NATIONAL PEMPHIGUS / PEMPHIGOID ASSOCIATION ITALY

VADEMECUM FOR AUTOIMMUNE BULLOUS DISEASE PATIENTS

This vademecum has been created for patients affected by autoimmune bullous disease and for their familiars and caregivers, who, for the first time, face a rare and almost unknown disease and, overwhelmed by questions and doubts, wish to have more information about it.

The ANPPI volunteers collected the most frequently asked questions and turned them to dermatologists, researchers and nurses involved daily in the diagnosis and treatment of these diseases. The main purpose of this vademecum is to provide basic information, so that everyone can face the therapeutic process with awareness and serenity and overcome the sense of loss that, almost inevitably, arises after such a diagnosis.

Another objective is to promote the management of the disease by encouraging collaboration between the patients' association and health professionals.

Note: all the briefly mentioned topics in this vademecum are described in depth on the website www.pemfigo.it

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1 BASIC INFORMATION

Are pemphigus and pemphigoid contagious diseases?

Pemphigus and Pemphigoid are autoimmune bullous diseases and are NOT contagious.

Are they hereditary diseases?

They are not hereditary, but few familiar cases have been described and observed. However, for both pemphigus and pemphigoid some genetically determined characteristics have been identified. We can therefore speak of a genetic predisposition to the disease that does not automatically determine its onset.

What is their origin?

The origin is generally unknown, although in some cases drugs, viruses, or particular foods, can act as triggers.

What is the cause of a bullous disease?

The onset of an autoimmune bullous disease is mainly due to the presence, in patients' blood, of circulating autoantibodies directed against some structures of the skin and/or mucous membranes (between these desmogleins (Dsg) 1 and Dsg3 in pemphigus, BP180 and BP230 in pemphigoid).

What is the difference between pemphigus and pemphigoid?

Both are autoimmune bullous diseases, caused by autoantibodies directed against different structures of the skin and mucous membranes.
In pemphigus autoantibodies are directed towards the more superficial (pemphigus foliaceus) and/or deep (pemphigus vulgaris) structures of the skin and/or mucous membranes; in pemphigoid they targets the junction between dermis and epidermis (in the skin) or between chorion and epithelium (in the mucous membranes).

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Is it possible to heal?

These are generally chronic diseases, that can heal in several cases. In any case, with appropriate treatment patients can experience prolonged and durable remission.

Is an autoimmune disease a predisposing condition for the development of other autoimmune diseases?

In some cases the coexistence with other autoimmune diseases is possible because the dysregulation of the immune system could facilitate their onset.

Are they disabling diseases?

It depends on their severity. n the more severe clinical forms, they could be disabling.

Are Is it possible to die for pemphigus or pemphigoid?

No, thanks to the use of steroids and new drug therapies, usually pemphigus and pemphigoid have a good prognosis and a favorable clinical course. The mortality for bullous diseases has been significantly reduced over the years.

Is there any specialized center for the treatment of pemphigus and pemphigoid?

These diseases must be treated in specialized dermatological centers. In Italy there are various specialized centers for the treatment of autoimmune bullous diseases. The list is available at this link: http://www.pemfigo.it/centri-di-riferimento-malattie-rare-in-italia/

2 DIAGNOSTIC INVESTIGATIONS

How is pemphigus or pemphigoid diagnosed?

The main diagnostic tests are: direct and indirect immunofluorescence and the dosage

of circulating autoantibodies (anti-Dsg 1 and 3 for pemphigus, anti-BP180 and BP230 for pemphigoid).

What is a skin biopsy?

Skin biopsy is a small surgical procedure performed under local anesthesia during which a small part of skin is taken. The sampling will cover the lesion if it is intended to perform histological examination and/or healthy skin adjacent to the lesion to perform direct immunofluorescence.

What is direct immunofluorescence?

It is an exam performed through a skin biopsy and can show the deposition of antibodies on the patient's tissue. It is an essential assay to confirm the diagnosis of autoimmune bullous disease.

What is indirect immunofluorescence?

It is an exam performed using a patient's blood sample and, like ELISA but in a less specific way, measures the presence of circulating autoantibodies specific for the diseases.

What are antibodies anti-Dsg1 and Dsg3 and anti-BP180 and -BP230 and -collagen VII?

These names indicate the autoantibodies that determine the onset of pemphigus (anti-Dsg), pemphigoid (anti-BP180 and -BP230) and acquired epidermolysis bullosa (another autoimmune pathology in which autoantibodies are directed towards collagen VII).

How can they be dosed?

They can be dosed through a simple blood sample; however, the titer (quantity) of these antibodies is not always related to the severity of the disease.
The titration (dosage by blood sampling) can be performed in different hospital

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centers: you can find the nearest one through the following link http://www.pemfigo.it/esami-antidesmogleine-pemfigo/

I have high anti-Dsg antibody titers but I feel fine and have no lesions: what should I do? do I have to worry?

No, but it would be useful to carry out a dermatological check-up and generally perform one every 6 months.

I have low/negative anti-Dsg antibody values but I have active lesions: what does it mean?

This could be a case of autoantibodies going towards other antigens. It is advisable to carry out a dermatological examination and generally perform a check up every 6 months.

3 THERAPEUTIC APPROACH

To date, what are the avalaible therapies for the treatment of pemphigus/pemphigoid?

The treatment of these bullous diseases is essentially based on the use of immunosuppressive drugs such as systemic corticosteroids, mycophenolate mofetil or sodium, azathioprine and others. In some cases, intravenous immunoglobulins may be used.
In the last decade in Italy the use of the biological drug anti-CD20 rituximab has been approved in patients suffering from pemphigus with severe disease and/or refractory

disease to conventional therapies. This drug can also be used in patients with bullous pemphigoid and mucous-membrane pemphigoid, as well as in acquired epidermolysis

bullosa in case of resistance to conventional therapies. Other specific therapies are still

in experimental phase: to be constantly updated periodically consult the site

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www.pemfigo.it

When is rituximab indicated in pemphigus patients?

In Italy, this drug is adopted as second line therapy in pemphigus i.e. when traditional immunosuppressive therapy has not been effective or has caused side effects (pharmacological toxicity, glaucoma, gastric ulcer, severe osteoporosis, severe diabetes mellitus, Cushing's syndrome for steroid therapy), and when there are contraindications to these therapies.

What is the cure for cicatricial pemphigoid (or mucous membranes pemphigoid with scarring?

The treatment of cicatricial pemphigoid involves the use of immunosuppressive drugs, such as those already indicated. In milder cases the use of dapsone may be useful, while in more severe cases the use of cyclophosphamide and rituximab is indicated. Topical corticosteroids and artificial tears can alleviate symptoms in case of eye involvement. In these patients, sometimes the removal of eyelashes may be indicated to avoid rubbing and traumas of the conjunctiva.

What is remission?

It is the complete absence of signs or symptoms of illness and can occur in the absence of drug therapy or in the presence of minimal therapy. In some cases a relapse can follow remission periods of variable length.

Have systemic corticosteroids to be taken lifelong?

In case of remission of the disease, which is possible after therapy with immunosuppressive drugs or rituximab, it is no longer necessary to take corticosteroids.

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4 MEDICATION OF LESIONS

Proper management of skin lesions is essential to promote healing, reduce pain and

risk of infection. For this it is necessary to follow the indications of an expert and specialized in wound care nurse and, for the oral cavity, to follow the indications of a dental hygienist trained on the recent specific care protocols for bullous diseases.

SKIN LESIONS:

Cleaning with clean warm water is recommended.
It is advisable to cover skin lesions with non-adherent dressing.
In case of exudate production (wounds often gets wet) it is possible to apply dressing such as hydrofibres, alginates and foams (also with the addition of silver).
In the absence of exudate (dry wound) hydrocolloid-based dressing and silicon contact dressing can be applied.
The specialist may prescribe antibiotic or corticosteroid-based ointments and antiseptic solutions.
NEVER apply adherent patches or dressings to the skin, but cover everything with soft bandages.

What to do with the blisters, can them be punched?

In case of mild clinical pictures it is possible to break the blister with sterile instruments (sterile needle) and with subsequent dressing of the skin lesion.

Pemphigoid is often very itching, what to take to alleviate it?

The dermatologist, after the visit, could prescribe an antihistaminic for itching. Unfortunately, in the more severe cases of pemphigoid, it is not always sufficient.

ORAL LESIONS:

For oral lesions it is essential to perform a correct oral hygiene following the instructions

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of an experienced dental hygienist. At home it is possible to use a soft bristle toothbrush that should be replaced every thirty days. Your doctor may prescribe antiseptics, topical steroids and local anesthetics. It is important to immediately recognize a candida infection or herpetic infection : therefore it is necessary to consult the dermatologist, when lesions not typical of pemphigus/pemphigoid are noticed.

5 SPECIAL PRECAUTIONS

Is it possible to schedule PREGNANCY, being affected by pemphigus/pemphigoid?

Yes, it is possible. However it is necessary to consult your dermatologist and gynecologist, as some therapies carry risks for the fetus. Among corticosteroids, prednisone is allowed, while immunosuppressants are contraindicated. It is preferable to avoid the use of Rituximab in pregnancy.

Who has a blistering disease must follow a particular diet?

There are no special dietary restrictions because the scientific evidence is insufficient to date. Some studies found a correlation between the intake of certain foods and the worsening of pemphigus symptoms. Among these foods there are for example garlic and onion, broccoli and cauliflower, some flavoring additives such as black pepper, wine, red fruits and coffee. Based on these studies, it may be suggested to evaluate the body's reaction following the intake of certain foods and, above all, often vary the daily choice of food.
In case of prolonged corticosteroid therapy and in the presence of oral lesions, it is advisable to consult a specialized nutritionist and adopt a healthy eating style.

What should you not do when you are being treated with Rituximab or other immunosuppressive drugs?

Vaccinations:
The use of vaccines containing living or attenuated viruses/microbes is contraindicated during immunosuppressive therapies. The other types of vaccines (against seasonal

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influenza, H1N1, tetanus and pneumococcus) can be practiced, but the protective effect may be less effective. Only for patients who have been treated with rituximab or other anti-CD20 drugs it is necessary to wait 4-6 months after the last infusion before performing the vaccination.

Infections:
It must be remembered that during treatment with the aforementioned drugs it is

easier to get an infection. Therefore it is necessary to follow hygienic/behavioral rules in order to limit the risks of a possible infection.

During short or long-term corticosteroid therapy should supplements or drugs be used to prevent side effects?

Your doctor may recommend vitamin D supplementation.
In patients at risk of osteoporosis, particularly post-menopausal women and men over 50 years old who have undergone prolonged systemic corticosteroid therapy (periods longer than 3 months), the specialist may also prescribe treatment with bisphosphonates (i.e. alendronate, risedronate).
When recommended by the specialist, topical and/or systemic antifungals, antivirals and antibiotics should be taken

Taking medium to high doses of corticosteroid, what routine clinical investigations should be performed and what values should be controlled?

- Blood counts, blood sugar, sodium and potassium should be checked periodically. Glycosylated hemoglobin should also be checked for diabetic patients
- Basic screening and prophylaxis of osteoporosis.
- Ophthalmological evaluation.
- The use of H2 blockers or proton pump inhibitors should be evaluated by the

- physician basing on the patient's characteristics.
- Evaluate the risk of thrombosis periodically.

- Contact a physiatrist if prolonged corticosteroid therapy is required.

Does corticosteroid cause sleep disorders?

Insomnia is a possible effect of steroid therapy. For this reason it is recommended to take this drugs in the morning. In cases of greater discomfort, mild sedatives can be used.

It is possible to have surgery for cataract? Surgical interventions are always allowed?

Before any surgical intervention it is mandatory to consult with the dermatologist

because in some cases it may be appropriate to postpone the operation or take special precautions.

Are there precautions for dental treatment?

Yes. It is necessary to communicate to your dentist the pathology you are suffering from, so that he can implement the necessary precautions.
In some cases, the dermatologist may prescribe steroid therapy in the days preceding and following the oral cavity surgery.

If it were necessary to make clinical investigations involving the contrast agent, would there be contraindications?

No.

Is it possible to do tattoos?

It is contraindicated to do tattoos in patients suffering from bullous diseases, particularly in the active phase of disease.

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Can you sunbathe and go to the sea?

Patients suffering from autoimmune bullous diseases should expose themselves with caution to direct sunlight, strictly avoiding skin erythema and exposure during critical hours. In the case of low vitamin D blood levels, the doctor may prescribe the use of

calcifediol or calcitriol (activated vitamin D).

6 RIGHTS

With pemphigus/pemphigoid, are you entitled to disability? Is there an exemption for pathology?

In Italy the disability for bullous diseases is attributable by the ASL, to which an application can be submitted, attaching a certificate drawn up by the dermatologist

and other suitable documentation.
There is an exemption for pathology for pemphigus and pemphigoid that can be requested in the centers identified for the treatment of bullous diseases, after the dermatological examination and confirmation of the diagnosis.

7 QUALITY OF LIFE

Can patients suffering from bullous diseases return to a normal life following an appropriate treatment?

It is certainly possible in the case of mild forms and/or with a good response to treatment. In many cases, in fact, therapies induce disease remission even for long periods. In the more severe cases, on the other hand, the quality of life strictly depends on the individual's response to therapies.
Psychological support, both individually and through mutual support groups, can be a valuable aid. Bullous diseases can put a strain on emotional balance and sharing experiences about one's daily life can be very useful.

This vademecum was created by:

Pemfigo Pemfigoide Italy National Association Steering Committee:
Sara Schifano, Filippo Lattuca, Carola Pulvirenti.
Silvana Bonelli, ANPPI member and patient with pemfigo volgare

In collaboration with the Istituto Dermopatico dell'Immacolata(IDI) -IRCCS, in particular with:
First Dermatological Division:
Doctors: Dott. Biagio Didona, Dott. Luca Fania, Dott.ssa Alessia Provini, Dott.ssa Jo Linda Sinagra, Dott. Francesco Moro, Dott.ssa Cinzia Mazzanti;
Nurse coordinator: Gabriele Alvetreti.
Researchers from the Molecular and Cellular Biology Laboratory:
Dr. Giovanni Di Zenzo, Dr. Adele Salemme

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