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Diagnostic & Management Challenges in Extrapulmonary Tuberculosis

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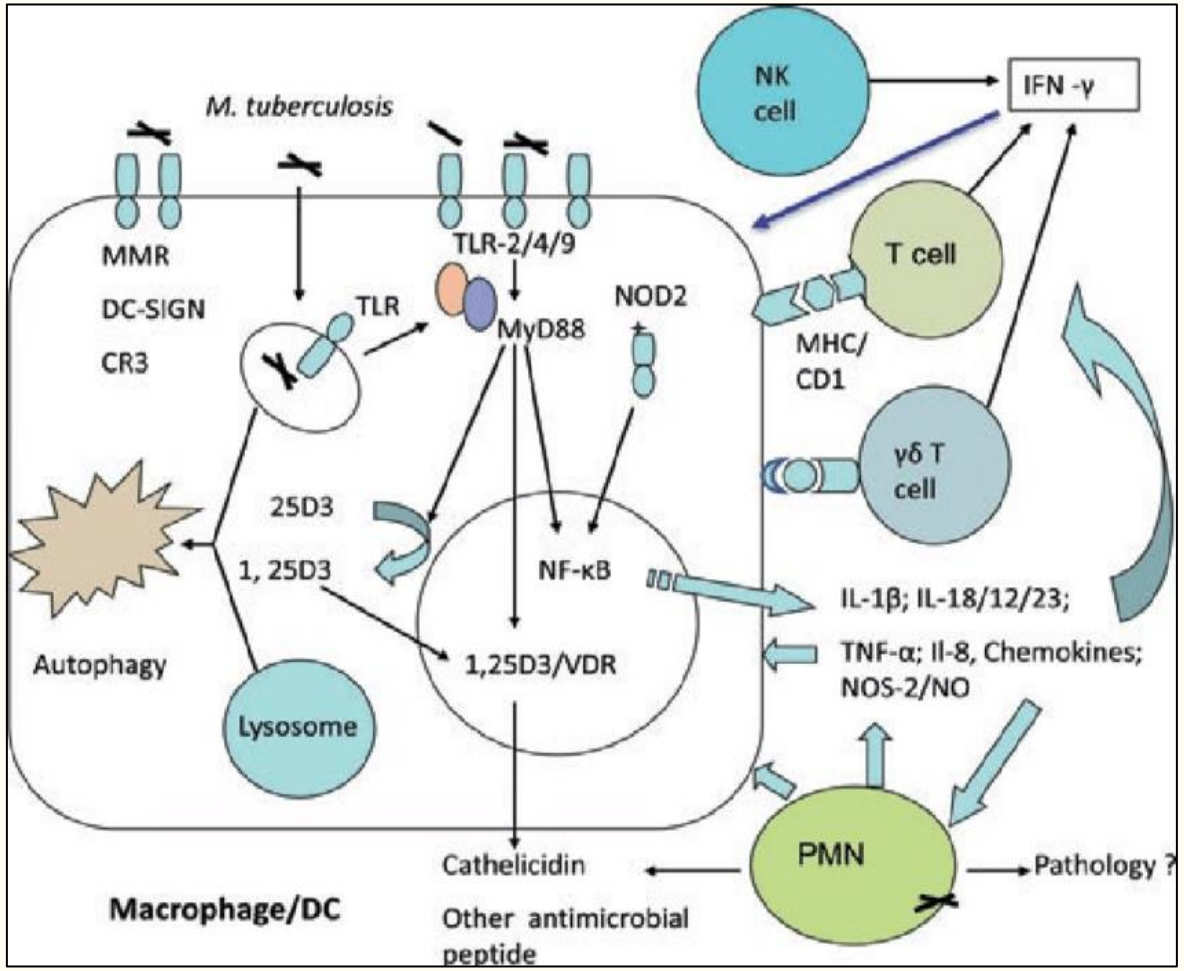
Extrapulmonary Tuberculosis : Receptors and Clinical Pathogenesis Hypothesis

Extrapulmonary Tuberculosis

- Pleural Tuberculosis
- Pericarditis Tuberculosis
- Lymphadenitis Tuberculosis
- Meningitis Tuberculosis
- Skin and Bone Tuberculosis
- Ocular Tuberculosis
- etc



Innate immunty to tuberculosis infection. M. tuberculosis is phagocytosed by macrophages and dendritic cells through membrane-bound receptors such as CR3, scavenger receptor, MMR, TLR, NOD2 and DC-SIGN. These lead to activation of macrophage signalling pathways (NF-kB), causing secretion of pro-inflammatory cytokines, chemokines, and antimicrobial molecules, and activation of VDR, which induces the expression of the antimicrobial peptides cathelicidin and ?-defensin. In addition, induction of autophagy mediates antimicrobial activity. PMN cells recognize and engulf M. tuberculosis and secrete antimicrobial peptides to kill bacteria. NK cells, ??T cells and CD1-restricted T cells are also be activated by specific ligands and cytokines, release cytotoxic factors and

DOI:10.13140/RG.2.2.16972.92802

Ayuningtyas *et al.*
Journal of Medical Case Reports (2022) 16:154
https://doi.org/10.1186/s13256-022-03376-w

Journal of Medical Case Reports

CASE REPORT Open Access

Confirmed severe acute respiratory syndrome coronavirus 2 encephalitis in cerebrospinal fluid: a case report

Triana Ayuningtyas[1*], Ronald Irwanto Natadidjaja[1,2,3], Chyntia Octaviani[1], Felly Sahli[1] and Hadianti Adlani[1,3]

Abstract

Background: Patients with severe acute respiratory syndrome coronavirus 2 infection show various clinical manifestations, including neurological . Altered consciousness due to severe acute respiratory syndrome coronavirus 2 encephalitis is a very threatening condition if not treated immediately.

Case presentation: We present the case of a 34-year-old Asian female who tested positive for severe acute respiratory syndrome coronavirus 2 infection using a nasopharyngeal swab sample and presented with acute changes in consciousness without typical respiratory symptoms. Empiric therapy was immediately and simultaneously given with cerebrospinal fluid analysis using polymerase chain reaction, which later also showed positive results for severe acute respiratory syndrome coronavirus 2 infection.

Conclusions: It is important to consider the diagnosis of severe acute respiratory syndrome coronavirus 2 encephalitis when a patient presents with acute altered consciousness and no typical respiratory symptoms. Early empiric therapy can improve patient outcomes.

Keywords: SARS-CoV-2, Encephalitis, Altered consciousness, Case report

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cells MDPI

Systematic Review

Encephalitis in Patients with COVID-19: A Systematic Evidence-Based Analysis

Md Asiful Islam [1,2,†], Cinzia Cavestro [3,†], Sayeda Sadia Alam [4], Shoumik Kundu [4], Mohammad Amjad Kamal [5,6,7,8] and Faruque Reza [9,*]

Ayuningtyas, T.; Natadidjaja, R.I.; Octaviani, C.; Sahli, F.; Adlani, H. Confirmed severe acute respiratory syndrome coronavirus 2 encephalitis in cerebrospinal fluid: A case report. *J. Med Case Rep.* **2022**, *16*, 1–4. [CrossRef]

Other Extrapulmonary infection – COVID-19

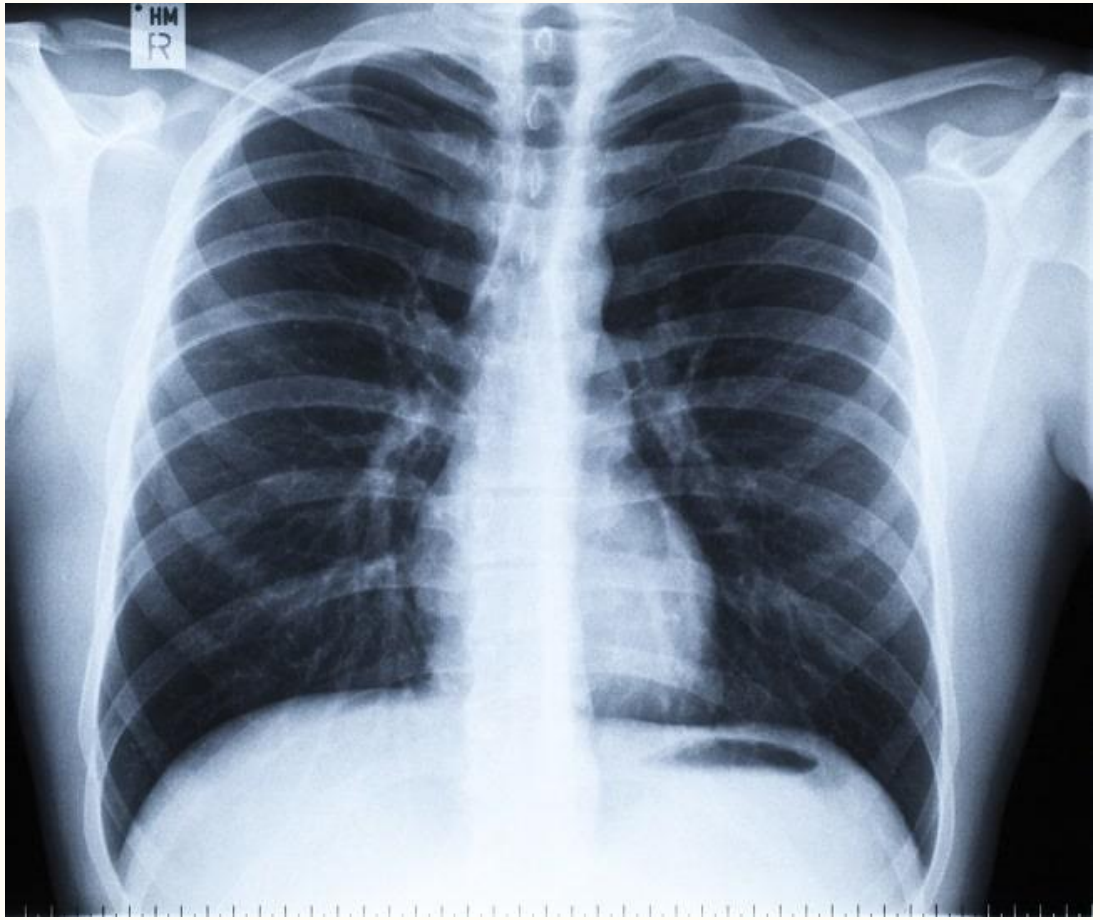
Receptors?

Diagnostic & Management Challenges in Extrapulmonary Tuberculosis

Extrapulmonary Tuberculosis : FUO Appearance - Case Presentation

Case Presentation

- Female, 65 y.o,
- 40 days fever, other vital sign is normal
- No cough, No shortness of breath
- Normal Complete Blood Count
- Negative Anti-HIV, Negative AFB
- Normal Malignancy Marker
- Normal Thyroid Function
- Normal CT Abdomen



Approach to the Adult Patient with Fever of Unknown Origin

ALAN R. ROTH, D.O., and GINA M. BASELLO, D.O., Jamaica Hospital Medical Center, Mount Sinai School of Medicine Family Practice Residency Program, Jamaica, New York

Category of FUO	*Definition*	*Common etiologies*
Classic	Temperature >38.3°C (100.9°F)	**Infection**, malignancy, collagen vascular disease
	Duration of >3 weeks	
	Evaluation of at least 3 outpatient visits or 3 days in hospital	
Nosocomial	Temperature >38.3°C	*Clostridium difficile* enterocolitis, drug-induced, pulmonary embolism, septic thrombophlebitis, sinusitis
	Patient hospitalized ≥24 hours but no fever or incubating on admission	
	Evaluation of at least 3 days	
Immune deficient (neutropenic)	Temperature >38.3°C	Opportunistic bacterial infections, aspergillosis, candidiasis, herpes virus
	Neutrophil count ≤ 500 per mm^3	
	Evaluation of at least 3 days	
HIV-associated	Temperature >38.3°C	Cytomegalovirus, *Mycobacterium avium-intracellulare* complex, *Pneumocystis carinii* pneumonia, drug-induced, Kaposi's sarcoma, lymphoma
	Duration of >4 weeks for outpatients, >3 days for inpatients	
	HIV infection confirmed	

AMERICAN FAMILY PHYSICIAN www.aafp.org/afp VOLUME 68, NUMBER 11 / DECEMBER 1, 2003

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases 32 (2023) 100377

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Epidemiology and factors associated with Extra-pulmonary tuberculosis in a Low-prevalence area

M. Rolo [a,1], B. González-Blanco [a,1], C.A. Reyes [a], N. Rosillo [b], P. López-Roa [a,*]

[a] Department of Clinical Microbiology and Parasitology, Hospital Universitario 12 de Octubre, Madrid, Spain
[b] Department of Preventive Medicine, Hospital Universitario 12 de Octubre, Madrid, Spain

Conclusions: Extra-pulmonary Tuberculosis have increased within our study period. A profound decline occurred in 2021 tuberculosis cases, probably due to COVID-19. Women, elderly population, and persons with previous history of tuberculosis are at higher risk of developing Extra-pulmonary tuberculosis in our setting.

Niu *et al. BMC Infectious Diseases* (2023) 23:488
https://doi.org/10.1186/s12879-023-08410-w

BMC Infectious Diseases

RESEARCH Open Access

The epidemiological characteristics and infection risk factors for extrapulmonary tuberculosis in patients hospitalized with pulmonary tuberculosis infection in China from 2017 to 2021

Tianshui Niu[1†], Fei He[1†], Jianshe Yang[2], Chengxi Ma[1], Jingyi Xu[1], Tianzhi Sun[1], Xin Zhang[1], Shuyi Chen[1] and Chuhui Ru[1*]

Abstract

Background Pulmonary tuberculosis (PTB) complicated with extrapulmonary tuberculosis (EPTB) infection can aggravate the disease, but there have been few reports.

Methods Retrospective analysis was used to collect the clinical data of PTB patients with pathogen positive in a teaching hospital from 2017 to 2021. We describe the incidence, the invasive site of EPTB patients, and analyze the infection risk factors for PTB with EPTB by univariate and multivariate logistic regression models. We also compared the complications, disease burden with chi-square test and rank-sum test.

Results A total of 1806 PTB were included, of which 263 (14.6%) were complicated with EPTB. The common invasive sites for EPTB were neck lymph nodes (16.49%), intestines (16.13%), and meninges (10.75%). Age ≤ 40 (OR = 1.735; 95%CI [1.267–2.376]; $P = 0.001$), malnutrition (OR = 2.029; 95%CI [1.097–3.753]; $P = 0.022$), anemia (OR = 1.739; 95%CI[1.127–2.683]; $P = 0.012$), and osteoporosis (OR = 4.147; 95%CI [1.577–10.905]; $P = 0.004$) were all independent risk factors for PTB infection with EPTB. The incidence of extrathoracic hydrothorax, intestinal bacterial infection, urinary tract bacterial infection, and abdominal bacterial infection were higher in patients with PTB with EPTB. PTB with EPTB patients also had longer median hospitalization durations (19 vs. 14 days), during which time they incurred higher total costs, laboratory test costs, imaging examination costs, and drug use costs.

Conclusion This study found important risk factors for PTB complicated with EPTB, such as age ≤ 40, malnutrition, anemia, and osteoporosis. PTB with EPTB patients have more extrapulmonary complications and higher hospitalization disease burden.

Fever of Unknown Origin Due to Liver Tuberculosis

April 2003 // DOI: 10.24871/41200322-25

Irman Firmansyah, Joko Jong, Noorwati Noorwati, Leo Nainggolan

Delayed diagnosis of extrapulmonary tuberculosis presenting as fever of unknown origin in an intermediate-burden country

•Jeong-Han Kim Eu Suk Kim, Kang-Il Jun, et al

BMC Infectious Diseases **volume 18**, Article number: 426 (2018) Cite this article

Fever of Unknown Origin Caused by Tuberculosis Author links open overlay panel,

Tuberculosis is an important cause of fever of unknown origin. Travel, age, dialysis, diabetes, birth in a country with a high prevalence of tuberculosis, and immunoincompetence are among the most salient risks. Associated physical findings, radiologic evaluation, and hematologic and endocrinologic abnormalities may provide clues to the diagnosis. Both noninvasive and invasive diagnostic modalities are reviewed. Because diagnosis may be elusive, therapeutic and diagnostic trials of antituberculous therapy should be considered in all patients with fever of unknown origin who defy diagnosis.

Infectious Disease Clinics of North America
Volume 21, Issue 4, December 2007, Pages 947-962

ATM ANNALS OF TRANSLATIONAL MEDICINE
AN OPEN ACCESS JOURNAL COVERING ALL SUBSPECIALTIES OF TRANSLATIONAL MEDICINE

Retrospective analysis of 1,641 cases of classic fever of unknown origin

Guanyu Zhou, Ying Zhou, Cejun Zhong, Hui Ye, Zhenzhen Liu, Yanbin Liu, Guangmin Tang, Junyan Qu, Xiaoju Lv

Center of Infectious Diseases, West China Hospital, Sichuan University, Chengdu, China

Conclusions: Infectious diseases are the principal cause of classic FUO, in which tuberculosis accounts for a large proportion. Non-infectious diseases that cause FUO are mainly connective tissue diseases and malignant tumors. Of the various causes of classic FUO, tuberculosis and lymphoma are relatively difficult to diagnose. In most cases, the causes of classic FUO can be ascertained.

Diagnostic and Treatment Challenges in Extra Pulmonary TB : FUO

Locate the Site of Infection
Diagnostic Modalities
Educate and Reassure
Patients
Finding the comorbidity

The role of IGRA in the diagnosis of tuberculosis infection, differentiating from active tuberculosis, and decision making for initiating treatment or preventive therapy of tuberculosis infection

Delia Goletti [1], Giovanni Delogu [2], Alberto Matteelli [3], Giovanni Battista Migliori [4]

Results: current tests for TB infection diagnosis as IFN-γ release assays or tuberculin skin tests are based on the detection of an immune response to Mtb in the absence of clinical disease. **The main limit is their low accuracy to detect progressors to disease.** New preventive treatments are available with short duration that are associated with better adherence. Options to register TB infections are presented.

Conclusions: **Tests to diagnose TB infection are available but they lack accuracy to identify the progressors from infection to TB disease**. Shorter preventive TB therapy are available but need to be implemented worldwide. A TB infection registry is crucial for improving the cascade of care leading to a better TB control.

•DOI: 10.1016/j.ijid.2022.02.047

. 2022 Nov:124 Suppl 1:S12-S19. doi: 10.1016/j.ijid.2022.02.047.

Comparison of PCR with the Routine Procedure for Diagnosis of Tuberculosis in a Population with High Prevalences of Tuberculosis and Human Immunodeficiency Virus

Lydia Kivihya-Ndugga,[1] Maarten van Cleeff,[2] Ernest Juma,[1] Joseph Kimwomi,[1] Willie Githui,[1] Linda Oskam,[2] Anja Schuitema,[2] Dick van Soolingen,[3] Lucy Nganga,[1,4] Daniel Kibuga,[5] Joseph Odhiambo,[1,4] and Paul Klatser[2,*]

PCR has great potential, but its evaluation in low-income countries has been limited. This study showed that PCR can be considered as an alternative to ZN in combination with CXR for the diagnosis of TB. However, cost-effectiveness studies and operational studies are required to support an evidence-based decision to introduce PCR for TB control in high-burden environments.

• J Clin Microbiol v.42(3); 2004 Mar PMC356878

Case Presentation

Female, 65 y.o

40 days fever, other vital sign is normal

No cough, No shortness of breath

Normal Complete Blood Count

Negative Anti-HIV, Negative AFB

Normal Malignancy Marker

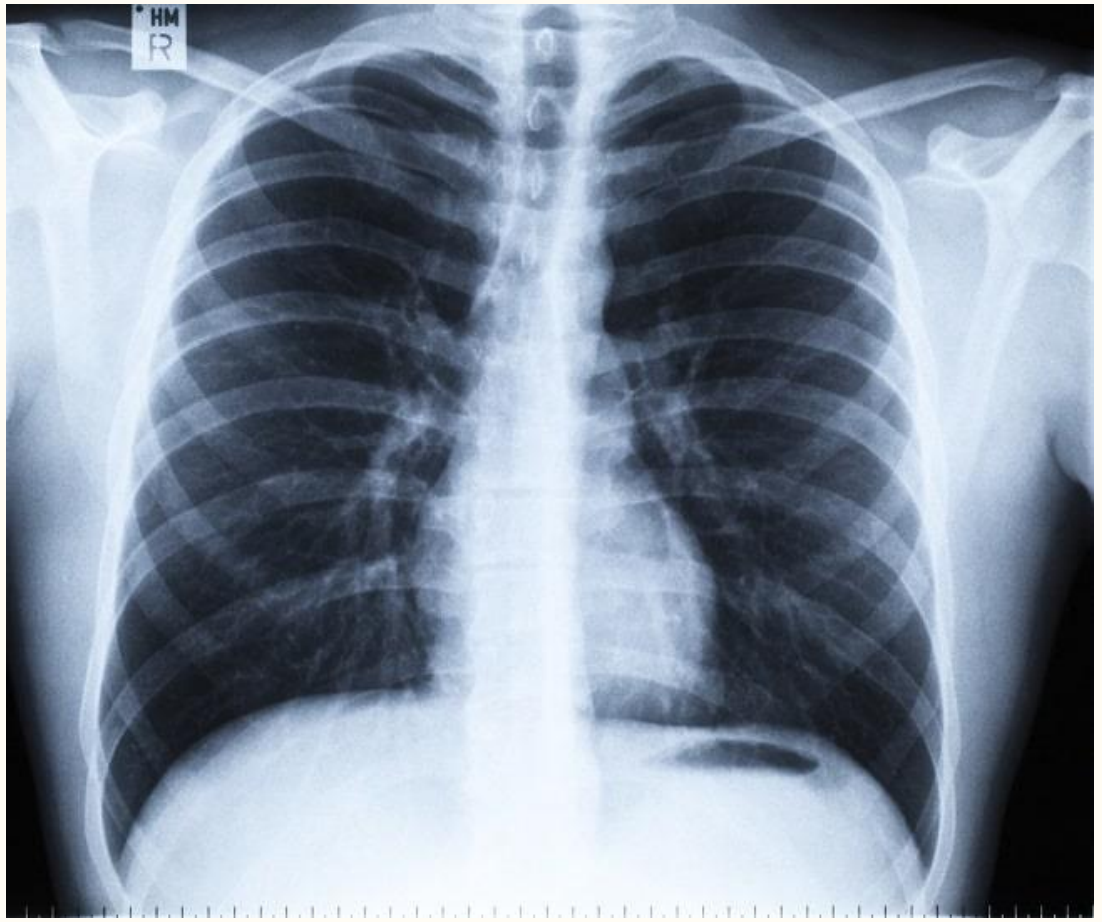
Normal Thyroid Function

Normal CT Abdomen

Next Findings :

IGRA (+)ve

ANA profile (+ve) –PCNA Antibody +1



QUESTION 1.

Should we treat patients with Anti-Tuberculosis in the case of FUO with Positive IGRA while the ANA Profile also show Positive Result ?

Is it really Extrapulmonary TB or Pulmonary TB or others?

Should we locate the TB site of Infection?
Where should we take specimen for PCR examination?

Other Medication Impact of FUO caused by Tuberculosis

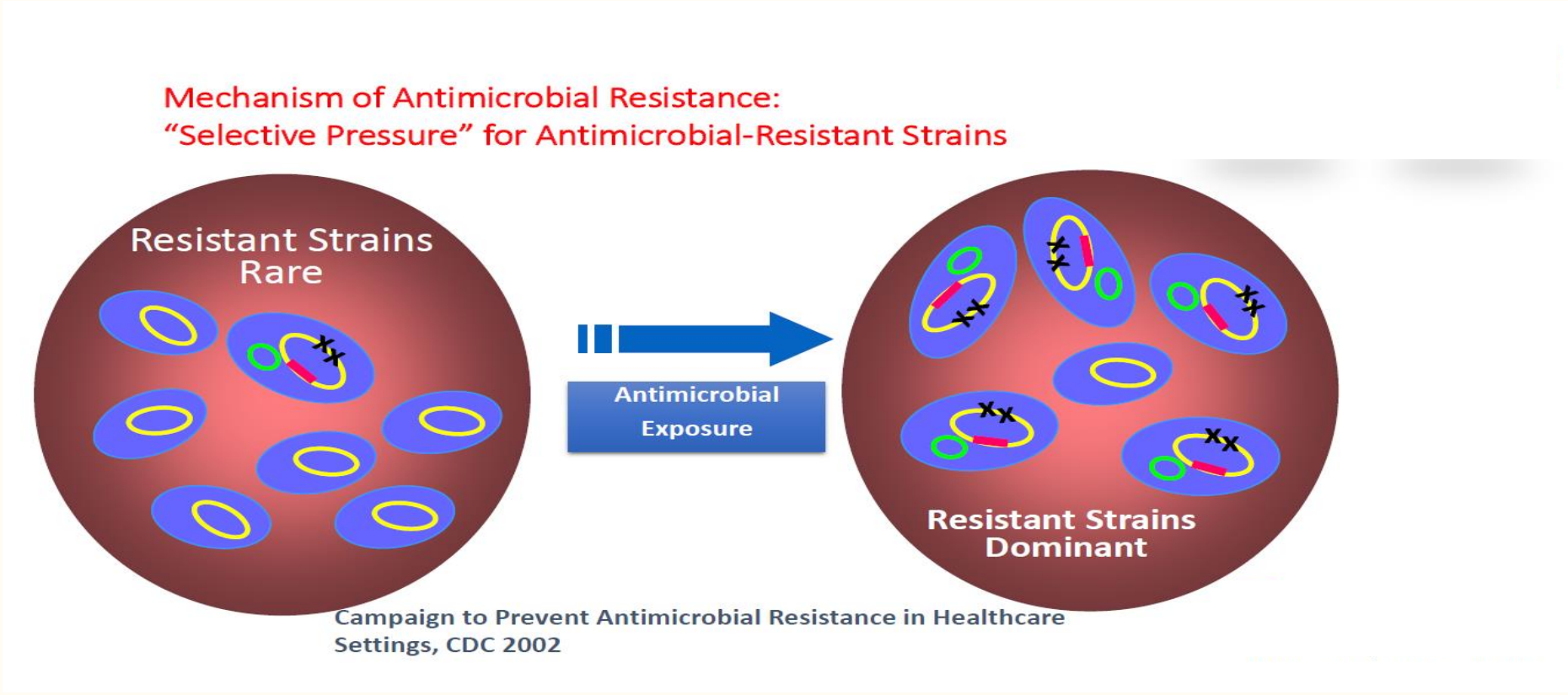
Extrapulmonary TB→ FUO
Antibiotics would be a first choice to be prescribed?

Prolong Antibiotic Used?

Next effect?

Antibiotic Overuse will result :

- Selective pressure
- Increase C. difficile infection risk



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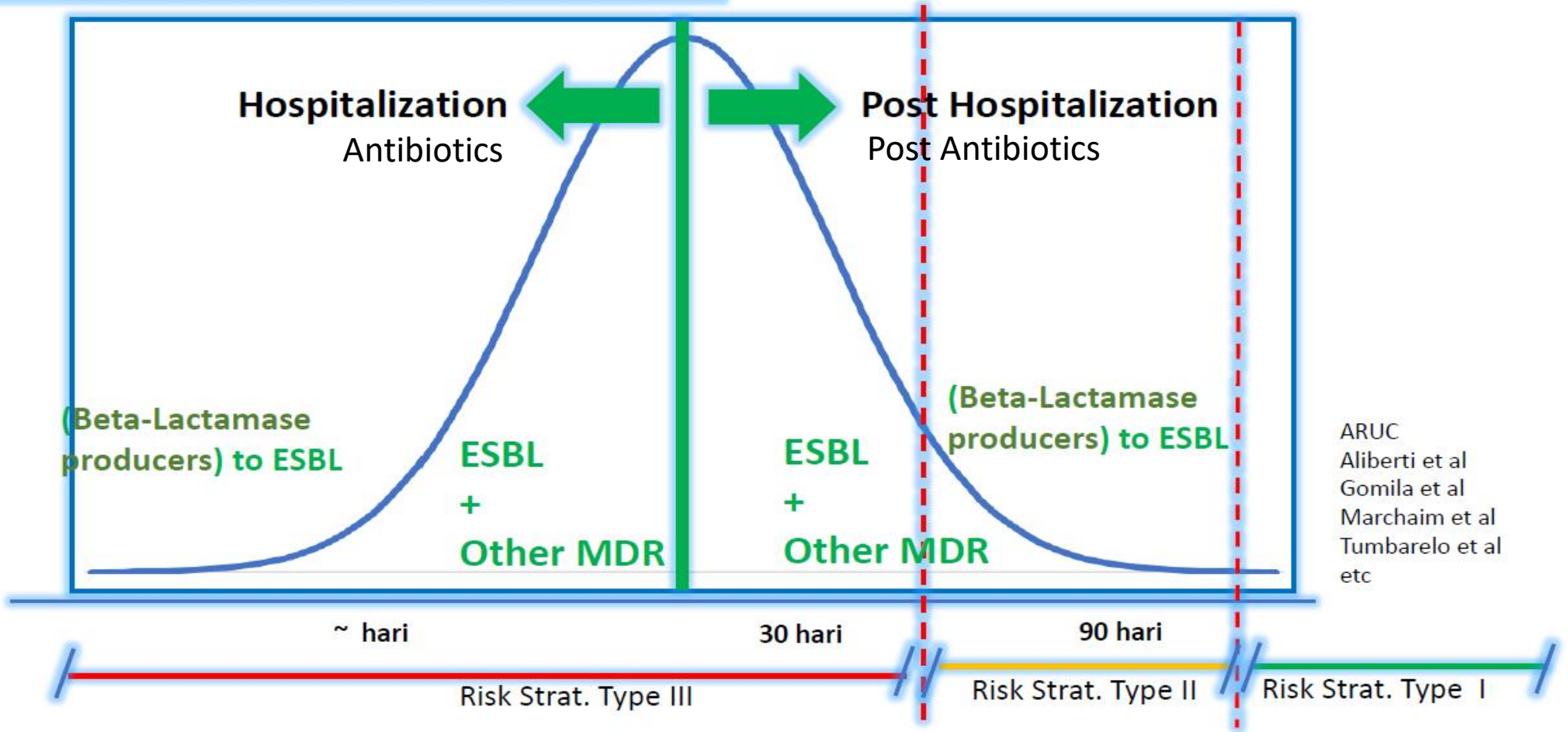

Risk Stratification based Microorganism Pattern

	Multisensitif		MDR				Prediksi	
			ESBL		Non ESBL			
	n	%	n	%	n	%	Sesuai	Tidak Sesuai
Gram Negatif								
Acinetobacter sp.	0	0,00	0	0,00	4	10,00	4	0
Pseudomanas sp.	0	0,00	0	0,00	7	17,50	7	0
Klebsiela pneumonia	15	26,32	2	22,22	6	15,00	21	2
Escheceria coli	18	31,58	7	77,78	6	15,00	28	3
Citrobacter koseri	0	0,00	0	0,00	1	2,50	1	0
Enterobacter sp.	1	1,75	0	0,00	1	2,50	2	0
Proteus sp.	0	0,00	0	0,00	2	5,00	2	0
Providencia stuartii	0	0,00	0	0,00	1	2,50	1	0
Pantoea agglomerans	1	1,75	0	0,00	0	0,00	1	0
Raoultella ornithinolytica	0	0,00	0	0,00	1	2,50	1	0
Serratia fonticola	1	1,75	0	0,00	0	0,00	1	0
Total	**36**	**63,15**	**9**	**100,00**	**29**	72,50	**69**	**5**
Gram Positif								
Staphylococcus aureus	4	7,02	0	0,00	1 *	2,50	5	0
Staphylococcus epidermidis	1	1,75	0	0,00	2 **	5,00	3	0
Enterococcus faecalis	4	7,02	0	0,00	2	5,00	5	1
Enterococcus faecium	1	1,75	0	0,00	1	2,50	1	1
Streptococcus sp.	8	14,04	0	0,00	4	10,00	12	0
Staphylococcus sp.	3	5,26	0	0,00	1	2,50	3	1
Total	**21**	**36,84**	0	0,00	**11**	27,50	**29**	**3**
TOTAL	**57**	**100,00**	**9**	**100,00**	**40**	**100,00**	**98**	**8**

* MRSA ** MRSE

	n	%	n	%	n	%
Multisensitif	54	94,74	3	5,26	57	100,00
MDR	44	89,80	5	10,20	49	100,00

Immunocompromised :

94.74% showed multi-sensitive findings in "NAIVE" medical history, while :

89.80% showed MDR with :

< 90 days history of antibiotic usage AND / OR

< 90 days history of hospitalization AND / OR

< 90 days history of medical devices usage

Journal of Hospital Accreditation, 2021
Vol 03, Edisi 2, hal 114-118

RONALD IRWANTO NATADIDJAJA[1,2], HADIANTI ADLANI[2], HADI SUMARSONO[2,3]

QUESTION 2.

Should we give the antibiotic for preventing the secondary infection, while we face the possibility of selective pressure and create the MDR colonization ?

EDUCATION

Benlutu, East Nusa Tenggara, 2022
High Endemic Area of Tuberculosis

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