Melioidosis in Bangladesh-an Update

Prof. Khwaja Nazim Uddin
Professor of Medicine
BIRDEM Genaral Hospital

Caused by Gm–ve bacteria

(Burkholderia pseudomellei)

motile,aerobic,nonsporeforming,oxidase(+)ve,nonfermenting,inherent property of drug resistant

Diabetes mellitus definite risk factor

Incubation period 2-3 weeks

(may remain latent > 25 years)

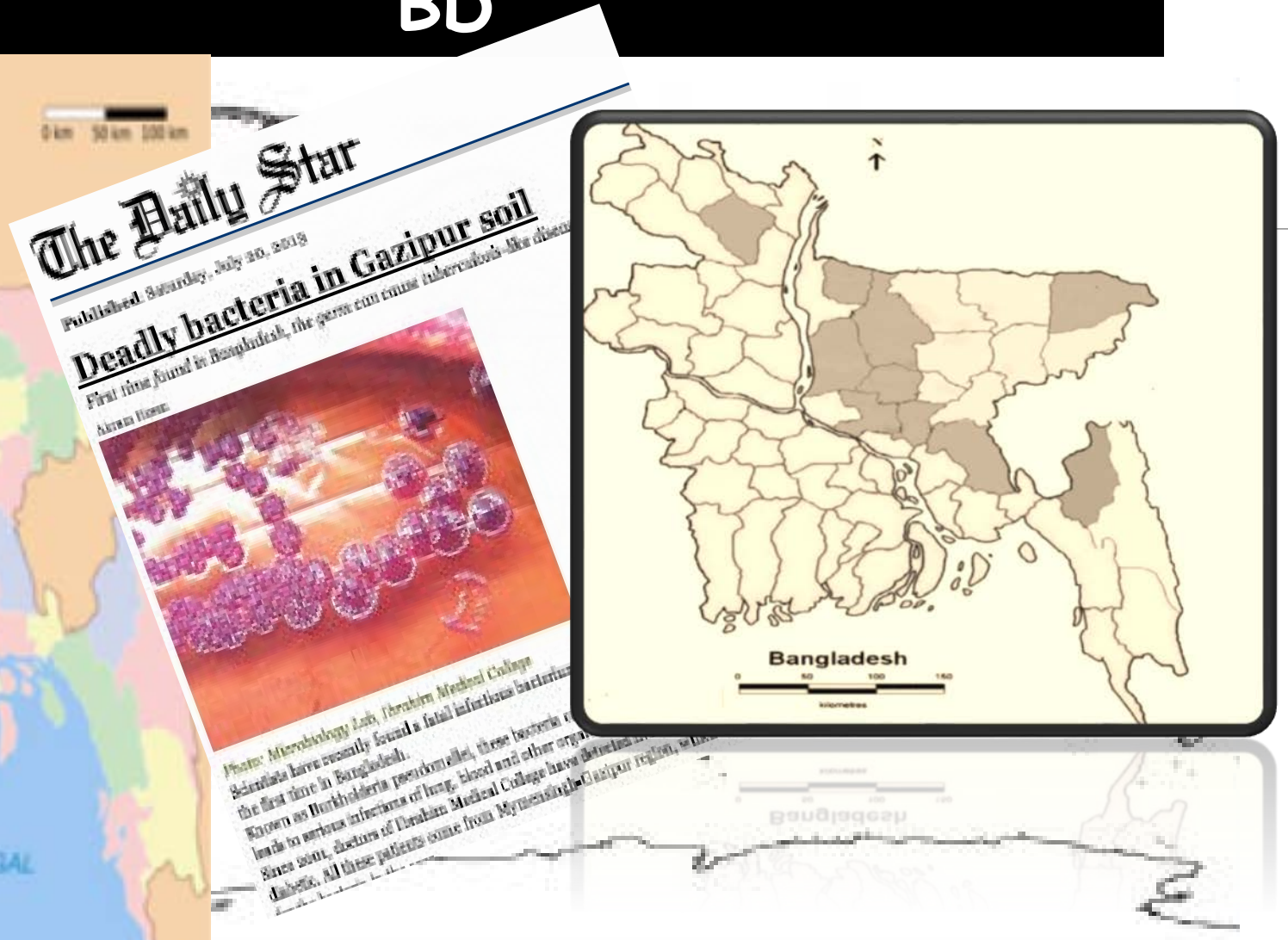
Mortality of melioidosis is 20 to 50% even with treatment

Category B bioterrorism

Disease of rice farmers

75% cases in rainy season

Worldwide distribution : Melioidosis in BD



Cheng AC and Currie BJ. *Clin Microbiol Rev* **2005**; 18:383-416.

Melioidosis in Bangladesh: *History*

First reported case of a foreigner (English steward), in BANGLADESH in 1964.

1st Bangladeshi case reported in foreign journal in 1988.

1st reported case in Bangladeshi journal in 2001.

Cases has been detected in 10 districts

Organism has been detected in the soil of Kapasia in Gazipur, June 2013.

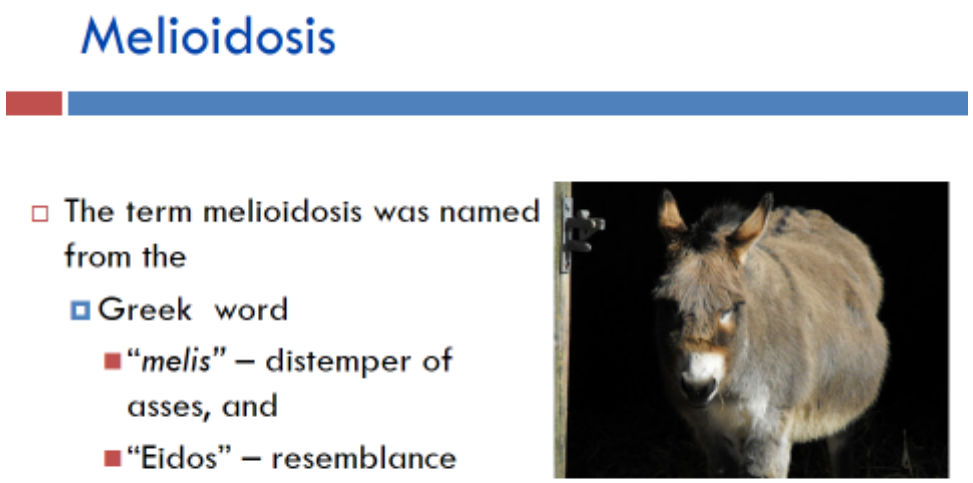
Bangladesh is now being designated as the 18th definite country for Melioidosis in the world

Melioidosis-Evolution of discovery

- Alfred Whitmore first described melioidosis in 1912
- The named melioidosis, was given by Stanton and Fletcher in 1932
- Bacterium has been variously known as Bacillus pseudomallei,

Bacillus whitmorii (or Bacille de Whitmore), Malleomyces pseudomallei, Pseudomonas pseudomallei, and,

- Since 1992, it is Burkholderia pseudomallei



Nothing is ever new!

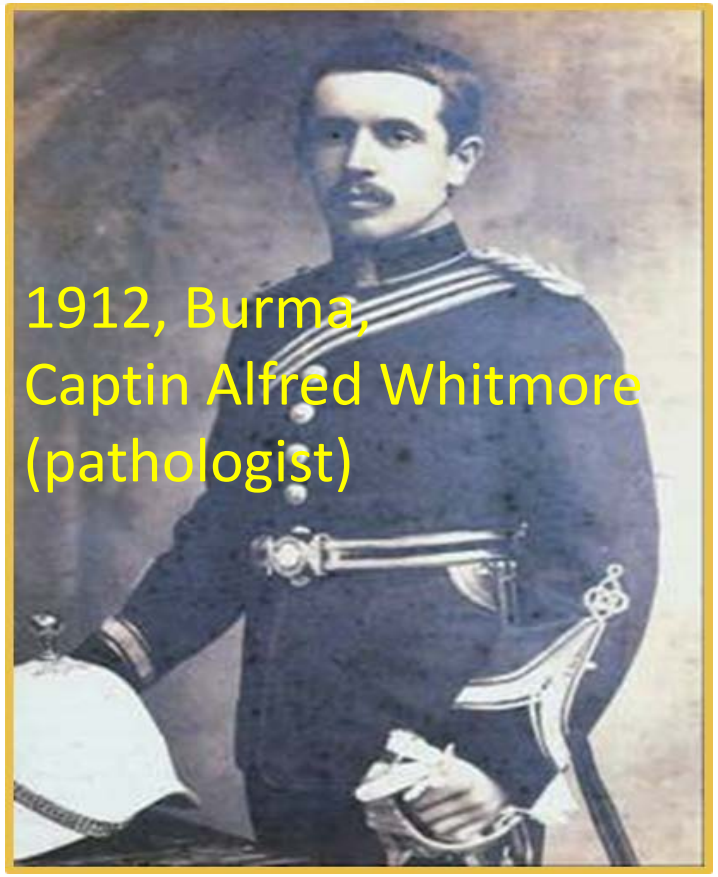
"MORPHINE INJECTOR'S SEPTICÆMIA" ("WHITMORE'S DISEASE").

BY H. H. G. KNAPP, M.A., M.D. (Oxon.), D. T. M. & H. (Camb.),

MAJOR, I.M.S.,

Rangoon.

My object in writing this note is to direct the attention of practitioners in India and elsewhere to this disease, in order that it may be further investigated, since it seems improbable that it is confined to Rangoon. The habit of injecting



1912, Burma,
Captin Alfred Whitmore
(pathologist)

World wide distribution

A DECADE OF EXPERIENCE OF THE UNITED KINGDOM'S MELIOIDOSIS DIAGNOSTIC SERVICE

H Malnick1, HA Englender1, DAB Dance2, MD Smith3, AJH Simpson4, TL Pitt1
1Centre for Infections, Health Protection Agency, UK; 2HPA Regional Laboratory Network, UK;3Taunton & Somerset Hospital, UK; 4DSTL, Porton Down, UK

- **1997 -2007, referred from UK, Europe, Brazil**
- **33 confirmed isolates of *B. pseudomallei* from individual patients**
- **22 patients were referred from UK hospitals**

Commonly with a history of travel in South East Asia or the Indian subcontinent

Thailand 9 Bangladesh 6* India 2 Malaysia 2 Vietnam 2

***6 cases occurred in 1998- 3 visited heavily flooded Sylhet district(Dance et al.1999).**

REFERENCES

- Abbink FC, Orendi JM, de Beaufort AJ. Mother-to-child transmission o
- Burkholderia pseudomallei.N Engl. J Med 2001;344:1171.
- Brent AJ, Matthews PC, Dance DAB, Pitt TL, Handy R. Misdiagnosing melioidosis.
- Emerg Infect Dis 2007;13:349.
- Dance DAB, Smith MD, Aucken HM, Pitt TL. Imported melioidosis in England
- and Wales. Lancet 1999;353:208.

Epidemiology

- Melioidosis accounts for
  - about 20% of all community-acquired septicemias in Northern Thailand and
    - 2000 to 3000 new cases are diagnosed every year
  - In Malaysia
    - Seroprevalence is 17-22% among rice farmers and
    - 26% in blood donors
  - In north Australia
    - 0.6 to 16% of children have evidence of infection by *B. pseudomallei*

    -Bangladesh:22-31% seropositive

NoC
W: 136
L: 62
Post
Rel. Pos -11.0 mm
SAG OBL T2 TSE MAS Cedlog
TSE-4000/120 (16)
BIRDEM
A SABUR 37 YRS
ID 1931612 M
3 Aug 2015/ 09:13
Head
Left
Slice 6 (9)
Rel. Pos 5.5 mm
SAG OBL T2 TSE MAS Cedlog

Melioidosis in Bangladesh
Socio-demographic characteristics (N-32).

- 32 cases (since 1988)
- Endemic: 26

  Mymensingh-Gazipur

  Sylhet
- Returning travelers: 6
- 31 were diabetic
- 25 were male

Method

- Previously published literatures
- information regarding melioidosis in and/or from Bangladesh.
- Medline, Banglajol search
- key words 'melioidosis',

  ' Bangladesh' *'Burkholderia psuedomallei'*
- local, unpublished cases, personal communication

Diagnostic Pathway

Indian J Orthop. 2010 Apr–Jun; 44(2): 216–220.
doi: 10.4103/0019-5413.61829
Copyright © Indian Journal of Orthopaedics
Burkholderia pseudomallei mu… (melioidosis) in India
Vivek Pandey, Sripath… Sarabjeet Singh…
© The Fellowship of Postgraduate Me…

Mel…
Postgrad Med J (1991) 67, 764 – 766
Missed Diagnosis
Melioidosis in a patient from Bangladesh
C.C. Kibbler[1], C.M. Roberts[2], G.L. Ridgway[1] and S.G. Spiro[2]
Departments of [1]Clinical Microbiology and [2]Respiratory Medicine, University College Hospital, London WC1E 6AU, UK.

Mel… within … acquir… were identifie… female rice farme… phadenitis and the oth… and renal calculi who wa… septicemia and septic arthri…

Summary: **A 54 year old Bangladeshi man presented with a history and chest X-ray appearances suggestive of pulmonary tuberculosis. Following deterioration 4 weeks later, he required ventilation. Although a blood culture isolate was subsequently found to be *Pseudomonas pseudomallei*, it was initially misidentified and dismissed as a contaminant. Further cultures demonstrated the organism, but the patient died, despite treatment with ceftazidime. The case illustrates the importance of taking a detailed travel history and having a high index of suspicion in patients from South East Asia and the Indian sub-continent, including Bangladesh, where the disease has not previously been considered endemic.**

…osis in Siem Rea… Cambodia
Vanaporn Wi… Sharon J. P… …it Amornchai,
…Tropical Medicine, …hidol University, …ne,

…ditorial
…XPLORED !
…mber of virulence factors. …III secretion system of *B.* …s bacterial invasion of epithelial …ular survival. The presence of …plex" is believed to be responsible for …t course of a rapidly fatal septicaemia.[3] …ology may show granuloma and necrosis …king caseation, suggestive of tuberculosis.
…elioidosis is rarely diagnosed in Bangladesh. In Bangladesh, the first case of melioidosis was reported in 1988 by ICDDR, B.[4] Subsequently, between 1988 to

Department of Microbiology, Bach Mai Hospital, 78 …
[b]Friedrich Loeffler Institute of Medical Microbiology, Ernst Moritz Arndt University …eifswald, Martin-Luther-Str. 6, 17489 Greifswald, Germany
[c]Department of Infectious Diseases, Bach Mai Hospital, 78 Giai Phong Road, Hanoi, Vietnam
[d]Robert Koch Institute, Burgstr. 37, 38855 Wernigerode, Germany
[e]Vietnamese Academy of Science and Technology, Institute of Biotechnology, 18 Hoang Quoc Viet, Hanoi, Vietnam

ELSEVIER
Transactions of the Royal Society of Tropical Medicine and Hygiene (2008) 102/S1, S10–S11
available at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevierhealth.com/journals/trst
…nce of melioidosis in Myanmar
…hin Thin Mar
…niversity of Medicine 2, Yangon, Myanmar
of th…
…tbach[b], …[b], Dinh Duy Khang[e],
THE ROYAL SOCIETY OF TROPICAL MEDICINE & HYGIENE

Melioidosis in BD: Presentation

Acute **(days)/fulminant – 4, septicemia reported**

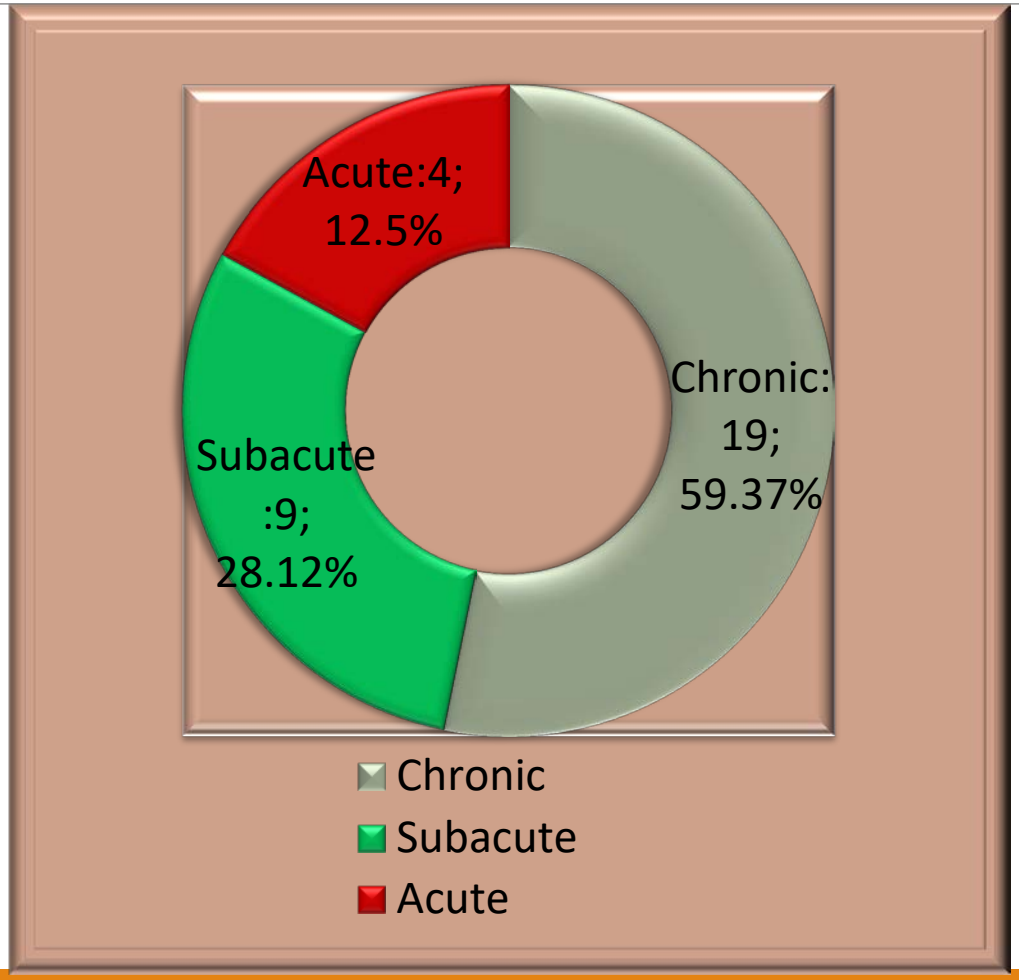
Subacute <2 months(9)

Chronic >2 months(19) **- commonest presentation mimicking tuberculosis**

Latent – with long incubation period

- May remain latent for years
- Reactivation occurs long time after exposure (after 62 years)

(described as Vietnamese time bomb**)– yet to know**

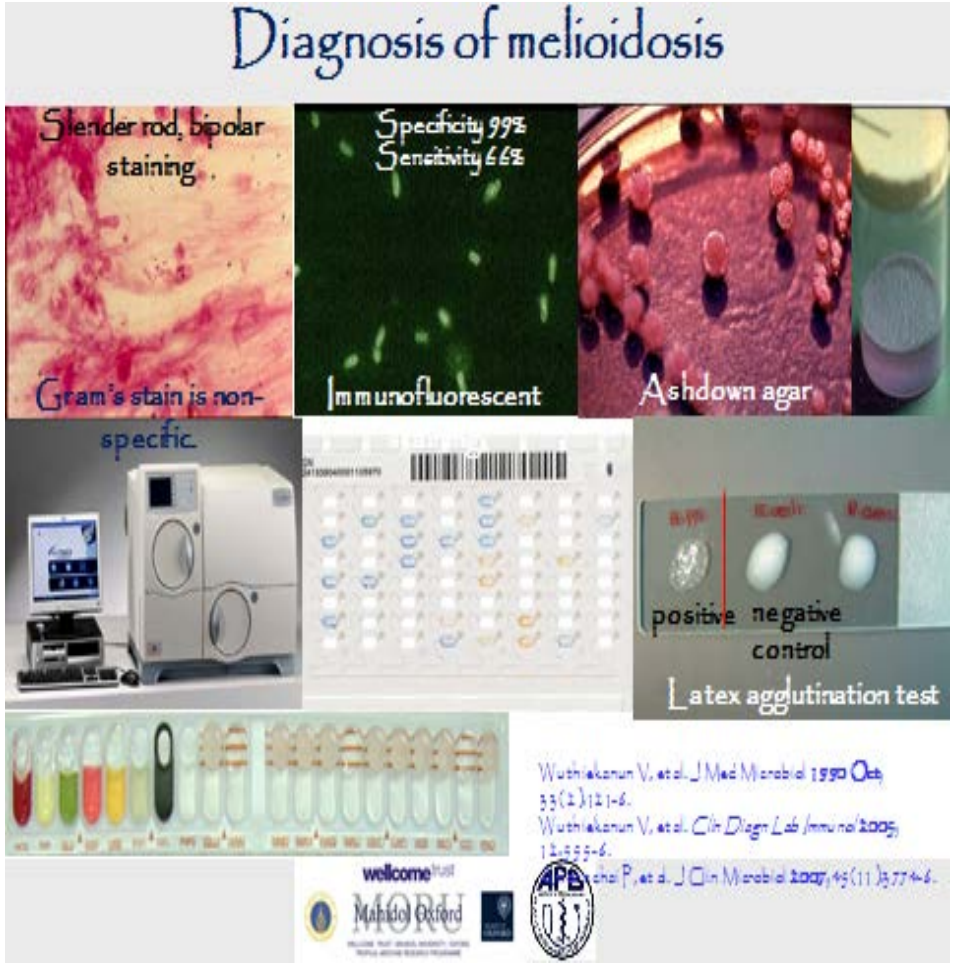


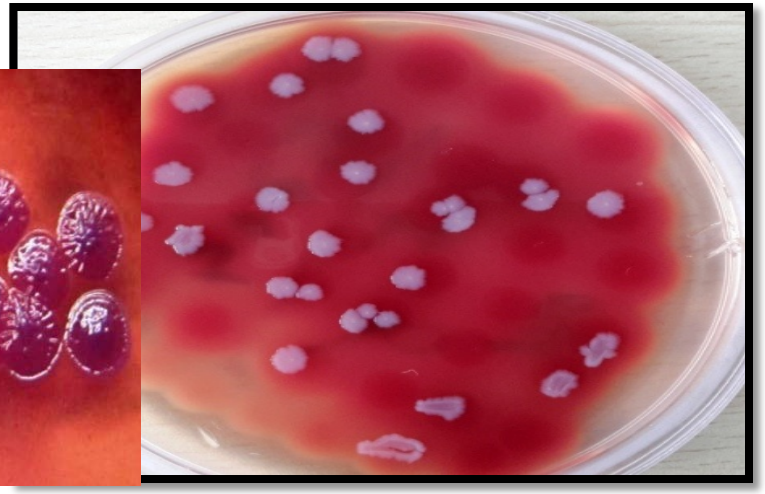
Melioidosis in BD: Laboratory diagnosis

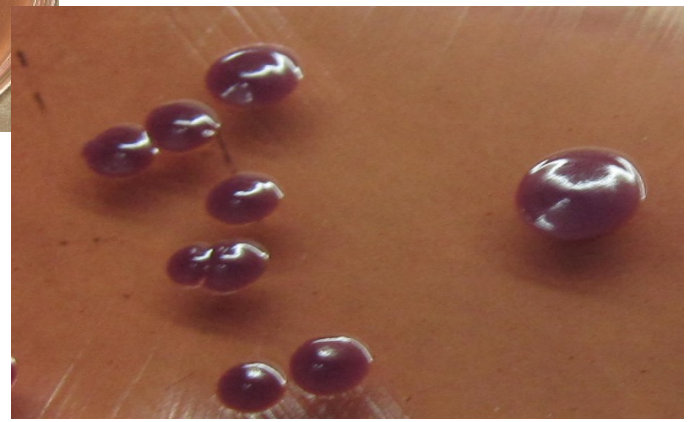
- *C/S:Mckonkey's Blood agar media*

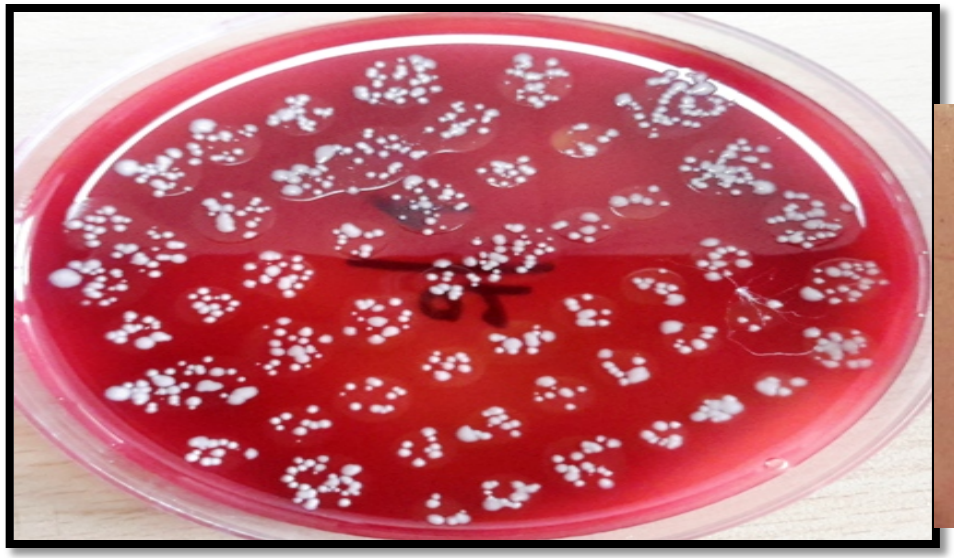
- **Ashdown's media only available in BIRDEM & IMC,**

  used in soil culture
- **PCR: done in some diagnosed cases**
- **Serology : Seroprevalence**
- **MLST**









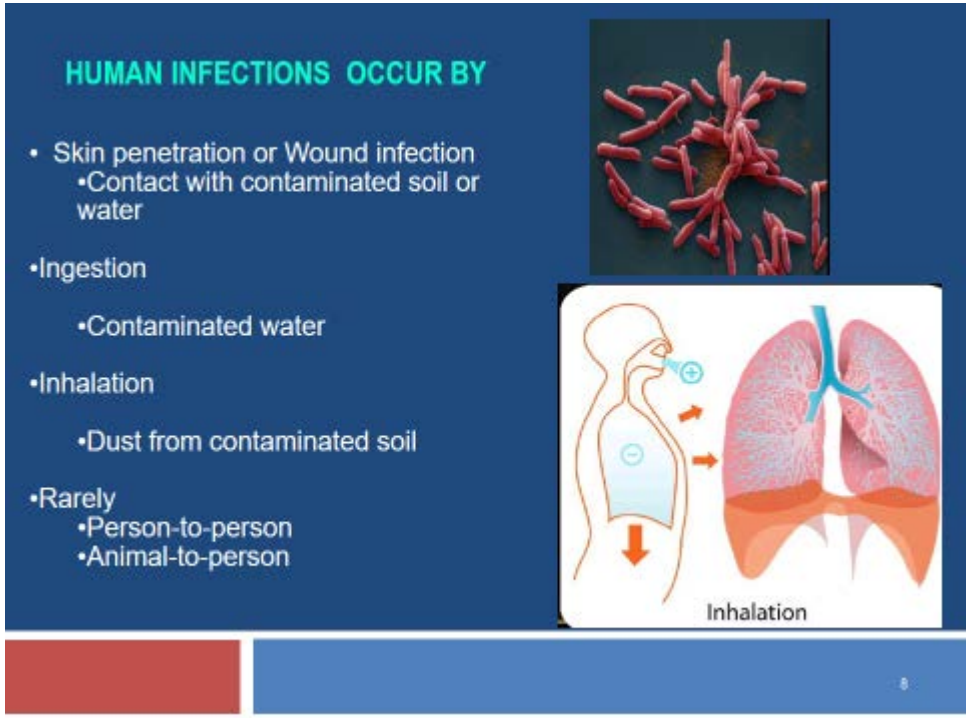
Bacteriology

How stronger bacteria is?

This bacteria is capable of surviving

- in prolonged nutrient deficiency (up to 10 yrs)
- in presence of antiseptic and detergent solutions
- in acidic environments at pH 4.5 for up to 70 days
- in dehydrated condition (soil water content <10% for up to 70 day)

How we get infected



Profile of our cases(32)

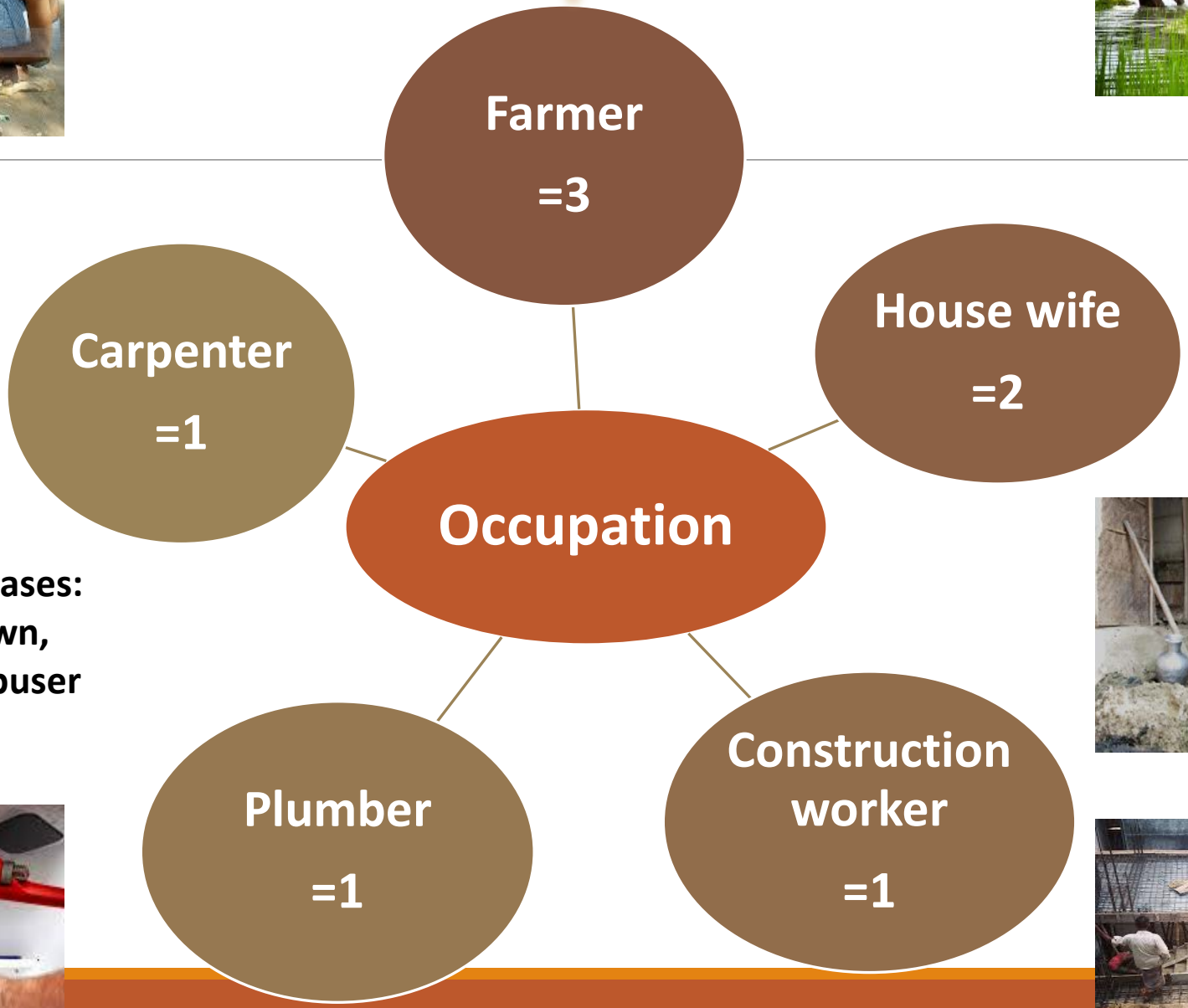
CLINICAL

DM	Abscess	joint	Lung	Skin	>3 Sites
31(97%)	13(40%)	9(28%)	9(28%)	7(22%)	8(25%

LABORATORY

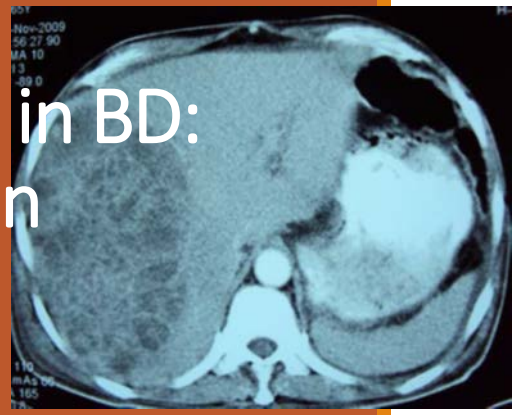
Blood C/S +ve	Pus C/S V+	Other C/S +ve	>one sample
13(40%)	9(28%)	10(31%)	19(60%)

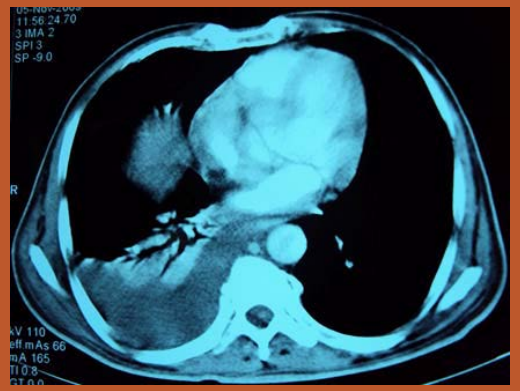
Occupation

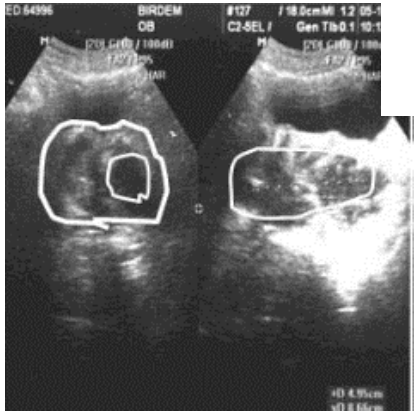


Rest of 3cases:
- **2 unknown,**
- **1 drug abuser**

Melioidosis in BD: Presentation

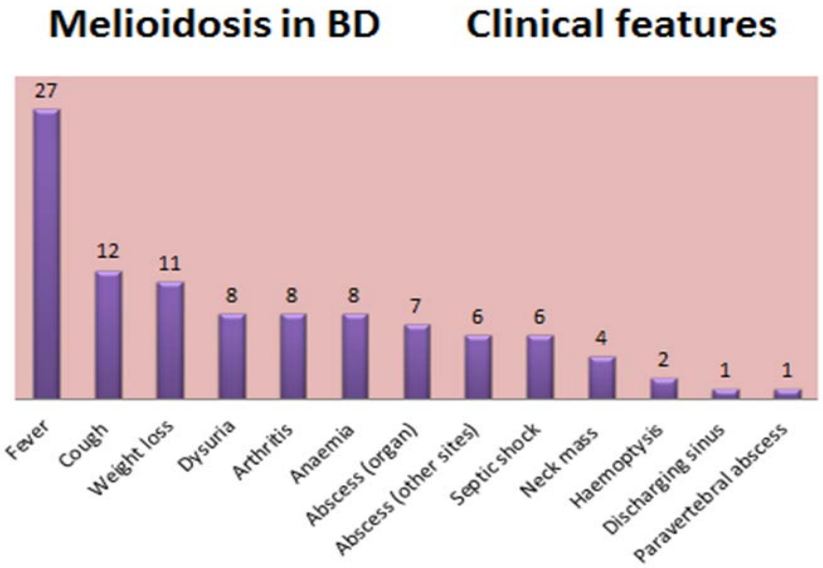






- **Focal : arthritis, liver abscess prostatic abscess, (no parotid abscess like Thailand children)**

History: **travel/dweller in endemic areas**

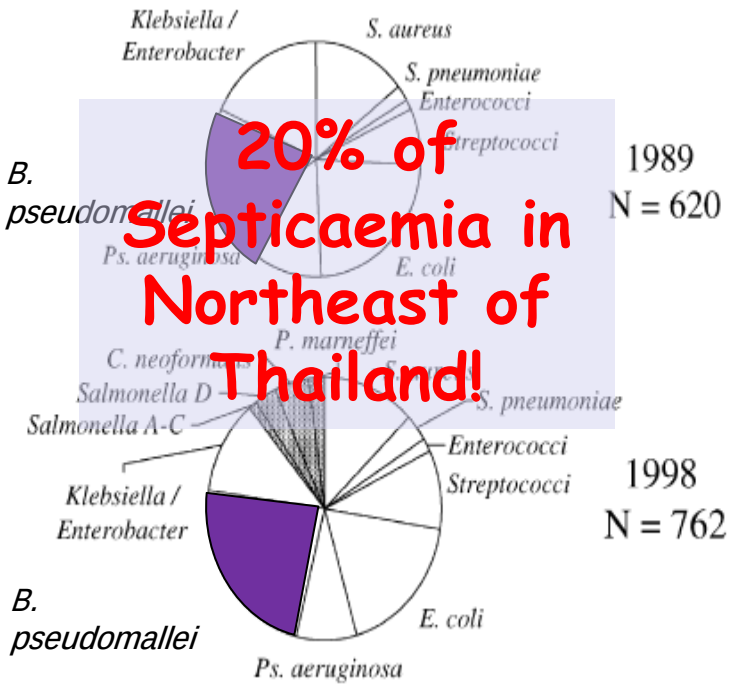


Systemic symptoms- Fever commonest (96%)

Fulminant:Pneumonia,septicemia

Disseminated disease: multi site/organ involvement

:High endemic area Melioidosis:



20% of Septicaemia in Northeast of Thailand!

Great mimicker
Internal organ abscesses
50% overall mortality

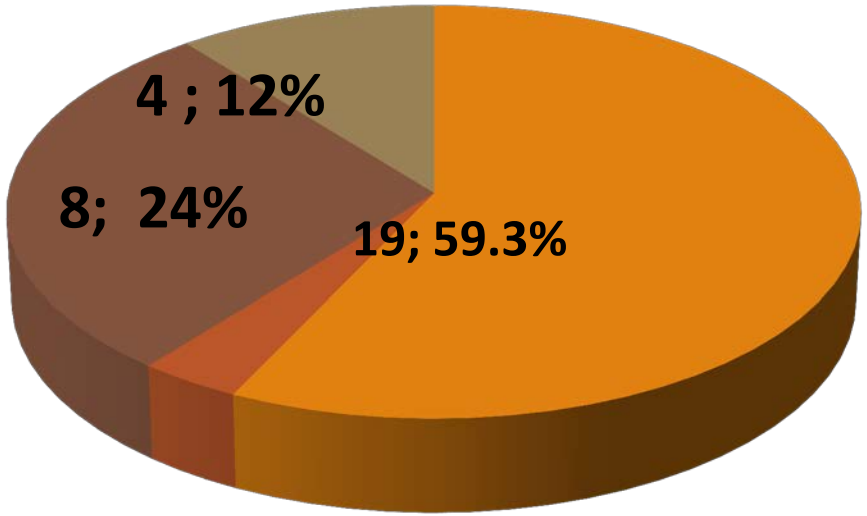
Required high dose iv antibiotic
Protracted course of antibiotic

Life-long follow up

Outcome summary of so far detected *cases(32 cases)*

19 cases responded to

- ***Initial IV:***
- Ceftazidime/imipenem/meropenum.
- ***Followup oral Rx:***
- Doxycycline and trimethoprim-sulfamethoxazole or amoxicillin-clavulanic acid.



- 1 case presenting with cutaneous manifestation was cured by oral antibiotics.

- 4 cases treatment was not mentioned
- 8 patients died despite treatment(25%)

Treatment (Initial acute phase)

Antibiotics	Dose	Duration	Cases
Ceftazidime	50-100mg/kg 2 gm 8 hrly daily	2 to 6 wks	14
Meropenem	25-50 mg/kg 1 gm 8 hrly daily	3 to 4 wks	09
Ceftazidime switched to meropenem	Do	4 wks	2
Meropenem followed by ceftazidime	Do	6 wks	1

3 cases died before culture report was received

- 2 of them were on ceftazidime
- 1 of them on ceftriaxone

Treatment (eradication phase): oral (3m)

Antibiotics	Dose	Duration	Cases
Doxycycline + Co-trimoxazole	1 tab (100 mg) 12 hrly (4mg/kg) + 2-3 tab (80-160/400-800mg) every 12 hrly	3 to 5 months	9
Doxycycline + Amoxicillin/ clavulanic cid	1 tab (100 mg) 12 hrly (4mg/kg) + 2-3 tab every 8 hrly (500mg/125mg)	3 months	5
Doxycycline + ciprofloxacin	Do + 1 tab (750 mg) every 12 hrly	3-4 months	2
Doxycycline/Co-trimo Xazole	Do	4-10 months	6
*Cured -12	*improved -7	*Death -8	*no relapse in 2-4 yrs. follow up

Case definitions

Cured resolution of clinical and laboratory parameters following completion of initial and maintenance therapy

Improved following initial treatment showed improvement(clinical + laboratory parameters) & is currently on maintenance therapy

Lost from follow up:initial therapy showed improvement(clinical and laboratory parameters) but following discharge missed their follow up visits

Relapse/Reinfection:S/S 6 months after complete disappearence

Initial acute-phase therapy for melioidosis.
**international concensus recommendation 2012

Patiemts	Drug	Dosage/Route	Frequency
With no complications	Ceftazidime 50mg/kg (up to 2g)	Intravenous	Every 8h
With neuromelioidosis	Meropenem 25mg/kg (up to 1g)	Intravenous	Every 8h

**Duration of acute-phase therapy is generally 10–14 days; however, >4 weeks of parenteral therapy may be necessary in cases of more severe disease

*****David Dance.Treatment and prophylaxis of melioidosis.International Journal of Antimicrobial Agents(2014);43:310-18*

Oral eradication-phase therapy for melioidosis. **international consensus recommendation 2012

Drug	Patient characteristics	Recommended dosage	Frequency
Trimethoprim/sulfamethoxazole (co-trimoxazole)	Adult, >60kg	160mg/800mg tablets	TwoTablet every 12 H
Trimethoprim/sulfamethoxazole (co-trimoxazole)	Adult, 40–60kg	80mg/400mg tablets	Three tablets every 12H
Trimethoprim/sulfamethoxazole (co-trimoxazole)	Adult, <40kg	160mg/800mg tablets	One tablet every 12H
Amoxicillin/clavulanic acid (co-amoxiclav)	Adult, >60kg	500mg/125mg tablets	Three tablets every 8H
Amoxicillin/clavulanic acid (co-amoxiclav)	Adult, <60kg	500mg/125mg tablets	Two tablets every 8h
Amoxicillin/clavulanic acid (co-amoxiclav)	Child	20mg/5mg per kg	Every 8h

** Recommended duration of therapy is a minimum of 12 weeks

**David Dance.Treatment and prophylaxis of melioidosis.International Journal of Antimicrobial Agents(2014);43:310-18

Literature review in Bangladesh

1.Melioidosis in Bangladesh: a case report. Trans R Soc Trop Med Hyg, 1988 by Strulens et al.

2.Melioidosis in Bangladesh- To see or not to see. Bang J Pathol(editorial)1998 by Haq JA

3.Melioidosis- A case report. J of Bang Coll of Physician and surgeon, 2001 by Uddin KN et al

4.Melioidosis-Case reports and review of cases recorded among Bangladeshi population from 1988-2014. Ibrahim Med Coll.J. 2014. Barai L et al

- 5. A case of fatal meliodosis presenting as septic arthritis and septicaemia. Bangladesh Crit Care J 2015 by Fatema et al
- 6. Melioidosis: Truly uncommon or Uncommonly diagnosed in Bangladesh? A case report. Birdem Medical Journal 2015. by Rahim et al.
- **7.8.9.10**
- continuing……

Presentation out side country

Jilani S Alam.Molecular characterization of B.Pseudomellei and it's seroprevalence.(abstract)1st south Asian Mellioidosis congress 2015 .India

Uddin K.N., Afroze S.R., Rahim M.A., Barai L., Haq J.A. Melioidosis in Bangladesh. ABSTRACTS OF THE ECIM 2015 . 14th EUROPEAN CONGRESS OF INTERNAL MEDICINE 14-16 OCTOBER, 2015 MOSCOW, RUSSIA.

Deceptive presentations mimicking Mycobacterium tuberculosis.Afroze S.R., Barai L., Rahim M.A., Rahman R., Uddin K.N.(Abstract)Poster 14th ECIM.Moscow,Russia.

Uddin K.N. Melioidosis in Bangladesh an update. ABSTRACTS OF THE17th WCIM 2016 in Bali,Indonesia.

Predicted global distribution of *B. pseudomallei* and burden of melioidosis (Nature Microbiology, 2016)

- Predicted breakdown by country (South Asia)

Country	Predicted Incidence	Predicted Mortality
India*	52306 (22335-124652)	31425 (13404-75601)
Bangladesh*	16931 (7814-37794)	9454 (4325-21621)
Sri Lanka*	1881 (705-4488)	619 (230-1501)
Nepal†	914 (317-2354)	502 (174-1353)
Pakistan*	442 (95-1718)	260 (58-1059)
Bhutan†	13 (5-42)	8 (3-24)

*Endemic but under-reported

† Predicted to be endemic but never reported

Bangladesh
Rangpur
Rangpur
Rajshahi
Rajshahi
Dhaka
Dhaka
Sylhet
Sylhet
Khulna
Khulna
Barisal
Barisal
Chittagong
Chittagong

Conclusion

Facts:

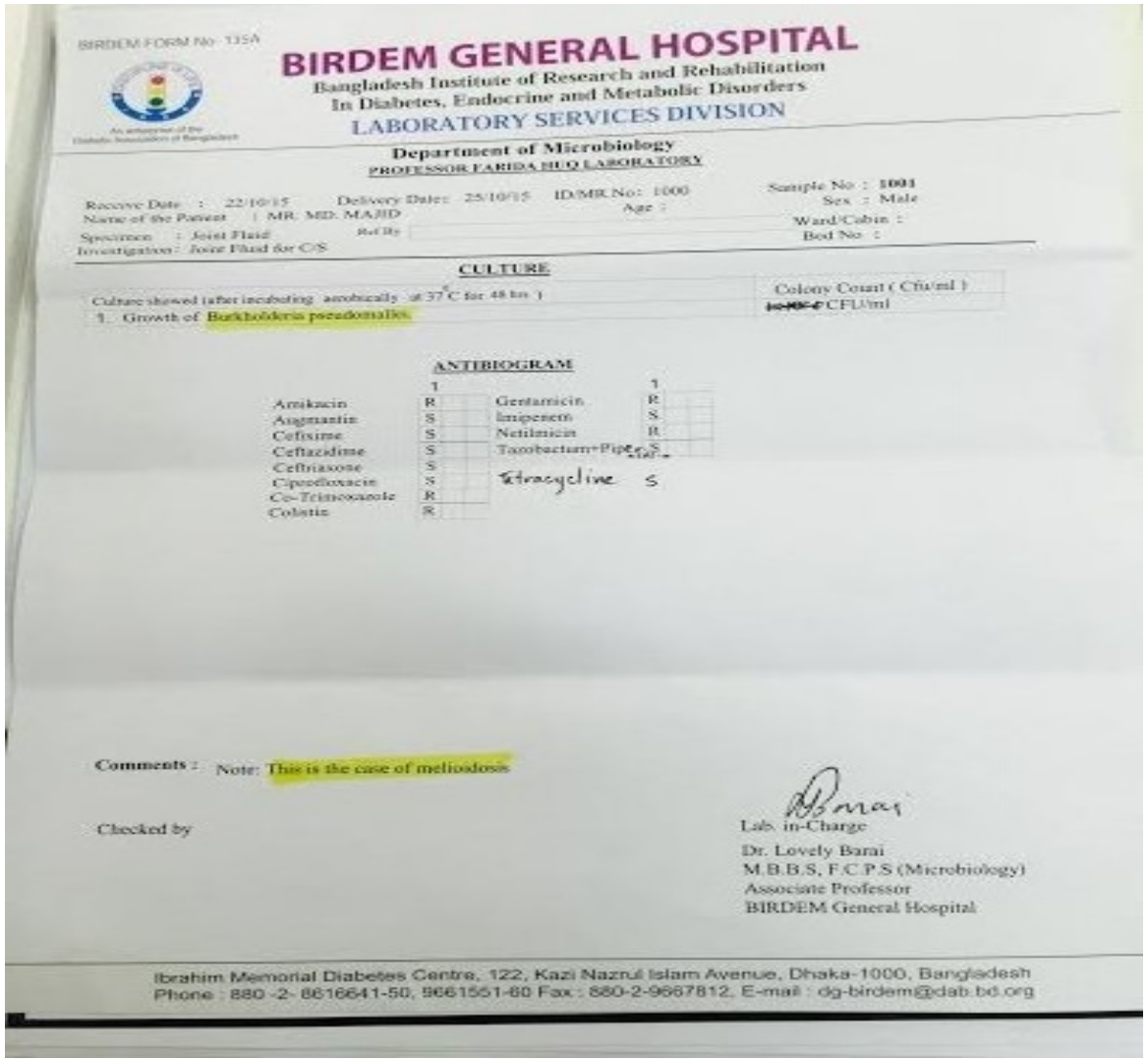
Melioidosis is probably far commoner in Bangladesh than currently recognised

Reality:

Melioidosis is an emerging infection in Bangladesh

We need systematic studies to detect the magnitude & extent of this disease.

Investigations



BIRDEM FORM No: 135A

BIRDEM GENERAL HOSPITAL
Bangladesh Institute of Research and Rehabilitation
In Diabetes, Endocrine and Metabolic Disorders
LABORATORY SERVICES DIVISION

Department of Microbiology
PROFESSOR FARIDA HUQ LABORATORY

Receive Date : 22/10/15 Delivery Date: 25/10/15 ID/MR No: 1000 Sample No : 1001
Name of the Patient : MR. MD. MAJID Age : Sex : Male
Specimen : Joint Fluid Ref By Ward/Cabin :
Investigation : Joint Fluid for C/S Bed No :

CULTURE

Culture showed (after incubating aerobically at 37°C for 48 hrs) Colony Count (Cfu/ml)
1. Growth of Burkholderia pseudomallei. CFU/ml

ANTIBIOGRAM

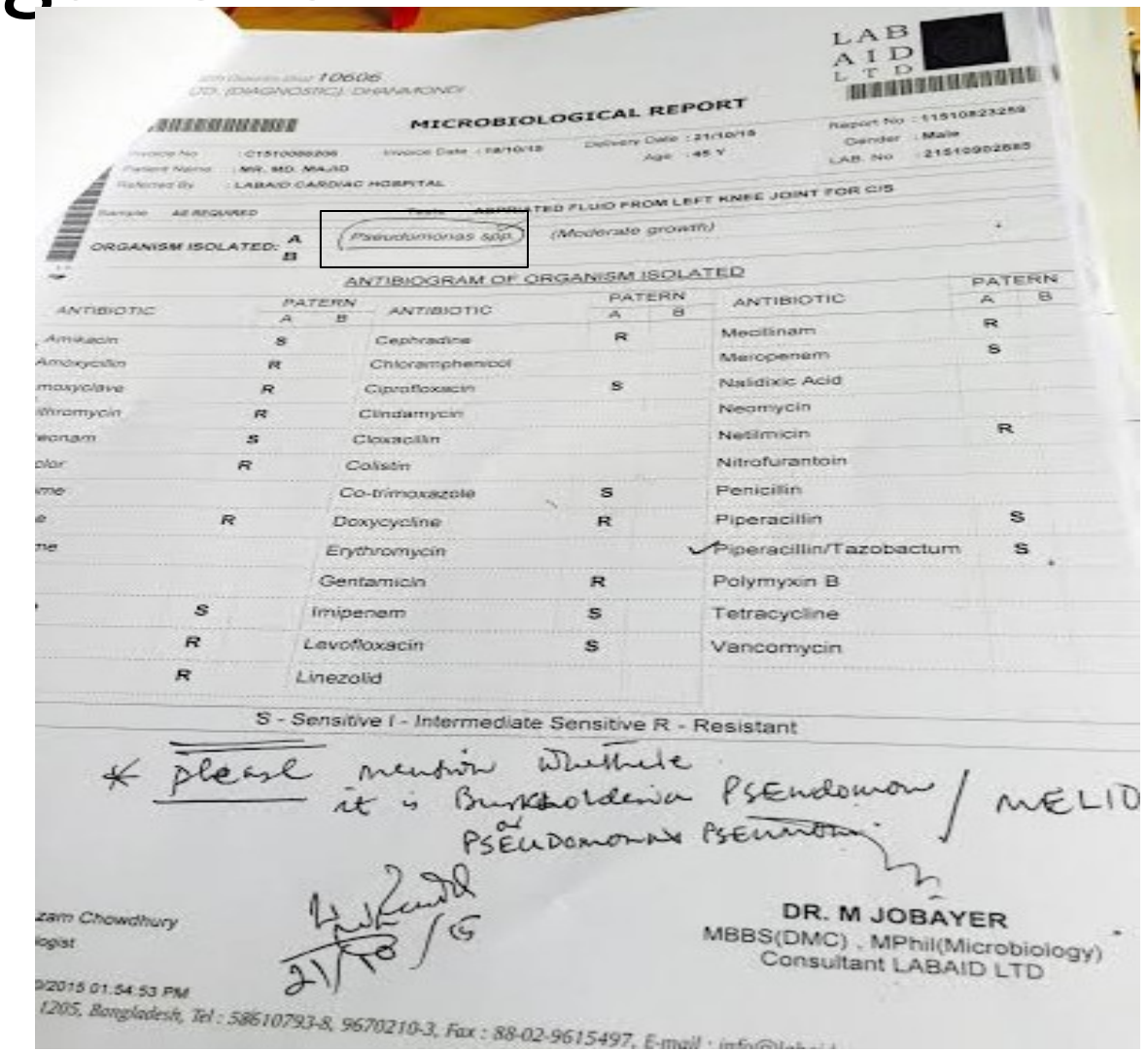
	1		1
Amikacin	R	Gentamicin	R
Augmentin	S	Imipenem	S
Cefixime	S	Netilmicin	R
Ceftazidime	S	Tazobactam+Pipe	S
Ceftriaxone	S	Tetracycline	S
Ciprofloxacin	S		
Co-Trimoxazole	R		
Colistin	R		

Comments : Note: This is the case of melioidosis

Checked by

Lab. in-Charge
Dr. Lovely Barai
M.B.B.S, F.C.P.S (Microbiology)
Associate Professor
BIRDEM General Hospital

Ibrahim Memorial Diabetes Centre, 122, Kazi Nazrul Islam Avenue, Dhaka-1000, Bangladesh
Phone : 880 -2- 8616641-50, 9661551-60 Fax : 880-2-9667812, E-mail : dg-birdem@dab.bd.org



LAB AID LTD

MICROBIOLOGICAL REPORT

Report No : 11510823259
Gender : Male
LAB. No : 21510902585

Invoice No : C1510090206 Invoice Date : 18/10/15 Delivery Date : 21/10/15
Patient Name : MR. MD. MAJID Age : 45 Y
Referred By : LABAID CARDIAC HOSPITAL

Sample : AS REQUIRED ABSTRACTED FLUID FROM LEFT KNEE JOINT FOR C/S

ORGANISM ISOLATED: A Pseudomonas spp. (Moderate growth)
B

ANTIBIOGRAM OF ORGANISM ISOLATED

ANTIBIOTIC	PATERN A	B	ANTIBIOTIC	PATERN A	B	ANTIBIOTIC	PATERN A	B
Amikacin	S		Cephradine	R		Mecillinam	R	
Amoxycillin	R		Chloramphenicol			Meropenem	S	
moxyclave	R		Ciprofloxacin	S		Nalidixic Acid		
ithromycin	R		Clindamycin			Neomycin		
eonam	S		Cloxacillin			Netilmicin	R	
olor	R		Colistin			Nitrofurantoin		
me			Co-trimoxazole	S		Penicillin		
e	R		Doxycycline	R		Piperacillin	S	
me			Erythromycin			Piperacillin/Tazobactum	S	
			Gentamicin	R		Polymyxin B		
	S		Imipenem	S		Tetracycline		
	R		Levofloxacin	S		Vancomycin		
	R		Linezolid					

S - Sensitive I - Intermediate Sensitive R - Resistant

* Please mention whether it is Burkholderia PSEUDOMONAS / MELIO or PSEUDOMONAS PSEUDOMALLEI

zam Chowdhury
logist

21/10/15

DR. M JOBAYER
MBBS(DMC) , MPhil(Microbiology)
Consultant LABAID LTD

9/2015 01:54:53 PM
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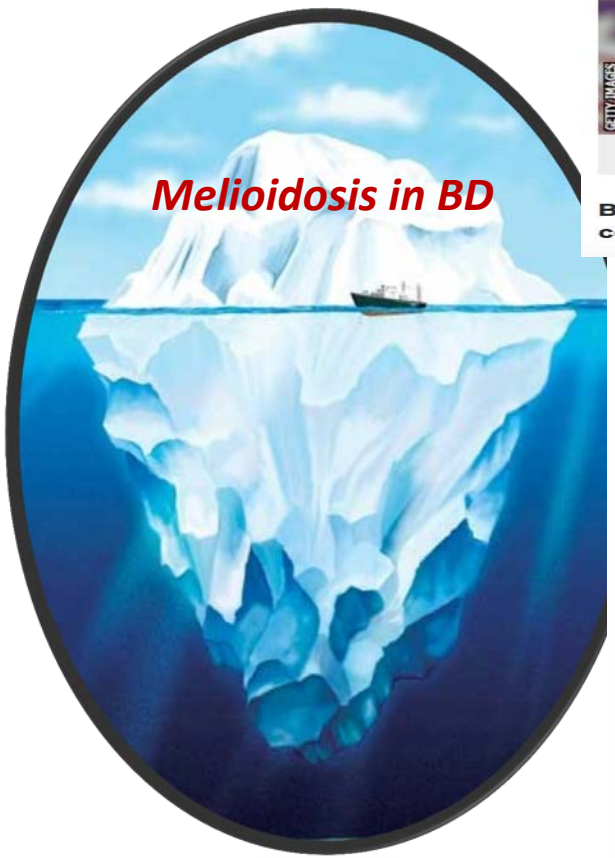
Take home messages

Clinician

- Should suspect any case with fever specially those with PUO
- Better to exclude Melioidosis before starting empirical treatment of TB

Microbiologist

- Should think of Melioidosis before discarding a specimen as contaminant
- Try to explore B.Pseudomellei in reports of Pseudomona spp



England v Bangladesh: Tourists collapse to 108-run defeat

By Matthew Henry
BBC Sport

12 minutes ago | Cricket | 9 Share

Alistair Cook and Ben Duckett had put on 100 for the opening partnership

Bangladesh claimed their first Test win over England as the tourists collapsed after tea on day three of the second Test in Dhaka.

Acknowledgement

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