food additives. Phenol is in cinnamon and cinnamic acid, and pinene. It is in tomatoes, potatoes, mangos, bananas and milk and milk products produced when cows consume phenol laced feed such as cottonseed.
- **Tannins**: Common sources of tannin are kola nuts, tea, coffee, raspberry, cherry, cranberry, blackberry, avocado, banana, apple, mango, pear, eggplant and grape skins, coffee and cocoa seeds, ginger, ginseng, garlic, rosemary, and arrowroot.

Patient Tips

Let your doctor know if some new symptom is occurring, doctors can't read minds. People with chronic illness often feel that their doctors are going to think they are chronic complainers if they are honest about how they are feeling. They may worry that their doctors will simply give them more prescriptions, adding to the many medications they are already taking. Another fear patients may have is that if they complain too much, their doctors may not want them as patients. It is much better to discuss what is going on and how it might be treated than to worry about what the doctor will think. The doctor may have the information you need, you just need to ask.

You can expect to have a variety of emotional responses. Typically, newly diagnosed patients feel the "anger, denial, bargaining, depression and acceptance" cycle identified by Kubler-Ross as a response to coping with a significant loss and major life changes. You may feel isolated from others and experience fear of the unknown future.

Understanding these responses and their causes will help you determine what works best for you in overcoming them. Be open and forthright with those around you. It is important that you do not blame everything that goes wrong on your illness.

Joining a support group for persons with chronic illness is very helpful to many patients. Professional counseling may be in order if you are unable to cope in spite of every effort to do so.

Understand that you did nothing to cause your illness and that life is not always fair. Bad things do happen to almost everyone at some time in a lifetime. It is how we deal with these life changes that makes the difference between a life of coping and a life of moping.

Dealing with the emotional aspect of having a chronic illness is a challenge. Often the unpredictability of a serious illness makes you feel out of control of your life and well-being. This can cause anxiety for both you and your family.

If you believe stress is related to increased incidence of lesions, it is wise to address and resolve those stress issues. Obviously, many causes of stress are not a matter of choice, but the manner in which an individual deals with the various sources of stress can be modified. One of the most common and effective ways to help reduce stress is to openly and honestly discuss it with a spouse, friend, or therapist. Having someone in your corner helps.

Basic Care

Minimize trauma to your skin. Avoid situations in which your skin could be touched or bumped, such as contact sports.

Ask your doctor for wound care instructions. Taking good care of your wounds can help prevent infection and scarring.

Use talcum powder or Vaseline. Generously sprinkling talcum powder or Vaseline on your sheets may help keep oozing skin from sticking.

Use lotions or dressings. To ease discomfort, treat sores and blisters with soothing or drying lotions or wet dressings. But, check with your doctor before using lotions or wet dressings for the first time.

Avoid spicy or acidic foods, as well as those containing garlic, onions or leeks. These foods can irritate or even trigger blisters.

Minimize sun exposure. Ultraviolet light may trigger new blisters.

Talk with your dentist about maintaining good oral health. If you have blisters in your mouth, it may be difficult to brush your teeth properly. Ask your dentist what you can do to protect your oral health.

Ask your doctor if you need calcium and vitamin D supplements. Corticosteroids can affect your calcium and vitamin D needs, so ask your doctor if you need a calcium supplement or any other additional nutrients.

Remember the Caregiver

Although you may be experiencing lots of changes and stressful situations, remember that the caregiver may also feel some of the same stress you do. Many caregivers change their usual work schedules to be able to provide as much care as possible; caregiving may be something new to them and can bring emotional changes.

Stay organized. That might be obvious advice, but it's easily overlooked. Daily life becomes very hectic when no proper plan was put into place, particularly when the disease is first diagnosed. Keep a plan of action so that the journey to remission can run more smoothly.

Break time. Caregiving can be stressful and the constant work may cause fatigue. Let your caregiver take breaks from time to time so that the stress doesn't become a part of the daily routine.

Helping without hurting. More often than not, a caregiver will be giving up personal time in order to provide care for the patient. Speak with your caregiver about including fun activities like going out to the park or giving the caregiver time alone into the schedule, that way you can both feel comfortable and relaxed without necessarily having to sacrifice self-indulgence.

Glossary of Medical Terms

Some of the terms used by doctors may be confusing and can bring more questions than answers. Below is a list of words and definitions to help you understand extensive information that a professional may give you.

Adrenal cortex: The outer portion of the adrenal gland located on top of each kidney. The adrenal cortex produces steroid hormones which regulate carbohydrate and fat metabolism and mineralocorticoid hormones which regulate salt and water balance in the body.

Antibody: a blood protein produced in response to and counteracting a specific antigen.

Antigen: Any substance that can induce a specific immune response with a specific antibody or specifically sensitized T-lymphocytes, or both.

Autoantibodies: Antibodies that react with self-antigens (autoantigens) of the organism that produced them.

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them.

B-cell: A type of white blood cell derived from bone marrow.

B lymphocyte - a lymphocyte derived from bone marrow that provides humoral immunity; it recognizes free antigen molecules in solution and matures into plasma cells that secrete immunoglobulin (antibodies) that inactivate the antigens

Cadherins: a class of type-1 transmembrane proteins.

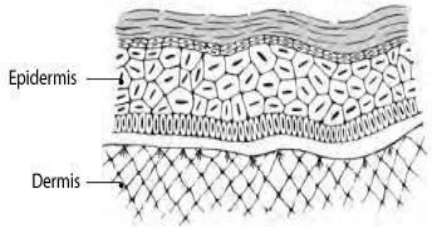
Corticosteroid corticoid: any steroid hormone produced by the adrenal cortex that affects carbohydrate, protein, and electrolyte metabolism, gonad function, and immune response; any similar synthetic substance, used in treating inflammatory and allergic diseases.

Dermal: Pertaining to or coming from the skin.

Dermatitis: Any inflammation of the skin.

Desmogleins: a family of cadherins consisting of proteins DSG1, DSG2, DSG3, and DSG4. They play a role in the formation of desmosomes that join cells to one another.

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis).



Exacerbate: to cause (a disease or its symptoms) to become more severe.

Glaucoma: Any of a group of eye diseases characterized by abnormally high intraocular fluid pressure, damaged optic disk, hardening of the eyeball, and partial to complete loss of vision.

Hematemesis: The vomiting of blood

Immunization: The process of inducing immunity to an infectious organism or agent in an individual or animal

Immunoglobulin: Also called an antibody.

Incidence rate: the probability of developing a particular disease during a given period of time; the numerator is the number of new cases during the specified time period and the denominator is the population at risk during the period.

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose.

Intercellular junctions: specialized regions on the borders of cells that provide connections between adjacent cells.

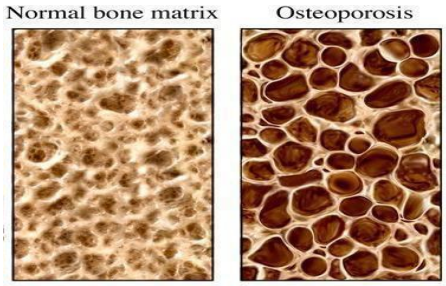
Lesion: An area of abnormal tissue change.

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases.

Mucocutaneous: Pertaining to or affecting the mucous membrane and the skin.

Mucous membrane: mucus-secreting membranes that lines body cavities or passages that are open to the external environment. (Also called mucosa)

Osteoporosis: A disease in which the bones become extremely porous, are subject to fracture, and heal slowly.



Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (=branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease).

Pigment: A substance that gives color to tissue. Pigments are responsible for the color of skin, eyes, and hair.

Predisposition: susceptibility to disease/condition.

Remission: A decrease in or disappearance of signs and symptoms. In partial remission, some, but not all, signs and symptoms have disappeared. In complete remission, all signs and have disappeared, although there is still pemphigus or pemphigoid in the body.

Risk factor: A habit, trait, conditioned, or genetic alteration that increases a person's chance of developing a disease.

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug.

Steroid: any of a large class of organic compounds with a characteristic molecular structure containing four rings of carbon atoms. They include many hormones, alkaloids, and vitamins.

Steroid therapy: Treatment with corticosteroid drugs to reduce swelling, pain, and other symptoms of inflammation.

Subcutaneous: Beneath the skin.

Superficial: Of, affecting, or being on or near the surface.

Suppression: Conscious exclusion of unacceptable desires, thoughts, or memories from the mind.

T-dependent antigen: One requiring the presence of helper cells to stimulate antibody production by B cells.

Tissue: A group or layer of cells that is alike in type and work together to perform a specific function.

Vulgaris: An affection of the skin, especially of the face, the back and the chest, due to chronic inflammation of the sebaceous glands and the hair follicles.

White blood cell: A type of cell in the immune system that helps the body fights infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others.

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Notes

Sources

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American Autoimmune-Related Diseases Association

And thou shalt honor – Edited by Beth Witrogen McLeod and Forward by Rosalynn Carter

This document has been reviewed by Dr. Victoria Werth, University of Pennsylvania, Philadelphia

1331 Garden Highway Suite 100

Sacramento, CA 95823

(855) 4PEMPHIGUS

(916) 922-1298

info@pemphigus.org

www.pemphigus.org