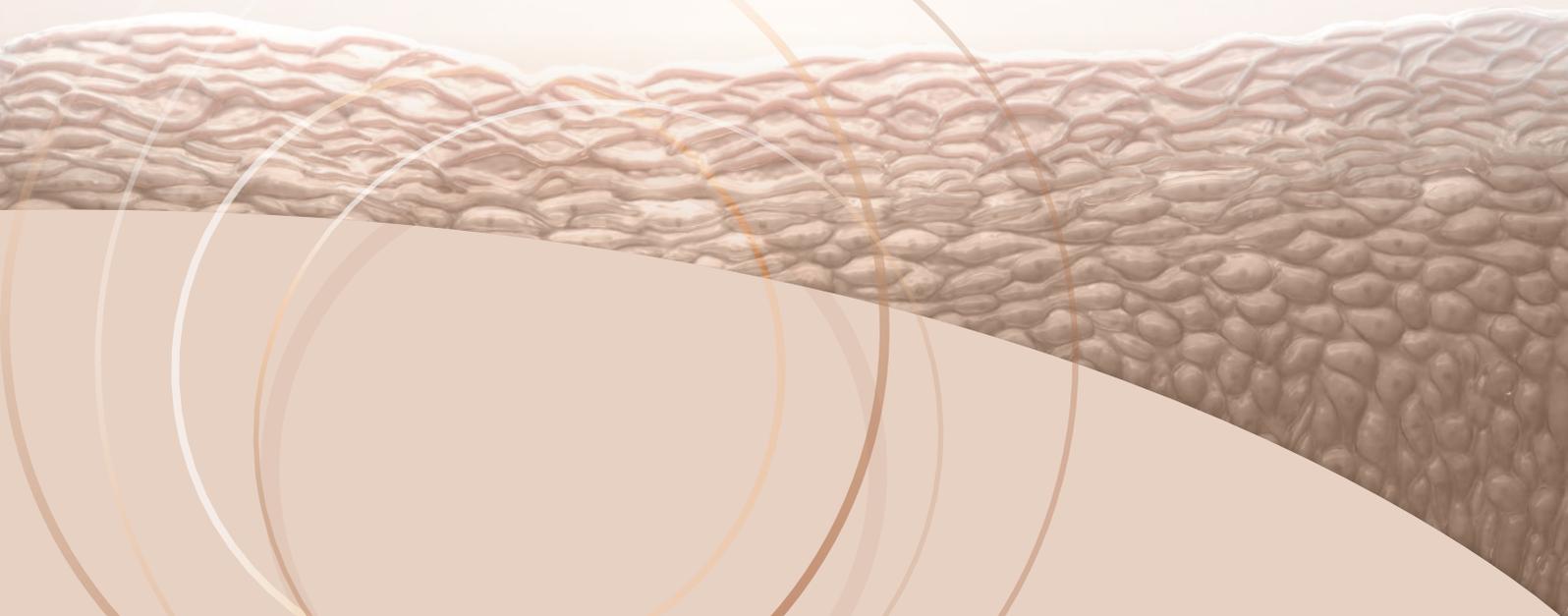


Information Leaflet for Patients

A detailed illustration of a skin cross-section, showing the epidermis and dermis. The epidermis is the upper layer, and the dermis is the lower layer. The illustration is rendered in shades of brown and orange, with a textured, wavy surface. Several overlapping circles in various shades of brown and orange are superimposed on the skin illustration, creating a sense of depth and focus.

CUTANEOUS IMMUNE COMPLEX VASCULITIS, SKIN-LIMITED CUTANEOUS IGA OR IGG/IGM VASCULITIS

(Formerly called: Allergic/Hypersensitivity Vasculitis)

The aim of this leaflet

This leaflet is designed to help you understand more about cutaneous immune complex vasculitis or skin -limited IgA or IgG/IgM vasculitis (formerly called allergic/hypersensitivity vasculitis). It tells you what this condition is, what causes it, and what can be done for treatment.

CUTANEOUS IMMUNE COMPLEX VASCULITIS, SKIN-LIMITED CUTANEOUS IGA OR IGG/IGM VASCULITIS

What are immunoglobulins (IgA, IgG and IgM)?

Immunoglobulins or antibodies are proteins made by the immune system to fight antigens, such as bacteria, viruses, and toxins. The body makes 5 different types of immunoglobulins to combat different antigens.

Immunoglobulin A (IgA): is found in high concentrations in the mucous membranes, particularly those lining the respiratory passages and gastrointestinal tract, as well as in saliva and tears.

Immunoglobulin G (IgG): the most abundant type of antibody, is found in all body fluids and protects against bacterial and viral infections.

Immunoglobulin M (IgM), which is found mainly in the blood and lymph fluid, is the first antibody to be made by the body to fight a new infection.

What is allergic vasculitis?

Cutaneous immune complex vasculitis, usually manifesting as skin-limited IgA or IgG/IgM vasculitis (formerly called: "Allergic/hypersensitivity vasculitis") belongs to the *cutaneous small-vessel vasculitides*, and is a disorder characterized by the inflammation of some small blood vessels located mainly in the skin, called *post-capillary venules*. Other small vessels located in the internal organs (like the kidneys (most frequently), bowels, or joints) may be affected as well. The disease is then referred to as systemic IgA vasculitis or *Henoch Schönlein purpura*, which on the skin has exactly the same symptoms as the skin-limited forms.

What causes allergic vasculitis?

Cutaneous immune complex vasculitis is thought to be mediated by immune complex deposition. In this form of vasculitis, circulating antigens in the body induce antibody formation. These antibodies bind to the circulating antigen and create immune complexes, which then deposit within vessels, activating complement and inducing inflammatory mediators. Inflammatory mediators, adhesion molecules, and local factors may affect the endothelial cells and play a role in the manifestations of this disease.

In half of cases, a trigger of cutaneous immune complex vasculitis can be identified, the most common of which include recent acute infections (eg. upper respiratory tract infections, viral hepatitis and HIV infection) or certain medications: antibiotics are the most common drugs to cause cutaneous immune complex vasculitis, particularly beta-lactams. nonsteroidal anti-inflammatory drugs and diuretics. However, almost all drugs and drug additives are potential causes.

Other causes or forms (variants) of *cutaneous immune complex vasculitis vasculitis* are:

- connective tissue vascular diseases (such as small vessel immune complex vasculitis in *systemic lupus erythematosus* or *Sjogren's syndrome*, whereas *vasculitis in rheumatoid arthritis* often also affects medium vessels)
- *malignancies/cancer* (mostly hematologic ones, and in rare cases, solid organ neoplasms)
- *inflammatory bowel diseases*
- chronic active *hepatitis*
- foods or food additives may also cause cutaneous immune complex vasculitis

In the other half of cases, no cause can be identified, so the cutaneous immune complex vasculitis could then be called "idiopathic."

Who is affected and what are the characteristics of allergic vasculitis?

Cutaneous immune complex vasculitis (as well as *systemic IgA vasculitis* or *Henoch Schönlein purpura*) may occur at any age (both children and adults), and in both men and women of all races, but it is slightly more common in women. It is characterised by three types of skin lesions: *palpable purpura* (violet-coloured, elevated skin lesions [*papules*] that do not change colour when pressed [“non-blanching”]), *retiform purpura* (violet-coloured, net-like or stellate erythemas that also do not change colour when pressed [“non-blanching”]), located primarily on the lower legs (due to inflammation of small vessels), *hemorrhagic blisters* sometimes developing into necrotic *ulcers*. These lesions are mainly located on areas that are prone to stasis like the ankles and shins, due to destruction of vessels with ensuing leakage of blood into the tissue (explaining the purpuric lesions).

What are the signs and symptoms of allergic vasculitis?

The skin lesions are asymptomatic in most cases, but sometimes they can be associated with an itching/burning sensation or local pain. Apart from the *palpable and retiform purpura*, and *ulcers*, signs and symptoms affecting beyond the skin can also occur, depending on the extent of the inflammatory reaction and involvement of internal organs, such as flu-like symptoms, abdominal pain, diarrhoea, bloody stool, joint and muscle pain.

How is it diagnosed?

The diagnosis of *cutaneous immune complex* or *IgA vasculitis* is made by a clinician by recognizing the characteristic skin lesion, by obtaining a physical examination, a careful medical history from the patient (as well as an extensive screening for possible triggers such as infections, inflammatory disorders, medication, etc.). It is very important to perform repeated urine analysis in order to detect or exclude renal involvement (as in systemic IgA vasculitis).

The diagnosis is confirmed by a skin biopsy, which involves the removal of a small skin sample under local anaesthesia, which will be further examined under a microscope by a pathologist.

How does it evolve?

Almost 90% of patients experience a spontaneous resolution of the skin lesions within only a few weeks, while 10% will have a chronic or recurrent disease at variable intervals (months to years).

Therefore, in patients with identified triggers (like drugs or treatable infections), the disease will disappear after eliminating the trigger, and it may not recur. Still, there are other cases with triggers like inflammatory diseases, chronic infections, *malignancies*, or “idiopathic cases,” in which the evolution and prognosis depends on the underlying condition and with an increased risk of recurrence. Additionally, when internal organs are also affected, the prognosis is worse.

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How is it treated?

First of all, your clinician needs to check any possible trigger and treat it (e.g. treatment of a certain infectious cause or discontinuing a certain medication). Aside from this, the treatment approach varies, taking into account the severity and extent of the disease.

In most patients, the lesions heal spontaneously after withdrawal of the trigger, but in some cases supportive or pharmacological treatment can be used. In the latter case, non-steroidal anti-inflammatory and antihistamine medications are used first. If there are hemorrhagic blisters, oral glucocorticoids are recommended to prevent formation of ulcers (steroids rather provide symptomatic relief, but do not treat the cause). The second choice includes colchicine or dapsone. Only rarely, if at all immunosuppressive agents (like methotrexate) and biological drugs (like infliximab or rituximab) are required. All treatments should be performed under the guidance of experienced, specialised clinicians.

How can I prevent the development of cutaneous immune complex vasculitis (skin-limited or systemic IgA vasculitis (Henoch Schönlein purpura)?

You should seek medical advice by seeing your general physician at the first cutaneous signs which may look like the ones described above with *cutaneous immune complex vasculitis*, in order to minimize, if possible, the evolution and extent of a possible systemic disease.

What can I do if I am diagnosed with it?

There are not many significant things you can do to influence the natural course of cutaneous immune complex vasculitis (as part of **skin-limited** or systemic IgA vasculitis). Avoidance of certain drugs that in the past were involved in the development of *vasculitis* may help to avoid another episode. ■

