IADVL

SIG RECALCITRANT DERMATOPHYTOSIS

NEWSLETTER

TINEA TIMES

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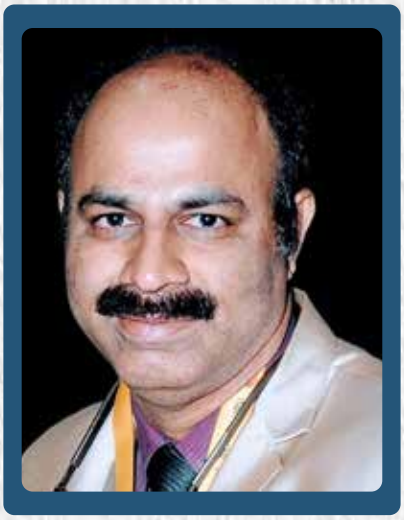

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News update

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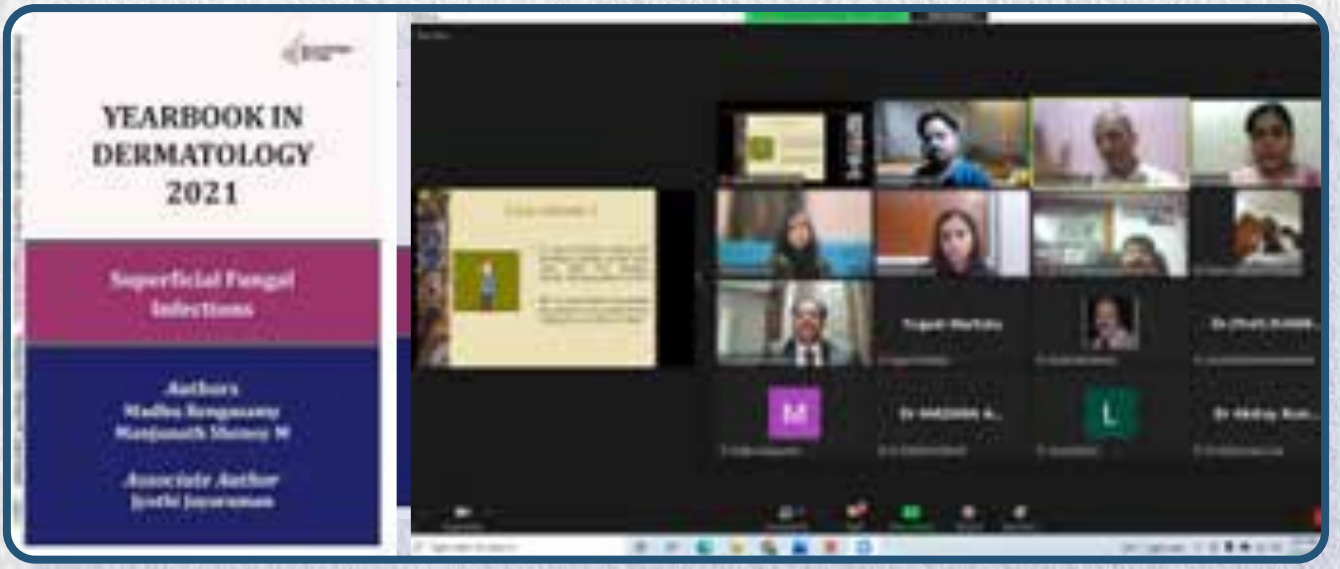

Activities by SIG members during 2021-22:

Four virtual CMEs were conducted by the members of the SIG in collaboration with IADVL EC and IADVL Academy during 2021.

CME 1 (29 th August, 2021): Dr. Sunil Dogra presented a lecture on 'emergence of epidemic of recalcitrant dermatophytosis- a historic update'. Dr. Venkata Chalam delivered a case-based discussion on the changing clinical profile of dermatophytosis. Dr. Ananta Khurana talked about 'laboratory diagnosis of dermatophytosis- practice vs research' and discussed the scenarios where we can use investigation like skin scraping for KOH mount in our practice. Dr. Kabir Sardana discussed 'the scientific basis and rationale of therapy in dermatophytoses'. A panel discussion was moderated by Dr. Nayankumar Patel on different aspects of dermatophytoses.

CME 2 (12th September, 2021): Dr. Yogesh S. Marfatia presented on the topic 'Reshaping of the epidemiology of dermatophytosis in the world and India'. Dr. Sunil Ghate discussed on 'dermatophytosis during the pandemic- the implications and challenges in teledermatology'. Dr. Shital Poojary delivered a lecture on 'non-pharmacological intervention and holistic approach in the management of dermatophytosis'. A debate was presented on the topic, 'combination of systemic antifungal therapy'. Dr. Anupam Das discussed for the notion and Dr. Deblina Bhunia was against it. A panel discussion was moderated by Dr. Ananta Khurana.

CME3 (17th October, 2021): Dr. Madhu Rengarajan presented a lecture on 'management of dermatophytosis in special scenarios like pediatric, pregnancy, lactation, co-morbidities, and poly-pharmacy'. A debate on the topic, 'factors responsible for the changing patterns of dermatophytoses- host vs agent' was presented by Dr. Deblina Bhunia (host factors) and Dr. Anupam Das (agent factors). Dr. Shivaprakash M. Rudramurthy discussed on 'antifungal resistance in dermatophytosis- mechanism, implication and clinical vs microbiological resistance'. Dr. Jyothi Jayaraman delivered a lecture on 'evolving molecules and the

future of antifungal therapy in dermatophytosis'. Dr. Yogesh S. Marfatia moderated a panel discussion.

CME 4 (7th November 2021): Dr. Shukla Das discussed 'the immunological basis of altered clinical manifestation of dermatophytosis with special reference to T. mentagrophytes'. Dr. Akshay Jain presented a case-based discussion on 'topical-steroid modified tinea- a diagnostic and therapeutic challenge'. Dr. Manjunath Shenoy presented a lecture on 'dermoscopy in dermatophytosis'. A debate was conducted on the topic 'conventional vs super-bioavailabe (SUBA) itraconazole'. Dr. Manjunath Shenoy discussed for SUBA while Dr. Nayan Patel spoke for conventional itraconazole. A panel discussion was moderated by Dr. Jyothi Jayaraman.

Take home messages from the CMEs:

- In recent times we have witnessed a tremendous change in clinical presentations of dermatophytosis resulting from the unscrupulous use of steroid containing combination creams. Extensive tinea which has a double edge involving large surface areas and affecting children and adults alike, with unusual sites like face, scalp, and ears is the norm. Tinea these days can mimic other diseases like atopic dermatitis, subacute cutaneous lupus erythematosus, pityriasis rosea, psoriasis, and others. Overlapping of Tinea with steroid-responsive dermatoses like eczema, pemphigus, and connective tissue disorders are common. Hence health education regarding the indiscriminate use of steroid-containing antifungals should be taken up by every Dermatologist to curb their menace
- Both the host as well as the agent factors are responsible for the changing scenario. Environmental changes, lifestyle and behavioral changes in host along with rampant topical steroid misuse are important contributing factors for recalcitrant dermatophytosis.
- A dramatic Indian-wide switch from T. rubrum to T. mentagrophytes has been observed recently. T. mentagrophytes "Indian ITS genotype" might be disseminated Indian-wide due to the widespread abuse of topical clobetasol and

other steroid molecules mixed with antifungal and antibacterial agents.

- The available diagnostic modalities for dermatophytoses include conventional methods (e.g.; direct smear examination, culture and histopathology) and advanced investigations like PCR/sequencing, antifungal susceptibility testing and genome analysis. Among these, the conventional KOH smear examination is essential in routine practice as it is a simple yet very useful investigation for the diagnostic purpose and also helps in the therapeutic monitoring. Others can be used for research purposes.

- Diagnostic criteria for the tinea capitis & onychomycosis based on the dermoscopic patterns have been established. It may be utilized for early diagnosis and institution of therapy. Dermoscopic features of glabrous tinea are not clearly established till date, though some findings may be helpful in the diagnoses.

- Irrational use of combinations of antifungals should be avoided. Checkerboard analysis can guide us to detect the possible synergistic combinations of antifungals, though a lot of studies and data are required for further recommendations.

- Proper history should be taken with regard to the intake of medications in patients with comorbid conditions. In all patients with steroid modified tinea, application of irrational combination creams has to be stopped immediately. Emollients to be applied regularly. All patients with dermatophytosis should be counselled regarding strict adherence to general measures and compliance to treatment.

Childhood dermatophytosis

Naïve tinea, localised, Infants, Hepatic failure – Only topical antifungals
Chronic, recurrent, steroid modified, extensive – Combination of topical and systemic antifungals for a longer duration
Neonates, infants, young children – Index case to be spotted and treated

Pregnancy

Systemic antifungals are to be avoided during first and second trimesters. Terbinafine is an FDA category B drug, but yet in the past, scarce human source precluded routine use during pregnancy. Nationwide, registry-based cohort study from 1997 to 2016 conducted in Denmark concluded that there is no increased risk of major malformation or spontaneous abortion among pregnancies exposed to oral or topical terbinafine.

Lactation

Fluconazole is a relatively safe option. Cream, gel or liquid products which are water miscible are recommended for application to the skin over the breast because ointments may expose the infant to mineral paraffin while feeding.

Patients with hypertension

- Azoles increase levels of Losartan, Nifedepine, verapamil. Reduction in dose of AHT/ monitoring
- Itraconazole with Nifedepine – pedal edema. Reversible edema of extremities in 0.4-3.5% and mild hypertension has been reported
- Hydrochlorthiazide increases levels of fluconazole
- Terbinafine increases levels of Beta blockers

Patients with dyslipidaemia

Fluconazole/ Itraconazole -

- Lovastatin, Simvastatin & Atorvastatin; comparatively less effect on Atorvastatin
- Fluconazole increases fluvastatin
- Rhabdomyolysis, rare severe adverse effect
- Concomitant administration of itraconazole increases risk of hepatotoxicity
- Itraconazole – no effect on Fluvastatin, pravastatin, rosuvastatin
- Fluconazole - no effect on pravastatin, rosuvastatin

Patients on anticonvulsants

Phenytoin, Phenobarbitone and carbamazepine reduce the level of Azole antifungals

Patients on anticoagulants

· Azoles and terbinafine increase the levels of warfarin

· Griseofulvin decreases levels of warfarin

Patients with tuberculosis

· Rifampicin, rifabutin, INH reduce the level of azoles

· Rifampicin reduces the levels of terbinafine

HIV patients – Drug interaction with ART drugs

· Nevirapine decreases itraconazole levels

· Indinavir and ritonavir increase levels of itraconazole

· Itraconazole increases levels of zidovudine, saquinavir, indinavir, efavirenz

· Patients with obesity, diabetes mellitus, hepatic, renal and cardiac diseases and those who are on immunosuppressant therapies also need special consideration of their conditions and drug interactions for successful and safe therapeutic outcomes (discussed later in the texts).

· Future of antifungal therapy encompasses research in five domains. Enhanced bioavailability, improved antifungal spectrum, diversity of targets, inhibition of virulence factors and to combat drug resistance. In this regard, newer formulations of traditional agents to improve penetration such as microsponges as carriers of eberconazole, newer azoles such as efinaconazole, pramiconazole, superbioavailable itraconazole, oxaboroles in onychomycosis, newer hydroxypyridones such as rilopirox and octopirox are a few recent advances. Use of silver nano particles, super oxide dismutase to prevent biofilm formation, heat shock proteins, drugs such as statins, cyclosporine to improve efficacy of traditional antifungals and study of sordarins as newer target molecules are some of the future prospects.

In eDERMACON 2022, a session on recalcitrant dermatophytosis was led by the SIG members. Dr. Manjunath Shenoy presented a lecture on 'Recent updates on dermatophytosis- clinical aspect' and Dr. Ananta Khurana talked about 'Recent updates on dermatophytosis- laboratory and investigation aspects'. A panel discussion was moderated by Dr. Nayankumar Patel and other SIG members participated as panelists. The session was chaired by Dr. R Madhu and Dr. Y. Marfatia.

Dr. Manjunath M Shenoy presented a lecture on " management of special situations of recalcitrant dermatophytosis" at the national conference of association of clinical dermatologists on 17th April 2022. He also authored an article in Forbes India (Aug 2021) entitled 'Ringworm Outbreak Of India: The Despicable Dermatological Disease'.

Dr. Madhu Rengarajan delivered a lecture on "IADVL Task Force Against Recalcitrant Tinea (ITART) Consensus on the Management of Glabrous Tinea (INTACT)" and moderated a panel on 'Management of recalcitrant superficial dermatophytosis'at DERMACON 2021 and on "Systemic therapy with Terbinafine in Current practice" at MIDDERMACON 2021. She has also delivered a lecture on "Topical antifungals – an Update" in a National Webinar on March 28th, 2021, "Management of dermatophytosis in special situations" in CUTICON TN 21, "Dermatophytosis – an Update" in a Webinar organised by IADVL Kerala on January 23rd, 2022 and on "Superficial fungal skin infections" on February 20th 2022 in a Webinar organised by Indian Medical Association Chennai Metro.

Dr. Nayankumar Patel has completed an IADVL granted study "Comparative evaluation of host immune response and cytokine signature pertaining toTh1 and Th2 immune arms in serum and tissue among patients of acute localized versus chronic disseminated dermatophytosis, hospital based observational study."" He also conducted a study "Recalcitrant dermatophytosis: Perception, Practice and Barrier study among dermatologists of India."

PUBLICATIONS:

'YEARBOOK IN DERMATOLOGY 2021 – Superficial Fungal Infections' was published during this period. Dr. Madhu Rengaswamy and Dr. Manjunath Shenoy were the authors of this book and Dr. Jyothi Jayaraman was the associate author.

Articles in journals:

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12. Khurana A, Agarwal A, Agrawal D, Sethia K. Re-emerging role of KOH smear examination in the era of recalcirant dermatophytoses. Dermatol Ther. 2021 Mar;34(2):e14891.

13. Jagadeesan S, Das A, Karunakaran A, Panicker VV, Anjaneyan G. A pilot study to evaluate the patient adherence to antifungal therapy in dermatophytosis: a possible contributory factor to the current epidemiclike situation in India. Clin Exp Dermatol. 2022 Feb 12. Epub ahead of print.

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Changing mycological ,epidemiological & mycological profile of dermatophytosis in India, **How does it affect dermatologist ?**

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In present era, dermatophytosis has become chronic and recurrent; clinical features have changed. Complete cure of infection has become an enigma for patients and dermatologists alike. There is need for higher dosage and longer treatment with systemic therapy. Only topical therapy has virtually become outdated and many topical agents are not useful. There is a higher incidence noticed amongst family members, infants and children.

Changing clinical features

Over the counter [OTC] potent topical steroid containing Fixed Drug Combinations [FDC] have altered clinical features and response to therapy. The dermatophytosis is clinically more extensive and involves erstwhile uncommon sites like face and scalp. Inflammatory and bullous like atypical lesions are common. Atypical presentations resembling lupus erythematosus, psoriasis, eczema, impetigo, rosacea etc are more common, steroid modified tinea with tinea incognito, pseudoimbricata, Majocchi's granuloma being seen.
Dermatophytosis is present in association with other dermatoses (many requiring corticosteroids as treatment) such as acne, eczemas, psoriasis, lichen planus, etc.

Atypical presentations are seen in healthy individuals, not only in immunocompromised individuals.

Indian scenario

There is a paucity of original studies of dermatophytosis and its treatment. It is becoming amply clear that experience-based treatment is ruling the roost and is proving to be more effective than the standard guidelines provided in current literature.
The factors contributing to the current scenario include environmental factors, erratic use of topical and oral antifungal agents, increased prevalence of Trichophyton mentagrophytes infections causing inflammatory lesions. Probably a growing resistance to antifungal agents may play an important role. One of the most formidable enemies that we have encountered in the recent times is the irrational FDC creams containing potent topical steroid, antifungal and antibacterial agent with three to five molecules in the product.
Today, dermatophytosis (especially chronic, recalcitrant, recurrent and resistant) have become the most common dermatologic condition seen in OPD in India. The dermatophytosis cases we see in hospitals represent just the tip of the iceberg of the epidemic seen in the community.

Clinical & Mycological Scenario

In chronic cases, T. rubrum is seen in 45% cases, while T. mentagrophytes is seen in 18%. Overall, T. rubrum still remains the most common infecting organism, but there is increasing prevalence of T. mentagrophytes. Topical Corticosteroid modified tinea is reported in 63% cases. Chronicity, female preponderance and increasing trend of intrafamilial cases is observed. Vineetha et al (2018) reported atypical clinical features like papules (follicular and non-follicular), arciform lesions, pseudo-imbricata in steroid modified lesions. MIC was high for fluconazole and griseofulvin but low for itraconazole (in chronic resistant cases).

Evolution of Dermatophytes- Global Scenario

Frequency of T. rubrum, T. interdigitale, T. tonsurans and M. canis has increased gradually. At present, T. rubrum is the leading pathogen for skin and nail fungal infections. M. canis, T. tonsurans and T. violaceum present as the predominant dermatophytes involved in tinea capitis. Global warming, population mobility, changes in human lifestyle, increasing obesity, altered cutaneous flora, virulence of the fungal species and advent of newer antifungal drugs will continually drive the dermatophyte evolution in the skin microenvironment.

T rubrum v/s T mentagrophytes

Trichophyton mentagrophytes complex is emerging as the major pathogen and is responsible for widespread and inflammatory lesions. T. rubrum survives in fomites lesser than T.mentagrophytes (<12 weeks as compared to >25 weeks) for the latter, highlighting the importance of disinfecton of clothes. A unique clad distinct from T. mentagrophytes/T. interdigitale complex with multidrug resistance has recently been identified. The reasons could be many fold- increasing use of corticosteroids

containing creams (with shift of steroid containing FDCs from beclomethasone to clobetasol) leading to lowered host immunity and persistence of new species.

Features of T. rubrum making it the commonest organism affecting humans

Many infected patients cannot elicit adequate CMI against T. rubrum. Antigen presentation is different compared to other dermatophytes, which prevents induction of immunity. Neonatal exposure to the fungus or molds which have cross reactivity to T. rubrum perhaps induces tolerance. Persistent infection induces suppressor T cells which leads to immune unresponsiveness.
The mannan of T rubrum is more immunosuppressive than of other dermatophytes. T. rubrum is not a very aggressive fungus, hence it evades immune surveillance. T. rubrum spores can survive on human skin and easily desquamate and survive on host skin. On finding correct environment of warmth and moisture, they readily colonise outgrowing normal flora.

Clinico-epidemiological profile of dermatophytosis in recent studies across India (Region wise)

North India (Rural Uttar Pradesh)- T. verrucosum and T. mentagrophytes were commonly found because majority population was rural and coming in close contact with cattle for dairy and farming.

High isolation rates in culture can also be due to poor hygiene and low socioeconomic strata of the study population.

South India (Karnataka, majority study population rural) - tinea corporis was commonest in adults and tinea capitis commonest in children (0-10years). Tinea unguim cases were highest in higher age group with other comorbidities like Diabetes and HIV/AIDS (concurrent with other studies).

North East India (Meghalaya- majority population with low socio-economic status): tinea pedis most common as majority people of Meghalaya tend to wear shoes and socks for prolonged periods irrespective of the weather and young population especially regularly plays sports and wears sports shoes for long durations.

North west(Jaipur, Rajasthan-largest group belonged to the lower middle class) -62.5% had disease duration >3 months (suggestive of chronicity). T. rubrum was commonest in tinea cruris with tinea corporis (rest of the sites, T.mentagrophytes was commonest)

Chronic Tinea and Host Immunity

Impact of long lasting dermatophytosis includes significantly lower cytotoxic effect of T cells against dermatophytes, suppression of lymphocyte proliferation, defect in antigen presentation, reduced phagocytic and killing ability. Skin reactivity to Trichophyton decreases with increasing skin chronicity. Chronic Dermatophytosis results in selective immune deficiency.

Host Factor – Barrier Defect

Barrier can play a crucial role in host defence. Dermatophyte penetrates stratum corneum and causes enhanced epidermal proliferation by several folds. There along with reduced skin hydration and increased transepidermal water loss results in barrier function impairment which is more frequent with atopic background and xerotic skin.

Barrier repair measures are the key to success of antifungal therapy in chronic dermatophytosis

Topical Corticosteroid application leads to immunosuppression, decreased epidermal proliferation and compromised barrier function. It can increase the penetration of fungus to dermis.

Literature states that the recovery of the hypothalamus takes about 14-30 days after cessation of corticosteroids. This explains the delay in clinical response seen in patients with steroid modified dermatophytosis, who will hence require an extended duration of treatment.

Tinea Incognito is characterised by minimal itching until steroid is applied. If steroid withdrawn, irritation/itching recur. The lesions are polymorphic with scattered papules, pustules and hyperpigmentation with diffuse blanching erythema and telangiectasia. Lesions are less scaly and margins are less raised.

Host factors leading to chronicity are comorbidities, immunocompromised state, cushing's syndrome (hypercorticism leading to chronic mycotic infection), diabetes. There is increasing use of systemic immunosupressants in management of many chronic conditions including malignancy. Non compliance for various reasons including affordability of medications is also a genuine concern.

Conclusion

There are drastic changes in environmental, epidemiological, clinical features and therapeutic considerations related to dermatophytosis. We often don't have laboratory backup helping us to decide an effective treatment. There is also lack of access to effective treatment (Itraconazole and newer topical agents which are expensive) to all the patients. Need of the hour is to evolve an effective strategy in managing chronic and recalcitrant dermatophytosis in a resource restrictive set up.

History taking in a patient of **dermatophytosis**

Dr. Akshay Kumar Jain
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History taking in a case of dermatophytosis begins with asking for the name of the patient, to know the identity of the patient and to establish a rapport with the patient. This is usually followed by asking the age of the patient, as some clinical subtypes of disease are more commonly found in certain age groups exemplified by tinea capitis which is common in pediatric age group.

We also enquire about the occupation of the patient to ascertain the physical activity of the patient and potential exposure to dermatophytes; for example patients involved in outdoor activities have increased sweating making them more prone to tinea and contact with infected animals may also lead to dermatophytosis. Education level of the patient often determines early visit to doctor, treatment seeking behavior, better personal hygiene and compliance to treatment and non-succumbing to steroid mixed combinations. Socioeconomic status determines the purchasing capacity of the patient, because increasing burden on pocket may lead to incomplete course of medications, causing recurrent and resistant tinea.

Residential address of the index case gives a rough idea about the locality of the patient, as certain species of tinea are more common in identified geographic regions. Marital status of the patient gives an idea about exposure to dermatophytes by intimate contact with the partner, in which case both the partners should be treated simultaneously to prevent recurrent disease. History of cultural and religious practices should also be elicited, for example tinea associated with finger rings or toe rings, tinea under threads worn on wrist and frequent washing of private parts in certain religious practices.

History of wearing clothes in hurry after bathing without drying skin should also be asked. These days, family history of dermatophytes is very important because children often acquire it from infected adults and if a family member is infected with disease, through cloth, linen, towels and bedding sharing, other family members also get infected. Lesions on face/other exposed parts/genital lesions cause social embarrassment to the patient often leading to poor quality of life. In the past few years we are encountering lesser number of treatment naïve fresh cases, while the number of patients with recurrent/chronic /recalcitrant disease is on the rise due to alteration in agent, host and environment, often treating such cases is often a challenge.

Over recent few years clothing pattern of our society has changed. Wearing of thick, occlusive tight clothes made of synthetic materials in tropical climate of our country leads to increasing entrapment of sweat creating moisture, high temperature the ideal conditions needed for fungal overgrowth and recurrent tinea. Due to lack of awareness in society, patients often resort to taking self-medication, improper drugs in inappropriate dose for inadequate duration leading to drug resistance and recurrent disease.

Widespread propaganda created by social media, certain pharma companies with vested interests, quackery and availability of easy to procure and affordable potent steroids and steroid containing medications have lead to alteration in host immunity leading to treatment resistant disease. Host immunity is often altered in diabetes mellitus and patients having other congenital/acquired disorders of immunosuppression, leading to chronicity of tinea in them.
In clinically atypical and tinea incognito cases laboratory diagnosis like KOH mount, culture and sensitivity, skin biopsy and molecular diagnosis are very helpful in identifying the organism and to select an appropriate medication according to the antifungal drug sensitivity pattern.

Examination of lesion of dermatophytosis, a **clue written between the lines!**

Dr. Sunil D Ghate
Consultant Dematologist, Dr Ghate's Skin Center,
Chembur, Mumbai

A classical lesion of dermatophytosis is described as erythematous, scaly plaque with central clearing and advancing margins. In recent years, that has changed & we see mostly atypical presentations. Many times, large plaques are seen. Multiple individual plaques can also be seen which coalesce to form larger lesions. The lesions can also be symmetrical. Interesting feature in present day dermatophytosis is that despite having long standing, extensive skin lesions, there is hardly any involvement of nails, palms or soles. Although, the clinical features are often atypical, one must still look for advancing margins, trailing scale & central clearing which may be seen somewhere on the lesion to diagnose it as dermatophytosis. The most important challenge is severe itching in cases of dermatophytosis.

Following definitions come handy.

1. Recurrent dermatophytosis: Reoccurrence of the glabrous tinea after 4 weeks of stopping treatment following clinical cure

2. Resistant dermatophytosis: Failure to eliminate dermatophytosis despite administration of one or more antifungal agents for an adequate dose and duration, based on clinical judgement due to proven mycological resistance to the drugs

3. Recalcitrant dermatophytosis: Persistent glabrous tinea, generally in settings like chronic, recurrent, corticosteroid-modified and resistant cases, with poor or no response to standard treatment

4. Corticosteroid modified tinea: Glabrous tinea whose morphology is altered due to topical or systemic corticosteroids, but is still recognisable or diagnosable

5. Tinea incognito: Glabrous tinea in which the morphology is markedly altered due to the suppression of inflammation by corticosteroids or other immunosuppressants such that it is not easily recognisable as tinea

6. Chronic dermatophytosis: Presence of glabrous tinea for a duration of six months or longer, continuous or recurrent, with or without treatment.

Following clinical presentations are becoming common

1. Eczematous lesions which may be difficult to differentiate from eczema.

2. Pustular lesions- Many cases are seen these days where the margins show pustules. In some cases, pustules can be seen all over the skin lesion. This needs differentiation from pustular psoriasis. Tinea is more itchy & responds to antifungals

3. Vesicular lesions- A classical case had small vesicles or papulovesicular lesions at the margins, but today's tinea can have prominent vesicobullous lesions.

4. Tinea pseudoimbricata- Ring within ring appearance of tinea lesions is due to application of potent steroids. Two or more concentric rings are seen

5. Majocchis granuloma- Tinea infection can go much deeper due to steroids use. The lesions present as papules or nodules in the pre-existing lesions of tinea.

Following areas are affected either alone or as an extension of lesions

1. Pinnae- Tinea involving pinnae called as tinea auricularis has become common. In fact, this affection as sole presentation wasn't described before.The lesions are erythematous, scaly. Multitude of folds due to anatomical shape of the pinna predispose to sweat retention in the concavities.

2. Eyelids- Tinea affects eyelids right upto the lid margins. The affection may be unilateral or bilateral. One must have high index of suspicion & look for advancing margins.

3. Genitalia-It was said before that tinea doesn't cross genito-crural fold. That no longer holds true. Quite a few cases are seen where male or female genitalia as well as the pubic areas are affected.

4. Lips- Lesions go right upto the lip margins. It is usually extension from the lesions on the cheeks, chin or nose.

5. Scalp- Glabrous tinea affects scalp in adults and is not uncommon. There is no involvement of the hairs. Sometimes, one must ask the patient to shave of scalp hair to visualise the lesions.

6. Exfoliative dermatitis- Although it has been mentioned in the books that dermatophytosis can be a cause of exfoliative dermatitis, these days more cases are being seen in the elderly or immunosuppressed individuals.

Tinea has been observed to mimic a wide variety of conditions including lupus erythematosus, psoriasis, lichenoid lesions, erythema multiforme, granuloma annulare, granuloma faciale, pityriasis rosea, seborrheic dermatitis, rosacea and annular syphilis, pustular psoriasis, Sweet's syndrome and impetiginized herpes. Signs of steroid adverse effects like striae, telangiectasis, atrophy, hypo & depigmentation, hypertrichosis, folliculitis etc may be seen in patients who have used steroids.

Dermatoscopy in dermatophytosis

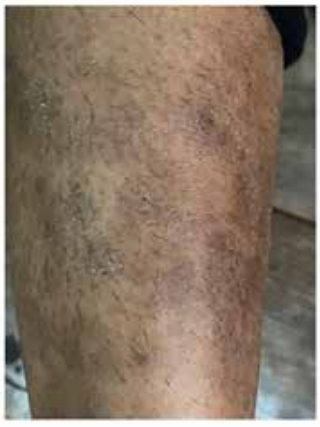
In dermatophytosis, dermoscopy shows a sensitivity of 94-95% and a specificity of 83%. In other investigations, such as potassium hydroxide (KOH), it is 73% and 45%, fungal culture (41%, and 77%) respectively.

Tinea Corporis

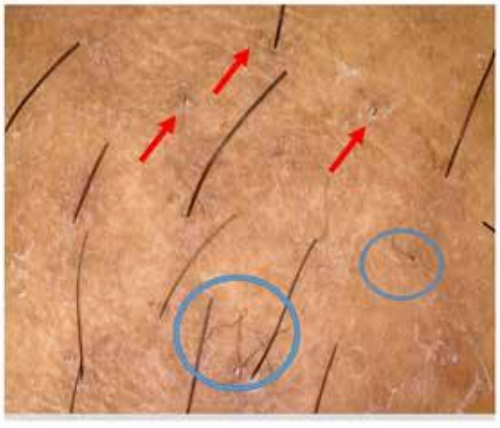
Dermoscopic findings of tinea corporis include diffuse, intense erythema, follicular micropustule; brown patches surrounded by a yellowish-white halo indicating hair follicle invasion. Follicular micropustules are predominantly visible in vellus hairs and inflammation can cause vellus hair loss.

Tinea Incognito

Dermoscopy of tinea incognito show the presence of Morse code hair (bar code like hairs) on the vellus hair are characterized by irregularly interrupted hairs with normally pigmented and paler narrowed intervals on dermoscopy, follicular micropustules and erythema. A new dermoscopic appearance, consisting of translucent and deformable hair that looks weak and transparent; breaks easily, possibly due to fungal invasion of the entire body of hair Dermoscopy is a fast, readily available test that can be performed at the bedside and recognition of the dermoscopic features are simple.



Tinea incognito-Ill-defined margins with no central clearing. The lesion look eczematous.



On dermoscoy, corkscrew hairs (blue circle), Broken hairs (red arrow) with perifollicular scales and interfollicular scales as well as dyspigmentation is seen. That clinched the diagnosis

Dermatophytosis and comorbidities

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Management of dermatophytosis in patients with systemic comorbidities is very challenging because of restricted therapeutic options. They may require modified treatment algorithms due to their increased propensity for adverse effects to anti-fungal agents, as a result of drug interactions or altered pharmacokinetics. Some of the commonly encountered co- morbidities are :Obesity, diabetes mellitus, hyperlipidemia, hepatic dysfunction, renal impairment, cardiac disorders (congestive cardiac failure, arrhythmias) , neurological conditions like epilepsy, transient ischaemic attack, infections such as tuberculosis, HIV infection, psychiatric illness etc wherein there is a potential risk for drug-drug interactions.

Geriatric patients: Although, elderly population is more commonly afflicted with medical co-morbidities, some such as obesity, diabetes mellitus, dyslipidaemia, cardiac disorders may be seen in the younger age group too. A healthy elderly patient may be treated in the same manner as an young adult. Changes in pharmacokinetics must be considered while deciding an appropriate antifungal drug in elderly patients with hepatic or renal dysfunction. It is pertinent to take a detailed medical history of each and every patient, prior to selection of an appropriate antifungal drug. Drug interactions are much less with terbinafine than with azoles, and hence, terbinafine is relatively a safe option in the elderly patients. However, geriatric patients with renal dysfunction will need alteration of dose based on the creatinine clearance.

Obesity: It is one of the major lifestyle diseases posing as a huge challenge in treatment of dermatophytosis of the glabrous skin. Persistence of dermatophytosis in skin folds, difficulty in application of topicals, large surface area and metabolic syndrome are some of the challenges encountered in the treatment in these patients. Counselling with regard to strict adherence of general measures plays a pivotal role in ensuring a successful therapeutic outcome.

Diabetes mellitus: Uncontrolled diabetes may predispose an individual to chronic/recurrent dermatophytosis and deeper infections such as Majocchi's granuloma. Azole antifungals act as substrates as well as inhibitors of cytochrome P450 (CYP450) enzymes and may alter the pharmacokinetic profile of coadministered drugs that are metabolized through the same pathway. Concomitant use of itraconazole increases the levels of sulfonylureas such as glicazide, tolbutamide, which may result in hypoglycemia.

Hepatic disease: Liver diseases that affect hepatic blood flow, protein binding and enzyme activity significantly alter drug pharmacokinetics. Cirrhosis is known to cause alterations in hepatic drug clearance. Some of the known risk factors for drug induced liver injury are concomitant alcohol intake, elderly patients, and drugs with significant hepatic metabolism. Transient, mild-to-moderate elevations in serum aminotransferase levels may be seen after administration of azoles or terbinafine, which is self-limiting most of the times. The pattern of serum enzyme elevations may be cholestatic or of severe hepatitis with acute liver failure. Hence in patients with pre-existing hepatic disease, use of systemic antifungals is not advocated. In patients who need prolonged or high dose therapy, regular monitoring of liver function is warranted.

The relative risk of liver damage to various antifungals is as follows: The relative risk (RR) of causing acute liver injury Ketoconazole (RR 228)> Itraconazole (RR 17.7) > Terbinafine (RR 4.2). Griseofulvin is not indicated in patients with hepatic failure. Fluconazole has a low incidence of hepatotoxicity.

Renal disease : Degree of renal insufficiency and pharmacokinetic properties of the antifungal agent, have to be considered while deciding the treatment options in patients with renal disease. Fluconazole due to high water solubility is primarily excreted by urine and hence dose reduction is needed in patients with altered creatinine clearance. Itraconazole is eliminated mainly through faeces and in lesser amount through the urine and is a relatively safe option in renal disorder. This drug does not need alteration in dosage in patients undergoing dialysis. In case of decreased creatinine clearance, both fluconazole and terbinafine require dose adjustment. If the creatinine clearance <50 ml/min, their doses are to be halved. In patients on regular dialysis: 100% dose after each dialysis; on non-dialysis days, dose may be reduced according to creatinine clearance. Close monitoring of the renal function tests is essential in these patients.

Cardiac disease: Itraconazole has been associated with congestive cardiac failure and must be avoided in patients predisposed to the same. Caution is advised in patients with ventricular dysfunction. Some potential complications noted are risk of developing pedal edema with concomitant use of itraconazole and nifedipine,

and rhabdomyolysis with use of itraconazole and statins. Terbinafine is a relatively safer drug, however potential drug interactions with beta blockers, antiarrhythmics – Class 1c flecainide and propafenone have to be kept in mind.

Immunosuppressive therapy: Patients with connective tissue disorders, autoimmune bullous disorders, solid organ transplant recipients, hematological and solid organ malignancies are most often on long-term immunosuppressive drugs and are hence, highly prone for chronic/ recalcitrant dermatophytosis. These patients require long duration of treatment.

Acid peptic disease: Proton pump inhibitors and antacids reduce the absorption of itraconazole, the bioavailability of which is only 55%. Advent of super bioavailable itraconazole has helped to solve this issue.

To conclude, it is always important to take a proper history regarding all the comorbidities and the details of the drugs, in patients with dermatophytosis. Combination of topical and systemic antifungals administered for a longer duration may be essential to achieve clinical cure in these patients. Duration of the treatment will depend on the clinical response. Use of emollients will improve the barrier function and provide symptomatic relief. Counselling regarding the compliance to general measures is the cornerstone of therapeutic strategy of dermatophytosis.

Investigations case of dermatophytosis: **When & Why?**

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Although the diagnosis of dermatophytosis of the glabrous skin - Tinea corporis/cruris/faciei is clinically obvious in most settings, the relevance of investigations lies in the following scenerios:

1. Atypical presentations: Erythrodermic (Figure 1), steroid modified disease, Majocchi's granuloma

2. To assess treatment response: Use of serial KOH smears

3. Culture and sequencing : To know the trends of prevailing species

4. Histopathology: Atypical clinical presentations where other diseases are also in consideration; esp. erythrodermic
cases

5. Antifungal susceptibility Testing (AFST): Important to know the current susceptibility patterns with antifungals of clinical use

6. Whole genome sequencing: for precise identification where inter strain differences are subtle. E.g the differentiation of T.indotineae (the currently prevalent Indian strain) from T.mentagrophytes s. str and T.interdigitale s. str has been seen to be difficult on morphological or physiological characteristics alone or even

with sequencing of the rDNA ITS gene, hence resulting in mis-labelling by laboratories. The process however requires specialised laboratory settings.

Smear examination

KOH smear examination in a simple procedure and an untreated case is rarely, if ever, negative when observed by experienced personnel. We use 40% KOH on skin smears to facilitate early dissolution. It is essential to collect small scales, or break bigger ones once coverslip is placed, to facilitate uniform clearance and obtain a good smear. A patient examination of multiple fields is essential, esp. when the patient has taken some partial treatment, which is a common clinical scenario. Serial examination while on treatment gives important clues about the effectiveness of ongoing treatment and heralds treatment failure when changes in hyphal morphology fail to develop within 2-3 weeks of treatment. (Figure 2) It is ideal to have a negative KOH documentation before stopping treatment. Even an apparently cleared area may yield scales on scraping which not uncommonly turns out to be positive. This is an important cause for recurrences and relapses and hence must be taken care of.

Fluorescent staining: An in house fluorescent stain, made with household fabric whiteners, gives a blue or green fluorescence to the fungi making it distinctly visible against the contrasting dark background. (Figure 3)

Culture, AFST and sequencing

A standard methodology for culture involves inoculation of specimens on two sets of SDA – one containing gentamicin and chloramphenicol and the other containing cycloheximide (0.05%) followed by incubation at 28°C for 2 weeks. Preliminary macroscopic phenotypic identification is done on potato dextrose agar (PDA) incubated at 28°C for 14 days and slide cultures prepared on PDA ,then mounted in lactophenol cotton blue are then examined microscopically for morphology.

AFST is performed as per the Clinical and Laboratory Standards Institute broth microdilution method (CLSI-BMD), using the M38-A2 guidelines with minor modifications. Recently, the upper limit wild type distribution MICs for common antifungals against the prevalent strain in the country have been published which gives a good reference point for future studies.

Molecular identification: Usually based on sequencing ribosomal internally transcribed spacer (ITS) region, which provides sufficient heterogeneity to allow separation of key species. Others: Tef1α

It has been recently agreed to that distinguishing the Indian genotype (recently named as T.indotineae) from T.mentagrophtyes s. str and T.interdigitale s. str may not be possible on morphological or physiological characteristics or sequencing of the rDNA ITS gene alone, and requires a multilocus approach combining ITS and Tef1-α genes with mating type genes HMG and α-box. A near complete dominance of this strain has been reported in isolates from our centre and from others from other centres in the country over past few years. The same has been identified/labelled as T.interdigitale/T.mentagrophytes type VII/ Trichophyton mentagrophytes-Trichophyton interdigitale complex in previous reports before the recent consensus on taxonomical aspects was achieved.

HISTOPATHOLOGY

If performed may show – sparse to occasionally dense chronic inflammatory infiltrate in the dermis along with hyphae and spores in the stratum corneum (better visualised with PAS staining) Neutrophilic pustules may be seen in the stratum corneum as well. (Figure 4)

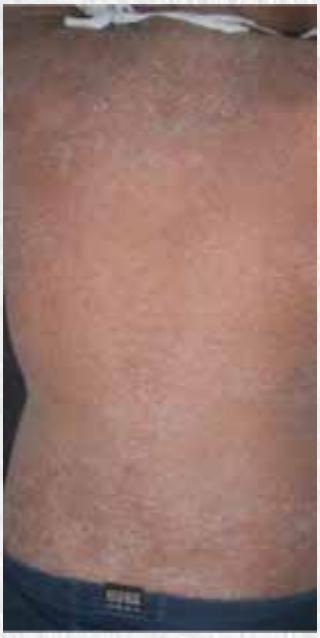

Figure 1:
Diffuse scaling with minimal erythema in a case of erythrodermic tinea corporis/cruris

Figure 2:
Left: Densely positive smear with branched septate hyphae. Right: With effective ongoing treatment – loss of branching, reduction in length and breaks within

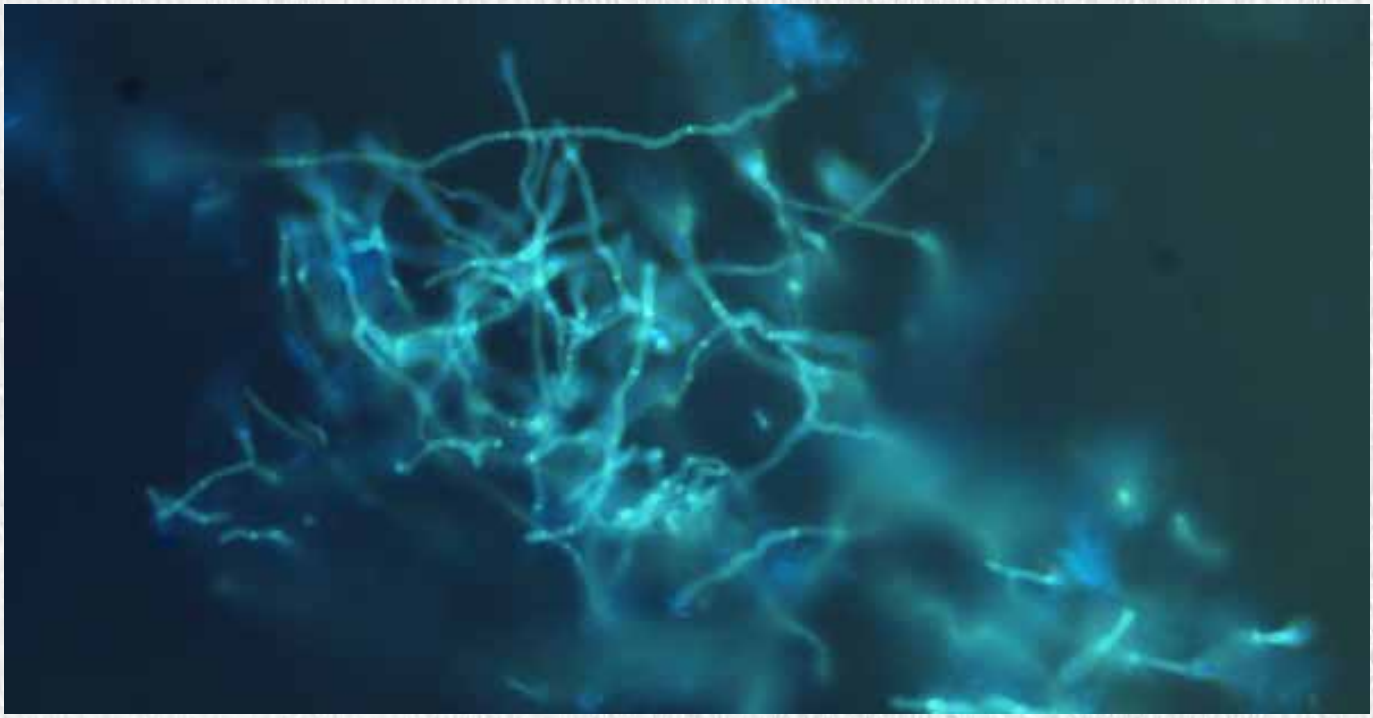

Figure 3:
Fluourescent green blue hyphae against a dark background using Ranipal fluorescent staining (Courtesy: Dr Shipra Suyal, Department of Microbiology, Dr RML hospital)

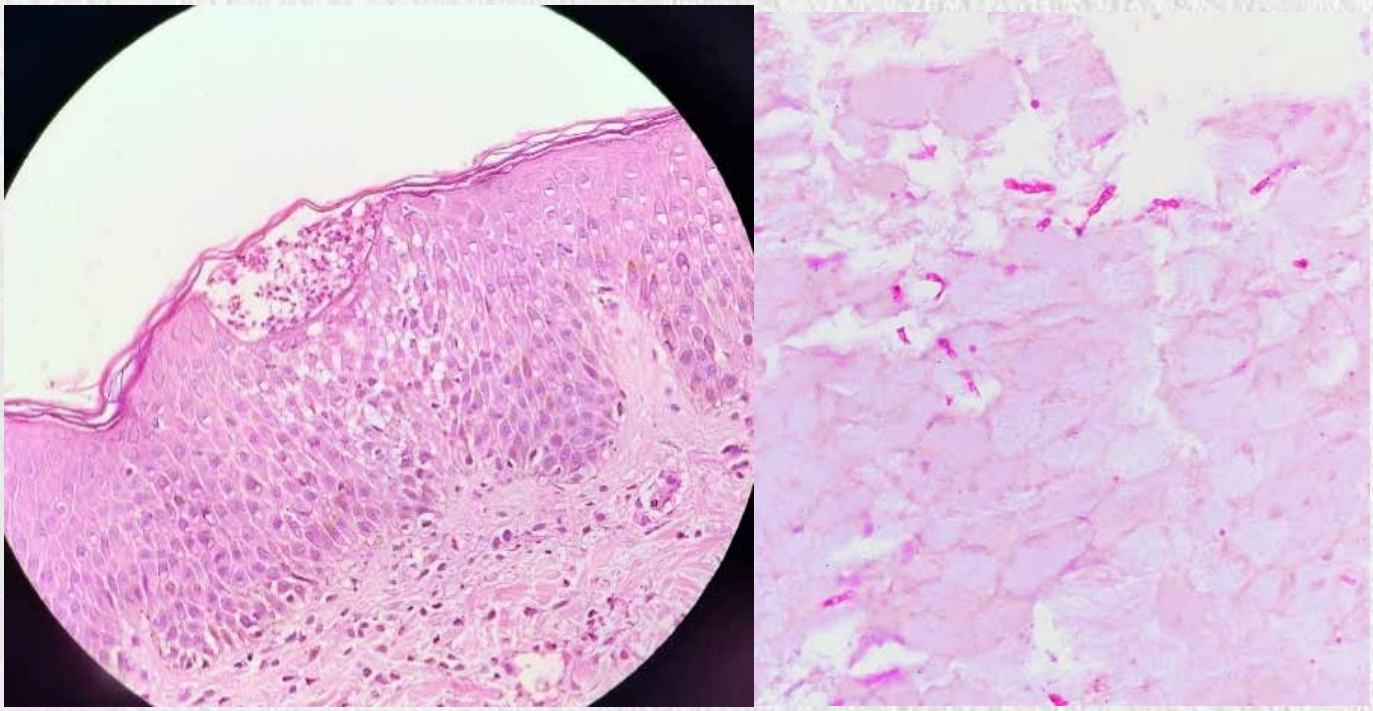

Figure 4:
Neutrophilic pustule in stratum corneum, along with hyphae. Right: Appearance of dermatophytic hyphae on tissue PAS staining (Courtesy: Dr Purnima Paliwal, Specialist, Pathology, Dr RML hospital)

Patient counselling in dermatophytosis: **walk the talk**

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Previous perception/Present scenario

Doctor patient communication lies in the very foundation of successful clinical outcome of doctor's efforts and patient satisfaction while treating any disorder. Making patient a part of decision making is considered essential component of patient-doctor interaction in modern medicine. Great amount of emphasis is given in this regard in literature on chronic conditions in dermatology like autoimmune, auto-inflammatory and malignant disorders.

Infectious diseases particularly superficial fungal infections, being amenable to cure with available antifungal medicine were considered to be goodwill builder for dermatologists till recent past. Prescribing correct medicine and ensuring proper treatment compliance was sufficient to cure the patient and leaving lasting positive impression of dermatologist on the patient. With the present epidemic of recalcitrant dermatophytosis in India many of these practice points need reconsideration by dermatologists. In the present epidemic, dermatologists are observing tremendous increase in number of cases of dermatophytosis characterized by severely inflamed lesions, chronicity, disseminated infections, involvement of multiple contacts and recurrence. Situation is further compounded by use of topical steroid containing fixed drug combination and exposure to systemic steroid rescribed by quacks. Dermatologist's armamentarium of oral and topical antifungal is limited to few molecules to manage this menace.

Why counselling is important

Spending few minutes in communicating with patient about disease and planned treatment is extremely important in present scenario. This will not only help identify patient's perception of treatment outcome and expectation from you, it will also help the dermatologist identify any limiting factors on part of patient like financial limitations, difficulty in regular follow up, occupational restriction related to clothing and hygiene etc.
We can also take this opportunity to discuss emerging scientific evidence related to present epidemic of dermatophytosis and how it changes the treatment plan in term of choice of antifungal and duration of therapy. Most importantly, it is pertinant to discuss factors related to recurrence and relapse with the patient about those which are known and which are yet unknown. This will not only help in compliance with treatment and instructions but reduce liability and accountability of dermatologist for unexplained recurrence or recalcitrance.
Over all counselling session will help bring down patient expectation from 'magical cure and absolute result' from doctor to 'best effort from doctor and equal participation of patient with expectation of a positive outcome'. Cost of therapy for dermatohytosis has increased considerably in recent time. Relapse or recurrence of disease leave patient with considerable dissatisfaction towards doctor if patient has not been made aware of same at outset. It goes without saying that good and continuous communication with patient, many a times helps doctor in avoiding unnecessary litigation which can arise out of unrealistic expectations.

Points to be included in counselling

1. Explain the diagnosis
Over past few decades rate of literacy as well as access to various sources of information have increased tremendously in India. Almost universal access to internet has made information regarding medical conditions available to patients. Few of these sources provide verified information while other spread misinformation and myths. In this context it is vitally important that patient is made aware of the diagnosis of tinea at outset. Special emphasis should be put on human to human transmission, infections nature of fungi, role of fomite etc.

2. Make patient aware about changing epidemiology and mycology.
Now enough data is available in scientific literature to suggest that present epidemic of dermatophytosis that India is witnessing mycological shift from Trichophyton rubrum to Trichophyton mentagrophyte (Indian genotype VIII). There are also multiple reports which document rising MIC of terbinafine in in-vitro susceptibility testing. Behavior of fungi is clearly anthropophilic and there is increase in cases of recalcitrant dermatophytosis which include chronic, recurrent and relapsing cases.
In this regard making patient aware of these emerging scientific details should be part of initial counselling. This will not only make patient aware about the epidemic but also prime for longer treatment, possible higher cost of therapy, importance of following hygiene instructions and most importantly possible recurrence despite of your best efforts. In absence of this, patient is more likely to discontinue treatment on initial clinical improvement, may perceive financial conflict of interest on part of dermatologist for use of relatively expensive

antifungal and may end up blaming dermatologist for any recurrence.

Counselling format used in our department
“You’ve a fungal infection of the skin also known as ringworm. Though this is a common skin infection in our country for the last few years, we’ve observed that it has become more difficult to manage. For example, it may become extensive, it spread to other body parts. Family members and close contacts are getting infected simultaneously. It persists for a longer time and often there is no adequate response to few drugs that we use. We’ve been seeing cases that are recurring despite therapy. Though we do not know all the factors responsible for change in the behavior of this disease in our country, we do know that some factors responsible are change in species of fungi, developing resistance to few of the antifungal drugs, use of over the counter creams which contain potent steroids, incomplete treatment which may leave behind some untreated fungi later causing recurrence and re-infection from infected family members.”

3. Explain about treatment and compliance.
Once patient is made aware of diagnosis and present scenario of epidemic next important step is to discussproposed plan of treatment in detail. Selection of antifungal molecule will depend on dermatologist’s analysis of present evidence and personal experience in particular geography but discussing this with patient in term of duration and dose is of vital importance to ensure treatment compliance. Most of the patients are expected to respond favorably in term of clinical improvement in initial days of therapy and tempted to discontinue therapy considering it as cure. Presence of fungus beyond advancing margin of lesions makes it necessary to apply topical therapy beyond margin of lesion. Clear instruction should be pass on not to share medicine with other family members even if they perceive that they have a similar condition. Few of the patients are extremely concerned for post inflammatory hyperpigmentation of tinea and consider treatment of tinea will take care of the same. Clear point on this, regarding possible slow disappearance of PIH is important on part of doctor.

Format used in our department
“I have prescribed some medicines along with the cream to clear your infection and reduce itching. Take the medicine as I instruct and do not miss any dose. The cream is to be applied twice daily on the affected area as well as up to 2 cm surrounding the affected area of the normal skin. As you take this medication, you may experience complete resolution of your itching and symptoms within few days but you’re not supposed to stop taking the medication unless advised by me. Come for a follow up consultation after 15 days and according to improvement I’ll decide on the length of the therapy. Do not share the prescription paper, the medicines or the cream with any of your family members or friends even if they have similar complaints. Each patient needs to visit dermatologist for proper diagnosis and treatment. After your infection has subsided, you’ll see some residual pigmentation in that area it’ll take some time to resolve so don’t worry about it.”

4. Explain regarding drug intake and possible drug interactions.

Depending upon the oral antifungal and antihistamine chosen by dermatologist, pertinent instruction on drug intake is necessary to ensure good bioavailability and sustained plasma levels of drug to inhibit growth of fungi. Patient's comorbidities and concomitant medication history evaluated at the time of history taking should guide counselling about drug interaction.

5. Explain about hygiene and host factors.
Proper personal hygiene without doubt plays extremely important role in management of dermatophytosis. Persistence of fungal spore on fomite is well documented. Instruction for proper washing and handling of personal belonging of patient is important to prevent relapse and spread of infection to other close contacts.

Format used in our department
"As this fungus can spread from close contact as well as personal belongings it is important to keep your clothes, linen and soaps separate. Wash your clothes in hot water in a separate bucket. Dry in sunlight and iron on the reverse side before wearing. Avoid washing clothes together in washing machine. It is also advisable that you take a bath twice a day and do not use any harsh soap or rub that area as this can irritate your skin and aggravate the itching. After bath let your body completely dry before applying the prescribed cream. Wear loose cotton underwear and clothes. Open toe footwear is preferable but if your profession demands close footwear then make sure you keep the area between your toes and your soles dry. You can use cotton socks for this that you can change twice daily. Keep your nails trim short and do not share your nail clippers with anyone else. If you have a western commode at home, then make sure you clean the seat before and after using."

6. Explain about management of close contacts.
In the present epidemic dermatologists across India are witnessing involvement of multiple family members and close contacts along with patient. Patient may or may not be aware of concomitant infection to other contacts. Reinfection from contacts can result in recurrence of tinea in patient. Patient must be made aware of importance of treating all infected person at same time.

Format used in our department
"Ask your family members and close contacts about similar complaints and bring them for treatment to me or to any other qualified dermatologist. It is important that all family members get treated at the same time."

7. Explain regarding over the counter (OTC) steroid hazards.
Detailed history taking regarding exposure to topical, oral or parental steroid should be standard operating protocol in a country like India. During counselling, patient must be made aware about immediate cessation of applying Topical steroid (TS) and not to use same in future at any point of time. Many patients are unaware that topical cream for itching that they buy directly from chemist contains topical steroid. Many are in fact happy with the temporary immediate relief they achieve with these creams owing to low cost of the same. Patient should be made aware about immunosuppressive effect of TS and the part it

plays in persistence and dissemination of infection. They may suffer from local adverse effects (AE) of topical steroid(TS) at the time of presentation. Patient may carry false impression that those AE will also be taken care by treatment of tinea. Here it is important on part of dermatologists to explain slow reversibility or irreversibility of AE. Also special emphasis should be made on possible exacerbation of inflammation when TS is discontinued. If not warned from beforehand, patient may perceive this as possible treatment failure and discontinue treatment with said dermatologist. We have come across patients who keep on applying TS without revealing to dermatologist because that cream(TS) gives much better relief in itching and burning than one prescribed by dermatologist!

Format used in our department

"Use of topical steroid may give symptomatic relief for a few days but it suppresses the local immunity and maintains infection in the skin which helps it to spread to other body parts so it is important to stop using over the counter creams which may contain steroid. You may experience increase itching or redness of that area once you stop these creams but you can visit me again. I'll make necessary changes in prescription to address the increase in symptoms but do not start using the over the counter cream again. Your skin already has few of the signs of adverse reaction to topical steroid (if present) which you have already used which may or may not (depending on type of AE) resolve gradually over the time."

Counselling during follow up visits

The patient should be asked about any complain of new lesions and persistent/new pruritus over the previous site of involvement as well as over any new site. This is to make sure that the patient is responding to treatment and to rule out any clinical signs of resistance to the prescribed drugs. Development of pruritus in any of the family members should be enquired so that their treatment can also be commenced simultaneously. It is advisable to cross check and confirm the medications bought by the patient. The patient should be instructed to maintain compliance with treatment and come for regular follow up as advised even if the lesions and pruritus resolve.

Two important point to be discussed during every follow up

1. Need to continue medication and all precautions discussed during first visit till dermatologist (usually 2-4 weeks beyond clinical remission) decides to stop. It is quite common for patient to discontinue treatment if they have symptomatic relief considering it as cure. Cost of therapy, aversion to take medicine are some of the factors responsible for this.
2. Many patients restore to TS application without informing dermatologist to achieve rapid symptomatic relief which they have experienced earlier with use of TS. Rebound inflammation and increase in symptoms being other factor which prompt patient to restore to TS use. Dermatologist must make detailed enquiry into this in reiterate need to avoid use of TS completely.

Dermatophytosis literature review of recent advances and future needs

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A brief overview of articles on the recent updates of epidemiological, mycological, immunological and antifungals in recalcitrant dermatophytosis have been included in this section.

1. **Jha K, Shaw D, Karim A, Narang T, Saikia B, Rudramurthy SM, Saikia UN, Dogra S. Immunological response and clinical profile in patients with recurrent dermatophytosis. Mycoses. 2021;64(11):1429-41.**
Evaluation of the host parameters in recurrent dermatophytosis that includes delayed type of hypersensitivity (DTH) response and immediate hypersensitivity (IH) and peripheral blood immune cells by flow cytometry have been studied in this article. Intradermal trichophytin skin test, estimation of the IgE, immunological and antifungal susceptibility tests were performed in 100 patients with recurrent dermatophytosis (RD) and 50 controls that included 25 healthy subjects and 25 acute dermatophytosis. Trichophyton mentagrophytes complex (95.84%) and T. rubrum (4.16%) were isolated. Almost 83 % cases had elevated Ig E levels. IFN-γ+ cells, Th1 cells, IL-17+ cells, Th17 cells were decreased, and IL-4+ cells were increased in patients with Rd. DTH response was negative in all RD cases. This study highlights the immunological aberration in the patients with RD, and compares the deviation of the immune response as compared to acute dermatophytosis and control.

2. **Shenoy MM, Rengasamy M, Dogra S, Kaur T, Asokan N, Sarveswari KN, Poojary S, Arora D, Patil S, Das A, Srivastava A, Katakam BK, Mahajan V. A multicentric clinical and epidemiological study of chronic and recurrent dermatophytosis in** India. Mycoses. 2022;65(1):13-23.

This is a study conducted by the special interest group of recalcitrant dermatophytosis by the IADVL academy. The study estimates the burden of chronic and recurrent dermatophytosis (CRD) in India by performing multicentric cross-sectional analysis. Total of 13 centres across India were employed for this purpose. Data was collected from the centres for 14 consecutive days, and various epidemiological and clinical data were analysed. Altogether, 41,421 patients were screened out of which 7174 (17.31%) patients had glamorous tinea that includes tinea corporis, tinea cruris and tinea faciei. Among them, 1999 (27.86%) patients were found to have CRD, with 78.08% being chronic and 21.95% being recurrent dermatophytosis. About half of them had family history of infection, topical corticosteroid misuse and sharing of fomites. Multiple site involvement was very common with tinea cruris being the commonest presentation. This study defines some of the important clinical and epidemiological aspects of CRD and highlights the gross differences from place to place and from centre to centre.

3. Tahiliani S, Saraswat A, Lahiri AK, Shah A, Hawelia D, Shah GK, Girdhar M, Rao PN, Raghav PA, Agarwal P, Kharkar RD, Gupta RP, Udare S, Hegde S, Haldar S. Etiological prevalence and antifungal sensitivity patterns of dermatophytosis in India - A multicentric study. Indian J Dermatol Venereol Leprol. 2021;87(6):800-6.
Dermatophytosis prevalence varies with season, geographical area, socio-economic factors and management strategies. Isolation of pathogenic dermatophytes, followed by in vitro antifungal drug susceptibility testing that were performed in this multicentric study. Patients from five cities across India that accounts to three hundred and ninetyfive patients were included. Clinical examination, direct microscopy with potassium hydroxide preparation, fungal culture and antifungal drug susceptibility testing were performed. Most common isolates were Trichophyton rubrum (68.4%), which was followed by T. mentagrophytes (29.3%). Isolation of T. mentagrophytes was more frequent in humid coastal environmental conditions (Mumbai and Kolkata), whereas T. rubrum was prevalent in non-coastal areas (Delhi, Lucknow and Hyderabad). Glabrous infections accounted for most of the infections, that included tinea corporis (71.4%) and tinea cruris (62.0%). Lowest MIC90 was detected for griseofulvin (0.25–3.0 µg/mL) as per the broth micro-dilution antifungal susceptibility. MIC of itraconazole was within the range (0.84 [0.252] µg/ mL). Highmean MIC was reported with terbinafine (0.05 [0.043] µg/mL). MIC values were favourable for the Luliconazole (0.29 [0.286] µg/mL), eberconazole (0.32 [0.251]) µg/mL and amorolfine (0.60 [0.306]) µg/mL showed favourable MIC profiles. Trends of in vitro resistance were noticed with terbinafine, however itraconazole, griseofulvin and newer topical antifungals showed good activity against the common fungal isolates.

4. Klinger M, Theiler M, Bosshard PP. Epidemiological and clinical aspects of Trichophyton mentagrophytes/ Trichophyton interdigitale infections in the Zurich area: a retrospective study using genotyping. J Eur Acad Dermatol Venereol. 2021;35(4):1017-25
Trichophyton mentagrophytes or Arthroderma vanbreuseghemii (telomorphic form) along with Trichophyton interdigitale are two different species that account for a large number of dermatophytosis across the world. It is difficult to differentiate them by conventional culture but it can be identified by internal transcribed spacer (ITS) genotyping. Epidemiologically and clinically, they differ significantly. The study

was conducted in the Switzerland (Munich), where epidemiology of Trichophyton mentagrophytes and Trichophyton interdigitale diagnosed based on ITS sequencing were analysed. Timeline for the study has been between 2009 and 2019 and the retrospective data were analysed. A total of 81 cases were studied and it was found that T. mentagrophytes infections affected younger and more frequently females. Head and body rather than feet and toenails were affected. Inflammatory lesions were found and it required a combination of systemic and topical antifungal for an effective management. Seven genotypes of T. mentagrophytes were identified with subtle changes in the clinical and epidemiological characteristics. It can be concluded that ITS genotyping allows identifying sources of infection and a possible terbinafine resistance which is prevailing in T. mentagrophytes.

5. He M, Zeng J, Mao Y, Zheng Y, Lian X, Chen H. Aetiological changes of tinea capitis in the Hubei area in 60 years: Focus on adult tinea capitis. Mycoses. 2021;64(12):1527-34.

Dermatophyte infection of the scalp hair, tinea capitis, is a common infection of children. It is uncommon but not unknown and the epidemiology in adults is not studied completely. Changes in the causative agent of adult tinea capitis in 60-year period in the Hubei area of China was studied in a retrospective descriptive study. In a single-center study, 164 adults with tinea capitis since 1960-2020 were included. Adults represented 14.7% of all cases on tinea capitis. It was more prevalent in males (91, 55.5%) but there was no statistical significance between genders. Ages of 18 and 29 years depicted higher prevalence. Commonest cause of adult tinea capitis was Trichophyton schoenleinii (78, 47.6%), followed by Trichophyton violaceum (58, 35.4%). Latter has become the leading pathogen in the recent years indicating a major epidemiological shift which could be due to the government programs intended to eradicate favus. Understanding the aetiology and epidemiology can help treatment and prevention of tinea capitis in adults.

6. Bonifaz A, Tirado-Sánchez A, Mercadillo P, Moreno-López LM, Fierro-Arias L, Araiza J, González GM. Clinical and mycological study of 42 cases of dermatophytic granuloma (Majocchi granuloma). J Dtsch Dermatol Ges. 2021;19(5):758-61

Keratophilic, filamentous dermatophytes remain limited to the stratum corneum. Deep tissue invasion rarely occurs due to local or general immunosuppression. Majocchi granuloma, deep dermatophytosis, disseminated dermatophytosis (Hadida's disease) and pseudomycetoma are some of the manifestations of such rare deep invasion. Forty-two cases of Majocchi granuloma seen by the authors over a period of 27 years (1993–2019) have been reviewed in this article. Females (27, 64.3%) outnumbered males. Mean age was 35.2 ± 10.56 years. Duration ranged from 2 to 14 months. Diabetes mellitus along with corticosteroids (topical and systemic) accounted to about 40% of the associated factors. Tinea pedis with onychomycosis was the diagnosis (78.5%) commonly noted with nodular lesions being the most common presentation (88%). Leg was the most frequent site (66.6%). Authors conclude that Majocchi granuloma should be suspected in diabetic and immunosuppressed patient presenting with unusual nodular lesions on the legs and feet.

7. Sardana K, Gupta A, Sadhasivam S, Gautam RK, Khurana A, Saini S, Gupta S, Ghosh S. Checkerboard Analysis To Evaluate Synergistic Combinations of Existing Antifungal Drugs and Propylene Glycol Monocaprylate in Isolates from Recalcitrant Tinea Corporis and Cruris Patients Harboring Squalene Epoxidase Gene Mutation. Antimicrob Agents Chemother. 2021;65(8):e0032121.
Current Indian epidemic of dermatophytosis has seen recalcitrant nature of infection that generally requires combinations of oral and topical drugs to improve cure rates. Identifying synergistic combinations of oral and topical antifungals is a challenge since there are few data on it. In this study, clinical isolates obtained from patients who had failed oral antifungals or had relapsed within 4 weeks of apparent clinical cure were studied in an in vitro analysis. Forty-two patients were enrolled and twenty-one isolates were identified by sequencing (all belonging to the Trichophyton mentagrophytes/T. interdigitale species complex) and subjected to antifungal susceptibility testing (AFST) and squalene epoxidase (SQLE) gene mutation analysis. Four clinical isolates with underlying SQLE gene mutations and one wild-type strain, were chosen for checkerboard studies using combinations of antifungal agents. Most isolates (n = 16) showed high MICs of terbinafine (0.5 to >16 µg/ml). All these isolates showed SQLE gene mutations. Combinations of itraconazole with luliconazole, terbinafine, ketoconazole and propylene glycol monocaprylate (PGMC) with luliconazole and with the triple combination of PGMC with luliconazole and ketoconazole were included. These synergistic combinations may be tested and further evaluated to counter the rising resistance among dermatophytes.

8. Shenoy M, Dhoot D, Mahajan H, Barkate H. An Open-Label, Randomized, Double-Arm Clinical Trial to Compare the Effectiveness and Safety of Super Bioavailable Itraconazole Capsules and Itraconazole Capsules in the Management of Dermatophytosis in India. Clin Cosmet Investig Dermatol. 2021;14:1367- 76.
A new oral formulation of itraconazole, called super bioavailable itraconazole (SBITZ), has been available in India since more than a year. With greater bioavailability than conventional itraconazole (CITZ), it could be a useful formulation to treat dermatophytosis. Objective of this study was to compare the efficacy and safety of SBITZ and CITZ in dermatophytosis. An open-label, randomized, double-arm clinical study was conducted and 70 adult patients diagnosed to have tinea cruris, tinea corporis, and/or tinea faciei were included. A treatment period of 4 weeks (CITZ 100 mg BID or SBITZ 50 mg BID) followed by an observation period for another 4 weeks was the study duration. Among the total, 59 (33 patients in the CITZ group and 26 patients in the SBITZ group) were included in the final analysis. Complete cure was achieved in 11 patients (33.33%) and 17 patients (65.38%) in CITZ and SBITZ group respectively ($p<0.05$), whereas mycological cure was achieved in 22 patients (66.67% and 84.61% in CITZ and SBITZ groups respectively) each ($p=0.14$). Recurrence was seen in 1/11 and 4/17 completely cured patients ($p=0.15$). Treatments were safe and well tolerated barring few adverse effects. This real-world evidence suggests the utility of both formulations of itraconazole in the management of dermatophytosis in India.

Tinea Quiz

Dr. Anupam Das
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1. Trichophyton mentagrophytes exhibits a rapid growth in primary culture within

a. 2-3 days
b. 5-7 days
c. 14-15 days
d. 28-30 days

2. Recurrent dermatophytosis has been defined as disease in which there is a recurrence of lesions within _____ after completion of treatment.

a. 2-3 weeks
b. 6-8 weeks
c. 10-12 weeks
d. 14-16 weeks

3. For confirmation and definitive identification of the dermatophytes, sequencing of ribosomal DNA (rDNA) targets which of the following?

a. ITS 1
b. 5.8S
c. ITS 2
d. All of the above

4. False statement about Trichophyton indotineae sp

a. Contained a nonsense mutation in squalene epoxidase (SQLE) gene
b. Trichophyton interdigitale-like strain
c. Isolated from Nepal and India
d. Highly terbinafine resistant

5. Choose the incorrect pair

a. ITS Type III : Europe
b. ITS Type VI : Australia
c. ITS Type VII : Thai
d. ITS Type VIII : India

6. Antifungal resistance to griseofulvin was first reported in

a. Trichophyton rubrum and Trichophyton tonsurans
b. Trichophyton rubrum and Trichophyton mentagrophytes
c. Trichophyton tonsurans and Trichophyton mentagrophytes
d. Trichophyton mentagrophytes and Trichophyton schoenleinii

7. False statement about epidemiological cut-off value

a. More relevant and practical than clinical breakpoint
b. Indicates to clinician whether an antifungal will be successful or not
c. Predicts clinical success
d. All of the above

8. Minimum inhibitory concentration of luliconazole for Trichophyton rubrum is

a. < 0.1 micrograms per milliliter
b. < 0.01 micrograms per milliliter
c. < 0.001 micrograms per milliliter
d. < 0.0001 micrograms per milliliter

9. Which of the following correctly describes the positioning of itraconazole in lactating mothers?

a. Risk I L3
b. Risk II L2
c. Risk III L3
d. Risk IV L2

10. Choose the correct statement

a. Fluconazole increases levels of oral contraceptives
b. Itraconazole decreases the levels of omeprazole
c. Terbinafine decreases levels of warfarin
d. Ketoconazole increases levels of sulfonylurea

Answers to tinea quiz

1-b, 2-b, 3-d, 4-a, 5-b, 6-a, 7-c,8-c, 9-d, 10-d

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