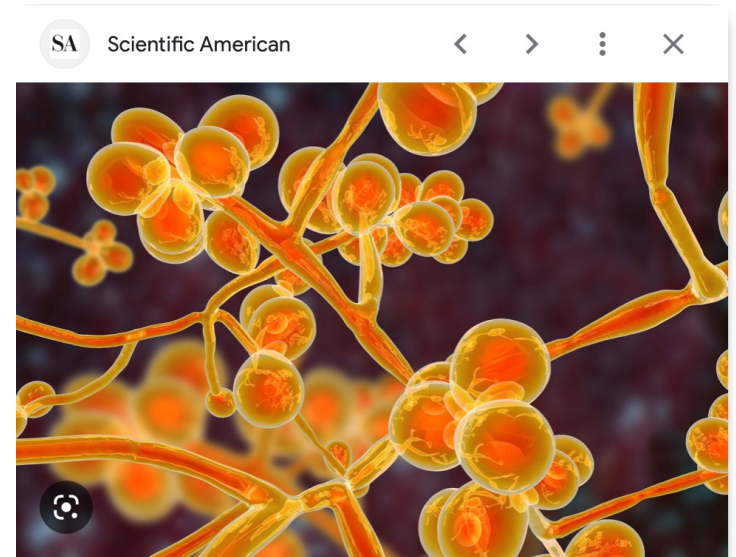


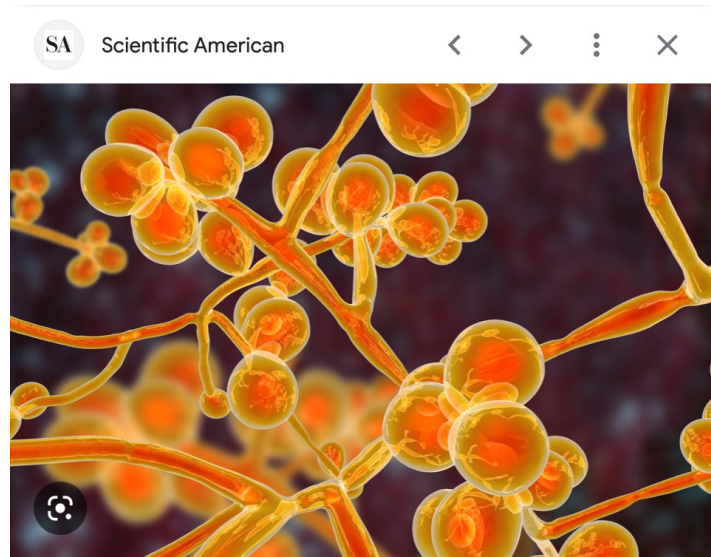
**Maui Derm 2023 NP/PA
Peds Infectious Disease
June 23, 2023**

Sheila Fallon Friedlander MD
Professor Emeritus, UCSD
Staff, Scripps Clinic San Diego



No conflicts

Fascinating, Frightening, Fungal Facts





The New York Times Magazine



6.11.2023

The Man Who Turned the World on to the Genius of Fungi

A vast fungal web braids together life on Earth.
Merlin Sheldrake wants to help us see it.

A Friendly Fungal Microbiome



6.11.23



THE LAST OF US PART I

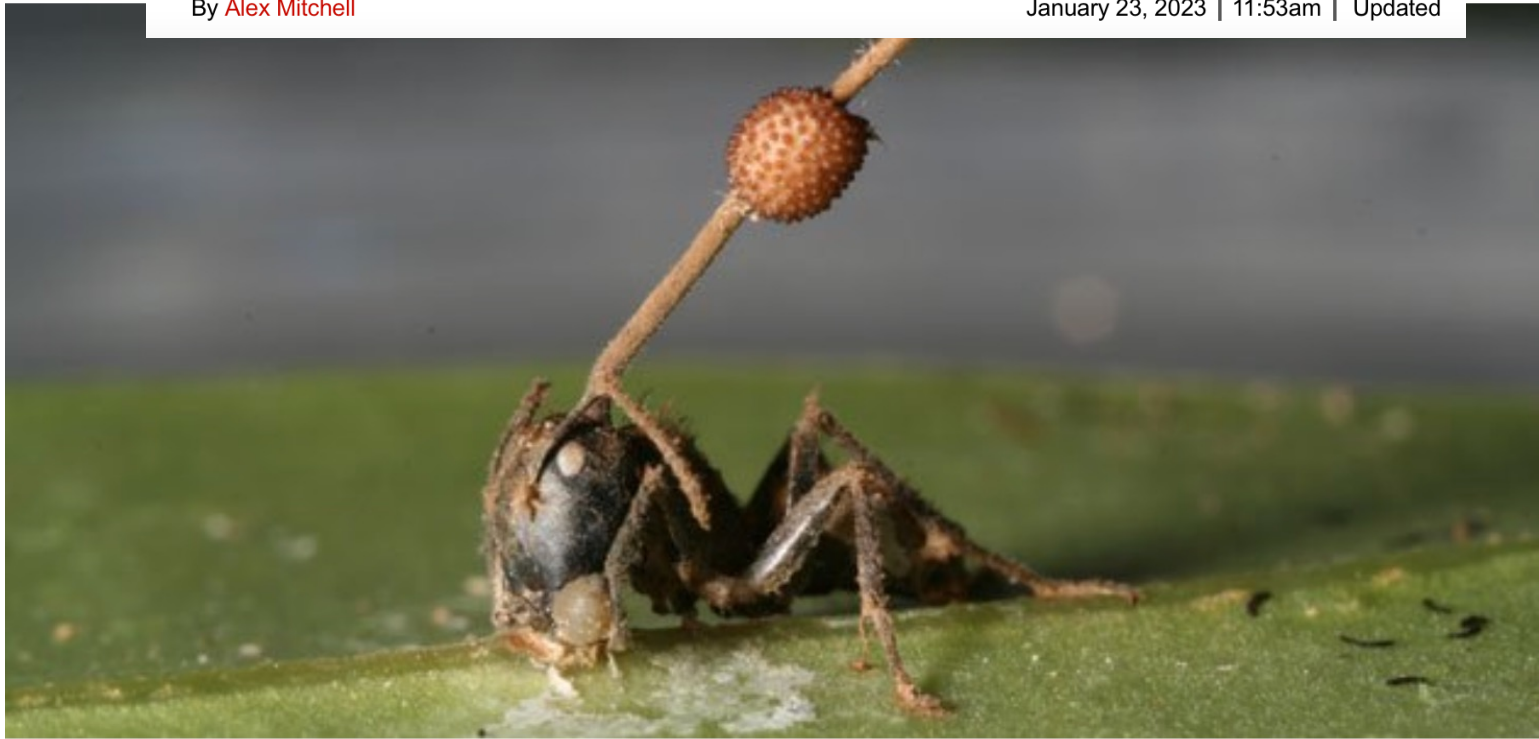
WEIRD BUT TRUE



'Last of Us' zombie fungus is real — and just one of many

By [Alex Mitchell](#)

January 23, 2023 | 11:53am | Updated

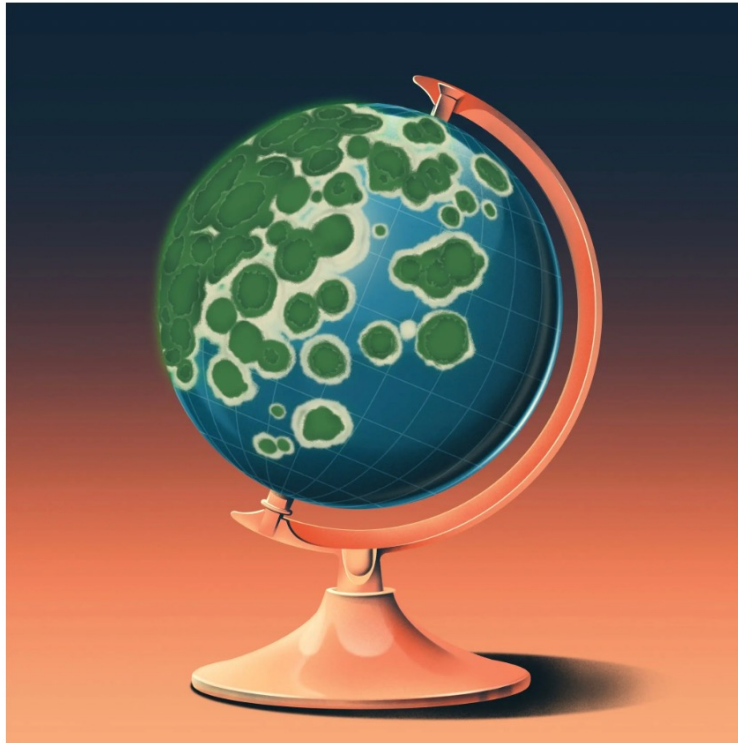


Some of the most successful zombie-masters are fungi from the genus *Ophiocordyceps*. In the jungles of Thailand, their victims are *Camponotus leonardi*, or carpenter ants. [David Hughes](#)

The New York Times

'The Last of Us' Is Right. Our Warming Planet Is a Petri Dish.

April 2, 2023



**Climate change
& ecosystem
destruction –**

**Provide
opportunities
for fungi to
attack man**



**This bug has spread
at an alarming rate in
health care facilities
and is concerning**

**CDC
March 20
2023**

Open Access

Perspective

On the Origins of a Species: What Might Explain the Rise of *Candida auris*?

by  Brendan R. Jackson ^{1,*} ,  Nancy Chow ¹,  Kaitlin Forsberg ^{1,2}, Anastasia P. Litvintseva ¹,
 Shawn R. Lockhart ¹,  Rory Welsh ¹,  Snigdha Vallabhaneni ³ and  Tom Chiller ¹

¹ Centers for Disease Control and Prevention, Division of Foodborne, Waterborne, and Environmental Diseases, Mycotic Diseases Branch, Atlanta, GA 30329, USA

² IHRC, Inc., Atlanta, GA 30346, USA

³ Centers for Disease Control and Prevention, Division of Healthcare Quality Promotion, Prevention and Response Branch, Atlanta, GA 30329, USA

* Author to whom correspondence should be addressed.

J. Fungi **2019**, *5*(3), 58; <https://doi.org/10.3390/jof5030058>

- Health care environment transmission –
- Colonization of human skin
- Expanding industrial farming
- Use of fungicides
- Global temperature changes

Isn't this an adult problem?

Open
Access
from BMJ

ARCHIVES OF DISEASE IN CHILDHOOD

[▶ View this article](#) [▶ Submit a manuscript](#) [▶ Open Access at BMJ](#) [▶ Contact us](#)

[Arch Dis Child.](#) 2018 Sep; 103(9): 891–894.

Published online 2018 Mar 15. doi: [10.1136/archdischild-2017-313960](https://doi.org/10.1136/archdischild-2017-313960)

PMCID: PMC6104675

PMID: [29545411](https://pubmed.ncbi.nlm.nih.gov/29545411/)

Candida auris, what do paediatricians need to know?

[Adilia Warris](#)

[▶ Author information](#) [▶ Article notes](#) [▶ Copyright and License information](#) [Disclaimer](#)

There's a new *Candida* in town...

First identified 2009 -Japanese ear..hence..auris
Simultaneous emergence in distinct locations
What's the problem?

ID difficult

NaCl & thermal tolerance 42*, MALDI/TOF & PCR)

Multidrug resistance, increased virulence factors

High mortality rates

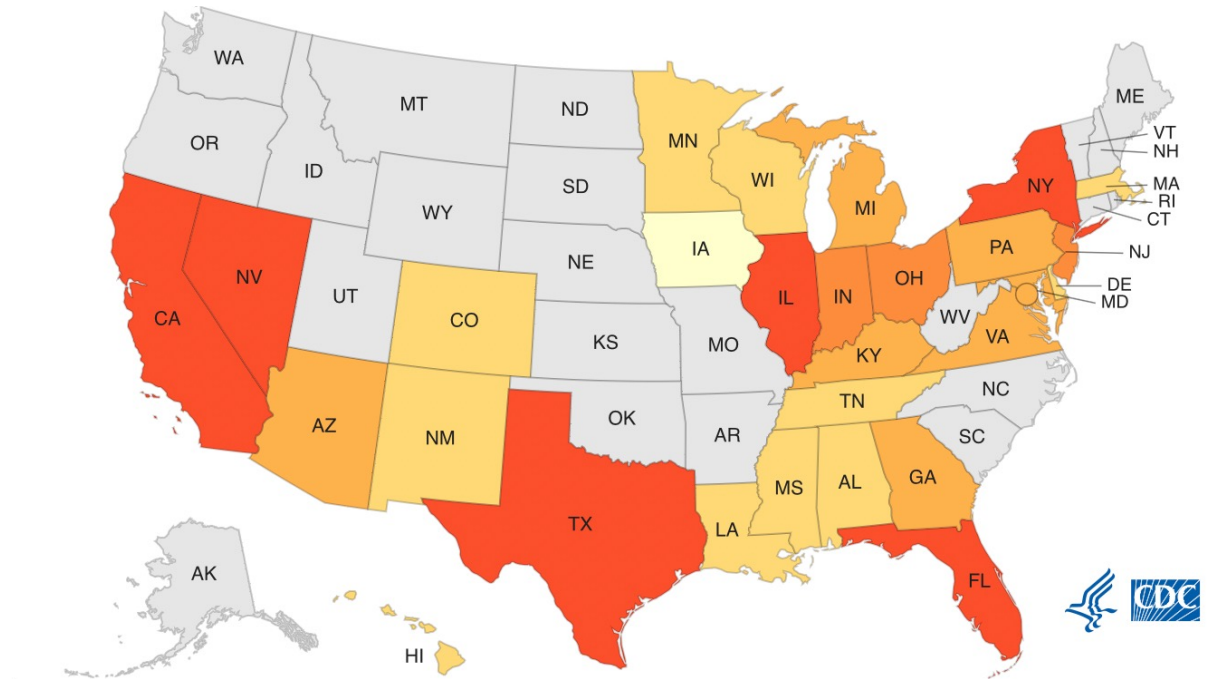
Long-term survival on biotic & abiotic surfaces – adherent to plastics

Du H et al PLoS Pathog 2020 Oct



How much risk is there?
Almost double
since 2021

Cases
2021 -- 1474
2022 -- 2377



Number of *C. auris* clinical cases through December 31, 2022

In 2022, there were 2,377 clinical cases and 5,754 screening cases.

- | | |
|--|---------------|
| ● 0 clinical cases and at least 1 screening case | ● 1 to 10 |
| ● 11 to 50 | ● 51 to 100 |
| ● 101 to 500 | ● 501 to 1000 |
| ● 1001 or more | |

How does *C. auris* differ from *C. albicans*?

Predominantly colonizes skin, rather than Gu/GI tract
It can grow at high temps! $>40^{\circ}\text{C}$,
Tolerates high salt conc $>10\%$ NaCl w/v
Persistence, survival on abiotic surfaces
Most resistant to fluconazole (44 - 100%), some
resistant to all available classes of antifungals

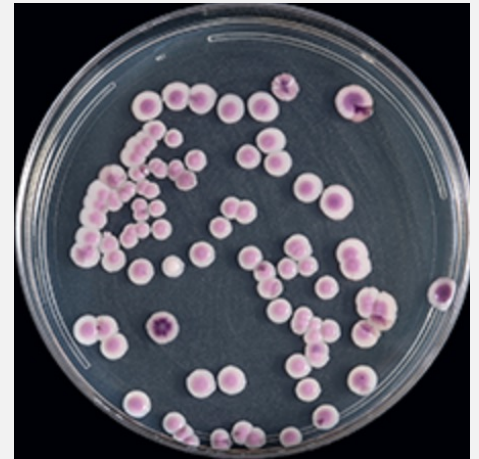
Risk factors include

Immunosuppression!

Diarrhea

Broad-spectrum antibiotics

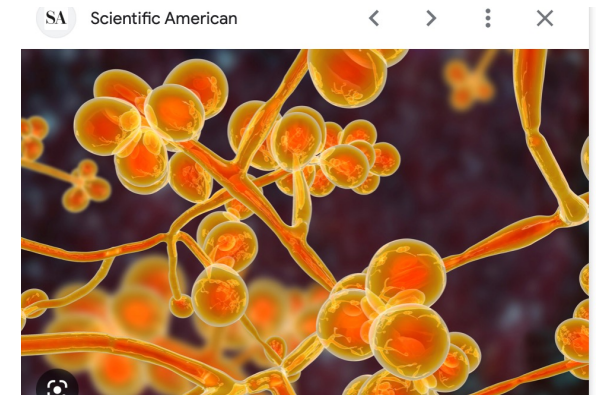
Tetracycline, minocycline tigecycline



C. Auris – the 1st MDR Candida species!

- C. auris - first Candida species - multidrug resistant (MDR)
- Pan-resistance as well!
- Hope - ibrexafungerp & fosmanogepix
- Virulence factors (genes which confer pathogenicity)
- Phenotypic switching - yeast to filamentous forms
- SAPS enzymes- adhesion, biofilm, host tissue degradation
- They can help evade immune system
- ? May inhibit PMN activity, avoid innate immune activity

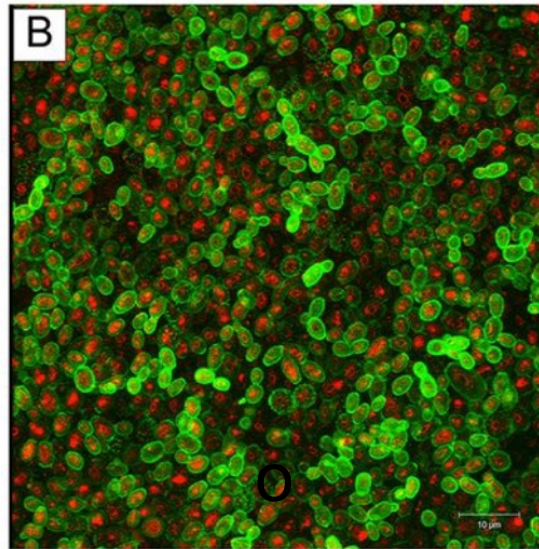
Sikora A et al Stat pearls Feb 19, 2023



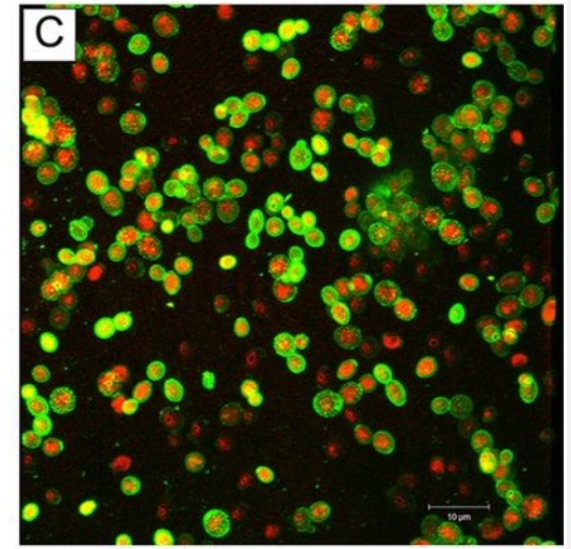
Clinical presentation

- Critically ill pts, immunocompromised, prior ab rx
- Non-specific!
- Mortality rates – 30-72%
- Affects the young & old

C. auris 31102



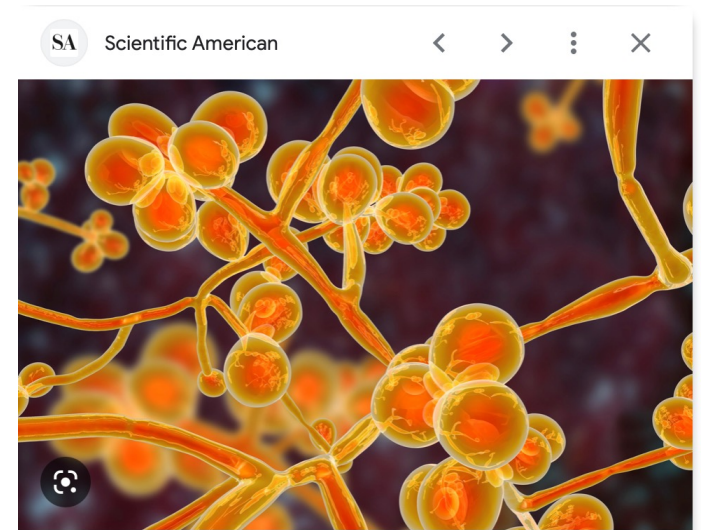
C. auris 31103



How do we get rid of this bug?

- What doesn't often work –
 - Purell, Lysol, Virex
- What does work?
 - Bleach agents – Cloriox, Oxycide, Oxivir TB
 - ?photodynamic rx – UVC light – longer exposures 20-30 mins

CDC, EPA



Candida auris

Fungal Diseases > Candida auris > Laboratorians and Health Professionals

Candida auris

General Information
about *Candida auris*

Tracking *Candida auris*

Laboratorians and
Health
Professionals

Surveillance

Identification

Antifungal

Infection Prevention and Control for *Candida auris*

[Español \(Spanish\)](#) | [Print](#)

The primary infection control measures for prevention of *C. auris* transmission in healthcare settings are:

- Adherence to [hand hygiene](#).
- Appropriate use of [Transmission-Based Precautions](#) based on setting.
- [Cleaning and disinfecting](#) the patient care environment (daily and terminal cleaning) and reusable equipment with recommended products, including focus on shared mobile equipment (e.g., glucometers, blood pressure cuffs).

In addition to these key points, considerations that are setting-specific are listed below:

[Dialysis clinics](#)

[Outpatient settings](#)

[Home healthcare settings](#)

Updated
Jan 17,
2023

EPA list of registered antimicrobials for *C. auris*

List P: Antimicrobial Products Registered with EPA for Claims Against *Candida Auris*

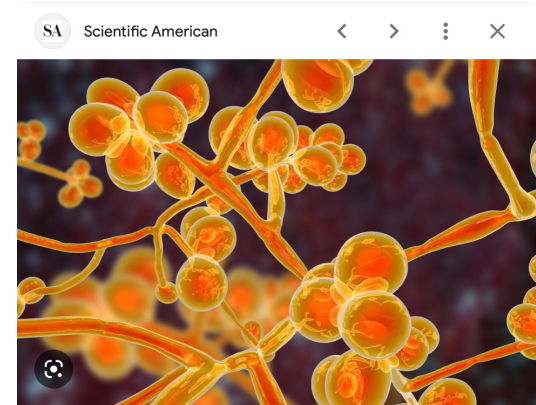
Registration	Active Ingredient	Product Brand Name	Company	Contact Time (minutes)	Formulation Type	Surface Types	Use sites
10324-214	Hydrogen Peroxide and Paracetic Acid	Maguard 5626	Mason Chemical Company	2	Dilutable	Hard Non-Porous (HN)	Hospital; Institutional; Residential
1677-226	Hydrogen Peroxide, Paracetic Acid and Octoanoic Acid	Virasept	Ecolab Inc.	4	Ready to Use	Hard Non-Porous (HN)	Hospital; Institutional
1677-237	Hydrogen Peroxide and Paracetic Acid	Oxycide™ Daily Disinfectant Cleaner	Ecolab Inc.	3	Dilutable	Hard Non-Porous (HN)	Hospital; Institutional
1677-262	Dodecylbenzenesulfonic Acid	Disinfectant 1 Spray	Ecolab Inc.	1	Ready to Use	Hard Non-Porous (HN)	Hospital; Institutional
1677-263	Dodecylbenzenesulfonic Acid	Disinfectant 1 Wipe	Ecolab Inc.	1.25	Ready to Use/Wipe	Hard Non-Porous (HN)	Hospital; Institutional
37549-1	Sodium Hypochlorite	Micro-Kill Bleach Germicidal Bleach Wipes	Medline Industries Inc.	2	Ready to Use/Wipe	Hard Non-Porous (HN)	Hospital; Institutional; Reside

Ammonia-based products suboptimal

Updated Feb 2, 2023

What do we do??

- FLUCONAZOLE a **no-no!**
 - Echinocandins **YES**
 - Combination therapies
 - Voriconazole & micafungin
 - Flucytosine & amphotericin B, flucytosine & micafungin, caspofungin
 - Ibrexafungerp – inhibits glucan synthesis of wall
 - Quorum sensing molecules (SMs)
 - Farnesol chemical signal formed by Candida species
 - Inhibits transition to hyphal phase, inhibits biofilm growth
 - Herbals ! Cinnamaldehyde, palmitic acid, essential & **oregano oils**- alpha caryophyllene
 - Medical grade honey – don't laugh alkaloids, flavonoids, bee defensin-1 & apidaecin
-
- Watkin R et al PaCthog Immun 2022;7:46-65
 - Bandara N et al Med Mycol 2022 April



What's going on here?



Wearing masks
Topical corticosteroids ineffective

[Pediatric Dermatology, Volume: 39, Issue: 2, Pages: 326-327, First published: 04 February 2022, DOI: \(10.1111/pde.14911\)](#)

> [Pediatr Dermatol](#). 2022 Mar;39(2):326-327. doi: 10.1111/pde.14911. Epub 2022 Feb 4.

Tinea incognito "mask" erasing as allergic contact dermatitis due to COVID-19 facial covering in children

[Eric P Cunningham](#)¹, [Natasha F Carter](#)²

Affiliations + expand

PMID: 35118710 DOI: [10.1111/pde.14911](#)

- 3 children initially thought to have contact dermatitis to masks
- Masks may have contributed to the *T. mentagrophytes* facial infection in each
- Think about this!
- Particularly if TCS don't help
- Ask about pets, exposures



Maskne –

Development of acne due to textile friction from mask....?akin to “chin-strap folliculitis”?

But many other conditions are associated with face masks

- Contact dermatitis-
 - Irritant or allergic
- Seb derm
- Perioral derm
- Rosacea
- Atopic derm



Maskne.....

Is it.....

- Contact dermatitis
 - Irritant
 - Allergic
- Acne (mechanical)
- Perioral dermatitis
- Seborrheic dermatitis
- Infection?
- **DON'T FORGET FUNGUS**



Pityriasis versicolor “maskerading” as maskne

7 cases 2-10 yrs

Hypopigmented spots on face

3-4 weeks

Cloth mask usage

KOH + ziti & meatballs

100% cure with topical antifungals



Speaking of facial rashes..

6 yo wearing mask
Topical steroids for
several weeks
Has some pets





**Adorable guinea pigs!
Tinea faciei from
Trichophyton Benhamiae**

JAMA Derm Iznardo et al 2021



Zoonosis.....Transfer from animals to us For ringworm...

Cats or dogs?
Guinea pigs
Cows
Goats
Pigs



Pet owners
Pet breeders
Livestock
Zoo workers
Can be transmitted
through..
Bedding,
grooming articles
Saddles, Carpets

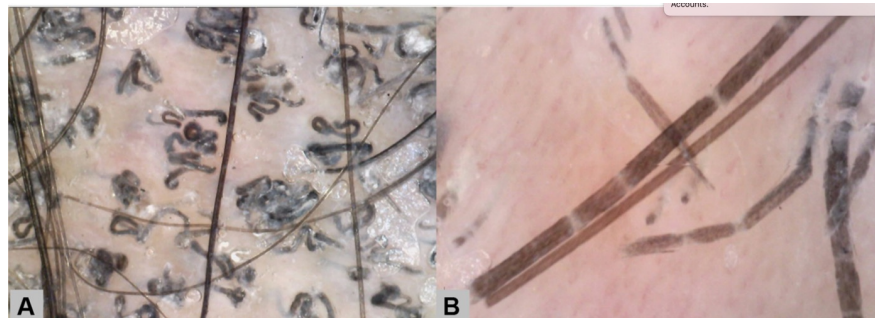
> [J Am Acad Dermatol.](#) 2023 Jan;88(1):166-167. doi: 10.1016/j.jaad.2021.12.010. Epub 2021 Dec 11.

Trichoscopy patterns of tinea capitis and their correlation with mycological culture results

Olívia Mercilene Meneses ¹, Aline Donati ², Fabiana O Silva ², Marcelo J Mimiça ³,
Carla J Machado ⁴, John Veasey ⁵

Affiliations + expand

PMID: 34906665 DOI: [10.1016/j.jaad.2021.12.010](#)

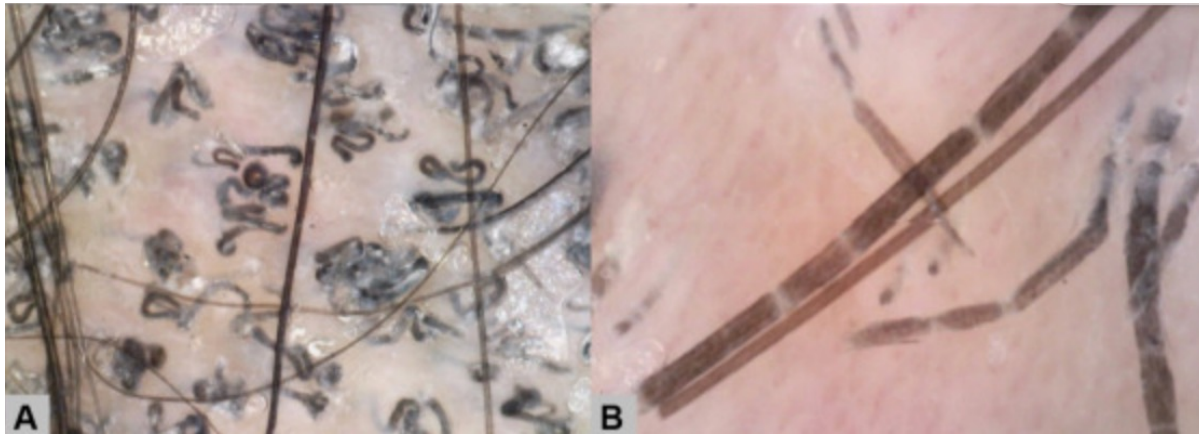


41 pts –culture & dermoscopy images

94.9% specificity curvilinear & monomorphic – T. tonsurans

85% specificity rectilinear - M. canis

Curved = endothrix - T. tonsurans
Straight = ectothrix. - M. canis



Meneses et al JAAD 2023

Fig 1 A, Trichoscopy of a lesion with the curvilinear monomorphic pattern presenting almost exclusively “curved” findings.

B, Trichoscopy of a lesion with the rectilinear monomorphic pattern presenting almost exclusively “straight” findings.

(Original magnifications [with liquid immersion]: A, x70; B, x170.)

Review > [Pediatr Dermatol.](#) 2022 Mar;39(2):167-172. doi: 10.1111/pde.14925.

Epub 2022 Jan 24.

Tinea capitis: An update

[Aditya K Gupta](#)^{1 2}, [Sheila Fallon Friedlander](#)^{3 4}, [Aaron J Simkovich](#)²

Affiliations + expand

PMID: 35075666 DOI: [10.1111/pde.14925](#)



Review > [Pediatr Dermatol. 2022 Mar;39\(2\):167-172. doi: 10.1111/pde.14925](#)

Epub 2022 Jan 24.

Tinea capitis: An update

[Aditya K Gupta](#)^{1 2}, [Sheila Fallon Friedlander](#)^{3 4}, [Aaron J Simkovich](#)²

Affiliations + expand

PMID: 35075666 DOI: [10.1111/pde.14925](#)



Diagnosis

- Trichoscopy – corkscrew, comma hairs, barcode
- PCR – but doesn't confirm viability of organism
- MALDI-TOF/MS matrix-assisted laser desorption ionization – time of flight mass spectrometry - compare database in silico matching mass spectra to sample

Tinea update - Treatment

- **Griseofulvin** – not always available in several countries
- **Terbinafine** (FDA approved pts >4 yrs of age) now commonly used, especially for Trichophyton species
- Resistance has been documented in both Microsporum & Trichophyton species – mutations in genes encoding squalene epoxidase
- Fluconazole & itraconazole alternatives, but 1 large RDBPCT showed suboptimal cure rates with fluconazole.
- If unresponsive, check compliance, repeat culture, KOH
- MICs sometimes available
- PDT off label



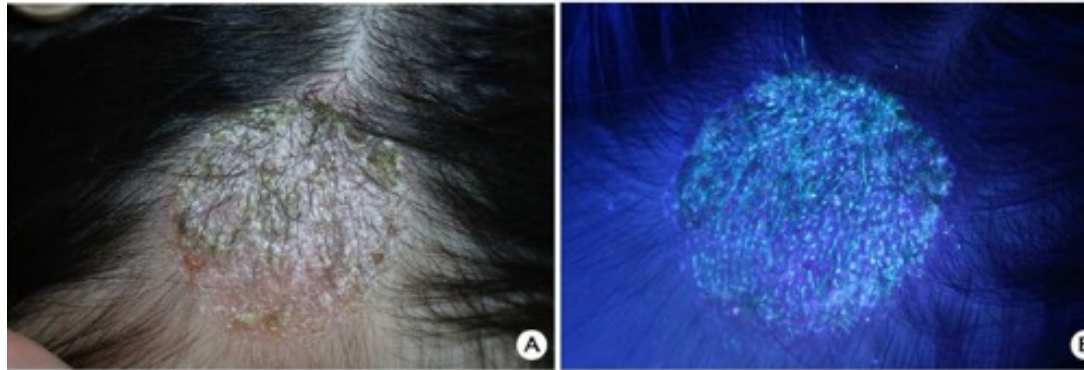
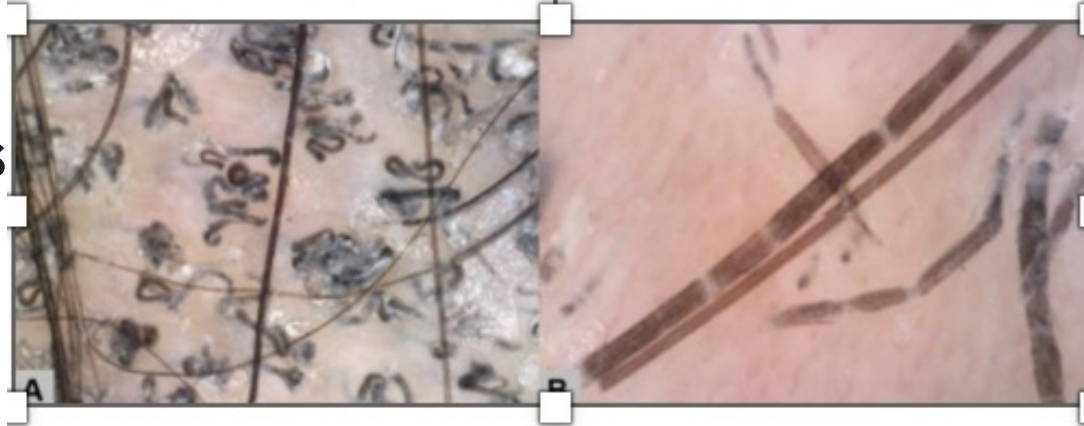
T. capitis – Dx & Rx

Terbinafine - best for *T. tonsurans*
Griseo – best for *Microsporum*

How to distinguish ?–
Wood lamp/trichoscopy

Griseofulvin 20-25 mg/kg/d
with food, max 1 gram.

Terbinafine – dosing options





Oral granules no longer available

But I use that dose utilizing tablets
FDA approval is for granules, not tabs

Usual Pediatric Dose for Tinea Capitis

4 years or older:

Oral granules:

Less than 25 kg: 125 mg orally once a day

25 to 35 kg: 187.5 mg orally once a day

Greater than 35 kg: 250 mg orally once a day

Duration of therapy: 6 weeks

Comments:

- Before using this drug, patients should be evaluated for evidence of chronic or active liver disease.

For Children, Some Experts Recommend:

Tablets: 5 mg/kg/day orally

Based on weight:

10 to 20 kg: 62.5 mg orally once a day

21 to 40 kg: 125 mg orally once a day

41 kg or more: 250 mg orally once a day

Tinea capitis – labs – How much is enough?



Griseofulvin

Not required if griseofulvin used ≤ 8 weeks

Terbinafine – controversial

FDA – baseline transaminase levels

AAP – above, but “some clinicians omit baseline labs in otherwise healthy children, with some f/u labs at 4-6 weeks if therapy prolonged”

Canadians – periodic monitoring if rx $>4-6$ weeks

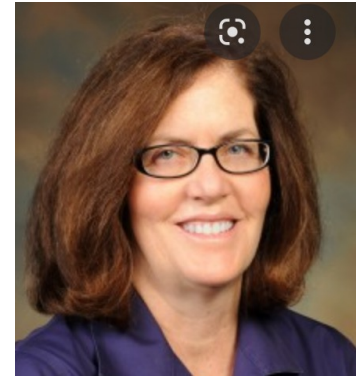
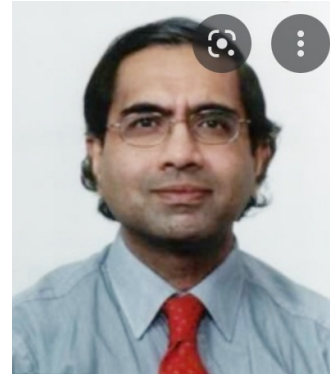
Wang/Lipner 100 children rx'd with terbinafine

4% abnl labs, all grade 1

Recent peds derm survey of onychomycosis practices
– got culture but not labs

Wang Y et al JAAD 2021

Tinea update – Lab monitoring – Authors’ recs



Obtain fungal culture on all suspicious kiddy hair/nails

Kids with any health problems,
on other meds – baseline and f/u lab 4-6 wks

Parents should be involved in the decision-making process in
otherwise healthy kids

Inform them of small risk of adverse effects

In healthy kids, many parents opt out of lab monitoring (I
agree with that approach)

Document your discussion!

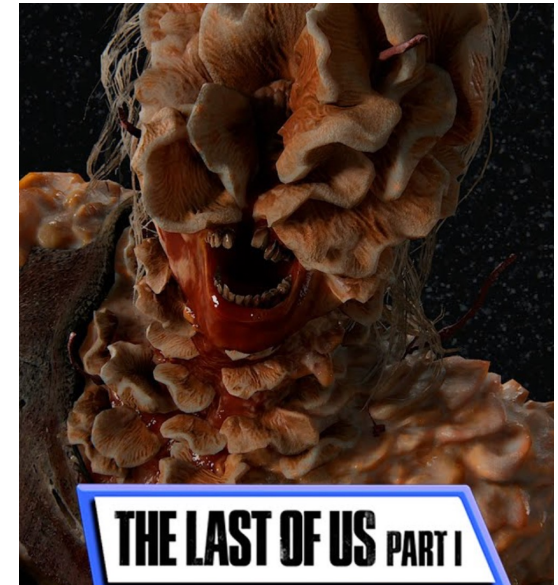
Tinea capitis– What about the carrier state & topical rx?



- No clear-cut large study results, but
- Risk benefit ratio favors using topical antifungal shampoos on infected patients and asymptomatic carriers
- When can pt return to school? No drainage & rx. AOK to go
- Not necessary to shave the child's head or wear a hat
- Potential fomites (brushes, linens hats) - boiling x 5 mins, or using a strong disinfectant such as bleach
- All pets and contacts should be queried/evaluated for symptoms

Fascinating & Frightening Fungi. – Summary

- **Beware Candida auris!**
 - Hard to dx, hard to eradicate
 - An increasing health risk
- **Don't forget that skin fungus is a great masquerader!**
- **Tinea capitis**
 - Trichoscopy helps!
 - Terbinafine usually a good choice for *T. tonsurans*
 - Labs may not be necessary



I really can't leave you without talking about molluscum

Prevalence rate in children
0-16yrs in the U.S. is

5.1% – 11.5%¹

1. Prevalence in the US of 5.1% to 11.5% in children aged 0-16 years. (Fam Pract. 2014 Apr;31(2):130-6).

Average time to resolution –
13 months



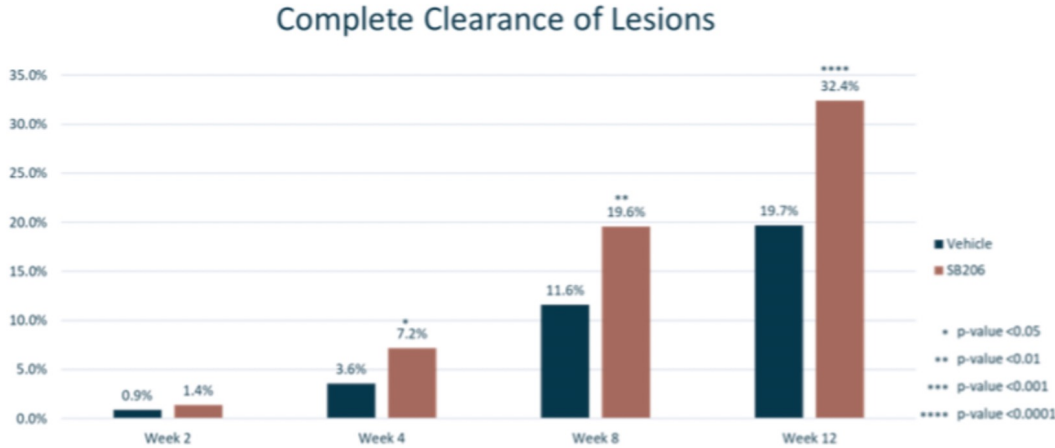
Berdazimer gel 10.3% - Home rx game-changer

Clinical Trial > JAMA Dermatol. 2022 Aug 1;158(8):871-878.

doi: 10.1001/jamadermatol.2022.2721.

Efficacy and Safety of Topical Nitric Oxide-Releasing Berdazimer Gel in Patients With Molluscum Contagiosum: A Phase 3 Randomized Clinical Trial

John C Browning¹, Carolyn Enloe², Martina Cartwright², Adelaide Hebert³, Amy S Paller⁴, David Hebert^{2,5}, Elaine Kearney Kowalewski⁶, Tomoko Maeda-Chubachi²



891 pts ≥ 6 mos of age
Qd x 12 weeks
32.4% vs 19.7% Clear
D/C rate 4%

NDA for Berdazimer Gel, 10.3% (SB206) for Treatment of Molluscum Contagiosum Accepted for Review by U.S. FDA with a PDUFA Goal Date of January 5, 2024

VP-102 (cantharidin) topical solution

**DESIGNED FOR RELIABLE,
AND TARGETED ADMINISTRATION**

Topical solution in a single-use applicator

Therapeutic class: Vesicant

Active ingredient cantharidin (0.7%) in a unique topical formulation

Single-use applicator to reduce cross-contamination and facilitate application of the topical solution

Small opening allows for targeting of affected skin

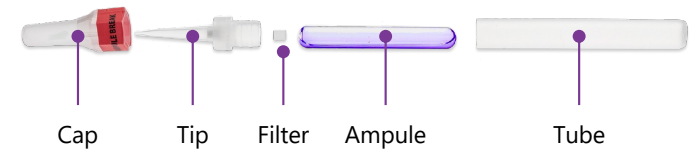
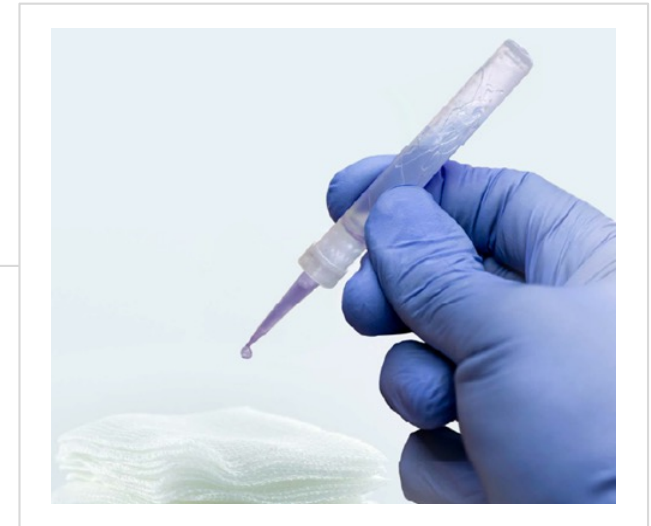
Physician administered in-office procedure

GMP-controlled, shelf-stable, consistent topical formulation

Visualization agent to identify treated lesions

Bittering agent to deter ingestion

Applied q 21 days for at least 3 rxs



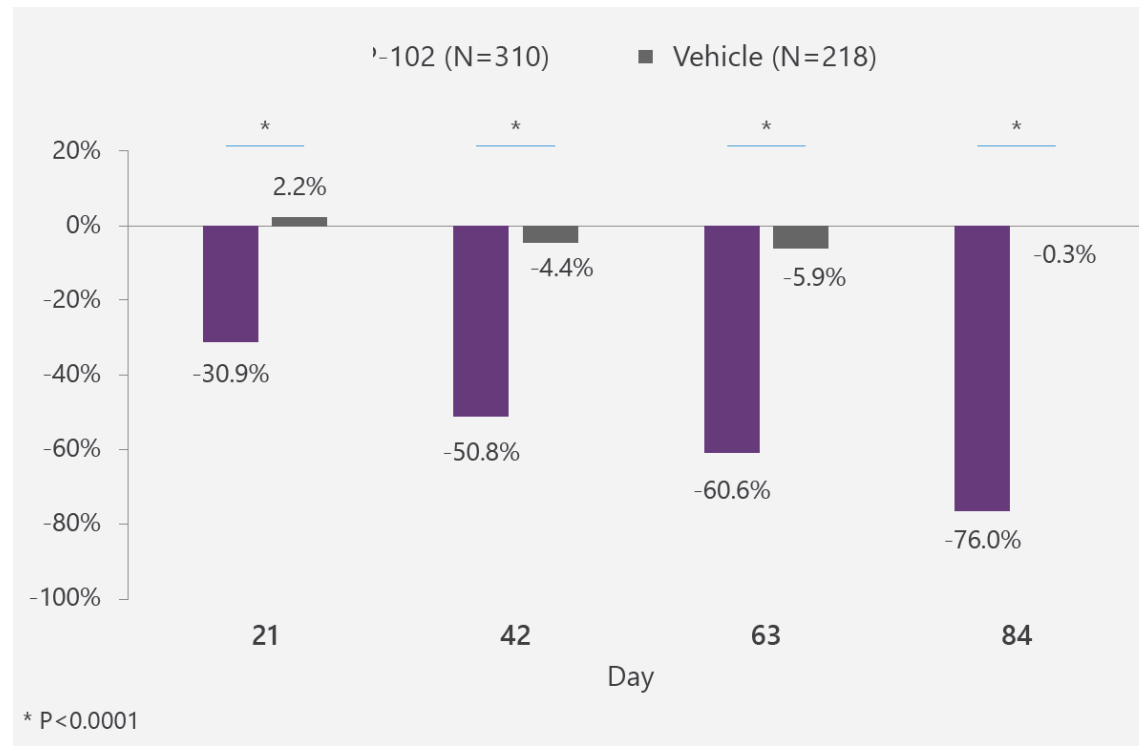
**Potential first FDA Approved therapy
for molluscum contagiosum**

Phase 3 Trials of VP-102 for the Treatment of Molluscum Contagiosum
Demographics
(Pooled, ITT population¹)

	VP-102 (n=310)	Vehicle (n=218)
Age (years)		
Mean (SD)	7.5 ± 6.7	6.8 ± 5.8
Median	6.0	6.0
Range	2-60	2-54
Age Group - no.(%)		
≥ 2 to 5 yr	137 (44.2)	106 (48.6)
≥6 to 11 yr	140 (45.2)	89 (40.8)
≥12-18 yr	22 (7.1)	18 (8.3)
≥ 19 yr	11 (3.5)	5 (2.3)
Gender – no. (%)		
Female	154 (49.7)	107 (49.1)
Male	156 (50.3)	111 (50.9)
Race or Ethnic Group – no. (%)		
White	277 (89.4)	202 (92.7)
Black or African American	13 (4.2)	8 (3.7)
Asian	6 (1.9)	1 (0.5)
American Indian/Alaskan Native	0	1 (0.5)
Other	14 (4.5)	6 (2.8)

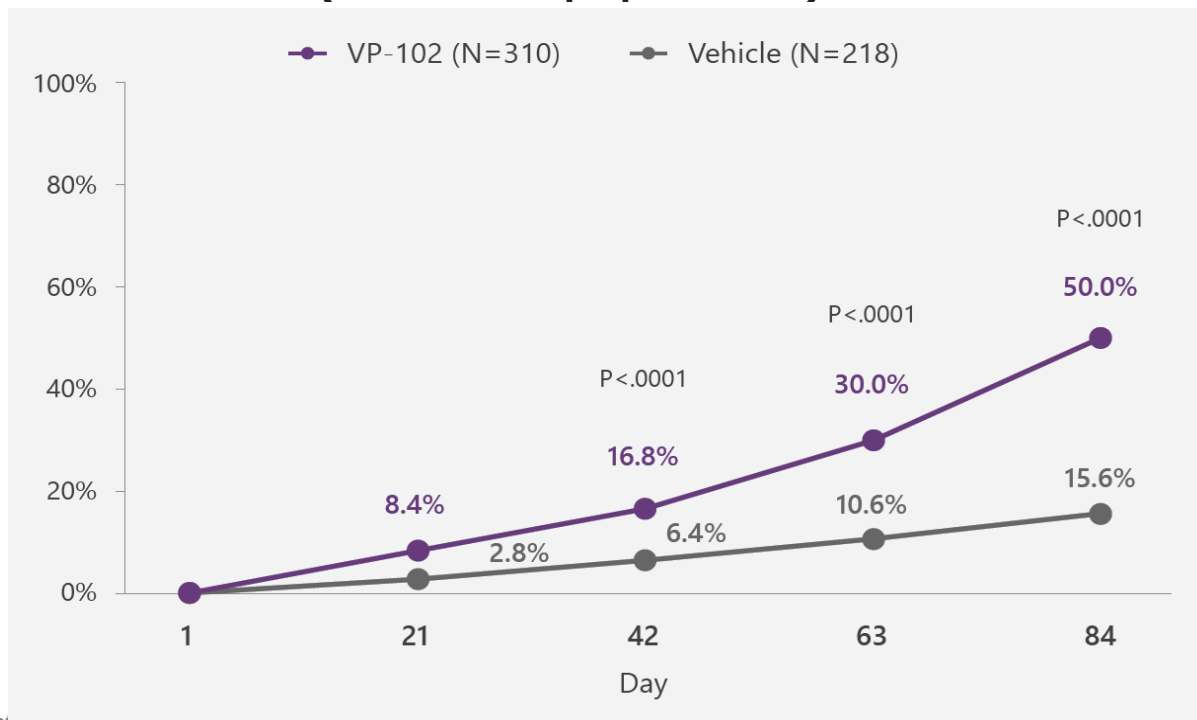
¹Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two phase 3 trials of VP-102 containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Arch Dermatol.* 2014;150(12):1211-1218.

Mean Percent Change in Molluscum Contagiosum Lesion Count from Baseline to Day 84 (Pooled, ITT population¹)



1. Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two randomized phase III trials evaluating VP-102, a drug-device combination product containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Am J Clin Dermatol*. 2021;22(2):257-265.

Percentage of Subjects with Complete Clearance of All Baseline and New Treatable MC Lesions at Each Time Point (Pooled, ITT population¹)



Note: no statistical significance reported at Day 21 in CAIR-2.

1. Eichenfield LF, Siegfried E, Kwong P, et al. Pooled results of two randomized phase III trials evaluating VP-102, a drug-device combination product containing cantharidin 0.7% (w/v) for the treatment of molluscum contagiosum. *Am J Clin Dermatol.* 2021;22(2):257-265.

Summary – Peds ID

Remain afraid of
ferocious fungi

There are several really
good topical molluscum
treatments on the
horizon!

