

A REVIEW ON ATOPIC DERMATITIS**Bhawna Malik***

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Corresponding Author*Dr. Bhawna Malik**Student Mission Chowk
Sonipat Haryana India.**1 INTRODUCTION****1.1 Skin**

Skin is the outer covering of the human body. Skin is one of the largest organs. Which establish 16% of the human body weight. Weight around 5kgs and cover about 2square meter area. It is a tissue in our body that duplicates the most and fastest.^[1] Skin is the layer of usually soft, flexible, outer tissue covering the body of a vertebrate animal. Your skin, along with your hair, nails, oil glands and sweat glands, is part of the integumentary system. "Integumentary" means a body's outer covering.^[2] Your skin have different thickness, colour, and

texture all over your body. For example- our head contains more hair follicles than anywhere else. But soles of our feet have none. In fact, soles of our feet and palms of hand are thicker than skin on the other areas of your body. And the thinnest skin of the human body is around eyes (eyelids and the skin under the eyes). It protects our internal organs from the environment using a multi-layered system of cushioning, a cellular barrier, and protective oils. Skin is more than just a protective barrier between our insides and the environment – it also plays an active role in maintaining our health, such as regulating body temperature by sweating when we're hot. It can also produce Vitamin D, which is important for the health of our bones, from sunlight. The skin1 is one of the largest organs in the body in surface area and weight. The skin consists of two layers: the epidermis and the dermis. Beneath the dermis lies the hypodermis or subcutaneous fatty tissue. The skin has three main functions: protection, regulation and sensation. Wounding affects all the functions of the skin. The primary function of the skin is to act as a barrier. The skin provides protection from: mechanical impacts and pressure, variations in temperature, micro-organisms, radiation and chemicals. The skin regulates several aspects of physiology, including: body temperature via sweat and hair, and changes in peripheral circulation and fluid balance via sweat. It also acts as a reservoir for the synthesis of Vitamin D. The skin contains an extensive network of nerve

cells that detect and relay changes in the environment. There are separate receptors for heat, cold, touch, and pain. Damage to these nerve cells is known as neuropathy, which results in a loss of sensation in the affected areas. Patients with neuropathy may not feel pain when they suffer injury, increasing the risk of severe wounding or the worsening of an existing wound.^[3]

Diagram of skin



Fig. no. 1.1: Skin surface.^[4]

Table 1.1 Function of skin.^[5]

Skin act as a protective barrier	The skin keeps bacteria and germs from entering your body and bloodstream and causing infections. It also protects against rain, sun and other elements.
Thermoregulation	Protect the body from cold or heat. Maintain a constant temperature. Achieved by alterations to the blood flow through the cutaneous vascular bed. The secretion, evaporation of sweat from the surface of the skin also help to cool the body.
Sensation	Skin is the “Sense of Touch” organ. It has receptor for touch, heat, cold, pain, pressure.
Secretion	It secretes sweat, oil, ear wax etc.
Chemical and immunological defence	The sweat, oil and waste of cutaneous glands contain the lactic acid and fatty acids which make the PH acidic to kill or slow down the growth of many bacteria and fungi.
Biochemical Reaction	In sunlight presence, Vitamin D called cholecalciferol is synthesised from a derivative of the steroid cholesterol in the skin. The liver converts cholecalciferol to calcidiol, which is then converted to calcitriol in kidneys. Vitamin D is essential for the absorption of calcium and phosphorus.
Colour	Melanin in the epidermis cells provide colour the skin.
Aids in diagnosis	Yellow colour of the skin indicate jaundice, pallor indicates anaemia, and shock etc. skin also reveals age of the person.
Healing of wounds	A great power of regeneration of the epidermis of skin helps in rapid healing of wounds.
Absorption	Skin absorb oil, fat-soluble vitamins, ointments etc. through the opening of sweat glands, hair follicles. If applied and rubbed.

1.1.1 Primary function of skin

1.1.2 Classification of skin (On the basis of characteristics)

Skin is classified according to: sebaceous secretion, hydration and sensitivity level. Thus, each type of skin will have its own characteristics and require different cares. The type of skin is determined by genetics, although it will also be affected by other factors and can change with time.

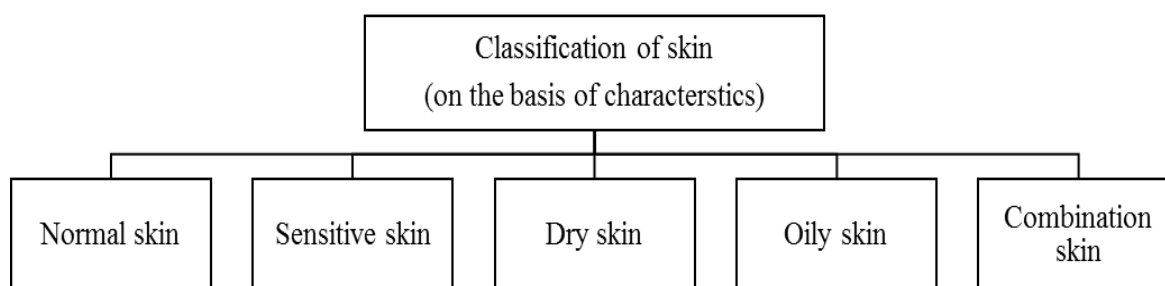


Fig. no. 1.2: Classification of skin.^[6]

Normal skin - This skin is neither too dry nor too oily. It has regular texture and a clean, soft appearance, and does not need special care.

Sensitive skin - Sensitive skin is more prone to react to stimuli to which normal skin has no reaction. It is a fragile skin, usually accompanied by feelings of discomfort, such as heat, tightness, redness or itching. This type of skin loses its barrier function, making it easy for microorganisms and irritant substances to enter it, and increasing the possibility of having an infection and allergic reactions. It is a delicate skin that needs more care to fight dryness, roughness and its usual appearance.

Dry skin - dry skin is caused by external factors such as the weather, low air humidity and immersion in hot water, and it is usually temporary. However, for some people it may occur more often and even be a lifelong condition. Since dry skin can crack leaving it more exposed to bacteria, although in general this is not serious, it may cause other skin disorders, such as eczema, or be more prone to infections if not properly managed. Dry skin signs and symptoms may vary depending on different factors such as age, health status or their cause. It is generally characterized by a feeling of tightness and roughness. It may also acquire an ashy grey colour, with occurrence of itching, redness and small cracks. Cracked skin is usually observed in very dry skin and presents small cracks, which, in more serious cases, may be deeper and even bleed.

Oily skin - Oily skin has a porous, humid and bright appearance. It is caused by excessive fat production by sebaceous glands, and usually determined by genetic or hormonal causes. It is frequent in adolescents and young people under 30 years old, and usually related with the occurrence of acne.

Combination skin - It is a characteristics of both dry and oily skin since the distribution of sebaceous and sweat glands is not homogeneous. The area with more oil is usually the forehead, nose, and chin, while the skin on the cheeks is normal or dry.

1.1.3 pH of skin

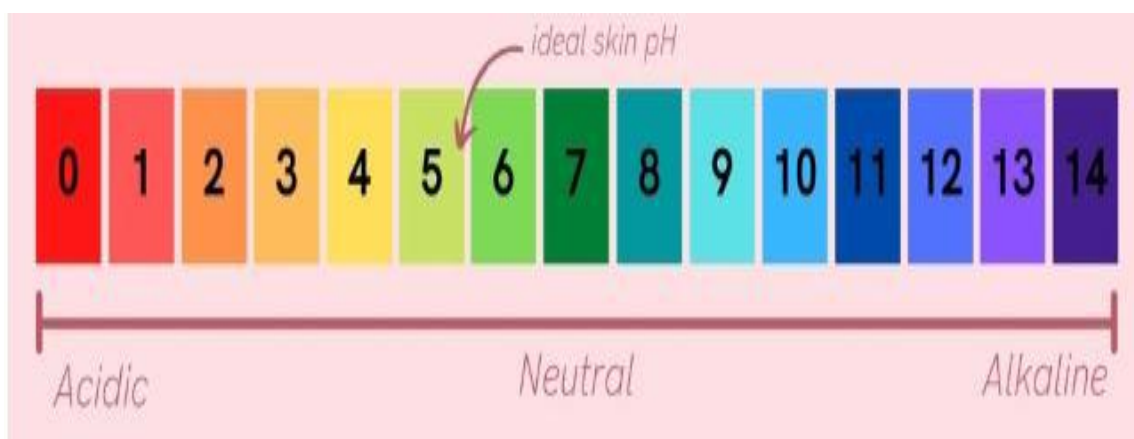


Fig. no. 1.3: pH of skin.^[8]

The ideal skin pH is between 5 and 5.5 for human, which is considered acidic. The skin's pH is constantly changing based on our diet, sleep, the products we are using, and environment you live in. Our skin type also plays a role in its pH. The pH of oily skin tends to range from 4 to 5.2, while the pH of dry skin is typically above 5.5. pH has a huge impact on our skin's barrier function, moisture retention, and microorganism environment. If our skin's pH is too alkaline (nine and above) the lipid layer of skin can be compromised, resulting in dryness and irritation. An acidic pH is optimal for proper hydration, and skin barrier function. Skin is protected by the acid mantle, a thin film on its surface composed of lipids from oil glands and amino acids from sweat that serves as a barrier, and a breakdown in this barrier leaves skin susceptible to inflammatory conditions, dehydration, and accelerated aging. An acidic pH helps keep our skin balanced, healthy, and radiant.^[7]

1.1.4 Skin structure

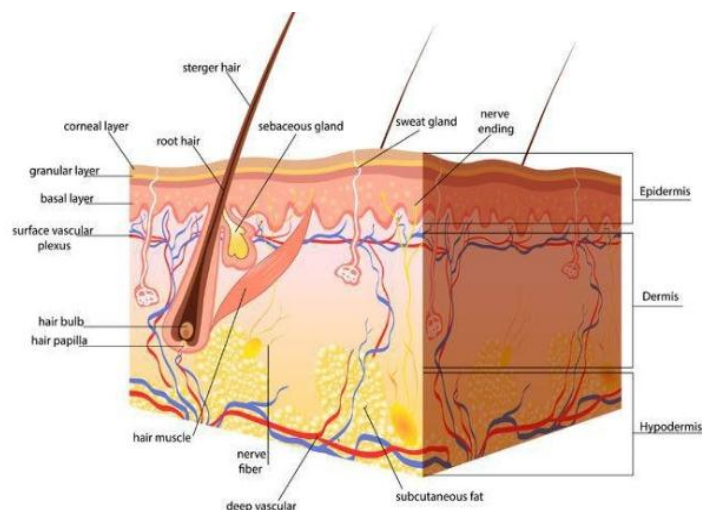


Fig. no. 1.4: Structure of skin. ^[9]

Layers of skin

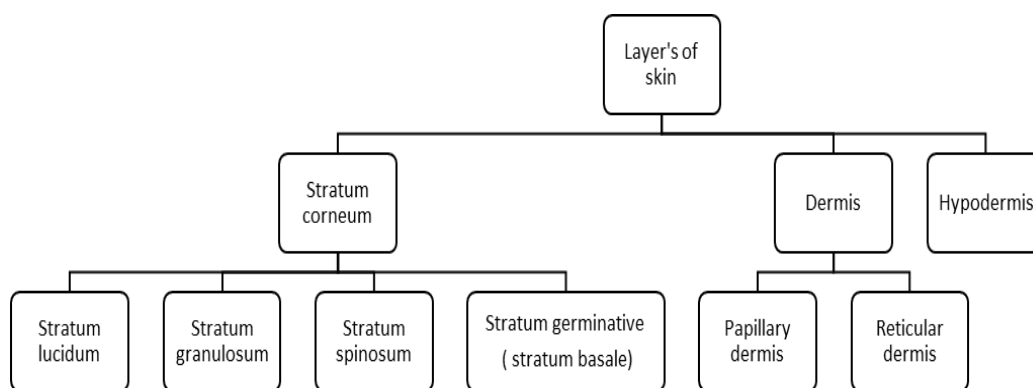


Fig. no. 1.5 layer of skin. ^[12]

Epidermis - It is the outermost layer of skin. It forms the waterproof, protective wrap over the body's surface. It contains no blood vessels.

Functions

- Give the skin its colour.
- To make new skin cells.
- Protect the body from the external environment.
- Epidermis contains no blood vessels.

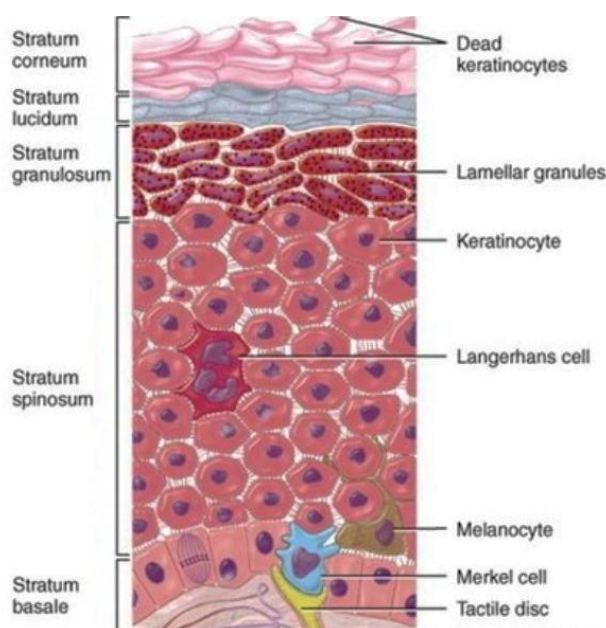


Fig. no. 1.6 epidermis layer.^[13]

Five layer of the epidermis^[10]

- Stratum corneum – It is the uppermost layer epidermis. It is consist of death cells.
- Stratum lucidum – It is the second layer of epidermis found in the only thick skin of the palm and soles.
- Stratum granulosum - Thin layer of cells in the epidermis lying above the stratum spinosum and help to form a waterproof barrier that functions to prevent fluid loss from the body.
- Stratum spinosum- It is a layer of the epidermis found between the stratum granulosum and stratum basal. This layer helps make your skin flexible and strong.
- Stratum Germinativum (stratum Basale) - It is the deepest layer epidermis. And contain keratinocytes, melanocytes, and merkel cells.

The epidermis has four main types of cells

1. **Keratinocytes (Skin cells)** – Originate in the stratum basal layer. It Produce keratin. Also regulate calcium absorption by the activation of cholesterol precursors by UVB light to form vitamin D.^[11]
2. **Melanocytes (Pigment-producing cells)** - Found in between of stratum Basale layer. Primarily produce melanin, which is responsible. For the pigment of the skin. Act as built-in sunscreen. Melanin produces during conversion of tyrosine to DOPA by enzyme tyrosine.^[11]

3. **Langerhans cells (Immune cells)**- Primarily found in the stratum spinosum layer. Play a significant role in antigen presentation. These cells express both MHCI and MHCII molecules, uptake antigens in skin and transfer to the lymph node.^[11]
4. **Merkel cells** – Found in stratum Basale .Found directly above the basement membrane. As the sensory receptor in the skin and make direct contact with sensory neurons of dermis. It Provide ‘sensation of Touch’.^[12]
5. **Dermis**- It is the thickest layer of the skin. It is made up of fibrous and elastic tissue. Thus, it provides strength and flexibility to the skin. The dermis consists of two layers: The papillary dermis, The reticular dermis.

Table 1.2: Difference between papillary Dermis and Reticular dermis.^[14]

<p>The papillary dermis – It is the more superficial of the two layers. It is relatively thin and is made up of loose connective tissue, which include: Capillaries, Collagen, Elastic fibres, Sensory neurons</p> <p>Function: It is important in temperature regulation. It can sense thing as heat, pressure.</p>	<p>The reticular dermis – It is the deeper and thicker layer of the dermis. It contains dense connective tissue, which include: Blood vessels, Fibroblast, Mast cells, Collagen fibres</p> <p>Function: It is providing structure and elasticity. It provide strengthen the skin.</p>
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Hypodermis layer^[15] –It is also called subcutaneous fascia. It is the deepest layer of skin and contains adipose lobules along with some skin appendages like the hair follicles, sensory neurons, and blood vessels. Its lies closet to muscle. It is made up of fat and connective tissue.

Functions

- Fat help to protect body from cold and absorb shock and damage to internal organs.
- This layer secrete hormone leptin. Which helps to regulate energy balance by inhibiting hunger.

1.2 Atopic dermatitis



Fig. no. 1.7: Atopic dermatitis.^[16]

It is a condition that causes one's skin to become dry, red, small bumps, itchy and rashes. Atopic dermatitis damage the skin barrier function loss of barrier function makes your skin more sensitive and more prone to infection and dryness. It is a pruritic inflammatory chronic condition that can come and go for years or throughout life.^[15] Eczema is a condition in which patches of skin become inflamed, itchy, cracked, and rough. Some types can also cause blisters. Many people use the word eczema when referring to atopic dermatitis, which is the most common type of eczema. The term atopic refers to a collection of conditions that involve the immune system. The word dermatitis refers to inflammation of the skin. Atopic dermatitis was described and named in 1933 by Fred Wise and Marion Sulzberger. Before 1933, however, the dermatological literature contained many clinical descriptions compatible with the modern diagnosis of atopic dermatitis. It has probably existed since antiquity many genes have been associated with atopic dermatitis, particularly genes encoding epidermal structural proteins and genes encoding key elements of the immune system. A recent and interesting genetic discovery is the documented strong association between atopic dermatitis and mutations in the filaggrin gene. The filaggrin gene is the strongest known genetic risk factor for atopic dermatitis. Around 10% of people from western populations carry mutations in the filaggrin gene, whereas around 50% of all patients with atopic dermatitis carry such mutations. Filaggrin gene mutations give rise to functional impairments in the filaggrin protein and thereby disrupt the skin barrier.

Infants^[17]

During infancy and up to 2 years of age, it is most common for a red rash, which may ooze when scratched, to appear on the: Face, Scalp, and Area of skin around joints that touch when the joint bends.



Fig. no. 1.8. Infant. S.^[18]

Childhood^[17]

During childhood, usually 2 years of age to puberty, it is most common for a red thickened rash, which may ooze or bleed when scratched, to appear on the: Elbows and knees, usually in the bend, Neck.



Fig. no. 1.9: Childhood.^[19]

Teens and Adults^[17]

During the teenage and adult years, it is most common for a red to dark brown scaly rash, which may bleed and crust when scratched, to appear on the: Hands, Neck, Elbows and knees, usually in the bend, Skin around the eyes, Ankles and feet.



Fig. no. 1.10: Teens and adults.^[20]

Other common skin features of atopic dermatitis include

An extra fold of skin under the eye. Darkening of the skin beneath the eyes. In addition, people with atopic dermatitis often have other conditions, such as:

- Allergies, including food allergies.
- Depression or anxiety.
- Sleep loss

Epidemiology

Atopic dermatitis is a common skin condition with significant associated social and financial burden. Atopic dermatitis affects adults and children with worldwide prevalence rates of 1-20%. International study of epidemiology and geographic variability in prevalence of Atopic dermatitis has been changed in different regions of the world. Nigeria, the United Kingdom and New Zealand had been areas of the highest prevalence; Latin America has emerged as a region of relatively high prevalence in follow up data. The prevalence of Atopic dermatitis seems to have reached a plateau around 20% in countries with the highest prevalence, suggesting that Atopic dermatitis may not be on a continued rise but that a finite number of individuals may be susceptible to the condition. Risk factors associated with increased prevalence include higher socioeconomic status, higher level of family education, smaller family size and urban environment.^[26]

1.2.1 Symptoms^[21]

- The rash often forms in the increase of your elbows or knees.
- Skin in areas where the rash appears may turn lighter or darker or get thicker.
- Small bumps may appear and leak fluid if you scratch them.
- Babies often get the rash on their scalp and cheeks.
- Dry skin
- Itching
- Thickened, cracked, scaly skin
- Raw, sensitive, swollen skin from scratching

1.2.2 Complications of atopic dermatitis it generally involve a worsening of Atopic dermatitis which may become widespread throughout the body and affect other organ systems. Thus, complications may lead to the development of new disease resulting from an Atopic dermatitis. Complication of atopic dermatitis may include:

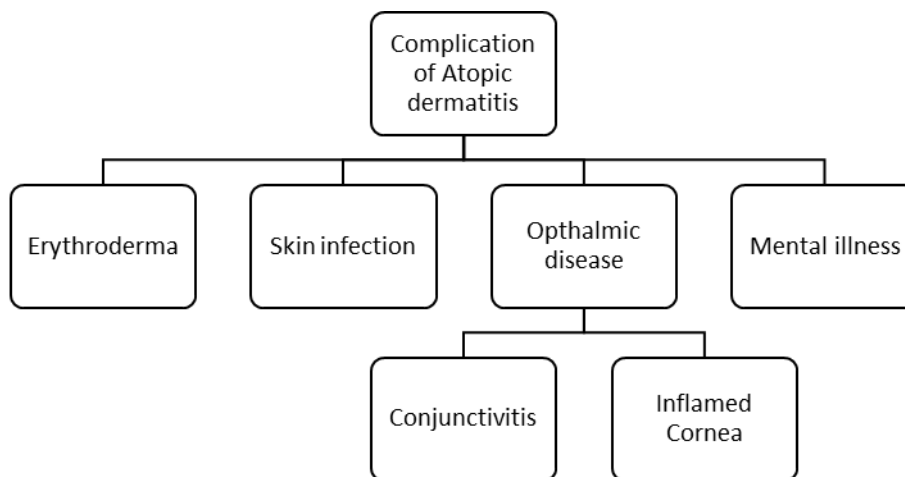


Fig. no. 1.10: Complication of atopic dermatitis.^[26]

Erythroderma

Erythroderma is a severe and potentially life-threatening inflammation of most of the body skin surface. It is an inflammatory skin disease with redness and scaling that affects nearly the entire cutaneous surface. This term applies when 90% or more of the skin is affected.



Fig. no. 1.11: Erythroderma.^[22]

Skin infection

Repeated scratching that breaks the skin can cause open sores and cracks. These increase the risk of infection from bacteria and viruses, including the herpes simplex virus.

Ophthalmic disease

Conjunctivitis (pink eye)

Inflammation or infection of the outer membrane of the eyeball and the inner eyelid. It covers the white part of the eyeball. Signs that you may have pink eye include: Pink (or red) colour to the eye, Watery, itchy eyes, Eyes sensitive to light, Wet, sticky or dry, crusty eyes



Fig. no. 1.12: Conjunctivitis.^[24]

Inflamed cornea (keratitis)

This eye disease occurs when the eye becomes infected or inflamed. Due to warning signs include your eyes feeling: Painful or uncomfortable, Sensitive to light, Gritty, Watery eyes.

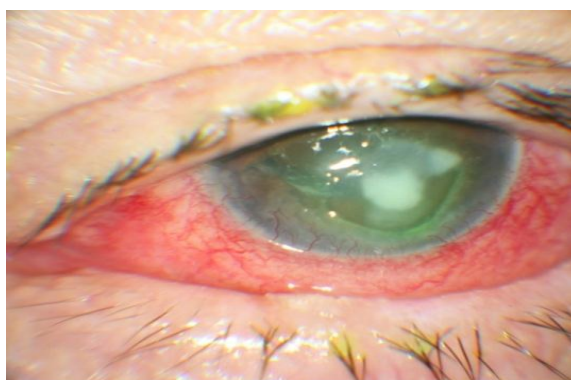


Fig. no. 1.13: Keratitis.^[25]

Mental illness- Adults with atopic dermatitis, or eczema, have significantly higher rates of anxiety and depression than those without dermatitis. Atopic dermatitis an inflammatory skin condition, may be linked to others forms of inflammation in the body that can affect your mental health.^[25]

1.2.3 Diagnosis

Severity of atopic dermatitis^[29]

A guide to visual assessment of Atopic dermatitis severity that also includes the evaluation of disease impact on quality of life and psychosocial well-being has been proposed as:

Mild – less than 5% body surface involved. Areas of dry skin, infrequent itching (with or without small areas of redness); little impact on everyday activities, sleep, and psychosocial well-being.

Moderate – 5-30% body surface involved. Areas of dry skin, frequent itching, redness (with or without excoriation and localized skin thickening), moderate impact on everyday activities and psychosocial well-being, frequently disturbed sleep.

Severe – More than 30% body surface involved.



Fig. no. 1.14: Redness.^[30]



Fig. no. 1.15: Swelling.^[31]



Fig. no. 1.16: Oozing.^[32]



Fig. no. 1.17: Scratch marks.^[33]



Fig. no. 1.18: Lichenification.^[34]



Fig. no. 1.19: Dryness.^[35]

Widespread areas of dry skin, incessant itching, redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking, and alteration of pigmentation); severe limitation of everyday activities and psychosocial functioning, nightly loss of sleep.

The diagnosis of Atopic Dermatitis is made clinically and based on historical feature, morphology (study of appearance, as cellular appearance, tissular appearance) and distribution of skin lesions (localized damage to the skin, like sunburn).

1.2.3.1 Scoring (SCORing Atopic dermatitis)^[46]

SCORAD is a clinical tool for assessing the severity of atopic dermatitis as objectively as possible.

Affected area (A) to determine extent, the sites affected by Atopic dermatitis are shaded on a drawing of a body. It is used to calculate the affected area (A) as a percentage of the whole body.

Head and neck 9%, Upper limbs 9% each, Lower limbs 18% each, anterior trunk 18%, Back 18%, Genitals 1%.

The score for each area is added up. The total affected area is 'A', which has a possible maximum of 100%.

Intensity (B) A representative area of eczema is selected. In this area, the intensity of each of the following signs is assessed as none (0), mild (1), moderate (2) or severe (3).

Redness, Swelling, Oozing/crusting, scratch marks, Skin thickening (lichenification), Dryness.

The intensity scores are added together to give 'B' (maximum 18).

Subjective symptoms(C) Subjective symptoms (itch and sleeplessness), are each scored by the patient or relative using a visual analogue scale where 0 is no itch (or no sleeplessness) and 10 is the worst imaginable itch (or sleeplessness). These scores are added to give 'C' (maximum 20).

Total score: The SCORAD for that individual is $A/5 + 7B/2 + C$

The maximum SCORAD score is 103.

Severity Scoring of Atopic Dermatitis index (SCORAD)

A: Extent (percentage of area involved)

Figures within parenthesis are used
For children under 2 years

B: Intensity

Criteria	Intensity	Means of Calculation
Erythema		Intensity items [average representative area]
Edema/papulation		0=Absence
Oozing/Crusting		1=mild
Excoriations		2=moderate
Lichenification		3=sever
Dryness*		*Dryness is evaluated on uninvolved skin

C: Subjective Symptoms (Pruritus and Sleep loss)

Visual analog scale (average for the last 3 Days or nights)

Pruritus (0-10) 0 10

Sleep Loss (0-10)

SCORAD : $A/5 + 7B/2 + C$

Fig. no. 1.20: SCORAD index.^[46]

1.2.3.2 EASI (Eczema Area and Severity index)^[37]

An EASI score is a tool used to measure the extent (area) and severity of Atopic dermatitis.

EASI score does not include a grade for dryness. Include only inflamed areas.

Body regions there are four body regions:

- **Head and Neck:** Face occupies 33% (17% each side), neck 33% (17% front and back) and scalp 33% of the head and neck region.
- **Trunk:** (Including genital area): Front occupies 55% and back 45% of the trunk
- **Upper limbs:** Each arm occupies 50% of the upper limbs region
- **Lower limbs** (Including buttocks): Each leg occupies 45% (front or back of one leg is 22.5%) and buttocks 10% of the lower limbs region.

Area score Area score is recorded for each of the four regions of the body. The area score is the percentage of skin affected by Atopic dermatitis for each body region.

Table no. 1.3: Area score.^[37]

Area score	Percentage of skin affected by atopic dermatitis in each region
0	0%
1	1-9%
2	10-29%
3	30-49%
4	50-69%
5	70-89%
6	90-100%

Severity score

Severity score is recorded for each of the four regions of the body. The severity score is the sum of the intensity scores for four signs. The four signs are: Redness, Swelling, Scratching, and Lichenification.

The intensity of each sign in each body region is assessed as: none (0), mild (1), moderate (2) and severe (3).

Table no. 1.4: Severity score.^[37]

Score	Intensity of redness, swelling, scratching, lichenification
0	None, absent
1	Mild
2	Moderate
3	Severe

Calculations

For each region, record the intensity for each of four signs and calculate the severity score.

Severity score = redness intensity + thickness intensity + scratching intensity + lichenification intensity

For each region, multiple the severity score by the area score and by a multiplier. The multiplier is different for each body site.

- Head and Neck: Severity score x area score x 0.1 (in children 0–7 years, x 0.2)
- Trunk: Severity score x area score x 0.3
- Upper limbs: Severity score x area score x 0.2
- Lower limbs: Severity score x area score x 0.4 (in children 0–7 years, x 0.3)

Table 1.5: Final EASI score.^[37]

Body region	Redness	Swelling	Scratching	lichenification	Severity score	Area score	Multiplier	Region score
Head/neck	–	+_	+_	+_	=_	X_	X 0.1(if ≤ 7 years, X 0.2)	=_
Trunk	–	+_	+_	+_	=_	X_	X 0.3	=_
Upper limbs	–	+_	+_	+_	=_	X_	X 0.2	=_
Lower limbs	–	+_	+_	+_	=_	X_	X 0.4(if ≤ 7 years, X 0.3)	=_
The final EASI score (0-72)								=_

Add up the total scores for each region to determine the final EASI score. The minimum EASI score is 0 and the maximum EASI score is 72.

1.2.3.3 Skin biopsy A skin biopsy is a procedure that removes a small sample of skin for testing. The skin sample is examine under a microscope to check for skin cancer, skin infections, or skin disorders determine whether Atopic dermatitis is present or if a different skin condition accounts for the rash. Biopsy results take three to seven days.

There are three main ways to do a skin biopsy

- A punch biopsy, which uses a special circular tool to remove the sample.
- A shave biopsy, which removes the sample with a razor blade
- An excisional biopsy, which removes the sample with small knife called a scalpel.



Fig. no. 1.21: Skin biopsy.^[38]

1.2.3.4 Skin prick test- Also called a puncture or scratch test, check for immediate allergic reactions to as many as 50 different substances at once. This test is usually done to identify allergies to pollen, mold, pet dander, dust mites and foods. In adults, the test is usually done on the forearm. Children may be tested on the upper back. Allergy skin tests aren't painful. This type of testing uses needles (lancets) that barely penetrate the skin's surface. After cleaning the test site with alcohol, the nurse draws small marks on your skin and applies a drop of allergen extract next to each mark. Then uses a lancet to prick the extracts into the skin's surface. A new lancet is used for each allergen.^[25]

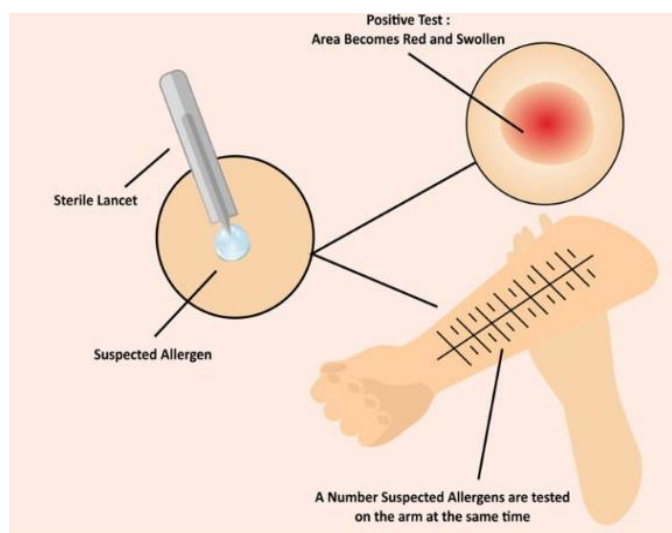


Fig. no. 1.22: Skin prick test.^[39]

1.2.4 Management of atopic dermatitis

Although there is no cure for atopic dermatitis. The doctor should have three Main goals in managing atopic dermatitis^[40]:

- Healing the skin and keeping it healthy.
- Preventing flares.

- Treating symptoms.

Management requires a multipronged approach that involves:^[41]

Patient education- It can be defined as the process of influencing patient behaviour and producing the changes in knowledge, attitudes and skills necessary to maintain or improve health. It is an important component of the management of atopic dermatitis. There was also a significant improvement in subjective assessment of severity, itching behaviour and emotional change.

Aeroallergens- Aeroallergens are various airborne substances or inhalants, such as pollens, spores, and other biological or non-biological airborne particles that can cause allergic disorders. So, keep surface in your home clean, clean dust mites. Ventilate your indoor areas well. Use air cleansers to clean indoor air.

Food allergens- An unpleasant or dangerous immune system reaction after a certain food is eaten. Approx. 50% of children with atopic dermatitis may have one or more food allergens. (Mainly food allergens have- cow milk, egg, wheat, peanut) Avoid food allergens by avoiding some food you are been allergen. Skin prick test is useful to find your food allergens.



Fig. no. 1.23: Common food aeroallergens.^[42]

Elimination of exacerbating factors- Exacerbating factors in atopic dermatitis that disrupt an already abnormal epidermal barrier include:

- Low humidity environments
- Manage stress and anxiety
- Dry skin

- Overheating of skin
- Exposure to detergents.

Avoiding these situations is helpful for acute flares as well as for long term management.

Hydration of the skin- Skin hydration is a key component of the overall management of patient with atopic dermatitis. Atopic dermatitis patient have dry skin as compare to normal skin. Bathing without moisturizer may compromise skin hydration. Bathing followed by moisturizer application provides modest hydration benefits. Moisturizers (are a good long-term solution)

- a. Lotion (lightest moisturizer)-
 - i. Water evaporates quickly.
 - ii. Lotion is not a best choice for AD.
 - iii. Example – CeraVe, cataphyll.
- b. Creams (semi-solid mixture)-
 - i. Daily moisturizing option for chronically dry skin.
 - ii. Example – Hydrocristine cream IP 1% w/w(cutisoft)
- c. Ointments (semi-solid mixture)-
 - i. Lower water content.
 - ii. Pure ointment is petroleum jelly
 - iii. Example - Aquaphor, Eucerin.

Plant derived products

1. Aloe vera gel – Aloe vera gel is a natural antibacterial moisturizer. Using aloe vera can hydrate the skin and may reduce the risk of Atopic Dermatitis becoming infected.
2. Coconut oil- Coconut oil is a safe and effective natural treatment for Atopic Dermatitis. It has antimicrobial properties, which make it effective at killing bacteria on skin. It also highly moisturizing and may reduce inflammation.
3. Ceramides- Ceramides restore skin water permeability and barrier function. Stratum corneum consist of a significantly high ceramide composition (50% from total lipids).
4. Ectoin- It is a natural compound found in high concentrations in microorganisms. It is a compatible solute which serves as a protective substance by acting as an osmolyte and thus helps organisms survive extreme osmotic stress. It used for the symptomatic treatment of AD. Ectoin dermatitis cream 7 % (EHK02) can build an ectoin hydro

complex on the skin providing: An effective protection against external stress factors. Stabilizing the skin barrier, moisturizing the dry skin.

Animal products

1. Lanolin (wool wax) - Sebaceous gland of sheep. Because of its high fat content. It prevents the evaporation of water from the skin. This keeps skin moisturized and helps the skin heal.^{[43][44]}
2. Horse oil-Horse oil is a by-product of horse meat. Horse oil is extracted from the fat of horses that are already farmed and processed for the purpose of meat consumption in countries throughout Europe and Asia. Folk ingredient used in the cosmetic industry. It shows antibacterial and anti-inflammatory property. It also keeps the skin moisturized and balance tone.^[45]

1.2.5 Pharmacological treatment

1.2.5.1 First line therapy - The initial or first treatment recommended for an Atopic dermatitis.

Topical moisturizers and bathing^[47]

1. Moisturizing has several key roles in treating the skin, including assisting in:
 - a. Repair of damaged skin barrier.
 - b. Maintaining skin hydration
 - c. Alleviating dry skin.
2. Patients with Atopic dermatitis should not over bath more than 5 to 10 minutes.
3. The water helps to eliminate allergens, sweat, and irritants.
4. Patients should avoid bathing with scented oils and fragrances.
5. Mild acid soaps are encouraged, scrubbing the skin is highly discouraged, and scrubbing the skin is highly discouraged and should be avoided.

Topical corticosteroids – Is used to treat inflammatory symptoms and signs of Atopic dermatitis including acute flares and itchiness. Topically corticosteroids are administered topically; however, successful administration depends upon obtaining an accurate diagnosis, choosing the correct drug, selecting the appropriate vehicle and potency, and the frequency of application. The vehicle selection depends on the region affected and the type of lesion present. It also functions to hydrate the skin and increase absorption.

Vehicle option include^[46]

- Ointments-Administered for thick lesions, the most potent vehicle.
Example – hydrocortisone valerate(0.02%), betamethasone dipropionate (0.05%)
- Creams- Less potent than ointment. Administration for acute inflammation and dermatitis.
Example- desonide (0.05%), colbestol propionate(0.05%)
- Lotions-Less greasy, work well in hair bearing regions.
Example – triamcinolone acetonide(0.1%)

1.2.5.2 Second line treatment –Also Known as subsequent treatment. Is a treatment come after the initial treatment

Antihistamine: It can reduced the serve itching, allergy caused by AD.

E.g. Diphenhydramine is an antihistamine used for pruritus and allergic reactions.

Oral Phosphodiesterase-4 (PDE-4) Inhibitors: An oral PDE-4 inhibitor is a nonsteroidal option for atopic dermatitis treatment. Example-Crisaborole topical (Eucrisa)

1.2.5.3 Third-line treatment when both initial treatment and subsequent treatment don't work.

Immunosuppressive and Anti-inflammatory agents- Long-term control of severe disease may require an immunosuppressive or anti-inflammatory agent. Such as:

- Methotrexate- It is an antimetabolite that inhibits dihydrofolate reductase, thereby hindering DNA synthesis and cell reproduction. Satisfactory response is seen 3-6 weeks following administration.
- Azathioprine- Azathioprine is an imidazolyl derivative of mercaptopurine.
It works by blocking the pathway for purine synthesis. The 6-thioguanine nucleotide metabolites mediate most of azathioprine's immunosuppressive and toxic effects.
- Cyclosporin –Cyclosporine has been demonstrated to be helpful in a variety of skin disorders.

It acts by inhibiting T-cell production of cytokines and ILs. Like tacrolimus and pimecrolimus (ascomycin), cyclosporine binds to macrophilin and then inhibits calcineurin, a calcium-dependent enzyme, which, in turn, inhibits phosphorylation of nuclear factor of activated T cells and inhibits transcription of cytokines, particularly IL-4.

Phototherapy – People with severe Atopic dermatitis may benefit from ultraviolet light therapy. Around 70% of Atopic dermatitis patient see an improvement after undergoing phototherapy. During phototherapy, doctor will shine UVB light on the affected area. The light helps reduce itchiness and inflammation, and the skin fight bacteria to prevent infection.



Fig. no. 1.24-photo therapy. [48]

Wet wrap therapy- After bathing and moisturizing, wrap wet strips of fibre or gauze around the affected areas. To this helps keep the skin hydrated and increase the action of medicated creams and moisturizers.

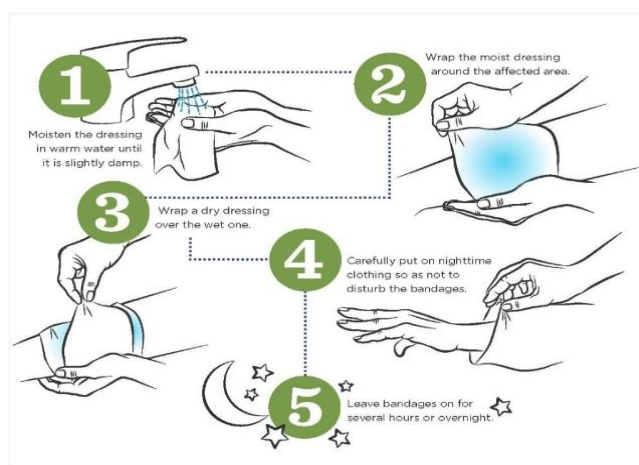


Fig. no. 1.25 wet wrap therapy. [49]

1.2.5.3 Advancement in treatment

Dupilumab^[50]– Is an injectable. Brand name – dupixent. Atopic dermatitis. It works by controlling the body inflammatory response. Dose - 300mg/2ml solution in a singled-dose. Medicine is given every 2 weeks as an injection. It also have a bioavailability of 64%, with the average concentration occurring one week after injection.

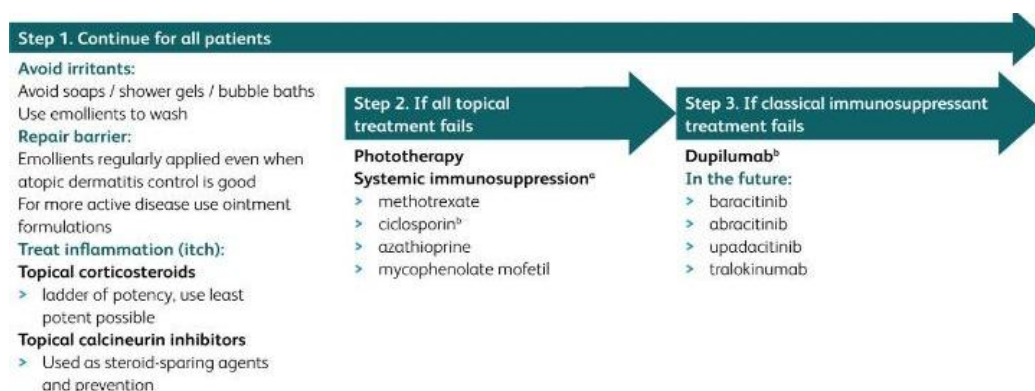


Fig. no. 1.26: Atopic dermatitis management.^[50]

Literature survey

- **Nutten et al (2015):** Improvement in the understanding of the interactions between the skin barrier, genetic and immunological factors. A better understanding of the key environmental risk factors that could be influenced, changed or modified is important for a better prevention of the disease.
- **Fennessy et al. (2000):** Atopic eczema is a common childhood disease, the prevalence of which seems to be increasing. Despite this relatively little is known of its epidemiology, particularly the social patterning of eczema during childhood, or its physical, psychological and social impact on children and their carers. that the atopic eczema during childhood may have more profound implications for the health and well being of children and their carers than is presently acknowledged by health care providers and public health policy. the majority of health service consultations for atopic eczema are within primary care. the bulk of care is provided in the home with relatively.
- **Teresita et al. (2020):** Atopic dermatitis is a chronic relapsing condition with a significant burden of disease, most commonly affecting the pediatric population. Atopic dermatitis patient. Knowledge and awareness of frequently associated conditions, whether in the realm of food allergies, contact allergies, or secondary infections, is paramount. In addition to the standard therapeutic armamentarium, the physician must also consider cultural practices and be knowledgeable of alternative therapeutic options. Referral to a specialist is recommended for recalcitrant cases of Atopic dermatitis, or when initiation of systemic immunosuppressive agents, phototherapy, or biologic agents is contemplated.
- **Park et al. (2019):** Wet wrap therapy with new garments could be easily done by parents. Wet wrap therapy may be effective and safe in controlling moderate-to-severe Atopic dermatitis in children.

- **Qian-Wen et al. (2019):** Atopic dermatitis is a disease resulting in significant somatic suffering and psychological disturbance. This meta-analysis identified that children and adolescents with Atopic dermatitis had higher risk of mental disorders compared to those without Atopic dermatitis. This review highlighted the importance of integrated, holistic, multidisciplinary management of pediatric Atopic dermatitis, which emphasizes the well-being of the whole person.
- **Afshari et al. (2016):** Atopic dermatitis is a disease that affects people from childhood and continues for a long term. Not only its annoying complications, but also sometimes the associated infections, necessitate different methods of treatment. In this review, several therapeutic strategies upon integrative medicine are introduced to provide the possibility to choose the desired treatment based on patient status including age, sex, lesion region and drug safety.
- **Sullivan et al. (2018):** An aloe vera can be effective for the treatment of eczema. It should be safe to use for most people. It is possible to mix aloe vera with another natural remedy, which may increase its effectiveness.
- **Maarouf et al. (2019):** The mechanism and effects of Dead Sea salt, hard water, commercial baby cleansers, oatmeal, rice, and natural oils as bathing additives for the treatment of atopic dermatitis. Bathing additives are useful adjuvant treatments for atopic dermatitis. Benefits of these compounds are derived from anti-inflammatory, antimicrobial, antioxidative, and skin barrier repair properties.

DISCUSSION

Marketed medicine

Table no. 1.6: Marketed medicine.^[51]

S. no.	Brand name	Drug	Type	Dose
1	Eucrisa	Crisaborole	ointment	Twice a daily
2	Elidel	Pimecrolimus	cream	Twice a daily
3	Aquaphor	Petroleum	ointment	Twice a daily
4	Dupixent	dupilumab	Injection	150mg/ml
5	lilly	baricitinib	Tablet	4 mg tablet once a day
6	protopic	tacrolimus	ointment	Twice a daily

Eucrisa belongs to a class of drugs called Phosphodiesterase-4 Inhibitors. It is not known if Eucrisa is safe and effective in children younger than 3 months of age. It is the first FDA (Food and Drug Administration)-approved topical prescription treatment for Atopic dermatitis in over a decade. Eucrisa contains (crisaborole) ointment, 2% (active ingredient)

and the following inactive ingredients: white petrolatum, propylene glycol, mono- and di-glycerides, paraffin, butylated hydroxytoluene, and edetate calcium disodium. It does not contain added fragrance. It is also PABA-free, paraben-free, and gluten-free.

Elidel Cream 10 gm belongs to a class of dermatological preparation called 'immunosuppressants' primarily used to prevent allergies including swelling, itching redness, heat and pain caused due to certain skin problems such as dermatitis (itchy, swelling of the skin) and eczema (itchy, cracked, swollen or rough skin). It is a prescription needed treatment. Each gram of Elidel Cream, 1% contains 10 mg of pimecrolimus in a whitish cream base of benzyl alcohol, cetyl alcohol, citric acid anhydrous, mono- and di-glycerides, oleyl alcohol, propylene glycol, sodium cetostearyl sulphate, sodium hydroxide, stearyl alcohol, triglycerides, and water.

Aquaphor medication is used as a moisturizer to treat or prevent dry, rough, scaly, itchy skin and minor skin irritations (such as diaper rash, skin burns from radiation therapy). Emollients are substances that soften and moisturize the skin and decrease itching and flaking. It is the over the counter drug. Active: Petrolatum (41%). Inactive: Mineral Oil, Ceresin, Lanolin Alcohol, Panthenol, Glycerin, Bisabolol.

Dupixent (dupilumab) is used to treat moderate-to-severe Atopic dermatitis that cannot be controlled with topical medicines applied to the skin. Dupixent is used for Atopic dermatitis in adults and children at least 6 years old. It is also used together with other medications to treat moderate-to-severe asthma that is not controlled with other asthma medicines. Dupixent is used only in adults to treat a condition called chronic rhinosinusitis (long-term sinus inflammation) that is associated with nasal polyps. Active ingredient: dupilumab Inactive ingredients: L-arginine hydrochloride, L-histidine, polysorbate 80, sodium acetate, sucrose, and water.

Baricitinib, sold under the brand name Olumiant. It is used to treat adults with moderately to severely active rheumatoid arthritis. It may be used as combination with methotrexate. It is indicated for the treatment of moderate to severe atopic dermatitis in adult patients who are candidates for systemic therapy. It is a prescription drug. Each tablet contains 2 mg of baricitinib and the following inactive ingredients: croscarmellose sodium, magnesium stearate, mannitol, microcrystalline cellulose, ferric oxide, lecithin (soya), polyethylene glycol, polyvinyl alcohol, talc and titanium dioxide.

Protopic contain tacrolimus is an immunosuppressive drugs. It is a prescription medicine used to treat the symptoms of Atopic dermatitis. Active Ingredient: tacrolimus, either 0.03% or 0.1% Inactive Ingredients: mineral oil, paraffin, propylene carbonate, white petrolatum and white wax.

CONCLUSION

Atopic dermatitis is a chronic condition which affect skin barrier function. The term atopic refers to a collection of conditions that involve the immune system. The word dermatitis refers to inflammation of the skin. Symptoms are it cause dry, itchy, inflamated, red skin. It can be worsen which cause complication in the patient of Atopic dermatitis. Which may further cause erythroderma, ophthalmic disease. It may be driven by secondary infection with bacteria or virus (eg herpes simplex virus). Atopic dermatitis can be trigger by various factor: allergens, smoke, low humidity, genetic. Diagnosis clinical tool for assessing the severity of atopic dermatitis. Most famous are SCORAD, EASI, skin biopsy. Skin prick test used to find out any allergic reaction. As there is no cure for Atopic dermatitis but we can manage it by various factor: patient education help to gain knowledge and skill necessary to maintain the health. avoid food allergens by avoiding some food you are been allergen. Atopic dermatitis have dry skin as compare to other normal skin. Applying moisturizer immedeatiely by bathing provides modest hydration benefit. Ointments are more preferable than cream and lotion. Regular application of moisturizers alongside treatment with topical corticosteroids form the foundation of treatment of all atopic dermatitis. Patients may present to the general medication with co-existing Atopic Dermatitis, and prescribing of other therapies such as oral corticosteroids, antihistamine, phosphodiesterase-4 inhibitors, immunosuppressive and inflammatory drugs. And some therapy like phototherapy, wet wrap therapy.

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