AVOID FLUOROQUINOLONES AS EMPIRIC THERAPY, RESERVE FOR TUBERCULOSIS

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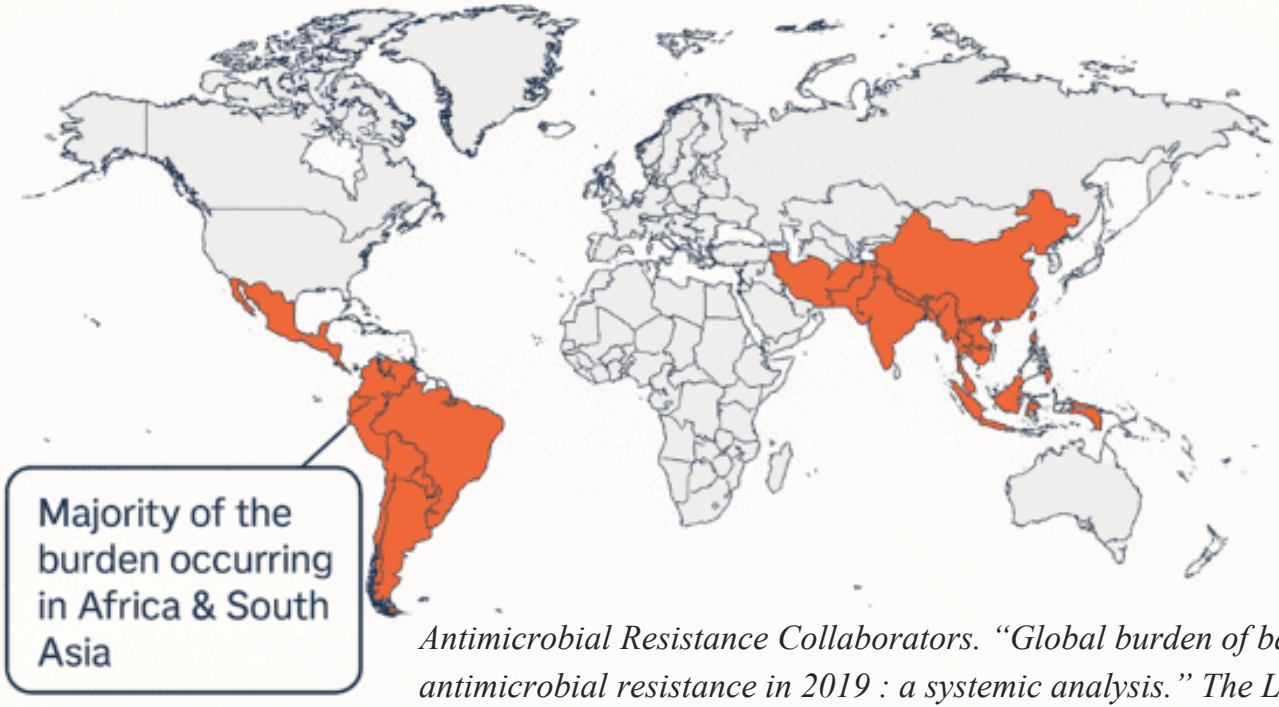
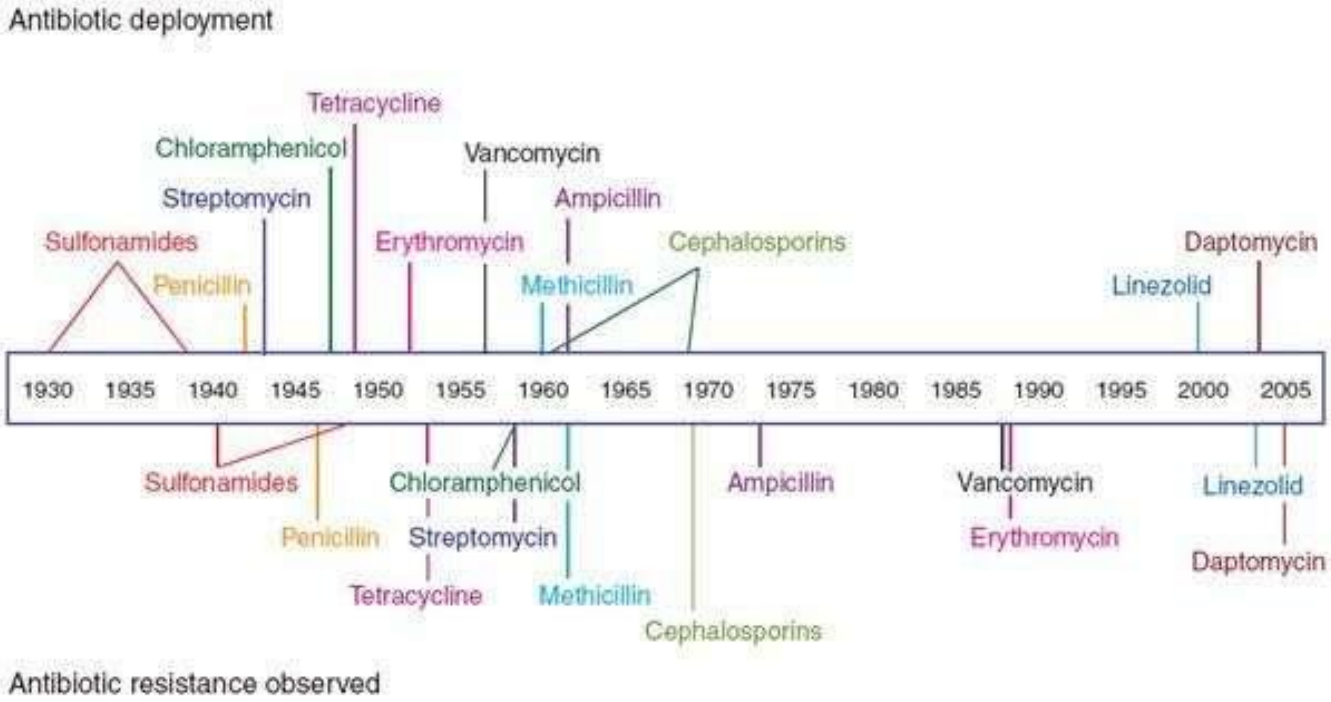
BACKGROUND / OBJECTIVE

ANTIMICROBIAL RESISTANCE: 1.27 MILLION DEATHS IN 2019

Surpassing HIV/AIDS, breast cancer, or malaria



Antimicrobial Resistance Collaborators. "Global burden of bacterial antimicrobial resistance in 2019 : a systemic analysis." The Lancet, vol. 399, no. 10325, 2022, pp. 629-655.



Source : Post-transcriptional regulation of porin expression in Escherichia coli and its impact on antibiotic resistance, Shusovan Dam (Picture from Clatworthy et al., 2007).

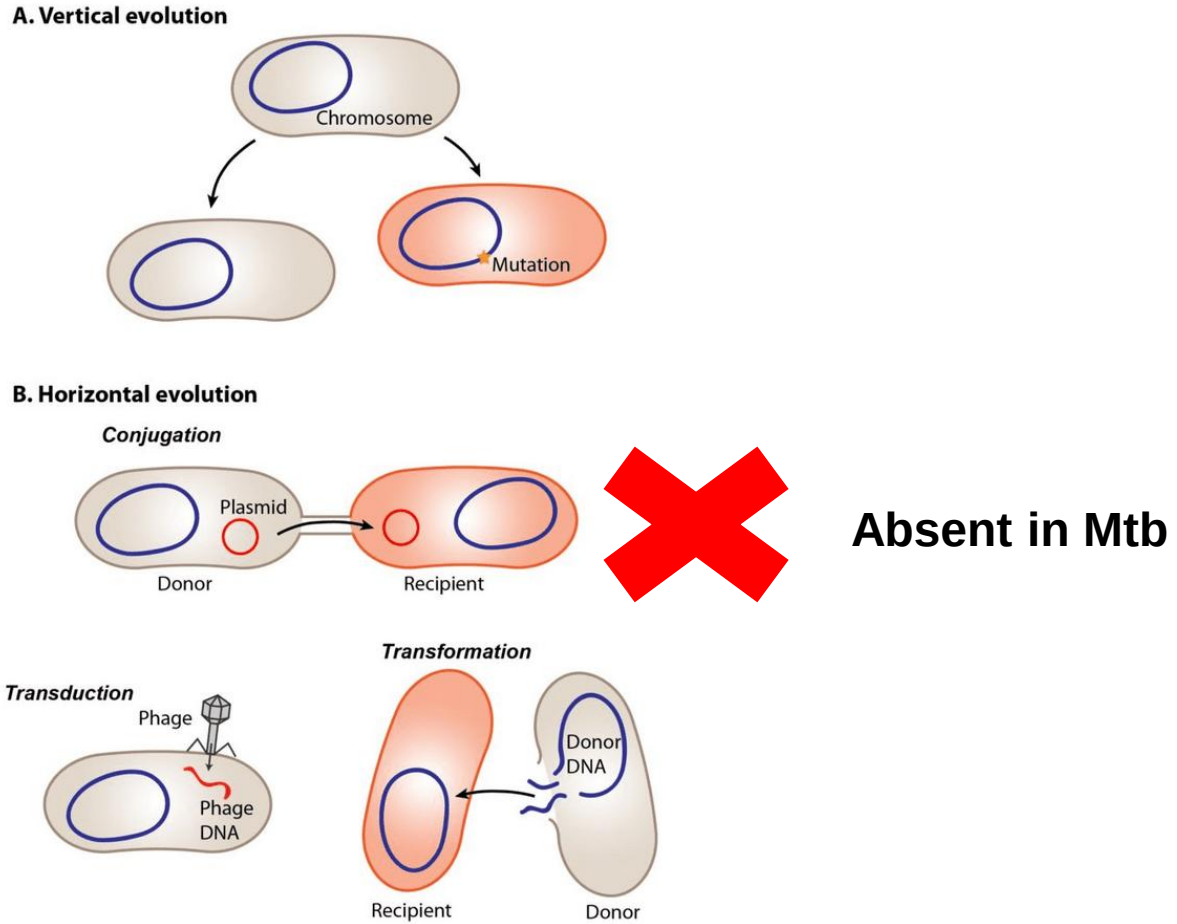
METHODOLOGY

Review of literature

Analysis of guidelines of WHO, IDSA & MoHP Nepal

RESULTS

UNDERSTANDING MECHANISM OF RESISTANCE AT MOLECULAR LEVEL

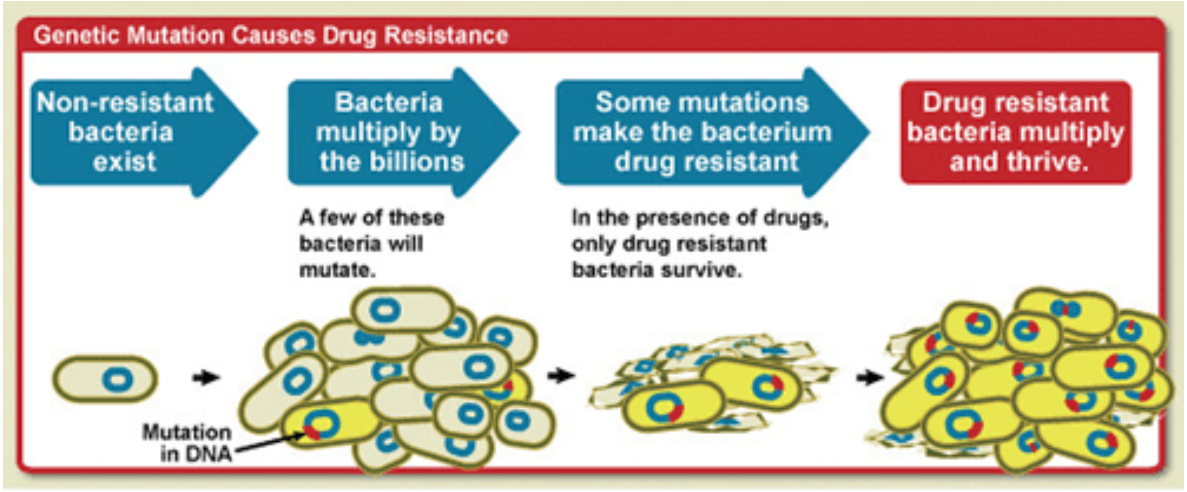


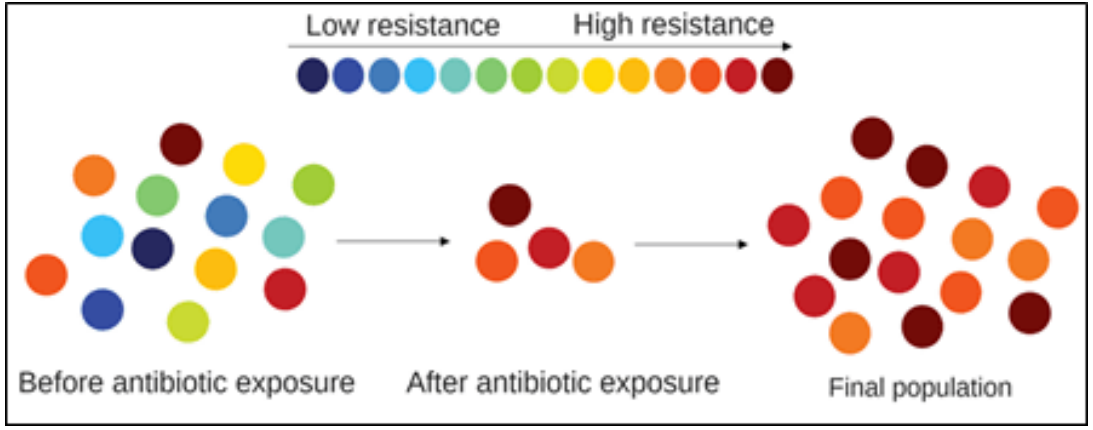
Source : https://www.futurelearn.com/info/courses/introduction-to-bacterial-genomics/0/steps/45331

Table: Types of Horizontal Gene Transfer in *Mycobacterium tuberculosis*

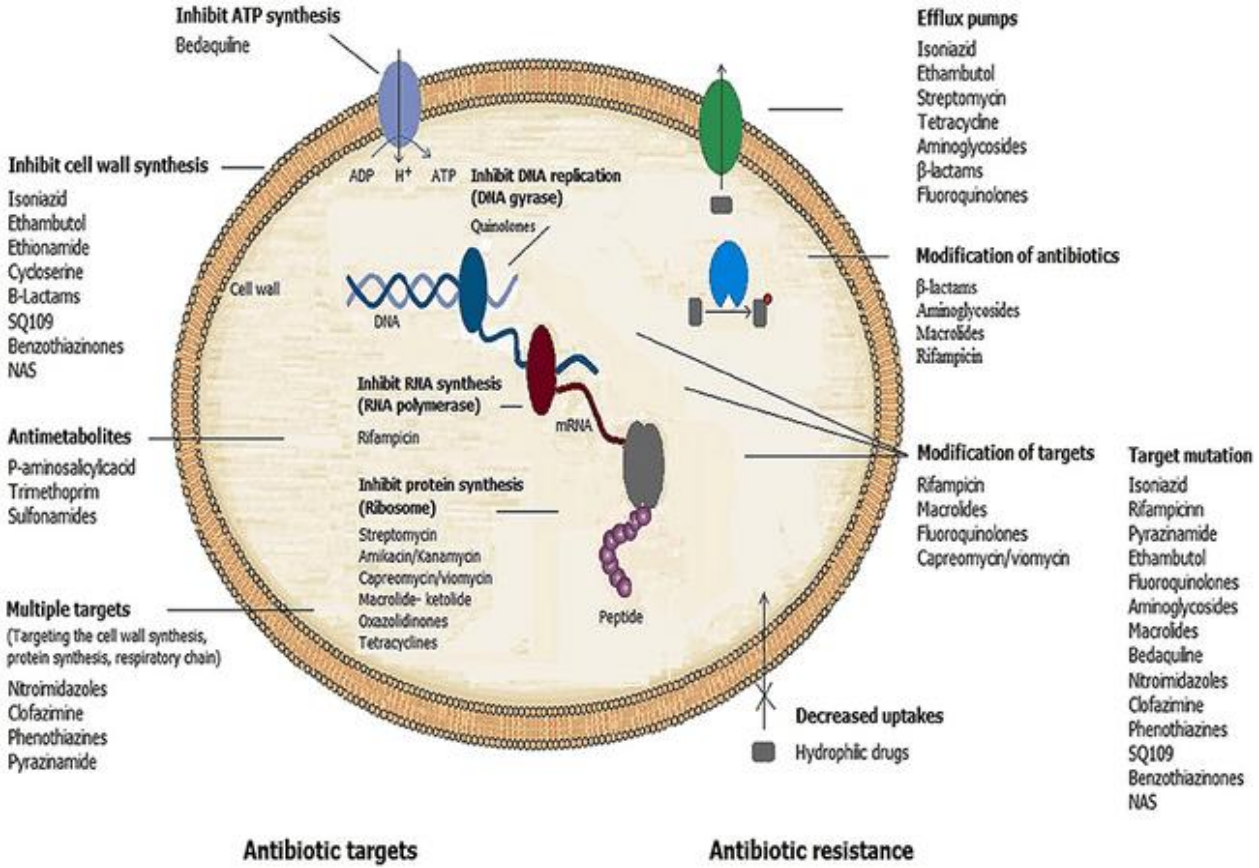
HGT Type	Description	Mechanism	Genes Potentially Transferred	Frequency	Clinical Relevance
Distributive Conjugal Transfer (DCT)	Chromosomal DNA exchange via cell-to-cell contact	Type VII secretion (ESX-1), distributive transfer	*katG*, *rpoB*, *inhA*, *embB*	10^{-4}–10^{-6} (in vitro)	Rare, experimentally observed
Mycobacteriophage Transduction	Phage-mediated transfer of chromosomal DNA	Generalized transduction by phages (e.g., D29)	*inhA*, *rpsL*, small segments	Unknown (very low)	Speculative, limited evidence
Transformation (Hypothetical)	Uptake of naked DNA from environment	Hypothetical competence, recombination	Any chromosomal mutation	Not quantified	Unproven, theoretical only

Mechanisms of drug resistance in Mycobacterium tuberculosis [State of the art series. Drug-resistant tuberculosis; Zhang et al; The International Journal of Tuberculosis and Lung Disease, Volume 13, Number 11, November 2009



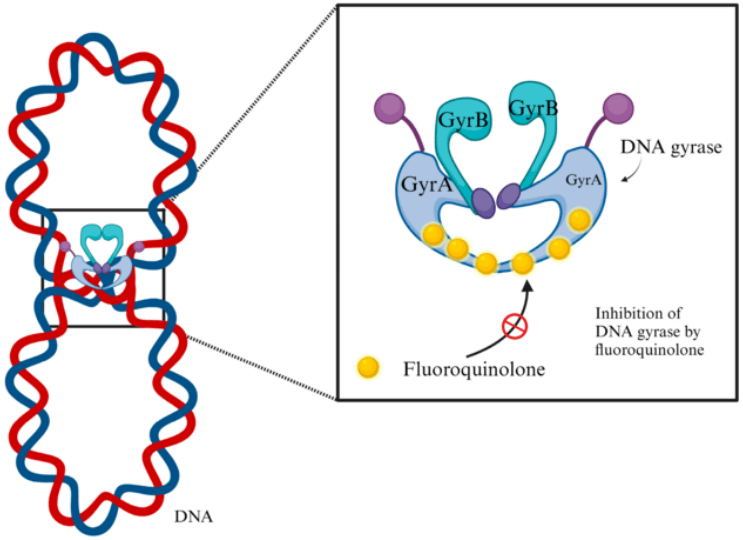


Drug Resistance in Mycobacterium tuberculosis and its Impact on Modern Medicine; Ifrah et al; DOI 10.26502/ami.93650076

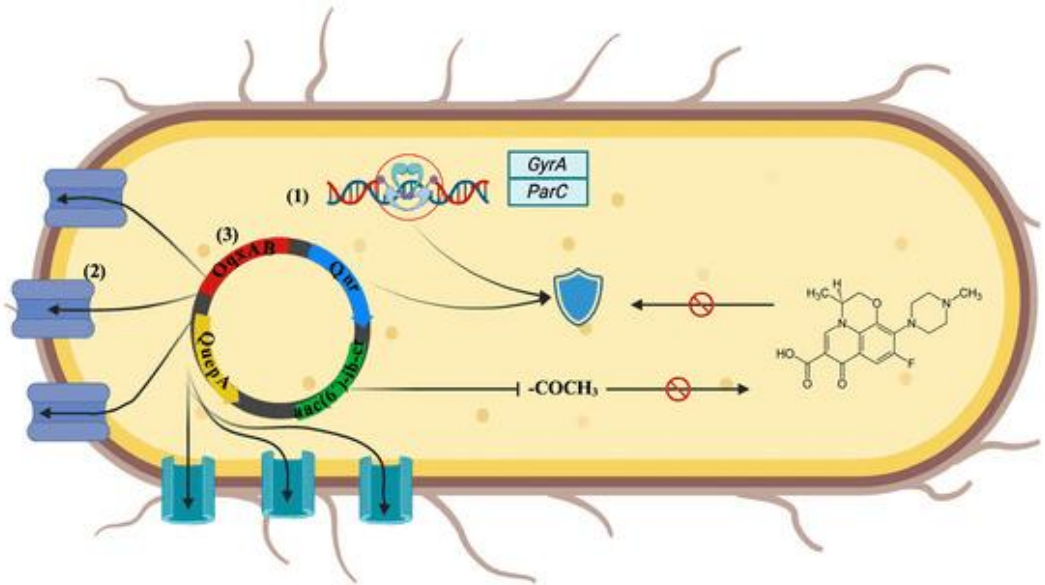


New Insights in to the Intrinsic and Acquired Drug Resistance Mechanisms in Mycobacteria; Mohammad et al; Front. Microbiol., 25 April 2017

LET’S TALK ABOUT FQs



Point mutation is enough for resistance !



Fluoroquinolone Resistance in Escherichia coli Causing Community-Acquired Urinary Tract Infections: A Systematic Review; Anna et al; Microorganisms 2024, 12(11), 2320; https://doi.org/10.3390/microorganisms12112320

WHAT HAPPENS IF YOU USE FQ FOR PNEUMONIA RX ?

Empiric Treatment of Community-Acquired Pneumonia with Fluoroquinolones, and Delays in the Treatment of Tuberculosis

Kelly E. Dooley, Jonathan Golub, Fernando S. Goes, William G. Merz, Sterling R. Timothy ✉

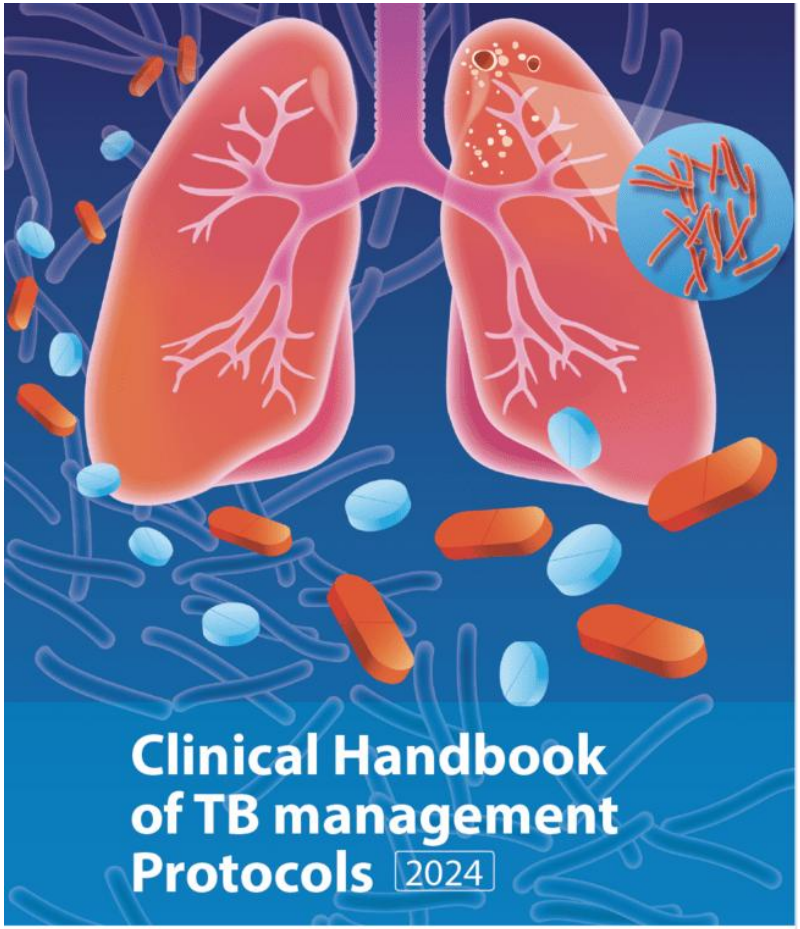
Clinical Infectious Diseases, Volume 34, Issue 12, 15 June 2002, Pages 1607–1612,
https://doi.org/10.1086/340618

Published: 15 June 2002 **Article history** ▾

Abstract

Fluoroquinolones, which are widely used to treat community-acquired pneumonia, also have excellent in vitro activity against *Mycobacterium tuberculosis*. A retrospective cohort study was conducted among adults with culture-confirmed tuberculosis to assess the effect of empiric fluoroquinolone therapy on delays in the treatment of tuberculosis. Sixteen (48%) of 33 patients received fluoroquinolones for presumed bacterial pneumonia before tuberculosis was diagnosed and treated. There were no differences between the group who did and the group who did not receive fluoroquinolones, except that patients who received fluoroquinolones were more likely to present with shortness of breath. Among patients treated empirically with fluoroquinolones, the median time between presentation to the hospital and initiation of antituberculosis treatment was 21 days (interquartile range, 5–32 days); among those who were not, it was 5 days (interquartile range, 1–16 days; $P = .04$). Initial empiric therapy with a fluoroquinolone was associated with a delay in the initiation of appropriate antituberculosis treatment.

WHY WE NEED TO PRESERVE FQ ?

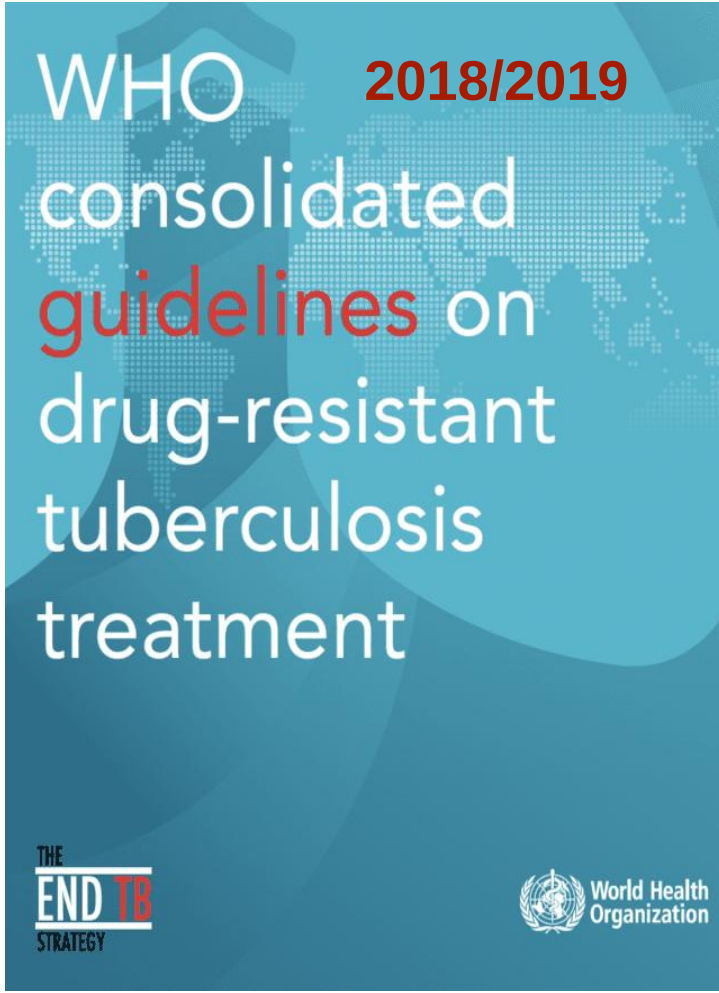


Clinical Handbook of TB management Protocols 2024

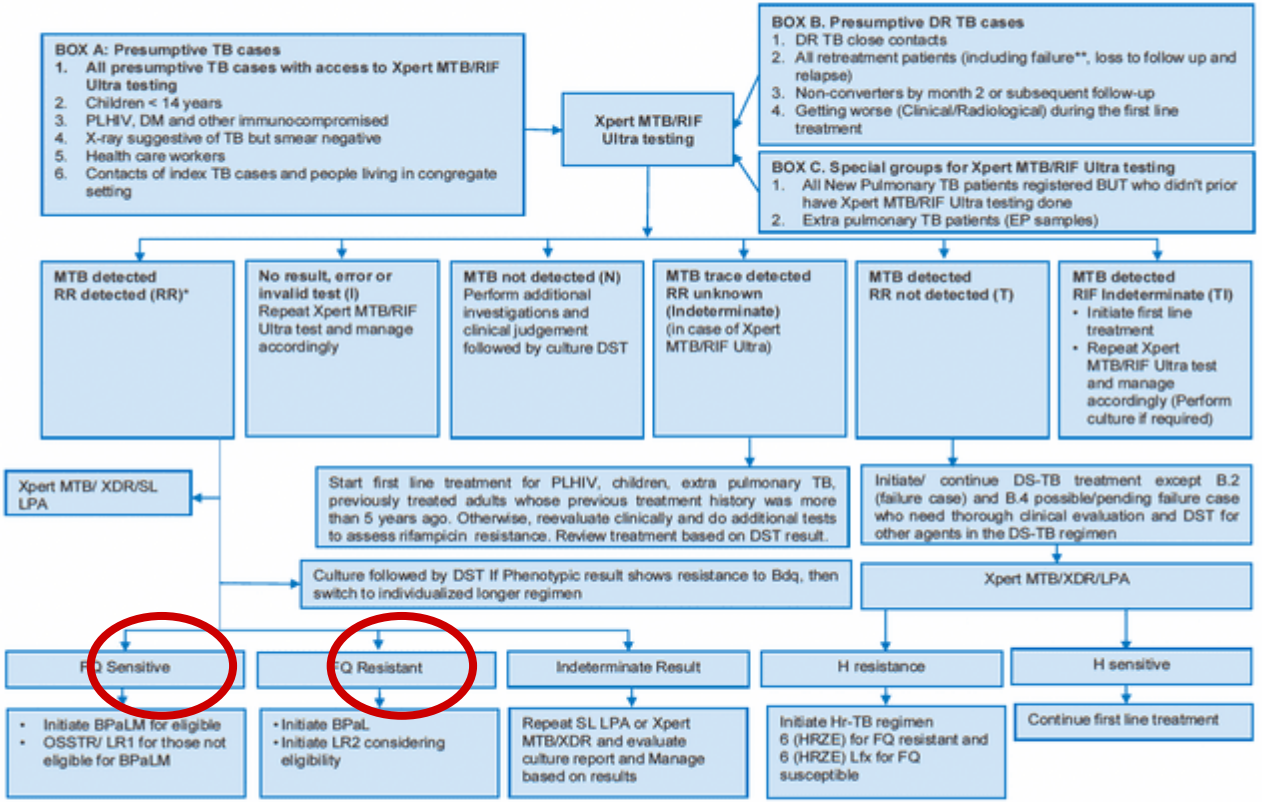
Government of Nepal
Ministry of Health and Population
Department of Health Services
National Tuberculosis Control Center

Table 2.1. Grouping of medicines recommended for use in longer MDR-TB regimens[1]

Groups & steps	Medicine	
Group A: Include all three medicines	levofloxacin *OR* moxifloxacin	Lfx Mfx
	bedaquiline[2,3]	Bdq
	linezolid[4]	Lzd
Group B: Add one or both medicines	clofazimine	Cfz
	cycloserine *OR* terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	ethambutol	E
	delamanid[3,5]	Dlm
	pyrazinamide[6]	Z
	imipenem–cilastatin *OR* meropenem[7]	Ipm–Cln Mpm
	amikacin (*OR* streptomycin)[8]	Am (S)
	ethionamide *OR* prothionamide[9]	Eto Pto
	p-aminosalicylic acid[9]	PAS



3.3 Decision tree for the diagnosis and treatment of MDR/RR TB



*For new cases with low risk of MDR/RR TB, clinician may consider to repeat the Xpert MTB/RIF/Ultra testing
** In failure cases, if H resistant diagnosed, consider to refer to the Tb specialists (NTCC)

3.4 Treatment of Multi-drug/Rifampicin Resistant (MDR/RR) TB

The key factors that define treatment regimen include drug-resistance profile, prior exposure to TB medicines and patient history, drug-resistance profile of close contacts, the patient's age, extent of pulmonary TB disease and localization of extrapulmonary TB lesions. The MDR/RR-TB treatment regimen are:

A. Shorter Regimen

- BPaLM/BPaL regimen – 6 months
- All oral standardized treatment regimen (OSSTR) – 9 months

B. Longer regimen (Standardized or Individualized): 18 months

Regimen	MDR/RR TB fluoroquinolone susceptible	Pre-XDR-TB	XDR-TB	Extensive pulmonary TB	Extrapulmonary TB	Age <14 years
6-month BPaLM/BPaL	Yes (BPaLM)	Yes (BPaL)	No	Yes	Yes - except TB involving CNS/meningitis, miliary TB, osteoarticular TB and pericardial TB	No
9-month all-oral regimen (OSSTR)	Yes	No	No	No	Yes - except TB involving CNS/meningitis, miliary TB, osteoarticular TB and pericardial TB	Yes
18 months Longer Regimen	Yes*/No	Yes*/No	Yes	Yes	Yes	Yes
Additional factors to be considered if several regimens are possible	Drug intolerance or adverse events					
	Treatment history, previous exposure to regimen component drugs or likelihood of drug effectiveness					
	Patient or family preference					
	Access to and cost of regimen component drugs					

BPaL: bedaquiline, pretomanid and linezolid; BPaLM: bedaquiline, pretomanid, linezolid and moxifloxacin, CNS: central nervous system; MDR/RR-TB: multidrug- or rifampicin-resistant TB; TB: tuberculosis; XDR-TB: extensively drug- resistant TB.

* When 6-month BPaLM/BPaL and 9-month regimens could not be used

CONCLUSIONS

SUMMARY

Tuberculosis can present as Community Acquired Pneumonia

Using FQ may initially improve that Pneumonia, but will ultimately worsen & even can change that drug sensitive TB to drug-resistant (FQ resistant) TB due to partial treatment

Now, if this turns out to be a MDR-TB, we will be losing our one of the most effective drug of treatment , that is FQ !!

So, reserve FB just for TB as other infections have other options to treat !

THANK YOU