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Dermatophytosis: An Updated Review of Epidemiology, Pathogenesis, Diagnosis, Antifungal Resistance and Treatment

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ABSTRACT:

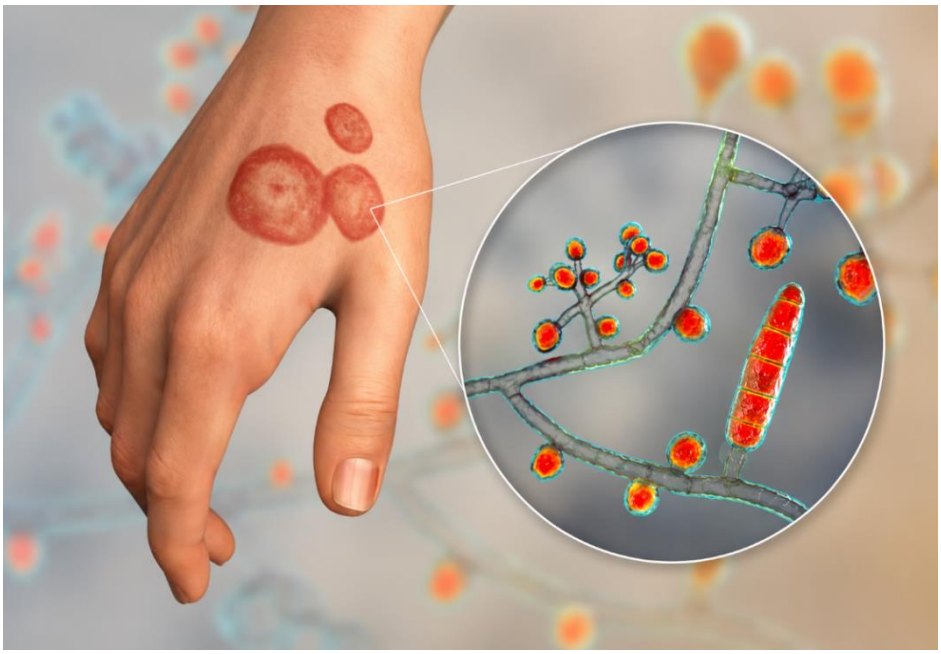
Dermatophytosis, commonly known as ringworm or tinea infection, is one of the most prevalent superficial fungal infections affecting keratinized tissues, including the skin, hair, and nails. It is primarily caused by dermatophytes belonging to the genera Trichophyton, Microsporum, and Epidermophyton. The infection can occur in different anatomical forms, including tinea corporis, tinea capitis, tinea pedis, tinea cruris, tinea faciei, tinea manuum, tinea barbae, and tinea unguium. Warm and humid environmental conditions, excessive sweating, close contact with infected individuals or animals, contaminated fomites, poor hygiene, and certain host-related factors contribute to the transmission and persistence of dermatophytosis. This review summarizes the current understanding of the aetiology, classification, pathogenesis, epidemiology, clinical manifestations, and diagnostic approaches used for dermatophyte infections. Conventional diagnostic methods such as direct microscopic examination using potassium hydroxide, fungal culture, dermoscopy, Wood's lamp examination, and skin biopsy, along with molecular diagnostic techniques, are discussed. Particular attention is given to the increasing emergence of antifungal-resistant dermatophytes, especially Trichophyton indotineae, and the molecular mechanisms associated with resistance to terbinafine and azole antifungals. Current pharmacological and non-pharmacological treatment approaches, including topical and systemic antifungal therapy, are also reviewed. The potential role and limitations of combination antifungal therapy and the use of non-antifungal agents as adjunctive treatments are highlighted. Overall, early and accurate diagnosis, appropriate antifungal selection, treatment adherence, and preventive measures are essential for improving therapeutic outcomes and reducing recurrence and transmission. Continued research into antifungal resistance, novel therapeutic strategies, and improved susceptibility testing methods is required to address the evolving challenges associated with dermatophytosis.

Keywords: Dermatophytosis, Ringworm, Trichophyto,; Microsporum, Epidermophyton, Antifungal resistance, Trichophyton indotinea, Terbinafine, Azoles, Diagnosis, Treatment.

1. INTRODUCTION :

Tinea corporis also known as “Ringworm” is a superficial dermatophyte infection of the skin, Other than on the hands (tinea manuum), feet (tinea pedis), scalp (tinea capitis), bearded areas (tinea barbae), face (tinea faciei), groin (tinea cruris), and nails (onychomycosis or tinea unguium), tinea corporis, also referred to as "ringworm," is a superficial dermatophyte infection of the skin. Dermatophytes from one of the three genera—Trichophyton, which causes infections on skin, hair, and nails; Microsporum, which causes infections on skin and hair; and Epidermophyton, which causes infections on skin and nails—are most frequently responsible for tinea corporis. Depending on whether their major source is human, animal, or soil, dermatophytes are classified as anthropophilic, zoophilic, or geophilic.

Physicians need to become familiar with the aetiology and management of tinea corporis because it is a common fungal infection that can be mistaken for many other annular lesions.1 (updated tinea corporosis)



Classification of Dermatophysis

Tinea corporis: an infection of the body that does not affect the hands, feet, groin, or scalp.
2. Tinea capitis: a hair and scalp infection.
3. Tinea pedis, also referred to as athlete's foot, is an inflating of the feet.
4. Hand infection (tinea manuum).
5. Tina faciei: a facial infection that is frequently confused with other dermatological conditions.

2. TRANSMISSION MODE CLASSIFICATION

The mode of transmission, which describes how the fungus infection spreads from one person to another or from an animal to a human, is used to categorize dermatophytosis. Typically, this classification consists of:

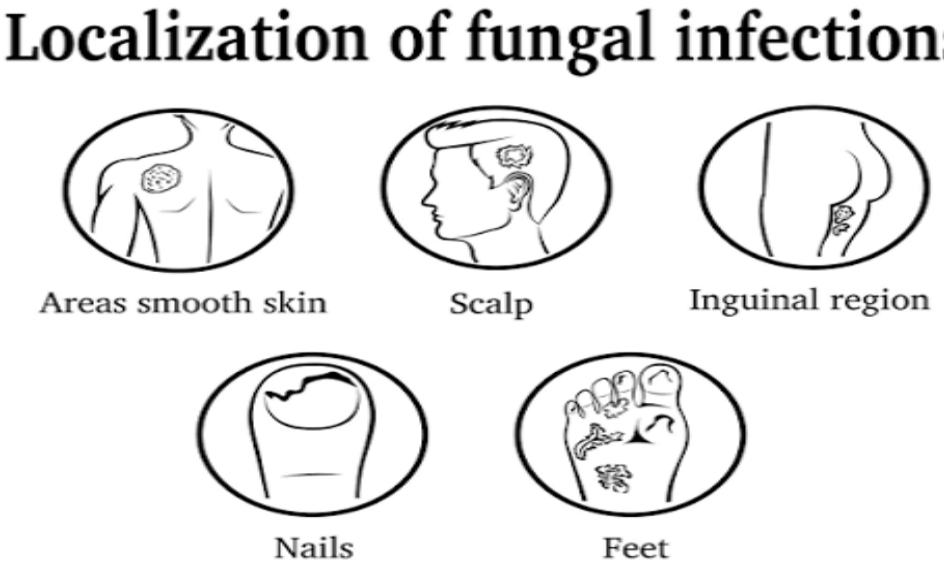
Anthropophilic Transmission: People are the main carriers of dermatophytes. In diseases like tinea corporis and tinea pedis, this type of transmission is common.

Dermatophytes can transfer from animals to people thru a process known as zoophilic transmission. Dogs, cats, and rats are examples of domestic animals that can act as reservoirs for dermatophyte infections, which can cause diseases like tinea corporis and tinea capitis.

Geophilic Transmission: Dermatophytes are gathered from the soil. Infections like tinea corporis and tinea pedis can be contracted from direct contact with contaminated soil or fomites.2 [a review of the system]

AETIOLOGY

Microsporum canis, T. tonsurans, and Trichophyton rubrum are the most common causes of tinea corporis. T. rubrum is the most frequent cause of tinea corporis in North America and the most frequent cause of dermatophytosis globally.T. tonsurans [updated tinea corporosis] is frequently the cause of tinea corporis subsequent to tinea capitis.Trichophyton rubrum has been the most prevalent species responsible for dermatophyte infections for the last 70 years. Eighty to ninety percent of the pathogenic strains are caused by T. rubrum.3. [tinea corporis stat pearls]

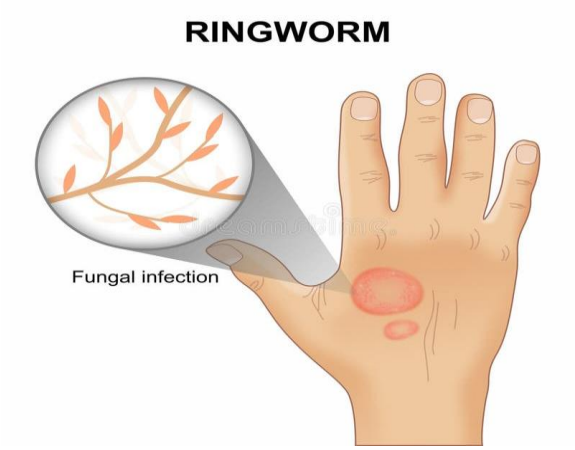


Symptoms and indicators:

The term "tinea" refers to the area of the body that is afflicted; for example, "tinea pedis" refers to an infection of the feet, while "tinea cruris" refers to an infection of the groin or crural folds. The degree of presentation is determined by organism virulence, host vulnerability, and hypersensitivity. The majority of the time, there is little to no inflammation; lesions with a scaling, slightly elevated border that are asymptomatic or mildly itchy may occasionally remit and recur. Typical signs of dermatophyte diseases include: • On glabrous skin, annular, erythematous, scaly plaques with a center clearing and an active elevated border (such as tinea corporis)

Itchy, white, macerated, and occasionally fissured lesions in intertriginous areas (such as tinea cruris or certain types of tinea pedis) • Scalp irritation (such as tinea capitis) and patchy baldness with scaling Onycholysis in onychomycosis, distal or lateral nail discolouration, thickness, and subungual debris All forms of dermatophyte infections are prone to chronicity and recurrence. Sometimes the inflammation is more severe and shows up as an inflammatory swampy lesion of the scalp (kerion) or as

abrupt vesicular or bullous disease (typically of the foot). Tinea incognito, also known as chronic or glucocorticoid-modified infectious lesions, may not have the typical characteristics.4



Ringwood's pathophysiology:

Dermatophytosis, also referred to as ringworm or tinea infection, is a superficial fungal infection mostly caused by keratinophilic fungi from the genera Epidermophyton, Microsporum, and Trichophyton. The skin, hair, and nails are examples of keratinised tissues that are infected by these fungi. Environmental variables, host immunological responses, and fungal virulence factors interact intricately in the pathophysiology of dermatophytosis.5

When fungal spores, or arthroconidia, come into touch with the skin's surface thru contaminated objects, dirt, diseased persons, or animals, the illness starts. The fungus use fungal adhesins and proteolytic enzymes to stick to keratinised tissue once they have reached a vulnerable host. Fungal colonisation and growth are facilitated by favourable environmental factors such warmth, moisture, perspiration, and poor hygiene.

Clinical symptoms include erythema, itching, scaling, vesicle development, and pustules are caused by inflammatory chemicals that are generated by fungus and diffuse into deeper epidermal layers. In contrast to anthropophilic species, zoophilic species typically cause more severe inflammatory reactions. When fungal pathogens avoid host immunity or when treatment is insufficient, chronic infection may result.

Six

Dermatophytes produce keratinolytic enzymes, such as keratinases, lipases, elastases, and proteases, to infiltrate the stratum corneum after adhesion. These enzymes break down keratin and supply the nutrients required for fungal growth and survival. The pH of the surrounding environment changes from acidic to alkaline during fungal metabolism, boosting enzyme activity and facilitating deeper fungal penetration into keratinised tissues.7

The most significant defence against dermatophyte infections is thot to be cell-mediated immunity. T-helper type 1 (Th1) immune responses increase the production of cytokines, especially interferon-gamma (IFN-γ), which stimulates macrophages and facilitates the removal of fungi. Thru the shedding of infected keratinised cells, inflammatory responses boost epidermal turnover and aid in the removal of

fungus.8
Chronic or recurrent infections can result from poor immune responses in certain people, particularly immunocompromised patients. Persistent dermatophytosis is linked to a predominance of Th2-mediated immune responses with elevated IgE and IgG4 production. Severe or invasive dermatophyte infections are more common in patients with diabetes mellitus, HIV infection, corticosteroid abuse, or genetic immunological abnormalities including CARD9 deficiency. 9

EPIDEMIOLOGY

One of the most prevalent superficial fungal infections that affect people worldwide is dermatophytosis. It is brought on by dermatophyte fungi that infiltrate keratinised tissues like skin, hair, and nails. These fungi primarily belong to the genera Trichophyton, Microsporum, and Epidermophyton. Due to the favourable environmental circumstances for fungal growth, the disease affects people of all ages and is regarded as a serious public health concern, especially in tropical and subtropical countries.Ten Over the past few decades, dermatophytosis has become much more common, particularly in developing nations like India. Disease transmission is greatly aided by hot and muggy weather, crowding, heavy perspiration, poor hygiene, occlusive clothes, and low socioeconomic level.

. The primary causal organisms of chronic and recurring dermatophytosis in India are Trichophyton rubrum and Trichophyton mentagrophytes complex. Increasing antifungal resistance among dermatophyte species has also been found in recent epidemiological research, making disease management more challenging.11 Although dermatophytosis affects both sexes, adult males are more likely to develop particular types, such as tinea cruris and tinea pedis, because to higher perspiration, occupational exposure, and tight clothes. Due to immature sebaceous gland activity and close social interaction in schools, children are more vulnerable to tinea capitis. Due to weakened immunity, diabetes, and poor peripheral circulation, elderly people are more susceptible to onychomycosis. Twelve Direct contact with sick people, animals, contaminated soil, or fomites like towels, shoes, combs, and clothes can spread the infection. While zoophilic species are typically contracted from infected animals, anthropophilic species are mostly transmitted from person to person. The rising incidence of infection has also been exacerbated by increased urbanisation, migration, the use of public facilities like swimming pools and gyms, and the abuse of topical corticosteroid combinations.13. A number of host-related conditions, such as diabetes mellitus, obesity, immunosuppression, HIV infection, malnourishment, and long-term corticosteroid medication, increase vulnerability to dermatophytosis. Additionally, weakened cell-mediated immunity and genetic predisposition

impact the recurrence and chronicity of an illness. Understanding geographical differences, spotting new resistant strains, and enhancing preventive and treatment approaches against dermatophytosis all depend on epidemiological surveillance. 14.

Clinical manifestations:

A superficial fungal infection that affects keratinised tissues like the skin, hair, and nails is called dermatophytosis. The type of dermatophyte causing the infection, the infection site, the host's immune system, the surroundings, and the length of the illness all affect the clinical signs. Erythematous, scaly, annular lesions accompanied by itching and inflammation are a frequent presentation of dermatophyte infections. The lesions frequently exhibit center clearing with active elevated edges, giving them the distinctive "ringworm" appearance. From moderate, asymptomatic scaling to highly inflammatory lesions with pustules and vesicles, infection severity varies.

One of the most prevalent types of dermatophytosis that affects the body's glabrous skin is tinea corporis. Usually, it appears as oval or circular erythematous plaques with a central clearing and well defined scaly edges.

In chronic infections, lesions may combine to produce polycyclic patterns as they progressively grow centrifugally. Frequent scratching can result in a secondary bacterial infection, and pruritus is a common symptom. Lesions can grow large and unusual in immunocompromised people.

Children are the main victims of tinea capitis, which damages the scalp and hair shafts. Patchy alopecia, broken hairs, black spots, generalised scaling, and inflammatory kerion development are among the clinical signs. While inflammatory types cause painful swampy swellings accompanied by pustules and lymphadenopathy, non-inflammatory variants may mimic seborrhoeic dermatitis. Alopecia with permanent scarring can result from serious infections that are left untreated. Compared to anthropophilic species, zoophilic dermatophytes typically cause higher inflammatory responses.

In adult guys, tinea barbae affects the areas of the moustache and beard. It frequently manifests as crusting lesions, pustules, nodules, and inflammatory follicular papules. Hair shafts come free and can be removed with ease. Zoophilic organisms obtained from domestic animals like livestock are often implicated. Additionally, patients may have localised lymph node enlargement, discomfort, and itching.15.

The groin, inner thighs, buttocks, and perineal area are all affected by tinea cruris, sometimes known as "jock itch." Due to friction, tight clothing, obesity, and profuse perspiration, it is more common in adult males. Clinically, it manifests as scaling, intense itching, and reddish-brown plaques with raised edges. Usually bilateral, the lesions have the potential to spread to other regions. Lichenification and hyperpigmentation are common outcomes of persistent infection. 16.

The interdigital areas of the feet are frequently affected by tinea pedis, generally referred to as athlete's foot. It manifests as burning, erythema, scaling, fissuring, and maceration. There are three main clinical variations: vesiculobullous, hyperkeratotic (moccasin type), and interdigital. The vesiculobullous variety is distinguished by painful vesicles and bullae, while the hyperkeratotic variant results in extensive scaling and thickening of the soles. Disease transmission is facilitated by communal bathing facilities, occlusive footwear, and persistent dampness.

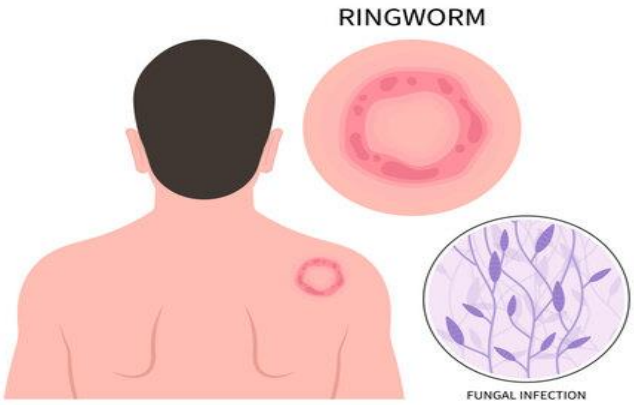
Nail discolouration, subungual hyperkeratosis, brittleness, thickness, and onycholysis are the hallmarks of tinea unguium, also known as onychomycosis, a fungal infection of the nails. Compared to

fingernails, toenails are more commonly impacted. The most prevalent clinical form is distal lateral subungual onychomycosis. People with diabetes, the elderly, and those with impaired immune systems are more vulnerable.

Walking, appearance, and quality of life can all be negatively impacted by a persistent nail infection. Non-bearded facial skin is affected by tinea faciei, which frequently manifests as erythematous, scaly plaques with hazy edges. The lesions could be mistaken for contact dermatitis, lupus erythematosus, eczema, or rosacea, delaying diagnosis. For some patients, sun exposure can exacerbate symptoms. Tinea manuum causes dryness, hyperkeratosis, scaling, and fissuring in the palms and interdigital areas of the hands. The "two feet, one hand syndrome" is often linked to tinea pedis.

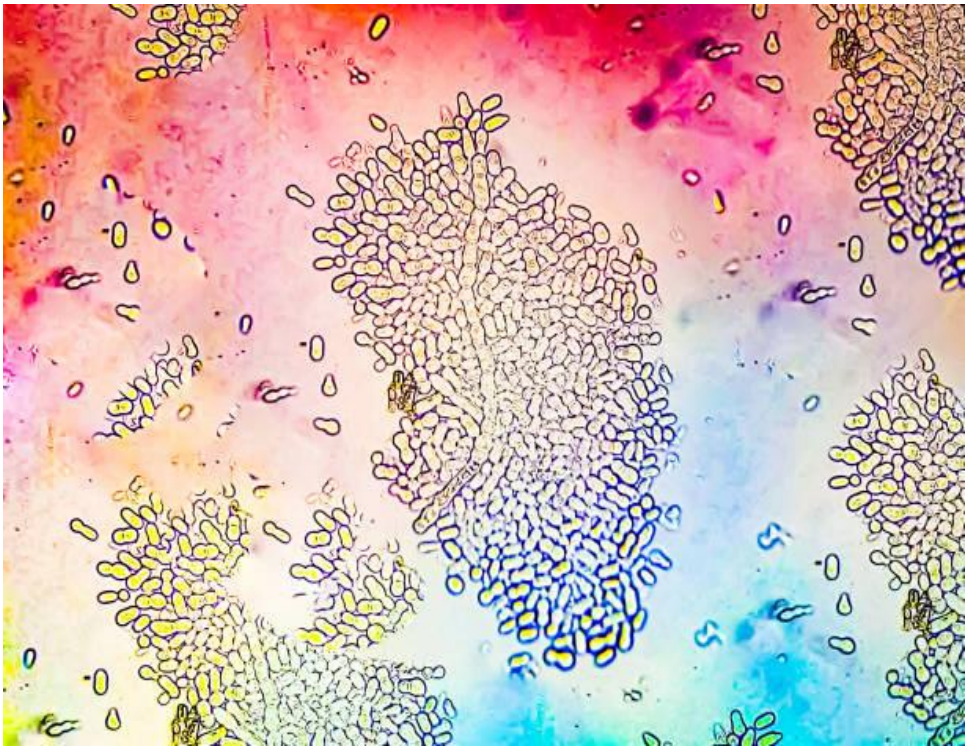
Identification and Diagnosis

1. Clinical Features: Symptoms and Signs Physical assessment:
   Take note of the lesion's redness, scaling, cracking, or distinctive ring patterns.
2. Methods of Diagnosis
   A.Direct Microscopic Analysis Method:
   1.Scrapethelesion'ssurface.
   2. Place the specimen in the KOH solution on a glass slide.
   3. Proteins, lipids, and keratin are broken down by KOH.
   4. Fungal structures become visible and resist digestion.
3. Staining: Visualisation is improved by optional stains like Parker Quink.
   Microscopic appearance
   Transparent, unpigmented, septate hyphae or arthrospores are known as dermatophytes.
   B. Culture of Fungi
   Goal: Verifies the existence and species identification of dermatophytes
   Media: Sabouraud's dextrose agar (neutral pH; dextrose, peptone, and agar). Growth characteristics: Complete identification may take up to four weeks, but they are visible within five to ten days. Size, shape, colour, texture, growth rate, spore pattern, and hyphal morphology are used for identification.
   C. Molecular Diagnosis
4. The goal is to differentiate species based on genetics.
   Methods:
   Conventional PCR is slower and less expensive.
   PCR in real time: faster detection
   Post-PCR analysis: very specific but sometimes time-consuming
   D. Dermoscopy
   Method: Apply gel or oil on the lesion Examine the shape of the fungus and the lesion.
   E. Biopsy of the Skin
   Use: To make a firm diagnosis or rule out other dermatoses (psoriasis, eczema). Method: Punch biopsy under local anaesthesia Fungal components seen under a microscope F. Wood's Lamp Analysis
5. Method: UV light that has been filtered (>365 nm wavelength) Results: Certain dermatophytes, especially those that infect hair, glow when exposed to UV light.18

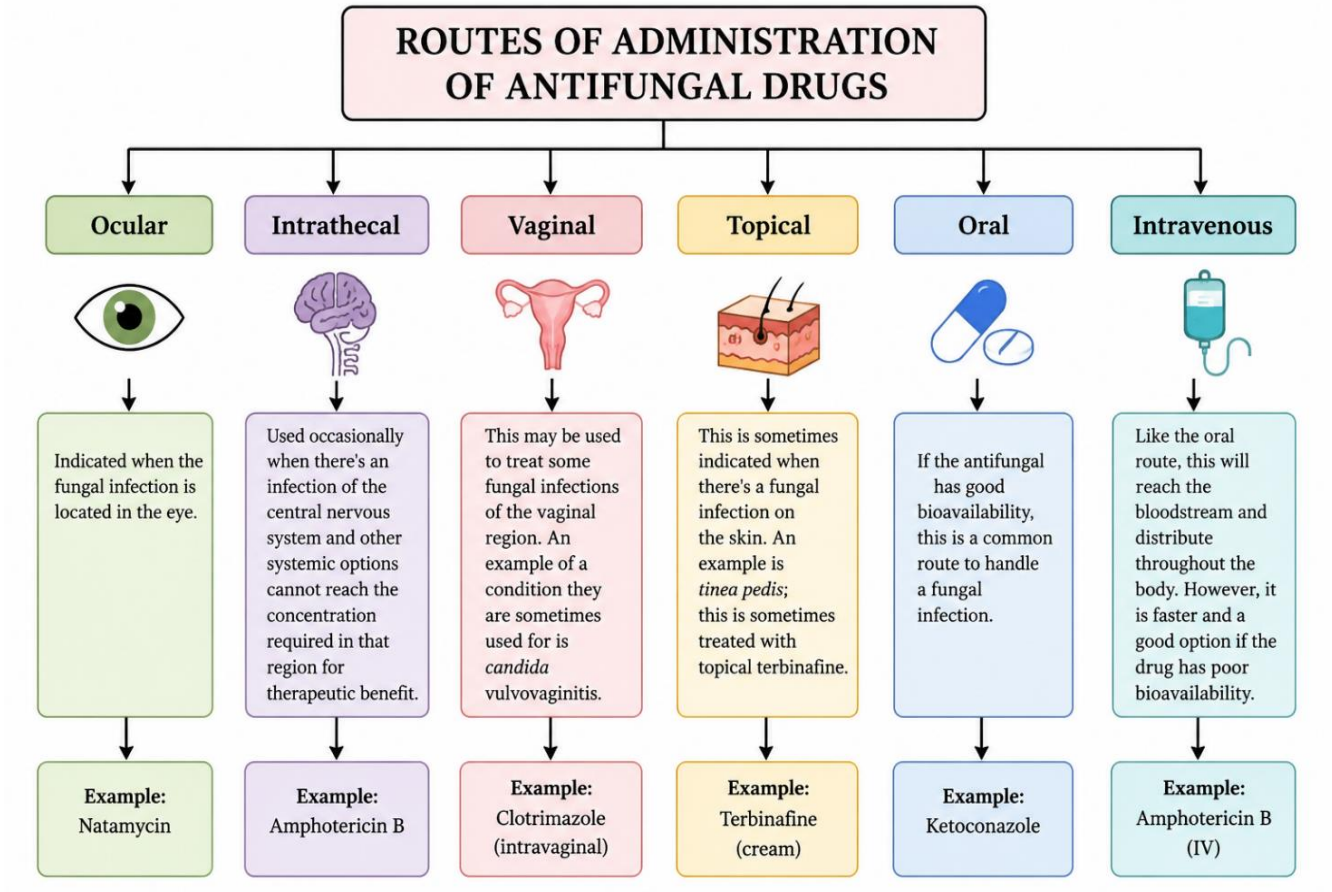


NEW RESISTANT DERMATOPHYTES

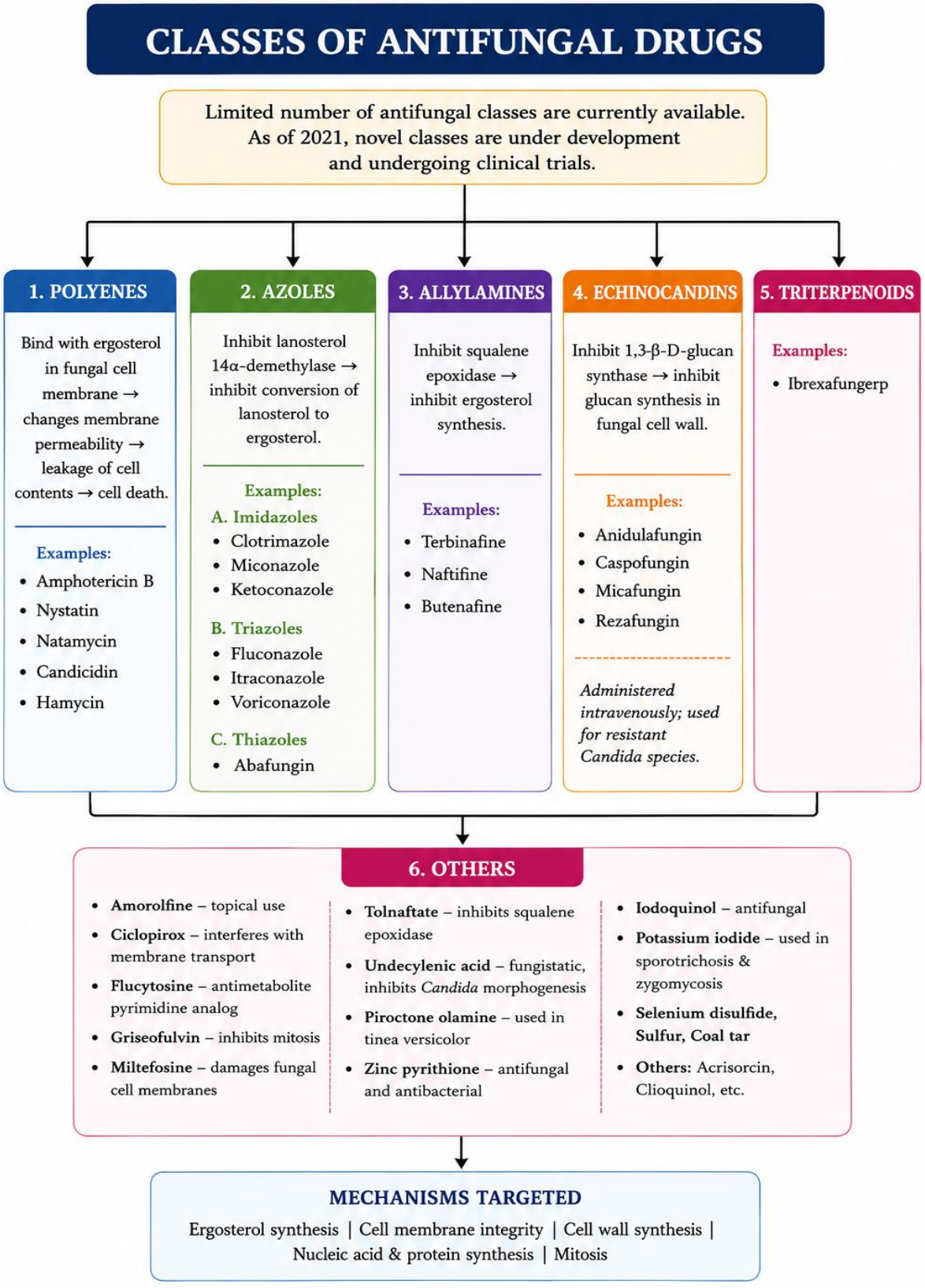
Dermatophyte resistance to terbinafine and azoles has gained attention again as a result of the appearance and worldwide expansion of T. indotineae. In 2003, the first instance of terbinafine-resistant dermatophytes was reported.The minimum inhibitory concentration (MIC) to terbinafine and other squalene epoxidase inhibitors was elevated in only one of the thirty T. rubrum strains that were isolated from onychomycosis patients who had not responded to oral terbinafine treatment for six months. Point mutations in the SQLE gene, which codes for squalene epoxidase, which is involved in ergosterol production, were later linked to terbinafine resistance19.Due to the concentration of these mutations in hotspots, important locations in the enzyme's amino acid sequence: 393Leu, 397Phe, 415Phe, and 440His. They are present in T. indotineae, T. rubrum, and T. interdigitale. Leu393Phe and Phe397Leu are the most commonly reported substitutions. In contrast to previous alterations like Phe397Ile, Phe415Ile, Phe415Val, and His440Tyr, they are linked to a marked increase in MICs to terbinafine. Outside of India, information on terbinafine resistance in dermatophytes can be found in the US, Europe, and Japan. With 4.3% (26/607) of T. interdigitale isolates and 3.6% (173/4,796) of T. rubrum isolates confirmed to be terbinafine resistant, the USA has recorded the highest rates of resistance to date.Elevated MICs to azoles are less frequently reported and are particularly concerning for isolates of T. indotineae . Drug efflux thru overexpression of ABC-type transporters and target overexpression thru an increase in CYP51 copy numbers are the two resistance mechanisms that have been identified thus far. These findings demand that the assessment of dermatophyte susceptibility to antifungal drugs be given more consideration. Testing for antifungal susceptibility in Trichophyton species. must be carried out on a regular basis, and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) has modified a standard broth microdilution method for the Trichophyton genus. Even for species that conidiate effectively, like T. mentagrophytes complex species, this method is still time-consuming, labour-intensive, and requires skilled workers due to the poor conidiation of some species, such T. rubrum.The development and evaluation of terbinafine gradient concentration stripes have produced disappointing outcomes. As an alternative, terbinafine-containing medium can be employed to assess if the strain exhibits a wild-type phenotype. Nonetheless, efforts must be made to convert in vitro MICs into pertinent clinical breakpoints for the various dermatophyte species and to create less expensive and complex methods that are simpler for non-specialist laboratories to employ in order to assess antifungal drug sensitivity.[20]



ROUTE OF ADMINISTRATION



CLASSES OF ANTIFUNGAL DRUGS



TREATMENT

Non-pharmacological methods

Wearing loose-fitting clothing made of cotton or synthetic materials that wick moisture away from the surface should be advised for patients. Socks ought to have comparable qualities. Before putting on clothing, areas that are susceptible to infection should be thoroughly dried. Additionally, patients should be counselled against sharing clothing and being barefoot.

Medical management with antifungals

Whitfield's ointment and Castellani's (Carbol fuchsin solution) paint are two examples of classical agents that are still in use but do not have a defined antibacterial effect. These remedies' effectiveness has not been thoroughly measured.The classification of frequently used antifungals is summarised in {Table}.Systemic therapy should be taken into consideration for lesions that cover a significant portion of the body's surface area and do not improve with repeated topical treatments.There isn't a conclusive study comparing topical and systemic antifungal medication to monotherapy. The pharmacokinetics of topical drugs are superior than those of systemic drugs.

Therefore, it is anticipated that the combination will have superior mycological clearance compared to systemic and topical treatment alone. For broad coverage and to avoid the establishment of resistance, combinations from various groups should be used. Compared to lower doses administered for longer periods of time, drugs administered over shorter periods of time with greater doses are less likely to cause resistance. Higher dosages of drugs with keratophilic and lipophilic properties will have a reservoir effect and improve mycological clearance.[21]

Table

Antifungal therapy classification according to structure

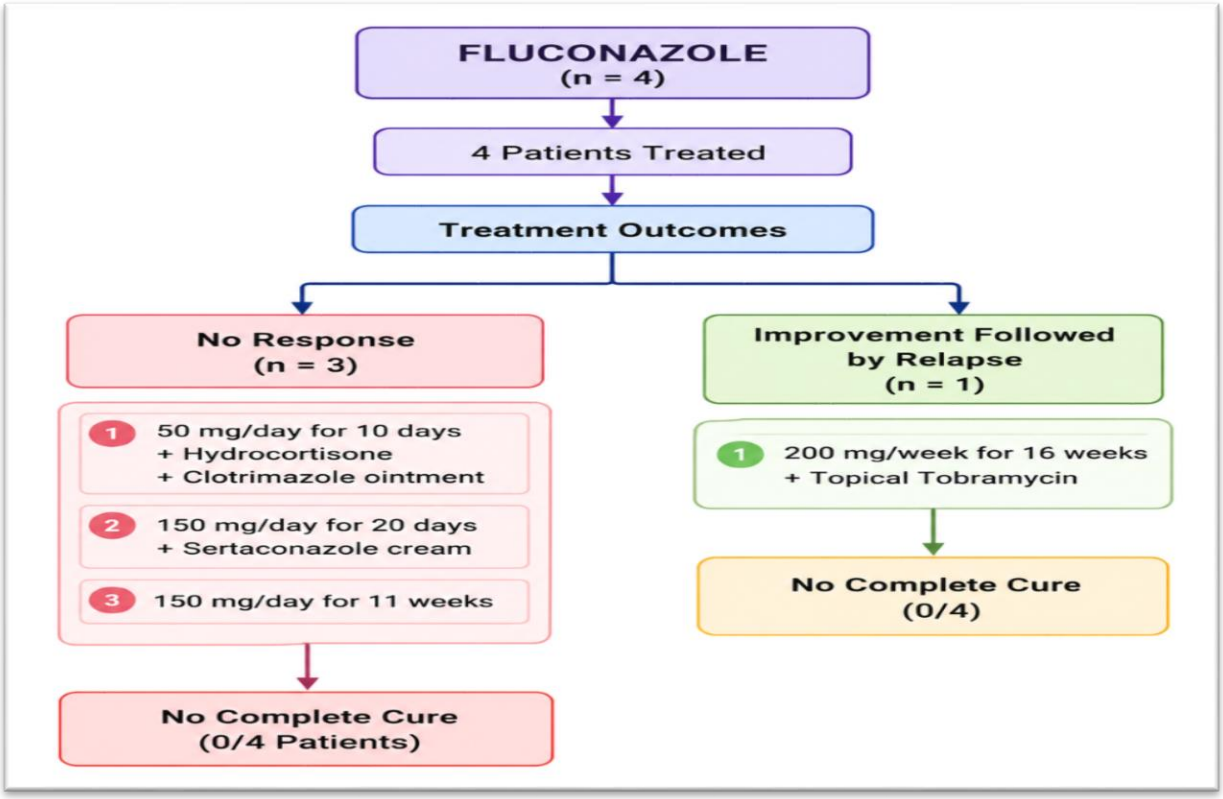
Antifungal class	Examples
Antibiotics	
Polyenes	Amphotericin B, nystatin, natamycin
Heterocyclic benzofuran	Griseofulvin
Antimetabolite	Flucytosine
Azoles	
Imidazoles	Topical - clotrimazole, econazole, miconazole, bifonazole, fenticonazole, oxiconazole, tioconazole, sertaconazole, berconazole, luliconazole, eberconazole
	Systemic - ketoconazole
Triazoles	Itraconazole, fluconazole (also topical), voriconazole, posaconazole, isavuconazole, posoconazole, ravuconazole, pramiconazole, albaconazol
Allylamines	Terbinafine, butenafine, naftifine
Echinocandins	Caspofungin, anidulafungin, micafungin, aminocandin
Sordarin derivatives	GR135402, GM237354
Cell wall antagonist	Capsofungin, micafungin
Other agents	Tolnaftate, ciclopirox, amorolfine, undecylenic acid, buclosamide, Whitfield's ointment, benzoyl peroxide, zinc pyrithione, selenium sulfide, azelaic acid etc., nikkomycins, icofungipen
Newer and potential therapies	Demcidin, macrocarpal C

Systemic antifungals' indication in dermatophytosis

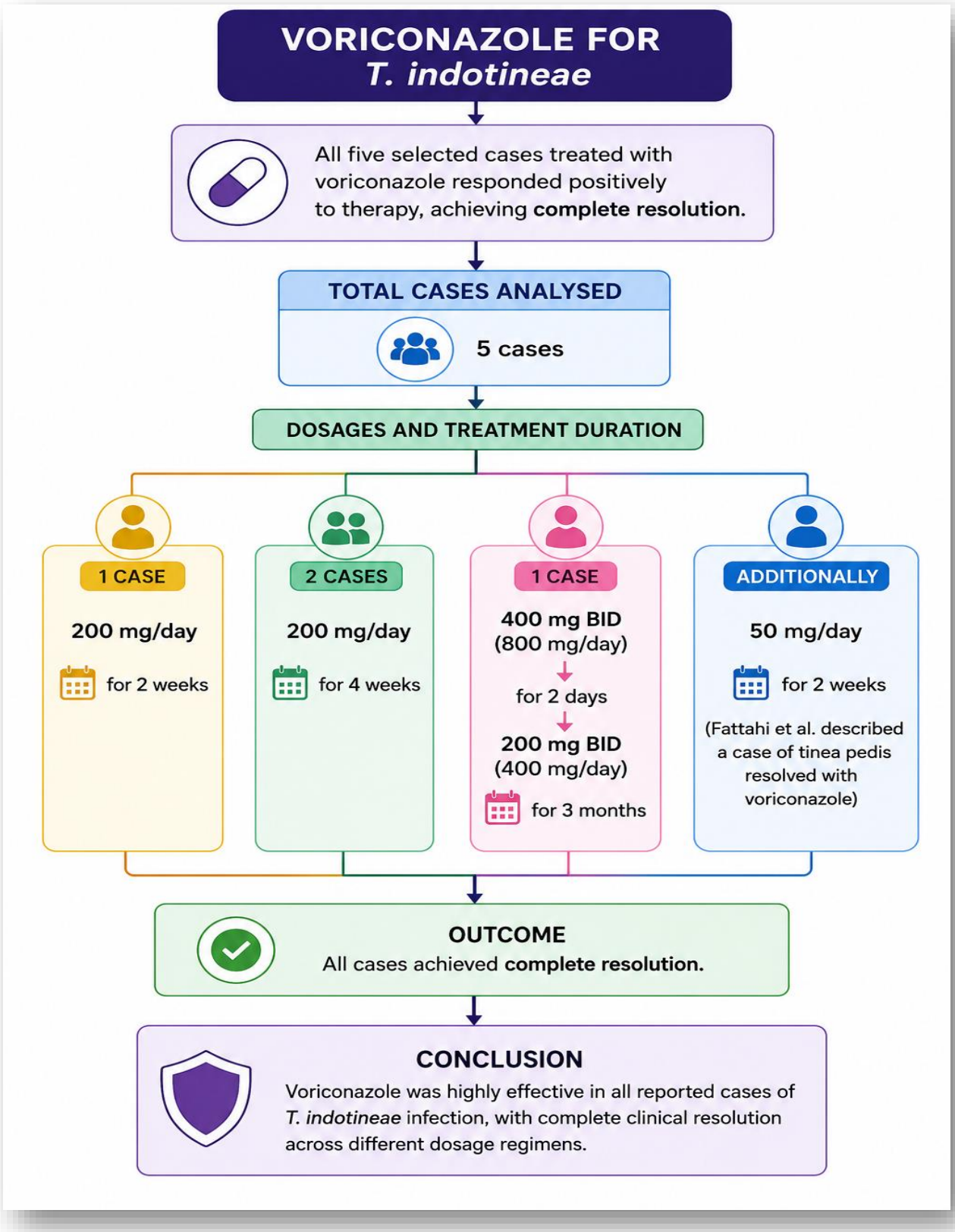
- Tinea capitis
- Tinea that affects the nails
- Tinea that affects many body parts at once, such as tinea cruris and corporis or tinea cruris and tinea pedis
- Tinea corporis, in which the lesions are especially large. However, the term "extensive disease" has no recognised definition. • Tinea pedis when the sole, heel, or dorsum of the foot are heavily affected, or when blistering occurs frequently and is bothersome.

MECHANISM OF ORAL DRUGS

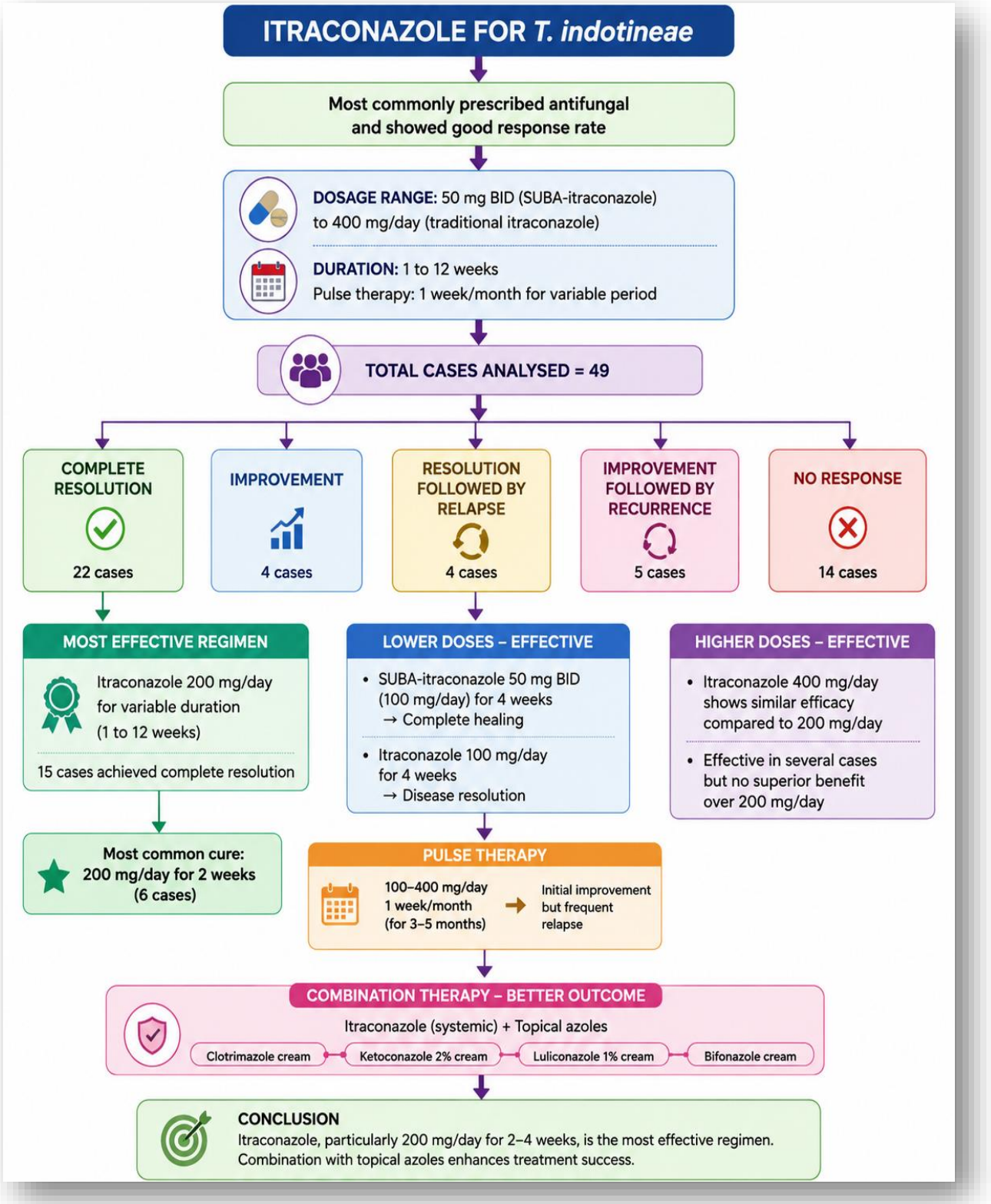
Oral Fluconazole



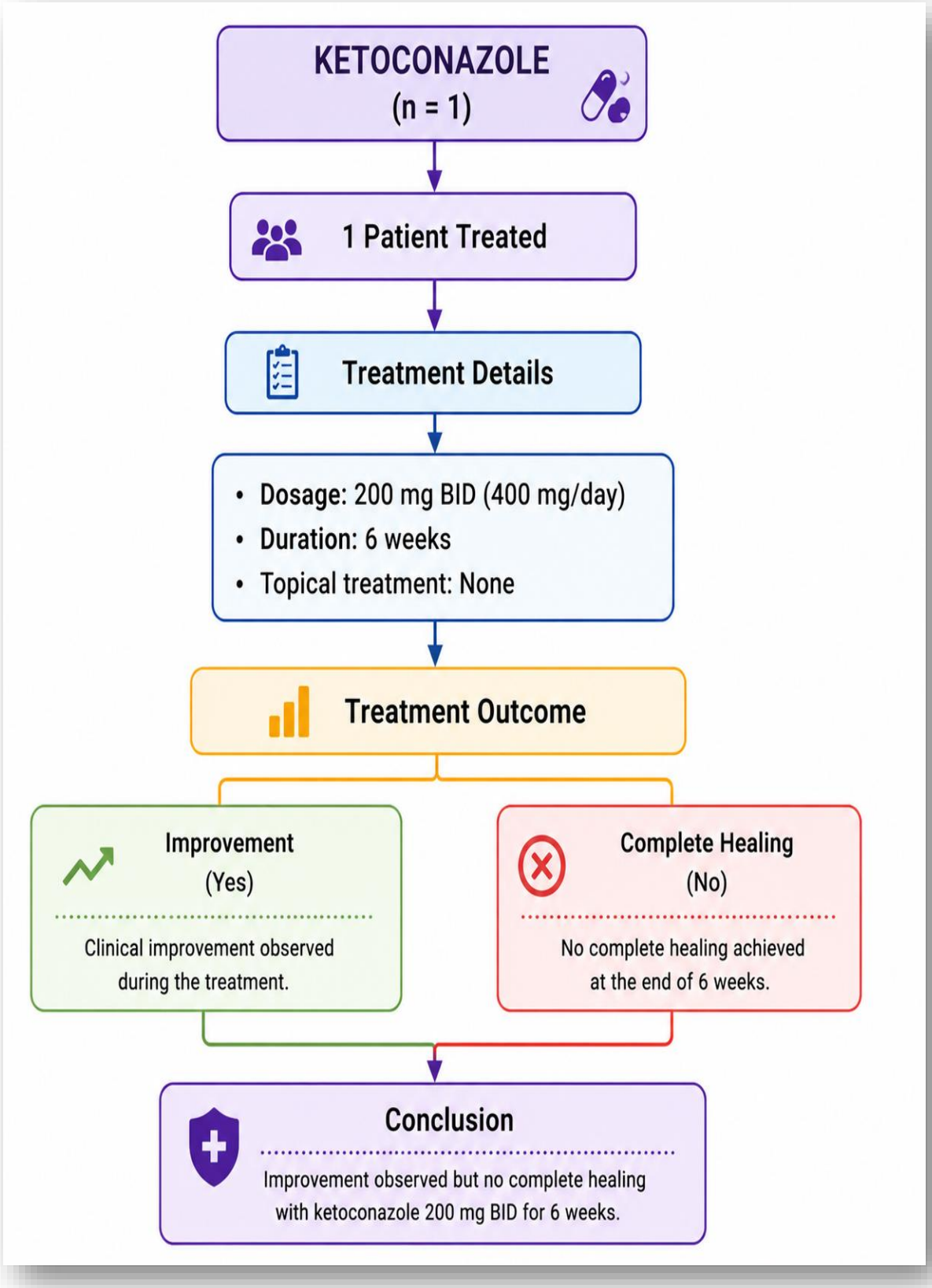
Oral Voriconazole



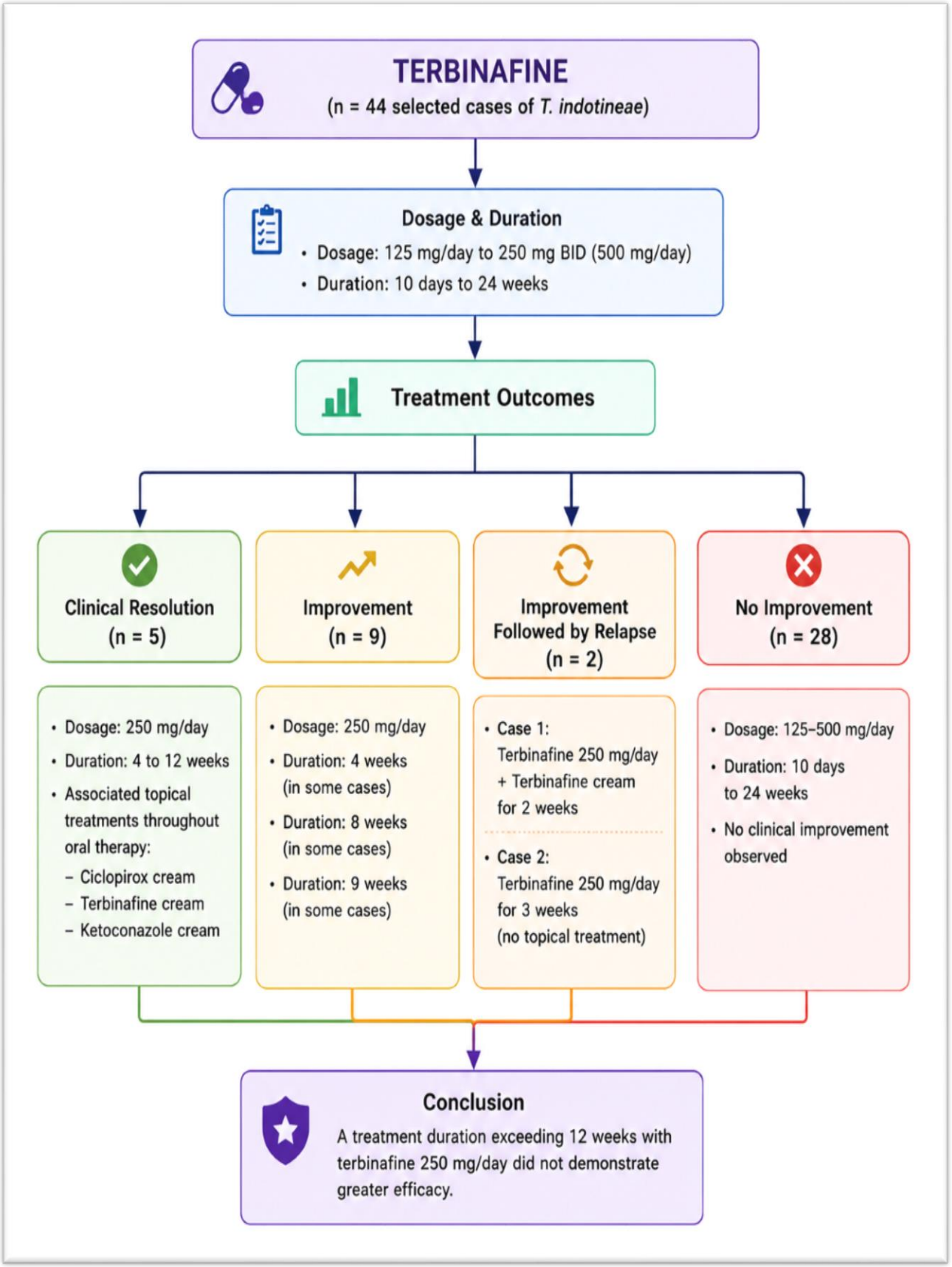
Oral Itraconazole



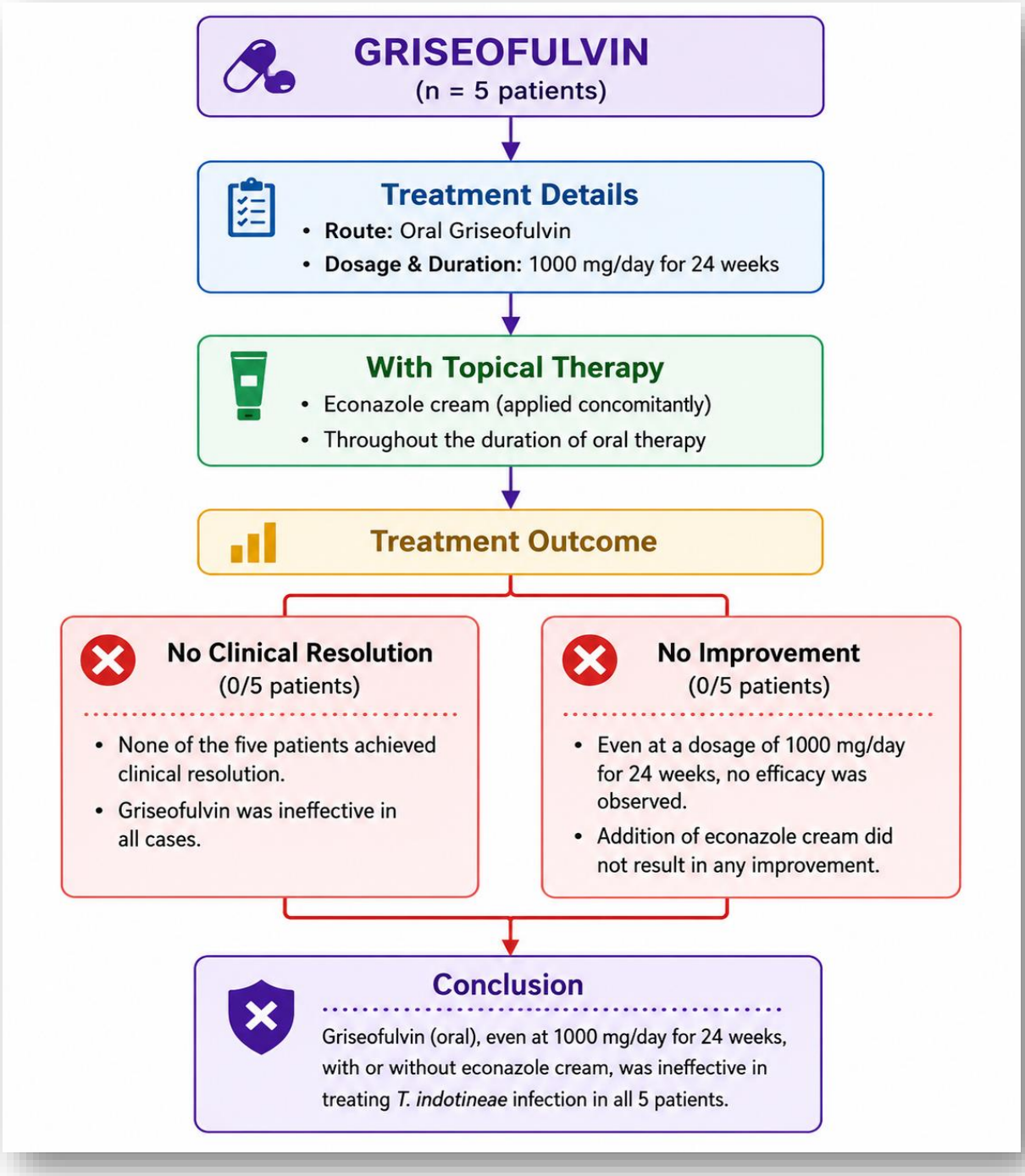
Oral Ketoconazole



Oral Terbinafine



Oral Griseofulvin [23]



COMBINATION OF SYSTEMIC ANTIFUNGALS

It is simplistic and unscientific to assume that using two or more effective medications with different mechanisms of action will result in a better outcome than using a single agent alone. This would likely lead to drug interactions, additional side effects, and an increase in the total cost of treatment.However, several combinations have been proposed and utilised without supporting data due to the decreasing effectiveness of formerly successful systemic antifungals.However, three sequential procedures are

necessary to establish and confirm synergistic antifungal medication combinations: 1) in vitro chequerboard testing or time kill curve technique to search for potentially synergistic combinations, (2) 3) evaluating the combination therapy in carefully planned clinical trials as the last stage to demonstrate or refute its usefulness, followed by in vivo animal model validation.A recent study from India looked at the effects of different antifungal combinations on clinical isolates from tinea corporis or cruris patients who showed little to no improvement after taking oral antifungals (itraconazole, terbinafine, fluconazole, or ketoconazole) in approved or higher doses for four to six weeks.One wild type strain and four isolates with elevated terbinafine MICs and SQLE gene mutations, were examined further, and itraconazole combinations with luliconazole, terbinafine, or ketoconazole were found to have an in vitro synergistic impact. Only a few combinations exhibiting in vitro synergy have demonstrated more performance than monotherapy in clinical studies on invasive mycoses, and it is crucial to keep in mind that in vitro synergy may not translate into a comparable in vivo benefit. In vitro MIC data on larger sets of unique isolates may also be necessary due to strain-to-strain variability. However, these data can be used to create clinical studies that are practical, suitable, and effective. Surprisingly, no large-scale study has yet shown the effectiveness or superiority of the combination treatment (oral with topical antifungal) compared with systemic antifungal used alone, despite the fact that topical antifungals are frequently co-prescribed with systemic antifungals in the treatment of tinea corporis or cruris. In contrast, topical and systemic antifungal combinations have proven to be more effective than oral antifungals alone for onychomycosis.proving that a systemic and topical antifungal combination is superior to an effective systemic antifungal alone, if any, Large numbers would be needed in the treatment of glabrous skin tinea because any difference, if any, is probably going to be minimal. The impact of systemic antifungal combinations in tinea corporis or cruris was investigated in two recent trials. When terbinafine 250 mg OD and itraconazole 200 mg OD were combined, Sharma et al. found that more patients in the combination group experienced "grade 4 improvement" after three weeks of treatment (90% in the combination group versus 50% in the itraconazole group and 35% in the terbinafine group). Although methodology explains the two terms differently, the results on endpoints are reported inconsistently, with "grade 4 improvement" and "cure" used interchangeably. It's interesting to note that the "cure rates or grade 4 improvement" reported for monotherapy are significantly greater than the cure rates reported by other authors in recent studies at comparable time periods. The effectiveness of a combination of terbinafine 250 mg/day and itraconazole 200 mg OD was investigated by another author group, with four more groups: itraconazole 100 mg BD, itraconazole 200 mg BD, terbinafine 250 mg OD, and terbinafine 250 mg BD.At four and eight weeks of treatment, the combination group and the itraconazole 200 mg and 400 mg groups did not significantly vary in cure rates, according to the authors. In contrast to the itraconazole 200 mg and 400 mg groups, which had cure rates of 17% and 76.6% and 19.6% and 80.4%, respectively, the combination group had cure rates of 18.9% and 79.2% at these time points.At 4 and 8 weeks, all itraconazole-containing groups showed greater efficacy than the terbinafine groups (cure rates of 23.4% and 33.3% with terbinafine 250 mg OD and BD, respectively, at 8 weeks).In contrast to the trial of Khurana et al. [84], where the itraconazole 400 mg group demonstrated considerably greater (final) cure rates than the 200 mg group, there was no discernible difference between the 200 mg and 400 mg groups. However, in this trial as well, the difference between the 200 mg and 400 mg groups did not become statistically significant until week 8 of treatment, which was Singh et al.'s time point of comparison.

Summary

According to a review of the literature, treating tinea corporis or cruris with a combination of two systemic antifungals (terbinafine and itraconazole) did not appear to offer any benefits above itraconazole alone. To get the most out of the small selection of medications against dermatophytes, clinical trials comparing various systemic–topical antifungal combinations based on the findings of in vitro chequerboard interactions are desperately needed.[24]

USE OF NON-ANTIFUNGAL DRUGS TO ENHANCE THE ACTION OF THE ANTIFUNGAL DRUGS

Few studies have looked at the impact of combining isotretinoin with antifungal drugs in order to use isotretinoin's effects on epidermal kinetics to provide an additional antifungal effect. In one instance, accutane 20 mg/day and itraconazole 200 mg/day administered for a month eradicated the infection in a patient who had previously undergone (short courses of) antifungals, according to Ardeshna et al.25. But Verma et al.[26] found that there was no additional benefit to combining isotretinoin 0.5 mg/kg with terbinafine 250 mg BD. After 4 weeks of treatment, both groups had comparable cure rates (43.18% in the combination group and 42.55% in the terbinafine monotherapy group) in 100 patients with recurrent tinea corporis or cruris. Although the statistical significance of this difference was not stated, Khattab et al.27 (2022, Egypt) reported a cure rate of 70% with itraconazole (200 mg/day) and isotretinoin (20 mg/day) combination and a cure rate of 53% with itraconazole alone.

. However, T. indotineae has not yet been extensively documented from Egypt, and this study did not do culture or species identification, thus its conclusions regarding T. indotineae infections are questionable.

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Drugs that mainly enter the stratum corneum thru sebum secretion, such as terbinafine and itraconazole, may not work well when combined with an agent that reduces sebum secretion, such as isotretinoin.28.Moreover, a quicker depletion of the drug reservoir at the infection site could result from accelerated keratinocyte turnover.29.Additionally, concurrent use of isotretinoin may result in a considerable reduction of itraconazole serum levels.Thirty Other medications that have shown antifungal efficacy in vitro, such as FK 506, cyclosporine, and statins, have not been shown to be useful in clinical trials.

Summary
Combining isotretinoin with antifungal medications is not supported by sufficient data. Moreover, it is impossible to overlook the combination's significant pharmacokinetic issues.[31]

Conclusion
One of the most prevalent superficial fungal infections affecting the skin, hair, and nails globally is dermatophytosis, also known as ringworm. It is mostly brought on by Trichophyton, Microsporum, and Epidermophyton species and is impacted by things like inadequate hygiene, a humid environment, intimate contact with infected people or animals, and immunocompromised circumstances. Effective management requires an early diagnosis made by laboratory testing and clinical evaluation. Despite the availability of numerous topical and systemic antifungal medications, treatment has become more difficult due to the rise of antifungal-resistant dermatophytes.
Reducing recurrence and transmission requires patient commitment to treatment, appropriate antifungal medicine selection, and preventive measures such maintaining personal hygiene and refraining from sharing personal things. To enhance treatment results and manage the increasing prevalence of dermatophytosis, ongoing research into novel antifungal drugs and resistance mechanisms is required.

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