



# A visit to the dentist

**CLINID conference**  
Hunter Ratliff  
03/20/2025

*Ages, dates, and other identifying information may have been changed  
I have no conflict of interest in relation to this presentation*

---

# Case #1

## Case 1: HPI

---

A **27 y/o M** with PMH including poorly controlled DM p/w **chronic groin wound drainage** & **productive cough**

# Case 1: HPI

---

A **27 y/o M** with PMH including poorly controlled DM p/w **chronic groin wound drainage** & **productive cough**

- Tenderness with purulent drainage from wounds
- High blood sugar
- Right sided chest tightness & productive cough
- Ongoing for “months”

# Case 1: HPI

---

A **27 y/o M** with PMH including poorly controlled DM p/w **chronic groin wound drainage** & **productive cough**

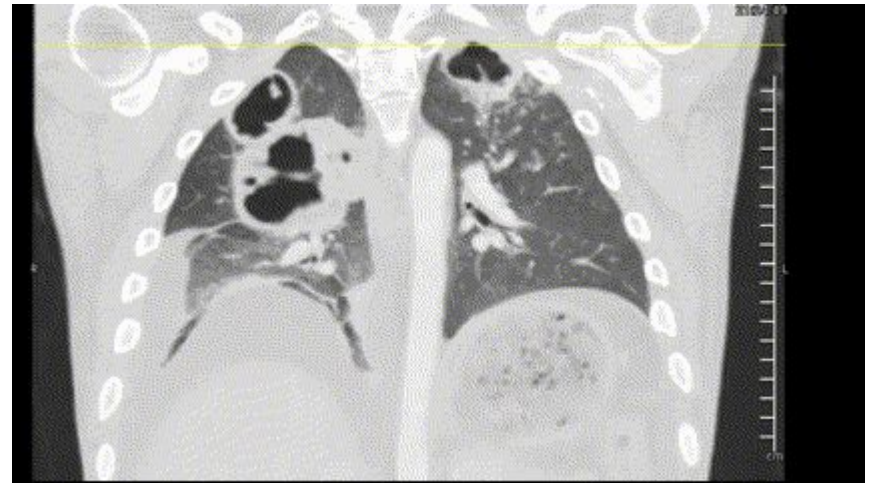
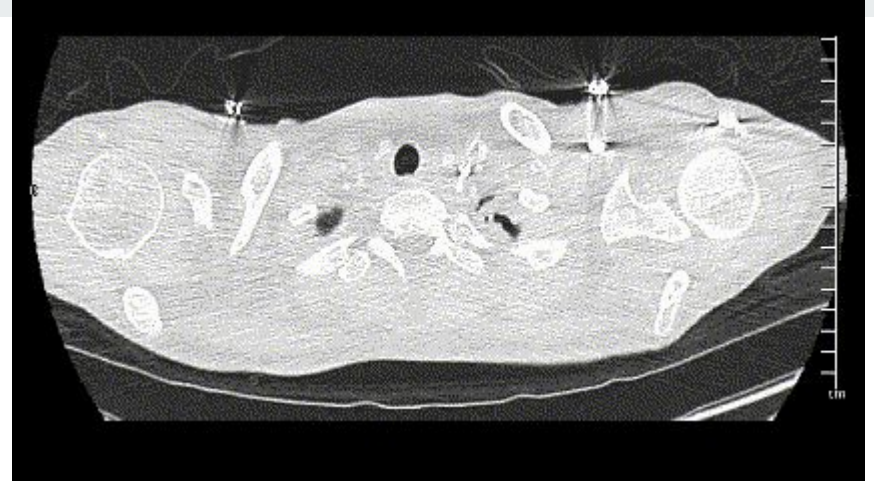
- Tenderness with purulent drainage from wounds
- High blood sugar
- Right sided chest tightness & productive cough
- Ongoing for “months”

## ROS

- No fevers, chills, night sweats
- DOE, but no dyspnea at rest
- Chronic diarrhea

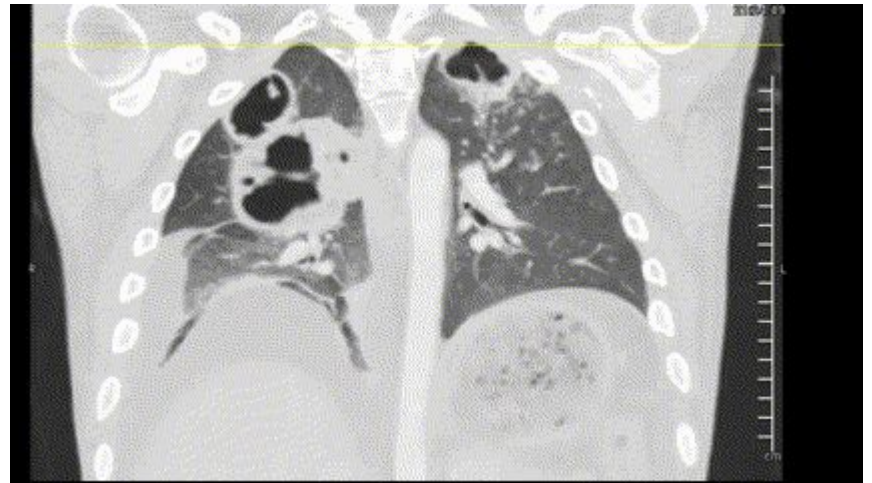
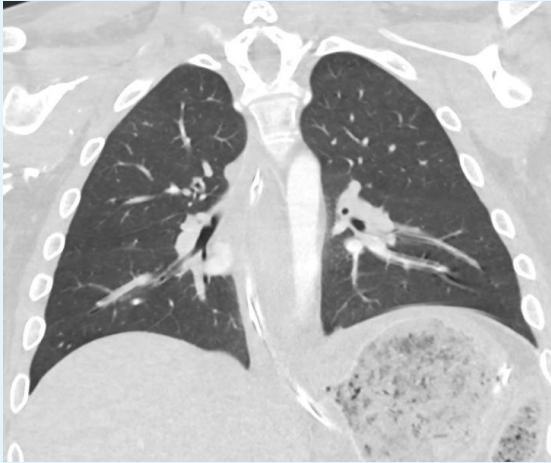
## Case 1: HPI

A **27 y/o M** with PMH including poorly controlled DM p/w **chronic groin wound drainage** & **productive cough**



# Case 1: HPI

Prior CT (5 months ago)



# Case 1: Social & Exposure History

|                                |   |
|--------------------------------|---|
| <b>Geographic &amp; Travel</b> | <ul style="list-style-type: none"><li>• The patient lives in <b>Ohio</b> with parents</li><li>• He denies recent foreign or domestic travel</li></ul>   |
| <b>Occupational</b>            | <ul style="list-style-type: none"><li>• Not working; no hobbies; doesn't do outdoor activities</li></ul>  |
| <b>Substance &amp; needles</b> | <ul style="list-style-type: none"><li>• Denies EtOH (prior ID notes state "alcohol abuse" in problem list)</li><li>• <b>Vapes tobacco</b></li><li>• <b>Smokes weed</b>, no other drugs; never IVDU</li><li>• Remote hx of <b>unprofessional tattoos</b></li></ul> |
| <b>Animals</b>                 | <ul style="list-style-type: none"><li>• No animals (including birds, bats), aside from <b>pet cat</b></li></ul>   |
| <b>Exposures</b>               | <ul style="list-style-type: none"><li>• No TB risk factors</li><li>• No exposures to soil; no dead/decaying wood or vegetation</li><li>• No water exposures (e.g. hot tubs, humidifiers)</li></ul>  |



# Case 1: Physical exam

---

Vitals: BP 102/61 (**on levophed**) | **Pulse 102** | Temp 36.6 °C | SpO2 94% | BMI 25.13 kg/m<sup>2</sup>

Gen: alert and oriented, NAD

Head/Neck: NCAT; trachea appears midline, no gross LAD

ENT: EOMI grossly, anicteric sclerae; **good detention**

Resp: normal respiratory effort, CTAB

CV: RRR; extremities perfused

GI: non-distended; no TTP

Neuro/MSK: moves extremities, CN exam normal

Psych: normal mood; appropriate affect

# Case 1: Chart review

---

## Multiple admissions for DKA

- A1c >15

## 3 months ago: NSTI groin & scrotum

- Done at OSH, so no micro records
- Completed abx while inpatient

## 2.5 months ago: Wheeling for wounds

- No surgical procedures done
- ID saw him there, was on Vanc/Unasyn for 4 days
- Pt declined OPAT
- Sent home on doxy/Augmentin

Micro: Lots of negative blood cultures in recent months

# Case 1: Chart review

---

## Multiple admissions for DKA

- A1c >15

## 3 months ago: NSTI groin & scrotum

- Done at OSH, so no micro records
- Completed abx while inpatient

## 2.5 months ago: Wheeling for wounds

- No surgical procedures done
- ID saw him there, was on Vanc/Unasyn for 4 days
- Pt declined OPAT
- Sent home on doxy/Augmentin

Micro: Lots of negative blood cultures in recent months

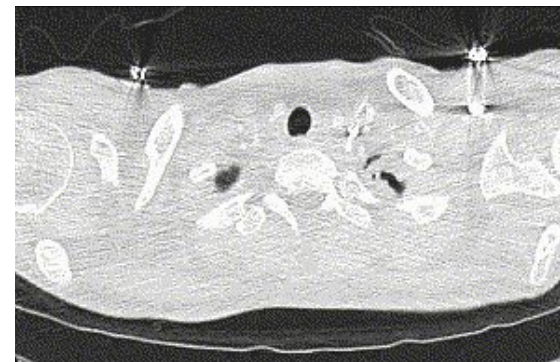
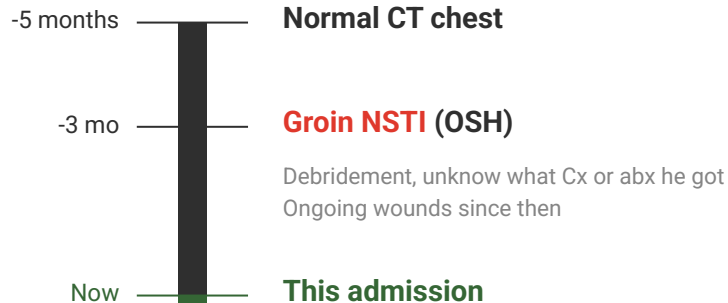
## Hospital course (thus far)

- Admitted to MICU w/ septic shock
- Groin I&D with general surgery
  - Left groin abscess at the site that was spontaneously draining
  - A moderate amount of pus was expressed from abscess
  - No true NSTI (per note)
  - Gram stain: GPC, yeast
- Pulm does bronch in OR
- ID consult on hospital day 2

# Case 1: Summary

A **27 y/o M** with PMH including poorly controlled DM, recent NSTI of groin p/w chronic groin **wound drainage** & **productive cough** and found to have **numerous cavitory lesions**

- ❖ **DDx?**
- ❖ **Workup?**



# Let's place some bets

## Mycobacterial

- Mycobacterium tuberculosis
- NTM: M kansasii, M abscessus, MAC

## Endemic mycoses

- Histo
- Blasto
- Cocci

## Other fungal

- Crypto
- Aspergillus
- Mucor

## Oral & anaerobes

- Streptococcus anginosus group
- Bacteroides, fusobacterium, prevotella



## Necrotizing bacteria

- Staph aureus
- Enterobacterales: Kleb, E cloacae
- Nonfermenters: Pseudomonas, Steno

## Filamentous gram positive rods

- Nocardia
- Actinomyces

# Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  |        |
| Asp PCR |        |
| MTB PCR |        |
| PJP PCR |        |

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      |        |
| Blasto Ag     |        |
| Crypto Ag     |        |
| Fungitell     |        |
| Asp GM        |        |
| uStrep Ag     |        |

| Micro         | Result       |
|---------------|--------------|
| Blood         |              |
| Urine         |              |
| OR (groin)    | GPC<br>Yeast |
| BAL (routine) |              |
| BAL (AFB)     |              |
| BAL (fungal)  |              |

# Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  | Neg    |
| Asp PCR | Neg    |
| MTB PCR | Neg    |
| PJP PCR | Neg    |

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      |        |
| Blasto Ag     |        |
| Crypto Ag     |        |
| Fungitell     |        |
| Asp GM        |        |
| uStrep Ag     |        |

| Micro         | Result       |
|---------------|--------------|
| Blood         |              |
| Urine         |              |
| OR (groin)    | GPC<br>Yeast |
| BAL (routine) |              |
| BAL (AFB)     |              |
| BAL (fungal)  |              |

## Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  | Neg    |
| Asp PCR | Neg    |
| MTB PCR | Neg    |
| PJP PCR | Neg    |

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      | Neg    |
| Blasto Ag     | Neg    |
| Crypto Ag     | ---    |
| Fungitell     | 34     |
| Asp GM        | Neg    |
| uStrep Ag     | Neg    |

| Micro         | Result       |
|---------------|--------------|
| Blood         |              |
| Urine         |              |
| OR (groin)    | GPC<br>Yeast |
| BAL (routine) |              |
| BAL (AFB)     |              |
| BAL (fungal)  |              |



# Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  | Neg    |
| Asp PCR | Neg    |
| MTB PCR | Neg    |
| PJP PCR | Neg    |

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      | Neg    |
| Blasto Ag     | Neg    |
| Crypto Ag     | ---    |
| Fungitell     | 34     |
| Asp GM        | Neg    |
| uStrep Ag     | Neg    |

| Micro         | Result       |
|---------------|--------------|
| Blood         | Neg          |
| Urine         | Neg          |
| OR (groin)    | GPC<br>Yeast |
| BAL (routine) | <b>GNR</b>   |
| BAL (AFB)     |              |
| BAL (fungal)  |              |

# Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  | Neg    |
| Asp PCR | Neg    |
| MTB PCR | Neg    |
| PJP PCR | Neg    |

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      | Neg    |
| Blasto Ag     | Neg    |
| Crypto Ag     | ---    |
| Fungitell     | 34     |
| Asp GM        | Neg    |
| uStrep Ag     | Neg    |

| Micro         | Result  |
|---------------|---|
| Blood         | Neg   |
| Urine         | Neg   |
| OR (groin)    | 4+ <b>Mixed GP &amp; GN</b><br>4+ <b>Strep Anginosus</b><br>3+ <b>CONS</b><br>2+ <b>C albicans</b><br>1+ <b>Proteus mirabilis</b> |
| BAL (routine) | <b>GNR</b> (gram stain)   |
| BAL (AFB)     |   |
| BAL (fungal)  |   |

## Case 1: Workup

| BAL     | Result |
|---------|--------|
| Asp GM  | Neg    |
| Asp PCR | Neg    |
| MTB PCR | Neg    |
| PJP PCR | Neg    |

| Serum / Urine    | Result        |
|------------------|---------------|
| Histo Ag         | Neg           |
| Blasto Ag        | Neg           |
| <b>Crypto Ag</b> | <b>1:1280</b> |
| Fungitell        | 34            |
| Asp GM           | Neg           |
| uStrep Ag        | Neg           |

| Micro         | Result   |
|---------------|--|
| Blood         | Neg  |
| Urine         | Neg  |
| OR (groin)    | 4+ Mixed GP & GN organisms<br>4+ <b>Strep Anginosus</b><br>3+ <b>CONS</b><br>2+ <b>C albicans</b><br>1+ <b>Proteus mirabilis</b> |
| BAL (routine) | >100k cfu <b>Kleb pneumo</b><br><b>Mucoid kleb</b> in the lab  |
| BAL (AFB)     | Neg  |
| BAL (fungal)  | Neg  |

## Case 1: Workup

| Micro         | Result   |
|---------------|--|
| Blood         | Neg  |
| Urine         | Neg  |
| OR (groin)    | 4+ Mixed GP & GN organisms<br>4+ <b>Strep Anginosus</b><br>3+ <b>CONS</b><br>2+ <b>C albicans</b><br>1+ <b>Proteus mirabilis</b> |
| BAL (routine) | >100k cfu <b>Kleb pneumo</b><br><b>Mucoid kleb</b> in the lab  |
| BAL (AFB)     | Neg  |
| BAL (fungal)  | Neg  |

| Date of CrAG | Titer           |
|--------------|-----------------|
| Day 2        | <b>1 : 1280</b> |
| Day 3        | <b>1 : 320</b>  |

4 fold  
decrease



HIV: negative  
CD4: 780 (56%, ratio 2.0)

## Case 1: Workup

| Micro         | Result   |
|---------------|--|
| Blood         | Neg  |
| Urine         | Neg  |
| OR (groin)    | 4+ Mixed GP & GN organisms<br>4+ <b>Strep Anginosus</b><br>3+ <b>CONS</b><br>2+ <b>C albicans</b><br>1+ <b>Proteus mirabilis</b> |
| BAL (routine) | >100k cfu <b>Kleb pneumo</b><br><b>Mucoid kleb</b> in the lab  |
| BAL (AFB)     | Neg  |
| BAL (fungal)  | Neg  |

| Date of CrAG | Titer           |
|--------------|-----------------|
| Day 2        | <b>1 : 1280</b> |
| Day 3        | <b>1 : 320</b>  |

| LP                      | Result                  |
|-------------------------|-------------------------|
| Opening Pr (cm H2O)     | 13                      |
| WBC (Neut, lymph)       | <b>50</b><br>(56%, 40%) |
| RBC                     | <b>875</b>              |
| Pro / Glu               | 40 / 131                |
| Biofire                 | Neg                     |
| Cx (routine/AFB/fungal) | Neg                     |
| India ink               | Neg                     |
| Crypto Ag               | Neg                     |

# Case 1: Next steps

A **27 y/o M** with PMH including **poorly controlled DM**, recent NSTI of groin p/w chronic groin **wound drainage** & productive cough and found to have **numerous cavitory lesions** that have grown mucoid **kleb pneumo**, but **serum CrAG** was also strongly positive

- ❖ Is this **kleb** or **crypto** (or **both**)?
- ❖ What do you do for **treatment**?

| Micro         | Result   |
|---------------|--|
| Blood         | Neg  |
| OR (groin)    | 4+ Mixed GP & GN organisms<br>4+ <b>Strep Anginosus</b><br>3+ <b>CONS</b><br>2+ <b>C albicans</b><br>1+ <b>Proteus mirabilis</b> |
| BAL (routine) | >100k cfu <b>Kleb pneumo</b><br><b>Mucoid kleb</b> in the lab  |
| BAL (fungal)  | Neg  |

| Date of CrAG | Titer           | W/O treatment |
|--------------|-----------------|---------------|
| Day 2        | <b>1 : 1280</b> | ←             |
| Day 3        | <b>1 : 320</b>  |               |

# Case 1: Hospital course

---

- Asked for **TTE** (normal), **CD4** (780, 56%, ratio 2.0)
- Initially on **Zyvox + Zosyn** (for NSTI) → **Unasyn**
- After LP was done, added **fluconazole 400**
- Signed off:
  - **Unasyn** → **Augmentin** x6 weeks (w/ repeat imaging)
  - **Fluconazole** (for 6 months?)

# Case 1: Hospital course

---

- Asked for **TTE** (normal), **CD4** (780, 56%, ratio 2.0)
- Initially on **Zyvox + Zosyn** (for NSTI) → **Unasyn**
- After LP was done, added **fluconazole 400**
- Signed off:
  - **Unasyn** → **Augmentin** x6 weeks (w/ repeat imaging)
  - **Fluconazole** (for 6 months?)
- Worsening **pleural effusion**, got chest tube
  - Pleural fluid also grew **kleb pneumo** again
- Started heading towards **neutropenia on Unasyn**
  - Switched to **ceftriaxone + Flagyl** → **cefpodoxime + Flagyl**
  - Still on **fluconazole**



# Discussion

---



Links to articles discussed  
here



---

# Hypermucoviscous *Klebsiella* *pneumoniae* (HmKp)

- Define HmKp and **distinguish it from classical *Klebsiella pneumoniae*** based on genetic & virulence factors
- Analyze the **geographic distribution of HmKp** highlighting its emergence as a global pathogen
- Recognize the **unique clinical manifestations of HmKp infections** and differences in disease severity compared to classical *Klebsiella pneumoniae* infections

# HmKp: What is it? [1.1]

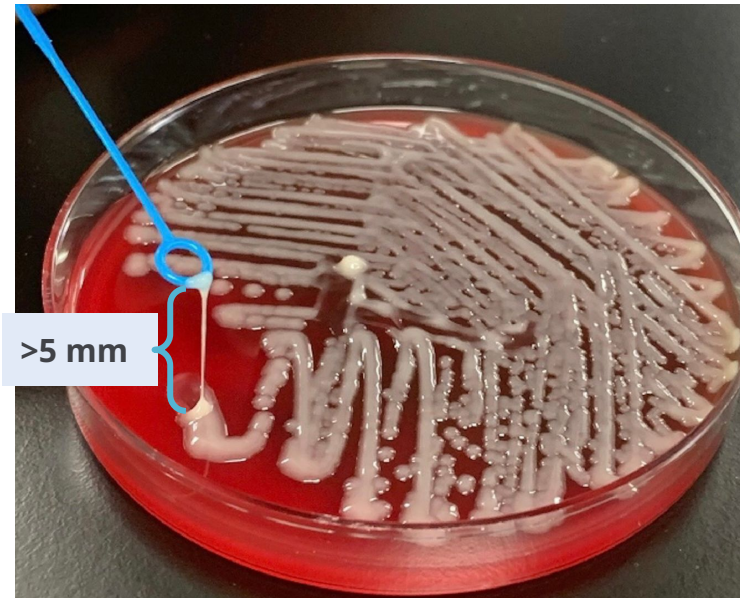
---

**Hypermucoviscous *Klebsiella pneumoniae*** (HmKp) is a phenotype of *K pneumoniae* that produces a thick, mucoid capsule

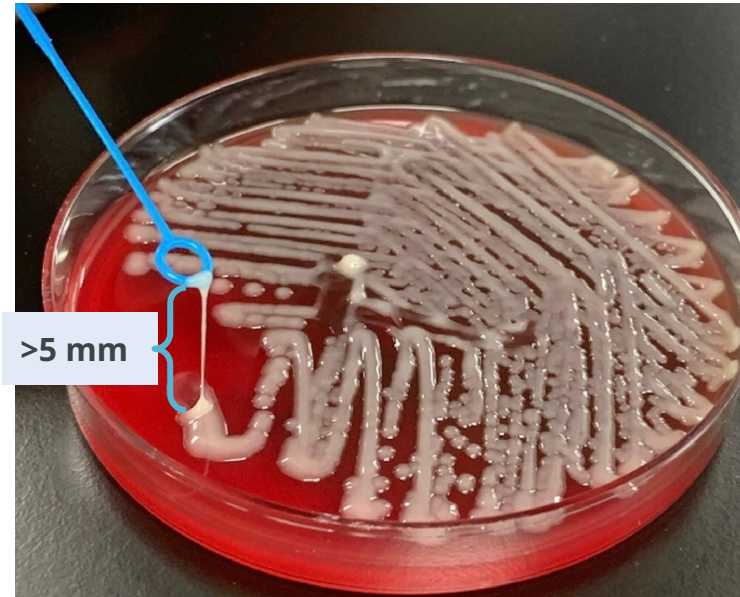
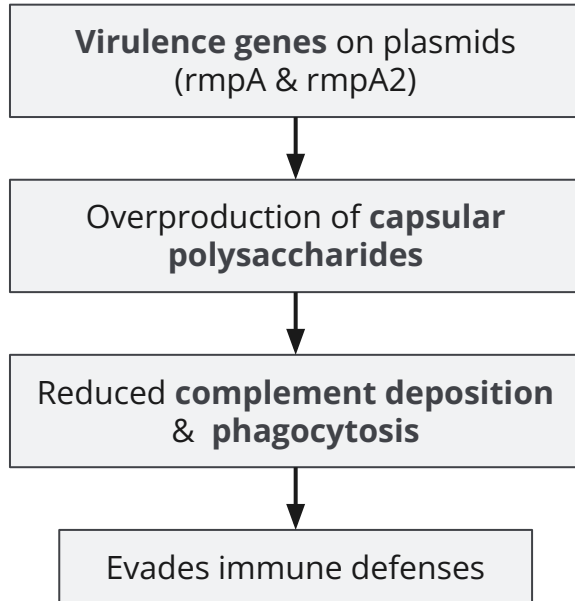
# HmKp: What is it? [1.1]

**Hypermucoviscous *Klebsiella pneumoniae* (HmKp)** is a phenotype of *K pneumoniae* that produces a thick, mucoid capsule

- Identified with the **string test**
  - Stretches over 5mm with an inoculation loop



# HmKp: What is it? [1.1]



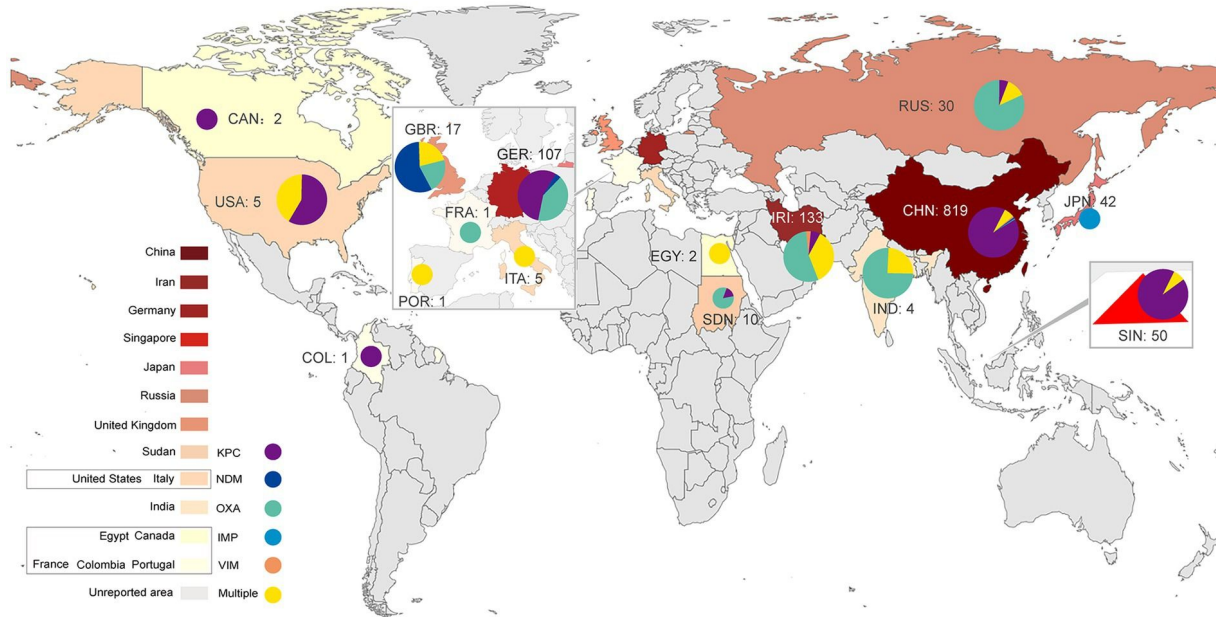
## HmKp: Who gets it? [1.1][1.2]

---

- Initial identified in **East/Southeast Asia**, but **spreading world wide**
- More often **community acquired** (as opposed to other strains of *K pneumo*)
  - Often younger, healthier folks
  - Immunosuppression isn't major risk factor, with the **exception of diabetes**

# HmKp: Who gets it? [1.3]

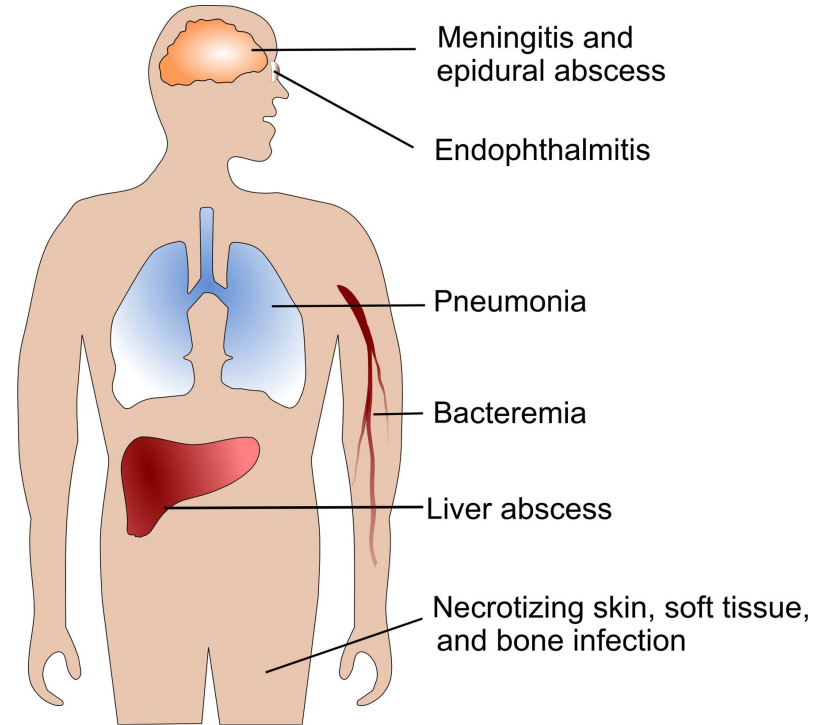
May be associated with **extensive antimicrobial resistance**, especially **internationally**



**Figure 1** [1.3]:  
Global distribution of CR-hvKP (2015–2022)

# HmKp: Clinical manifestations [1.1][1.4]

- High risk for **metastatic spread** (12-28%)
- Classically: **liver abscess in healthy adults**
- Most common sites
  - Meningitis
  - Pleural empyema
  - Endophthalmitis
- Many reports with NSTIs (as was maybe our case)
- Has been reported to seed almost anywhere



**Figure 1 [1.4]:** Common sites of primary and metastatic infections caused by hvKp





# Evidence Bayes'ed medicine

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

- Review **Bayes' theorem and its applications** (without talking too much about math)
- Highlight the key relationship between **pre-test probability and testing characteristics** (sensitivity, specificity)

# Bayes theorem

---

- Named after Thomas Bayes
- Law of conditional probability

## Bayes Theorem

$$P(A | B) = \frac{P(B | A) P(A)}{P(B)}$$

# Bayes theorem

---

- **Posterior:** Probability the “hypothesis” being true, given observed “evidence”

## Bayes Theorem

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

**H** = hypothesis

**E** = evidence

**A | B** = means “A given B”

# Bayes theorem

- **Posterior**: Probability the “hypothesis” being true, given observed “evidence”
- **Likelihood**: Probability that “evidence” occurs if “hypothesis” is true

## Bayes Theorem

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

**H** = hypothesis

**E** = evidence

**A | B** = means “A given B”

# Bayes theorem

- **Posterior:** Probability the “hypothesis” being true, given observed “evidence”
- **Likelihood:** Probability that “evidence” occurs if “hypothesis” is true
- **Prior:** The pre-test probability the “hypothesis” is true

## Bayes Theorem

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

**H** = hypothesis

**E** = evidence

**A | B** = means “A given B”

# Bayes theorem

- **Posterior:** Probability the “hypothesis” being true, given observed “evidence”
- **Likelihood:** Probability that “evidence” occurs if “hypothesis” is true
- **Prior:** The pre-test probability the “hypothesis” is true
- **Evidence:** The probability of the “evidence” occurring (regardless of “hypothesis”)

## Bayes Theorem

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

**H** = hypothesis

**E** = evidence

**A | B** = means “A given B”

# The good news

You don't need to do the math!

The important takeaway is that the **chance our hypothesis is right, given the evidence** is *equally* influenced by of **BOTH**

- The **quality of the test** (e.g. sensitivity, specificity)
- The **pre-test probability** (e.g. the base rate)

## Bayes Theorem

$$P(H | E) = \frac{P(E | H) P(H)}{P(E)}$$

**Posterior:** Probability the “hypothesis” being true, given observed “evidence”

**Likelihood:** Probability that “evidence” occurs if “hypothesis” is true

**Prior:** The pre-test probability the “hypothesis” is true

**Evidence:** The probability of the “evidence” occurring

# What the pre-test probability?



How often would you expect this to be caused by cryptococcus?

- One in 10?
- One in 20?
- One in 50?
- One in 100?
- One in 1000?

A **27 y/o M** with PMH including **poorly controlled DM**, recent NSTI of groin was found to have **numerous cavitory lesions**

- BAL: **Kleb pneumo**
- No risk factors for Cryptococcus
- No fungal growth or yeast on slides



# Serum cryptococcal antigen

| Serum    |          | CrAg EIA |          |
|----------|----------|----------|----------|
|          |          | Positive | Negative |
| CrAg LFA | Positive | 96       | 7        |
|          | Negative | 0        | 94       |

**Sensitivity** =  $96 / (96 + 0) = 100\%$

**Specificity** =  $94 / (94 + 7) = 93.1\%$

|      |          | Disease   |           |
|------|----------|-----------|-----------|
|      |          | Positive  | Negative  |
| Test | Positive | True Pos  | False Pos |
|      | Negative | False Neg | True Neg  |

Sensitivity =  $TP / (TP + FN)$

Specificity =  $TN / (TN + FP)$

# Serum cryptococcal antigen

| Serum    |          | CrAg EIA |          |
|----------|----------|----------|----------|
|          |          | Positive | Negative |
| CrAg LFA | Positive | 96       | 7        |
|          | Negative | 0        | 94       |

## Likelihood ratio

$LR+ = \text{sensitivity} / (1 - \text{specificity})$

$LR+ = \text{Pr}(T+ | D+) / \text{Pr}(T+ | D-)$

$LR+ = 1 / (1 - .931) = 14.5$

Sensitivity =  $96 / (96 + 0) = 100\%$

Specificity =  $94 / (94 + 7) = 93.1\%$

# Post-test probability



How often would you expect this to be caused by cryptococcus?

- One in 10?
- One in 20?
- One in 50?
- One in 100?
- One in 1000?

# Post-test probability



How often would you expect this to be caused by cryptococcus?

- One in 10?
- One in 20?
- One in 50?
- One in 100?
- One in 1000?

Among 44 cryptococcosis patients with DM2 as the only identifiable risk factor for disease, the annual incidence of cryptococcosis was 0.001% (**1 in a thousand**), with a prevalence of 0.002%. [1.5]

**Sensitivity:**

0 % 100 %

0 10 20 30 40 50 60 70 80 90 100

**Specificity:**

0 % 93 %

0 10 20 30 40 50 60 70 80 90 100

**Set Prevalence**

Disease prevalence: 1 per 1,000 (0%)

**Numerator**

1 affected 100 affected

0 10 20 30 40 50 60 70 80 90 100

**Denominator**

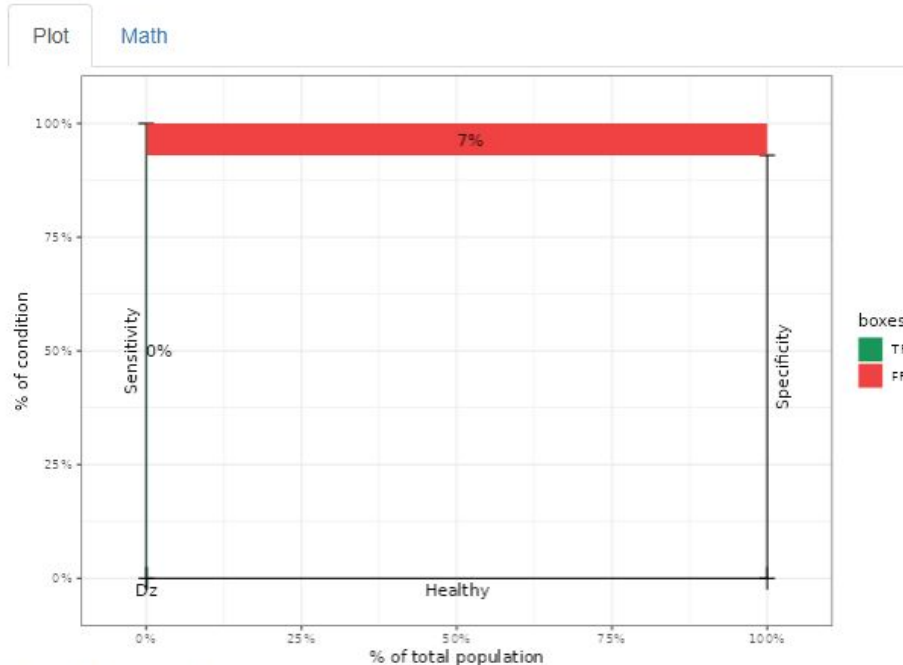
Per 1,000 ▼

## 2 x 2 table

|          | Has Disease | No Disease |
|----------|-------------|------------|
| Test (+) | TP: 0%      | FP: 7%     |
| Test (-) | FN: 0%      | TN: 93%    |

## Positive Predictive Value

Among those who test positive, 1% will actually have the disease



## Show which cases?

- Both  Test positive  Test negative

**Sensitivity:**

0 % 100 %

0 10 20 30 40 50 60 70 80 90 100

**Specificity:**

0 % 93 %

0 10 20 30 40 50 60 70 80 90 100

**Set Prevalence**

Disease prevalence: 10 per 100 (10%)

**Numerator**

10 affected 100 affected

0 10 20 30 40 50 60 70 80 90 100

**Denominator**

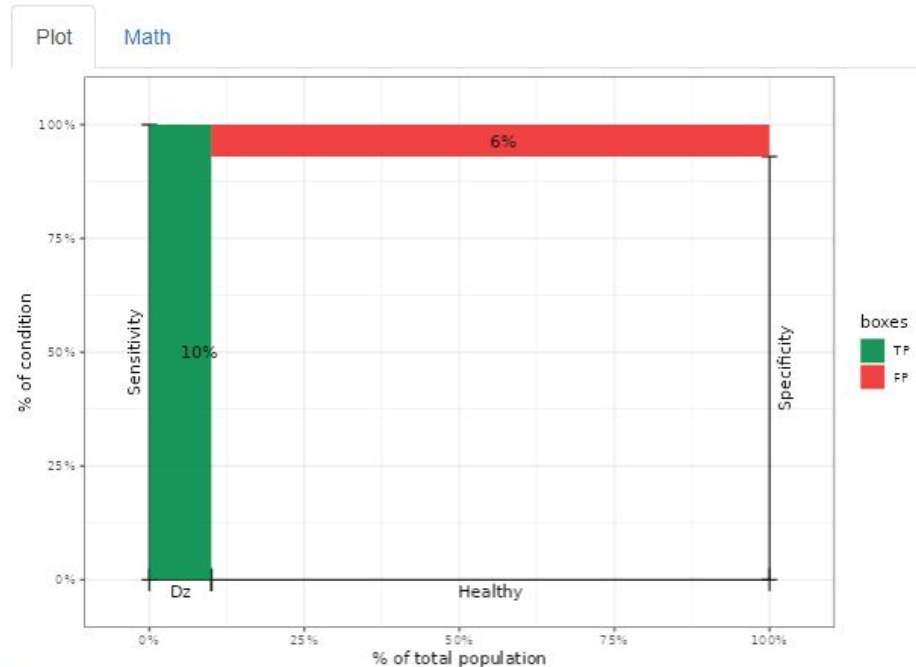
Per 100 population ▼

## 2 x 2 table

|          | Has Disease | No Disease |
|----------|-------------|------------|
| Test (+) | TP: 10%     | FP: 6%     |
| Test (-) | FN: 0%      | TN: 84%    |

## Positive Predictive Value

Among those who test positive, **61%** will actually have the disease



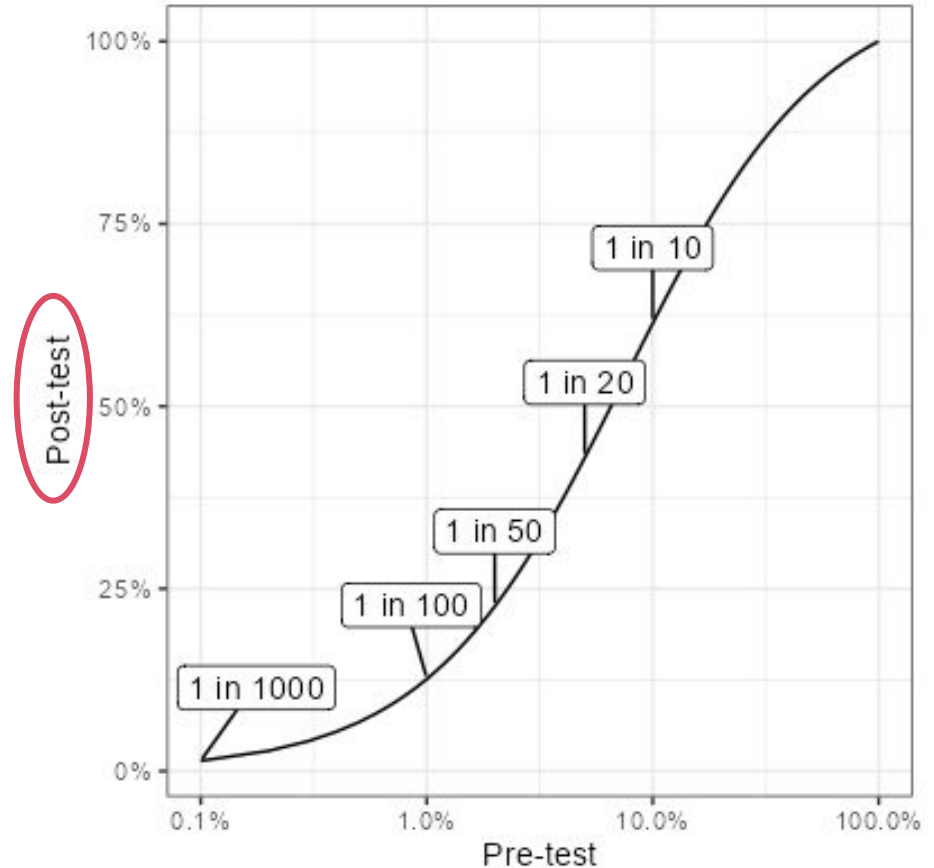
## Show which cases?

Both  Test positive  Test negative

# Post-test probability

How often would you expect this to be caused by cryptococcus?

- One in 10? **Pr(post) = 61.7%**
- One in 20? **Pr(post) = 43.2%**
- One in 50? **Pr(post) = 22.8%**
- One in 100? **Pr(post) = 12.8%**
- One in 1000? **Pr(post) = 1.4%**



---

# Case #2



## Case 2: HPI

A 22 y/o M with no PMH who p/w **subacute cough**

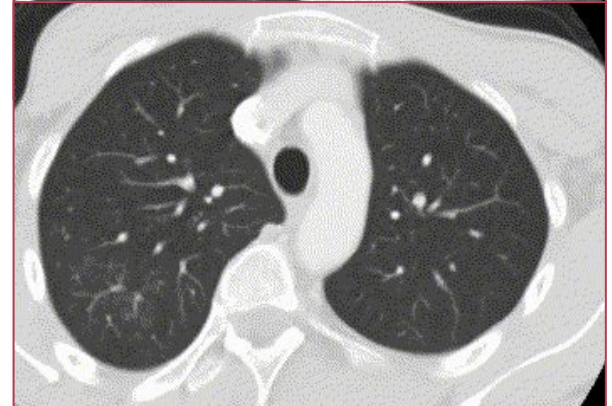
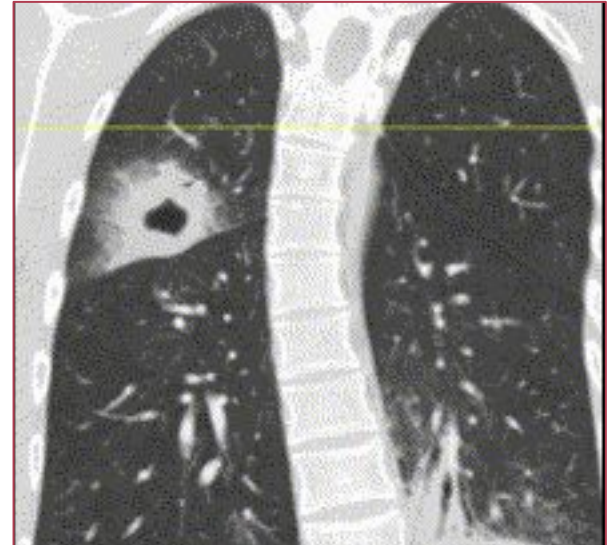
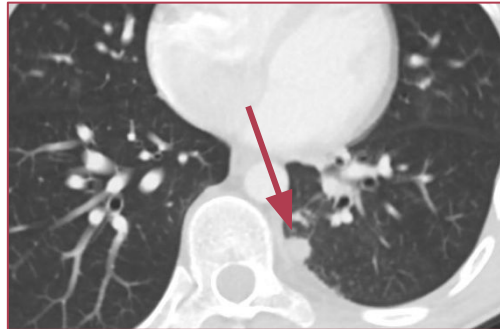


## Case 2: HPI

A **22 y/o M** with no PMH who p/w **subacute cough**

### CT chest impression

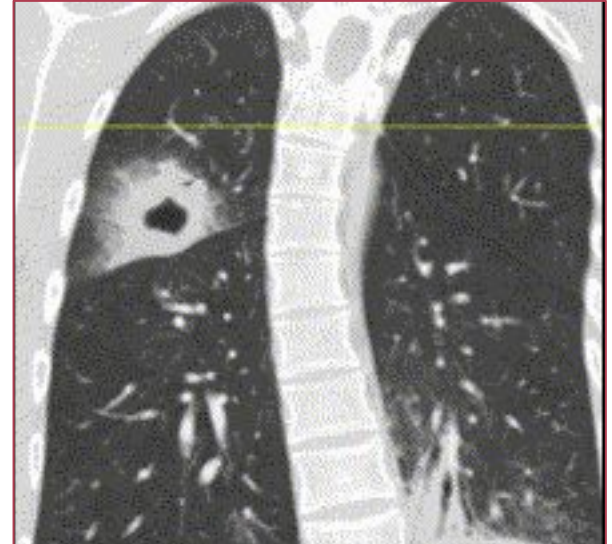
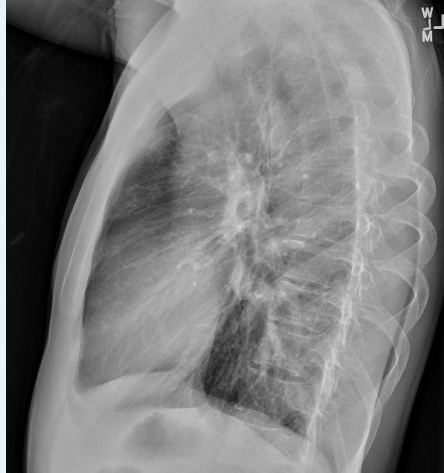
- Ill-defined **4 cm** thick-walled cavitary mass **posterior RUL**
- **10 mm** round subpleural nodule **posterior medial LLL**



## Case 2: HPI

A **22 y/o M** with no PMH who p/w **subacute cough**

Prior XR (14 months ago)



## Case 2: HPI

---

A **22 y/o M** with no PMH who p/w **subacute cough**

- **4 weeks ago: sore throat** → **fevers, cough**, anorexia
- After **7-10 days**, still having **productive cough**
  - But **all other symptoms resolved**
  - **Never took antibiotics**
- Went to urgent care due to cough
  - Obtained CXR → Sent to ED





## Case 2: HPI

---

A **22 y/o M** with no PMH who p/w **subacute cough**

- **4 weeks ago**: sore throat → **fevers, cough**, anorexia
- After **7-10 days**, still having productive cough
  - But **all other symptoms resolved**
  - Never took antibiotics
- Went to urgent care due to cough
  - Obtained CXR → Sent to ED
  
- **Cracked a tooth 4 years ago**, but **no new symptoms**
- Had routine dental cleaning (**2 weeks ago**)
  - This was well after onset of fever & cough
  - Says **exam & X-rays** were normal



## Case 2: Social & Exposure History

### Geographic & Travel

- The patient lives in **Tennessee** (between Nashville & Memphis) for **past year**
  - Before that, lived in **Washington state** for **a few years**
- Visits parents in **Morgantown** frequently
- A **few months ago**, some time in **northern California** for a family reunion
- Has driven through the **Southwest states** (Arizona, Texas), but did not spend much time there
- Only **international travel** has been to **Canada** (Alberta/BC area)

## Case 2: Social & Exposure History

|                                       |   |                                       |   |
|---------------------------------------|---|---------------------------------------|---|
| <p><b>Geographic &amp; Travel</b></p> | <ul style="list-style-type: none"> <li>The patient lives in <b>Tennessee</b> (between Nashville &amp; Memphis) for <b>past year</b> <ul style="list-style-type: none"> <li>Before that, lived in <b>Washington state</b> for <b>a few years</b></li> </ul> </li> <li>Visits parents in <b>Morgantown</b> frequently</li> <li>A <b>few months ago</b>, some time in <b>northern California</b> for a family reunion</li> <li>Has driven through the <b>Southwest states</b> (Arizona, Texas), but did not spend much time there</li> <li>Only <b>international travel</b> has been to <b>Canada</b> (Alberta/BC area)</li> </ul> |                                       |   |
| <p><b>Environmental exposures</b></p> | <ul style="list-style-type: none"> <li>Did live in house with <b>?mold</b></li> <li>No <b>caves, landscaping, wood,</b> or <b>dust/dirt/soil</b> exposure</li> <li>Helping parents with their <b>house renovations</b></li> </ul>   | <p><b>Occupational</b></p>            | <ul style="list-style-type: none"> <li>Doordash driver in TN</li> </ul>                                   |
|                                       |   | <p><b>Substance &amp; needles</b></p> | <ul style="list-style-type: none"> <li>NoEtOH, tobacco, drugs</li> <li>No tattoos or piercings</li> </ul> |
|                                       |   | <p><b>TB</b></p>                      | <ul style="list-style-type: none"> <li><b>No TB</b> risk factors</li> </ul>                               |

## Case 2: Social & Exposure History

|                                       |   |                                       |   |
|---------------------------------------|---|---------------------------------------|---|
| <p><b>Geographic &amp; Travel</b></p> | <ul style="list-style-type: none"> <li>The patient lives in <b>Tennessee</b> (between Nashville &amp; Memphis) for <b>past year</b> <ul style="list-style-type: none"> <li>Before that, lived in <b>Washington state</b> for <b>a few years</b></li> </ul> </li> <li>Visits parents in <b>Morgantown</b> frequently</li> <li>A <b>few months ago</b>, some time in <b>northern California</b> for a family reunion</li> <li>Has driven through the <b>Southwest states</b> (Arizona, Texas), but did not spend much time there</li> <li>Only <b>international travel</b> has been to <b>Canada</b> (Alberta/BC area)</li> </ul> |                                       |   |
| <p><b>Environmental exposures</b></p> | <ul style="list-style-type: none"> <li>Did live in house with <b>?mold</b></li> <li>No <b>caves, landscaping, wood, or dust/dirt/soil</b> exposure</li> <li>Helping parents with their <b>house renovations</b></li> </ul>  | <p><b>Occupational</b></p>            | <ul style="list-style-type: none"> <li>Doordash driver in TN</li> </ul>                                   |
|                                       |   | <p><b>Substance &amp; needles</b></p> | <ul style="list-style-type: none"> <li>NoEtOH, tobacco, drugs</li> <li>No tattoos or piercings</li> </ul> |
|                                       |   | <p><b>TB</b></p>                      | <ul style="list-style-type: none"> <li><b>No TB</b> risk factors</li> </ul>                               |
| <p><b>Animals</b></p>                 | <ul style="list-style-type: none"> <li><b>Rodent exposure</b> (cleaned <b>mouse feces</b>) w/o appropriate PPE</li> <li>While working as delivery driver, <b>he pet a cat</b> on the street (unclear if feral)</li> <li>Otherwise, <b>no other animal exposures</b> (including <b>birds, bats</b>, pets)</li> </ul>   |                                       |   |



## Case 2: Exam & initial labs

---

Vitals: BP 100/57 | Pulse 62 | Temp 37.1 °C | SpO2 98% | BMI 18 kg/m<sup>2</sup>

Gen: alert and oriented, NAD, physically fit

ENT: EOMI grossly, anicteric sclerae, MMM; **good detention**

Resp: normal respiratory effort, CTAB

CV: RRR

GI: no TTP

Neuro/MSK: moves extremities

**CBC w/ diff**: Normal

**BMP**: Normal

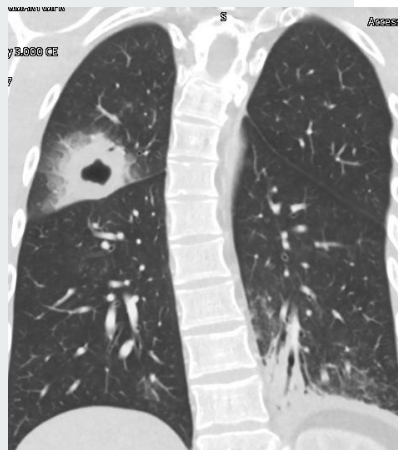
**LFTs**: Not available

**HIV**: Negative

# Case 2: Summary

A **22 y/o M** with no PMH who p/w **subacute cough** x 1 month

- New 4cm RUL cavity, 1cm LLL nodule (vs XR 14 mo ago)
- Lots of fun travel & exposures
- Some dental issues?
- HIV negative



-3 years

## Living in **Washington State**

- Lived in a house with “mold”
- International travel to British Columbia

-1 year

## Moved to **Tennessee**

- Normal CXR around this time
- Travel to **northern California**
- Did cross **country trips** too
- House renovations (in WV)

-1 month

## **Fever, cough, sore throat**

Self resolved after 7-10 days

-3 weeks

## **Symptoms gone aside from cough**

Did go to the dentist

Now

## **Admission**

# Let's place some bets

## Mycobacterial

- Mycobacterium tuberculosis
- NTM: M kansasii, M abscessus, MAC

## Endemic mycoses

- Histo
- Blasto
- Cocci

## Other fungal

- Crypto
- Aspergillus
- Mucor

## Oral & anaerobes

- Streptococcus anginosus group
- Bacteroides, fusobacterium, prevotella



## Necrotizing bacteria

- Staph aureus
- Klebsiella pneumoniae
- Pseudomonas, E cloacae, Steno

## Filamentous gram positive rods

- Nocardia
- Actinomyces

## Case 2: Workup

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      |        |
| Blasto Ag     |        |
| Crypto Ag     |        |
| Fungitell     |        |
| Asp GM        |        |
| Strep Ag      |        |
| Legionella Ag |        |
| QuantGOLD     |        |

| BAL            | Result |
|----------------|--------|
| Asp GM         |        |
| Asp PCR        |        |
| MTB PCR        |        |
| PJP PCR        |        |
| Legionella DNA |        |

| Micro         | Result |
|---------------|--------|
| Blood         |        |
| BAL (routine) |        |
| BAL (AFB)     |        |
| BAL (fungal)  |        |

## Case 2: Workup

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      | Neg    |
| Blasto Ag     | Neg    |
| Crypto Ag     | Neg    |
| Fungitell     | <31    |
| Asp GM        | Neg    |
| Strep Ag      | Neg    |
| Legionella Ag | Neg    |
| QuantGOLD     | Neg    |

| BAL            | Result |
|----------------|--------|
| Asp GM         | Neg    |
| Asp PCR        | Neg    |
| MTB PCR        | Neg    |
| PJP PCR        | Neg    |
| Legionella DNA | Neg    |

| Micro         | Result |
|---------------|--------|
| Blood         | NG     |
| BAL (routine) | NG     |
| BAL (AFB)     | NG     |
| BAL (fungal)  | NG     |

**Any other tests?**

## Case 2: Workup

| Serum / Urine | Result |
|---------------|--------|
| Histo Ag      | Neg    |
| Blasto Ag     | Neg    |
| Crypto Ag     | Neg    |
| Fungitell     | <31    |
| Asp GM        | Neg    |
| Strep Ag      | Neg    |
| Legionella Ag | Neg    |
| QuantGOLD     | Neg    |

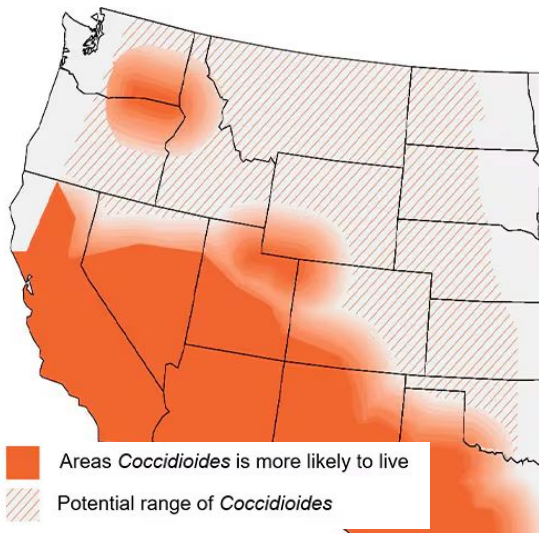
| BAL            | Result |
|----------------|--------|
| Asp GM         | Neg    |
| Asp PCR        | Neg    |
| MTB PCR        | Neg    |
| PJP PCR        | Neg    |
| Legionella DNA | Neg    |

| Micro         | Result |
|---------------|--------|
| Blood         | NG     |
| BAL (routine) | NG     |
| BAL (AFB)     | NG     |
| BAL (fungal)  | NG     |

**K**ARIUS?

Any other tests?

# Case 2: Workup



Areas *Coccidioides* is more likely to live  
 Potential range of *Coccidioides*

| BAL            | Result |
|----------------|--------|
| Asp GM         | Neg    |
| Asp PCR        | Neg    |
| MTB PCR        | Neg    |
| PJP PCR        | Neg    |
| Legionella DNA | Neg    |

| Micro         | Result |
|---------------|--------|
| Blood         | NG     |
| BAL (routine) | NG     |
| BAL (AFB)     | NG     |
| BAL (fungal)  | NG     |

-3 years

## Living in Washington State

- Lived in a house with "mold"
- International travel to British Columbia

## Coccidioides antibody, serum

**Complement fixation**  
Antibody detected (**1:2**)

**Immunodiffusion**  
Antibody not detected

## Case 2: Workup

---

### Complement fixation

Antibody detected (**1:2**)

All serum titers  $\geq 1:2$  should be **considered evidence indicative of coccidioidomycosis**, although **titers of 1:2 and 1:4 should be confirmed by immunodiffusion testing**. Titers exceeding 1:16 usually reflect disseminated disease. In general, higher titers are correlated with disease severity, and changes in serial titers are of prognostic value.

A **negative CF test does not**, however, **rule out diagnosis**. Only **70% of patients with cavitary diseases are positive**, and only **30% of patients with nodular disease are positive**.

### Immunodiffusion

Antibody not detected

The immunodiffusion (ID) procedure correlates both in sensitivity and clinical utility with the CF test. The ID test, which **detects IgG** directed to the "F" antigen, becomes positive within 4 weeks after infection and remains **positive throughout clinically active disease**. **It is most useful in confirming the specificity of low CF titers**, where lines of identity are formed with reference antisera. Positive ID reactions are diagnostic for coccidioidomycosis and usually indicate active or recent disease and remain detectable for up to 1 year thereafter.



# Case 2: Workup

## Complement fixation

Antibody detected (1:2)

All serum titers  $\geq 1:2$  should be **considered evidence indicative of coccidioidomycosis**, although **titers of 1:2 and 1:4 should be confirmed by immunodiffusion testing**. Titers exceeding 1:16 usually reflect disseminated disease. Titers of 1:2 and 1:4 are associated with disseminated disease, and titers of 1:2 are of particular significance in patients with no other explanation.

A **negative** complement fixation test can **rule out** coccidioidomycosis in patients with no other explanation.

Prior XR (14 months ago)



## Immunodiffusion

Antibody not detected

The immunodiffusion (ID) procedure correlates both in sensitivity and clinical utility with the CF test. The ID test, which **detects IgG** directed to the "F" antigen, becomes positive within 4 weeks after infection and remains **positive throughout clinically active disease**. It is **most useful in confirming the specificity of low CF titers**, where lines of identity are formed with reference antisera. Positive ID reactions are diagnostic for coccidioidomycosis and **usually indicate active or recent disease and remain detectable for up to 1 year** thereafter.

# Coccidioides

---



Links to articles discussed  
here

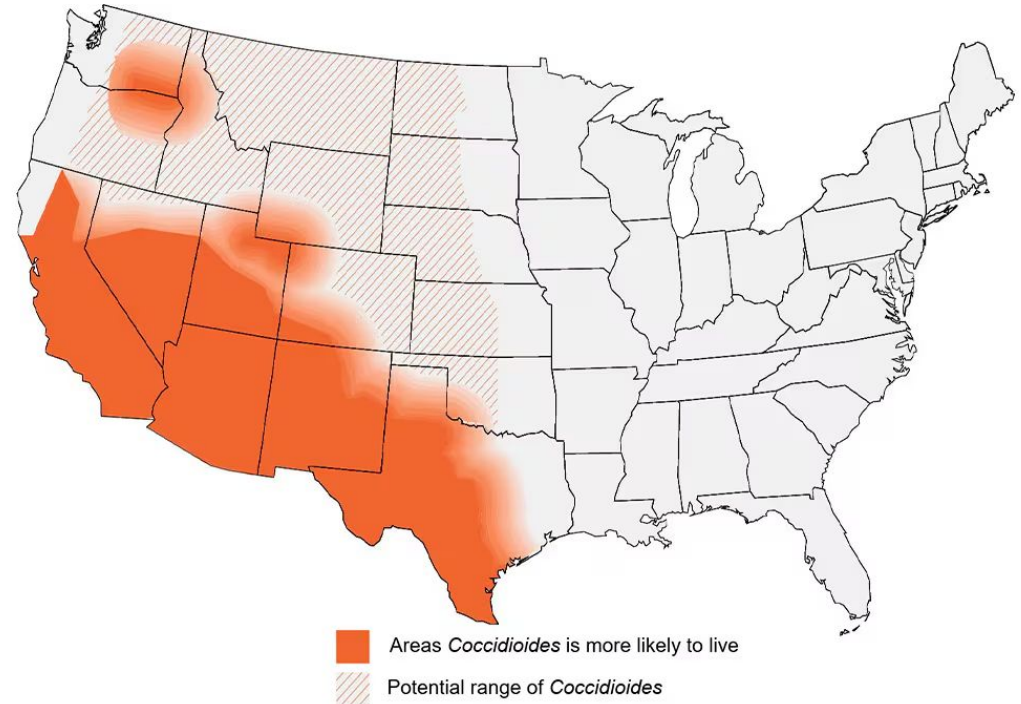


# Coccidioides

- Describe the **epidemiology** of **Coccidioides**, including geographic distribution & seasonal patterns
- Explain the modes of transmission and **key risk factors** for **Coccidioides** infection
- Discuss the **diagnostic approaches** for **coccidioidomycosis**, including serologic testing, culture, and molecular methods
- Characterize the **spectrum of disease** caused by **Coccidioides**

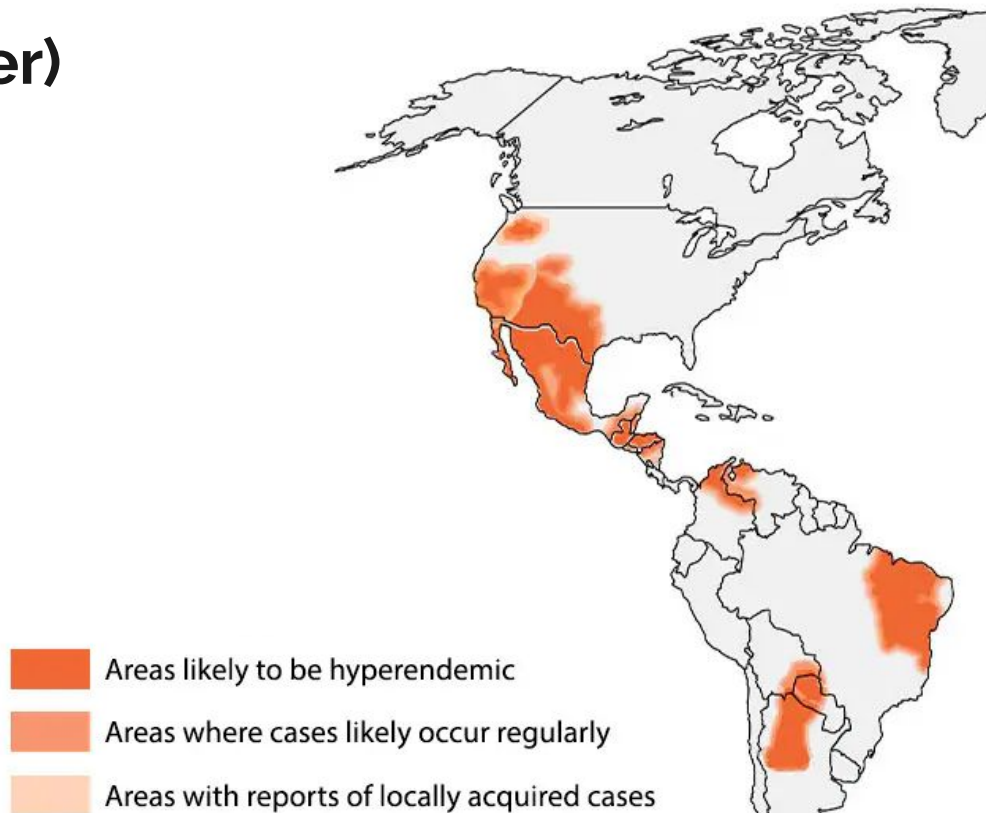
# Coccidioides (Valley fever)

- California, AZ, Washington
  - *Coccidioides immitis* more common in California
  - *C posadasii* elsewhere
  - No clinical difference

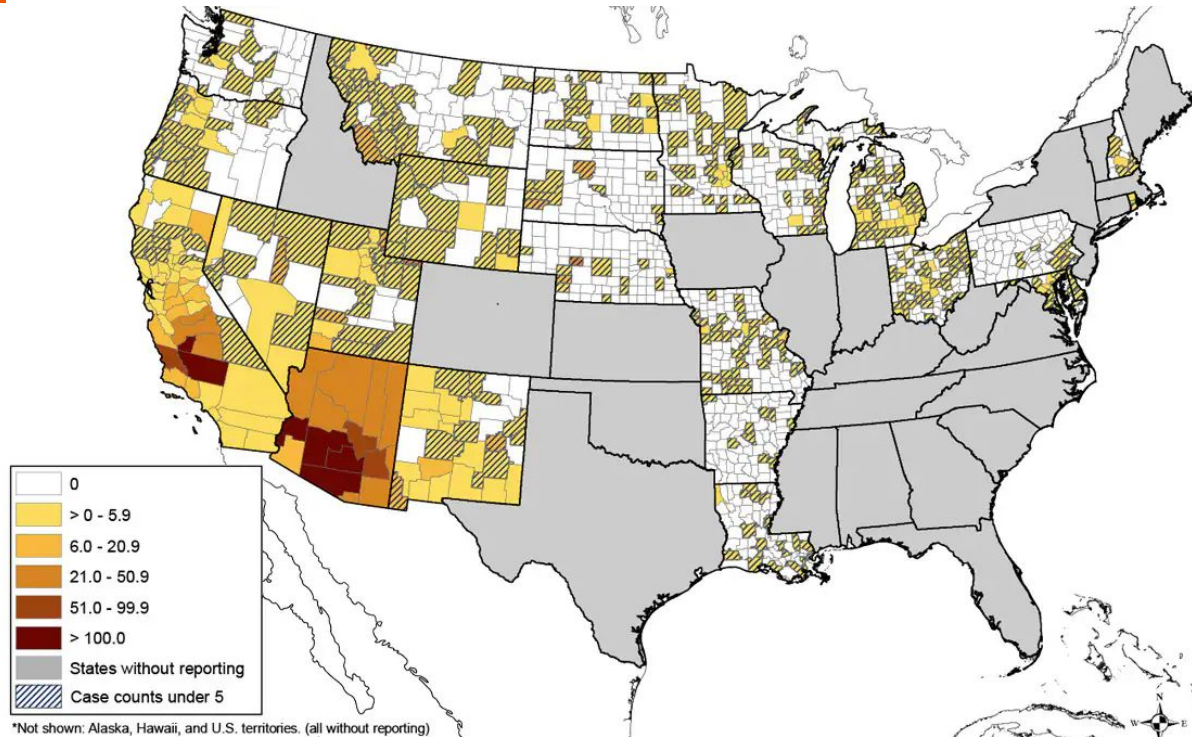


# Coccidioides (Valley fever)

- California, AZ, Washington
  - *Coccidioides immitis* more common in California
  - *C posadasii* elsewhere
  - No clinical difference
- Also seen in Mexico, Central America, and some areas of South America



# Coccidioides (Valley fever)



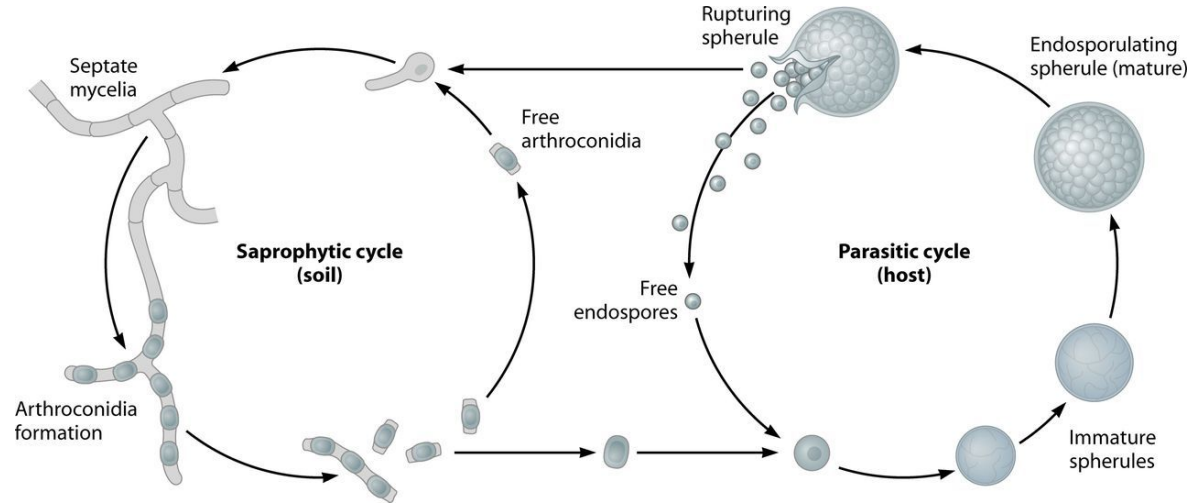
County incidence (per 100,000) from 2011 - 2017 <https://www.cdc.gov/valley-fever/areas/index.html>

# Coccidioides: Transmission [2.1]

Inhalation of **arthroconidia** from contaminated soil

- Dust storms
- Construction
- Earthquakes

More common in the dry season



# Coccidioides: Diagnosis [2.2]

---

**Most common:** EIA (screen) → immunodiffusion (confirmation)

- May have false negative early in the disease (re-test 1-3 weeks later)
- EIA is prone to false positives
- If immunodiffusion is positive → quantification should be done (either QID or CF)



# Coccidioides: Diagnosis [2.2]

---

**Most common:** EIA (screen) → immunodiffusion (confirmation)

- May have false negatives early in the disease (re-test 1-3 weeks later)
- EIA is prone to false positives
- If immunodiffusion is positive → quantification should be done (either QID or CF)

**Complement-fixation** (CF) assay was the original method of diagnosis

- Still helpful in running on the CSF
- Not as sensitive or specific as ID

# Coccidioides: Diagnosis [2.2]

**Most common:** EIA (screen) → immunodiffusion (confirmation)

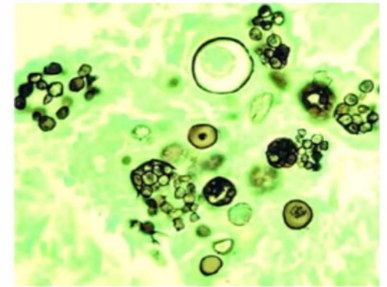
- May have false negatives early in the disease (re-test 1-3 weeks later)
- EIA is prone to false positives
- If immunodiffusion is positive → quantification should be done (either QID or CF)

**Complement-fixation (CF)** assay was the original method of diagnosis

- Still helpful in running on the CSF
- Not as sensitive or specific as ID

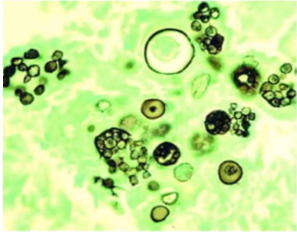
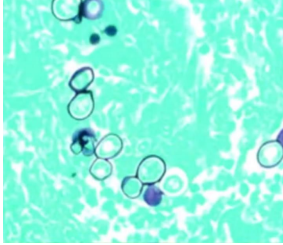
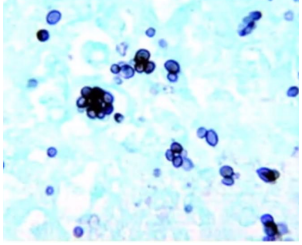
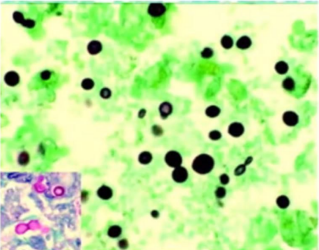
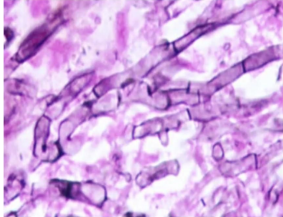
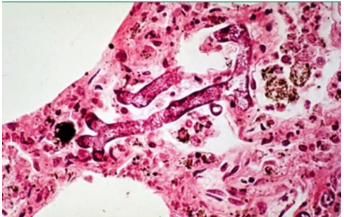
**Culture:** Coccidioides grows on most media

- Growth usually evident within a week



Spherules with multiple endospores - coccidioidomycosis

Adapted from [@TheIDTrivia](#), [@GeraldMD](#), & Febrile [podcast #69](#)

|     | Coccidioidomycosis   | Blastomycosis  | Histoplasmosis   |
|-----|--|--|--|
| BAL | <p>Spherules with multiple endospores</p>                   | <p>Broad based, single-budding</p>   | <p>Small yeast, narrow based budding. May be in macrophages</p>           |
|     | Cryptococcus   | Aspergillosis  | Mucor and Rhizopus   |
| BAL | <p>Narrow budding yeast with mucicarmine (+) capsules</p>  | <p>Septate hyphae<br/>Acute angle branching<br/>Forms conidial heads</p>  | <p>Ribbon-like hyphae<br/>Right angle branching<br/>Rare septations</p>  |

Adapted from [@TheIDTrivia](#), [@GeraldMD](#), & Febrile [podcast #69](#)

|                | <b>Coccidioidomycosis</b> | <b>Blastomycosis</b>                         | <b>Histoplasmosis</b>                         |
|----------------|---------------------------|--|---|
| Risk factors   | Working in dusty areas    | Working, playing, or hunting in wooded areas | Chickens, barns, caves, or any bird droppings |
| B-D glucan     | +/-                       | No   | +/-   |
| Galacto-mannan | No                        | +/-  | +/-   |

|                | <b>Cryptococcus</b>               | <b>Aspergillosis</b>                                | <b>Mucorales</b>                     |
|----------------|-----------------------------------|---|--------------------------------------|
| Risk factors   | Steroids, AIDs, sarcoid, liver dz | Steroids, neutropenia, transplant, viral infections | DM, DKA, steroids, burns, transplant |
| B-D glucan     | No                                | Yes   | No                                   |
| Galacto-mannan | +/-                               | Yes   | No                                   |

# Coccidioides: Spectrum of disease [2.1]



- Majority of patients (2/3) are asymptomatic



Asymptomatic

# Coccidioides: Spectrum of disease [2.1]



Primary pulmonary disease

- In endemic areas, can account for 1 in 4 cases of CAP
- Often self limiting, some will have “multiple visits for unimproved symptoms (despite abx)”



Asymptomatic

Pulmonary

# Coccidioides: Spectrum of disease [2.1]



Primary pulmonary disease

- In endemic areas, can account for 1 in 4 cases of CAP
- Often self limiting, some will have “multiple visits for unimproved symptoms (despite abx)”
- **Systemic symptoms**: Fevers, night sweats
- **Immunologic**: **arthralgias** (“desert rheumatism”), erythema nodosum, erythema multiforme
- **Labs**: One in four have **peripheral eosinophilia**

Asymptomatic

Pulmonary

# Coccidioides: Spectrum of disease [2.1]

## Primary pulmonary disease

- Systemic symptoms: Fevers, night sweats
- Immunologic: arthralgias, erythema nodosum, erythema multiforme
- Labs: Eosinophilia

These do not mean they have disseminated disease!

## Radiographically

- Unilateral (upper > lower) infiltrate
- Associated hilar LAD
- Nodules &/or cavities (4-8%)

Asymptomatic

Pneumonia

Nodules



# Coccidioides: Spectrum of disease [2.1]

---

**Disseminated disease** is rare

- **Skin and soft tissue:** Granulomatous infections (*not the immunologic phenomena*)
- **Bone & joint:** May progress to osteomyelitis
- **Others:** GU, peritoneum, eyes, pericardium

Asymptomatic

Pneumonia

Nodules

Disseminated

# Coccidioides: Spectrum of disease [2.1]

---

**Disseminated disease** is rare

- Skin and soft tissue
- Bone & joint
- Others
- Most feared is **CNS**
  - Most common symptom: headache
  - 95% mortality if untreated
  - High rates of relapse

Asymptomatic

Pneumonia

Nodules

Disseminated

# Coccidioides: Spectrum of disease [2.1]

**Disseminated disease** is rare

- Skin and soft tissue
- Bone & joint
- Others
- Most feared is **CNS**
  - Most common symptom: headache
  - 95% mortality if untreated
  - High rates of relapse

## CSF studies

- Common to have eosinophilia
- Uncommon to grow on Cx

Asymptomatic

Pneumonia

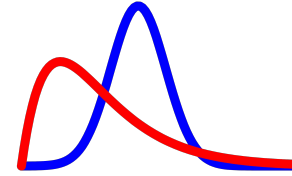
Nodules

Disseminated

# Learning points & take aways

---

# Learning points & take aways



- Hypermucoviscous *Klebsiella pneumoniae* (HmKp) is a **thick, mucoid** phenotype of *K pneumoniae* (**string test**),
  - Predisposition to cause **more severe infections** in **immunocompetent hosts**
  - Likes to **metastasize**: Liver, CNS, lungs, brain
  - Can have **extensive antimicrobial resistance**, especially internationally
- *Coccidioides* is most often **asymptomatic or mild pulmonary infections**, but can be severe in immunocompromise
  - Risk factors: Travel to the **Western US** + **dry dirt/soil exposure**
  - Testing for *coccidioides* is multi-step, and subject to **false positives & false negatives**
- Interpreting the test results depends on both the nature of the test itself and the **pre-test probability**
  - You don't need to know Bayes Theorem itself, but [online calculators](#) can help improve our numeracy