Allergic skin diseases is considered as an “umbrella term” which includes three main clinical entities:

- atopic dermatitis,
- urticaria/angioedema and
- allergic contact dermatitis.

Cutaneous findings are also seen during the course of adverse drug reactions, insect allergy and food hypersensitivity. However, here we will focus on main dermatoallergic diseases.

**Atopic Dermatitis (AD):**

AD is a chronically relapsing inflammatory pruritic skin disease that may be regarded as the dermatologic manifestation of atopic diathesis. It is commonly associated with allergic rhinitis and/or allergic bronchial asthma.

There are a number of studies reporting an increasing prevalence of AD. It is an important problem especially in developed countries. AD begins before the age of 5 years in almost 85% of cases. The patient’s age, psychological status, associated respiratory allergies, nature and stages of skin lesions (acute, subacute, chronic) and intensity of AD should be considered and therapeutic management should be individually tailored.

That patients’ education is one of the indispensable parts of therapy must always be kept in mind. AD patients should avoid triggering factors (sweating, food and inhalant allergens, infections etc.) and
irritants (wool and synthetic clothing, soaps and irritating skin care products, hot water etc.).

Therapeutic approaches in AD is outlined below:

1. Topical treatment
   - Skin hydration and emollient use:
     This is the basic therapy for AD patients. Dryness of the skin and dysfunction of the cutaneous barrier system cause transepidermal water loss, and result in inflammation and pruritus. Emollients / moisturizers (creams or ointments) should be applied within 3 minutes after bathing to retain hydration.
   - Topical corticosteroids (TCS):
     Topical corticosteroids are the mainstay of acute AD flare-up therapy. They may be used in all stages of AD.
   - Topical calcineurin inhibitors (TCI):
     Pimecrolimus and tacrolimus are anti-inflammatory molecules which are effective in AD with a good safety profile. Transient burning sensation is the most frequently observed side effect. The use of TCI in children younger than 2 years is currently not recommended.
   - Topical antimicrobial agents:
     Fusidic acid and mupirocin might be used in order to eradicate S. aureus for infected lesions of AD. Since long-term treatment may cause development of resistant strains, topical antibiotics should be applied for only 10-14 days.

2. Systemic treatment
   - Systemic corticosteroids:
     Long-term oral therapy should be avoided because of serious side effects. A Short course of systemic corticosteroid therapy may be considered in acute exacerbations.
   - Systemic antibiotics:
     Systemic antibiotics should be used for generalized bacterial secondary cutaneous infections in AD for about 10 days. Maintenance therapy for prolonged periods may result in colonization of methicillin-resistant S aureus.
• Antihistamines:
The therapeutic value of antihistamines are very limited in AD. First generation antihistamines may bring some benefit with their sedative effect. Long-term treatment with cetirizine of infants with AD might help to reduce the duration and the amount of TCS used.

• Cyclosporine A:
Cyclosporine A was found to be effective in AD. However its use should be limited to severe, treatment-resistant cases because of possible side effects.

• Immunosuppressive agents (azathioprine, methotrexate):
They may be effective in severe cases.

• Omalizumab:
Anti-IgE may be a reasonable alternative in severe refractory AD cases with high IgE levels.

3. Phototherapy:
Acute AD flares may respond to phototherapy. Narrow-band UVB (311-313 nm), UVA (320-400 nm), UVA-1 (340-400 nm), PUVA or bath-PUVA therapy are the commonly accepted ones. TCS may be combined with these modalities. Phototherapy shouldn’t be used in children younger than 12 years.

4. Allergen-specific immunotherapy (IT):
IT in AD is controversial. A recent multi-center, randomized trial which investigated the efficacy of house dust mite immunotherapy in cases with AD revealed a dose-dependent improvement and reduced the need for TCS.

A stepwise therapeutic management based on the intensity of the disease seems reasonable in AD:

• Mild AD or only dry skin: Skin hydration, emollients / moisturizers, avoidance of irritants, elimination of triggering factors.

• Mild to moderate AD: In addition to the general supportive measures outlined above, low-mid potency TCS and / or TCI
- Moderate to severe AD: Mid-high potency TCS and/or TCI
- Recalcitrant, severe AD: Systemic therapy and phototherapy.

Use of probiotics (Lactobacillus GG) in primary prevention of AD is still a matter of debate.

Urticaria / Angioedema:
While urticaria is characterized by itchy wheals, painful or non-pruritic swelling of the subcutaneous and submucosal tissues are defined as angioedema. It seems reasonable to use “urticaria” as a wide term of a disease spectrum ranging from localized urticarial wheals to severe angioedema.

Recent classification of urticaria according to the EAACI/GA2LEN/EDF guideline is shown below:
1. Spontaneous urticaria: Acute urticaria, chronic urticaria (CU)
2. Physical urticaria: Cold contact urticaria, delayed pressure urticaria, heat contact urticaria, solar urticaria, dermographic urticaria (symptomatic dermographism), vibratory urticaria/angioedema
3. Other urticaria disorders: Aquagenic urticaria, cholinergic urticaria, contact urticaria, exercise-induced urticaria/anaphylaxis

Even if “urticaria / angioedema” is usually evaluated under the main title of “allergic skin diseases”, allergic factors may play causative role in some cases of acute urticaria.
The role of food, drug, latex and contact allergens are very limited in chronic urticaria.
The lifetime prevalence of acute urticaria is 15-20%.

In most cases, underlying factors (drug, infections etc.) are recognized, and therapeutic management with oral antihistamines is satisfactory.
However, short-course of oral corticosteroid therapy should always be considered in moderate to severe cases with acute urticaria.

Chronic urticaria, defined as the occurrence of wheals for a minimum of 6 weeks, is an extremely disabling condition and it is associated with angioedema in almost 50% of patients. Anti-FcεRI or anti-IgE autoantibodies have been detected in a subgroup (30-50%) of chronic idiopathic urticaria (CIU) which is called as “chronic autoimmune urticaria” (COU).

In addition, about one-fifth of CU patients is associated with thyroid autoimmunity.

In general, cases of COU are more resistant to therapeutic approaches. CU is triggered by multiple factors including infections /infestations, autoreactivity, non-allergic hypersensitivity (non-steroid anti-inflammatory drugs: NSAIDs, food additives) and malignity on the basis of a genetic predisposition.

The first and most important step in therapeutic management in all urticaria cases is to obtain a detailed history regarding possible triggering and etiologic factors.

Following items should be investigated meticulously:

- Time of onset
- Frequency, duration and diurnal variation of wheals
- Shape, size, colour and distribution of wheals
- Appearance and colour of lesional areas after resolution of urticarial plaques (hyperpigmentation or purpuric changes ⇒ vasculitis ?)
- Associated angioedema
- Associated symptoms: Itching, burning, pain
- Family history of atopy
- Importance of physical factors in the appearance of lesions: Cold, heat, mechanical traumas, pressure, vibration, water, ultraviolet light etc.
- Triggering factors: Food, insect sting, emotion etc.
• Use of drugs: Non-steroid anti-inflammatory drugs, hormones, alternative remedies etc.
• Associated systemic symptoms: Fever, weight loss, fatigue, abdominal pain, lymphadenopathy etc.
• Associated other diseases, infections and infestations
• Occupation and hobbies

Treatment of CIU is a difficult task which requires close patient-physician collaboration. Avoidance of known eliciting stimuli (drugs, stress, parasites, helicobacter pylori etc.) brings benefit in all cases.

However, it is impossible to find any triggering factor or underlying disease in most patients. Cases of COU should be more closely examined and followed. Second-generation H1 receptor antagonists are still the mainstay of therapy. Step-wise algorithmic approach will be reasonable in the treatment of CU:

1. Second generation antihistamines
2. First generation antihistamines or doxepin can be added, or the dose of second generation agents are increased
3. Short-term oral corticosteroid therapy may be added
4. Second generation antihistamines + anti-leukotrienes
5. Thyroxine can be considered if there is evidence of thyroid autoimmunity
6. Cyclosporin A
7. Other therapies: Sulfasalazine, dapsone, colchicine, IVIG, plasmapheresis, methotrexate, warfarin, mycophenolate mofetil, tacrolimus

Physical urticaria is not defined as “chronic urticaria” in the light of the recent classification.

Avoidance of physical stimuli is the basic rule in the therapeutic management.

However, some cases of physical urticaria (delayed pressure urticaria, cold urticaria etc.) are resistant to standard antihistamine therapy.
The most important and frequently encountered physical urticarias are reviewed below.

- **Dermographic urticaria:**
  Dermographic urticaria or its severe form, symptomatic dermographism (SD) is characterized by an exaggerated response (itching associated with burning) to a minor stroking, rubbing or scratching.
  It may respond to second generation antihistamines or ketotifen. In resistant cases, the antihistamine dose may be increased.
  SD is a distressing disease; even light pressure or rubbing from clothes, the movement of collars or cuffs may provoke urticarial reactions.
  Although it is defined as an “idiopathic” disease in most textbooks, we documented a close temporal relationship between SD and psychic factors, drug reactions and scabies

- **Delayed pressure urticaria (DPU):**
  Typical lesions of DPU are deep, painful swellings developing 2-6 hours after exposure to a pressure. Carrying a heavy bag by a strap on the shoulder, wearing tight belt or tight shoes may provoke DPU. It is an important occupational problem for manual workers. Almost one-third of patients with CIU has been shown to be associated with DPU. DPU poorly respond to treatment approaches.
  Second generation antihistamines may be tried, but they are usually ineffective.
  Anti-leukotrienes may be added to antihistamines. Oral corticosteroids may be effective in high doses, however their long-term use should be avoided because of well-known side effects. Promising results have been obtained with dapsone and sulfasalazine. IVIG and etanercept may be tried in resistant cases.
  We obtained the best result with sulfasalazine in a DPU patient unresponsive to high dose oral antihistamines, anti-leukotrienes and oral corticosteroids (personal observation)
Acquired cold urticaria (ACU):
ACU is defined as immediate urticarial reaction to cold. Systemic symptoms ranging from headache, wheezing and visual disturbance to anaphylactic shock with angioedema may develop in some patients following widespread cold exposure (for example, during aquatic activities).
Patients should avoid exposure to cold and abrupt transitions from warm to cold as well. Most patients with ACU respond to high dose antihistamines, up to four times the daily recommended dose. Anti-leukotrienes may be added to antihistamines.
In some patients, antibiotic therapy might be considered, even if there is no underlying infection.
Systemic corticosteroids, cyclosporin A and anti-IgE should be considered in resistant cases.

Allergic Contact Dermatitis:
Allergic contact dermatitis (ACD), a delayed-type hypersensitivity reaction to allergens, is one of the most common skin diseases with a great socio-economic impact.
Elimination of the contact allergen and cross-reacting substances is the basic rule in the treatment of ACD. However, avoidance may not be easy, especially in occupational ACD.

Therapeutic agents and methods available for ACD are outlined below:
- Topical agents: Corticosteroids, antimicrobials, emollients / moisturizers, barrier creams, immunomodulators (TCI: pimecrolimus, tacrolimus)
- Systemic agents: Corticosteroids, antibiotics, cyclosporin A, azathioprine
- Phototherapy

Topical corticosteroids are the mainstay of therapy in ACD.
Basic principles of dermatologic therapy is valid for ACD, AD and all other eczematous lesions: While corticosteroid lotions and creams are
chosen in acute eczematous stage, ointments are used in chronic phase.

The potency of topical corticosteroids and localization of lesions (face, trunk, palm etc.) should also be considered. In general, it is reasonable to use high potency corticosteroids initially and switch to less potent ones as the disease improves.

Tacrolimus and pimecrolimus have been found to be effective in the treatment of nickel-induced ACD. A multicenter, randomized, vehicle controlled, 3-week study with pimecrolimus cream, twice daily with overnight occlusion was also effective in the treatment for chronic hand dermatitis. Systemic corticosteroids may be used in acute stage of ACD. Their use should be confined to severe, resistant and/or widespread cases. A short course of oral antibiotic therapy is very effective in secondarily infected ACD. Cyclosporin A and azathioprine may be tried in resistant cases. Ultraviolet radiation; PUVA, UVB and bath-PUVA may bring benefit in generalized ACD, or in cases of unresponsive to standard therapeutic approaches. UV therapy should be individually tailored and be managed by physicians experienced in phototherapy.

REFERENCES: