Emerging and Complex Ringworm in Newcomer Populations Webinar

Thursday, August 22, 2024

Minnesota Center of Excellence in Newcomer Health

CENTER OF EXCELLENCE IN NEWCOMER HEALTH MINNESOTA

Acknowledgment

The Minnesota Center for Excellence in Newcomer Health is supported by *1 NU50CK000563* from the U.S. Centers for Disease Control and Prevention.

The Minnesota Medical Association facilitated the CMEs.

No financial conflicts of interest.

Learning Objectives

- Recall prevention measures for dermatophytosis
- Describe the epidemiology, diagnosis, and treatment of emerging and complex dermatophytosis
- Identify key areas where clinicians, public health, and the public can help stop the spread of emerging and complex ringworm

Today's Speakers

Dallas Smith, PharmD, MAS

Mycotic Diseases Branch
Centers for Disease Control and Prevention

Sheila Roy, MD, MPH

Immigrant and Refugee Health Branch
Centers for Disease Control and Prevention

(Moderator)

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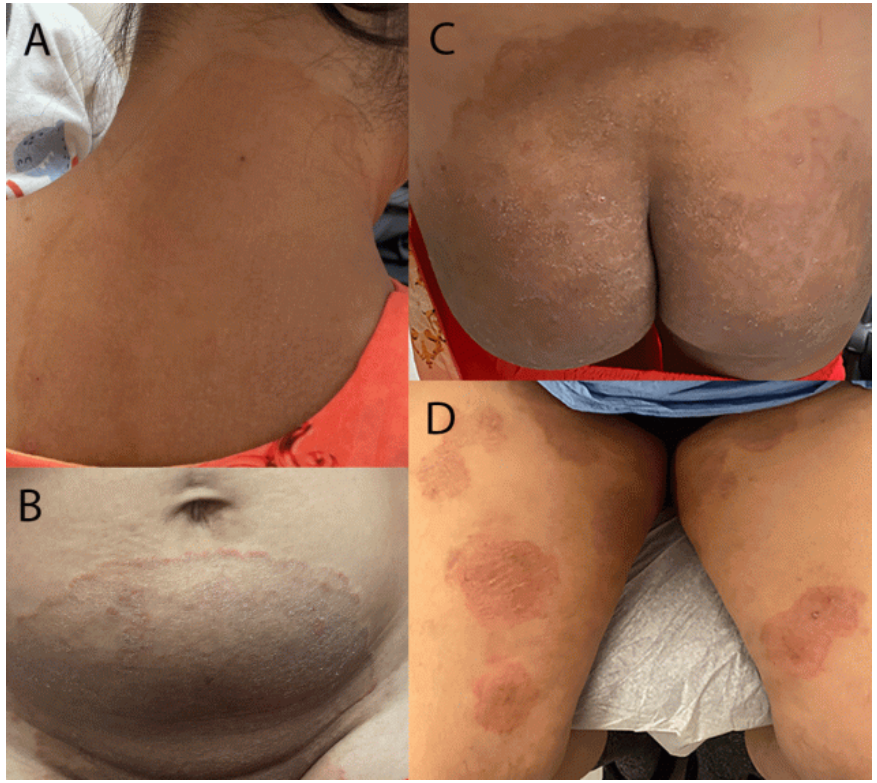
Case #1

A 26-year-old man presents to a primary care clinic in Minnesota…

- Chief complaint: extensive rash on neck, abdomen, thighs, groin, and buttocks
  - Rash started three months ago



Caplan AS, Chaturvedi S, Zhu Y, et al. *Notes from the Field:* First Reported U.S. Cases of Tinea Caused by *Trichophyton indotineae* — New York City, December 2021–March 2023. MMWR Morb Mortal Wkly Rep 2023;72:536–537.

Past medical history indicates the patient is relatively healthy

- HIV negative
- No chronic diseases
- No family history of hypertension or cancer

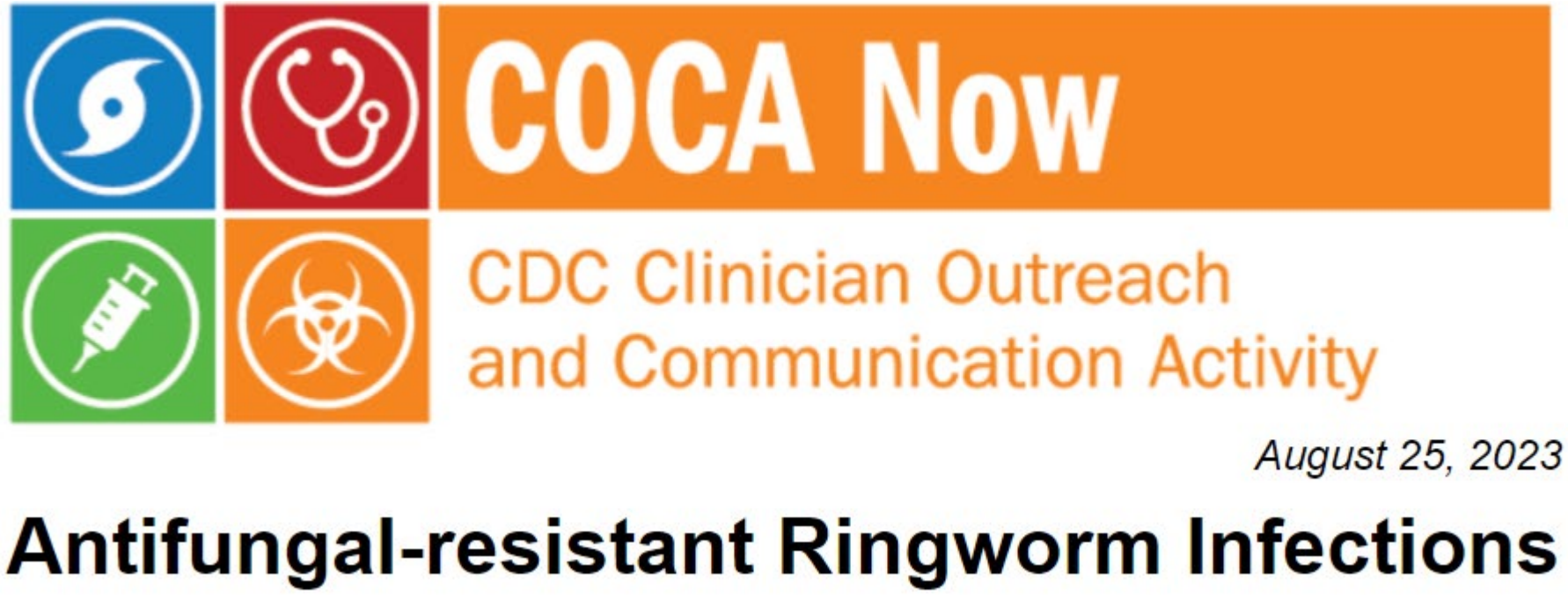
Polling question #1:
With the available information, what would be your next step? (select all that apply)

- Take skin scrapings and examine under microscope on potassium hydroxide wet mount
- Prescribe an antifungal-corticosteroid cream to cover fungal and non-infectious skin conditions
- Obtain further patient information like social and travel history
- None of the above

Upon further patient interviewing, you learn that:

- He denies any sexual intercourse with men
- He traveled to India to visit friends about 3 months ago. The rash started while in India
- After returning to Minnesota, he went to the emergency room three times:
  - Visit 1: prescribed hydrocortisone 2.5% ointment and diphenhydramine
  - Visit 2: clotrimazole cream
  - Visit 3: four weeks of oral terbinafine
- All topical medications resulted in no improvement
- His family members have similar rashes that started after his return

You stumble across this CDC health alert after exploring differential diagnoses



COCA Now: Antifungal-resistant Ringworm Infections (emergency.cdc.gov/newsletters/coca/2023/082523.html)

From the CDC health alert, you learn….

- About the spread of a new species of dermatophyte that is resistant to topical antifungals and oral terbinafine
- How to conduct additional testing to identify this new species
  - You subsequently obtain a culture from the patient and send it out

While awaiting lab results, you start the patient on itraconazole following considerations from the American Academy of Dermatology

AAD: Emerging Diseases Resource Center
(www.aad.org/member/clinical-quality/clinical-care/emerging-diseases)

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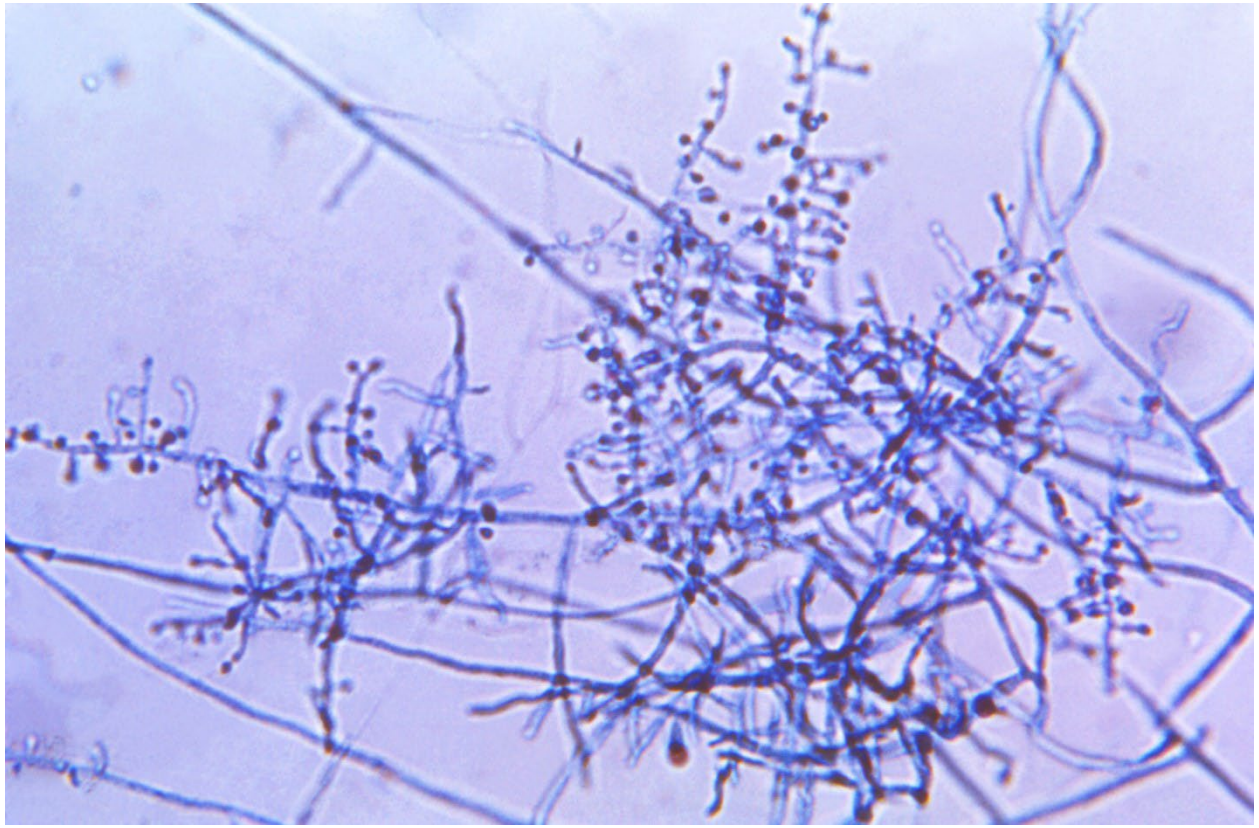
A few weeks later, the laboratory reports that the culture was identified as *Trichophyton indotineae*



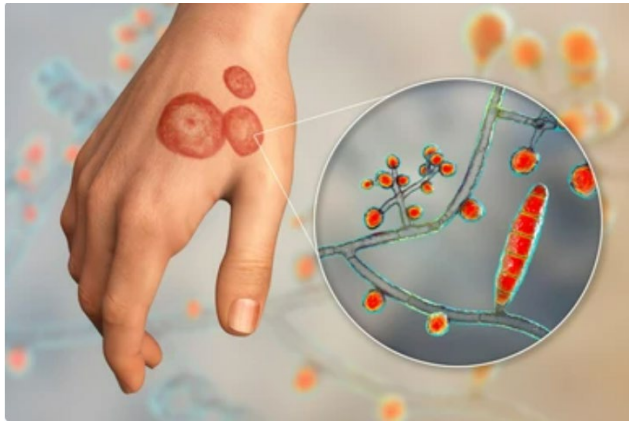
AAD: Recognizing *Trichophyton indotineae*
(www.aad.org/member/clinical-quality/clinical-care/emerging-diseases/dermatophytes/recognizing-trichophyton-indotineae)

Polling question #2:
Have you heard, suspected, or diagnosed *Trichophyton indotineae* before? (select all that apply)

- Yes, I have diagnosed *Trichophyton indotineae*
- Yes, I have suspected that a patient has had *Trichophyton indotineae*
- Yes, I have heard of *Trichophyton indotineae*
- No, I have never heard of *Trichophyton indotineae*

Dermatophytosis, or “tinea” or “ringworm”

Trichophyton mentagrophytes



Tinea corporis (forearm)

COURTESY OF DR. SHEILA TORRES.

COURTESY OF DR. SHEILA TORRES.

Ringworm on cat and dog

- **It is estimated that the lifetime prevalence in human and animals is about 20%**
- **Are fungi that invade and grow on the skin of mammals**
- **Spread easily among people and animals via fomites**
- **Cause itching, scaling, ring-shaped lesions**

Among the dermatophytes, there are at least 40 species known to cause disease in humans

Three main genera:

- *Epidermophyton*
- *Microsporum*
- ***Trichophyton***

Ecology (primary habitat associations):

- **Anthropophilic**
- Zoophilic
- Geophilic

TABLE 3. Current synopsis of dermatophyte species and congeners: ecological classification, host preference, and endemicity

Anthrophilic species (area of endemicity)	Zoophilic species (typical host)	Geophilic species
E. floccosum	*M. canis* (cat, dog)	*E. stockdaleae*
M. audouinii (Africa)	*M. equinum* (horse)	*M. amazonicum*
M. ferrugineum (East Asia, East Europe)	*M. gallinae* (fowl)	*Microsporum* anamorph of *A. cookiellum*
T. concentricum (Southeast Asia, Melanesia, Amazon area, Central America, Mexico)	*M. persicolor* (vole)	*M. boullardii*
T. gourvilii (Central Africa)	*T. equinum* (horse)	*M. cookei*
T. kanei	*T. mentagrophytes* (two sibling species and variants; rodents, rabbit, hedgehog)	*M. gypseum* (complex of three species)
T. megninii (Portugal, Sardinia)	*T. sarkisorii* (Bactrian camel)	*M. nanum*
T. mentagrophytes (complex of two species)	*T. simii* (monkey, fowl)	*M. praecox*
T. raubitschekii (Asia, Africa, Mediterranean)	*T. verrucosum* (cattle, sheep, dromedary)	*M. racemosum*
T. rubrum		*M. ripariae*
T. schoenleinii		*M. vanbreuseghemii*
T. soudanense (Subsaharan Africa)		*T. ajelloi*
T. tonsurans		*T. flavescens*
T. violaceum (North Africa, Middle East, Mediterranean)		*T. gloriae, T. longifusum*
T. yaoundei (Central Africa)		*T. phaseoliforme*, *T. terrestre* (complex of three species), *T. vanbreuseghemii*

***T. rubrum*, *T. mentagrophytes*, and *M. canis* are the most common specie in hospital isolates**

Clinical presentation

Main clinical forms:

- Body (Tinea corporis)
- Foot (Tinea pedis)
- Scalp (Tinea capitis)
- Groin folds (Tinea cruris)
- Nails (Tinea unguium)

CDC: Public Health Image Library (PHIL) (phil.cdc.gov/Default.aspx)

Diagnosing ringworm by visual inspection alone is often inaccurate: testing can help

- Fungal and non-fungal rashes can look very similar
- Studies show frequent misdiagnosis, which can lead to inappropriate treatment
- Diagnostic testing: KOH preparations, culture, PCR can help

Quality of life impact

- Stigma
- Missed work/school
- Patients with diabetes: bacterial superinfection

https://phil.cdc.gov/Default.aspx

https://www.physio-pedia.com/Cellulitis#/media/File:Classic_celulitis.PNG

https://santamariatimes.com/news/local/santa-maria-animal-shelter-continues-battling-ringworm-outbreak/article_b000e5b7-78ec-53c5-8691-580e9555677c.html

- **Outbreaks (affecting humans and animals)**
- **Substantial health care burden**

Classic treatment

Topical antifungals usually effective

https://www.gettyimages.com/

- **Severe infections (which often occur in patients with immunocompromising conditions) may require oral antifungals**
  - terbinafine
  - griseofulvin
  - azoles

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Emergence of antifungal-resistant dermatophytosis

› Mycoses. 2019 Apr;62(4):336-356. doi: 10.1111/myc.12878. Epub 2019 Feb 20.

The current Indian epidemic of superficial dermatophytosis due to Trichophyton mentagrophytes–A molecular study

Pietro Nenoff [1], Shyam B Verma [2], Resham Vasani [3], Anke Burmester [4], Uta-Christina Hipler [4], Franziska Wittig [1], Constanze Krüger [1], Kolja Nenoff [1], Cornelia Wiegand [4], Abir Saraswat [5], Rengarajan Madhu [6], Saumya Panda [7], Anupam Das [7], Mahendra Kura [8], Akshay Jain [9], Daniela Koch [1], Yvonne Gräser [10], Silke Uhrlaß [1]

Multicenter Study › Mycoses. 2020 Jul;63(7):717-728. doi: 10.1111/myc.13091. Epub 2020 M

Alarming India-wide phenomenon of antifungal resistance in dermatophytes: A multicentre study

Andreas Ebert [1 2], Michel Monod [3], Karine Salamin [3], Anke Burmester [4], Silke Uhrlaß [2], Cornelia Wiegand [4], Uta-Christina Hipler [4], Constanze Krüger [2], Daniela Koch [2], Franziska Witti
Shyam B Verma [5], Archana Singal [6], Sanjeev Gupta [7], Resham Vasani [8], Abir Saraswat [9], Rengarajan Madhu [10], Saumya Panda [11], Anupam Das [11], Mahendra M Kura [12], Akshy Kumar [13], Shital Poojary [14], Sibylle Schirm [15], Yvonne Gräser [16], Uwe Paasch [17], Pietro Nenoff [2]

Affiliations + expand

Epidemic-like scenario of dermatophytosis in India

Nenoff P et al (2018) Mycoses

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By 2023, cases of ringworm caused by *Trichophyton indotineae* were detected in 6 continents

Most U.S. cases are linked to international country travel and migration

Adapted from: The rapid emergence of antifungal-resistant human-pathogenic fungi (www.nature.com/articles/s41579-023-00960-9) | Nature Reviews Microbiology; Messina F et al., (2023) **Med Mycol Case Rep**.; Mosam A et al (2023) **Public Health Bulletin**

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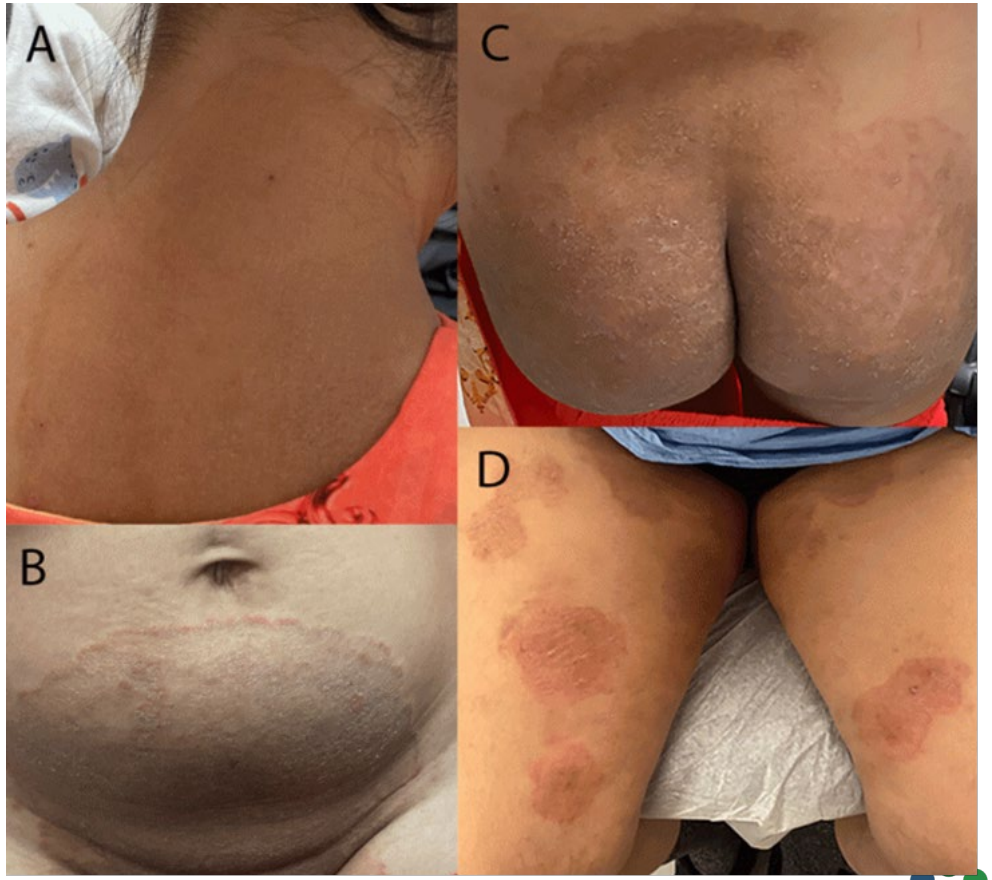
First Reported Cases of Ringworm Caused by *Trichophyton indotineae* in the United States — New York City, December 2021–March 2023

- 2 cases in NYC with severe ringworm caused by *T. indotineae*
- Patients had diagnostic delays, received multiple rounds of antifungal treatment
- Both patients were immunocompetent
- 1 patient had recent travel to Bangladesh; other patient lacked known exposure
    - Potential local U.S. transmission



CDC MMWR: Notes from the Field: First Reported U.S. Cases of Tinea Caused by *Trichophyton indotineae* (www.cdc.gov/mmwr/volumes/72/wr/mm7219a4.htm)

JAMA Network™

From: **Clinical Course, Antifungal Susceptibility, and Genomic Sequencing of Trichophyton indotineae**

JAMA Dermatol. Published online May 15, 2024. doi:10.1001/jamadermatol.2024.1126 Caplan et al, 2024

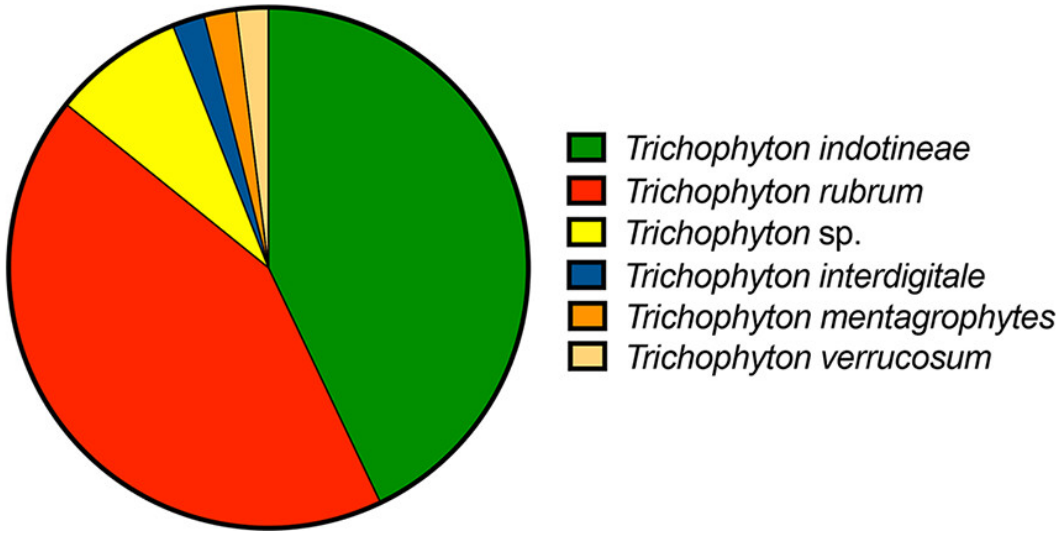
Case series describing the first 11 NYC cases

- 9 patients with recent travel to Bangladesh
- Extensive diagnostic delays
- Frequent terbinafine failure at standard doses
- Prolonged itraconazole therapy needed

T. indotineae has been present in the U.S. since at least 2017

- North American dermatophyte isolates received at a fungal diagnostic reference laboratory
- 18.6% of isolates were resistant to terbinafine
- *T. indotineae* has been present in North America since at least 2017
- *T. indotineae* detected from more than 10 states and several Canadian provinces

Species distribution for 49 terbinafine-resistant dermatophytes



Cañete-Gibas et al, 2023

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

MYCOLOGY
August 2023 Volume 61 Issue 8 e00562-23
https://doi.org/10.1128/jcm.00562-23

Terbinafine resistance-conferring SQLE epoxidase mutations in nearly 4% of *Trichophyton* isolates

- 15,683 toenail samples were collected across the U.S. from patients with abnormally shaped or colored nails suspected of onychomycosis
- Of these 5,894 dermatophyte samples, *Trichophyton* was identified as the main etiological agent at 94.7% (5,584 of 5,894)

J Invest Dermatol. 2023 Dec;143(12):2476-2483.e7. doi: 10.1016/j.jid.2023.04.032. Epub 2023 May 24.

Detection of Squalene Epoxidase Mutations in United States Patients with Onychomycosis: Implications for Management

Aditya K Gupta [1], Elizabeth A Cooper [2], Tong Wang [2], Shruthi Polla Ravi [2], Sara A Lincoln [3], Vincent Piguet [4], Laurence R McCarthy [3], Wayne L Bakotic [3]

Recent case of sexually-transmitted *T. indotineae* in Philadelphia

- Healthy woman in her 20s, likely acquired infection in Bangladesh from male partner and spread to a new partner in U.S.
- Patient suffered misdiagnosis and ineffective treatments for >1 year before correct diagnosis
- Infection was resistant to terbinafine but improved with itraconazole

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Potential Sexual Transmission of Antifungal-Resistant *Trichophyton indotineae*

Stephanie Spivack, Jeremy A.W. Gold, Shawn R. Lockhart, Priyanka Anand, Laura A.S. Quilter, Dallas J. Smith, Briana Bowen, Jane M. Gould, Ahmed Eltokhy, Ahmed Gamal, Mauricio Retuerto, Thomas S. McCormick, and Mahmoud A. Ghannoum

With resistant ringworm strains, culture results may not tell the whole story

- KOH preps and microscopy cannot distinguish *T indotineae* (frequently resistant strain) from other common dermatophyte species (*T mentagrophytes*, *T interdigitale*)
- Advanced molecular techniques (PCR with sequencing) needed for definitive diagnosis
- Laboratory capacity is limited
- Treatment should be started before getting laboratory results back

Outpatient antifungal stewardship is critical to address the emergence of this superficial fungal disease

Misuse of combination creams containing highly-potent steroids, antifungals, and antibacterials has been linked to emergence of resistant dermatophytes

Hypothesis

- Altered host immune response
- In vitro resistance of the causative fungi

What does antifungal-corticosteroid use look like in the United States?

Dermatology Online Journal || **Original**

Volume 25 Number 8| August 2021| 25(8):4

The continued inappropriate use and overuse of combination topical clotrimazole-betamethasone

Nicholas D Flint[1*] BS, Jamie L W Rhoads[2*] MD MS, Ryan Carlisle[1] BS, Meganne Ferrel[1] BS, Zachary H Hopkins[3] MD, Aaron M Secrest[2,4] MD PhD

[*]Authors contributed equally

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Limited national data for prescribing of these combination products

Insurance claims analysis found frequent, potentially inappropriate use of clotrimazole-betamethasone dipropionate

- Among >100k adults prescribed clotrimazole-betamethasone dipropionate
  - Only ~30% had a fungal diagnosis
  - ~15% had a diagnostic test
  - Most were prescribed by primary care providers
- Prescribing to children and for intravaginal use was observed
- Highlights opportunities to increase clinician knowledge and promote alternative treatment strategies

Striae of the axillae appeared after using Lotrisone cream continuously for 3 months.

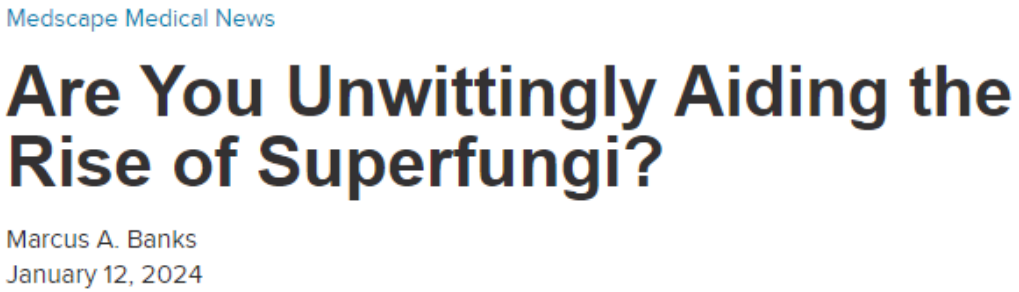
Striae of the groin after long-term use of group V topical steroids for pruritus. These changes are irreversible.

Figure 2-19 Striae, steroid induced.

https://drclementlo.com/refer/index.php/dermatology-habif?view=article&id=240&catid=123

Topical antifungal prescribing is **very** common in the U.S.

- In 2021 Medicare Part D data:
  - ~6.5 million prescriptions for topical antifungals or antifungal-corticosteroids (enough for 1 prescription per every 8 beneficiaries)
  - Most common prescriber types were PCP (40%) and NPs/PAs (21%)
  - Top 10% of prescribers prescribed ~44% of all prescriptions
  - Nearly 1M clotrimazole-betamethasone prescriptions written


Medscape Medical News

Are You Unwittingly Aiding the Rise of Superfungi?

Marcus A. Banks
January 12, 2024

MMWR

Topical Antifungal Prescribing for Medicare Part D Beneficiaries — United States, 2021

Key take homes about antimicrobial-resistant ringworm

- Confirm superficial fungal infections through diagnostic testing, if possible, before starting treatment
- Consider antimicrobial-resistant dermatophyte infection in patients who present with widespread ringworm, particularly when lesions do not improve with first-line topical antifungal agents.
  - Consider in patients with recent international travel, particularly South Asia
- Correct identification of *T. indotineae* requires advanced molecular testing, available at select public health and specialized academic labs.
- Antifungal stewardship efforts are needed to minimize the misuse and overuse of antifungal drugs and corticosteroids, including both prescribed and over the counter formulations.
- More data are needed to understand the burden of antifungal-resistant dermatophyte infections globally.

Case #2

A 33-year-old male presents to an STI clinic in Florida…..

- Chief complaint: scaly rash on genital area

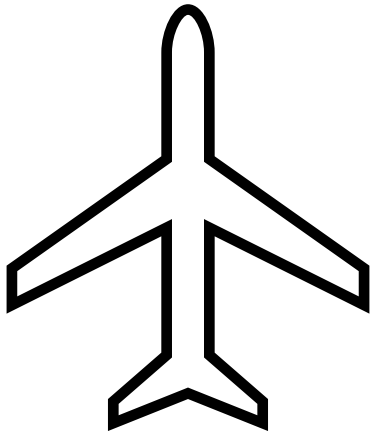
JAMA Network: Potential Sexual Transmission of Tinea Pubogenitalis From TMVII (jamanetwork.com/journals/jamadermatology/article-abstract/2819235)

Past medical history indicates the patient is immunocompetent

- Taking pre-exposure prophylaxis
- No HIV or immunocompromising conditions

Social and travel history

- Traveled to Europe before developing lesions
  - Reported multiple male sexual partners while traveling
  - Visited a sauna 2 months before developing skin lesions
- Reported shaving and waxing the pubic region and denied pet exposure



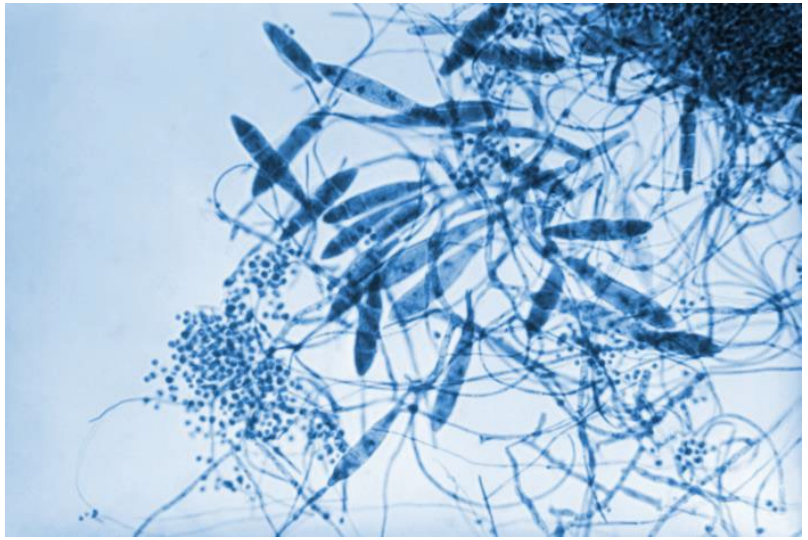
Polling question #3:
What infections would be in your differential at this point? (select all that apply)

- Mpox
- Molluscum contagiosum
- Lice
- Psoriasis
- Contact dermatitis
- Dermatophytosis
- Syphilis

https://wwwnc.cdc.gov/eid/article/29/7/23-0025-f1

You obtain skin scrapings, and the culture grows *T. interdigitale*

- You've recently learned about *T. indotinae*
  - *T. indotinae* can look like *T. interdigitale*, so you send the culture to be sequenced
- You start the patient on oral terbinafine as the patient hasn't tried any antifungals yet



CDC PHIL: Trichophyton mentagrophytes Details (phil.cdc.gov/Details.aspx?pid=22306)

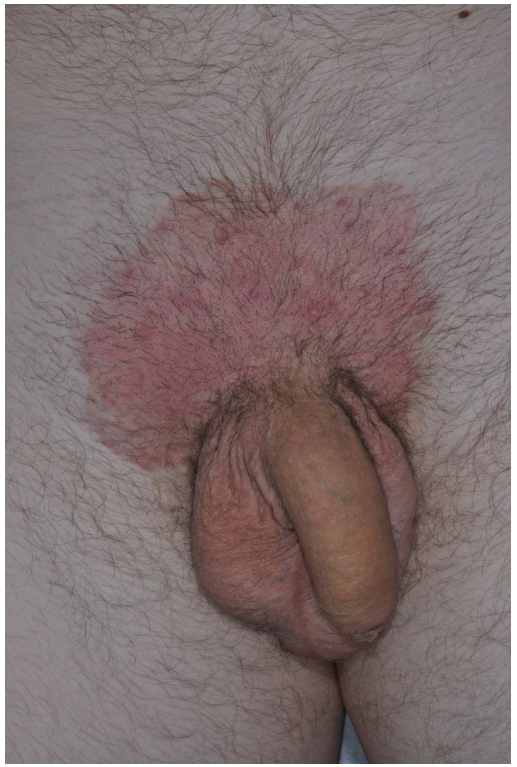
After two weeks, the laboratory reports the culture is *T. mentagrophytes* internal transcribed spacer (ITS) genotype VII (TMVII)

Polling question #4:
Have you heard, suspected, or diagnosed TMVII before? (select all that apply)

- Yes, I have diagnosed TMVII
- Yes, I have suspected that a patient has had TMVII
- Yes, I have heard of TMVII
- No, I have never heard of TMVII

A specific dermatophyte strain (*Trichophyton mentagrophytes* genotype VII [TMVII]) is often implicated in tinea genitalis cases in Europe

- A specific internal transcribed spacer (ITS) genotype of *T. mentagrophytes*, genotype VII (TMVII), was reported for cases of suspected sexual transmission, most frequently tinea genitalis.
- TMVII causes highly inflammatory, painful, and persistent lesions, mostly of the pubogenital area.
- Some reports describe association with sexual tourism in Southeast Asia or with genital shaving.



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4680168/

Figure 1 | Extensive erythematous plaque with numerous papules and pustules and purulent discharge on the mons pubis (tinea genitalis profunda) and annular erythematous macules on the thighs and abdomen (tinea corporis).

https://pubmed.ncbi.nlm.nih.gov/37365896/

Study from France (January 2021–September 2022): "Sexually Transmitted *Trichophyton mentagrophytes* Genotype VII Infection among Men Who Have Sex with Men"

- **Case series, 13 MSM with TMVII infection.**
- **Important case features:**
  - Delayed diagnoses
  - Initial misdiagnosis as bacterial STIs
  - Severe infections requiring hospitalization for pain
  - Scarring, permanent hair loss
  - Prolonged antifungal treatment
  - Resistance to antifungals not noted
    - Patients improved on topical antifungals, terbinafine (first-line oral antifungal for ringworm), itraconazole.

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https://wwwnc.cdc.gov/eid/article/29/7/23-0025-f1

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First case of TMVII identified in U.S. in June 2024

- Recent travel to Europe and within the U.S. prior to lesion development
  - Multiple male sexual partners while traveling
- Started on terbinafine with improvement
  - Switched to itraconazole due to persistent infection

Observation

June 5, 2024

Potential Sexual Transmission of Tinea Pubogenitalis From TMVII

Avrom S. Caplan, MD[1]; Michelle Sikora, BS[1,2]; Arianna Strome, MD[1]; et al

» Author Affiliations | Article Information

JAMA Dermatol. 2024;160(7):783-785. doi:10.1001/jamadermatol.2024.1430

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More epidemiologic and clinical data needed to understand prevalence, risk factors, affected population, optimal treatment

- Current data are limited to case reports and small studies
- Cases of TMVII genital ringworm infection are increasingly being reported in U.S.; vigilance is needed
- Increased laboratory capacity needed to detect unusual ringworm clusters, including emerging species
- Antifungal stewardship important to improve patient outcomes and preserve available treatments

Thank you!

fungaloutbreaks@cdc.gov

Questions?

Center of Excellence Reminders!

Subscribe to Center of Excellence in Newcomer Health Updates (https://public.govdelivery.com/accounts/MNMDH/subscriber/new?topic_id=MNMDH_463) for training announcements and other guidance and resources.

Upcoming trainings at Trainings: Minnesota Center of Excellence in Newcomer Health (www.health.state.mn.us/communities/rih/coe/webinars.html)

NEWCOMER HEALTH

This ECHO series increases medical providers' knowledge of the resettlement and health issues of newcomers, including refugee, immigrant and migrant (RIM) populations.
It reviews resettlement pathways, evidence-based screening recommendations, and more common diagnoses and treatment approaches for pediatric and adult populations.

Sessions include brief didactic presentations by immigrant health experts and discussion of participant-submitted cases. Participants are highly encouraged to submit de-identified patient cases for group discussion and expert consultation.

Project ECHO COLORADO

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ONGOING MONTHLY VIRTUAL SESSIONS
Last Tuesday of the month
8:00 AM PT | 9:00 AM MT | 10:00 AM CT | 11:00 AM ET

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echocolorado.org/echo/newcomer-health/

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UPCOMING SESSIONS

July 30
Hepatitis B and C in Pediatrics

AUGUST 27
Care Coordination - Specialty Care Needs

SEPTEMBER 24
Dermatologic Considerations for Newcomers

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Thank You!

Please remember to complete your evaluation

CareRef

- CareRef is a tool that guides clinicians through conducting a routine post-arrival medical screening of a newly arrived refugee to the U.S.
- Output is based on the current CDC Domestic Refugee Screening Guidance.
- CareRef recommends screening tests and other preventive care based on the demographic and geographic factors that contribute to risk.

CareRef (https://careref.web.health.state.mn.us)