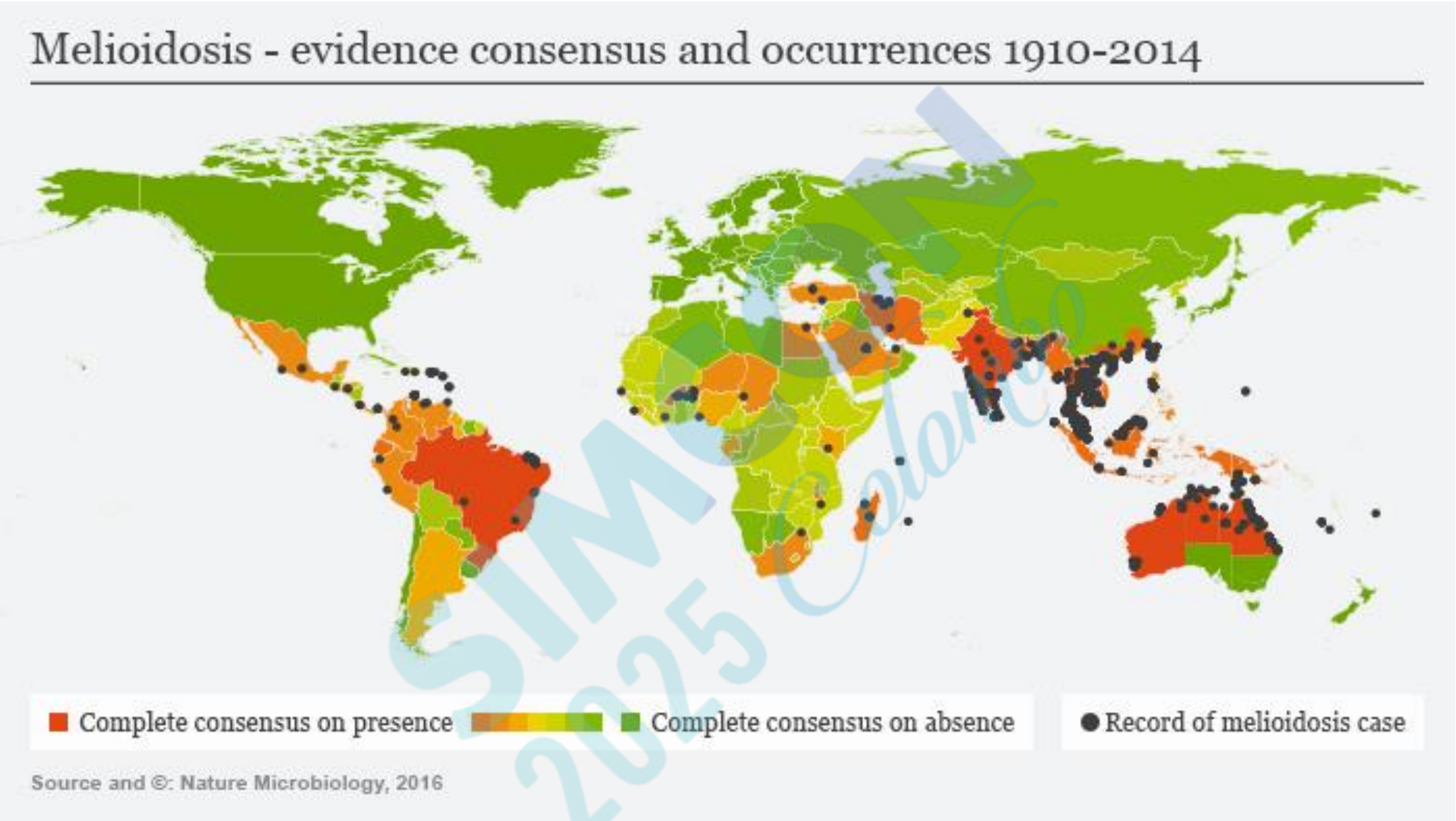
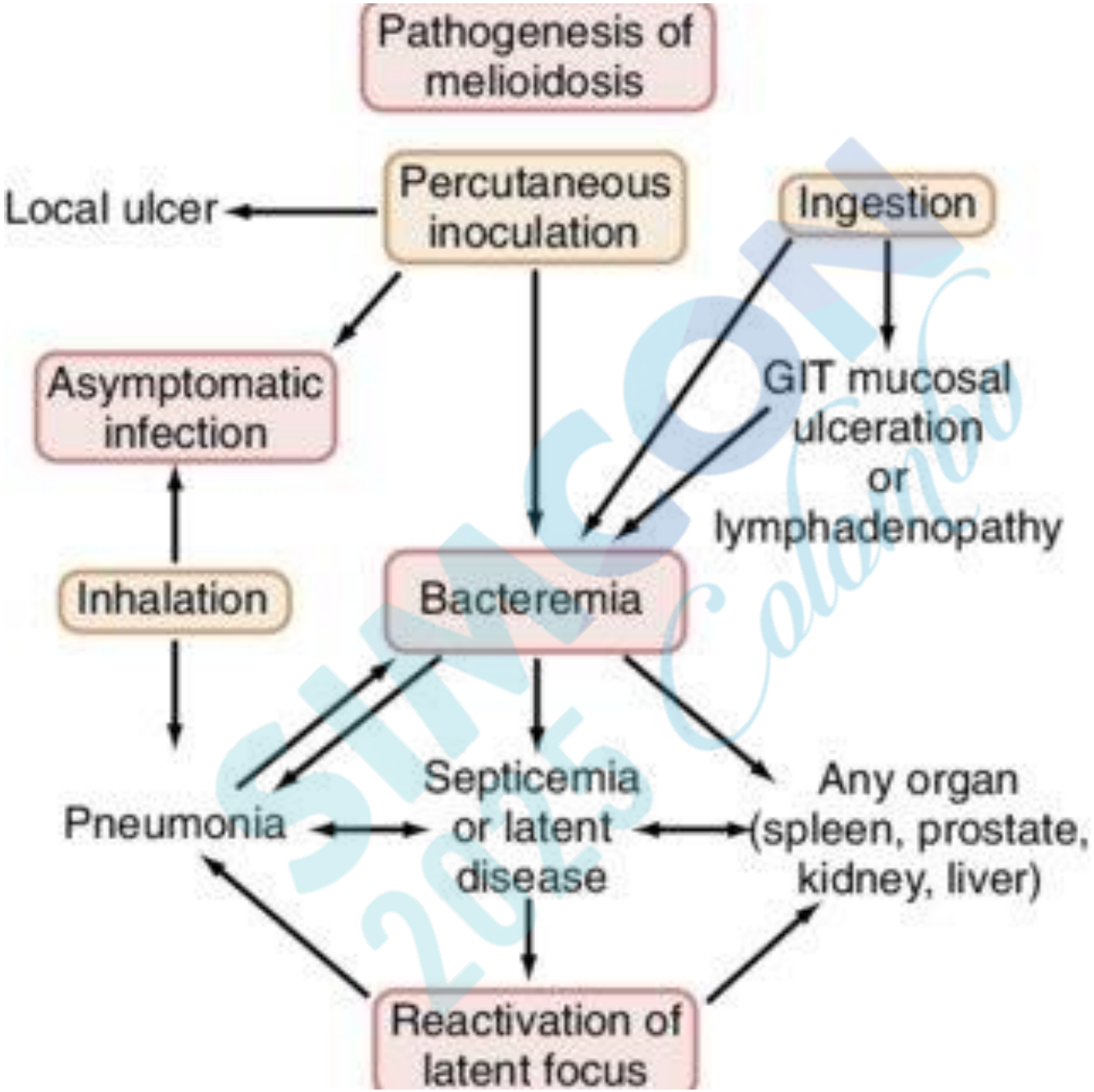
# Melioidosis

Dr Amit A Saraf
MD FRCP (London, Edinburgh, Glasgow) FACP (Philadelphia) FICP FCPS
Director Dept of Internal Medicine & Group Head Quality Control
Jupiter Hospitals, Mumbai, India

Dr Saraf

Dr Saraf




Pathogenesis of melioidosis
Percutaneous inoculation
Local ulcer
Ingestion
Asymptomatic infection
GIT mucosal ulceration or lymphadenopathy
Inhalation
Bacteremia
Pneumonia
Septicemia or latent disease
Any organ (spleen, prostate, kidney, liver)
Reactivation of latent focus

# Case 1

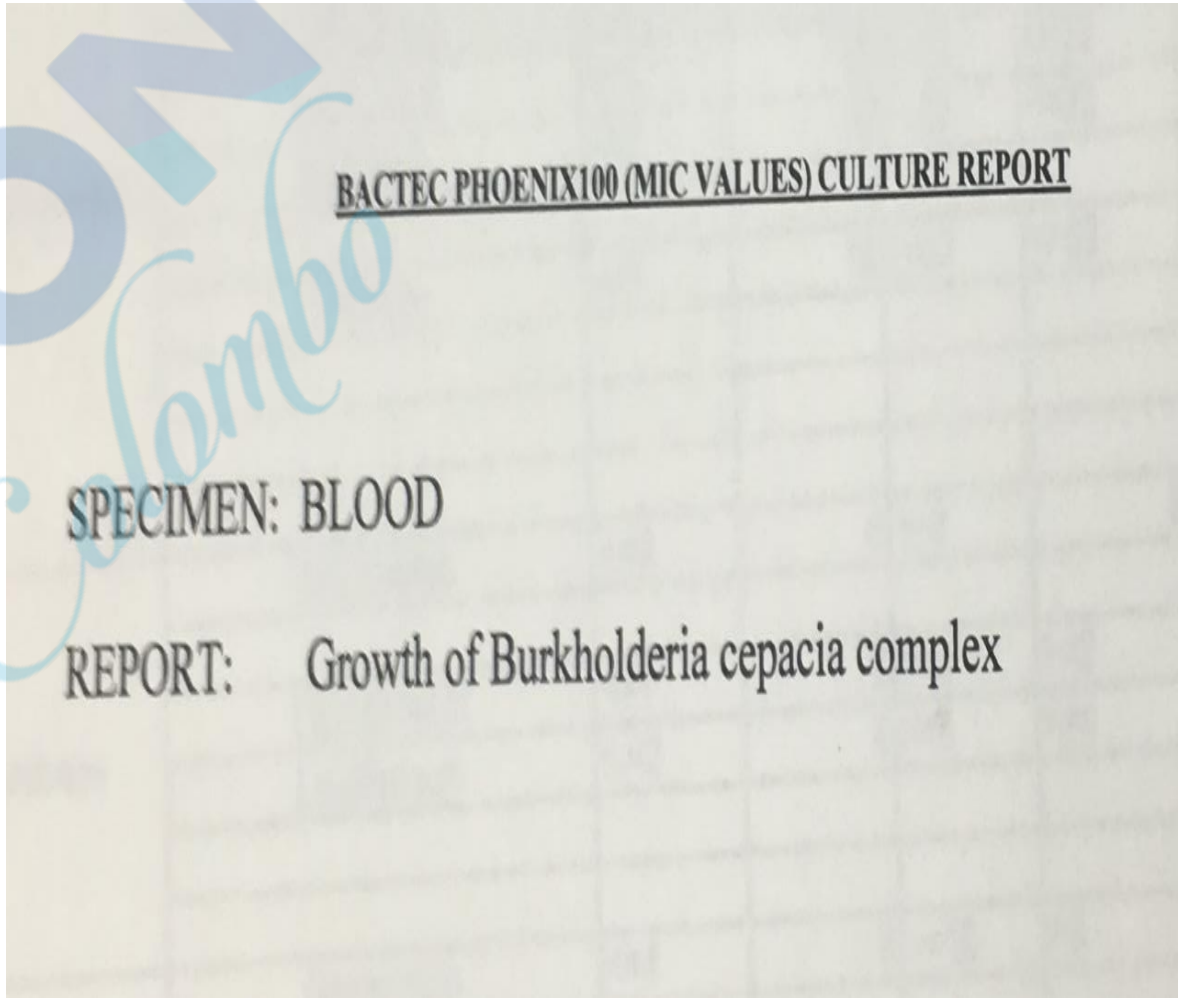
- 67/M resident of Goa, presented with:

- Fever– 6 days
- Mild increase in frequency of urination– 6 days

- Fever– high grade, a/w chills, no diurnal variation, responded initially to antipyretics but persisted

- Investigations revealed a normal count, normal USG (A) and the blood culture grew Burkholderia cepacia

- He was started on TMP/SMX elsewhere as per the culture report



BACTEC PHOENIX100 (MIC VALUES) CULTURE REPORT

SPECIMEN: BLOOD

REPORT: Growth of Burkholderia cepacia complex

- The fever responded to the TMP/SMX and he was alright for 7 days
- 4-5 days after the TMP/SMX was stopped he started getting fever again
- Repeat testing revealed a TLC– 12,000 (N – 87), a Creat of 3.0 and an HbA1c of 7.8
- 3 repeat blood cultures were sent and a CT of abdomen was done to look for a focus
- There was also a history of soil exposure as the patient had walked to the beach on wet soil near his house

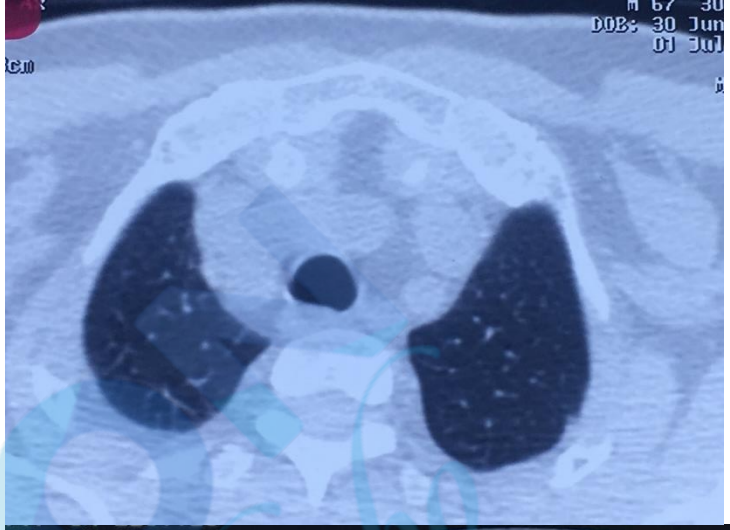
| Antimicrobial Class | Antimicrobial Agent | MIC INTERPRETIVE CRITERIA(microgram/ml) CLSI Guidlines S | I | R | MIC OF PATIENT ISOLATE | RESULT |
|---|---|---|---|---|---|---|
| ß- lactamase Inhibitor Combinations | Amoxicillin+ Clavulanic acid | <=8/4 | 16 / 8. | >=32/16 | >=16/8 | R |
| | Piperacillin/ Tazobactum | <=16/4 | 32/4-64/4 | >128/4 | >=32/4 | R |
| | Cefoperazone/ Sulbactum | <=16/4 | 32/4-64/4 | >128/4 | <=32/4 | INTERMIDIAT |
| Cephalosporins | cefuroxime | <=8 | 16 | >=32 | >=32 | R |
| | cephalexin | <=8 | 16 | >=32 | >=32 | R |
| | cefoxitin | <=8 | 16 | >=32 | >=32 | R |
| | ceftazidime | <=8 | 16 | >=32 | 8 | S |
| | ceftriaxone | <=8 | 16 | >=32 | <=32 | R |
| | cefepime | <=8 | 16 | >=32 | <=32 | R |
| | Cefixime | <=8 | 16 | >=32 | <=32 | R |
| Quinolones | Norfloxacin | < =2 | 4 | >=8 | 8 | R |
| | Ciprofloxacin | <=1 | 2 | >=4 | >=2 | R |
| | Levofloxacin | < =2 | 4 | >=8 | >=4 | R |
| Aminoglycosides | Gentamicin | <=4 | 8 | >=16 | >8 | R |
| | Netilmycin | | | | | |
| | Amikacin | <=16 | 32 | >64 | >32 | R |
| Aztreonam | Aztreonam | | | | 16 | R |
| Carbapenems | Ertapenem | < = 2 | 4 | > = 8 | 8 | R |
| | Imipenem | < = 2 | 4 | > = 16 | >4 | R |
| | Meropenem | < = 2 | 4 | > = 8 | >4 | R |
| Penicillins | Ampicilin/SULBACTUM | | | | 16 | R |
| Miscelleneous | colistin | | | | >4 | R |
| | linezolid | | | | | |
| | Clindamicin | | | | | |
| | Vancomycin | | | | | |
| | Fosfomycin w/G6P | | | | | |
| | Doxycycline | | | | | |
| | Tigecycline | < = 1 | 4 | > = 8 | 1 | S |
| Folate pathway inhibitors | Trimethoprim-sulfamethoxazole | | | | <=1/19 | S |
| | Trimethoprim | | | | 4 | R |
| | Nitrofuraitoin | <=32 | 64 | >128 | >128 | R |

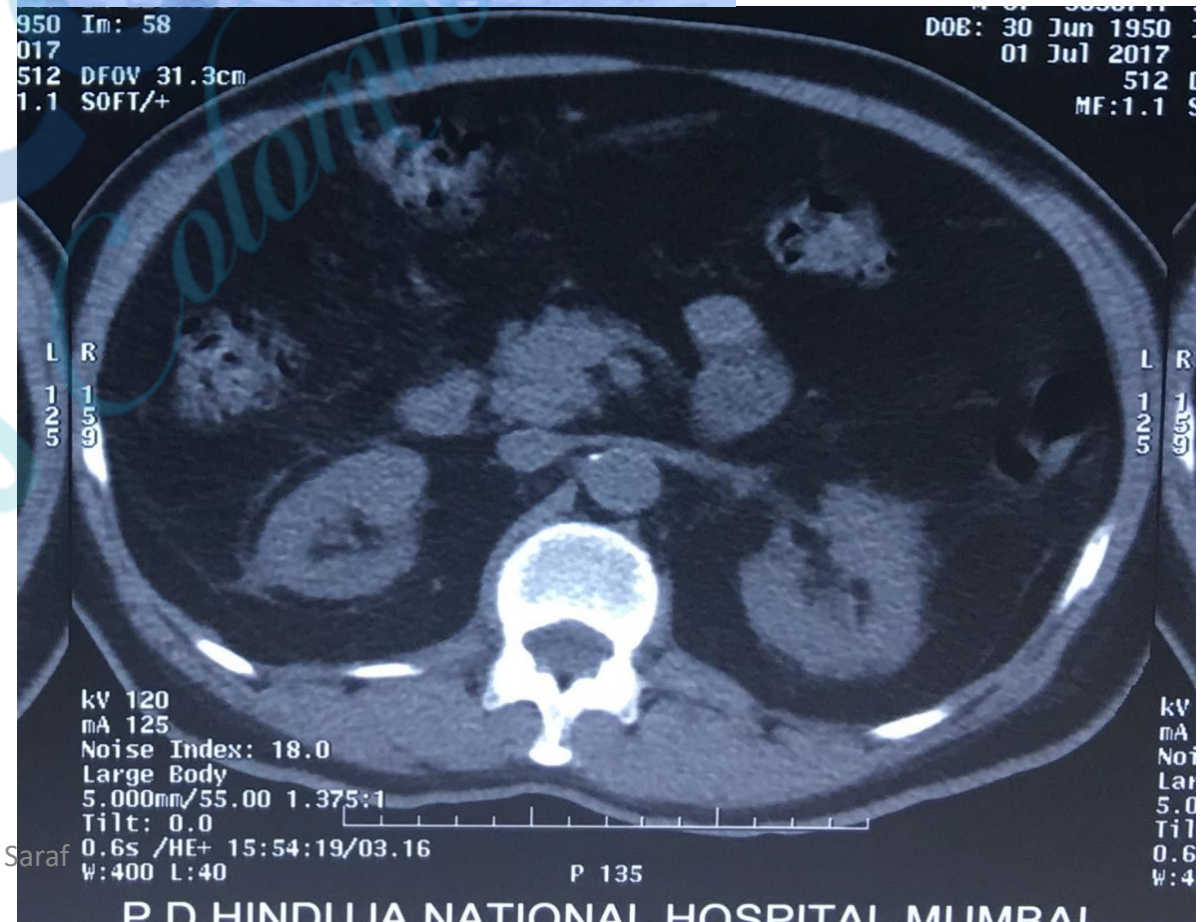
RESISTANCE

Dr Saraf
Off Power House Road, Near St. Sabastian Chapel (Pandava Chapel), Aquem, Margao, Goa.
Tel. Nos.: 0832-2735773, 2735774, Email: shradhanaikgaonkar@gmail.com Mobile: 9975764336

- CT– B/L mild perinephric fat stranding and small kidneys

- The blood cultures sent had started growing GNB





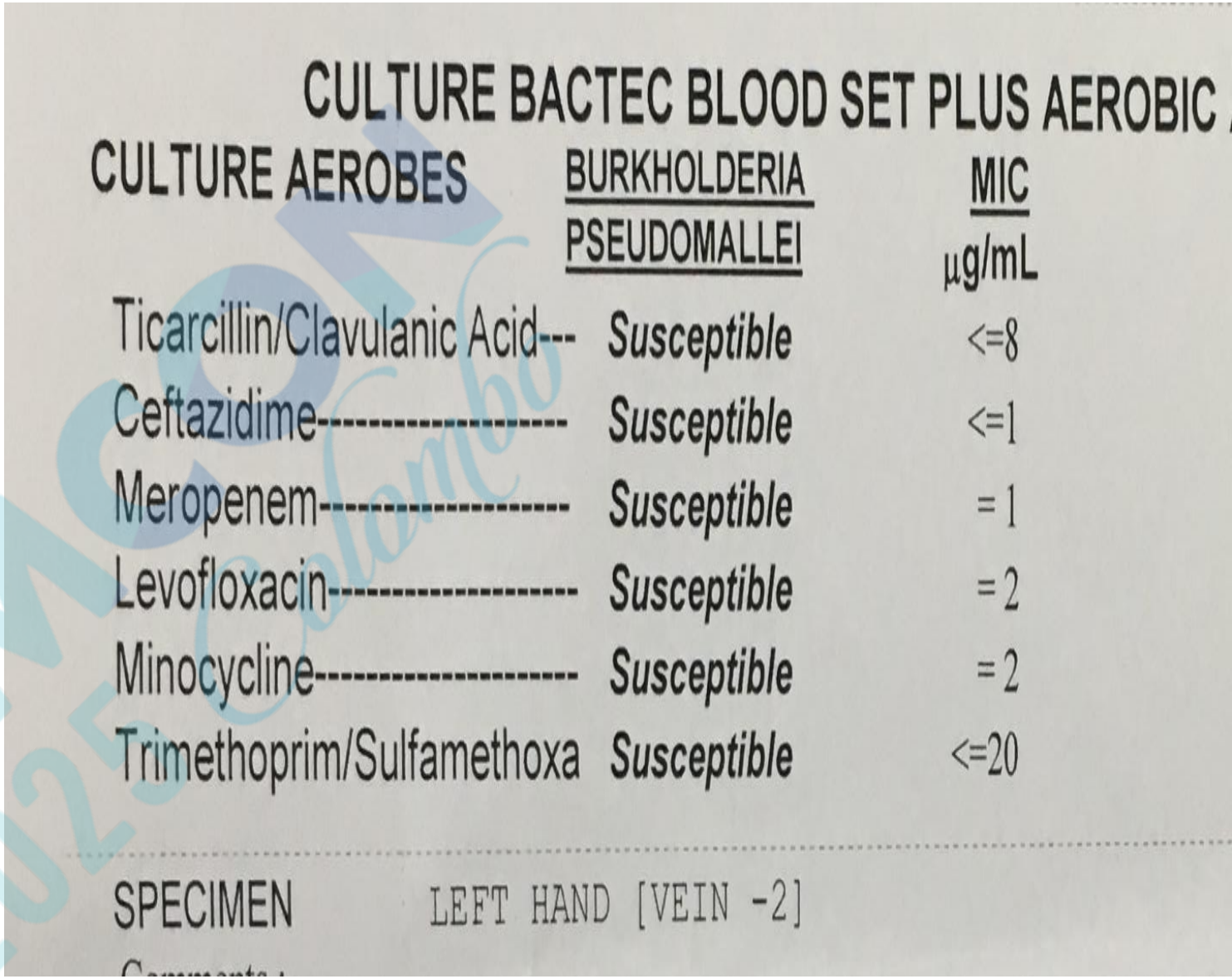
# To summarize

- This was an elderly male with uncontrolled unrecognized diabetes, with likely acute on chronic renal failure, with GNB bacteremia and a blood culture done earlier which had revealed Burkholderia cepacia
- He had also responded well to TMP/SMX

- The diagnostic possibilities were-

| | Community acquired GNB bacteremia | Blood culture Day 1/1– B cepacia | B/L perinephric fat stranding | DM | Response to TMP/SMX |
|---|---|---|---|---|---|
| UTI (Pyelonephritis) | ✓ | X | ✓ | ✓ | ✓ |
| B cepacia UTI with bacteremia | X | ✓ | +/- | - | ✓ |
| Melioidosis | ✓ | +/- (older identification systems can misidentify B pseudomallei as B cepacia | ✓ | ✓ | ✓ |

- Burkholderia cepacia can be a contaminant due to povidone-iodine which may be used as a sterilizer before collecting blood via a venipuncture
- Hence, the diagnosis of UTI with the B cepacia as a contaminant was almost as good a fit as melioidosis
- The GNB from Day 3/3 blood cultures turned out to be Burkholderia pseudomallei



CULTURE BACTEC BLOOD SET PLUS AEROBIC

| CULTURE AEROBES | BURKHOLDERIA PSEUDOMALLEI | MIC µg/mL |
|---|---|---|
| Ticarcillin/Clavulanic Acid--- | *Susceptible* | <=8 |
| Ceftazidime---------- | *Susceptible* | <=1 |
| Meropenem---------- | *Susceptible* | = 1 |
| Levofloxacin---------- | *Susceptible* | = 2 |
| Minocycline---------- | *Susceptible* | = 2 |
| Trimethoprim/Sulfamethoxa | *Susceptible* | <=20 |

SPECIMEN LEFT HAND [VEIN -2]

- Final diagnosis– Melioidosis septicemic form
- The patient was put on an intensive phase of IV Ceftazidime and oral TMP/SMX
- Gradually he improved and was discharged
- The plan was to continue the oral TMP/SMX for 6-12 months

# Lessons

1. Burkholderia pseudomallei may be misidentified by automated blood culture systems like Vitek, Bactec etc. It is misidentified as B cepacia, Pseudomonas, Acinetobacter and related species

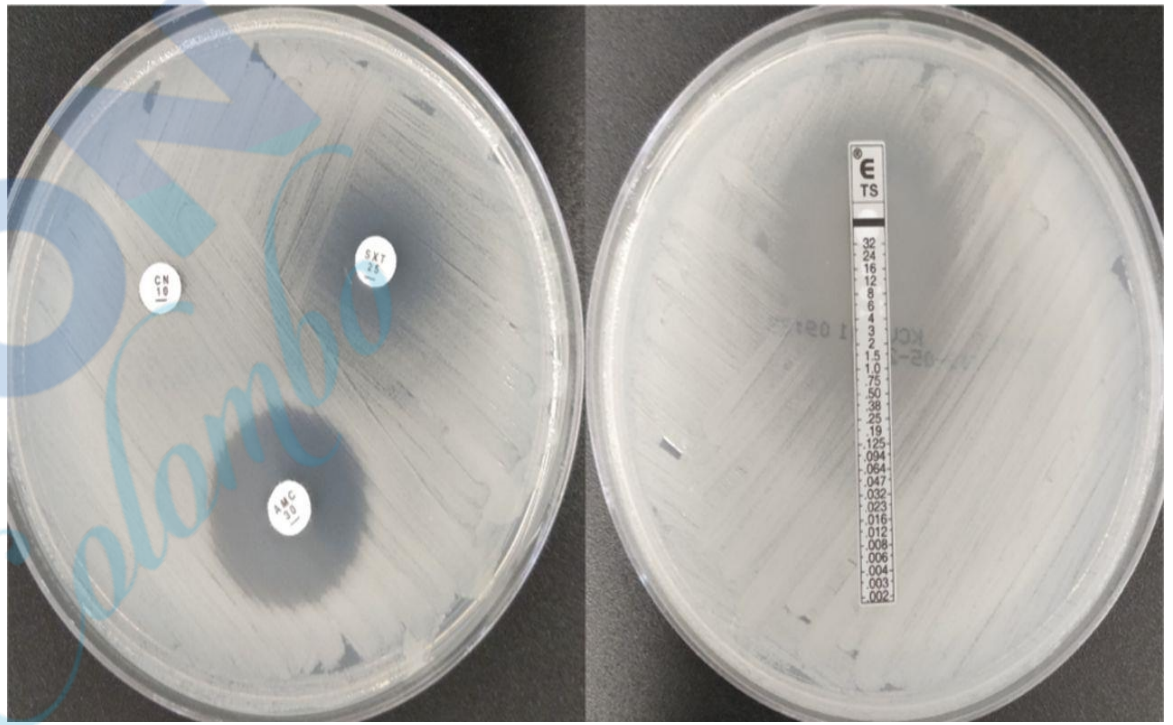
2. Burkholderia cepacia can be a contaminant from the use of povidone-iodine prior to venipuncture

3. Burkholderia cepacia is an uncommon cause of community acquired syndromes and should be viewed with suspicion in a patient coming from the community

# When misidentified, how to differentiate?

1. Colony morphology

2. Susceptibility to Amoxy-Clav, but resistance to Colistin, may be a hint that the isolate identified as Pseudomonas or Acinetobacter might be something else



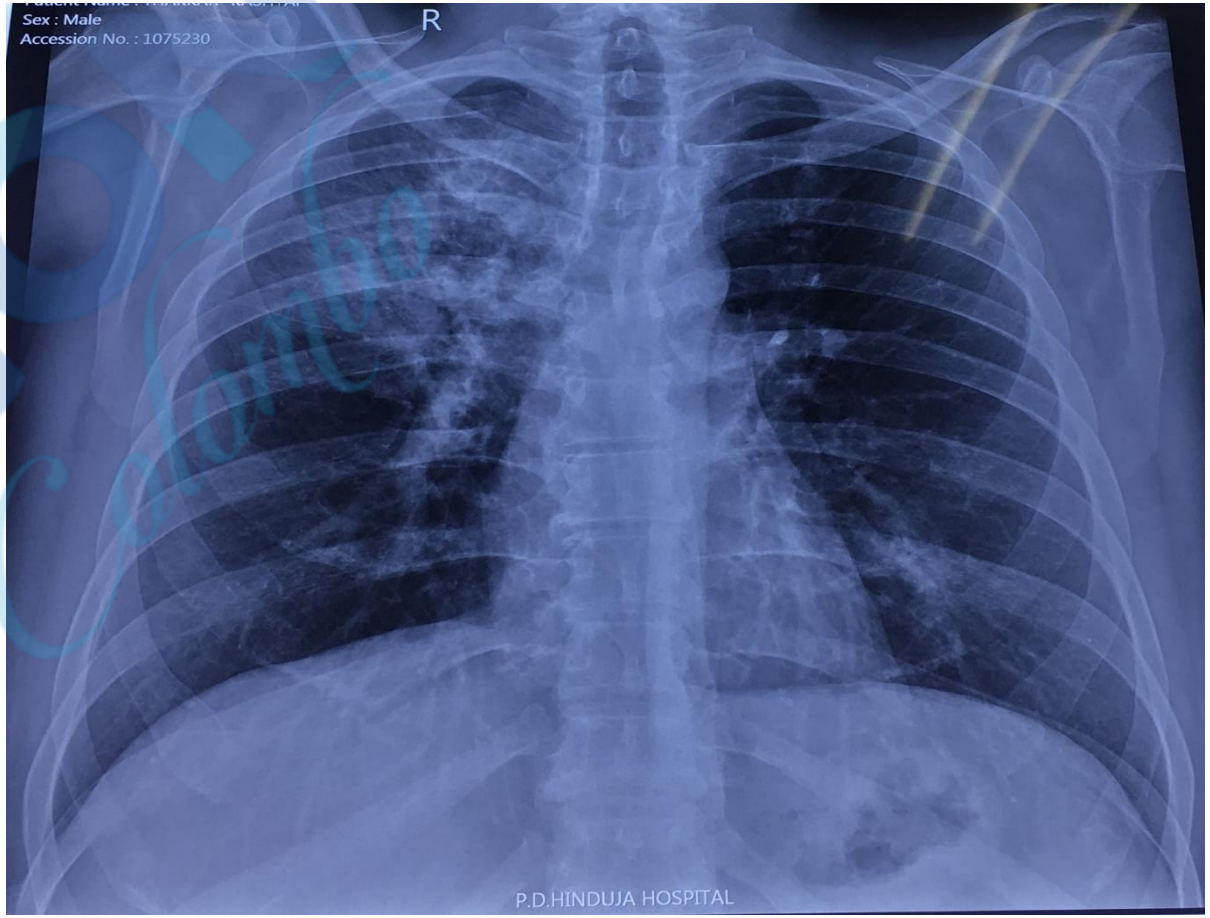

*Double zone of susceptibility around TMP/SMX*

# Case 2

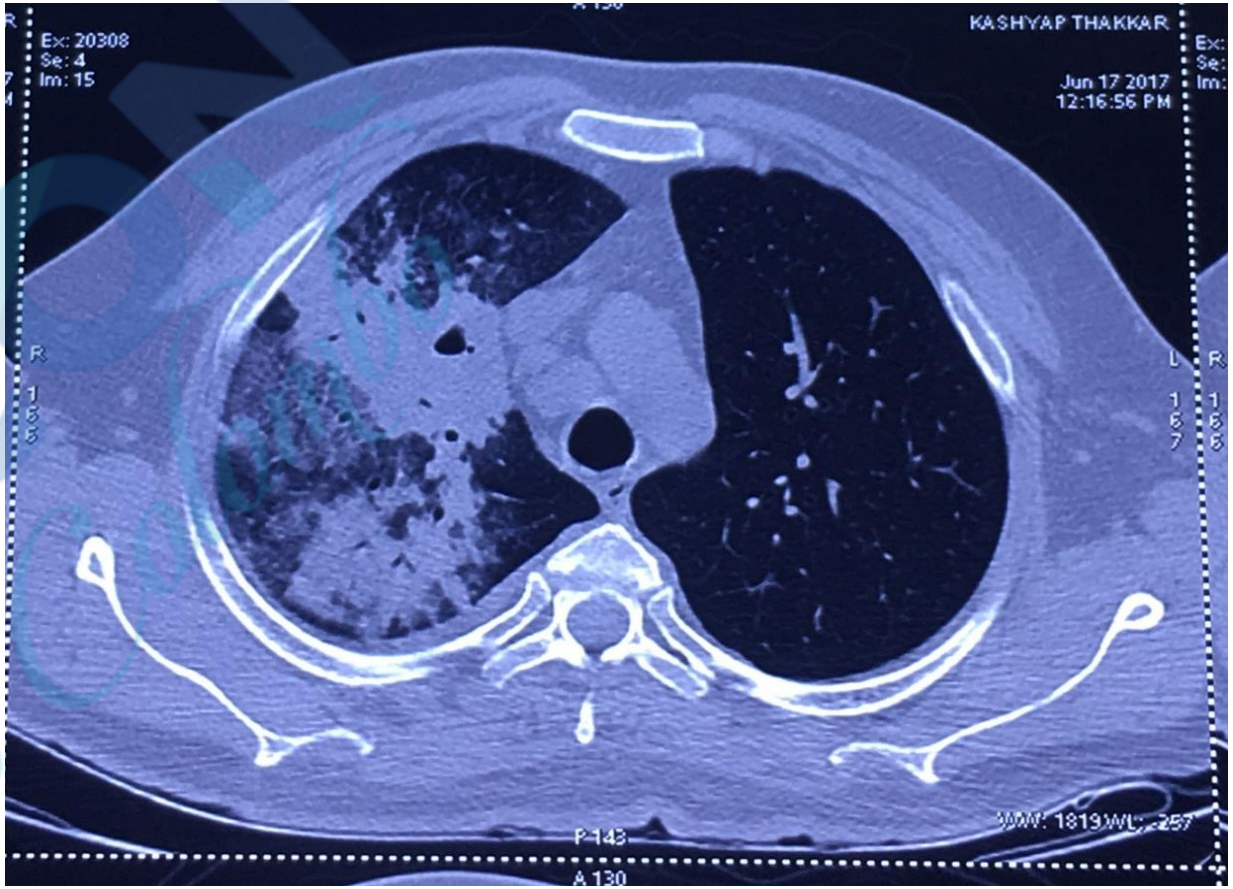
- 43/M smoker, alcohol abuser, with uncontrolled DM (HbA1c– 12.5%) and chronic pancreatitis, presented in July 2017 with:

- Fever– 20 days
- Cough– 20 days

- Fever– Sudden in onset, high-grade, a/w chills and rigors with no diurnal variation
- Cough– Scanty mucoid expectoration, no hemoptysis



- He also gave a history of travel to the west coast near Goa 1 year back
- Investigations revealed a TLC– 12,500 (N 78)
- He was treated elsewhere with Clarithromycin and Levoflox, with no response
- A sputum culture revealed Enterobacter cloacae
- A CT chest & abdomen– Consolidates in right lung & coarse echotexture of the liver



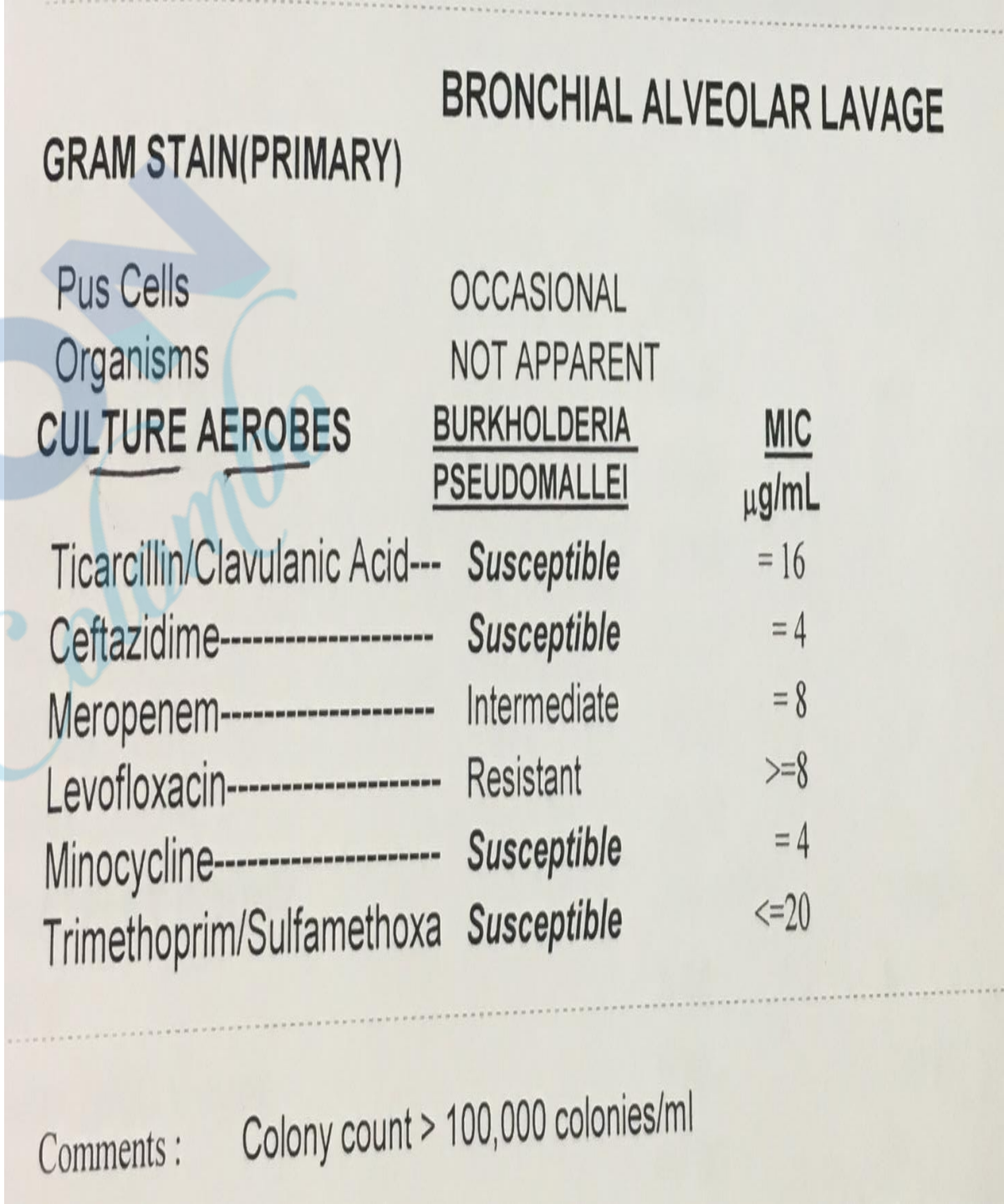

*Nodular multifocal consolidates in right lung*

# On suspicion of TB, a bronchoscopy was done

- Specimens were sent for GeneXpert, Bacterial Culture and TB MGIT

# Melioidosis!

- The result came as a surprise to the primary team. And finally, an ID ref was sought
- The diagnosis was Pulmonary form of Melioidosis
- The patient was started on IV Ceftazidime and oral TMP/SMX in a weight-based regime
- Slowly the patient responded and was discharged with instructions to abstain from alcohol and restricting travel to coastal areas in the monsoon season



BRONCHIAL ALVEOLAR LAVAGE

GRAM STAIN(PRIMARY)

| | |
|---|---|
| Pus Cells | OCCASIONAL |
| Organisms | NOT APPARENT |

| CULTURE AEROBES | BURKHOLDERIA PSEUDOMALLEI | MIC µg/mL |
|---|---|---|
| Ticarcillin/Clavulanic Acid--- | *Susceptible* | = 16 |
| Ceftazidime---------- | *Susceptible* | = 4 |
| Meropenem---------- | Intermediate | = 8 |
| Levofloxacin---------- | Resistant | >=8 |
| Minocycline---------- | *Susceptible* | = 4 |
| Trimethoprim/Sulfamethoxa | *Susceptible* | <=20 |

Comments : Colony count > 100,000 colonies/ml

# TB and Pulmonary Melioid can mimic each other

| Similarities | |
|---|---|
| Risk Factors– Uncontrolled DM, Alcoholism, Steroids | |
| Subacute to chronic community acquired pneumonia | |
| Predilection for upper lobes, intracellular organisms which need prolonged treatment | |
| **Differences** | |
| **TB** | **Melioid** |
| Low grade fever, with evening rise | Can start with High grade fever |
| Normal counts | High counts |
| No response to routine antibiotics for CAP | May respond to 3rd gen cephalosporins, FQN's |
| Consolidates and cavities more common | Multifocal Nodules, which coalesce<br>B/L interstitial pattern also known |
| No such seasonal variation | Cluster in the monsoon season, H/O travel to coastal area may be a clue to the diagnosis |

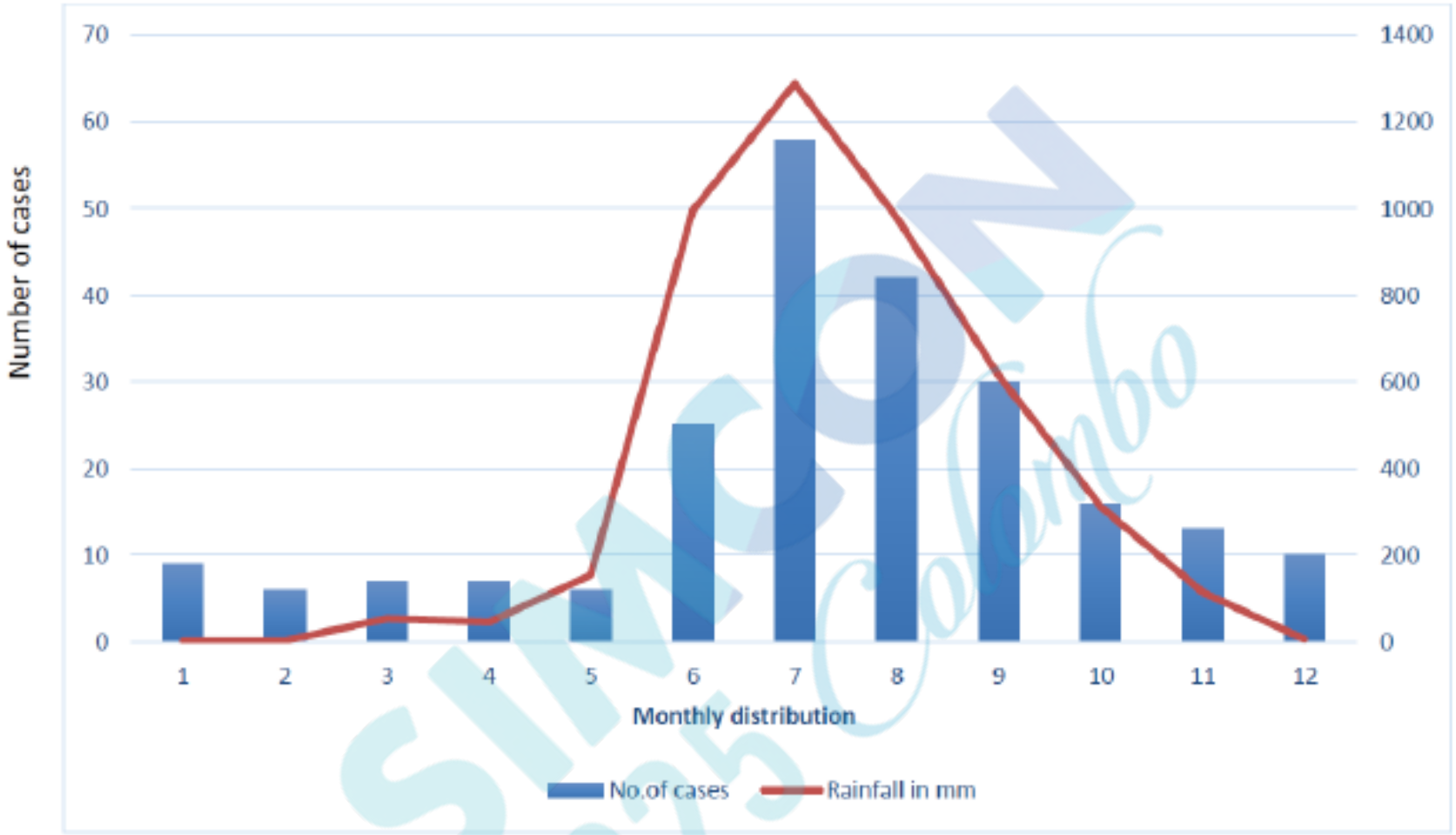
# Clues in this case

- High grade fever
- High counts
- Travel to endemic area
- Nodular coalescing opacities

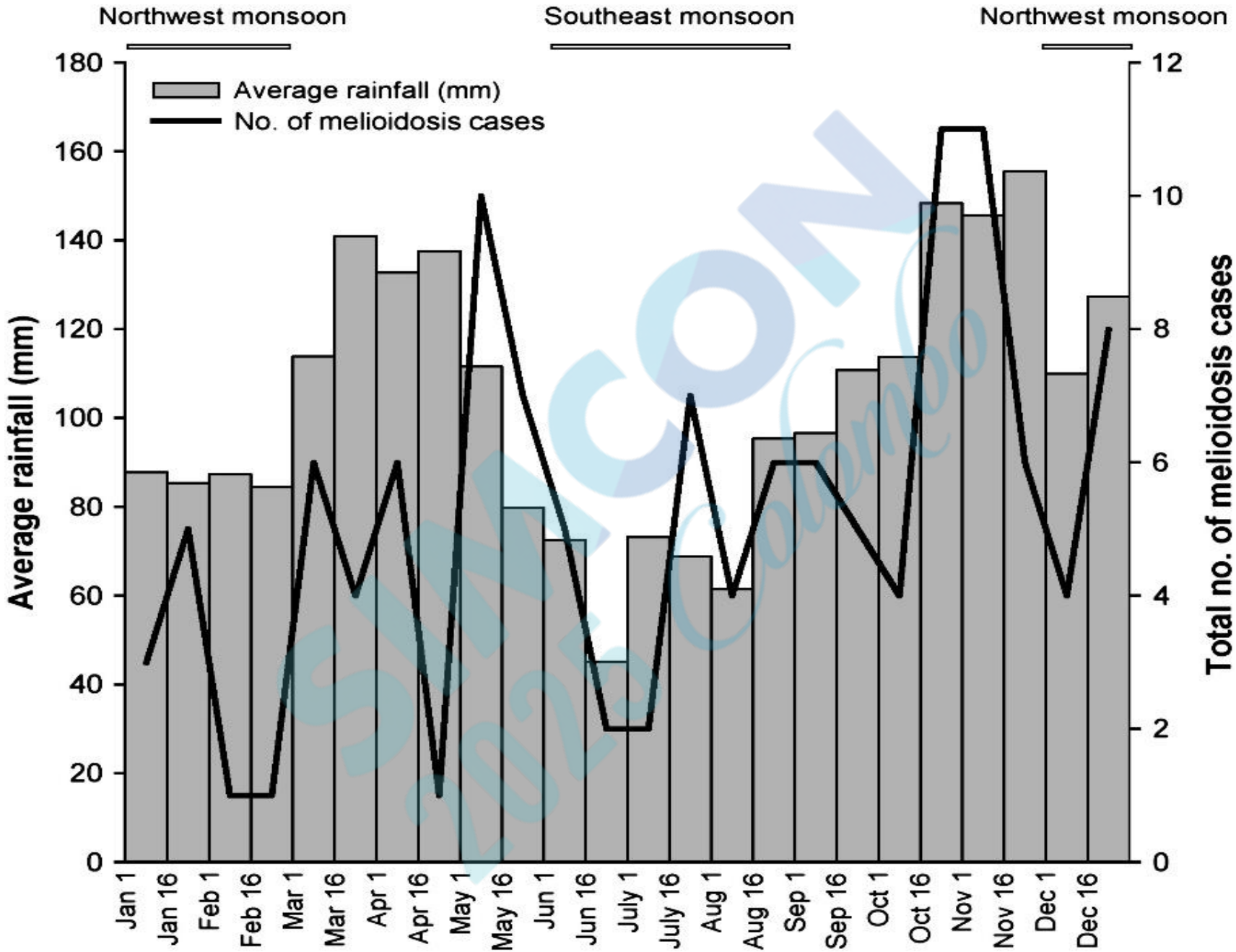
- The Enterobacter grown from the sputum culture was likely a colonizer, as it is not a common cause of CAPs

- In a publication a few years back, Vidyalalakshmi K et al presented a series of 22 cases which were initially diagnosed as TB and later confirmed to be Melioidosis
- Eight cases mimicked Pulmonary TB, five tubercular arthritis, three tubercular spondylitis, two tubercular lymphadenitis, two splenic abscess and one each mimicked tubercular pericarditis and parotid abscess
- In their analysis they concluded that neutrophilic leukocytosis was the one test result which was more common in the melioid group, although TB is known to cause leukemoid reactions on occasion

# Why July?




| Month | Season |
|---|---|
| October–February | Post-monsoon |
| March–May | Summer |
| June–September | Monsoon |



# Case 3

- 61/M, alcoholic (since 40 years), IHD post CABG and PTCA, resident of Mumbai, hailing from Ratnagiri and had paid a recent visit to his village

- Came with the chief complaints of–
- Fever with chills– 40 days
- Left sided chest pain– 40 days

- Fever– Insidious in onset, intermittent in type, associated with an evening rise, initially low grade which progressed to high grade and it was associated with chills, weight loss (14 kg's) and night sweats

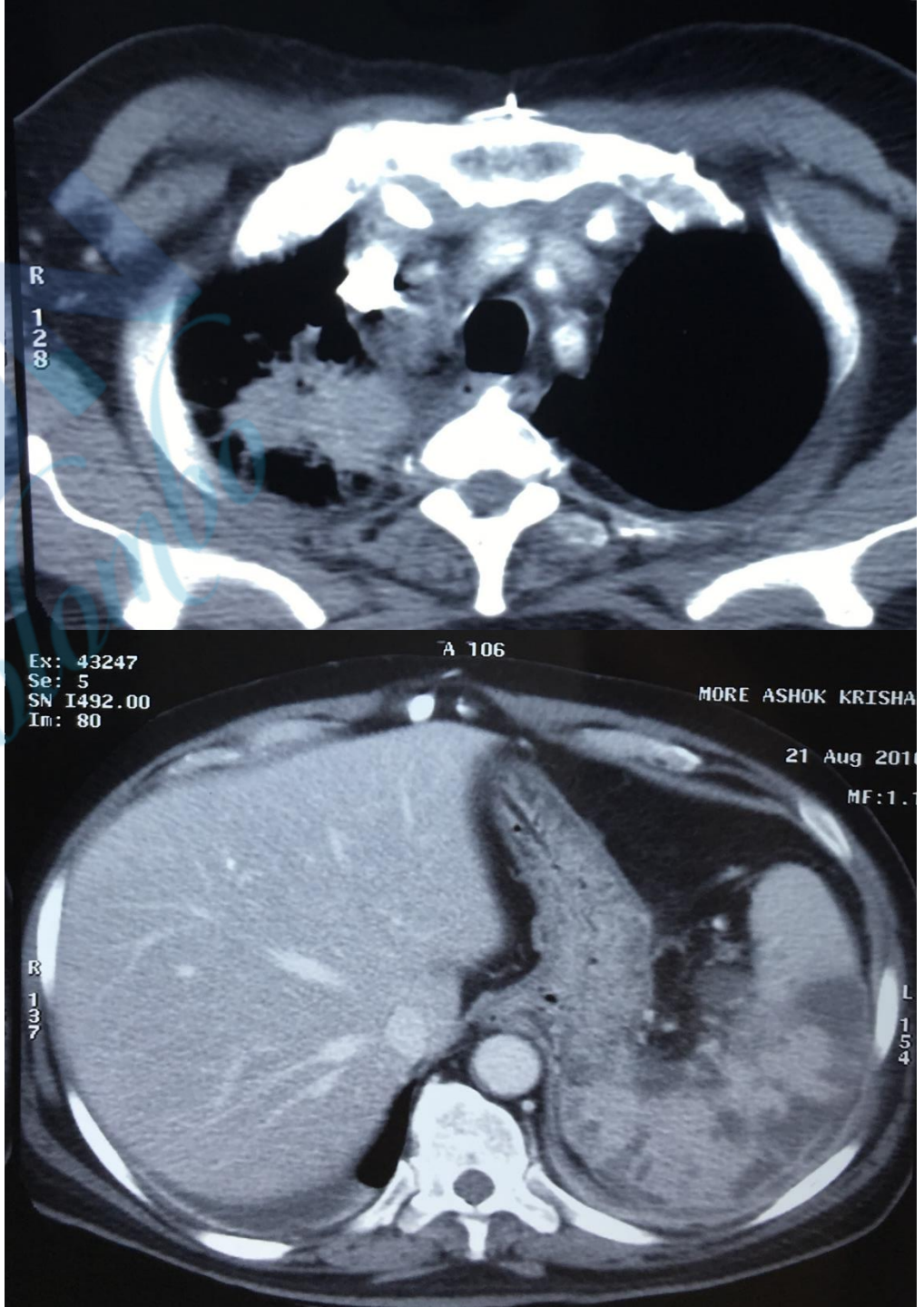
- Initial workup: TLC– 15,770 (N71, L25), CXR– Right UZ infiltrate and incidentally detected DM

- He received Cefpodoxime and then Cefixime for a total of 10-12 days elsewhere. There was a partial response to this treatment in the form of defervescence, but the fever came back after a few days

- CT (A + C)–

1. Right upper lobe consolidation with early cavitation, mediastinal adenopathy

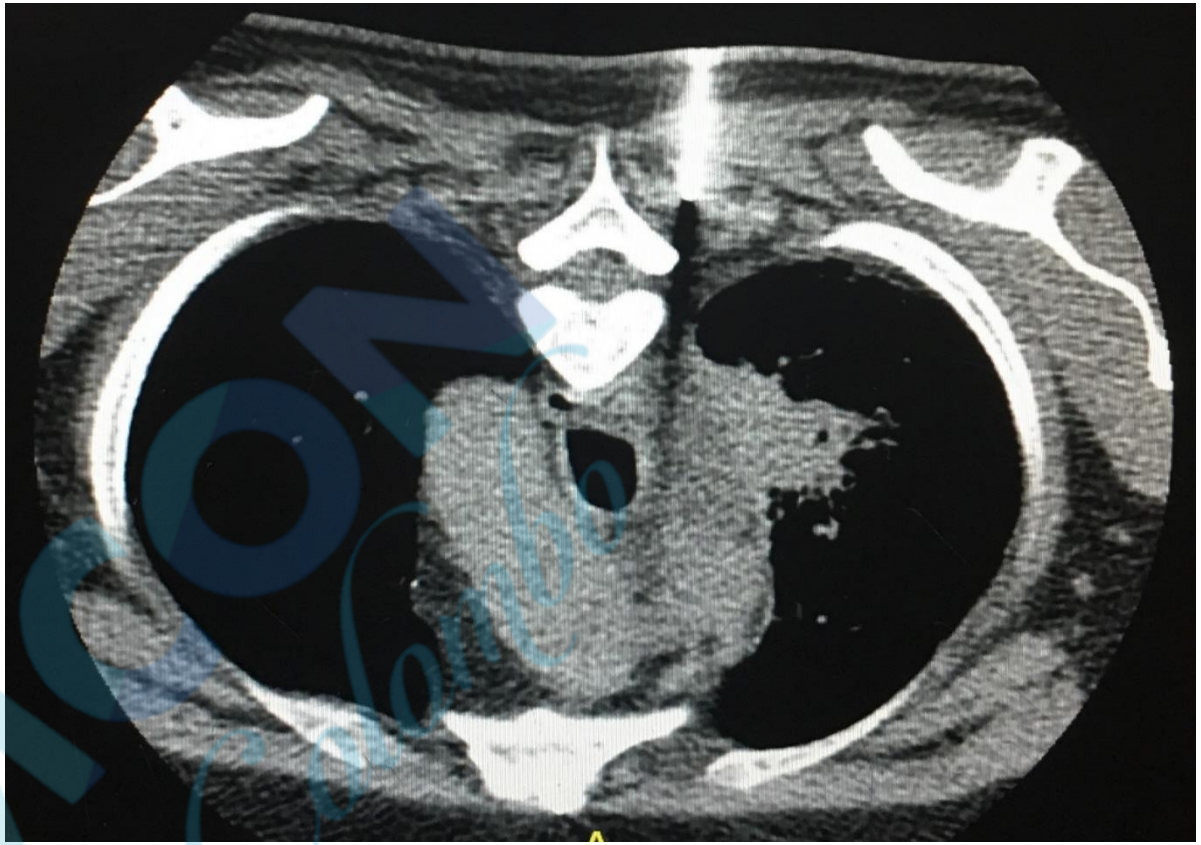
2. Multiple hypodense lesions in spleen with varying sizes S/O micro-abscesses



# Finally Melioidosis, because….

| | Right UZ consolidate with cavity, mediastinal adenopathy | Splenic deposits | High TLC, partial response to 3rd generation Cephalosporins | No response to ATT |
|---|---|---|---|---|
| Melioidosis | ✓ | ✓ | ✓ | ✓ |
| TB | ✓ | ✓ | X | X |
| Lymphoma | X | ✓ | X | - |
| IE | X | ✓ | ✓ | - |

- CT guided FNAC– Neutrophil predominant inflammatory changes

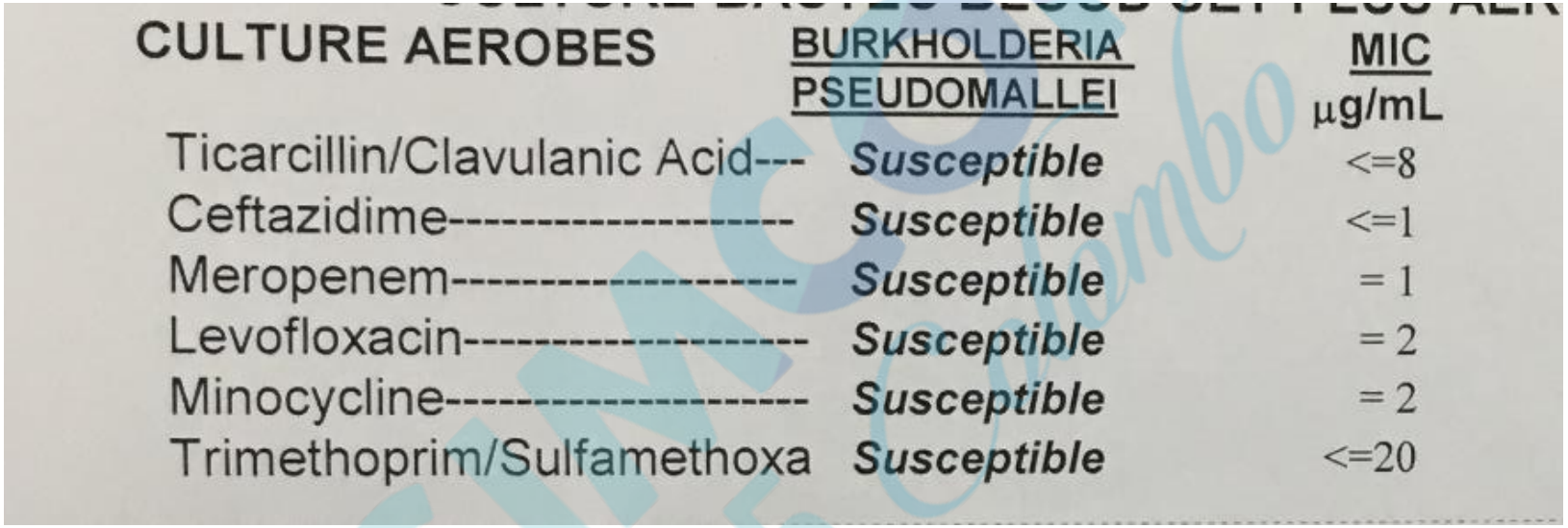


***CT-GUIDED ASPIRATION FROM MEDIASTINAL LYMPH NODE***

***Number of slides :*** Received 2 ml of thick brownish coloured fluid. 4 direct smears were prepared.

***Microscopy :***
Smears show dense neutrophil predominant inflammatory exudates mixed with many degenerating histiocytes and necrotic material in the background.
There are no granulomas.

- Culture of the CT guided aspirate– Burkholderia pseudomallei!



| CULTURE AEROBES | BURKHOLDERIA PSEUDOMALLEI | MIC µg/mL |
|---|---|---|
| Ticarcillin/Clavulanic Acid--- | *Susceptible* | <=8 |
| Ceftazidime---------- | *Susceptible* | <=1 |
| Meropenem---------- | *Susceptible* | = 1 |
| Levofloxacin---------- | *Susceptible* | = 2 |
| Minocycline---------- | *Susceptible* | = 2 |
| Trimethoprim/Sulfamethoxa | *Susceptible* | <=20 |

- He was started on Inj Ceftazidime 2 gm iv 8 hrly and TMP/SMX DS – BD
- 3 days later he developed severe right ankle joint pain
- Joint fluid aspiration was done and sent for joint fluid routine and culture
- The joint fluid also grew B. pseudomallei!
- He responded to the above treatment and was discharged
- Planned for 6 weeks of therapy with Ceftazidime and TMP/SMX Followed by TMP/SMX for a total of 1 year of therapy

- Case 1– Bacteremic/Septicemic form
- Case 2– Subacute necrotizing CAP
- Case 3– PUO with lung consolidation and splenic abscesses

# Why such varied presentations??

- Inoculum dose
- Route of transmission
- Virulence of infecting strain
- Host immune status

The American Journal of Tropical Medicine and Hygiene

The American Society of Tropical Medicine and Hygiene

# Clinical, Bacteriologic, and Geographic Stratification of Melioidosis Emerges from the Sri Lankan National Surveillance Program

Harindra D. Sathkumara, Adam J. Merritt,

[...], and Aruna Dharshan De Silva

*Some Multi Locus Sequence Typing types were correlated with certain clinical presentations.*

# Differential diagnosis

- It varies with the presentation that the patient has come with and the localization:

| Acute pneumonia | Acute sepsis | Hepatosplenic abscesses | Parotitis | Chronic pneumonia |
|---|---|---|---|---|
| CAP | Bacterial sepsis | Dimorphic fungi | Mumps | TB |
| | | TB | | Nocardia |
| | | Lymphoma | | NTM |
| | | | | Aspergillosis |

# What does this have to do with melioid?

Case Reports > N Engl J Med. 2022 Mar 3;386(9):861-868. doi: 10.1056/NEJMoa2116130.

# Multistate Outbreak of Melioidosis Associated with Imported Aromatherapy Spray

Jay E Gee [1], William A Bower [1], Amber Kunkel [1], Julia Petras [1], Jenna Gettings [1], Maria Bye [1], Melanie Firestone [1], Mindy G Elrod [1], Lindy Liu [1], David D Blaney [1], Allison Zaldivar [1], Chelsea Raybern [1], Farah S Ahmed [1], Heidi Honza [1], Shelley Stonecipher [1], Briana J O'Sullivan [1], Ruth Lynfield [1], Melissa Hunter [1], Skyler Brennan [1], Jessica Pavlick [1], Julie Gabel [1], Cherie Drenzek [1], Rachel Geller [1], Crystal Lee [1], Jana M Ritter [1], Sherif R Zaki [1], Christopher A Gulvik [1], W Wyatt Wilson [1], Elizabeth Beshearse [1], Bart J Currie [1], Jessica R Webb [1], Zachary P Weiner [1], María E Negrón [1], Alex R Hoffmaster [1]

Affiliations + expand

PMID: 35235727 DOI: 10.1056/NEJMoa2116130

## Abstract

Melioidosis, caused by the bacterium *Burkholderia pseudomallei*, is an uncommon infection that is typically associated with exposure to soil and water in tropical and subtropical environments. It is rarely diagnosed in the continental United States. Patients with melioidosis in the United States commonly report travel to regions where melioidosis is endemic. We report a cluster of four non-travel-associated cases of melioidosis in Georgia, Kansas, Minnesota, and Texas. These cases were caused by the same strain of *B. pseudomallei* that was linked to an aromatherapy spray product imported from a melioidosis-endemic area.

# Take Home Message:

- Burkholderia pseudomallei can present as:

✓Bacteremia/Septicemia

✓Community Acquired Pneumonia

✓PUO with lung consolidation and splenic abscesses

✓Aerosol use (from endemic areas)

- So…..Be Aware and Be Vigilant for this diagnosis!!

# Thank You!