



allergies

Basic comprehensive protocol

 **STANGEST**

Comprehensive therapeutic approach to food allergies

Allergic diseases represent a high percentage of the consultations in small animal clinics. In the last 10 years, research on the pathogenesis and treatment of allergies has evolved tremendously. In this bulletin, we will make a quick review of the factors related to the development of an allergic dermatitis. With this we want to highlight the importance of going past the implementation of a short-term symptomatic treatment. Understanding the underlying causes of the disease is key for applying a long-term comprehensive treatment, establishing measures against the factors that can be handled, always adapted to the needs of each patient and to the situation and the expectations of its owner.

Aetiology and pathogenesis

Allergic diseases include a range of hypersensitivity reactions to one or more allergens. The most common allergic processes in the veterinary clinical practice are food allergies, atopic dermatitis, flea allergy and contact allergy.

Most allergies in cats and dogs show up with pruriginous and inflammatory processes that cause the animal to scratch and/or lick itself, causing lesions and even secondary infections.

Multiple factors implied in the onset of the skin inflammation and the itching have been described (Figure 1). It is difficult to ascertain which is the primary cause, because these factors interact and may feedback themselves reciprocally, thus increasing the intensity of the allergy manifestations.

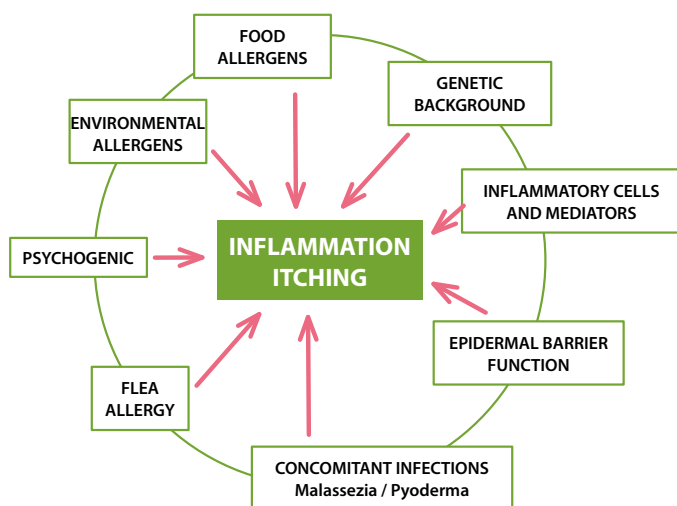


Figure 1. Main pathogenic factors implied in the development of skin inflammation and itching. Adapted from Saridomichelakis & Olivry, 2016.

Keys for diagnosis

A thorough clinical examination and anamnesis are essential for a correct diagnosis of the allergy and the choice of the therapeutic treatment.

- Habitat: Are other animals/owners affected?
- Presence of fleas or other parasites
- Coincidence with a specific situation: Vaccines? Changes?...
- Age of onset
- Seasonality
- Features of the itching: intensity, pattern of the lesions...
- Diet
- Previous and current treatments

Before considering a food or environmental allergy it is necessary to rule out other diseases that cause itching: mange, flea bite allergy, etc.

Key concepts

- **Atopic dermatitis:** it is an inflammatory and pruriginous condition with a genetic predisposition component that involves characteristic clinical manifestations related to IgE antibodies mainly directed against environmental allergens.
- **Food intolerance:** adverse reactions against certain foods that do not involve the immune system. They are mediated by metabolic (e.g. lactose or gluten intolerance), pharmacological (caffeine intolerance) factors, etc.
- **Food allergy:** immune-mediated adverse reaction. The body considers a part of the food as something strange, and the immune system response against it is activated.

Some kinds of allergy can be diagnosed with a test. We must evaluate if the result may help in the treatment of the allergy or if it will only provide information.

FACTOR	TESTS
Environmental allergens	Clinical examination Intradermal or allergen-specific IgE test
Food allergens	Food restriction-reintroduction
Skin barrier function	Trans-epidermal water loss
Concomitant skin infections	Clinical examination. Cytology
Flea allergy	Clinical examination. Detection of fleas or their droppings
Psychogenic	Clinical examination. Clinical history

Intestinal permeability as a background in allergy cases

Skin manifestations of food allergy are indistinguishable from those of atopic dermatitis. Up to 40% of the dogs with atopic dermatitis symptoms show sensitisation to food allergens. In case of showing atopic dermatitis symptoms, especially if it has a non-seasonal pattern, we should analyse if the animal has developed a food allergy.

A damaged intestinal wall may allow partially digested molecules with a high molecular weight to pass through it, which would have never happened with a healthy gut mucosa. This is why the immune system considers them as something exogenous and starts a reaction against them, causing an allergic response. Therefore, there is inflammation, recruitment of more immune cells..., and a positive feedback mechanism is triggered that perpetuates the mucosal damage, that is seen at a systemic level: itching, inflammation, dry skin, alopecia, etc.

Causes of intestinal permeability

1. **Previous use of drugs:** NSAIDs, corticoids, antibiotics...
2. **Intestinal dysbiosis:** gut microbiota imbalance to the detriment of beneficial bacteria. Candidiasis is normally present in many cases and it must be treated with antifungal drugs.
3. **Chemical sensitivity and secondary inflammatory processes** against synthetic additives or other irritants.
4. **Enzyme insufficiency and malabsorption:** extra-di-

gestive disorders, such as pancreatitis, cirrhosis, etc. may cause problems at the gut level. The arrival of inadequately digested proteins to the colon allows them to be digested by bacteria, that produce residues that damage the gut microbiota and the mucosa.

5. **Consumption of poor-quality diets.**
6. **Nutritional deficiencies:** the intestinal permeability and the associated inflammatory process also feedback the nutritional deficiencies.
7. **Food allergy.**
8. **Autoimmune diseases** (rare).

State-of-the-art hypoallergenic food contains hydrolysed proteins, so amino acids, and not whole protein molecules, pass through the intestinal barrier. This controls the allergy symptoms significantly, because allergic reactions are reduced.

But it is necessary to underline that the primary cause of the problem are not proteins, but **intestinal permeability:** an epithelial barrier that is damaged and that cannot exert its protection role against exogenous molecules: antigens, pathogens, toxins, poorly digested food, etc. Due to this, we must search for the cause of this damage on the gut mucosa and try to repair it as soon as possible. It is only in this way that the entrance of these high molecular weight proteins (that on many occasions would not come into contact with the immune system) will be avoided, and so the immune response will not be triggered.

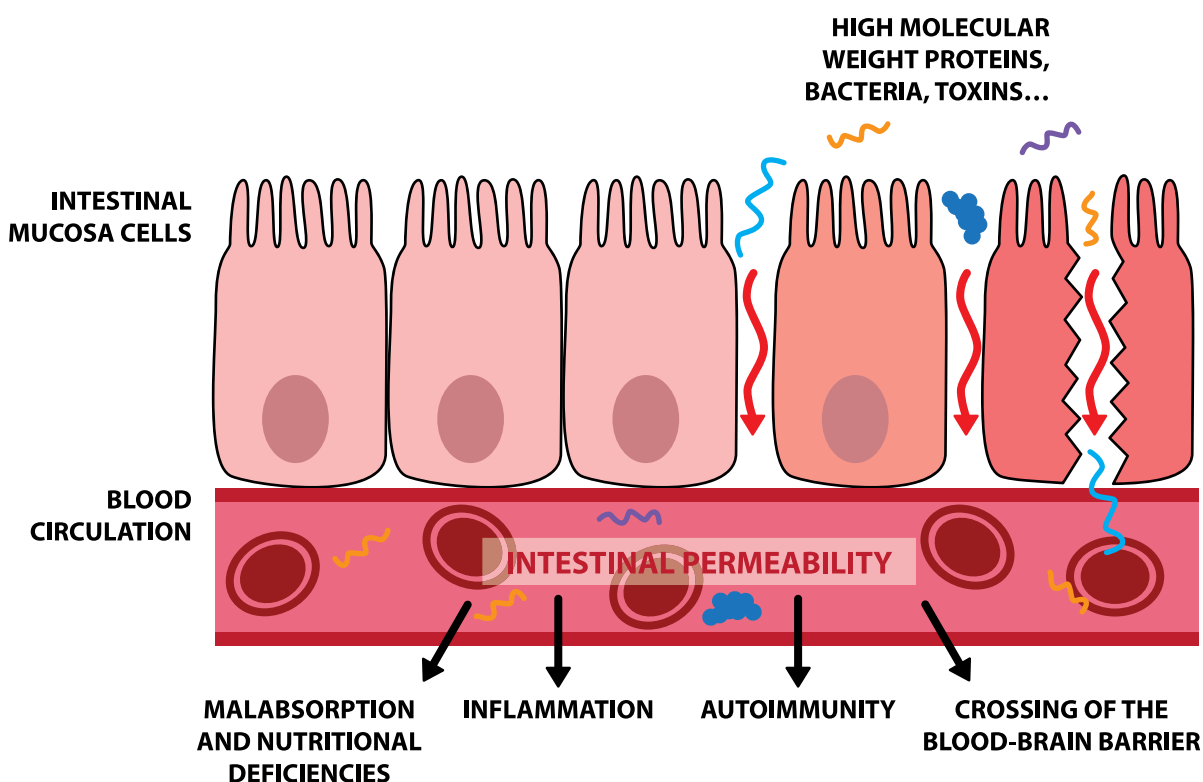


Figure 2. When the integrity of the gut mucosa is compromised, an intestinal permeability problem appears: the epithelial barrier is unable to control the entrance of exogenous substances, that enter the bloodstream and can cause a series of reactions at a systemic level.

Comprehensive therapeutic options for allergy

Restoration of gut health

This is the key for the comprehensive therapeutic approach of food allergy, because it is to be found in the origin of many of the cases. The gastrointestinal tract is considered as an ecosystem that is based on three pillars: **the epithelial cells, the immune system and the gut microbiota**, and all of them must be taken care of.

The epithelial barrier is the first defence mechanism against the entrance all kind of allergens, pathogens and poorly digested glycoproteins. In the case of allergies, there are many factors that compromise the integrity of the gut epithelium: inflammatory processes, diarrhoea, gut dysbiosis... **GlutaVet** can facilitate the regeneration of the intestinal mucosa, because it contains a precursor of glutamine, a conditionally essential amino acid that exerts a protective and regenerative effect on the intestinal mucosa. It also acts as an energy source for enterocytes, lymphocytes and macrophages, so the immune system is supported at the gut level.

The consumption of prebiotics and probiotics, such as **Floravet Complex**, help the microbiota to develop harmonically, exerting positive effects on the gut health, among which we must underline:

- The strengthening of the immune system: e.g. the regulation of the Th2/Th1 balance.
- The decrease in the pathogenic agents such as bacteria, parasites, Candida...
- The drop in the food intolerance symptoms.
- The prevention and treatment of diarrhoea.

Repairing of the skin

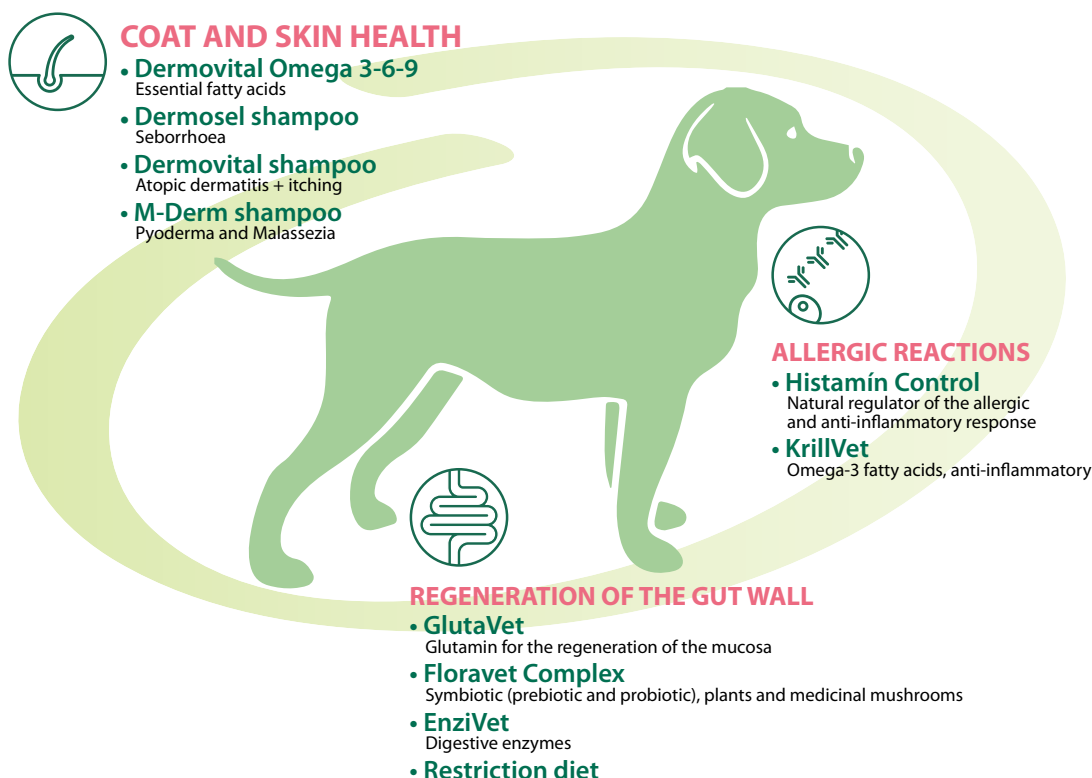
The restructuration of the epithelial barrier by means of fatty acids or shampoo therapy are deemed as key steps for the long-term treatment of atopic dermatitis (Saridomiche-lakis & Olivry, 2016).

Dermovital Omega 3-6-9 is a supplement suitable for repairing and maintaining the integrity of the skin barrier. It contains essential fatty acids, as well as MSM, biotin, zinc and selenium, and it is a great nutritional support for skin metabolism.

Therapy with **dermatological shampoos** helps to control skin infections (Malassezia, pyoderma...), as well as exerting a moisturising and soothing action.

The normalisation of the skin barrier through these supplements allows to:

- Prevent the entrance of allergens through the reduction of the allergenic load settled on the coat and the skin, and reinforce the physical barrier represented by the skin.
- Reduce the itching and the inflammation.
- Moisturise and soothe the skin, avoiding the excessive trans-epidermal water loss.
- Reduce the secondary infections.



Management of the allergic reactions

The entrance of the allergen causes a response of the T and B cells, that produce IgE antibodies that pre-activate the mast cells. The contact with the allergen causes the degranulation of the mast cells, and molecules such as histamine, leukotrienes and interleukins (which have a direct responsibility in the activation of allergic processes related to inflammation and itching) are released. Therefore, the damage to the skin barrier is worsened, and the entrance of new allergens is facilitated, and this feedbacks the allergic process.

There are nutritional supplements, such as **Histamín Control**, that help to modulate the response of the immune system: a key step for normalising the allergic reactions. These supplements can act at different levels in the chain reactions, being conducive to the following: rebalancing the Th1/Th2 populations, inhibiting the mast cell's degranulation, reducing the pruriginous processes... This effect may be increased with the concomitant use of **KrillVet**, thanks to the anti-inflammatory effects of its omega-3 fatty acids.

We must not forget... The communication with the owner

One of the greatest challenges in the treatment of allergies is achieving a good relationship with the owner; a relationship based on trust and commitment. When the cause of the allergy is unknown or it cannot be avoided, the allergy becomes an incurable chronic disease, and thus it can be very frustrating for the owner and the veterinarian.

There is not a single, effective and well-defined therapy for the treatment of allergies. Each case is different and implies a comprehensive customised therapy. Therefore, the establishment of a good relationship with the owner is key so the veterinarian can handle their expectations, financial situation and degree of commitment. The most appropriate treatment for allergies is the one that implements measures that are adapted to the clinical needs of the animal and the owner's situation.

ACTION	THERAPEUTIC OPTIONS
Reduce the allergic reactions	<ul style="list-style-type: none"> ● Histamín Control ● KrillVet ● Immunosuppressants, anti-inflammatory drugs
Improve the gut health	<ul style="list-style-type: none"> ● GlutaVet ● Floravet Complex ● EnziVet ● Restriction diet ● Dermovital Omega 3-6-9
Avoid the release of mediators of inflammation	<ul style="list-style-type: none"> ● Histamín Control ● KrillVet ● Glucocorticoids, cyclosporine, oclacitinib
Reinforce the skin barrier	<ul style="list-style-type: none"> ● Dermovital Omega 3-6-9 ● Topical treatments
Treat the concomitant skin infections	<ul style="list-style-type: none"> ● M-Derm Shampoo (<i>Malassezia</i> and Pyoderma) ● Dermosel Shampoo (seborrhoea) ● Dermovital Shampoo (pruritus) ● Topical antiseptics
Control the ectoparasites	<ul style="list-style-type: none"> ● Natural repellents: Stanvet® Life , Pulvex ● Environmental insecticides: Pulfin
Handle psychogenic factors	<ul style="list-style-type: none"> ● Measures to reduce stress ● KrillVet ● Anxiolytics

Food allergies basic comprehensive control

Objectives

• SHORT TERM:

- Reduce itching and inflammation.
- Promote the healing of the skin.
- Promote the repairing of the gut wall.
- Control the secondary infections, if present.

• LONG TERM:

- Identify the underlying cause and try to avoid it.
- Management of the allergic reactions during the periods of exposure.
- Reinforcement of the epithelial barriers.

Newly-affected animal

Characteristics:

- It shows the symptoms for the first time.
- Young or adult animal.
- Generally, only itching, without lesions. Sometimes, sporadic short-lived diarrhoea.
- Check the current and the past months diet and its quality (amount of cereals, synthetic additives, etc.).
- Check vaccines and parasites.
- Optional: food allergy tests (we can wait and see the evolution).

Therapeutic protocol in newly-affected animals

For 1 month:

- **Histamin Control + GlutaVet:** 1 pill / 10 kg of weight, 2 times/day.
- **Change the diet** for one of these options:
 - Hypoallergenic food.
 - Natural elimination diet: the recommendations in Vicent's book (2016) may be followed.
 - A single protein source: beef, turkey, rabbit, chicken, fish. 20 g/kg of weight, in 2 meals.
 - Boiled or steamed vegetables may be added. It may eat all the fruit that it wants or likes between meals
 - Dogs: reintroduce carbohydrates gradually (e.g. potato) after 2 weeks, avoid cereals.

It is a transitional, but not a complete diet. The goal is to repair the intestinal mucosa and to try to detect the trigger of allergy. So, ideally, we will try not to use NSAIDs nor inhibitors of the allergic reactions with the aim of trying not to inhibit the symptoms of the inflammatory reactions and not producing confusing results.

Evolution

Depending on the chosen diet, check the evolution 30-45 days later:

- Hypoallergenic food: if there is an improvement, keep it for 2 months at least. Try to return to the normal food gradually. If the symptoms appear again, return to the hypoallergenic food or the natural diet permanently.
- Natural elimination diet: if there is an improvement, begin to add another kind of meat, offal and raw bones.

In this case (newly-affected animal) it is normally not necessary to improve the gut microbiota nor treat the permeability problem intensely, except in more complex cases in which the animal has been treated intensely with NSAIDs.

Werner Ulrich

Veterinarian - wernerul@gmail.com

Graduated in Veterinary Medicine from the University of Cordoba in 1975. He has worked in small animal clinical practice since then, after training in the Animal Medical Center of New York and in several private clinics in Germany. In the last 15 years, after questioning the conventional medical methodology partially, he has directed the clinical practice towards a more natural and less aggressive medicine.



Cristina Moncunill

PhD in Biomedicine - st.cristina@stangest.com

Graduated in Biology from the University of Barcelona in 2011. She took PhD studies at the Bellvitge Campus, in Barcelona, together with stays at the CECAD, in Germany. She currently works as Product Manager at Stangest, applying her expertise in physiology to improve the health of pets.



Chronic patient

Characteristics:

- Intense itching. Hives. Bad-looking skin and coat (it already denotes nutritional deficiencies). On many occasions, different lesions are seen.
- It has been treated several times with conventional symptomatic therapy, and it improves with it, but the animal relapses after suspending it, sometimes immediately and sometimes after some months.
- There can be digestive disorders with flatulence and with or without diarrhoea.
- Several hypoallergenic foods have been tried. When there is a relapse, there is a tendency to change the food brand.
- The therapy has been changed (prednisone, cyclosporine, oclacitinib, etc.), and frequently the patient has been treated by many veterinarians.

Supporting diagnostic tests:

- If they have not been carried out yet, we can resort to a blood antibodies test. In some cases, desensitising vaccines have been used after identifying some allergens, but the therapy has been discontinued due to several reasons (cost, adverse reactions that have needed a therapy with corticoids, etc.).
- Thyroid gland test.
- Biopsies.

Tests for *Candida*

The intestinal permeability is a problem that appears in a severe form in chronic patients, and it is generally accompanied by an important alteration of the gut microbiota. The treatment of chronically allergic animals causes intestinal dysbiosis, that can facilitate the proliferation of *Candida*. Therefore, it is recommendable to make a stool test to ascertain the presence of this pathogenic mould.

Pathological consequences of the presence of *Candida*

- Production of histamine → they favour allergy.
- Consumption of vitamin B6 → they cause a deficit.
- Secretion of neurotoxic substances → tiredness and anxiety.
- Zinc deficit → drop in the activity of the macrophages against *Candida*.
- Imbalance of the gut microbiota.

How to fight *Candida*?

- **Diet:** avoid the nutrients that may be used by *Candida* for its proliferation: carbohydrates, fermented products, sulfur amino acids, etc.

- **Antifungal medication:** **Dermovital Omega 3-6-9** and **Biotin B Complex** contain biotin, that acts by inhibiting the growth of *Candida* from its yeast to its pathogenic mould form.

- **Repopulation of the gut microbiota:** such as **Floravet Complex**, at high doses.

Therapeutic protocol in chronic patients

For 45 days:

- **Histamin Control + GlutaVet:** 1 pill / 10 kg of weight, 2 times per day. If the itching is very intense, the dose of **Histamin Control** can be doubled during the first 10 days and then reduce it to the maintenance dose.
- **Natural elimination diet** exclusively. The possibilities of providing commercial diets have already come to an end.
- **Floravet Complex**, a symbiotic based on prebiotics and probiotics. 1 envelope per day.
- Try to **remove, progressively** the previous therapy (immunosuppressants, anti-inflammatory drugs) that does not work fully or that the client does not wish to keep using due to the side effects that it causes and the cost that they entail.
 - If the itching is intense, return, temporarily, to prednisone at the minimum effective dose (start with 0.25 mg/kg of weight, 1-2 times per day –test out–) for 1 week or 10 days while the animal starts to eat the natural diet. It is better if we can administer the dose every other day. After 10-20 days discontinue it gradually.
- If flatulence or short-lived sporadic diarrhoea are seen, make an exocrine pancreatic function test and start a therapy with pancreatic enzymes (**EnziVet**), mixed with food.

Evolution

Once an improvement is seen, if it persists, the administering of the aforementioned supplements can be discontinued gradually, based on the veterinarian's opinion, and start the:

- Supplementation with fatty acids, such as **Dermovital Omega 3-6-9** or **KrillVet**, krill oil that is very rich in omega-3 fatty acids. They can be administered from the beginning, but their absorption will be optimal when the intestinal villi have been repaired. In the case of cats or of small animals, fatty acids can be administered in liquid form: **Dermovital gots**.

Keep the **natural diet** and then add offal and raw bones of the same animal species before changing to another species. If there is a relapse, repeat the tests for *Candida* and the treatment against it: **Dermovital Omega 3-6-9** or **Biotin B Complex**.

References

- Day, M. et al., 2013a. Expert Views from a Roundtable on Canine Allergic Disease.
- Day, M. et al., 2013b. Expert Views from a Roundtable on Canine Allergic Disease Itchy Dogs – Part 2 Building a Clinical Toolbox for Treating Allergic Patients.
- Hensel, P. et al., 2015. Canine atopic dermatitis: detailed guidelines for diagnosis and allergen identification. *BMC Veterinary Research*, 11, p.196.
- Marsella, R. et al., 2012. Current understanding of the pathophysiologic mechanisms of canine atopic dermatitis. *Journal of the American Veterinary Medical Association*, 241(2), pp.194–207.
- Saridomichelakis, M.N. & Olivry, T., 2016. An update on the treatment of canine atopic dermatitis. *The Veterinary Journal*, 207, pp.29–37.
- Vicent, Verónica, 2016. *Dieta BARF para perros*. CreateSpace Independent Publishing Platform.



DIGESTIVE

Floravet Complex /
GlutaVet / EnziVet



COAT AND SKIN

Dermovital Omega 3-6-9 /
Dermatological shampoos



ALLERGIES

Histamín Control /
KrillVet

To obtain more information

Video
<http://bit.ly/2uqAQ1h>



Experiences
<http://bit.ly/2twJ7UL>

