Nail Fungi - onychomycosis

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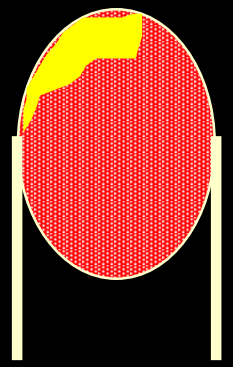
Causes of onychomycosis

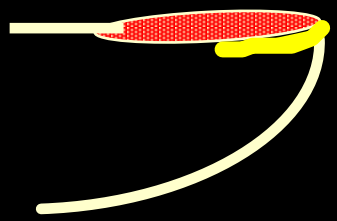
- Dermatophytes – *T.rubrum, T,interdigitale, T.violaceum*
- *Candida albicans*
- Others – *Neoscytalidium, Fusarium, Aspergillus* spp. *Acremonium, Scopulariopsis,*
- Disputed - Malassezia

Classification of onychomycosis -1

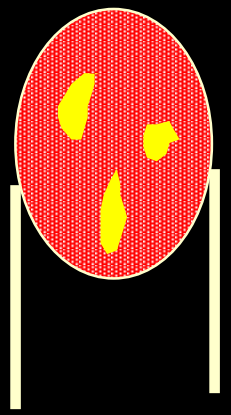
Distal & lateral subungual



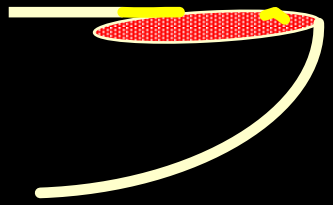
DLSO



Superficial white

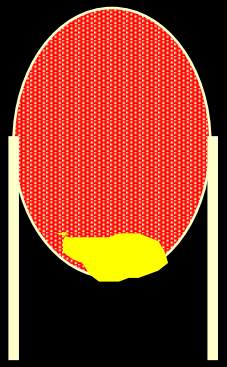


SWO

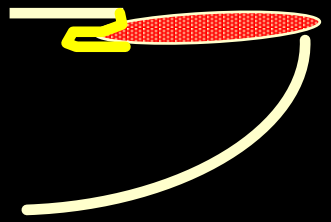


Classification of onychomycosis - 2

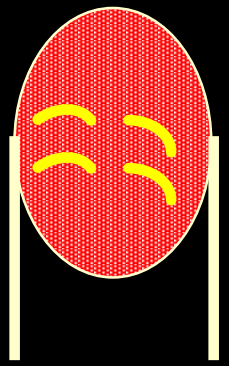
Proximal subungual



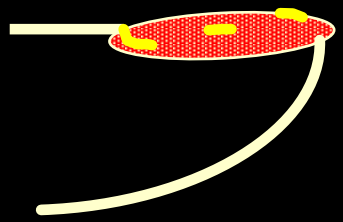
PSO



Endonyx

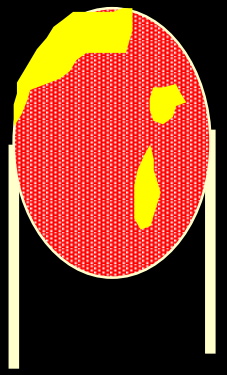


ENO

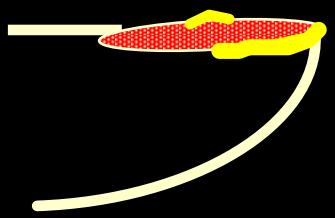


Classification of onychomycosis - 3

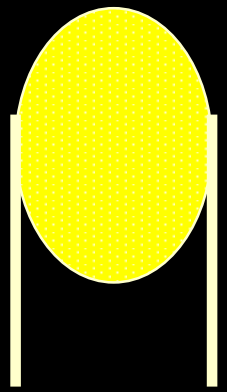
Mixed



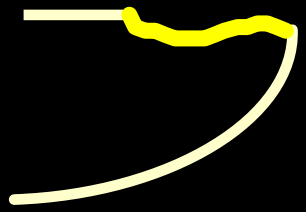
MO



Totally dystrophic



TDO



These are all
superficial white onychomycosis

Onychomycosis revised classification Hay & Baran 2011

- **Distal and lateral subungual onychomycosis – DLSO**

- **Superficial onychomycosis (white or black) – SO**
  a) ***patchy*** **or** ***transverse***
  b) ***originating from beneath the proximal nail fold***
  - patchy
  - transverse (striate)

  c) ***with deep penetration*****. The fungi invade from superficial to deep aspects of the nail plate**

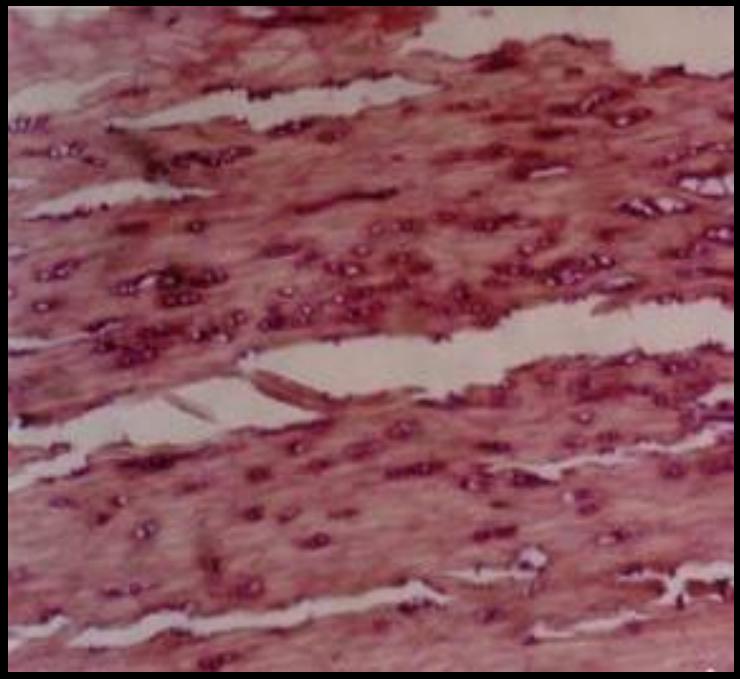
- **Endonyx onychomycosis – EO**

- **Proximal subungual onychomycosis - PSO**
  a) ***Patchy***
  b) ***Transverse (striate, longitudinal)***

- **Mixed onychomycosis – MO : eg DLSO plus SO, SO plus DLSO**

- **Totally dystrophic onychomycosis- TDO .**

Plus option to add organism X and paronychium and colour eg black DLSO due to *T.Rubrum*

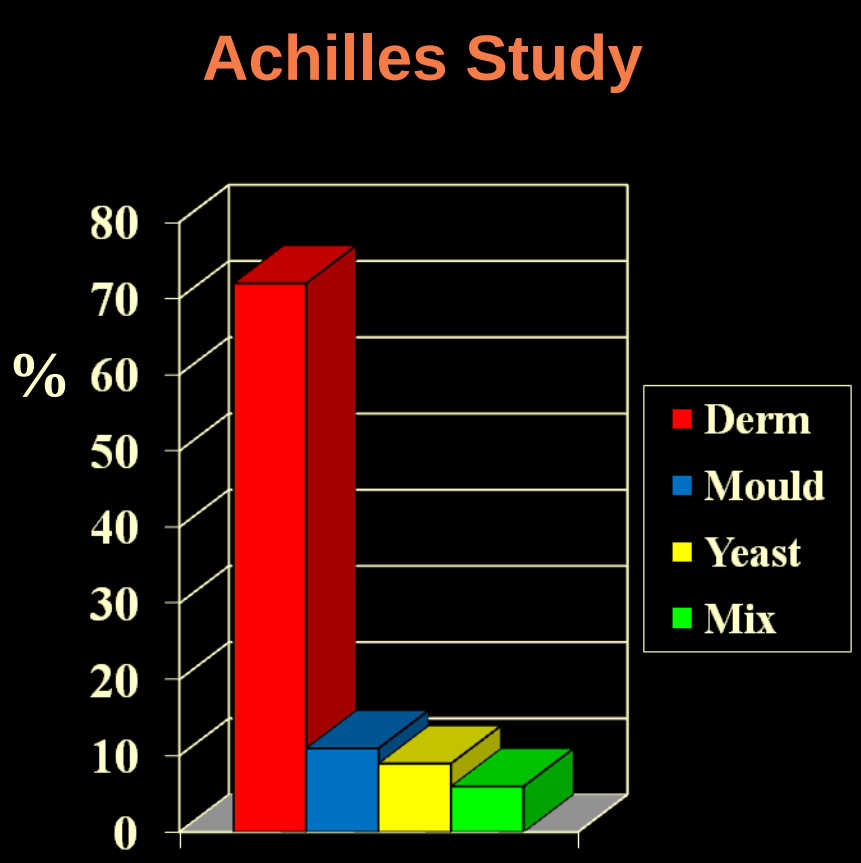


SWO with deep invasion

Onychomycosis in Europe
(Burzykowski et al, Mycoses 46. 496, 2004)

- Range 3%-22% depending on methodology
- Questionnaire v Clin v Lab
- Achilles survey(GP 76475) /study (Derm 19588) :

  (1997 and 1998)
  - Over 20 European countries
  - Over 96,000 subjects
  - Onychomycosis in 23.9%
- Variation in prevalence eg Spain 7% Russia over 60%
- Age an increasing risk



Is it possible to diagnose onychomycosis accurately clinically ?

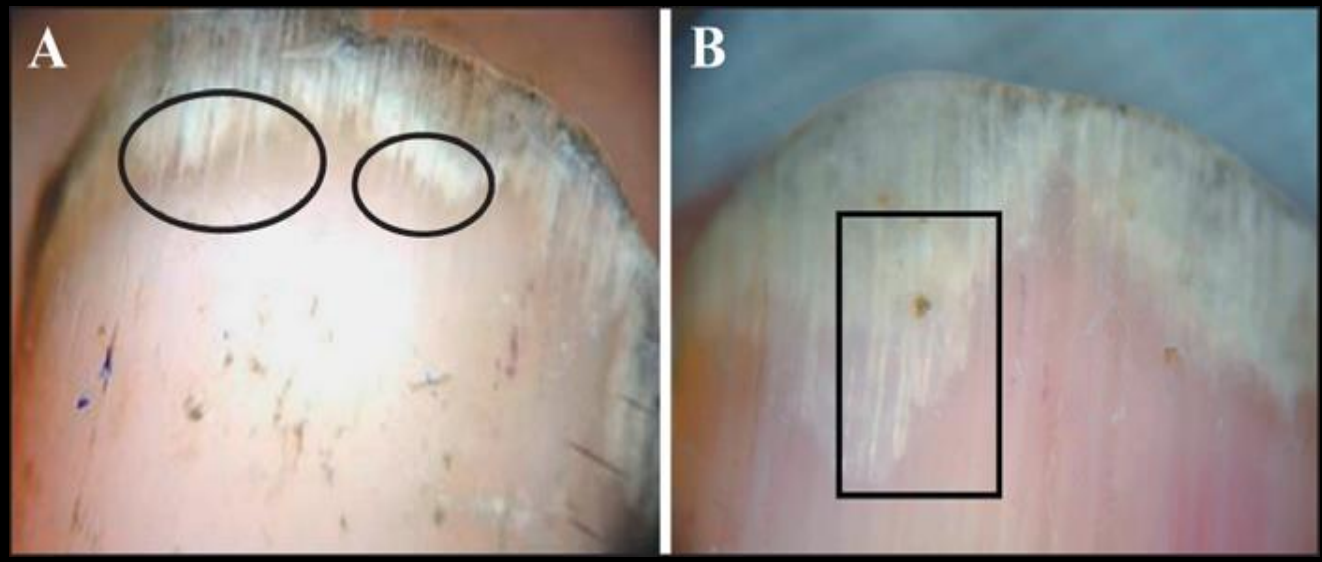
- 209 patients with abnormal nails. Final 169
- Case = positive microscopy and culture
- 54 Cases (derm >90%)
- Questionnaire
- Multiple log regression

Significant findings with onychomycosis

1) Scaling on 1 or both soles
2) White crumbly patches on the nail surface
3) Abnormal colour of the nail plate
4) History of tinea pedis in the last year

Dermoscopy – onychomycosis

Useful , but requires training
Onychomycosis – shows solid structures within onycholysis. Jagged proximal edge within spikes



Confirming the diagnosis in the laboratory

- **Direct microscopy** for fungal cells eg (potassium hydroxide 10% , Negative stains, Fluorescent whiteners, PAS). **Rapid**
- **Culture** (Sabouraud's agar). **Takes 5-14 days to make diagnosis**
- **Histopathology** – often specific because of fungal morphology
- **Molecular genetic** – little u… PCR – use of different … of analysis
- MALDI-ToF

Advantage:
speed,accuracy
Disadvantage:
availability,
use of directs

Matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) - Mass spectrometry

Rapid
In use in microbiology laboratories
Accurate even compared with PCR based approaches

Nenoff et al Med Mycol. 2012 – analysis of dermatophytes v ITS rRNA. Agreed in 283/285. Not *T violaceum*

Table 1

Identification of the 381 clinical dermatophyte and *Neoscytalidium* isolates by MALDI-with the Andromas system

Group and species	No. (%) of isolates		
	Total	Accurately identified	No spectral acquisition[a]
Dermatophytes			
E. floccosum	5	5 (100)	0
T. rubrum	158	154 (97.5)	4 (2.5)
T. mentagrophytes var. *interdigitale*	82	80 (97.6)	0
T. soudanense	50	36 (72)	14 (28)
T. tonsurans	26	23 (88.5)	3 (11.5)
T. erinacei	1	1	0
M. langeronii	26	21 (80.8)	5 (19.2)
M. canis	12	11 (91.7)	1 (8.3)

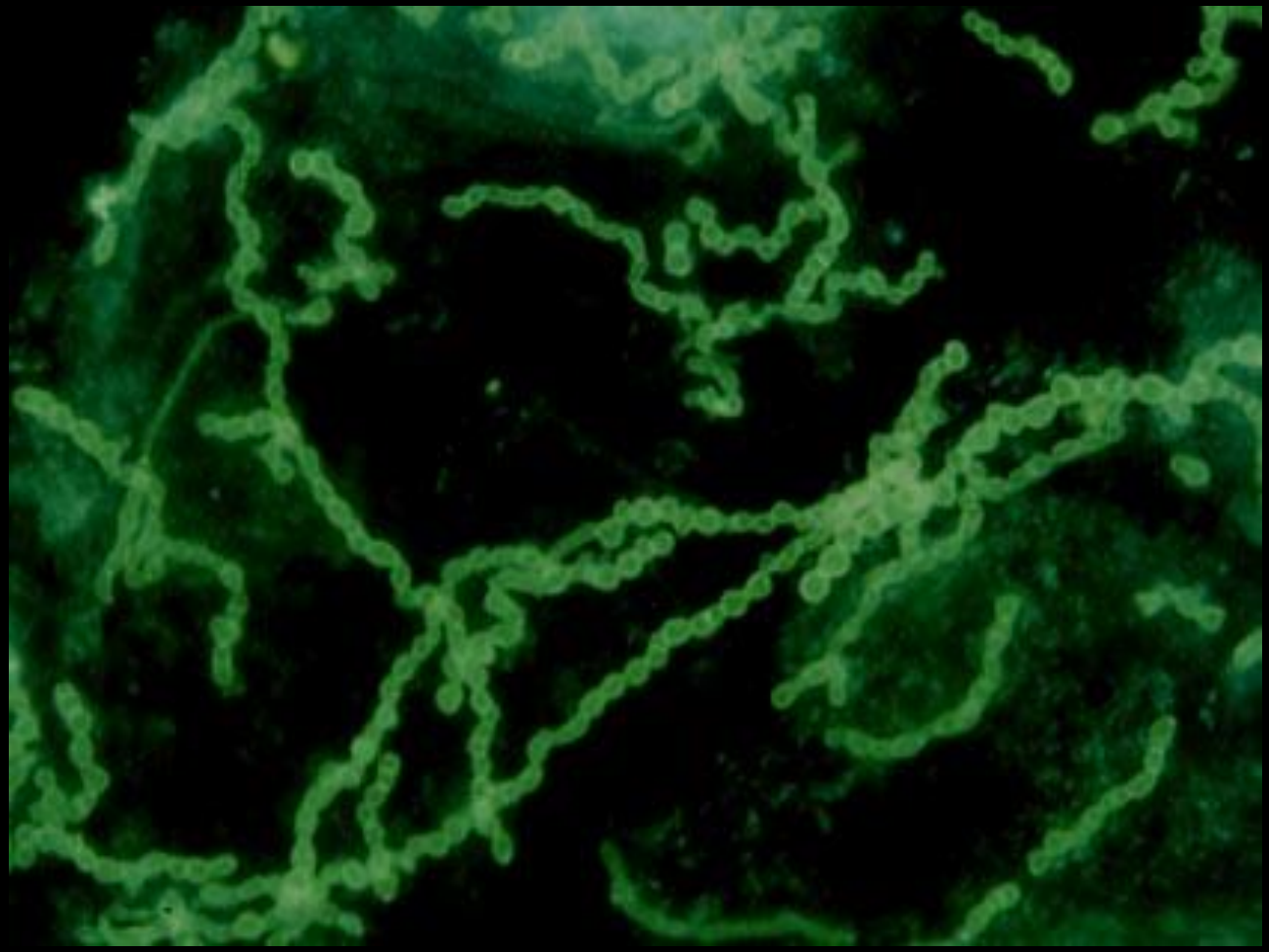
Alshawa et al 2012

Dermatophyte arthrospores (KOH)

Scopulariopsis brevicaulis

Neoscytalidium spp

Dermatophyte arthrospores (Calcofluor)



10% higher yield versus directs alone

Modified Periodic acid Schiff stain

Quality of Life, Onychomycosis, - why do patients seek treatment

- Lubert (1999) USA . Pain and discomfort
- Drake et al (1999/1998) Internat/USA - difficulty in trimming (76%), embarassment (74%), pain (48%), shoe discomfort (38%).
- Whittam et al (1997) UK. Discomfort of toes, problems with all footwear
- Triggers to treatment - symptoms, appearance, “infection,” but expectation of recovery, side effects.

Topical therapies & onychomycosis

Topicals

- Azoles - Cream or solution 1% = 2-12%
- Tioconazole 28% = 12-45%
- Efinaconazole 10% = 15-18%
- Tavoborole 5 % = 7-9%

Urea mix

- Bifonazole + urea = 14%-90%

TUDDS

- Amorolfine = 25 - 65%
- Ciclopiroxolamine = 6-9%

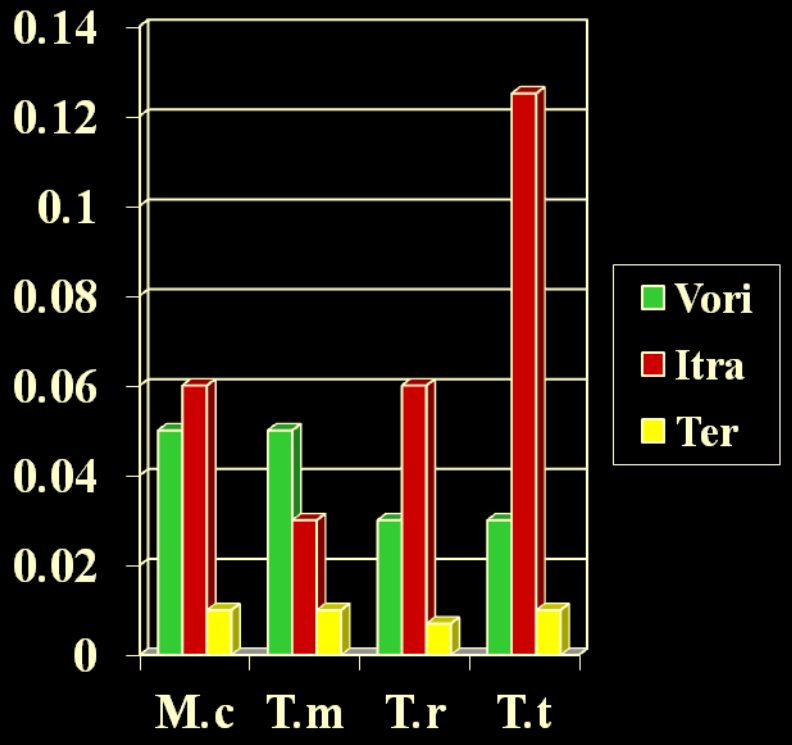
Systemic therapies & onychomycosis

- Griseofulvin 25% - 65%
- Ketoconazole 28% - 75 %
- Terbinafine 45 % - 85%
- Itraconazole 35% - 84%
- Fluconazole 37% - 62%
- Posaconazole 54% - 70%

Voriconazole – dermatophytes & superficial mould pathogens

- Susceptible in vitro
- Active against *M.canis* in animal model (Saunte 2007)
- Cure or stabilisation of deep *Scytalidium* infections – MIC 0.03 to 0.5 mg/L (lower than terbinafine, itraconazole)
- Others – *A.fumigatus* >0,05, *Fusarium* c 4

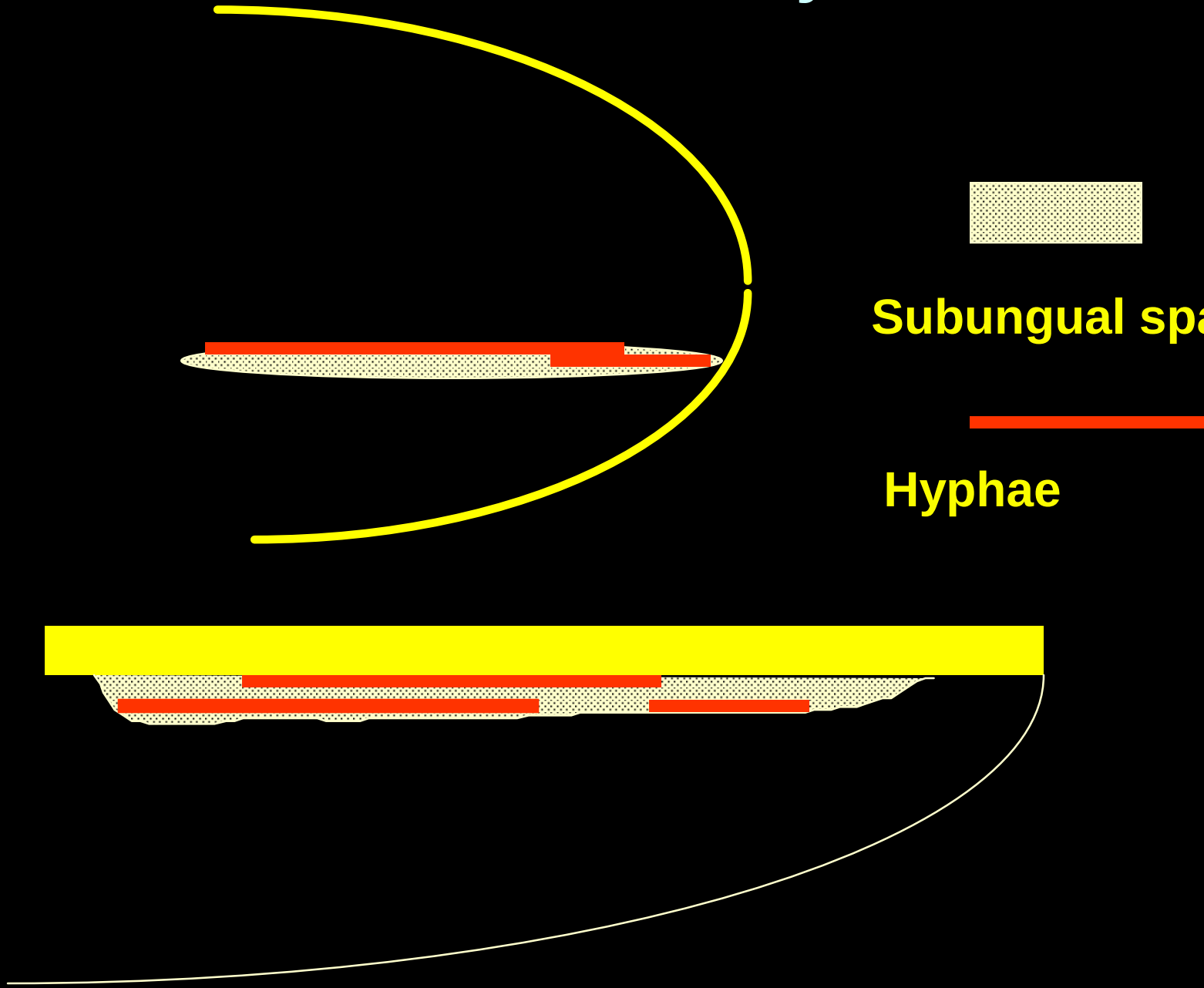
MIC 50s Dermatophytes



Reasons for Treatment Failure

- **Compliance**
- **Penetration**
- **Bioavailability**
- **Drug interactions**
- **Resistance**

Bioavailability



Trichophyton rubrum

Resistance in superficial mycoses – the practicalities

- Rare
- **Mainly with Candida spp**

a) secondary to low dosage in face on immunosuppression eg untreated HIV/AIDS

b) primary resistance eg *C.glabrata* (fluconazole)

- **Dermatophytes** – V rare e.g

a) terbinafine >4mg/L *T.rubrum* (Mukherjee 2007)

b) itraconazole > 32mg/L *T.rubrum* (Mendez-Tovar 2007)

Management of difficult cases

- Should I test for drug resistance ?
- What about the new drugs ?
- Can I prevent relapse ?
- When do i use surgery ?
- What are useful combinations of drugs ?

Laser Treatment

- **Laser choice eg Nd:YAG 1064-nm laser, Fotona XP**
- **Duration and spacing of treatments**
- **Long terms follow up**
- **Place of adjunctive antifungal therapy**

Since 2010, the FDA has approved seven laser devices to be used as a *cosmetic treatment* for the ‘temporary increase in clear nail growth in patients with onychomycosis.

Clinical/mycological study of in vitro and in vivo responses to laser for onychomycosis

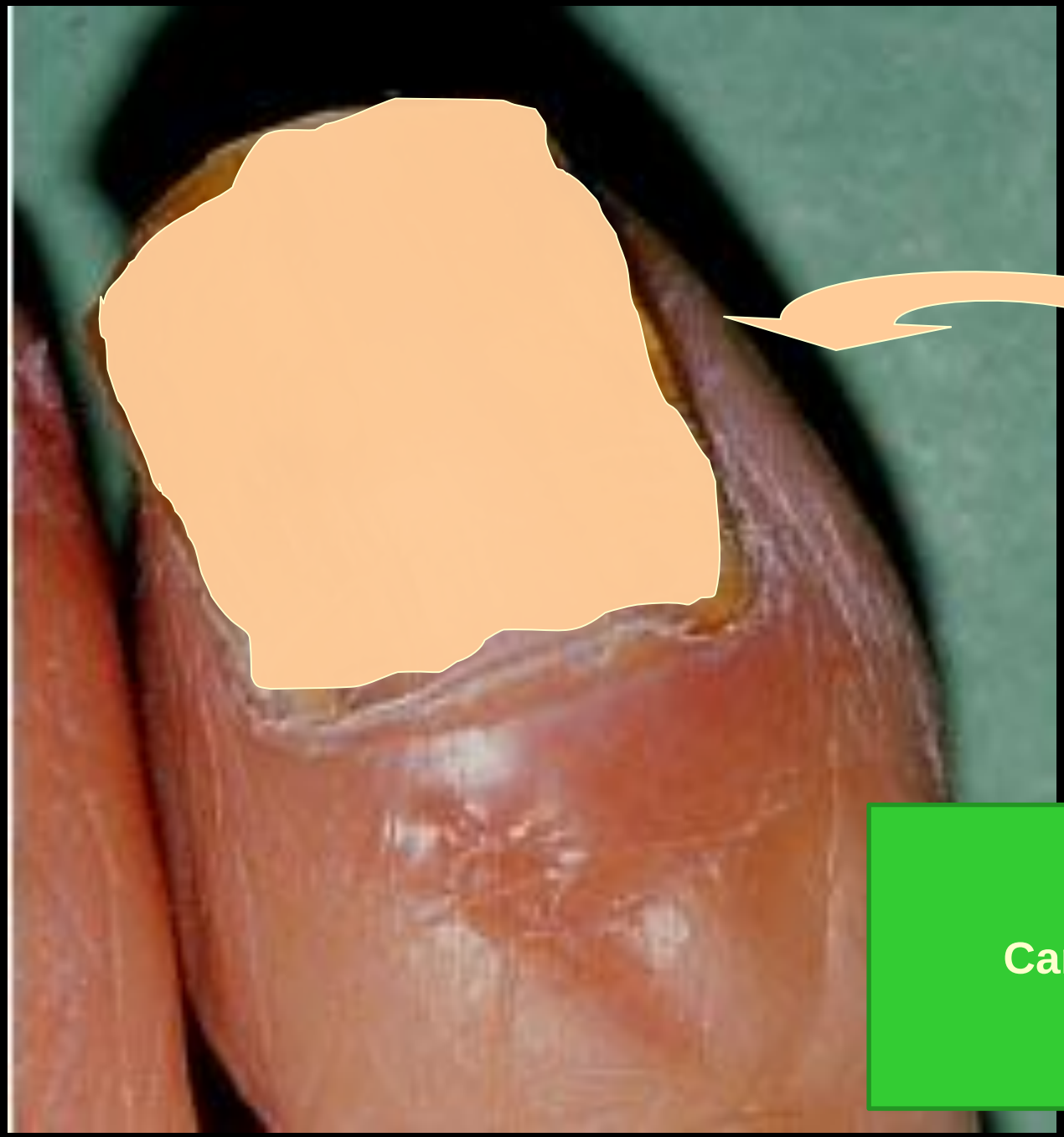
- **Carney et al 2013 JAAD**
- **Used Nd:YAG 1064**
- **In vitro killing after 15 min**
- **But 5 sessions of treatment resulted in no change in microscopy, culture or severity after 6 months**

Severity index after laser Rx

Nail	Baseline OSI score	Wk-5 OSI score	Wk-24 OSI score
1	2 (Mild)	1 (Mild)	1 (Mild)
2	1 (Mild)	2 (Mild)	1 (Mild)
3	1 (Mild)	9 (Mild)	4 (Mild)
4	4 (Mild)	4 (Mild)	9 (Moderate)
5	2 (Mild)	2 (Mild)	2 (Mild)
6	26 (Severe)	26 (Severe)	30 (Severe)
7	12 (Moderate)	12 (Moderate)	18 (Severe)
8	12 (Moderate)	12 (Moderate)	12 (Moderate)
9	18 (Severe)	18 (Severe)	25 (Severe)
10	16 (Severe)	16 (Severe)	16 (Severe)
11	12 (Moderate)	12 (Moderate)	12 (Moderate)
12	16 (Severe)	16 (Severe)	16 (Severe)
13	35 (Severe)	26 (Severe)	26 (Severe)
14	35 (Severe)	35 (Severe)	26 (Severe)

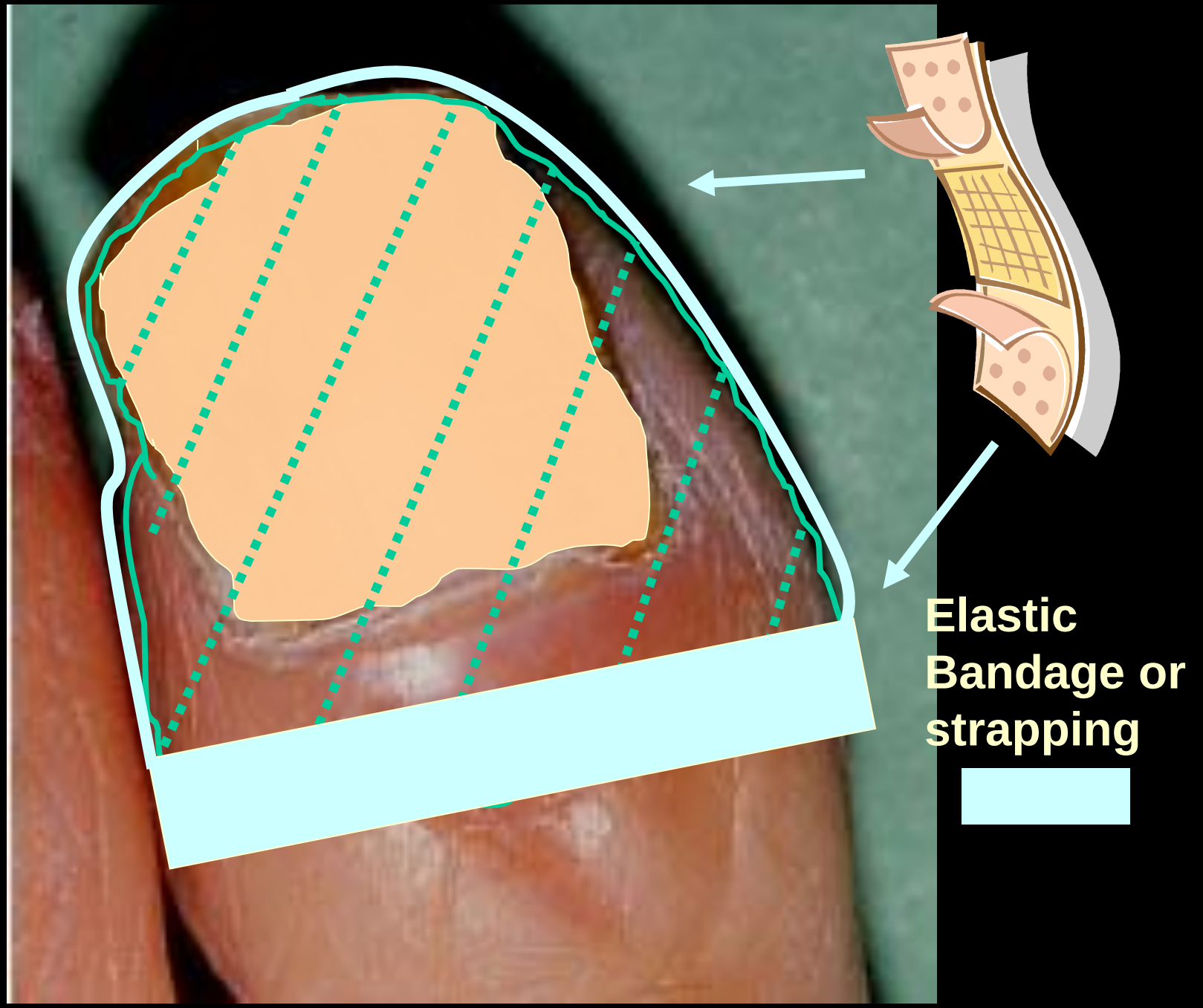
Other treatments

1. **Photodynamic therapy** (5-aminolevulinic acid (ALA), methyl aminolevulinate, and methylene blue (MB). Cure rates 43-100% at 12 months . Better with regular treatment for 6/12
2. **Iontophoresis** – Terbinafine gel – 40% cure
3. **Drilling with topical terbinafine** - clinical improvement but without cure
4. **Surgical or chemical ablation**



40%
Urea

Canespro

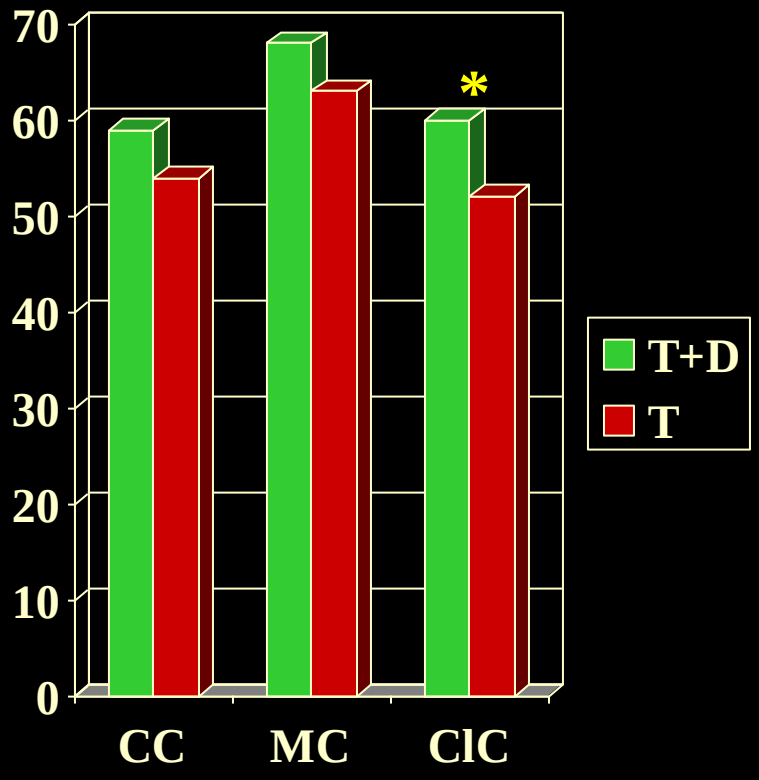

Elastic
Bandage or
strapping

Use nail clippers or surgical scissors to remove affected nail

Remove debris & lightly curette nail bed.

Oral therapy plus debridement of the nail plate (Jennings MB 2006)

- 255 on terbinafine 12 w, 249 on terbinafine plus debridement
- No effect of duration of disease or extent on cure rate
- No description of debridement techniques
- 48w follow up

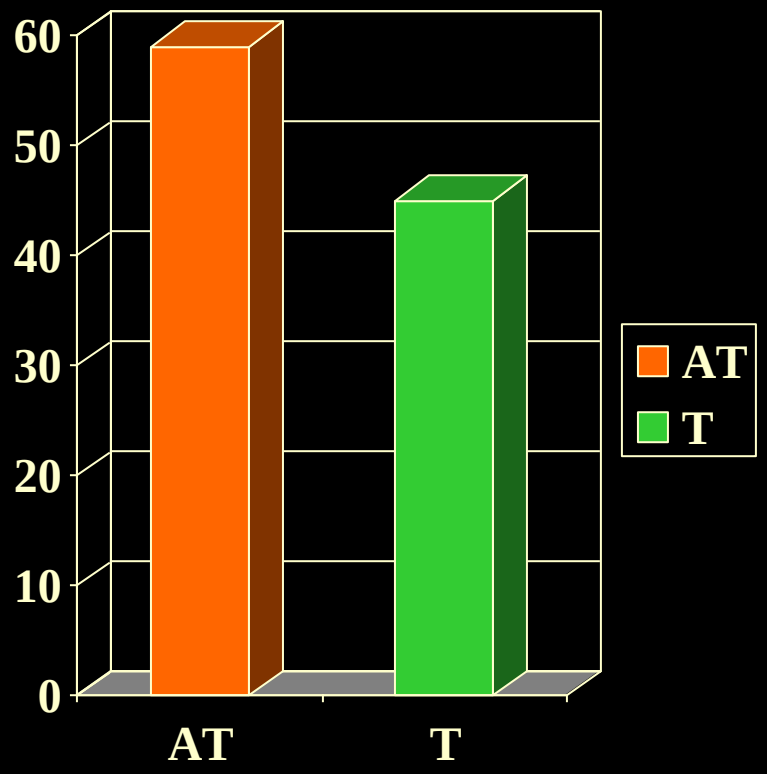


Can one use combinations of drugs e.g. oral/oral or oral/topical ?

Amorolfine and terbinafine for onychomycosis

(Baran, Sigurgeirrsson et al BJD 2007 157 149)

- Multicentre open label – matrix involved
- 249 patients with advanced toenail onychomycosis
- Amorolfine/terbinafine 12 w(AT), terbinafine 12 w (T)
- Final assessment – 18 months. Clinical cure plus negative mycology



Treatment of recalcitrant tinea corporis with combination terbinafine (250 mg daily) & itraconazole (100mg daily)

- 6 patients referred with treatment unresponsive tinea corporis
- Failed on >6 months terbinafine
- 3 were on systemic steroids, 1 ichthyosis
- MICs for both terbinafine & itraconazole in normal range

Organism	End (4-6m)	FU (6 m)
T.rubrum (5)	5	3 2 relapsed
M.canis (1)	1	1

Case 1

A 53 year old male with involvement of 6 toe nails.
This has been present for 5 years at least.
He has no relevant medical history apart from the fact that he and his son have hay fever

Trichophyton rubrum **is isolated**

Would you carry out any further examinations ?

How would you treat him ?

Case 2

A 43 year old female presents with one infected toe nail. This has been present for 2 years.
She has Type 1 diabetes mellitus
***Trichophyton rubrum* is isolated**

Would you carry out any further examinations ?

How would you treat her ?

Case 3

A 57 year old female music teachers presents with one infected toe nail. This has been present for 10 years.
She has no underlying diseases

***Paecilomyces lilacinus* is isolated**

How do you interpret this result?

How would you treat her ?

Case 4

A 54 year old male presents with two infected toe nails. This has been present for 5 years. He has myelodysplastic syndrome but requires no treatment

***Fusarium solani* is isolated**

How do you interpret this result?

How would you treat him ?

Case 5

A 54 year old female who works as a caterer in a primary school presents with three dystrophic finger nails. She is well apart from well controlled hypertension This has been present for 1 year
***Candida parapsilosis* is isolated**

Do you carry out any other investigations ?

How would you treat her ?

Case 6

A 46 year old female presents with four dystrophic finger nails. Her toe nails are normal. But She has Raynaud's phenomenon She has SLE and 4 years previously went into chronic renal failure, subsequently requiring a renal transplant. She is maintained on tacrolimus and prednisolone.

Candida albicans **is isolated and hyphae seen in nail**

How would you treat her ?