

**Allergy:**

**With regard to the immunologic mechanisms associated with the allergic reaction, which cell type plays the most significant role in allergy?**

T. Lymphocytes are the immune cell that regulate almost all immunologic responses. The Langerhans's cells survey the environment in the epidermis and process antigens for the T. Lymphocytes. The T-cells then produce specific cytokines depending on the immune response which is most appropriate for the given antigen based on the antigenic protein, the route of exposure (percutaneous vs. subcutaneous vs. intravenous), and the relative dose of the antigen. The cytokines that are produced then signal all of the subsequent cell types to respond by infiltrating the tissue and producing their signature cell products which produce the actual changes in the tissue which we can recognize clinically.

With allergy, T. Lymphocytes (TH2 cells) produce cytokines that attract mast cells and eosinophils which then amplify the allergic signal and produce inflammatory mediators. These cause vasodilatation, vessel leakage, stimulation of the nerves, and alterations in normal skin function (sweat glands, sebum, etc). When the dog comes into the exam room, we recognize these changes as erythema, edema or urticaria, pruritus, and our favorite secondary folliculitis or yeast dermatitis.

**What role does the Mast cell play questions?**

Mast cells are actually not very smart. They have limited ability to recognize or process antigens and pretty much respond to signals from other cells. Basically, mast cells act like giant megaphones amplifying the message that they receive then blasting the tissue with inflammatory mediators.

**Why to certain allergic diseases (Pollen allergy, food allergy, scabies) have similar clinical patterns? Specifically, why do these diseases affect the ear pinnae, face, feet, and axilla?**

**(Hint: Which cell type is predominantly distributed in these regions of the skin?)**

Since mast cells are the most significant amplifying cell in the allergic response, wherever mast cells tend to congregate will be the areas or skin regions where symptoms develop. In the dog the areas around the ear, mouth, feet, and axilla have more mast cells. Therefore, if an allergen is inhaled or absorbed and has a general affect on the entire body, the face, ears, feet, and axilla will receive the majority of the mast cell's inflammatory mediators and have the most dramatic symptoms. This is why atopy, food allergy, and scabies can look exactly alike with lesions ranging from very mild (almost subclinical) to severe total body wipe out.

**What changes take place in the epidermis and immune system that allow secondary infections to be so common in patients with allergic dermatitis? Specifically why do most dogs with allergies have secondary bacterial pyoderma or Malassezia dermatitis?**

1. Sebum - alterations in the production and chemical makeup decrease its antimicrobial efficacy.
2. Moisture - changes in the amount of glandular secretions and chemical makeup increase skin moisture and decrease its antimicrobial effects. Additionally the dog's licking and chewing increases the moisture of the skin surface.
3. Adhesion - changes in the actual keratinocytes of allergic individuals promote the adhesion of organisms.
4. Crusts - the pruritus/itch induces skin damage which allows the formation of crusts which can serve as a source of nutrients for the organisms. Additionally, the damaged epidermis allows invasion.
5. T-lymphocyte (helper subtype 2) - is ineffectual at preventing or eliminating infections caused by bacteria or yeast. This T-cell response in fact promotes a hypersensitivity reaction to these organisms which worsens the clinical disease.
6. Pruritus - staph and yeast normally inhabit the oral cavity and the skin around the mouth and anus. The licking and chewing of the allergic dog spreads the organisms across the skin surface

## **How is otitis caused by allergies?**

For the same reason that the skin is predisposed to developing secondary infections, the ear canal is likewise affected. In fact the ear canal is basically a tube of skin that is closed off at 1 end (with the tympanic membrane) and open at the other. All of the changes that occur in the skin caused by the inflammatory mediators of the allergic response can be amplified by this tube effect and create an almost perfect culture media with an incubator environment. Perfect for Staph or yeast...

## **How do the following drugs work to treat allergies?**

**(What is the mechanism of action and the cell that is targeted by each drug?)**

### **Steroids**

### **Antihistamines**

### **Hyposensitization vaccine**

### **Staphage lysate**

### **Cyclosporine**

Steroids affect almost every aspect of the immune system which accounts for its superb efficacy in reducing inflammation and controlling the symptoms of allergy. However, every other cell in the body is also affected by steroids due to its very imprecise targeting. These effects on the other (non immune system cells) tissues create the adverse symptoms which limits the usefulness of this medication. There is no other drug that has such a broad spectrum of anti-inflammatory activity but likewise there is no other drug that has such a broad spectrum of adverse tissue effects.

Antihistamines work by targeting the histamine receptors and blocking the response that is associated with the activation of these receptors. Therefore the effects of histamine on the vessels and nerves is blocked (no vasodilatation, erythema, edema, pruritus, etc). Unfortunately histamine is only one of the many inflammatory mediators and antihistamines do very little for the prostaglandins, leukotrienes, proteases, etc. Therefore the allergic symptoms are reduced by antihistamines but not completely eliminated.

Hyposensitization vaccine is somewhat of an unknown therapy with regard to its mechanism. The latest theory and research indicates that the desensitization vaccine pushes the immune response away from the TH 2 reaction and towards a more normal TH 1 lymphocyte response. With this comes the gradual down regulation of the allergic response as the T. Helper 2 cells are reduced in their activity and number. The vaccine is able to achieve this results by altering the route of antigen administration and the relative dose. The body responds differently to the relatively high dose of antigen injected into the deeper tissues and promotes tolerance.

Staphage lysate is believed to work in a similar manner to the desensitization vaccine. The staphage lysate likely pushes the immune response away from the T-helper 2 lymphocyte reaction.

Cyclosporine is probably the most specific - well targeted immune modulating medication that we have. Cyclosporine targets the calcineurin in the T-lymphocytes and inhibits their activity. If the allergic T-helper 2 lymphocytes are effectively deactivated then the allergic response grinds to halt. Since cyclosporine only affects the T-cells there are very few side effects with this drug but these benefits are not cheap. Currently, it costs approximately \$100 a month to treat a cocker spaniel size dog. Needless to say if we have a big Labrador we quickly become priced out of this therapy.