Multidrug resistant Tuberculosis

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Introduction

Tuberculosis remains a major cause of morbidity and mortality globally, one of the causes are multidrug resistant tuberculosis (MDR-TB). MDR-TB refers to tuberculosis that is resistant to both rifampicin and isoniazid. Almost 20% of all TB strains worldwide are resistant to at least one major TB drug, approximately 10% are isoniazid monoresistant . Multidrug resistant tuberculosis with additional resistance to any fluoroquinolone (such as ofloxacin or moxifloxacin) and also any one of the three second line injectable agents (amikacin, capreomycin,kanamycin)is designated as extensively drug resistant tuberculosis (1). Rapid diagnosis and effective treatment are two of the most important strategies tuberculosis(TB)control program to prevent ongoing transmission of disease and to improve patient outcomes (2).

Mechanism and causes of resistant

The 2 reasons why multidrug resistance continues to emerge and spread are:(3)
- mismanagement of TB treatment.
- person-to-person transmission.

The mechanism of resistance in mycobacteria (figure 1-1):(3)
- Cell wall: more than 60% of the cell wall is lipid, mainly mycolic acids. This extraordinary shield prevents many pharmacological compounds from getting to the bacterial cell membrane or inside the cytosol.
- Efflux pumps: a second layer of defense in the cell membrane. These transport proteins pump out potentially harmful chemicals from the bacterial cytoplasm back into the extracellular space.
- A third barrier is the propensity of some of the bacilli to hide inside the patient's cells, thereby surrounding themselves with an extra physicochemical barrier that antimicrobial agents must cross to be effective.

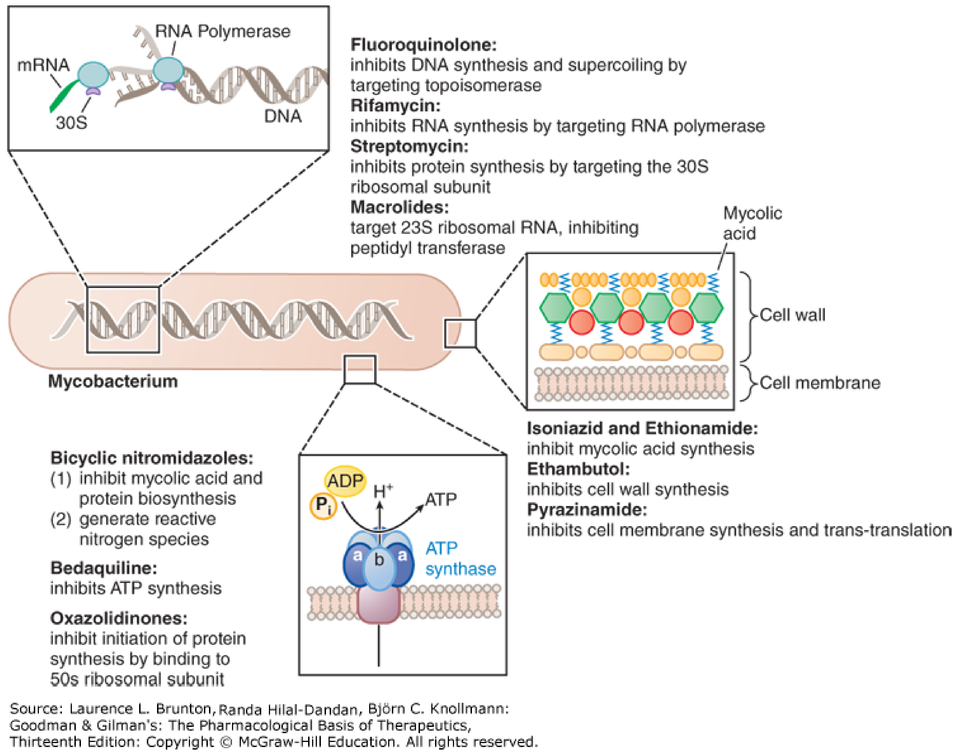

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Fig.1-1 Mechanisms of resistance in mycobacteria

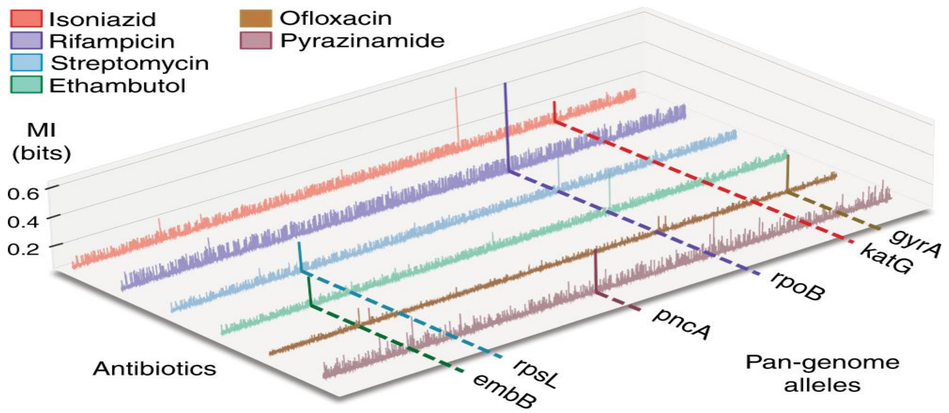

Fig.1-2 genes associated with MDR-TB

GeneXpret

- Drug resistance can be detected using special laboratory tests which test the bacteria for sensitivity to the drugs or detect resistance patterns. These tests can be molecular in type (such as Xpert MTB/RIF) (figure 1-3) or else culture-based.
- GeneXpert MTB/RIF assay is a nucleic acid amplification (NAA) test which simultaneously detects DNA of Mycobacterium tuberculosis complex (MTBC) and resistance to rifampin (RIF) (i.e. mutation of the rpoB gene) (figure 1-2) in less than 2 hours. In comparison, standard cultures can take 2 to 6 weeks for MTBC to grow and conventional drug resistance tests can add 3 more weeks.
- This system integrates and automates sample processing, nucleic acid amplification, and detection of the target sequences (4).
- Composed of: (4)

1. GeneXpert System.
2. GeneXpert Cartridge .
3. Sample reagent.

Fig.1-3 GeneXpert

Conclusion

- Drug-resistant TB (DR-TB) remains a serious threat to control because there is higher associated morbidity and mortality.
- Development of specific techniques to rapidly detect multidrug resistance is important thing.

References

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