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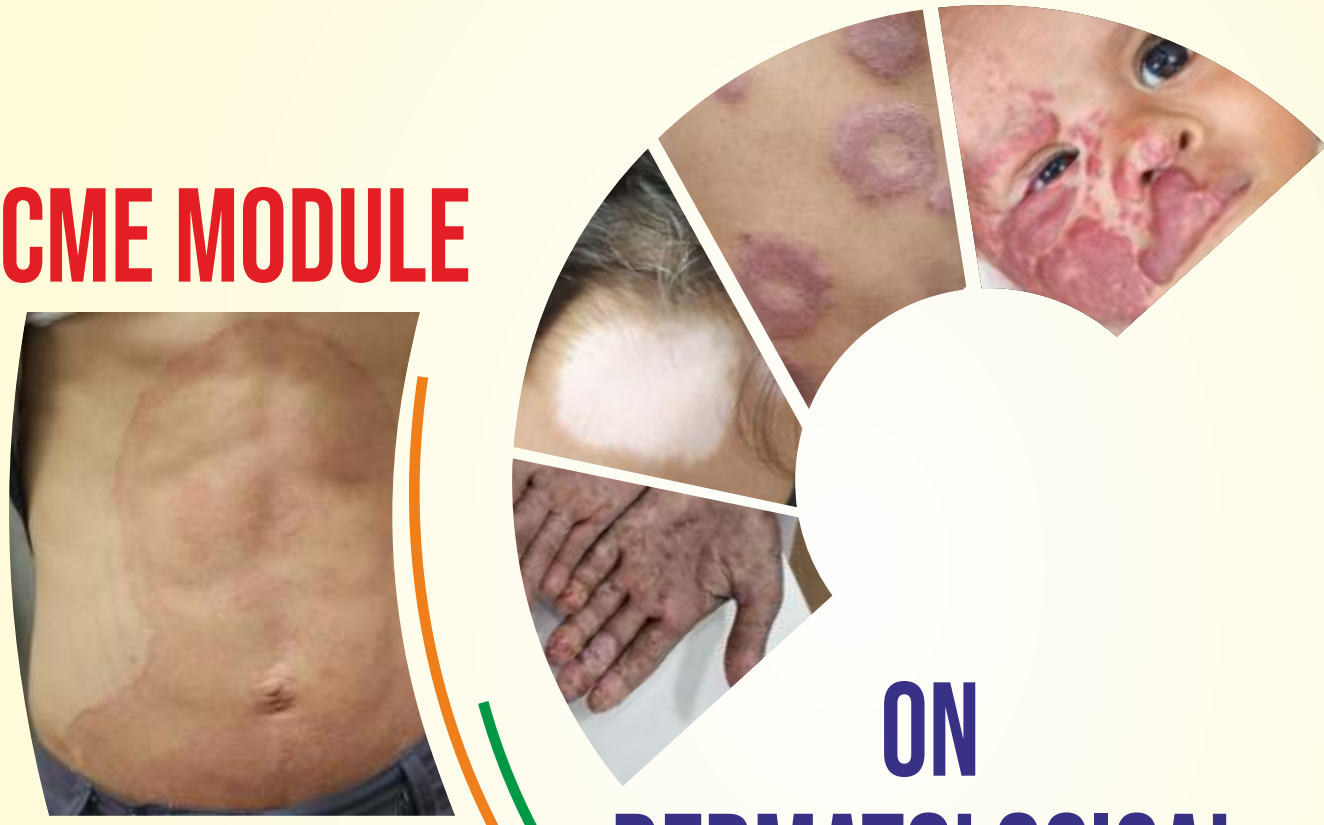
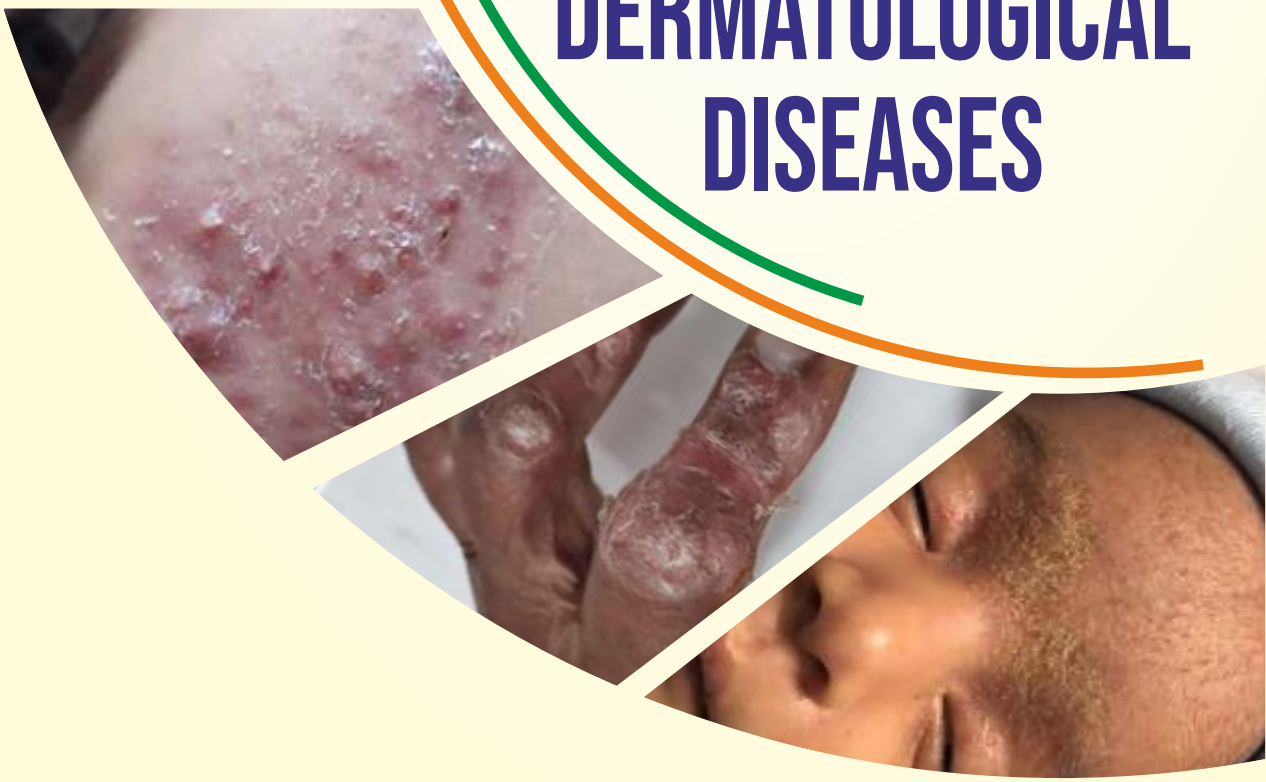
CME MODULE



ON DERMATOLOGICAL DISEASES



STATE INSTITUTE OF HEALTH AND FAMILY WELFARE
UTTAR PRADESH

AKNOWLEDGEMENTS

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MESSAGE

Shri Brajesh Pathak
Hon'ble Deputy Chief Minister
Minister of Medical Health and Family Welfare
Department Government of Uttar Pradesh

Continuing Medical Education (CME) module is a tool for medical professionals to stay abreast of the rapidly evolving practices in medical and medicine. In the COVID era, it has become more essential for medical officers to keep up with the mode of treatment and management developing in conjunction with the feedback from the medical community.

The medical officers at primary and secondary levels face a lot of issues in diagnosing common skin diseases. There has been an increase in skin diseases in last decade. In the popular mukhya mantri arogya melas at PHCs more than 25% patients have been reported to have come for treatment of skin issues alone. Medical officers at these levels face a huge burden of updating themselves in absence of CME programmes designed for them.

This CME module has been generated keeping in mind the footfall of skin diseases. The treatment portion has been discussed in detail as well as customization of same to patients with different needs. The module also takes care of composite interpretation of recent developments in diagnosing, prevention and primary management of dermatological disorders. I hope this manual despite being a CME presentation is complete comprehensive document containing all information required for Medical Officers to enhance their skills and knowledge, ultimately leading to improved health care services to the masses.

I would like to congratulate SIHFW, the lead author and other subject matter experts in developing such a comprehensive module in such a short period. I hope this CME module will provide much needed dose of dermatological information to medical officers and relief to common man in terms of better treatment.

(Brajesh Pathak)


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MESSAGE

Shri Mayankeshwar Sharan Singh

Hon'ble State Minister
Medical Health and Family Welfare
Department Government of Uttar Pradesh

I am happy that the State Institute of Health & Family Welfare, Uttar Pradesh (SIHFW) through this module on Continuing Medical Education (CME) for medical professionals is to stay abreast of the rapidly evolving practices in medical and medicine. In the COVID era, it has become more essential for medical officers to keep up with the feedback from the medical community.

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To address to this situation, this CME module on Dermatological Diseases for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh has been developed by State Institute of Health & Family Welfare (SIHFW), Uttar Pradesh with the help of subject matter experts as part of CME initiative specially designed for medical officers

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(Mayankeshwar Sharan Singh)


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FOREWARD

Shri Partha Sarthi Sen Sharma

Principal Secretary
Department of Medical, Health and Family Welfare
Government of Uttar Pradesh

Continuing Medical Education (CME) module is a mechanism for medical professionals to stay abreast of the rapidly evolving practices in medical and medicine. In the COVID era, it has become more essential for medical officers to keep up with the mode of treatment and management developing in conjunction with the feedback from the medical community.

The medical officers at primary and secondary levels face a lot of issues in diagnosing common skin diseases. There has been an increase in skin diseases in last decade. Medical officers at these levels face a huge burden of updating themselves in absence of CME programmes designed for them. They have very little time to pursue knowledge and skill development with the duty of managing their centre and government policies.

To assuage and remedy this situation, this CME module on Dermatological Diseases for Medical Officers in Provincial Health & Medical Services in Uttar Pradesh has been developed by State Institute of Health & Family Welfare (SIHFW), Uttar Pradesh with the help of subject matter expert as part of CME initiative specially designed for medical officers

This CME module has been generated keeping in mind the footfall of skin diseases. The manual despite being a CME presentation is complete comprehensive and yet crispy containing all information required for Medical Officers to enhance their skills and knowledge, ultimately leading to improved health care services to the masses.

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(Partha Sarthi Sen Sharma)


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MESSAGE

Dr. Renu Srivastava Varma

Director General Medical & Health Services
Uttar Pradesh

Continuing Medical Education (CME) module is a mechanism for medical professionals to stay abreast of the rapidly evolving practices in medical field and medicine.

The medical officers at primary and secondary levels face a lot of issues in diagnosing common skin diseases. There has been an increase in skin diseases in last decade. Medical officers at these levels face a huge burden of updating themselves in absence of CME programmes designed for them. They have very little time to pursue knowledge and skill development with the duty of managing their centre and government policies.

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This CME module has been generated keeping in mind the footfall of skin diseases. It was observed that dermatophytoses, scabies, dermatitis, psoriasis, acne and vitiligo alone are responsible for 60% to 70% of skin OPDs hence these diseases have been covered extensively. The treatment portion has been discussed in detail as well as customization of same to patients with different needs. Dermatology being a visual specialty it was prudent to add disease defining photographs contributed by the experts of Department of Dermatology Balrampur Hospital Lucknow.

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(Dr. Renu Srivastava Varma)


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MESSAGE

Dr. Anita Joshi

Director General Family Welfare,
Directorate of Family Welfare
Uttar Pradesh

Continuing Medical Education (CME) module is a mechanism for medical professionals to stay abreast of the rapidly evolving practices in medical and medicine.

The medical officers at primary and secondary levels face a lot of issues in diagnosing common skin diseases. Medical officers at ground levels face a huge burden of updating themselves in absence of CME programmes designed for them. They have very little time to pursue knowledge and skill development with the duty of managing their centre and government policies.

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(Dr. Anita Joshi)


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MESSAGE

Dr. Deepa Tyagi

Director General (Training)
Medical and Health Services
Uttar Pradesh

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(Dr. Deepa Tyagi)


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ACKNOWLEDGEMENT

Dr. Rajaganapathy R.

Director
State Institute of Health and Family Welfare
Uttar Pradesh

The purpose of Continuing Medical Education (CME) is to facilitate life-long learning among Medical Officers so that their practices may reflect the best medical care for their patients. The goal of CME is to help Medical officers enhance their performance in practice, in turn enhancing patient care and satisfaction.

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I congratulate the faculties at SIHFW & Dr.M.H.Usmani for coming up with the CME module. I am looking forward to a wider dissemination of this module and feedback on its efficacy in the coming months.

(Dr. Rajaganapathy R.)


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INDEX

CME 1

DERMATOPHYTOSES

Introduction

Synonyms: Superficial fungal infection, Tinea

Dermatophytoses are fungal infections of skin and its appendages which are localized in superficial layers. They are the most common fungal infections worldwide and are the 4th most common cause of human disease. Prevalence as per WHO data is around 25%. Prevalence is more in the tropical countries. Dermatophytosis, does not contribute to mortality but has huge morbidity and has emerged as a public health issue. More than 300 million people suffer from fungal infections (systemic, superficial sungal infections & deep fungal infections) worldwide.

Fungal infections	
Superficial Fungal infection	Infection of dead keratinized tissues of skin, nail and hair. It includes both dermatophytosis and non dermatophyte mould , candidiasis and tinea versicolor
Deep fungal infection	Infect the subcutaneous tissue e.g Mycetome, sporotrichosis, chromobastomycosis
Systemic or systemic fungal Infections	Systemic internal organs involved e.g Cryptococcosis
Opportunistic Fungal Infections	Caused by normal flora or saprophytes that invade when host defenses are weak e.g aspergillosis, zygomycosis

Prevalence of Superficial Fungal infections in India and Uttar Pradesh

Dermatophytes are a large group of related fungi that invade keratin and derive their nutrition from it. Recent prevalence of dermatophytosis in India ranges in various studies from: 36% -78%.

Dermatophytosis compromises almost 30% to 50% of the patients attending dermatology outpatient departments in both in the government and private setups of Uttar Pradesh, thus making it the most common disease of Skin. There is an increase in prevalence of dermatophytosis over the past 10–15 years with isolation of some uncommon species. Recurrent dermatophytosis is fast emerging as a challenge in India.

Why this increase in prevalence?

Many Reasons

- Short incubation period
- Tropical or subtropical geography
- Treatment duration very long up to 12 months especially in toes
- Very few antifungal drugs to fall back upon and with increase in resistance against backdrop of development of new anti fungal drugs not taking place, is a issue of great concern.
- Increasing trend of steroid mixed antifungal use
- Trend of poor population especially urban poor taking steroid mixed creams from over the counters of medical stores and not visiting the specialized OPD's.

Classification:-Dermatophytes are divided into 3 main genera

Distinguished by morphology of large multicellular macroconidia that are produced

- **Trichophyton (24 species)**
- **Microsporum (17 species)&**
- **Epidermophyton (2 species)**

Superficial Fungal infections named after part of body they affect in clinical practice

· **Tinea capitis;** infection of the scalp. Common species (*T Tonsurans, M audouinii)*

· **Tinea corporis;** infection of the body. Common species (T Rubrum, Mentagrophyte)

· **Tinea cruris;** infection of the groin. Common species (T.Rubrum, E Flocossum)

· **Tinea unguium;** infection of the nails. Common species (T Rubrum, Mentagropyte)

· **Tinea barbae;** infection of the beard. Common species (T. verrucosum, Mentagrophyte)

· **Tinea manuum;** infection of the hand Common species. T. Rubrum,mentagrophyte)

· **Tinea pedis;** infection of the foot

Ecological Divisions		
Anthrophophilic (human to human transfer)	Restricted to human skins. Produce mild but chronic lesions	T.Mentagrophytes, T. Rubrum, T. Interdigitale,T. Tonsurans, T> Violaceum, M Audouinni
Zoophilic (animal to human transfer)	Animal origins. Produce high inflammation	M.Canis, T. Verrucosum, M.Equinum
Geophilic (soil to human transfer)	Originating in soil	M.gypseum, Mnanaum,

These 3 groups are not sharply demarcated. Geophilic may contaminate animals which may infect humans

Why top layer of skin involvement in Tinea

· Dermatophytes are fungi that invade keratin and derive their nutrition from it. They implant on the skin by secreting keratolytic enzymes that dissolve keratin by adherence of arthroconidia (takes

2hrs) and literally eat it away and move farther in all direction with the active margins being inflammatory. Leading to ring like morphology. Due to its moving ring the Romans thought it was a worm. Tinea is a Latin word for worm. Inflammation, they cause is due to metabolic products of the fungus or delayed hypersensitivity which involves dermis and malpighian layers. There appears to be a certain amount of substrate preference as different species vary widely in invading nails and hairs.

· They do not invade mucosa as they require keratin for growth. The entire human body is covered by keratin from head to hairs and nails except mucosa and scrotum which does not have keratin top layer.

Predisposing factors

· Tropical humid climate. Sub Himalayan belt has more tinea infection than any other district in Uttar Pradesh.

· Low socioeconomic status with overcrowded living place in urban areas.

· Sharing of clothes, combs and towels in poor socioeconomic settings.

· Ease of bathing facility a issue in urban poor. Unable to maintain personal hygiene.

· Profuse sweating in manual labor population.

· Friction with tight clothes, synthetic type innerwear in upper class.

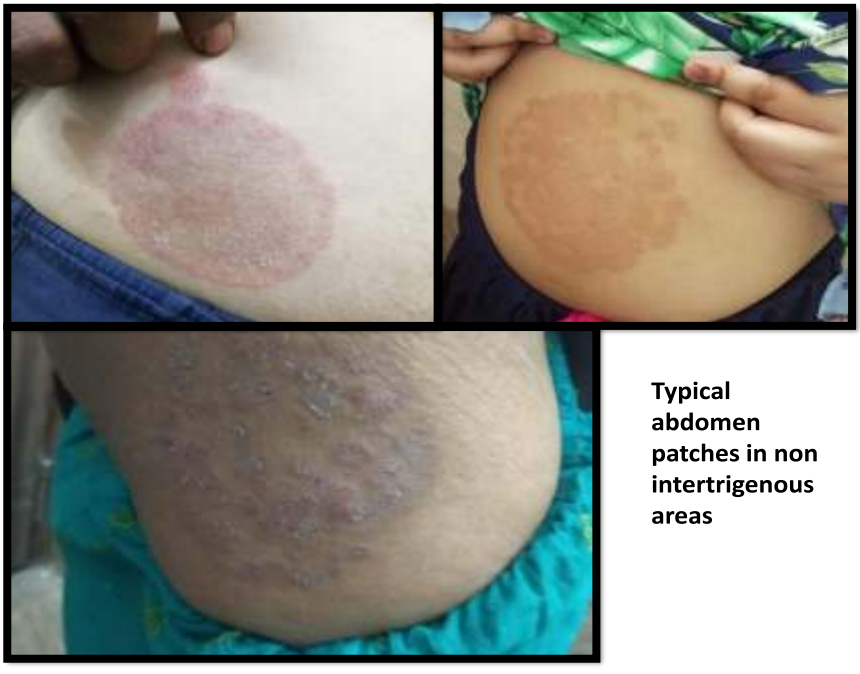
· Immunosuppressed patients, HIV, Congenital immunodeficiencies, patients on corticosteroids, immunosuppressive drugs, Cushing's disease, malnutrition and diabetic patients are more prone.

· Pet animals with tinea are of great concern as a predisposing factor and hence require regular checkups.

Symptoms

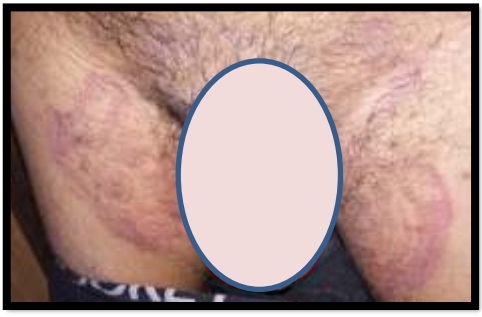
· Irritation, Redness, Scaling, Itching, Swelling, Strae & atrophy due to steroid overuse.

In extensive tinea infection where morphological features are modified by various factors, some portion of infection still reflects classical features. Here lies the importance of observing the entire skin, palm, nails & soles.



Typical abdomen patches in non intertrigenous areas

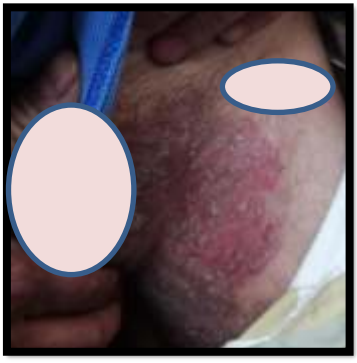
Changing Morphology Beyond Classical Features



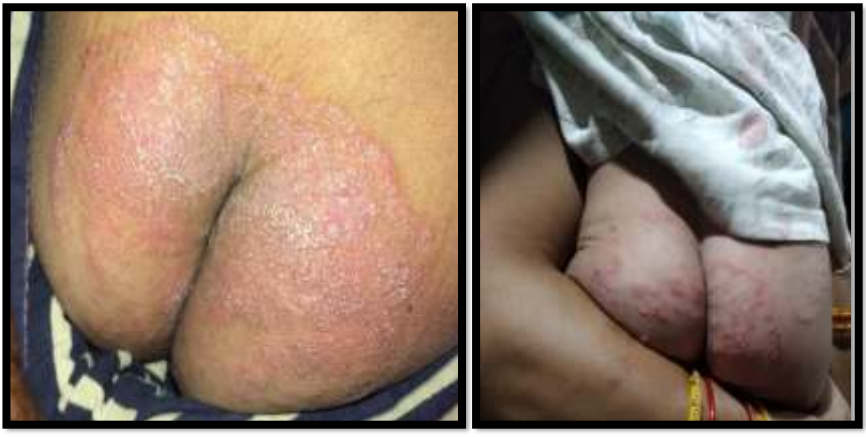
Double ring or multi ring lesions in the groins and spreading up to lower abdomen is now more common feature

Highly inflammatory burning red lesions without classical central clearance

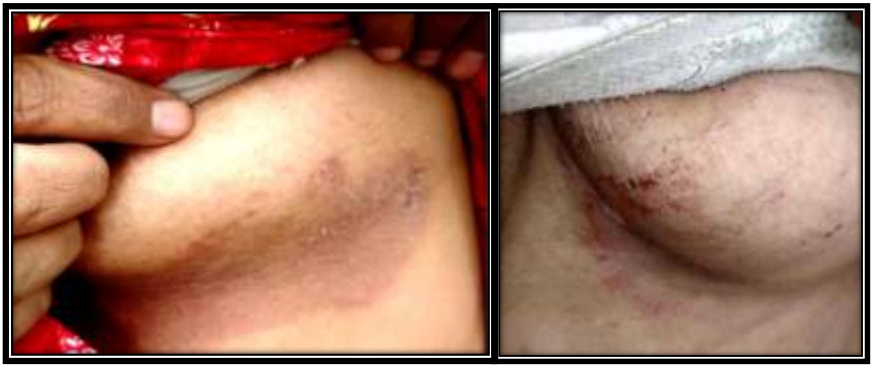
Change in morphology from Tinea of last decade is obvious



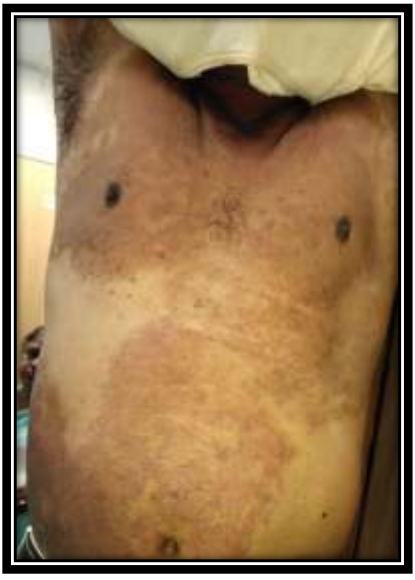
Large sized, erythematous plaques with active border with pustular lesions in gluteal area are now seen more

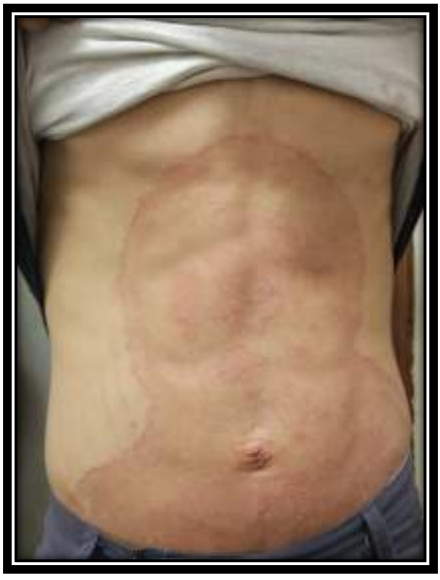


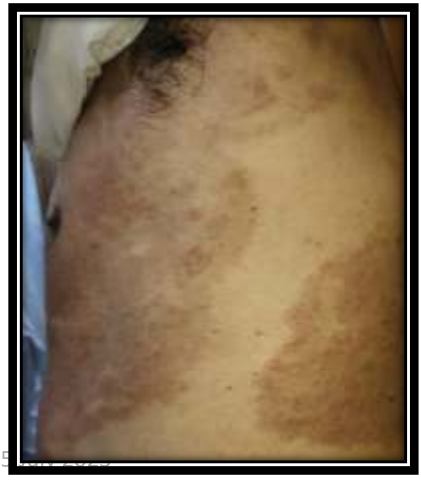
Typical infra mammary spread. Common site of infection in females



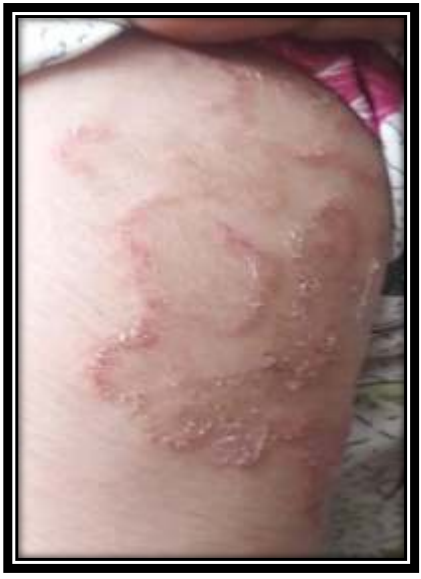
Widespread Large lesions on abdomen common now

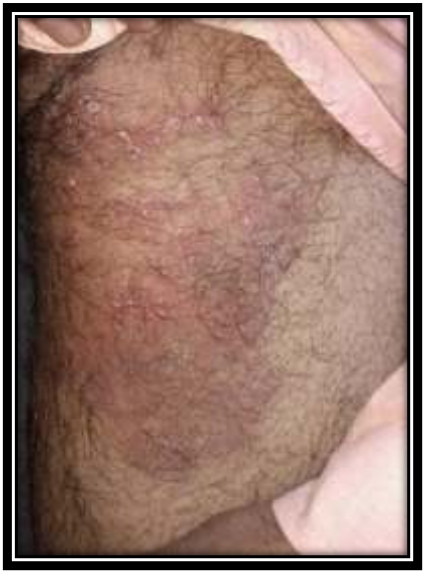




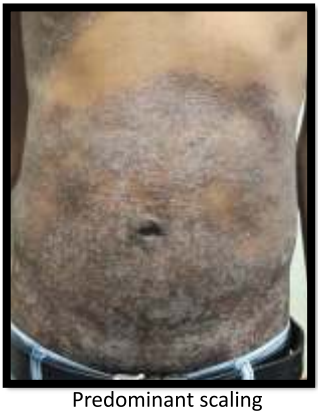


Giant lesions many times involving whole abdomen.
Phantom tinea formed by confluence of two or more large lesions, increasingly more and more body surface area involved.

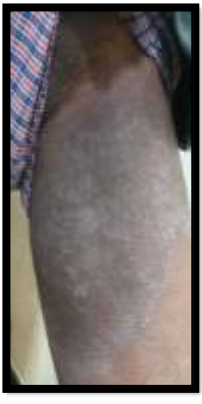


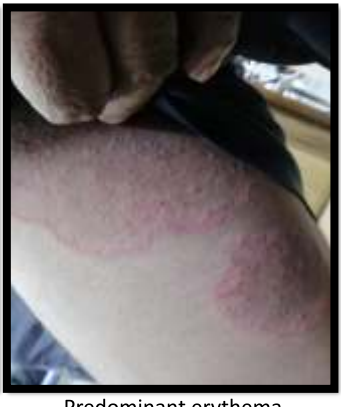


Scaly plaques with an erythematous edge.
Multiple rings in large area now more common



Predominant scaling

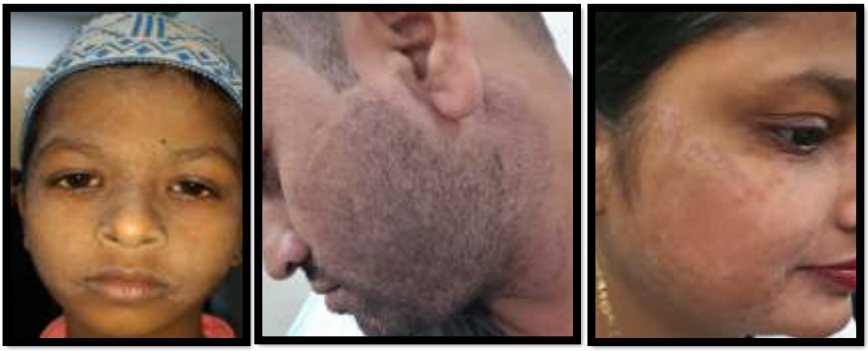




Predominant erythema

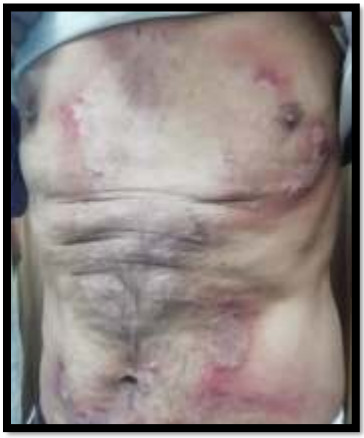
White scales with peripheral accentuation and outward direction of scale peeling are strong indicator of Tinea infection

Tinea Faciei

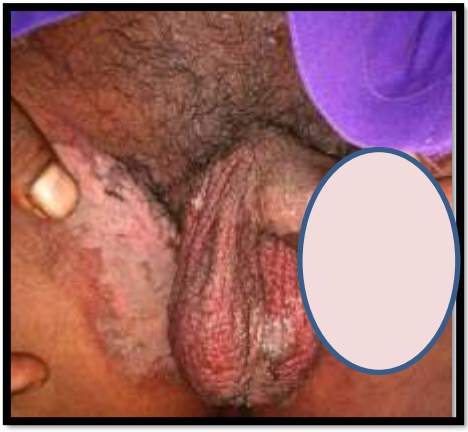


Increase in cases of Tinea Faciei

Change in Morphology due to irritant application



Darovin application

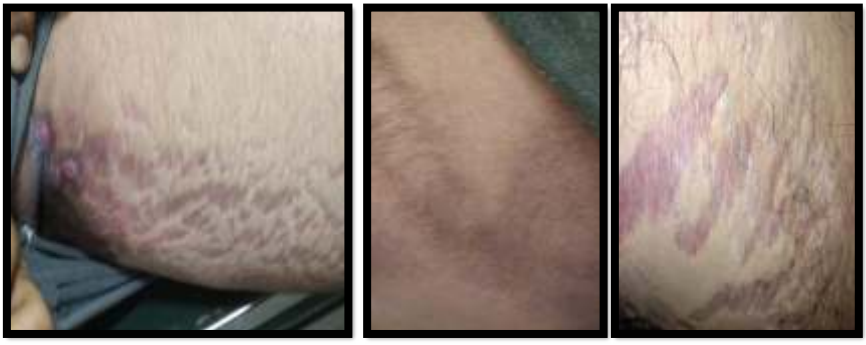


Zalim Lotion application

Irritant applied Tinea Lesions.
Common irritants are Darovin cream, Zalim lotion.

Darovin (Dithranol) & Zalim lotion (mixture of acids) is a common treatment application used by quacks to chemically burn the tinea infected skin.

Change in morphology due to potent topical steroid misuse



Side effects striae, thinning of skin with backdrop of active tinea

Tinea Capitis

Kerion

Grey patch

Black dot

Found usually in children. Natural Resistance to Tinea capitis in adults is due to fungistatic fattychain in sebum at puberty.

Healed Kerion with scarring

Kerion with folliculitis type sterile pustules

Tinea Capitis:-Clinical feactures		
Clinical type	**Clinical features**	**Common Organisms**
Gray patch	Presents as patches of partial hair loss, numerous hairs are broken at different lengths and become dull gray and lusterless due to the over coating by arthrospores	Microsporum audouinii
Kerion	Presents as an inflamed boggy and indurated tender swelling that is studded with broken or unbroken hairs, vesicles, and pustules. Painless removal of hair differentiates it from follitulitis. There may be sinus formation and crusting with matting of adjacent hair. Lymphadenopathy and secondary bacterial infections may be present.	Trichophyton verrucosum Trichophyton Mentagrophytes Agents of tinea capitis M. Audounii and T. Schoenleinii have been replaced by T.Tonsurans in recent times
Black dot	The hair shaft is extremely brittle and breaks at the level root of the scalp. The remnants of the hair left behind in the infected follicle appears as a black dot on clinical examination	Trichophyton Tonsurans Trichophyton Violaceum Trichophyton Soudanense

Onychomycosis

Onychomycosis is fungal infection of nails of fingers and toes. It affects 14% of population and is responsible for 50% of nail dystrophy. Prevalence is more in old age group. Diabetes, immunosuppressents and peripheral vascular disease are other risk factors.

Various clinical variants are

1. DLSO (Distal and lateral subungual onychomycosis)
2. PSO (Proximal subungual onychomycosis)
3. WSO (White sub ungula onychomycosis)
4. TDO (Total dystrophic onychomycosis)

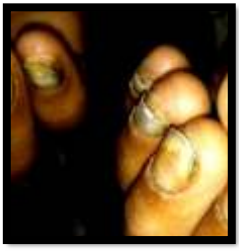
DLSO: - This is invasion of stratum corneum of hyponychium of distal

and lateral nail bed. Infection spreads proximally along ventral nail plate. Clinically presents as yellowish discoloration and subungual hyperkeratosis. Tunnelling is a sign of DLSO.

PSO:- In PSO invasion of fungus is in proximal nail bed from it spreads distally. Clinically presents with transverse leukonychia and onycholysis. Paronychia is common.

WSO:- In WSO invasion of fungus is via nail plate from top. It presents as white lesion on nail plate.

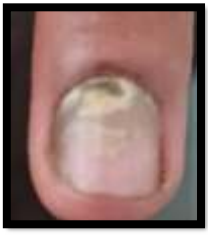
TDO:- This is the most severe variant of the disease. Clinically presents as thickened abnormal nailplate and keratotic debris. May be painful.



DLSO

DLSO

DLSO with Tunneling



PSO

WSO

NAIL DYSTROPHY

ONYCHOMYCOSIS
•DLSO (commonest)
•PSO
•WSO
•NAIL DYSTROPHY

Low incidence of tinea ungium was observed in patients with chronic reoccurances.

Presence of non dermatophytes adds to the recalcitrant nature of infection
Diabetics are more prone to develop onycomycoses esp of toenail

Causes of shift in clinical presentation of tinea

· Shift in spectrum of fungal biodata (T.Rubrum to T.Mentagrophyte are mostly mutant variant)

· Shift in morphology due to irritant and topical steroid use

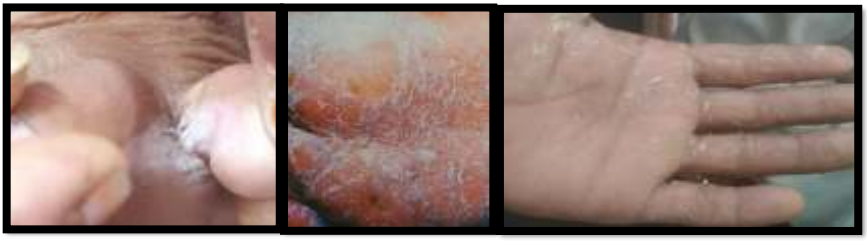
· Shift in steroid use (change from mild Betamethasone valerate to potent Clobetasole)

· Shift in usage and dosage of common drugs due to misuse by untrained.

· Resistance of common antifungal drugs.

· Overuse of agriculture fungicide adding to menance

Tinea Pedis & Mannum



INTERTRIGO TINEA PEDIS TINEA MANNUM

Current scenario of Tinea infection

· Increased frequency of tinea patients in almost all skin OPDs.

· Repeated Re-occurances.

· Chronic infection despite treatment for over 6 months.

· Resistance to fungal drugs is increasing.

· Deviation in clinical presentation.

· In the last 5 years there seems to be an epidemiological transformation of species in India. Many studies done across India have still found *Trichophyton Rubrum* , to be the most common organism, however the prevalence is much less when compared to the past.

· Now *Trichophyton mentagrophytes* has emerged as the dominant pathogen with an increased prevalence in comparison to what was seen in the past. Mutated variants are considered as drug resistant.

· T. Mentagrophyte exhibits a rapid growth in the primary culture within 5–7 days.

T.rubrum survived for <12 weeks on a towel while T. mentagrophytes is said to be surviving for >25 weeks on towels

· 92% samples from India showed mutated strain of T Mentagrophte in a study, which is supposed to be the cause of so called resistance to therapy.

· At 30^{0} C, 16% of fungi matter is found in rinse cycle. Fungi can be transmitted to uncontaminated clothing in wash. This fact highlights the importance of disinfection of clothes which could be best done by washing in hot water at 60°C to 70° C for 45 minutes and or drying in sunlight for a prolong period of 8 to 10 hrs, as sunlight is considered to be the most effective disinfectant for dermatophytes. Hot iron press on both sides of clothes (which is difficult with terricot clothes and undergarments with elastics) is other option for disinfection.

· Tinea is now common all round the year, even in winter months. Previously it was in summer and rainy season only.

· Clinically more aggressive large giant lesions getting commoner. Classical central clearance is not found in many lesions. Unusual distribution in non intertrigenous highly common

· Incidence of tinea faciei and tinea incognito increasing

· Previously Betamethasone valerate was steroid which was combined to antifungals but now clobetasole is offered by pharma units. Topical antifungal with potent steroid cream application resultants in striae, thinning of skin and more complications with a change of morphology also. Abuse of tropical steroid facilitates the persistence of fungal elements.

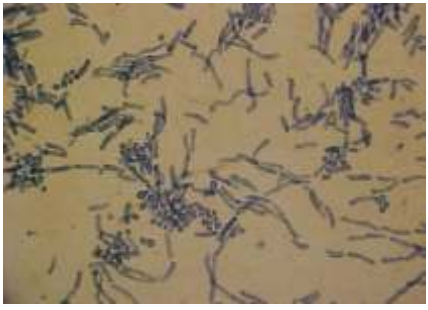
· Treatment failure, re-occurance and relapse are on the high especially among those sharing family beds and with family member

having the disease.

· Cases in high socio economic status on the rise.

· Urbanization, tight fitting clothes, high end synthetic undergarments, shoes with synthetic nylon socks, tight Jeans culture on the rise are new predisposing factors.

Investigations



KOH is Key Test and is underutilized in both Private and Goverment setups

KOH Wet Mount Preparations

Whenever in doubt, perform KOH Examination, especially in cases of tinea incognito. Sample to be collected from all sites, if extensive lesions are present.

Very easy to perform with very limited logistics

· A slide.

· Scrape border of lesion.

· Apply 1-2 drops of KOH 20% and heat gently

· Examine at 50x

· Look for hyphae

Other Tests

Fungal Cultures

(Very difficult to perform in comparison to bacterial cultures. Not easily available at most of the centers except research Labs)

Culture Mediums Used

- DTM (Dermatophyte Test Medium)
- Sabouraud's agar Media

Culture

- Cultures are difficult to perform and drug sensitivity even more complicated to access.
- Culture requires 1-4 wks as organisms are slow growing.
- Fluorescent microscopy is also employed for evaluation which has has a sensitivity of 96% and a specifity of 90%.
- Molecular techniques are now utilized which identify sequences from fungal ribosomes; others identify more specific DNA sequence which allows genus & species identification also.

Newer techniques are costly and not available at routine centres

Clinical classification and definitions of reoccurrence and resistance

Resistance or Reoccurrence conundrum

- Re-occurrence is loosely defined as reoccurrence of signs and symptoms within a few weeks of apparent cure. At Balrampur Hospital we have taken 6 weeks duration between clinical cure and relapse as boundary to call next occurrence as new infection, if the first occurrence was treated properly at our centre alone for full course of 6wks
- Some centers are defining relapse after 3 wks as re-occurrence as

effect of Terbinafine and Itraconazole lasts more than 3 wks in skin

· Fungal resistance can either be microbiological (in vitro) or clinical

· Clinical resistance also referred by many as chronic dermatophytosis is the persistence of infections beyond 6 months even after continuous therapy and elimination of reservoir of fungus (accepted personnel hygiene, adequate washing and sun drying of clothing and treating all affected family members simultaneously). Clinical resistance is due to host or drug related factors. More than 70% of patients with clinical resistance are those using terbinafine and itraconazole along with steroid mixed topical. At our centre where counseling for elimination of reservoir is done regularly the cure rates are better and negligible clinical resistance has been found.

· Microbiological (In Vitro) resistance depends on fungal factors arising due to genetic alteration in the fungi.

· Microbiological resistance is non susceptibility of a fungus to an antifungal agent in vitro susceptibility testing in which the MIC of the drug exceeds the susceptibility breakpoint of that organism. This may be primary or secondary

· Most common fungi responsible for resistance in India is T. Mentagrophyte complex characterized by a particular genotype called T. Mentagrophytes (ITS) type which is endemic in India and is resistant to widely used drug terbinafine

· Standard susceptibility testing appropriate drug dosing and use of combinational antifungal therapy will be helpful in combating fungal resistance.

Management-1

Proper Diagnosis

· Proper diagnosis is must.

· Do KOH examination if possible(may be used extensively as very little logistic is required)

Management -2

Counseling

· Counseling of patients of all categories on for correction of predisposing factors and elimination of reservoir of fungal elements from patient contact and environment.

· Hygiene- daily bath, scrub bath with any soap or moisturizing soaps. Antifungal soap adds to cost and contact time of drug in them is insufficient. Dry skin before wearing clothes

· Wear Dry loose cotton undergarments Avoid tight fitting fashionable undergarments

· To remove reservoir of fungal element from clothing where they can survive for up to 6 months

· All clothes to be washed after dipping in hot water at 60 degrees for 45 minutes (this option is difficult) or

· Sun dried for prolonged period for 8 to 10 hrs and to be worn after 3 to 4 days (Best option for poor resource setting) And or

· If possible every day or in rainy season with no sun, clothes to be hot iron pressed on both sides (least effective option as undergarments with elastic and terricot clothing do not allow for proper hot pressing)

· All linen, bed sheets, comb and clothing especially towels shall be separate for all members of family

· Treatment of all affected family members simultaneously and for duration as decided by medical officer and special focus on

completing the duration with strict compliance of doses.

· Treatment of co morbidities, if any

In absence of above counseling, pharmacological treatment likely to fail.

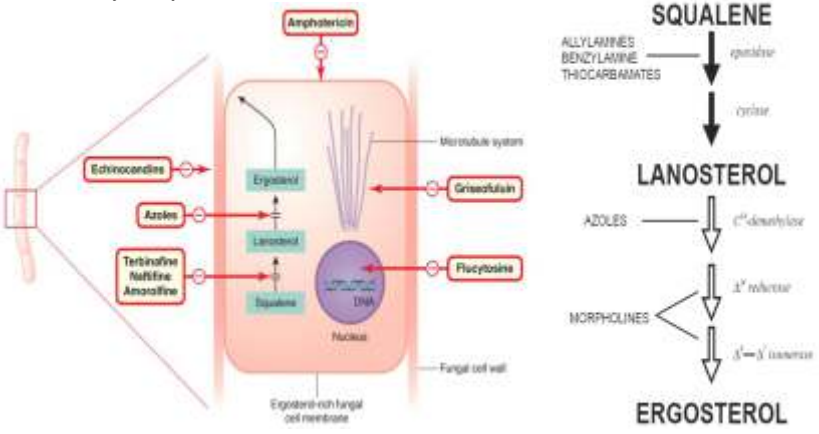
Management - 3

Pharmacological drugs available for use

TOPICALS		ORALS	
Azoles (topical)	**Other Topicals**	**Oral Azoles**	**Other Oral Drugs**
• Clotrimazole • Miconazole • Ketaconazole • Efinaconazole • Oxyconazole • Eberconazole • Luliconazole • Sertaconazole	• Allylamines • Thiocarbamates • Morpholenes • Ciclopirox • Polyenes (amphotericin B, Nystatin & Natamycine) • Fluropyrimidines (5FU & 5FC)	• Fluconazole • Ketaconazole • Itraconazole • Vericonazole • Posaconazole	• Griseofulvin • Terbinafine

Antifungal therapy is the mainstay of treatment

Location, severity and reoccurrences decide the molecule. Selection is basically emperical.



Mechanism of Action

Knowing mechanism of action is important as when clinical cure is delayed, oral and topical with different MOA are used.

Class	Drugs	Mechanism of Action
Allylamines	Terbinafine. (Fungicidal) Benzylammine (Butenafine)	Inhibition of enzyme Squalene epoxide leads to deposition of squalene leading to fungal cell death
Microtubule inhibition	Griseofulvin	Microtubule interferes with mitosis to form multinucleated, stuned and curled hypae. Hence called curling factors.
Imidazole	Clotrimazole , Ketoconazole Miconazole , Eberconazole,	All Azoles are C14 D Methylase enzyme inhibitors
Imidazole	Fentikonazole	Additional action blocking cytochrome oxidases and peroxidases. Antiinflamatory action strong
Imidazole	Bifonazole	Additionally Microsomal HMG CoA reductase inhibition. Dual mode of action fungicidal effect
Imidazole	Sertakonazole	Additionally It has a Benzothiophene ring which mimics trptophan and increases the drugs ability to form pores in fungal cell membrane. Ant-iinflamatory action is the highest among azoles
Imidazole	Luliconazole	Additionally has Reservoir effect and highest antifungal activity vs T. species
Triazoles	Fluconazole ,Itraconazole	C14 D Methylase enzyme inhibition
Morpholen	Amrolphene	C14 Reductase and 7,8 isomerase inhibitor
Hydroxy pyridone	Ciclopirox	Acts through chelation of metal ions-inhibits cytochrome oxidase catalase and peroxidase which results into intracelular degradation of toxic peroxidase which in turn inhibits cellular uptake of essential compounds and alters cell permeability
Fluropyrimidine		Synthetic structural analog of DNA nucleotide cytosine
Polyene	Amphotericin B Candicidin , Natamycin	Forms micropores in fungal cell membrane through which ions aminoacids and water sol substance move out

Points to be considered while selecting oral drugs

· Terbinafine working very well in western countries and USA but not as effective in India. Terbinafine resistance is inherent among mutated isolates of T Mentagrophytes. Only category B in pregnancy antifungal.

· Griseofulvin has short spectrum and effective for tinea capitis for children but limited use in adults however since went into disuse in last decade, resistance is very minimal.

· Fluconazole is broad spectrum, most overused and supposed to be not working in conventional doses. Resistance as high as 90 percent reported in some studies. Liposomal formulations of nanofluconazole have better activity as compared to conventional fluconazole but currently unavailable freely.

· That leaves Itraconazole which has broad spectrum and is now extensively used to the extent of misuse.

· Ketaconazole oral use has been withdrawn by USFDA in USA due to mortalities because of drug induced idiopathic fulminant hepatitis

· Vericonazole and Posaconazole are very costly and do not justify use in superficial fungal infection as they have high serum concentration and cross blood brain barrier so must be preserved for systemic fungal infections.

Points to be considered in selecting topical anti fungals

· Local applications have more options than oral.

· Old generation azoles clotrimazole was found to be less effective (35-40% efficacy) in many studies and miconazole fares slightly better. Luliconazole was found to be most effective in same studies. Terbinafine is not working as expected despite microbiologically not resistant.

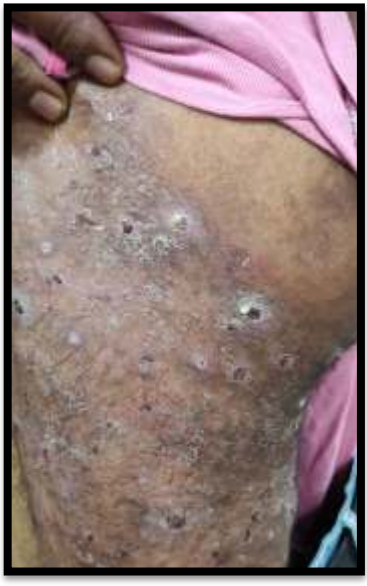
· Except oxiconazole, luliconazole and some preparation of

eberconazole all have twice daily applications. So despite high cost oxi , eber and luli are still comparatively cheap being once daily dosing.

· Amrolfine, ciclopirox have different mode of action than azoles hence many clinicians prefer them. Ciclopirox works in mentagrophytes even.

· The best local applicant CICLOPIROX is supplied free in government hospitals of Uttar Pradesh.

· One finger tip unit of drug is to be applied for one palm size area and application must extend beyond 2 cm outside the active border of ring.



Tinea with secondary bacterial infection

Oral antifungal agents

Drug	Doses	Side effects	Interactions	Remark
Griseofulwin	500mg (microionised) OD after fatty meal preferably at night	Contraindicated in porphyria and hepatic failure and SLE.	Level is decreased by Barbiturates.	Sweat channels potentiates entry of drug in S.corneum.
		Headache nausea common.	Potentiates level of Alcohol	Mostly used for tinea capitis however approved for pedis unguium & corporis also
		Vomiting diorrhea angular stomatitis gastritis.	Decreases level of warfarin OCP Cyclosporin and Salicylates	
		Hepatotoxicity		
		Leucopenia neutropinea basophilia are other S/E		
		Renal side effects, Albuminuria without renal insuffuciency are uncommon		
Drug	**Doses**	**Side effects**	**Interactions**	**Remark**
Fluconazole	Regular dose 150-300mg per wk. Exceptional doses150 mg once daily for 28 days is also being used with CBC,LFT,&KFT monitoring every 2 wks	Contraindicated along use with quinidine Nausea vomiting diorrhea headache are common	Level decreased by Rifampicin. Level increased by thiazides.	Transported through eccrine sweat channel in dermis and s corneum. Eliminated through renal system 80%
		Alopecia TEN, SJS syndrome haematological S/E uncommon. Rarely anaphylaxis oligourea, fatigue, malaise and fever	Increses level of sulfonylureas, nifedipine losartan, omeparazole theophyline, phenytoin carbamazepine, cyclophosphamide, warfarin, ributin, statins and cyclosporine.	
Drug	**Doses**	**Side effects**	**Interactions**	**Remark**
Itraconazole	100mg BD conventional as well as SB100 mg bd. (65mg SB bd is considered equal to 100mg bd conventional)	Contraindicated in ventricular dysfunction and cardiac failure	Level is decreased by antacids proton pump inhibitor ranitidine rifampicin phenytoin phenobarbitone carbamazepine INH.	Delivered in skin by passive diffusion from plasma at peak level. That is why 200mg od is inferior to 100mg BD dosing
		Implicated in cardiac and fluid related adverse events with edema as most common event.	Level increased by Erythromycin ciproflox indinavir ritonavir.	
		Worsening of existing hypertension. (Stoppage of drug improves resolution of symptoms but adverse events may persist in 10-15% of patients)	It decreases level of OCP. It Increses level of sulphoneureas nifedipine omerazole phenytoin alprazolam midzolam cyclophosphamide indinavir.	

Oral antifungal agents

Drug	Doses	Side effects	Interactions	Remark
Itraconazole		Pregnancy is C/I Can cause tachcardia Other S/Is TEN SJS nausea vomiting pancreatitis constipation dizziness, p.neuropathy, UTI raised liver enzymes. Peripheral edema pulmonary edema rarely mayagia, arthralgia, erectile dysfunction & menstrual disorders	Increses level of sulphoneureas nifedipine omerazole phenytoin alprazolam midzolam cyclophosphamide indinavir.	
		Other S/Is TEN SJS nausea vomiting pancreatitis constipation dizziness, p.neuropathy, UTI raised liver enzymes. Peripheral edema pulmonary edema rarely mayagia, arthralgia, erectile dysfunction & menstrual disorders		

Drug	Doses	Side effects	Interactions	Remark
Terbinafine	250-500 od	Contrindiacated in chronic active liver disease and low creatinine clearance.	Level is decreased by rifampicin.	Inherent resistance against against T. mentagrophyte mutants.
				Elimination route is 70% renal
		S/E Neutropenia and LE.	Increased by fluconazole cyclosporine	
		TEN SJS are not frequent.	Increases level of TCA betablockers	
		Alopecia diarrhea nausea depressive symptoms hepatic injury are more frequent. Haematological S/E uncommon. Other S/E are Serum sickness photosenstivity vertigo, arthralgia taste and smell disturbanance		Only Cat B pregnancy antifungal However risk benefit ratio must be weighed upon.

Duration of treatment

· For Tinea cruris, corporis; - At least one skin turn over time (28days) and recommended to exceed 2 wks beyond clinical cure. I.e. total duration 4-6wks. If symptoms persist KOH must be done and if positive then emphasis must be placed on counseling as explained in management above rather than searching for magical drugs.

· For capitis, pedis and manuum duration of treatment is 6-8wks

· For nails duration is 6 months

· For toes duration is 12 months

Special Situations /Pregnancy and Lactation

· Terbinafine is pregnancy Cat B drug and can be used in both pregnancy and lactation

· Griseofulvin and Fluconazole are contraindicated in pregnancy. Fluconazole can be used in lactation but not griseofulvin.

· Itraconazole – animal studies have revealed evidence of dose related toxicity embryological and teratogenecity

· Itraconazole- in lactation data is limited. However the drug in milk gives a approx serum concentration of 5mg/kg that are recommended for children hence risk benefit ratio is to be weighed

Photodynamic (PDT) and Laser therapy for nails

· Not popular yet as logistics are costly. Tool at tertiary care centres only.

· Recent advance especially for patients presenting contraindications to the use of systemic antifungals.

· *T. rubrum*, a causing agent in approximately 90% of onychomycoses, is capable of metabolizing 5-aminolevulinic acid to protoporphyrin IX, and that PDT brings about significant reduction of its growth.

· No resistance from fungi and the lack of cumulative or mutagenic effects allows for repeated treatments.

· S/E -Discomfort is reported by patients during illumination, as well as local phototoxic reactions.

· Nd YAG laser (wavelength of 1064nm) has been proven a promising option for treating onychomycoses

· Main advantages of laser treatment are the bactericidal and fungicidal effect.

· Laser light provokes local hyperthermia, destruction of pathogenic microorganisms and stimulation of the reparation process.

· The success of the clinical use of lasers depends on the wavelength used, the exiting energy, pulse duration, exposure time, point size, type and color of the targeted tissues.

Customization of Treatment

1. Proper diagnosis. If any confusion go for KOH wet mount. Counseling as detailed earlier must, without which pharmacological therapy likely to fail.

2. If skin area involved less than two palm size then local alone may be sufficient. Start with ciclopirox ointment

3. If more than 2 palm size areas involved or scalp, nails, palm and soles involved go for both oral and local antifungals. Start with fluconazole in regular doses of 300mg/week or if extensive then at tertiary care exceptional dose of 150 per day for 4 weeks under monitoring may be used. At our centre fluconazole and ciclopirox in appropriate doses result in more than 80 percent cure rate.

4. At seconadary or tertiary care centres, if no clinical response in 4 weeks and KOH still positive then add on one more local applicant of different mechanism of action. Response rate increases to beyond 90

percent and If still no response in another 2 weeks then add one more oral in terbinafine in regular dose of 250mg. At our centre if terbinafine works then 250 daily dose is sufficient and if it does not work then 500 daily also fails. For rare cases at 2 orals and 2 locals for 4 weeks response rate is nearly 100 percent.

5. Chronic dermatophytosis which is not healing even after 6 months of appropriate treatment is very rare. At our centre we had just 2 such cases in last 5 years. At tertiary care vericonazole 150 bd and local Amphotericin B once daily may be used for 3 weeks. We used this combination to achieve cent percent cure in chronic dermatophytosis.

6. Antihistaminics may be used for short duration to control pruritis

7. In pregnancy and lactation local applicants only to be used. If required then terbinafine may be used as only category B oral antifungal with risk benefit ratio clearly weighed upon. Do not use in first trimester.

CME 2

SCABIES

Introduction

· Scabies word is derived from Latin SCABERE meaning to scratch. In Uttar Pradesh disease is called as "KHUJLI" reflecting the key symptom.

· Scabies is caused by mite Sarcoptes Scabiei var human, Notoedres cati (infesting mostly Cats) and Scabiei var canis (infesting mostly Dogs) Notoedres cati and Scabiei var canis are physiological variant of a single species. Their host specificity is not complete, but they usually survive for only a short period on another host especially humans.

· Currently scabies patients comprise 10% of Skin OPDs

Scabies Mite

Important considerations of life cycle of scabies

· Adult female mite is twice the size of male and the main difference is presence of sucker on the fourth leg which is the bristle in female.

· The mite walks on the surface of skin at a speed of about 2.5cm/min. Burrows are created at the base of stratum corneum at rate of 2-3 mm/day. Burrowing time is about 8 hrs mainly at night.

· Copulation occurs in a small burrow excavated by the female. Burrow is not confined to the stratum corneum but is inclined downwards into the epidermis.

· Female mite lays eggs in groups of 2-4/day and the total number of eggs laid is 40-50 in its life span of 4-6 wks

· Eggs hatch after 3-5 days into larvae. Larvae mature into adult mite in about 4-6 days. The maturation cycle lasts about 14-21 days. Adult females live in host for about a month.

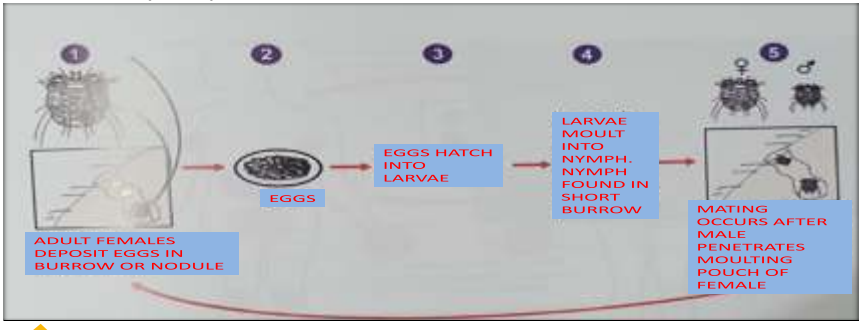
· Mite feeds on liquid oozing from the cells it has chewed only. The female mite survives away from the host for a maximum of 2-3 days at room temperature. The mites survive on fomites for not more than 72 hours so they do not play a major role in spread.

· In classical scabies average adult patient, mites are 5-12 in number. In crusted scabies (found in unattended patients / vagabonds) millions of mites may be present.

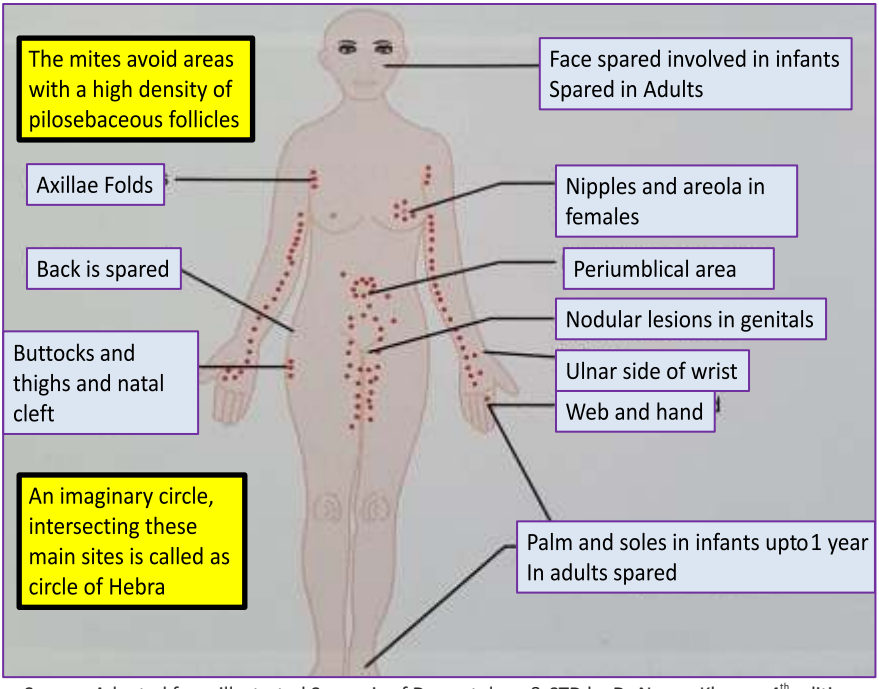
Transmission epidemiology

· A close physical contact for 20-30 mins is sufficient for transmission. Immature and fertilized female mites are implicated in transmission.

· Family contact is responsible for 40% of secondary attack. Frequent source for introduction is through known contacts, family and friends (90%)



Common sites of infestation in human



Source; Adapted from illustrated Synopsis of Dermatology & STD by Dr Neena Khanna 4th edition

Areas where scabies lesions are present

Immune response

· Immune response is still not very well known however delayed hypersensitivity response is important. In primary infection the symptoms appear slowly after a lapse of 4-5 wks as delayed hypersentivity takes approximately 4 wks to precipitate symptomatically. Once patient is symptomatic mite population dramatically reduces, leaving only 5-12 mites at maximum due to mechanical removal and immunological response.

· The development of immunity neither ensures elimination nor does it confer immunity against re-infestation .Though the number of mite reduces, spontaneous cure, without treatment is not achieved.

Diagnosis and Clinical features

· Diagnosis is essentially clinical and pruritis is key symptom which leads to diagnosis, so much so that the disease itself is called “khujli” in northern India

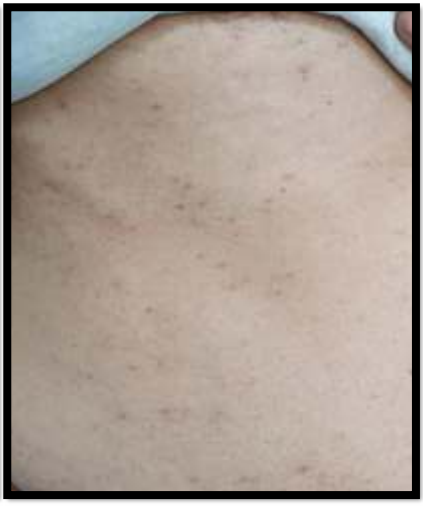
Primary lesions

· **Burrows** – pathognomic lesions

· Papules-erythematous papules commonest lesion. Excoriation present more often. Excoriated papules most common sign

· Vesicles & Bullae both may be present

· Nodules are usual in genitals and axillae. A nodular lesion on genitals of a child is almost diagnostic as STDs are ruled out due to non sexual age group.

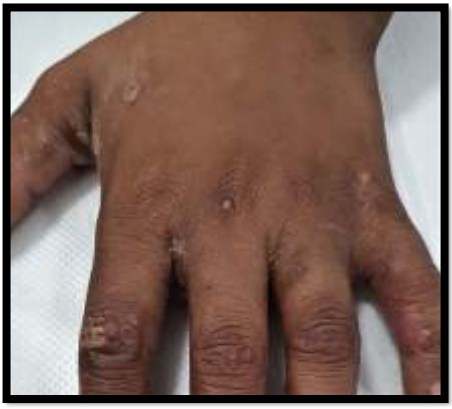


Both immediate and delayed type hypersensitivity is involved. The papules are reactive papules due to delayed hypersensitivity

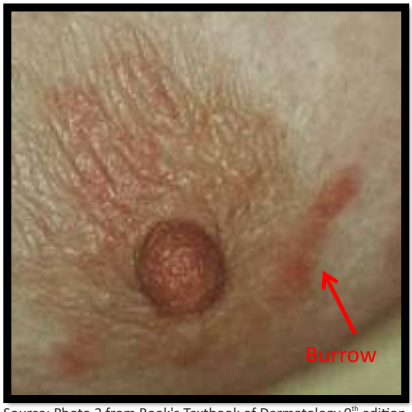
Symptoms appear slowly after a lapse of 4-5 wks
Symptoms appear within 24 hrs in re-infestation

DD of Excoriated Papules

- Scabies (by far commonest)
- Papular Urticaria
- Dermatitis herpetiformis
- Geneotii Crostii syndrome



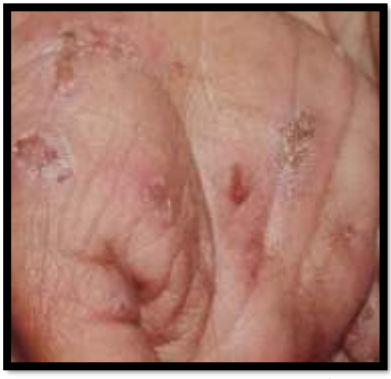
Pruritic excoriated papules and vesicle and pustule in web and hand



Source; Photo 2 from Rook's Textbook of Dermatology 9th edition

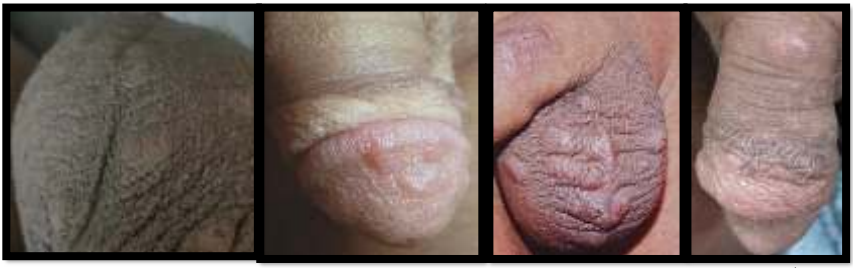
Burrow near areola

Involvement of palm and soles



Source; Photo from Rook's Textbook of Dermatology 9th edition

Distinct feature of neonatal scabies is involvement of face neck and infant scabies is involvement of palm and soles. In neonatal and infant scabies there is tendency to form vesicle and pustules early, lack of burrows, poor feeding failure to thrive. Once scratch comes secondary eczamatization and infection is present.



Source; Photo 2 from Rook's Textbook of Dermatology 9th edition
Source; Photo 3 from IADVL text book of dermatology 3rd edition

Nodular lesions on genitals

Nodules are common in genitals of young child and young male adults. Persistent nodules are reddish brown extremely pruritic excoriated.
Male genitalia and axillae are commonest site. Associated with classical lesions in 2/3rd of patients
Pt with longer duration of untreated or inadequately treated scabies are more likely to develop nodular lesions

Scabies of clean

· Scabies mite may infest in clean hygiene population also but lesions are few and are commonly on the genitalia and thigh. Classical sites are spared. Very few papules may be present but burrows are uncommon. Sometimes present as chronic urticaria due to itch at times here and there.

Pruritis without lesions are also found in

· Hepatitis

· Uraemia

· Senile pruritis

· Drugs statins clofazimine rifampicin

Hence differentials above to be ruled out before making a diagnosis of scabies of clean.

Crusted scabies

· Crusted scabies is the most extreme type of infestations remarkably asymptomatic, more than million mites, marked crusting

and psoriasis like plaques in usual scabietic sites. It was first time reported in Lepers in Norway

· Found in uncared for persons only

· If not in uncared group search for other causes of immunosuppression, Hansen's, Turner & Down syndrome

· In addition to palm & soles head and neck lumbosacral areas may be involved in adults. Generalized lymphadenopathy may be present.

· Nail are dystrophic and discolored and masses of horny debris may accumulate under the nails

· Involvement of characteristic sites and occurrence of classical scabies in family

Complications of Scabies

· Secondary bacterial infections

· Glomerulonephritis (immune complex mediated) due to streptococcal infection

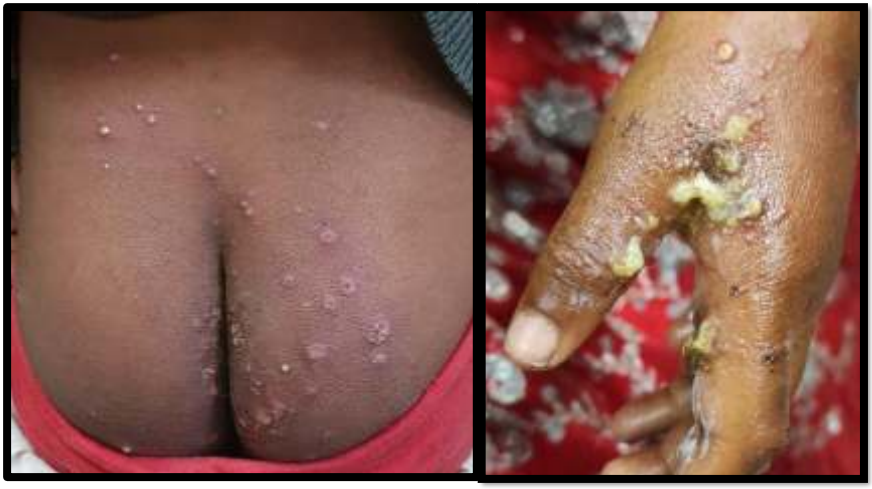
· Eczematization

· Post scabietic pruritis

· Persistent delusions of parasitosis

· Septicaemia, bacterial endocarditis and death have been reported in association with scabies especially in immuno-compromised

Infected Scabies



Infected scabies pustules in natal cleft and hand

Management

· General measures are important to treatment

· Entire family to be treated as one unit, even non-symtomatic members. (Even close contact if possible)

· All bed-sheets, pillow cover and "chader" and quilts to be washed in hot water temp >80^{0}c Or

· If unable to do so then sunbathe (hot sun) quilt etc for more than 4hrs Or

· If old clothes unable to wash, keep them in isolation in plastic bags atleast for 3 days

· All clothes in Elmira need not be washed. Mites do not survive more than 3 days in any case outside human body.

· Before applying drug for first time a shower is advised but not scrub bath

· Drug should be applied below from neck down.

Drug	Indications	Remarks
Permethrin, 5% cream	Treatment of Scabies. May also be used for pediculosis	Advantages: Can be used in infants >2 months of age, in pregnancy/lactation. Rinse after 8-12 Hrs
Benzyl Benzoate, 25% emulsion/lotion	Cure rates are only slightly inferior to permethrin if applied properly	Limitations:Irritation after application. Not to be used in children<2 years

Recent Meta-analysis has suggested that permethrin is the most effective drug in Scabies

- Permethrin cream 60 gms or lotion 50 ml is sufficient for average Indian adult.
- Applied overnight, all over the body below the neck as thin film like done in oiling of body.
- Special attention to be paid to ensure that all areas where propensity of mite is high not to be left, e.g. genitals, lower abdomen, web of fingers, natal cleft and areola. Take bath, next morning. All family members under one roof to be treated simultaneously. (In Tinea all affected family members to be treated simultaneously.
- The other option is ivermectin, the **only oral antiscabiatic**. Given in doses of 6 mg stat to children between 2 to 12 yrs and 12 mg stat to all above 12 yrs as a single stat dose.
- Very good option in large closed groups, such as jail inmates and hostels. Not well studied in aged below 2 yrs and not recommended in aged population.

Management of complications

Pruritis

· Oral antihistaminics (levocetrizine, CPM and others)

· In long standing cases hypersensitivity may last up to 3wks so antihistaminics may be continued for 3 - 4 wks

Infection which at times lead to sepsis

· Oral and local antibiotics e.g. framycetin locally and oral antibiotics covering staph and streptococcus e.g. amoxyclav are recommended.

Eczematization

· Eczematization is common due to scratch reaction and local moderate steroid once daily for a 1-2 wks are sufficient e.g. betamethasone valareate

Management is same at all level of cares (Primary Secondary and Tertiary)

Customization of Treatment

1. Proper diagnosis must along with diagnosis of complications if any.

2. Counseling must and general management as detailed earlier to be followed religiously otherwise reinfection from family members and fomites common.

3. Apply permethrin as detailed before and give stat doses of ivermectin as per age. Single application of permethrin is sufficient. If required to be repeated then do it after 14 days.

4. Antihistaminics must for 2-3 weeks. In some cases where pruritis continues antihistaminics may be continued for upto 4 weeks

5. Treat complications if any.

CME 3

PSORIASIS

Introduction

Psoriasis is a chronic inflammatory papulosquamous disease characterized by presence of well demarcated erythematous plaques with typical fish like silvery scales. It is a T-cell immune mediated genetically determined disease affecting skin, nail and joints with an unpredictable course of remission and relapses.

Prevalence is approx 2-3% in India. However in specialized skin OPD's of UP government Hospitals, it is 5% of total OPD making it a top ten dermatological disorder for seeking treatment .

Epidemiology

Psoriasis can first appear at any age. At Balrampur Hospital Lucknow our youngest patient was 3 months old child and oldest 80 year old age with first time clinical features of psoriasis. The disease is uncommon before teenage and more than 80% of patients are below 50 years of age. It has a bimodal peak. First peak incidence is at 20-25 years (early twenties) and second peak is at 45-50 Year (late forties).Both sexes are equally affected. Most patients worsen in winter than in summer. Trauma has been documented to cause psoriasis at site of injury (Koebner phenomenon). The time between injury and onset of psoriasis is approx 1 to 2 weeks.

Infections especially streptococcal phanyngitis, dental sepsis abscess, staphylococcus aureus, yeast malassezia and candida species are known to exacerbate disease in genetically prone patients. HIV infection also aggravates but psoriasis incidence is not increased in HIV positive population.

Certain drugs precipitate psoriasis in genetically prone like lithium, beta blockers, antimalarials & NSAIDs. Some drugs like

cabamezepine, ACE inhibitors, calcium channel blockers, sodium valproic acid have been implicated in exacerbation of psoriasis. Withdrawal of oral caticosteroid precipitates psoriasis. Sun exposure can induce psoriasis in few prone individuals especially in HLA Cw6 association.

Psychological issues like mental stress predisposes to early onset and exacerbation of disease. Smoking has also been implicated in onset of psoriasis in prone individuals. Alcohol exacerbates psoriasis. High dose of estrogen and hypocalcinimea has also been implicated in precipitation of psoriasis in prone persons.

Pathogenesis

· Genetic linkages are clear and more research is going on. Up to now nine Psoriasis genes (PSOR 1-9 genes) have been identified.HLA antigens HLA-Cw6, HLA-B13, HLA-27 increases association of early precipitation

· There are increased familial cases. 35-73 % concordance in monozygotic twins and 12-22% concordance in dizygotic twins has been found. First degree relatives are at increased risk.

· Inheritance is basically mutifactorial (Autosomal dominant with incomplete penetrance) requiring polygenic and environmental factors for its clinical expression

· Th17 pathway is now considered as key inflammatory cascade. Auto immune cascade in psoriasis is basically formed by T-cell (Th1) response with increased cytokines IFN-Y IL2, IL6, IL15, IL17 IL22 and IL23 and reduction in IL10 which leads to epidermal proliferation, shortening of epidermal cell cycle and faster and increased shedding of epidermal cells. In a normal healthy individual 6.5 pounds of epidermal cells are shed every year.

Histopathological features

1. Epidermal hyper proliferation with increase in proliferating cell compartment in basal and suprabasal level.

2. Parakeratosis (Presence of nuclei in stratum corneum), acanthosis, suprapappilary thinning. Collection of neutrophills in spinous layer (Munro's micro abscess).

3. Dermal vasculature especially vertical capillary loops are dilated elongated tortuous and twisted with proliferation of vascular endothelium with lymphocytic infiltrate in dermis.

Types

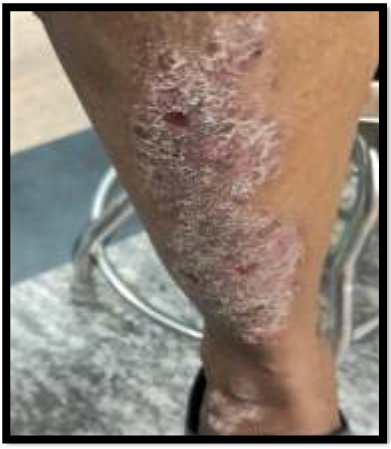
- Chronic Plaque Psoriasis CPP (Classical Psoriasis or Morphological protype) is most common presentation
- Guttate psoriasis (acute onset pattern)
- Erythrodermic psoriasis
- Palmoplanter psoriasis
- Pustular psoriasis (considered acute onset pattern)
    - Generalized pustule
    - Localized
    - Palmoplanter pustulosis
    - Acrodermatitis continua of Hallopeau
- Psoriatic arthritis

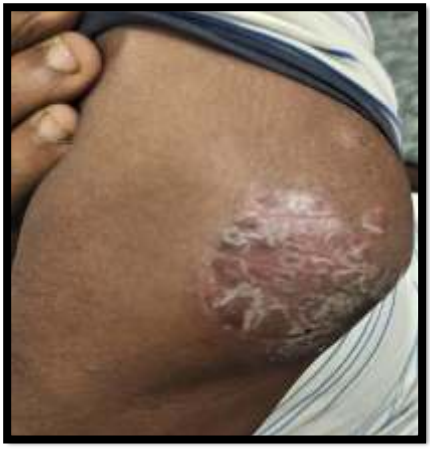
Clinical features

Morphology of Chronic Plaque Psoriasis (CPP)

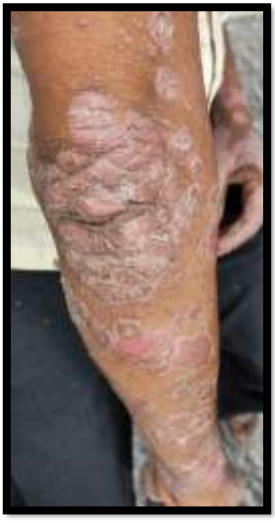
- Sharply demarcated salmon pink (deep red in white population) in untreated lesions with mild induration with semi adherent **fish like silvery** scales. Treated plaques with local steroid shows a hypo pigmented halo due to depletion of PgE2 (Woronoff'f ring). Initially

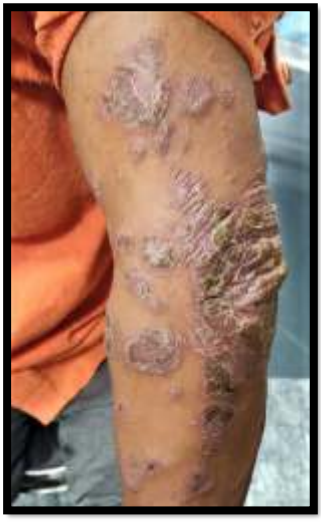
lesions are discoid but as they grow may merge to form polycyclic gyrate geographic annular lesions. Size and number of lesions vary with person to person. Lesions are found on all parts of body but are usually prominent on extensors, knees, elbow and lumbosacral area.

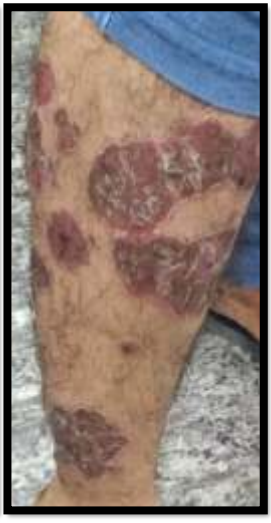




Psoriatic plaque well defined erythematous, indurated with fish like silvery scales







Typical lesions of chronic plaque psoriasis with fish like scales, on a salmon pink background

Differentiating CPP (scale) and Dermatitis (crust)

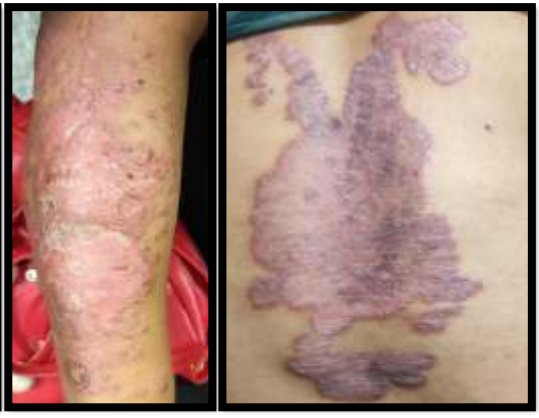
Grattage Test is used to confirm psoriasis and to differentiate it from crusts of dermatitis

· A tilted glass slide which is used to scrap gently the scales. The silvery nature of scales (d/t air trapped) is increased.

· Removal of scales further reveals a smooth red glossy adherent membrane (Membrane of Burckeley)

· If this glossy surface is scrapped further pin point bleeding spots appear on surface. (Auspitz sign) This is due to elongation of vertical capillary loops in dermal papillae and thinning of suprapapillary epidermis.

Extensive psoriatic plaques with typical scales

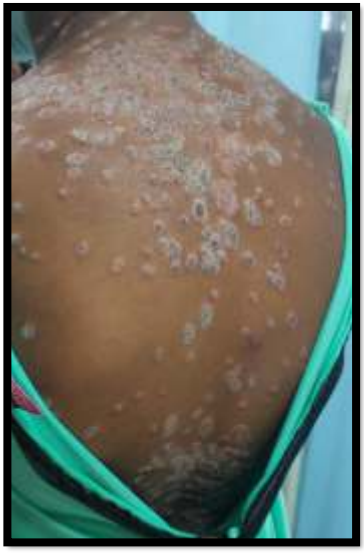


Chronic plaque psoriasis under treatment with few scales in extensors of hand and lumbosacral area (typical sites)

Morphology of Guttate Psoriasis

Small rain drop (guttate) like deep red papules with silvery scales (sparing of palm and soles) usually found on trunk which appear after episode of URTI/tonsillitis/sore throat and dental abscess/sepsis. Guttate psoriasis is more common in young adults. Prognosis with spontaneous remissions occurs during course of the disease in few weeks after treatment with appropriate antibiotics.

Rupoid Psoriasis at lumbosacral area

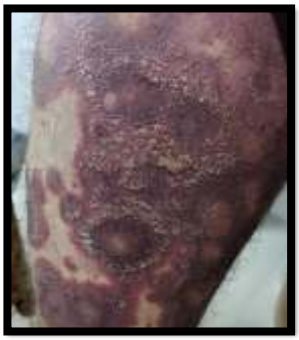


Scaly lesions all over trunk after a bout of tonsillitis

Morphology of Pustular Psoriasis

Sterile pustule evolves from an erythematous background. Considered as an acute precipitation form, usually precipitated by withdrawal of oral corticosteroid or overuse of irritant like dithranol. It is generalized all over body (Von ZumBusch type) or localized affecting palm and soles only, often called as palmoplanter pustulosis. It is often associated with fever, tenderness and chills. Pustules are easily damaged forming what is known as lakes of pus. Pustules come in waves; propensity to converting into erythroderma (high mortality) is common.

A rare form is acrodermatitis continue of hallopauea where digits are involved and pustulosis starts at tip of finger or toes and ascends locally sometimes may evolve in generalised pustular psoriasis. The tip of finger is painful and bony extension leads to osteolytic changes of distal phalynx.



Generalized Pustular Psoriasis with pustular lesions on erythematous background

Morphology of Erythrodermic Psoriasis

Erythroderma is associated with significant mortality. The plaque merge to form uniform reddish skin >90% involvement with marked scaling with itch. Complications like hypopthermia, electrolyte imbalance contribute to mortality. Pustular Psoriasis has more propensities to convert to erythroderma. Irritant effect of Dithranol and withdrawal of systemic steroid precipitate erythroderma.

Erythroderma is also caused by

- Dermatitis
- Drug reactions
- Pemphigus Folacius
- PRP, T cell lymphoma
- Unknown causes >25%

Erythrodermic Psoriasis with diffuse scaling involving >90% of BSA with erythema

Psoriatic Arthritis

Almost 10-40% of patient of psoriasis have joint involvement and in a few joint disease surface even before skin lesions. All patients are rheumatoid factor negative (seronegative) and a strong HLA-B27 association

Classification criteria for psoriatic arthritis (CASPER). A score of 3 is sufficient for diagnosis of psoriatic arthritis.

Classification criteria for psoriatic arthritits (CASPAR)		
Entry criteria: Inflammatory articular disease of the joints, spine or enthesis		
Psoriasis	Current psoriasis Personal history of psoriasis	2 1
	Psoriasis in a first-or-second-degree relative	1
Typical psoriatic nail involvement	Onycholysis, pitting, hyperkerotosis	1
A negative test for rheumatoid factor	Any method except latex agglutination	1
Dactylitis	Current dactylitis or History of dactylitis	1
Radiological evidence of juxta articular new bone formation		1

Clinical types of Psoriatic Arthritis (Ps-A)

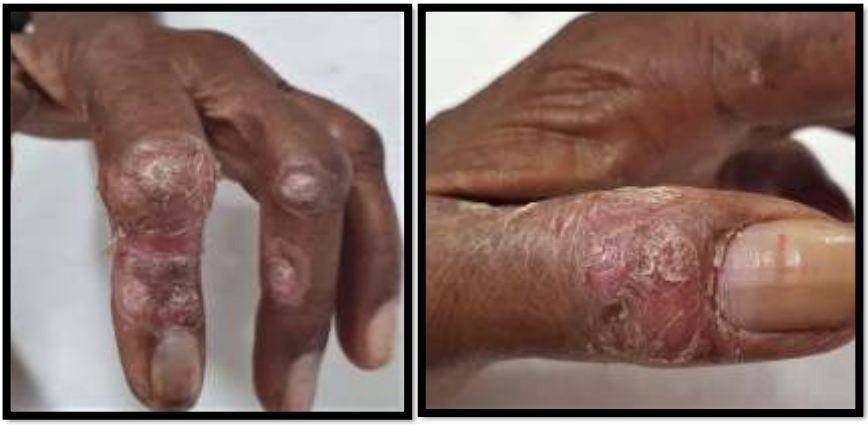
· **Asymetrical oligoarthritis**- It is the most common type involving single joint or few IP joints.

· **Digital IP arthritis-** It is the most classic form involving DIP. RA typically involves PIP. The affected finger nails are also involved with pits all over nails (usually more than 20).

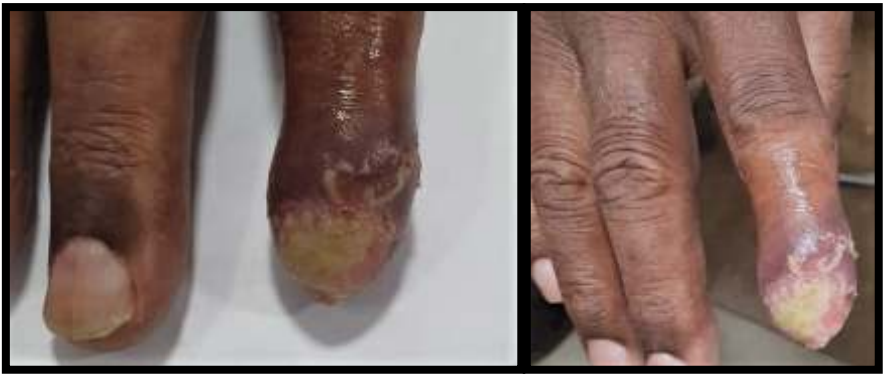
· **RA type-**Involves PIP joints and is present in approx 15% of patients & is symmetrical. Less severe type.

· **Axial type-** Rare type associated with ankylosing spondylitis and sacroillitis. Associated with HLA-B27.

· **Arthritis Mutilans-** Rare form affecting less than 5% of all PS-A where gross resorption of digits takes place.



Typical Psoriatic arthritis of IP joints



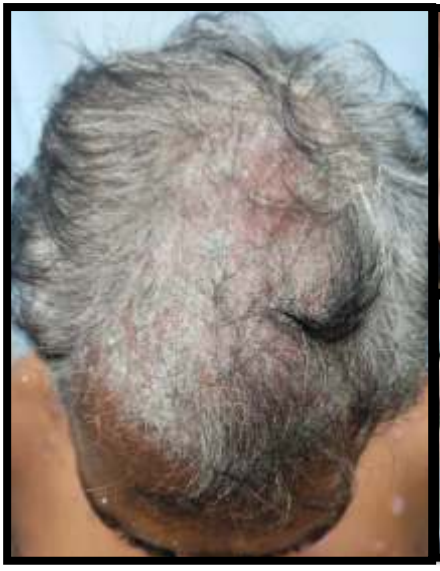
Acrodermatitis continua of Hallopeau

Regional modification due to part affected

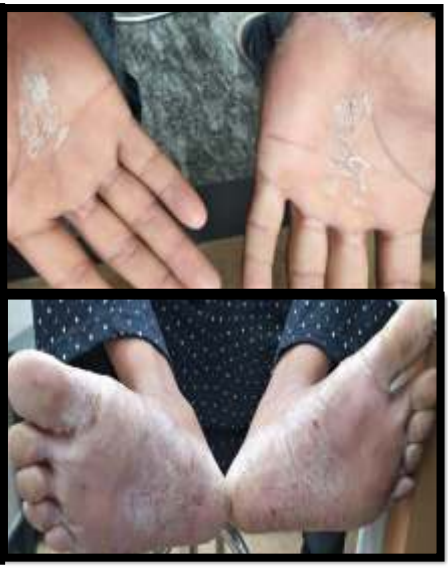
Scalp Psoriasis- Well defined localized indurated white scaly plaques which have to be differentiated from scales of seborrheic dermatitis which are greasy yellowish.

Flexural Psoriasis (Inverse Psoriasis)- Psoriasis plaques are usually found on extensors of body and in rare event it is present on flexural, intertrigenous areas of axila, inframamary region and inguinal areas. The well demarcation of lesion is key point to be noted and is to be differentiated with tinea and candida which are more common lesions of intertrigenous areas.

Palmoplanter- Lesions are very common in central Uttar Pradesh. Usually bilateral symmetrical well defined. Scales are adherent and do not often give silvery appearance as in other parts & eythema is not prominent. To be differentiated from irritant contact dermatitis of palm and soles.



Scalp psoriasis



Palmoplanter Psoriasis; adherant scales with well defined plaques

Diagnosis

Diagnosis is based on clinical morphology of salmon pink well demarcated plaque with fish like scales in classical chronic plaque psoriasis and in other types also diagnosis is based on morphology. In case of doubt or otherwise investigation of choice is Biopsy & Histopathology.

Severity scale

Clinical evaluation is done with **PASI** (Psoriatic Area severity Index) which takes into account erythema, induration and scaling of head, upper and inner limb and trunk. Takes time and proper recording, hence in a busy OPD likes ours for treatment purposes BSA is used.

Management

Pretreatment Activity & Counseling

· Emotional support is absolutely required as morbidity increases poor quality of life.

· Counseling about disease is a must by clinician in first visit.

· Most of patients are worried up to how long treatment will continue. It is not life long as waxing and waning nature of disease and with minimum treatment morbidity can be controlled. Nature of treatment is suppressive and not curative as disease is genetic in nature.

· Precipatory factors to be identified individually and corrected. Drugs/ Smoking/Weight to be managed.

Treatment Tools Available

· **PHOTOTHERAPY**

  · NBUVB 311nm Chambers

  · PUVA Chemotherapy

- **Topical therapy (local applicants)**
  - Moisturizers/ Petrolatum jelly
  - Coal Tar 3-6% solutions/gel/ointments
  - Dithranol 0.25-2%
  - Calcipotriol 0 .005% (Vit D analog)
  - Tazoretene 0.05-1% (Vit A analog)
  - Potent topical steroids
  - Clobetasole propionate
  - Halobetasole
  - Betamethasone dipropionate
  - Potent steroids plus salicylic acid combination
- **Systemic Agents (oral)**
  - Methotrexate (MTX) (the most common agent used in India.)
  - Acitretin-(Vit A analog)(used extensively in pustular psoriasis)
  - Cyclosporin (second fastest acting @5mg/kg/day dose)
  - Apremilast (PDe4 inhibitor)- Minimal S/E, may be used unmonitored
  - Tofacitinib (JAK I & III Inhibitor)
- **Biologicals**
  - Inflixizumab- (Fastest acting, preferred in erythroderma)
  - Eternacept (TNF-alfa inhibitor)
  - Adalizumab (most commonly used biological)
  - Secukinumab- (IL-17 inhibitor)
  - Risankizumab IL-23 inhibitor

At primary and secondary care centres topical, and immunosuppressant and MTX are prefered and at tertiary care centers topicals, immunosuppressant plus Apremilast and Tofacitinib and or biologicals may be used.

Topicals

Agent	Application style	Indication	S/E	Remarks
Coal Tar 3-6% CT with salicylic acid as lotion and shampoo and or combined with ketaconazole to cover SD is also used.	Daily application or and may be followed by UV exposure	CPP with BSA<10%	Allergic Contact Dermatitis Chemical folliculitis	Very Safe Improved response when combined with salicylic acid Most products have a typical smell. CT shows best results when pure and when purified loses some of its antipsoriatic properties.
Dithranol 0.05%, 0.25-2% combined with or without salicylic acid	Concentration (0.25-2%) applied for 10-30 minutes. Protect surrounding skin with Vaseline/petrolatum To be avoided on face, flexures and genitals.	CPP when surface area involved is small	Irritation Iirritant contact dermatitis with discoloration of skin which is removed very quickly	Short contact is safe. Irritant effect is highest among topicals used by trained dermatologists only now
Calcipotriol 0.005% may be combined with topical steroids	Twice daily application. Do not exceed 100 g/week		Avoid in extensive psoriasis due to chances of Systemic absorption	Colorless (does not stain skin or clothes like coaltar or daithranol) Easy to apply Irritation is negligible considered good option but cost is key road block in poor patients
Tazarotene 0.05-0.1% Can be combined with topical steroids	Once daily application If irritation, reduce duration of contact	Localized CPP on small areas	Irritation is only second to diathranol in most patients Reduces scaling and plaque thickness but not erythema	Newer topical retinoid costly

Systemic agents			
Drug dosage	**Indications**	**S/E**	**Monitoring**
Methotrexate (MTX) Used in doses of 5mg-25mg /per week. Maximum doses to not exceed 25mg/ per week. Yearly cumulative dose not to exceed 1gm. Median weekly dose is 15mg. children 0.2-0.7mg/kg/wk Drug may be given in divided doses or single weekly dose. Effects and side effects are same in single or divided doses Add folic acid 5mg for 2-3 days/wk but not on day of MTX administration. Reduces haematological S/E	It is effective in all type of psoriasis. Palmoplanter and Debilitating psoriatic arthritis respond well to MTX Most common drug used, as cheap easy to use and all dermatologists are well trained in use and monitoring	**Commonest** S/E is nausea and gastric erosion. Pancytopenia most dreaded s/e. severe Anemia. **Hepatotoxicity:** Highly hepatotoxic If SGPT increases by 2X then continue,@3x alert and at 4X (160)stop the drug Hepatic scan after every 3.5 to 4gm of cumulative dosage to rule out hepatic fibrosis **Bone marrow suppression:** manifests as leucopenia and thrombocytopenia **Teratogenicity and mutagenicity:** **Category D drug in pregnancy. C/I in lactation** Use contraception: for 1 month in females and 3 months in males.	**Baseline:** CBC, LFT, KFT and Chest X-ray must be done before starting. **Follow up:** CBC and LFT biweekly x 6 weeks; then 4-8 weekly. **KFT** yearly if suspicion of kidney dysfunction. Then do creatinine clearance and if >30% decrease then drug may be considered to be stopped. Do KFT more regularly and titrate dose, if KFT impaired. Avoid concurrent use of aspirin, sulfonamides, tetracyclines, frusemide. Or reduce dose of Mtx.

Methotrexate restores the immunosuppressive functions of of T-regulatory cells and down regulates IL-17. Low dose MTX has anti-inflammatory action and also leads to accumulation of adenosine in tissue and potential inhibition of leucocyte accumulation.

Before starting MTX, a baseline of CBC, LFT, KFT must be done and if higher doses are selected then screening for HepB, HepC, HIV and latent TB should also be done. This is however mandatory when biologic therapy is started. Biologic therapy should be stopped for 6-12 months before giving live vaccines

Drug dosage	Indications	S/E	Monitoring
Acitretin 25-50 mg Start with 25 mg daily in adult. Max 50mg daily	In Pustular psoriasis psoriatic erythroderma it is more effective	**Commonest s/e**. Cheilitis, dryness of mouth, vagina and eyes .Peeling of skin and pruritus**.** **Use of emollients becomes a necessity.** in women of child-bearing age **Body clearance time is 2-3 years hence contraception by 2 methods if used.** Elevation of triglycerides and cholesterol**. Avoid in familial hypertriglcerimia** Liver toxicity Ossification of paraspinal ligaments are other s/e of note In acse of low backache then xray lumbosacral spine urgently.	**Baseline** **CBC ,LFT and Lipid profile and before starting** Baseline, at 4 weeks, and then 3 monthly stop acitretin if lipids raised or add a lipid-lowering agent. Yearly X-ray of spine for monitoring ossification of paraspinal ligaments. **Pregnancy precaution absolute or drug not to be used if likely to get pregnant**
Cyclosporine Dose of 5mg/kg/day in erythroderma. Dose reduced to 3.5mg/kg/day when erythema subsides. Regular dose is 2.5mg to 3.5mg/kg/day	Used in all types of psoriasis but Pustular psoriasis Psoriatic erythroderma respond very well. Much less hepatic damage. Cat B drug in pregnancy	**Hypertension:** mild-moderate in 30% to 40% of patients. Treat with calcium-channel blockers (amlodipine) Avoid diuretics (worsen real function) and beta blockers (worsen psoriasis) **Pancytopenia and GI erosion are much less than MTX** • **High level of Nephrotoxicity.**	**Base line** **CBC LFT KFT at baseline befor starting** **BP :** Daily initially and then weekly x 4wks **Serum Creatinine:** Baseline. Then weekly and later monthly. Dose reduction by 25-50%, if serum creatinine level rises to 30%> baseline. Drugs withdraw if creatinine level persistently elevated, despite dose reduction.

Biological drugs

Drugs	Mechanism of action	Route	Dose	Side effects
Risanki-zumab	Targets the subunit p19 of IL-23 and inhibits it without interfering with subunit p40 that is shared with IL-12	Subcutaneous	150 mg(two 75 mg injections)administered by SC injection at week 0, week 4, and every 12 weeks thereafter	Mucocutaneous oppurtunistic infections candida infections, malignancies lymphoma
Secuki-numab	Binds to, and blocks the biological activity of IL-17	Subcutaneous	300 mg on week 0, 1, 2, 3 and 4 followed by 300 mg every 4 weeks	Mucocutaneous oppurtunistic infections candida infections, malignancies lymphoma
Etanercept	Blind to and neutralizes the activity of TNF-α	Subcutaneous	50 mg twice weekly for 13 weeks, then 50 mg once weekly	URTIs, Sinusitis, Rarely, opportunistic infections(TB), malignancies(lymphoma,nonmelanoma, skin cancers)
Infiximumab	Blind to and neutralizes the activity of TNF-α	Intravenous	5 mg/kg on week 0, 2 and 6, then every 8 weeks	URTIs, Rarely, opportunistic infections(TB), malignancies (lymphoma, nonmelanoma, skin cancers)
Adalimumab	Blind to and neutralizes the activity of TNF-α	Subcutaneous	80 mg initial dose, then 40 mg every 2 weeks, starting 1 week after initial dose	URTIs, Rarely, opportunistic infections(TB), malignancies (lymphoma, nonmelanoma, skin cancers)
Usteki-numab	Targets the shared protein subunit p40 of IL-12 and IL-23. Thereby it inhibits the action of these two cytokines, secreted by the myeloid dendritic cells upon activation of naïve T-cells into Th-1 And Th-17-cells	Sub cutaneous	45 mg (<100 kg) or 90 mg (>100 kg) on week 0, 4 and 14 (weekly)	Nasopharyngitis, URTI, Headache, fatigue

Source; Adapted from IADVL recent advances in dermatology by editor in-chief Shital Poojary 2nd edition

Customization of treatment

Customization of treatment depends on age, occupation, sex, general health, type and extent of disease. Disease severity index PASI is used to assess severity as well as response, however in busy OPD it is difficult to calculate hence body surface area has been used with great success.

In Less than 10% BSA involvement

Topical alone may be used.

- Emollients- **Key component**-always to be used in all form of skin involvement.
- A. Topical steroid (potent) - on less scaly lesions.
- B. Salicyclic acid up to 3% when combined with potent steroid increases penetration and 6% salicylic acid acts as keratolytic agent and may be used when thick fish like scales are present. Tachyphylaxis occurs usually after 6-8 weeks and if stopped for 4-6weaks it again regains effect.
- To cover up for Tachyphylaxis period.

Out of coal tar/ Dithranol (High irritant effect)/ Tazoretene/ Calcipotriol one of them may be used. Calcipotriol is considered comparatively the best but initial effect is delayed for up to 2 weeks. May be used for 4-6 weeks, till topical steroid are used again or may be continued (with cost implications)

In 10-30% BSA Involvement

Topicals emollients, topical steroids and calcipotriol all three may be used initially but if no appreciable improvement in lesions, oral agents may be added.

The most common oral agent is **Methotrexate** (MTX). Methotrexate when given judiciously and with required appropriate monitoring is safe. Instructions and dosage should be clearly written on

prescription in both medical and Hindi script to not only make patient but also the dispensing pharmacist to understand. Most calamities with MTX have occurred when used daily or used unmonitored. **Acetretin** is used more in pustular psoriasis, where cyclosporine is also equally effective. **Aperimilast** is new addition and can be given un-monitored but is effective in 50-60% of cases and where effective is a very good drug.

Apremilast is phosphodiesterase 4 (PDE4) inhibitor and leads to increase in cAMP which ultimately decreases the proinflammatory cytokinines (TNF alfa, IL23,IL12 and increases IL10. Monitoring is not required as with other immunosuppresent use in psoriasis. Headache , vomiting and diorrhea are common side effects and resolve by 2wks of use. Doses may be started from 10mg once daily to maximum of 30mg twice daily in an adult.

Tofacitinib is a new agent and experience of Indian dermatologists is not much, however it is said to be effective. Tofacitinib is Janus Kinase Inhibitor and interferes with JAK signal transduction and activation of a transcription signaling pathway. Monitored drug unlike apremilast. CBC, LFT and KFT are monitored and also PT INR. It should be tapered off slowly in 4-6 months. Sudden withdrawal has been associated with aggressive relapse.

At tertiary centres if psoriasis is not controlled on immunosuppresents, PDE4 inhibitor or JAK inhibitor then biologicals may be initiated. Cost implications are too high to be routinely used even in private setups. Adalizumab, Eternacept are commonly used biologicals.Inflixizumab is the fastest acting and most commonly used in erythrodermic psoriasis.

Suggested Treatment ladder

Mild plaque Psoriasis without Psoriatic Arthritis

First line:

- Potent topical corticosteroid
- Vitamin D analog
- Coal tar
- Dithranol
- Second line:
- NB- UVB or PUVA
- Excimer laser

Moderate to severe plaque Psoriasis without Psoriatic Arthritis

First line:

- NB-UVB or PUVA

Second Line :

- Methotrexate
- Cyclosporin
- Acitretin
- Apremilast

Third line:

- Adalimumab
- Etanercept
- Infliximab
- Secukinumab
- Ustekinumab

Moderate to severe plaque Psoriasis with Psoriatic Arthritis

First line:

- Methotrexate
- Apremilast

Second line :

- Adalimumab
- Etanercept
- Infliximab
- Ustekinumab
- Secukinumab

Third Line

- Combination therapy

Source; suggested treatment ladder adapted from Postgraduate Dermatology by Kaushik Lahiri & Abhshek De 2022 edition

Choice of therapy rests with treating physican and titration of response

More than 60% of cases of psoriasis have achieved good results with topical steroid, moisturizer and methotrexate at our centre.

CME 4

ECZEMA/DERMATITIS

Introduction to Eczema/Dermatitis

Eczema is a heterogenus group of inflammatory skin disease characterized by extreme pruritis, erythema, edema, papules, vesicles, oozing/crusting scaling and or lichenification.

Term eczema and dermatitis have often being used one for other however, eczema is non-specific and describes morphological features of “boil out” or weeping lesion while dermatitis is specific group of skin inflammation and is a broader umbrella which includes eczema.

Incidence & prevalence of eczema/dermatitis varies from country to country and with environment and life style within communities also. In Balrampur Hospital Lucknow Skin OPD approximately 10% of all OPD consists of dermatitis of various types, making it the top 10 skin disease for treatment seeking.

Eczema/Dermatitis is classified as Endogenous (something inside the body "endogen” that makes person prone) & Exogenous (Some chemical/irritant/" exogen" that damages skin)

The various types of dermatitis are differentiated into above classification as follows;-

Endogenous Dermatitis	Exogenous Dermatitis
Atopic Dermatitis(AD)	Irritant Contact Dermatitis(ICD)
Seborrheic Dermatitis(SD)	Allergic Contact Determatitis (ACD)
Nummular eczema	Photo dermatitis
Asteototic eczema	Infective Dermatitits
Stasis dermatitis	
Pompholyx	
Pityriasis Albae	
Lichen Simplex Chronius(LSC)	

Pre disposing factors

- Genetic- white race more prone
- Age- in very old age sensitivity decreases
- Drugs- In on steroid/Immunosuppressive, classical clinical feature are not precipitated.
- Dry skin is more prone
- Socioeconomic status- Nickel polished artificial Jewelery wearers more prone.
- Local plantation- Parthenuim grass highly allergic

Clinical features

Before diagnosing dermatitis/eczema one must have clear sense of ruling out. Tinea (approx. 50% of) skin OPD and psoriasis (5% of OPD) and then look for manifestation of 1) Pruritis 2) Erythema 3) Edema 4) Papules 5) Vesiculation 6) Oozing (weeping Lesions) & 7) Lichenification (Thickening, Increased skin markings hyper-pigmentation)

Lastly while focusing on above features pattern of presentation also helps in diagnosing as most of dermatitis have a typical pattern.

Diagnosis is basically clinical.

Investigations

Biopsy and histopathology (H/P examination) where clinical features are helpful (few cases)

Spongiosis in acute phase and psoriasiform pattern in chronic stage is found in H/P examination.

Radioallergosorbent test or RAST which is commonly done in name of allergy testing has high financial implication and efficiency is not up to the mark and is not recommended by most of dermatologists

Types of Common Dermatitis in clinical practice.

Atopic Dermatitis

Introduction

Atopic dermatitis is an endogenous dermatitis which is chronically relapsing, inherited, inflammatory skin desease with extreme pruritis and typical morphology.

The prevalence is estimated at 7.9% in 6-7 years and 7.3% in 13-14 year age groups. In Indian subcontinent the presence is 3-4.2% which is much less than American and European continents. It is approximately 1 to 2 % of total Skin OPD at Balrampur Hospital Lucknow.

Genetics has an important role in expression of disease and approximately 80 candidate genetic sequences have been identified with filaggrin gene mutation as key risk factor. Filaggrin deficiency contributes to dry skin due to defective epidermal barrier and there is impairment of adaptive and innate immunity. Increased susceptibility of bacterial viral and yeast infections have triggering role. Environmental factors like change in season, humidity allergens chemical soaps and psychological stress are also involved. Defective IgE increased in >80% of cases and increased expression of IgE receptors of B cells.

Genetics, Environment, Infections, Immnulogies, loss of skin barrer all combine together in expression of Atopic dermatitis.

Clinical Features

Typical Morphology

AD has 3 different patterns

1. Infantile age group pattern,
2. Childhood age group and
3. Adult pattern.

Earliest onset is commonly between 2-6 month of age and 60% developing the disease in first year of life. 2/3rd of patients who develop disease clears by 1.5 years of age and only rest proceed to have childhood phase, of which 70% also clear by 12 year of age. Few patients develop symptoms for first time in as adult.

- **Key** symptoms are –
  - Extreme pruritis
  - Typical morphology and distribution of lesion.
  - Dermatitis which is chronic or chronically relapsing
  - Personal or family history of atopy (asthma allergic rhinitis and atopic dermatitis)

Important symptoms on which AD may be suspected are:

- 1) Extremely dry skin 2) Infections 3) Dannie Morgan folds 4) Itching when sweating 5) Wool intolerance 6) Facial erythema
- Other symptoms of suspection are based on Haniffin and Rajka's criterion

1) Cataract 2) Cheilitis 3) Recurrent conjunctivitis 4) Facial pallor with or without erythema 4) Food intolerance 5) Hand dermatitis(irritant type) 6) Elevated IgE level 7) Immediate type I skin reactivity 8)Keretoconus 9) Keratosis Pilaris 10) Nipple eczema 11) Palmer hyperlinearity 12) Perifollicular accentuation 13) Pityriasis albae 14) White Dermatographism 15) Vulvar and Perianal dermatitis 16) Infra auricular, Retroauricular and infranasal fissuring 17) Atopics also develope urticaria frequently

UK working group criterion of diagnosis atopic dermatitis are:

Itchy skin plus (Three of the following features):

- History of flexural dermatitis
- Onset under the age of two years

- Personal history of asthma
- History of dry skin
- Visible flexural dermatitis

Typical morphology

In infantile group pattern (after 2 month to 1-1/2year of age)

· Extremely pruritic erythematous papules and vescicles which often ooze. Scaling, excoriations, crusting and secondary infection are also present.

· Typically begins on face, forehead, chin, scalp with sparring of diaper area. Lesions may involve rest of body especially extensors.

· Perioral and nasolabial folds are other areas which may be spared. Although course is chronic but most of the lesions resolve by 18 months of age.

Childhood phase (1- 1/2 year to 12 years)

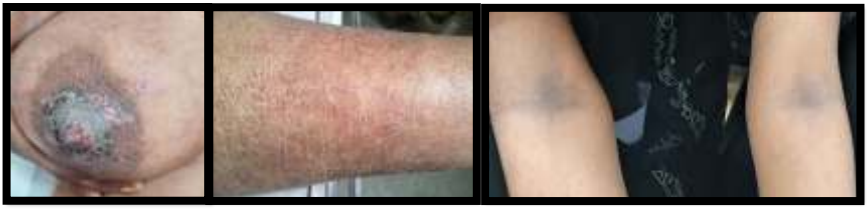
· Extremely itchy plaques on the flexures mainly on elbows, knees and neck, wrist and ankles.

· Erythema, oozing, crusting and lichenification reticulate hyper pigmentation on sides of neck may be present.

Adult phase

· Extremely itchy leathery lichenified plaques on flexures cubital fosae and popliteal fosae and sometimes involvement of wrist, ankles, face and neck.

· Nummular eczema, cheilitis and nipple eczema may also be present.



Nipple eczema | Dry Skin in Atopic | Flexural dermatitis

Diagnosis

Diagnosis of atopic dermatitis is basically clinical and strong suspection is important on criterion discussed above.(Hanifin and Rajka's). Suspected person's lesion matched with typical morphology to arrive at the diagnosis. UK working group criterion is more easily followed in diagnosing.

Investigations

Very few lab tests can confirm the disease hence emphasis is on clinical diagnosis. However serum IgE is being done routinely as more than 80% have elevated levels (normal up to 200 IU/ml. Food allergy tests (Rast method) have less than required accuracy level and are not advised routinely . A new test double blind placebo controlled food challenge (DBPCFC) is in consideration, not popular yet.

Management

· **General baseline measures are very important**

· Counseling parents/patient about the disease, its nature and chronic course, giving education material and explaining about the avoidance of triggers go a long way in management.

· Reassurances as relapses are frequent.

· Counseling on avoidance of scratching, although difficult but breaks itch-scratch cycle.

· Avoiding drying soaps. Bathing should be daily but of short time with luke warm water. Antiseptic and medicated soaps to be avoided. (Financial implication of medicated soaps heavy and evidence of benefit poor) After bathing immediately apply emollient or moisturizer.

· Apply moisturizer /emollient on all affected areas and dry skin area 2-3 times per day. Recent concepts are that use of skin barrier protection creams may prevent AD. Emollients form corner stone of

treatment and the most important part of general management.

· Avoidance of trigger is the 2nd most important part of general management.

· Avoid extreme of temperatures.

· Avoid woolen /synthetic clothing. Loose cotton, full sleeve shirts and full pants to be promoted.

· Wash sweat or pat dry with cotton towel.

· Avoid extreme detergents during washing of clothes.

· Avoid exposure to pets, pollens, house mites.

· Evidence of improvement on diet restriction is lacking and should not be followed as nutrition status suffers until and unless evidence of food allergy is present.

Available tools for treatment

Topical Applicants

· Moisturizer as discussed in general measure.

· Topical steroid (potency as per skin condition)

· Steroid sparing agents (Tacrolimus)

· Treatment of infection/ topical antibiotics

Systemic Therapy

Available tools for treatment

· Immnosuppresents

· Newer agents JAK Inhibitor(Tofacitinib)

· Antihistaminic

· Oral steroid

Discussion on tools available and their customizations

Moisturizer as discussed in general measures is primary focal point of general management.

Topical corticosteroid (TCS)

Topical steroids are First line of management in mild to moderate AD.

Choice of topical steroid depends on patient's age, chronicity of disease, potency of steroid. As a rule potent steroid (Clobetasole propionate, Betamethanone dipropionate & Halobetasole) should be avoided on face genatalia, axilla and inguinal areas.

Start with lower potency in infants and children (desonide, hydrocortisone and clobetasole butyrate) and if response is poor in 1 to 2 weeks then moving over to medium potency (fluticasone, mometasone) may be considered.

Monthly application of TCS should not exceed 15 gms in infants, 30 gm in children and 60 gms in adolescent and adults.

Long term use gives classical known side effects like atrophy, strae and hypertrichosis and other side effect like perioral dermatitis and osteopenia. So the duration of local application should be short and steroid sparring agents then brought in. After 4-6 week tachyphylaxis occurs. Usually once a day use is preferred.

Steroid sparing agent (Calcineurin inhibitors)

Calcineurin inhibitors (**Tacrolimus** 0.03% & 0.1% & **Pimecrolimus** 1% cream)are used.Tacrolimus 0.03% is (FDA approved for age 2 years and above) and pimecrolimus 1% are used even in children less than 2 years of age and do not have atrophy telangiectasia or strae as side effects and can be used for prolonged period unlike local steroids. Irritancy and stinging sensation on damaged skin are prominent side effects. Tacrolimus is now considered as key drug in management of atopic dermatitis as it increases the duration between two reoccurrences.

Treatment of infection

Prevalence of S.aureus on atopic skin is 60%-100% of patients and correlate with severity of dermatitis. Hence a short term use of local antibiotics. (Framycetin/fusidic acid/mupirocin) is recommended and if systemic infection is present then oral antibiotics (Amoxicillin, Cefadroxil, Cefuroxime, Cefixime) are preferred.

Oral Steroids

Systemic steroids are not preferred. However a short term less than a wk are used by few dermatologists if immunosuppressant cannot be initiated in an aggressive disease due to some contraindications.

Antihistaminics

Antihistaminics use to improve itch is controversial and evidence of benefit is not proved however sedating first generation antihistaminic (hydroxizine, clorpheniramine maleate) may be used where sleep is disturbed. In reality every dermatologist uses antihistaminics. If sleep is disturbed then growth hormones are not secreted and growth suffers in infants and children

Systemic immunosuppressant.

They are third line therapy when 1st and 2nd start failing or in severe wide spread and recalcitrant AD.

Currently methotrexate, azathioprine, mycophenolate mofetil and cyclosporine are used. Methotrexate with its low cost is used excessively but cyclosporine is considered as best choice. Only cyclosporine is approved in western countries, for severe AD in children. Dose of cyclosporine is 3-5 mg/kg/day maximum up to 1 year. Monitoring of BP & S.creatinine is necessary. Creatinine clearance in case kidney involvement is suspected. A 30% deterioration in C.clearance is a sufficient alert for consideration to stop the drug.

Methotrexate (MTX) is more popular (available, easy to administer in weekly dosage and cheap). Dose of 0.2-0.7 mg/kg per week shows good improvement in approx 75% of children 3-18 yrs of age. CBC LFT, KFT are to be monitored. Weekly dose not to exceed 25 mg and yearly cummulative dose not to exceed 1gm. After every 3.5-4 gm of cumulative dose administration liver fibroscan is to be done to rule out hepatic fibrosis.

Azathiopriene (AZA) in dose 2.5 -3.5 mg/kg/day and **Mycophenolate Mophetil** (MMF) in doses of (40-50 gm /kg/day are other drug used. MMF has favorable long term side effects. MMF efficiency in children is not well studied.

New Agents

Tofacitinib (JAK inhibitor) in dose of 10mg bd has shown significant clinical improvement. A dose of 11mg SR is also been used in adults.

Suggestive Treatment ladder for Management of Atopic Dermatitis

Mild AD	• Basic skin care • Avoidance of triggers • Emollients • Counselling
Moderate AD	• Basic skin care • Avoidance of triggers • Emollients • Topical steroids • Topical immunomodulators-calcineurin • Inhibitors • Oral antihistamines • Counselling
Severe AD	• General skin care • Avoidance of triggers • Emollients • Systemic corticosteroids • Immunosuppressants • Oral anthistamines • Counselling

Source; adapted from Postgraduate Dermatology by Kaushik Lahiri & Abhshek De 2022 edition

Choice of therapy rests with treating physician and level of care.

Moisturizer, topical steroids, short course of antibiotics and Tacrolimus has provided very good relief in more than 80 percent of cases at our centre.

Seborrheic Dermatitis (SD)

Introduction

This is a very common endogenous dermatitis. The areas rich in sebaceous glands, scalp, nasion, eyebrows, nasolabial folds, retroauricular region, presternal, interscapular regions, pubic area and fluxures are sites involved in isolation or in combination.

It has a bimodal peak of incidence. First peak occurs in infancy while the other in third to fourth decade in adults. Children are not usually affected. SD is more common in HIV infection, Parkinson's disease and patients taking Lithum and Haloperidol. It is more common in males than females. The disease runs a chronic course with relapses.

Pathogenesis

It has strong association with over growth of commensal skin yeast malassezia species especially furfur and responds to antifungal therapy thus proving a link however exact pathogenesis is not yet determined.

Seborrheic dermatitis involving scalp with hypopigmentation

Clinical feature and morphology

A) Infantile age group.

Asymptomatic, begins on scalp as thick adherent greasy yellowish scale (cradle cap) usually self limiting mostly within 6 months. May involve other seborrheic sites.

B) Adult Phase

Lesions are usually in scalp with less greasy yellowish scales and erythema. The other seborrheic areas get involved with erytrematous macules to thin plaques with scales which may not be greasy yellowish but dry fine and sometimes white.

C) Trunk involvement in adults

Several patterns are present on trunk

· **Petaloid pattern-** commoner pattern on chest (trunk) reddish brown papules with peri follicular greasy scales resembling flowers petals.

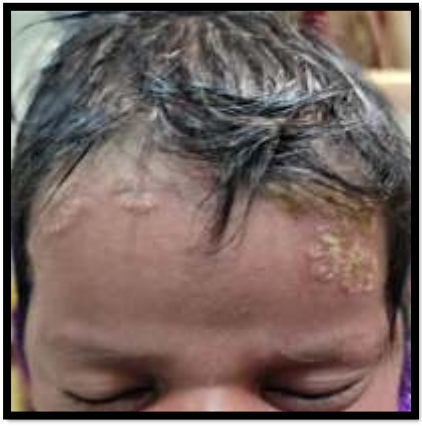
· **Pityriasiform pattern-** rare form generalized macules and patches as in pityriasis rosea.

· **Generalized type-** severe variety, whole body may be involved. May progress to Seborrheic folliculitis- erythroderma.

· **Erythemetous follicular papules.**

· **Flexure types-** Sharply dermarcated erythema with greasy scales with (crusted fissures in fold). Secondary infection and eczematization may also occur.

Infantile seborrheic dermatitis



Follicular papular greasy scales infantile SD

Diagnosis

Diagnosis is clinical on basis of pattern and involvent of seborheic areas. The pattern is so specific that to miss SD is difficult.

Other diseases in seborrheic distribution are (All are comparatively rare)

1. Pemphigus folaceous
2. Darier's Disease
3. Langerhan's cell Histiocytosis

Treatment

Cure is not permanent and treatment is aimed at control of symptoms and prevention of relapse.

Azoles (oral and local)

Azoles are antifungal (Fluconazole, Clotrimazole, Miconazole, Ketaconazole, Luliconazole) and are key drugs both in oral and topical forms in management of seborheic dermatitis.

Fluconazole 400 mg stat (single dose in adults) is sufficient although 150 mg once a week continuous for 4-6 week is preferred dosage. Oral is given in HIV, multiple relapse cases & in extensive lesions. In infantile age group topicals alone are sufficient.

Topical Ketakonazole as shampoo or stay on lotion or cream is preferred local azole. In infant clotrimazole or miconazole cream are azoles of choice.

Topical steroid alone or in combination with azoles are required when erythema is too extensive and in an exudative lesion. For scalp involvement in adults shampoos with steroid and ketaconazole are also available.

At our centre we have used combination of oral fluconazole and topical clotrimazole to good effect in treating most of the cases.

Contact Dermatitis

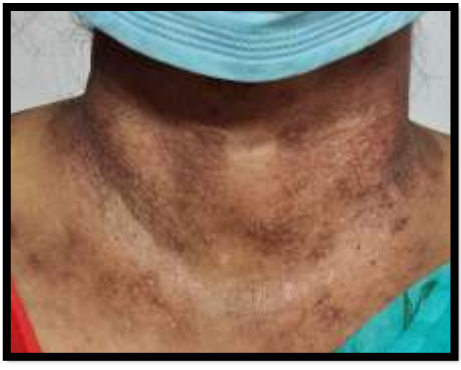
Contact Dermatitis is caused by direct damage due to chemicals (80%) usually industrial (solvents/ Acid-Alkali) or household items (detergent/ soaps water). The damage is direct and it induces cytokinines which lead to clinical manifestation of damage. The other 20% is due to allergic contact which is mediated by type IV hypersensitivity when the chemical (allergen) is present to Langerhan's cells (antigen presenting cells) and the damage is caused via IL-1 & IL-2 through sensitized T-cells.

Predisposing factors

Dry skin is more susceptible as well as atopic skin. Occupationally exposed (motor mechanics, hair dressers, betel shop workers and cement worker) are more susceptible.

Allergic Contact dermatitis caused by makeup

Patient had h/o Atopic dermatitis since childhood



Artificial jwellery causing irritant contact dermatitis

Differences between allergic and irritant contact dermatitis		
Feature	Allergic	Irritant
Itch	+++	++
Pain	++	+++
Vesicles	++++	+
Pustules	+	+++
Hyperkeratosis	++	++++
Fissuring/hyperkeratosis	++	++++
Delay after contact	Days	Minutes to hours

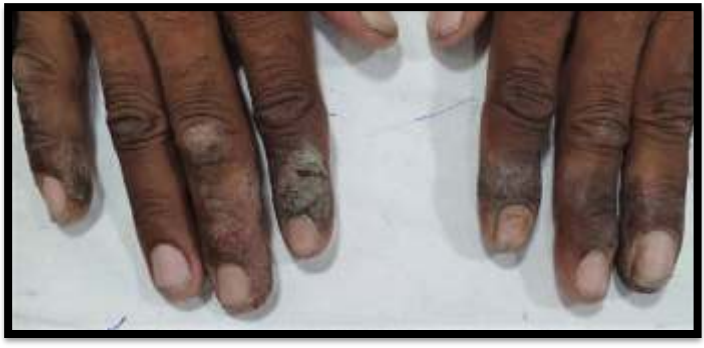
Source; Adapted from Marks JG contact and ocuupational Dermatology 2016

Clinical Features

Acute irritant contact: - Usually after single exposure leading to dryness, erythema and vesiculation. Lesions are localized to exposure site.

Chronic irritant contact: - Cumulative insult with dryness, erythema scaling are prominent with fissuring rather than vesiculation.

Allergic contact: - Presents a few week after first exposure. The distribution of lesion is strongly suggestive of allergic contact eg chromium allergy in hands via cement which contain hexavalent chromium, eyelids (cosmetics). Repeated contacts with allergen increases chances of developing hypersensitivity. All body parts are allergic but most of the time lesion manifest only in area of direct contact. Most of the time allergy is permanent.



Allergic /Irritant contact dermatitis due to cement

Allergic contact dermatitis in painter

Agents causing ACD

Plants: -

- Parthenium hysterophorus (strong sensitizer)

Chemical dye: -

- PPD (Paraphenylediamine)

Metal:-

- Nickle (artificial jewellery)
- Chromium hexavalent (cement) strong sensitizer
- Chromium trivalent (cement) weak sensitizer

Drugs: -

- Neomycin

Cosmetics:-

- Fragrance (deodorant)
- Formaldehyde (Bindi glue)

Rubber:-

- Mercaptans (Leather processing)
- Thiourams (rubber gloves)

Investigation of choice for ACD is patch testing. Dermatitis if not responding to emollients & topical steroids should be patch tested.

Treatment

The basis of treatment for both ICD & ACD is avoidance of Exogen/allergens. In ICD there is proportionate decrease in clinical feature while in ACD complete avoidance is required.

Topical corticosteroids in appropriate potency to be applied, for symtomatic relief. Emollient help in replacing skin barrier. In more chronic and severe cases systematic corticosteroids and systematic immunosuppressant may be required.

CME 5

ACNE

Introduction

Acne is a chronic inflammatory disease of sebaceous gland with high morbidity, decreasing patient's quality of life. It is one of the most common skin disease and in Balrampur Hospital Lucknow 5% of total daily skin OPD is for Acne alone. Male & females are equally affected however the number of female patients is more than male probably due to increased cosmetic sensitivity in females. Nodulocystic acne is 5-10 times more common in males.

The disease starts in puberty /teenage and spontaneously resolve by fourth decade but still in many individuals have acne eruption even in fifth decade of life.

Acne affects approximately 85% of population at some point in their lives. The effects of acne extended beyond skin and lead to psychological distress and depression although it is not a life threatening medical condition. Dietary restrictions on class of foods or any specific food has not been demonstrated to be of benefit in treatment of acne. How ever low glycemic diet benefits in acne has been proposed by few researchers. Chocolates and milk in large quantity to be avoided.

Pathophysiology

Sebacious glands are associated with hair follicle and rest between follicle and the epidermis. The activity of the gland is controlled by androgens however acne is not a disease of total circulatory hormones. The sebacious glands contain and enzyme called 5 alfa-reductase, which converts less potent testosterone into more potent dihydrotestosterone, which is directly responsible for gland activity.

Four pronged factors which result in acne are as follows:

1)	Increased sebum production and change in sebum quality	↑ 5HT receptor sensitivity (end organ sensitivity) ↑ DHEAS & DHT ↑ Size and number of lobules of sebaceous gland ↓ Reduced level of Linoleic acid, leading to retention of sebum.
2)	Increased colonization of propionibacterium acnes (commensal)	Proliferation of P. acnes & Release of Lipase & Proteinase
3)	Retention of Hyper--keratosis of infundibulum of sebacious gland	Occlusion of Pilosebacuous orifice by Keratinous plugs.
4)	Inflammation of sebaccus follicle	Ductal epithilium produces endogenous cytokines initiating an inflammatory cascade which causes rupture of comedones & distended follicle which attracts dermal interleukins & result in more intense inflammation.

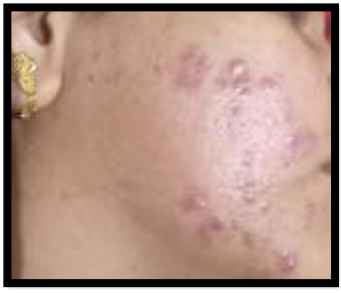
Clinical features & Morphology

Acne presents as with comedones, papules, pustules, nodules, pseudocysts, sinuses, keloids, hypertrophic scars and acne scars.

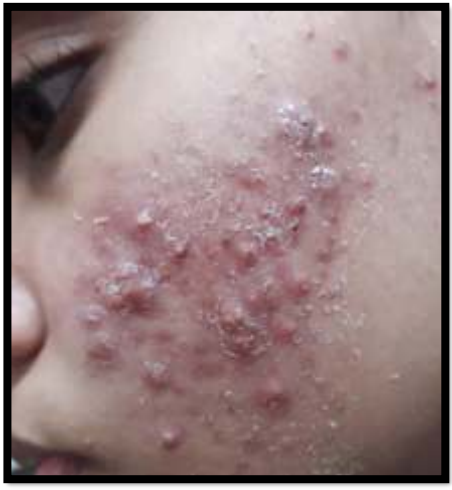
Acne has been classified on basis of clinical presentation

Comedonal Grade I	Comedone is a hair follicle infundibulum that is dilated and plugged with keratin and dried sebum. Comedone is pathognomic sign of acne If the opening is dilated then the due to oxidation the content in follicular opening turn black. (Black heads) If there is no visible opening & the content are below the level of the epidermis then they appear white.(white heads)
Papulopustular Grade II	Papules & pustules (sterile) along with any number of comedones. Heals with scars which may be present as circumstantial evidence
Nodule cystic (Grade III	Nodules & Cysts (due to rupture of sebaceous glands) (Not a true cyst) and sometimes two cysts and interconnected by sinuses along with comedones, papules & pustules of any number.Nodulocystic acne always heals with scarring

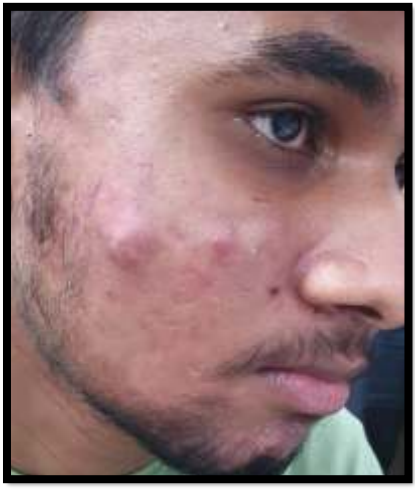
Senile comedones



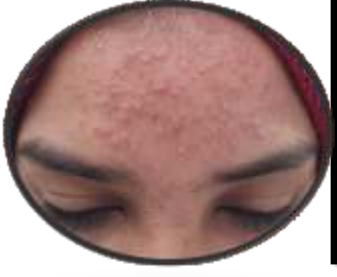
Acne after facial massage



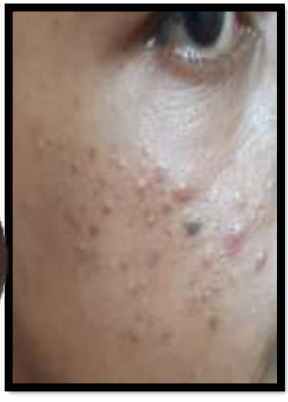
Comedones, papules and pustules in grade II Acne



Nodules and pappules



Mostly comedonal acne



Adult Acne first eruption at 25yr of age

Lesion occurs in seborrheic zones more frequently in face, upper chest, upper back, upper arms (Sebaceous glands of vellous hairs are larger in size and have more end organ sensitivity. Pathognomic lesion (identifying) is comedone.

Variants

Neonatal acne

No comedones, only papulopustular lesions. Erupt 2to3 weeks after birth.

Due to excessive androgenic activity.

Infantile acne

Due to presence of maternal hormones in the child. Common in males. Comedones as well as papules and pustules may be present. Onset is 3 to 6 month of birth and may sometimes last up to 2-3 years.

Acne Excoriee

Excoriations mimicking acne lesions due to picking and excoriating lesions in cheek. Seen usually in young girls. Primary lesions of acne are very few. Associated with OCD, depression and anxiety.

Adult Acne

Mostly in adult females >25 year of age. Lesions are few usually on lower face, mandibular area, chin involvement is characteristic. Associated with PCOS, ovarian tumor and congenital adrenal hyperplasia.

Other associated disease may be obesity, hirsutism, acanthossis nigricans. PCOS and hormonal work up are part of management in adult acne .

Acne Fulminans

Acute onset with fever crusted lesions on sternum & around clavicle associated with myalgia and arthralgia. Abscess and ulcers are usually present. High chances of scarring.

Acne Conglobata

Adolelescant & early childhood acne usually grade III with inflamed tender nodules especially in back. Comedones are multiporous. May

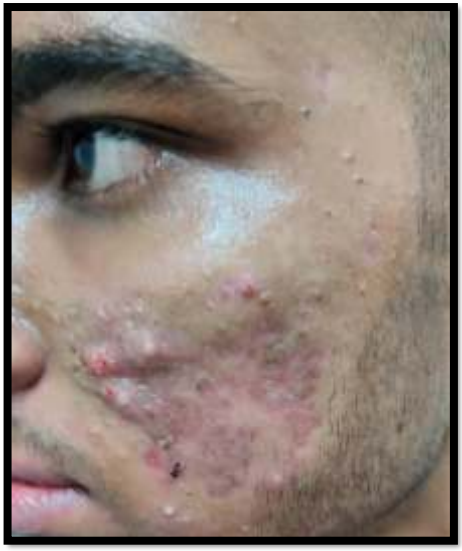
be associated with follicular occlusion syndrome. (Triad of acne conglobata, dissecting folliculitis of scalp & hidradenitis suppurativa and sometimes pilonidal sinus also).

Acneiform eruptions

Follicular eruption usually papulopustular are similar in appearance to acne but does not involve 4 pronged acne pathogenesis

- Acne due to repeated friction e.g. arm pit due to crutcles
- Acne due to topical chemicals leading to blockage of pilosebecious canal.
- Cosmetic acne due to blockage caused by cosmetic products.
- Occupational acne due to cutting oil (chlorinated hydrogenated oils)are non inflamed with only comedones in axila, neck back, malar and retro auricular area.

Abscess and cyst in grade III Acne



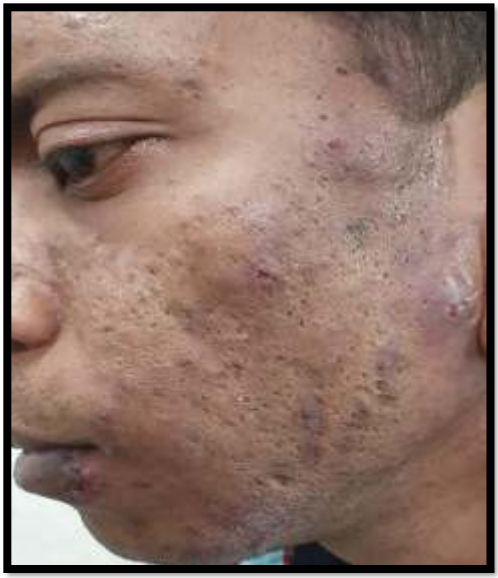
Polymorphic features of nodules,cysts papules and comedones

Complications of acne

1. Cosmetic disfigurement due to acne scars, hypertrophic scar, keloid and perifollicular elastolysis.

2. Post inflammatory hyperpigmentation

3. Depression due to cosmetic sensitivity.



Acne scars Icepick,Boxscar& Rolling scars

Management

History is important to identify variants

Classify patients in comedonal, papulopustular and nodulocystic and truncal involvement for management. Sudden onset are usually due to drugs (Corticosteroids topical & Oral both, Anabolic steroid, Lithium, Isoniazid, Phenytion Progestin Cyclosposine) and gradual onset are usually pathological. Occupational are due to exposure to cutting oils and cosmetic items. Cosmetics, occupational cutting oils, drugs have to be withdrawn and predisposing factors attended.

Investigations

A) In Hormonal acne

· AMH (Antimullerian Hormone) predicts PCOS to a great extant.

· DIHEAS, Prolactin, LH,FSH, TSH and ultrasound to check ovaries for polycystic lesions

B) Routine fitness tests before starting isotretinoin CBC,LFT & Lipid profile and S. electrolytes before starting spirinolactone)

Treatment tools available

Orals **Drugs**	**Role in acne treatment**	**Remarks**
oral antibiotics • Erythromycin, clinadamycin and azithromycin cephalosporine • Doxycycline, minocycline and • Amoxycilin and cephalexin • trimethoprim-sulfamethoxazole	• Reduces, P. acne infection • Antimetalloproteinase activity reduces inflammation	• Antibiotics Should not be used beyond 6-8 weeks continuously • Adult doxi dose is 100mg and minocycle 50 to 100mg and in extended relaese form 45 to 55 mg ER
Oral isotretinion	Acts on all four stages of pathogenesis	• Dose0.5-1 mg/kg/day • Low dose also works usually given in 20mg per day for 3-4 months • Key drug in nodulocystic and truncal acne and in other types may be used if nothing else works
Hormonal therapy: • Combined OCP • Spironolactone	• Reduces androgen relese, sex hormone binding globulin, and free testosterone • Spironolactone blocks androgen receptor • Reduces 5-a reductase activity	Used in female acne-due to hormonal imbalance, not responding to conventional treatement, and or clinical signs of hyperandrogenism with normal biochemical profile. spironolactone dose 25-50mg per day not to exceed beyond 8-12 wks

Topicals Topical drugs	Role in acne treatment	Remarks
• Retinoids- adapalene, tretinoin, and tazarotene	Comedolytic, anti comedogenic and anti-inflammatory action	• Chance of retinoid dermatitis (irritant effect) and photosensitivity • Can be combined with topical antibiotics or BPO (first line in mild and moderate) • Tazarotene is pregnancy category X,
Benzoyl Peroxide (BPO)	• Antibacterial action by free radical release • Reduces antibiotic resistance • normalises hyperkeratinization and also reduces p acnes	• Combined with topical retinoid or topical antibiotic • irritant effect present to be applied on acne lesions only
Topical antibiotics- Clindamycin and erythromycin	Reduces P.acne infection	• Prolonged use and monotherapy can cause antibiotic resistance • Combined with topical niacinamide, retinoids, or BOP • Pregnancy category B
Topical dapsone (5%)	Anti-inflammatory action	• Can be combined with topical retinoids • used as maintainance antibiotic for 8-12 wk • Mild irritant effect
Salicylic acid-0.5-2%	Comedolytic and anticomedogenic	Used as adjuvants as peel or daily face washes

Source; adapted from Postgraduate Dermatology by Kaushik lahiri & Abhshek de 2022 edition

Isotretinoin-(Vitamin-A derivative)

One of the most widely used drugs in management of acne. It is a category “X” drug in pregnancy. The body clearance time is approximately 4 weeks. Hence should not be used in pregnancy or in likely to get pregnant. The first year of married like is high risk as a majority of couples conceive during first year itself regardless of socioeconomic status in India.

Daily dosage is 0.5 to 1mg. However the experience says 20 mg daily in over 40 kg bodyweight is sufficient. Total cumulative dose per year should not exceed 120 mg/kg/year. Dose of 20mg daily in an average adult for 3-4 month is sufficient.

Common side effects are extreme dryness, hair loss, myalgias, vertebral hyperostosis and pseudo tumor cerebri. Monitoring of LFT & Triglycerides is mandated every 4-6 weeks. Drug has potential to cause depression and hence should not be used in primary depression cases.

Customization of Treatment

Points to remember

1. Management is designed to remove predisposing causes and to reduce morbidity and complications as it is a chronic disease with relapses.

2. Nodulocystic and truncal acne respond well to oral isotretinoin and without it do not heal.

3. In Grade I and II start with one oral antibiotic and one local antibiotic. The best one in oral category are Doxycline/Minocyclin and in local category Clindamycin /Oxenoxacin. If no response in 3-4 weeks add Benzyl peroxide 2.5% local application or adapalene with Benzylperoxide combination. If response not adequate in another 3-4 week then add oral isotretinoin.

4. In grade III & Truncal acne, oral isotretinoin may be started from beginning. Oral antibiotics may be continued for 3-4 weeks & then withdrawn. Topical antibiotics may be changed to maintenance antibiotic Dapsone or Benzoyl peroxide (BOP) or BOP adapalene combination 12 to16 weeks of therapy is usually sufficient.

5. Salycylic acid peel/face wash/Benzyl peroxide face wash may be may be used as adjuvant. Dryness must be watched.

6. In androgen producing pathology such as PCOS, cyperoterone acetate may be used for long term up to 6-24 months. Spironotolone in dosage of 50 mg is other drug used (at tertiary care). Spironolactone has emerged as an alternative to antibiotics due to issue of antibiotic resistance for most of common anti acne antibiotics. Electrolyte imbalance issue has to be monitored however in under 30 years of age with normal kidney functions the need to stop spironolactone due to electrolyte imbalance has been rare.

7. In cases with post inflamatory hyperpigmatation azleic acid (10-20%) is a good option as it reduce PIH and has mild antibiotic and anti inflammatory & comedolytic activity.

8. Cases for surgical procedure to be separated and oral and topical therapies to continue as required

9. Realistic expectations in treatment must be set on first visit itself. Acne therapy in combination of oral/topical and adjuant is extremely successful when used properly and appropriately by a well trained medical officer/dermatologist

Summary of Management

1. Classify & identify predisposing causes and address them.

2. At primary and secondary level start with oral and local antibiotics. If acne aggression is not reducing add BOP.

3. If appreciable decrease not happening add isotretinoin. In cases where isotretinoin is to be started early, start it. Keep a watch on S/e and precautions. Isotretinoin to be started at tertiary care.

3. In case of no response add BOP+ adapalene and or spironolactone and in PCOS cyperoterone or spirinolactone may be started by specialist at tertiary care

4. Cases for surgical procedures to be identified and proceeded upon. Peeling, I/L Triamcinilone and comedone extraction at primary and secondary care. Rest of procedures to be done at tertiary care.

Procedures in Acne Treatment

S.No	Procedure	Done For
1	Comedones	Comedone extraction withspecial come done extractor only for open and closed comedones
2	Abscesss	Drain abscess
3	Phenolization of abscess wall	in recurrent abscess
4	Hypertrophic scar and keloid	Intralesional Triamcelelone For severe nodular acne, abscess, hypertrophic, or keloidal scars Dose-10 mg/mL to be diluted with normal saline to 2.5 mg/ mL. 0.1 mL is given at each site.
5	Chemical peeling Salicylic acid, mandelic acid, retinol, glycolic acid, black vinegar containing peel and TCA	as adjuvant in PIH cases, TCA cross done in ice pick spots
6	Spot peeling with TCA	Ice pick scar respond well to TCA
7	Subcision	for rolling scar
8	Scar excision punch grafting	for mostly boxer scar
9	Microdermabrasion Dermaroller and dermaplaning	For all scar except box scars
10	Laser, Ablative and fractional laser	for all types of scars
11	Autologous fat transfe, fillers	for depressed scars

The experience of our centre is that oral and topical antibiotics along with 5 percent salicylic acid peel results in good improvement in more than 50 percent of cases (level one care therapy) and when combined with oral isotretinoin (secondary and tertiary level therapy) the results are beyond 90 percent.

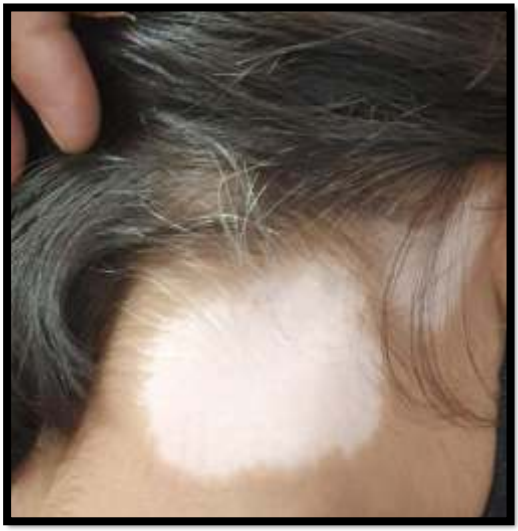
Abscess and cysts are drained as per requirement and other procedures are done after 3 months when aggressive acne eruption stops.

CME 6

VITILIGO

Introduction

Vitiligo is an acquired disorder of well demarcated milky white patches or macules. In the USA only 23% patients of vitiligo seek treatment while in India due to social pressure of taboo of having "Safed daag" almost 100% seek treatment in specialized skin OPD's. Vitiligo is one of the top ten treatment seeking dermatological disorder at Balrampur Hospital Lucknow.



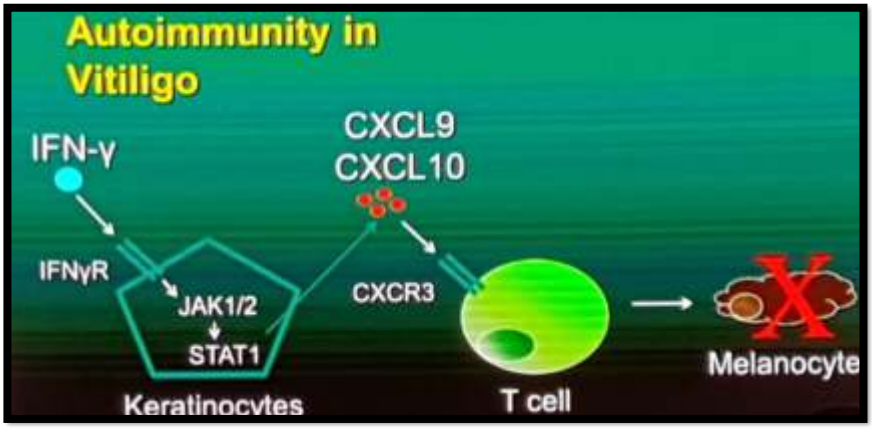
Typical milky white circumscribed patch

A term leucoderma is also in use which includes all "white" lesion of skin including vitiligo. Contact with monobenzyl ether of hydroquinone and substituted phenol used in footwear industry and PTBH in formaldehyde used in stuck-on bindi leads to depigmentation and white lesions due to other disease as in DLE are all included in Leucoderma.

Vitiligo has a multi factorial and complex pathogenesis. 20%-30% have a positive family history. Reported in monozygotic twins. Several susceptibility loci on chromosomes are under study on chromosome 1, 4, 6, 7, 8, 17c & 22.

Many hypotheses for pathogenesis have been proposed

1. Autoimmune destruction



Autoimmune destruction of melanocyte is the top theory explaining pathogenesis of melanocyte destruction in vitiligo.

Other important features in immunochemical & other studies are:

· Lack of DOPA-positive melanocyte in epidermis of vitiligo skin.

· KIT reception protein which is present in melanocyte differentiation is absent.

· Overlap with endocrinopathies hypo and hyperthyroidism Addison's disease & Alopecia Areata.

· Antibodies against tyrosinase releated proteins in melanocyte.

· Dermal infiltration is of CD8+ T-cells.

· In vitiligo patients melanocytes have increased oxidate stress, (resulting in cell death) and which is important for cellular apoptosis.

· Defective free radical defenses.

· Destruction of melanocyte form metobolites.

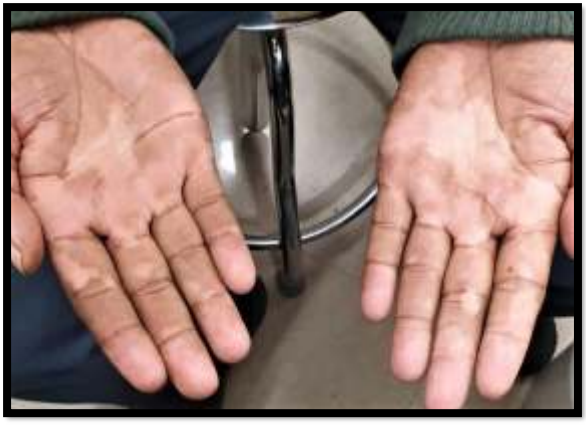
· Membrane lipids of melanocytes becomes defective.

· Destruction of melanocyte form by products of neurochemical substances (toxins released from nerve endings-explaining segmental vitiligo.)

· Two phenotype segmental & non-segmental are there.

· Nutritional hypothesis of deficiency in phenylalanine, selenium and copper.

Combined theory joining all above hypothesis has been proposed, that all above converge in genetically prone with stress, accumulation of toxin from nerve, autoimmunity, defective cellular environment, impaired melanocytes, cellular oxidative stress and abnormal immunologic reaction to contribute for pathogenesis.



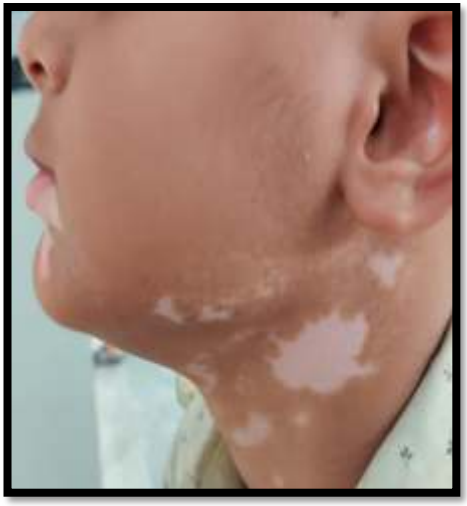
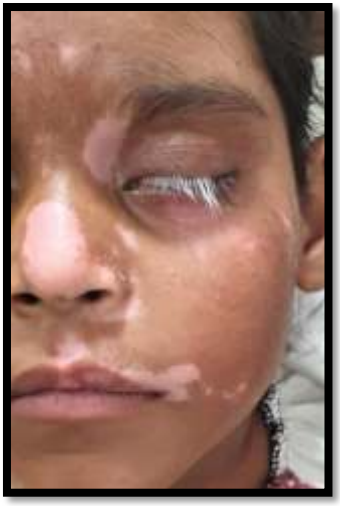
Vitiligo palm and soles are usually recalcitrant to treatment

Pattern of Vitiligo

Generalized vitiligo
Acrofacial vitiligo
Segmental vitiligo

Bad prognostic factors

Long standing disease
Leucotrichia/poliosis
Acrofacial lesions
Lesions on bony prominences

Segmental and facial Vitiligo in child with poliosis

Differential diagnosis

Other disorders having milky white appearance

- Albinism
- Piebaldism
- Waarden burg syndromes
- Chediak –Higashi syndrome
- Griscelli syndrome
- Chemical leucoderma
- Post inflammatory depigmentation
- Lichen sclerosus et atrophicus.

All above DDs are rare in comparison to vitiligo and any milky white patch or macule must be thought of as vitiligo until and unless it is ruled out, at primary and secondary care levels.

Management

For treatment purpose vitiligo is divided into two categories.

1) **Progressive; -** Where number of lesions or size of lesion is increasing. Progressive vitiligo means that autoimmunity is active and mini oral pulse of steroid & or Azathioprine immunosuppressant or Tofacitinib (JAK Inhibitor) has to be used. In progressive vitiligo if surgery is performed it invariably fails with boundaries of lesion showing koebnerization and redevelopment of white lesions. Trichrome vitiligo and scaloping of boundary of lesion are signs of progressive vitiligo.

2) **Stable; -** Where number & size of lesion remains constant for at least 1 year. Stable vitiligo means that autoimmunity is not active and repigmentation effort may be taken up with psoralens & or sun exposure and vitiligo surgeries can be performed.

Disease course

Onset is insidious and gradually size and number of lesion increase for a period of months and even years. The disease process then halts for a few years to again progress.

Treatment tools available

- Oral corticosteroids In mini oral Pulse (2 days every week)
- Oral immunosuppressant (Most common used is Azathioprine)
- JAK inhibitors (Tofacitinib)
- Topical Steroid
- Tacrolimus 0.1%
- Decapeptide Topical
- Narrow Band UVB
- Psoralens plus phototherapy & Psoralens+UVA

- Excimer lasers
- Surgical therapies
  a. Minipunch
  b. Melanocyte Tranfer Blister Method for small areas
  c. Melnaocyte culture Transfer for large areas
  d. Microneedling and 5FU /Phenolization
  e. Thin split graft

11. Tattooing
12. Depigmentaion with MBEH
13. Psychological support-Camouflaging systems and colors

Oral Therapy

Oral corticosteroid in mini oral pulse (MOP) is standard therapy. Dexamethasone 4mg on 2 consecutive days every week is preferred option. Prednisolone and methylprednisolone in equivalence may be given. (Dexa 0.75mg is equal to 5 mg of Prednisolone and 4 mg of Methylprednisolone)

The advantage of mini oral pulse is that routine side effects of steroid are minimized and therapy may be given for 6-8 months continously.

If the progress is not halted then Azathioprine @ not less than 2.5 mg/kg body weight in divided does may be added to mini oral pulse. Azathioprine as standalone therapy without steroid is a bit inferior in halting progress when compared to combined therapy.

A new drug Tofacitinib (JAK inhibitor I &III) in doses of 5 mg BD is new entrant. As standalone therapy along with sun exposure or UVB is very promising with repigmentation in more than 60% of cases except in recalcitrant areas of knuckles, knees, ankles, palm and soles. Monitoring as in immunosuppressant is to be done CBC, LFT, KFT as well as eye on DVT is to be kept.

Topical therapy

Topical steroid the most potent ones gives better result for small areas. Higher potency Clobetasol propionate, Halobetasole and Betamethasone work better than medium potency Mometasone & Fluticasone. The catch point is that prolong application results is stirae, atrophy and telangectasia. Hence consensus is to apply for a short period of time (less than 1-2 months). On thin skin neck face low & medium potency local steroids are recommended.

Tacrolimus 0.1% has emerged as a prominent steroid sparring agent and has been reported from very good results to only as good as vaseline. However the consensus is that it results in repigmentation especially in face in children.

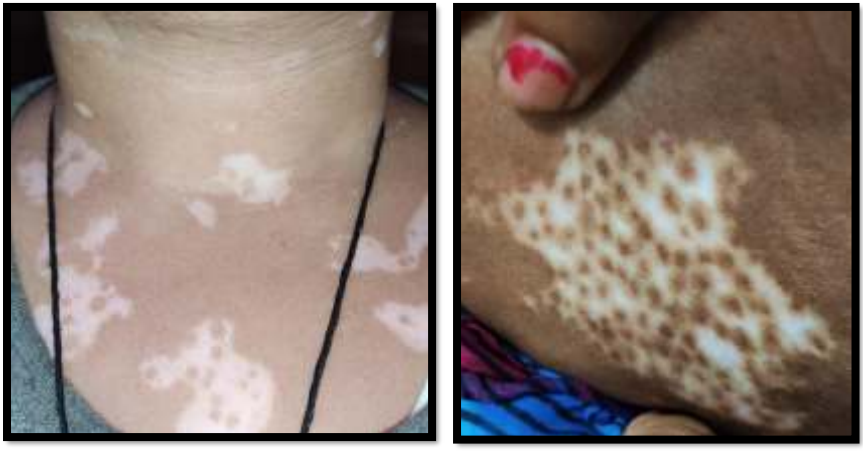
Decapeptide local application has emerged as a new concept in vitiligo in children on face. The results are variable.

Psoralens and sun exposure or UVA/UVB exposure. Mono Psoralens (8-Mop) are applied locally followed by sun exposure or UVB/ exposure on alternate days (Topical PUVA).Usually used for repigmentations. Multiple combination topical gels and oils of psoralens derived from florocuramine bearing plants have come up for repigmentation.

Oral Psoralen may also be given Mono Psoralens (8-Mop)@ at 0.3 mg/kg on alternate days & Tripsoralen (4, 5, 8, TMP)@ 0.4-0.6 mg/kg/on alternate days and sun exposure after 2 hours of intake. (Oral PUVA).

Ophthalmic evaluation is mandated after every 6 months due to its side effects on retina and cataract formation. Total treatment required varies between 60 to 300 exposures with complete repigmentation in few cases and acceptable pigmentation in most of cases. Oral PUVA has been discontinued at our hospital due to burden of 6 monthly ophthalmic examinations on department concerned because of large number of cases.

Narrow band UVB (NBUVB-311 nm) is perhaps the best therapy and acceptable in children and pregnancy also. However better results are achieved using NBUVB chambers rather than hand held devices. Excimer lasers are also used.



Healing vitiligo with small macules of color regeneration

Popular Treatment Modes for Vitiligo			
	First Line	Second Line	Third Line
Topical	Local steroids	Tacrolimus 0.1% or	If skin involvement more than 50% then depigmentation of normal skin (MBEH)
Radiation	UVB narrow band 311 nm	Topical psoralen & UVA	
	Oral psoralens+sunlight Oral psoralens +UVA	Excimer Laser 308 nm	
Systemic	Weekly pulse of corticosteroid	Immunosuppresives most popular azathioprin	
Surgery	NA	NA	Vitiligo Surgery

Treatment in children

To treat children is difficult with apprehensive parents wanting magical therapy all the time and most of drugs for halting progression of vitiligo are contraindicated in children.

Oral steroid, immunosuppressant are used with extreme caution and at our centre we do not use them in children under 12 years of age. Tofacitinib has not been trialed in children below 8 yrs of age.

The **best therapy is NBUVB (311 nm)** and in case not available then Tacrolimus, topical steroid & decapeptide are used with variable results.

Psychological support is extremely important to both parents and child

Summary of Medical Management

1. At primary care start with mini oral pulse of steroid if progression does not halt add local steroid as per skin condition monitor for s/e. In most cases progression halts in 6-8 months. If it does not add, at secondary centre with Local Purchase facility, azathioprine and monitor S/E.

2. Tacrolimus may be used in children on face so also decapeptide. Both have financial implications and to be used at tertiary care with Local Purchase (LP) facility.

3. Surgical procedures and psoralens addition with (ophthalmic monitoring) to be done at tertiary care.

4. NBUVB if available at all level of care.

5. If more than 50% of body area involved then the pigmented area is treated with MBEH to depigment colored areas to give a uniform color.

6. Camouflage colors hide the white patches cosmetically for few hours and are widely used. They are part of psycological support.

Surgical therapy

Vitiligo Surgery

Vitiligo surgery is third line of treatment for those who have stopped responding to drug therapies and have stable disease (i.e the white patches have not increased in size or number for 1 year).

Surgical procedures are designed for replication of melanocytes in white patches by various techniques. Commonly used procedures are:

- Autologous Thin Thiersch's grafting
- Suction blister (epidermis)graft
- Autologous miniature punch grafting
- Cultured melanocytes transplant
- Therapeutic wounding by
- Derma-abrasion
- Laser ablation by CO_2 laser
- Needle puncture after chemical cautery (20% TCA or 88% phenol)
- Excision and repair
- Cosmetic tattooing

The best results have come from **cultured melanocytes transplantation**; however this is not popular mainly due to complexities and cost of culture systems. **Suction blister grafting** has provided equally good results but is only suitable for areas of size of 6-20 cm^2. This technique in initial stage of development needed heavy mechanical apparatus for artificial blistering which was the main reason of its non-use in eastern countries but this issue was handled well by Indian dermatologists especially Dr. Satish Sawant who used common 10-20 ml syringes and triway canula to produce blisters at donor site and popularized the technique through

workshops all over the country. The color gain is very good and scarring is minimal as dermis is left intact. At Balrampur Hospital Lucknow this is primary vitiligo surgery done. **Miniature punch grafting** is also a very popular technique for areas as large as 10-30 cm^2 but cobble stoning and cosmetic damage to donor site if large number of grafts are taken are major disadvantages. **Autologous Thin Thierch's grafting** mastered by plastic surgeons was time immemorial surgery performed for vitiligo. Relatively large areas can be treated in short time by placing split thickness grafts on recipient site prepared by derma-abrasion. Major disadvantages being risk of hypertrophic scarring at both donor and recipient site and raising of skin. Mostly performed by plastic surgeons. Koebner phenomenon (Spreading of vitiligo due to surgical stress) is common. Therapeutic wounding is used for small patches with 20-25% success in generation of color and when nothing works tattooing is done. Tatooing disadvantages are color mismatch and koebnerization and developement of new vitiliginous areas.

Suction Blister Grafts

This is the simplest and the most popular method of transferring melanocytes.

Procedure

Pigmented epidermis of usually from thigh is separated by production of suction blisters that separate skin above the dermo-epidermal junction. The top of blister is removed and directly applied to derma-abraded recipient site. Approx 100-200 mm Hg of negative pressure is required to separate epidermis from DEJ. This pressure is created by sucking 30 ml air from 10 ml syringe and 50 ml from 20 ml syringe which are placed over surgically prepared and anaesthetized anterior to anterolateral aspect of thigh and placing the negative pressure for approx.2- 3 hrs which is routine blistering time.

The recipient area is prepared surgically and anesthetized by 2%

lignocaine and derma abraded till the level of papillary dermis. Pin point bleeding heralds the papillary dermis during derma abrasion which can be done by mechanical derma abrader or electrical abrader or CO_2 laser. We are using mechanical derma abrader. After the blister is formed the top is removed from donor site and spread over glass slide to remove any debris of fibrin/protenaceius materials stuck to basal layer which contains melanocytes. The graft is then transferred from glass slide to recipient area and dermal side of graft comes in contact with the papillary dermis of recipient area. The graft is spread with jeweler's forceps. The area is then covered with antibiotic dressing.The donor site is also dressed the same way.

Antibiotics and oral corticosteroids are given for 7 days after which the dressing is removed. The melanocytes are transferred and normal skin color is obtained in 1-3 months.

Various steps of blister transplant

Advantages

Simple and safe method can be done with minimum of equipment, most of which are available even in a **PHC level hospital**. No Scar formation as in thin thierch's grafting or cobblestoning as in miniature punch grafting. Color matching is very good or slightly hyper pigmented. Success rate is very high.

Disadvantages

Beyond an area of $20cm^2$ it is not feasible and is not suitable for acral parts and body folds. Some residual hypopigementation may be left between the margins.

Complications

- Hyper pigmentation
- Infection and non-uptake of melanocyte
- Keloid formation
- Koebner phenomenon

The results of suction blister are very good in small patches, lips and segmental vitiligo and hence have become vitiligo surgery of choice even in logistic starved situations or where melanocytes culture transplant cannot be done.

Suggested Readings :

1. Illustrated Synopsis of Dermatology and Sexually Transmitted Diseases by Dr Neena Khanna 5th Edition, Publisher Reed ELSEVIER India Pvt Ltd

2. Andrews' Diseases of the Skin 12th Edition 2016, Publisher ELSEVIER

3. Rook's Textbook of Dermatology 9th Edition Publisher WILEY Blackwell

4. Post Graduate Dermatology First Edition by Dr Koushik Lahiri & Dr Abhishek De Publisher Jaypee

5. IADVL text book of Dermatology 5th edition by Dr S. Sacchidanand, Publisher Bhalani

6. IADVL Recent advances in Dermatology 2nd edition by Dr Shital Poojary, Publisher Jaypee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