Information sheet for patients affected by MUCOUS MEMBRANE PEMPHIGOIDS (cicatricial pemphigoid, epidermolysis bullosa acquisita, linear IgA dermatosis with mucosal involvement)

These information sheets were written in collaboration with the Reference Centre for Autoimmune Bullous Diseases and the Pemphigus-Pemphigoïde France patient association.

Dear Sir or Madam,

This sheet is intended to provide you with information on mucous membrane pemphigoids. It is not a substitute for a medical consultation.
Its purpose is to promote dialogue with your doctor. Feel free to ask him or her to specify any points that do not seem sufficiently clear to you and to ask for additional information on your particular case.
Indeed, some of the information contained in this sheet may not be adapted to your case: it is important to remember that each patient is different. Only your doctor can give individualised and adapted information.

The disease

What are mucous membrane pemphigoids?

The term mucous membrane pemphigoid includes several closely related diseases such as cicatricial pemphigoid (CP), epidermolysis bullosa acquisita (EBA) or linear IgA dermatosis with mucosal involvement.

These are autoimmune diseases: which means that the body, following a disruption of the immune system*, produces antibodies against its own mucous membranes or skin (autoantibodies).

** Immune system: the set of defences of an organism (in particular white blood cells and antibodies) that normally allow it to recognise what belongs to its body and to defend itself against what is foreign to it (microbes for example). In this disease, it is mistaken and removes by mistake the skin and/or mucous membranes.*

Are these diseases serious?

The severity depends on the mucous membranes affected: damage to the eyes, throat and oesophagus can be severe.

Prolonged treatment is necessary in all cases.

What are the symptoms of mucous membrane pemphigoids?

1- ACTIVE LESIONS

As the name suggests, lesions in mucous membrane pemphigoids occur predominantly or exclusively on one or more mucous membranes. The mucous membranes involved are in decreasing order of frequency: the mouth, the conjunctiva of the eyes, the ENT region (Ear-Nose-Throat/ pharynx-larynx), the anus, the genital region and the oesophagus, the urethra and the trachea.

The symptoms depend on the mucous membrane(s) affected, for example:
-bleeding, discomfort when brushing teeth and/or eating when the oral mucosa is affected,
-dry cough and voice modification when the throat (larynx) is affected,
-in the eyes, the disease is often painless, giving the impression of simple conjunctivitis at first.

On the skin, the blisters are generally tight and surrounded by normal skin. They are sometimes very small, so we talk about vesicles.

Sometimes these blisters and vesicles rupture quickly and are then not noticed by the patient; only wounds (also called erosions) remain.

2- SCARS

The lesions progress by forming scars (or fibrosis) that sometimes permanently damage the affected mucosa.

These scars sometimes have serious consequences, especially in the eyes and throat (larynx).

On the skin, after disappearance, the lesions leave clearer, hollow scars, sometimes with small white cysts (milium cysts).

What are they caused by?

Mucous membrane pemphigoids are autoimmune diseases, they are caused by autoantibodies that prevent the attachment systems between the first two layers of the skin and mucous membranes from functioning.

The causes of this immune system disorder are not yet well known. Rarely can specific drugs be used to promote the development of these diseases.

Who can be affected?

Mucous membrane pemphigoids can affect people of all ages, ethnic origins and genders.

How many people are affected?

These are very rare diseases (about 1 new case per million inhabitants per year in Western Europe).

How do we explain the symptoms?

The structure of the skin is very similar to that of the mucous membranes that line the mouth, throat, oesophagus, eyelids, external genitalia, anus and in some patients the nose and throat (larynx). The most superficial layer of the skin is called the epidermis and the layer immediately below is called the dermis. For mucous membranes, we speak of epithelium (instead of epidermis) and chorion (instead of dermis).

Mucous membrane pemphigoids are autoimmune diseases caused by autoantibodies. These autoantibodies cause a detachment between the epithelium and the chorion. This leads to the formation of blisters, commonly called "bubbles", containing a liquid. These blisters form at a place called the dermo-epidermal or chorio-epithelial junction or basement membrane (see diagram below).

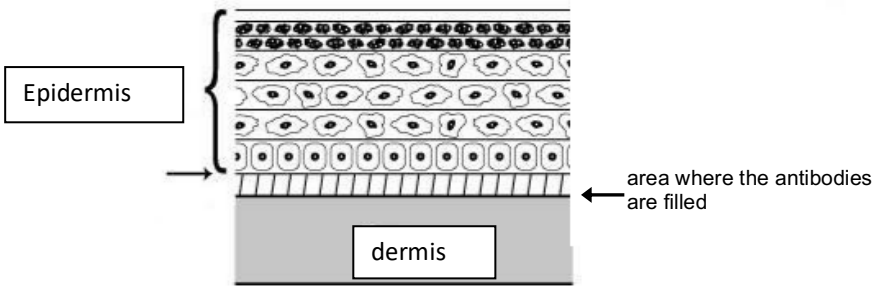

Diagram representing the epidermis (surface layer of the skin) and the dermis (deep layer).

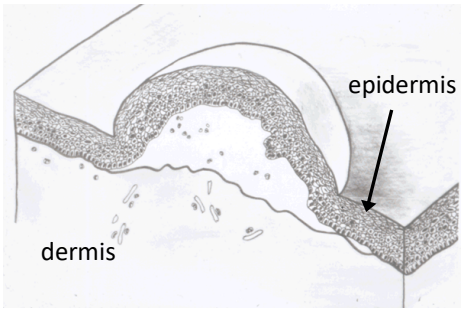

Diagram representing a blister. *C. Prost-Squarcioni*

Excerpt from the International Pemphigus Foundation website http://www.pemphigus.org

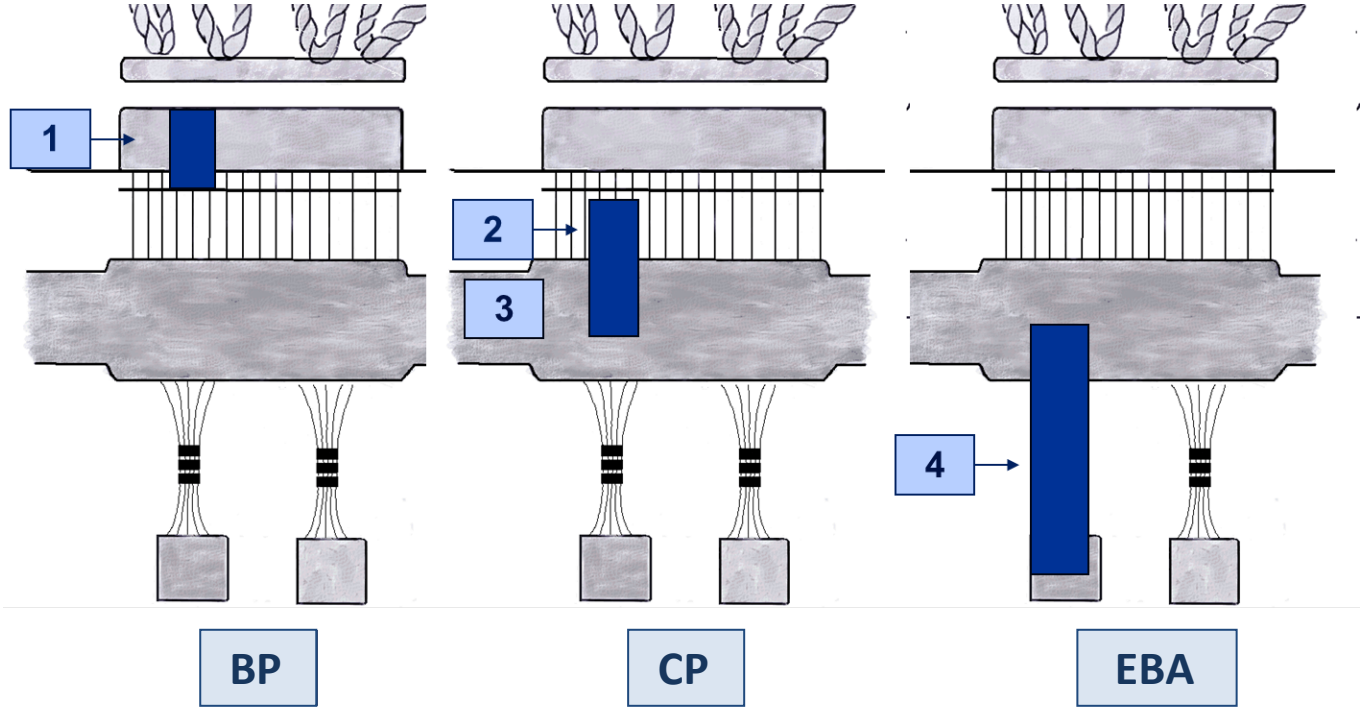

Diagram showing the details, after very high magnification under an electron microscope, of the dermal-epidermal junction (between the epidermis and the dermis in the skin) or chorio-epithelial junction (between the epithelium and the chorion in the mucosa). Bullous pemphigoids (BP), CP and EBA are distinguished by the precise site of antibody deposition (schematized as blue rectangles). *According to C. Prost-Squarcioni*

Are they contagious?

No, these diseases are not contagious.

Are they hereditary?

Mucous membrane pemphigoids are not hereditary, although there is a genetic predisposition. Some genes transmit a terrain that predisposes to

the development of these diseases; but even in people who carry this gene, the risk of triggering the disease is extremely low.

Family forms are therefore extremely rare and there is no reason to worry family members about this. No genetic testing is required.

How are they diagnosed?

The dermatologist examines the appearance, number and location of blisters and small wounds left by bubbles (erosions). This is the clinical analysis.

Under local anaesthesia, (s)he takes two samples of small fragments of the skin or mucous membranes (biopsies). These analyses will allow us to see:
- at what depth the detachment is located and blisters are formed. This is the histological analysis.
- autoantibodies that attack the junction membrane (basement membrane) between the epidermis and dermis. This is the direct immunofluorescence analysis.
- immunomicroscopy is only practiced in some specialized laboratories. It allows us to see more precisely where autoantibodies are located and to differentiate mucous membrane pemphigoids or other autoimmune blistering diseases.

A blood test may be performed to determine the type and amount of autoantibodies. This is the biological analysis (most often using ELISAs).

How do they evolve ?

The disease evolves over time by successive outbreaks. It can be severe if left untreated.

As the blisters disappear, they leave scars and sometimes small white cysts (milium cysts) that will fade over time.

With the treatment given at the beginning (attack treatment), blisters and erosions cease to appear within a few weeks or months. The disease is said to be "controlled" and treatment is gradually reduced, becoming milder. This lighter treatment (maintenance treatment) is necessary for several years or even for life to avoid relapses.

Treatment, care, follow-up

Is there a treatment for these diseases?

Effective treatments are available.

Care is generally carried out in two phases:
- Initial treatment (attack treatment) usually involving high doses of medication to stop the progression of the disease and achieve healing of the lesions.
- Disease control treatment (maintenance treatment) to maintain remission (no relapse), usually continued for several years or even for life.

Since these diseases can affect several mucous membranes, their management must involve several specialists (= multidisciplinary): the dermatologist generally coordinates care and, depending on the case, seeks the help of stomatologists, ophthalmologists, ENT specialists, proctologists and even gastroenterologists and gynaecologists. Depending on the condition (especially eye or laryngeal damage), the choice of medication must be adapted.
Treatment is most often based on dapsone (Disulone®), sometimes sulfasalazine (Salazopyrine®), doxycycline (Tolexine®, Doxy 100®, Doxylis® or many other generics) or colchicine (Colchicine® or Colchimax®). These drugs do not prevent the production or binding of autoantibodies but limit their damage (action on associated inflammatory phenomena).
In severe forms (such as those affecting the eyes or throat), immunosuppressants (drugs that block the production of autoantibodies) such as cyclophosphamide (Endoxan®), rituximab (Mabthera®, Rixathon®), cyclosporine (Neoral®, Sandimmun®) or mycofenolate mofetil (CellCept® and its generics) are often added.
In some forms with a very inflammatory onset or in very severe cases (larynx and/or eyes), general corticosteroid therapy may be necessary for a short period of time until other associated treatments (dapsone, sulfasalazine or immunosuppressants) become effective.

Local treatments with corticosteroids in creams, mouthwashes or eye drops may also be useful to optimise improvement and comfort.

In case of pain, analgesic treatments are available.

At the beginning of the disease in the period before diagnosis, and in the interval between the initiation of treatment and the control of the disease, hospitalisation is sometimes necessary.

Is psychological support desirable?

Psychological support may sometimes be considered, at the beginning of the disease and in its severe forms, when there is a strong impact on the patient's quality of life.

Can these diseases be prevented?

These diseases cannot be prevented.

Living with mucous membrane pemphigoids

In general, when the disease is controlled through treatment, the patient's daily life is virtually unchanged outside the constraints of treatment and possible side effects.

No treatment is contraindicated but it is advisable to check for possible interference with corticosteroids and/or immunosuppressants.

In case of mouth disease, careful oral hygiene and appropriate care are recommended. Your dermatologist or stomatologist will advise you.

A detailed fact sheet with tips for the daily life of patients with bullous disease (skin hygiene, clothing, nutrition, sun protection, physical activity) is available on the website of the National Reference Centre for Autoimmune Bullous Diseases http://www.chu-rouen.fr/crnmba.

Where can you be treated?

In a dermatology department located in a hospital centre.

In France, there is a reference centre and several competence centres for the management of autoimmune bullous diseases (contact details on the

website of the national reference centre for autoimmune bullous diseases http://www.chu-rouen.fr/crnmba).

To know more

Where can I get more information?

How to connect with other patients with the same disease?

There is a French patient association "Association Pemphigus Pemphigoïde France" created by patients and their families in March 2005.

URL: http://www.pemphigus.asso.fr
Contact Numbers for questions and information requests:
*Hélène Facy (Paris region): +33 (0)687 114 026
* Bernadette Dejean (Western and Southern regions): +33 (0)683 395 320
*Jenny Vernet (Eastern and Northern regions): +33 (0)634 686 87457
Telephone number of the association's headquarters: +33 (0)143 252 5 4288

There are also websites dedicated to all rare diseases:

http://www.orpha.net

http://www.maladiesraresinfo.org (+33 (0)156 535 38136 non surcharged call)

This website provides answers to any questions that you may have during corticosteroid treatment:

http://www.cortisone-info.fr