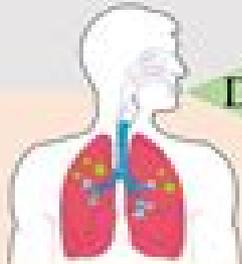


- Programmatic Strengthening Across TB Care Continuum
- Case Finding:
 - Rigorous deployment of cough analysis technologies
 - Investigation of breath sampling/skin patch approaches
 - Use of GIS mapping approaches to identify transmission hotspots
- Case Notification
 - Increase notification in private sector
- Improve Diagnostic Methods:
 - Rapidly progress point of care detection of resistance
 - Whole genome sequencing / Targeted sequencing
 - Eliminate cost restraints*
 - Increase data pool regards genotype:phenotype associations*
 - Further investigations to detect heteroresistance as a proxy for transmission leading to poor outcomes*

- Prophylaxis, Increase Available Treatments:
 - in adults
 - in vulnerable populations (HIV, children)
- Who Transmits the Disease?
 - Investigate fundamental differences in transmission of drug sensitive vs. drug resistant TB
 - Investigate role of sub-clinical TB in driving transmission of drug resistant TB
- Impact of Covid-19 on:
 - Diagnostic pickup
 - TB-Covid-19 coinfections
 - Further transmission of drug resistant TB due to effects on health systems



DR-TB



Environmental transmission of drug resistant bacteria



Bacterial mechanisms driving drug resistance

- Tolerance Factors
 - The pathway from tolerance to resistance
 - Investigating efflux pumps, pathway redundancies, drug target modifications*
- Dormancy (role in drug tolerance and persistent infection)
- Heterogeneity
 - Division and cell cycle, heterogeneity in cell size
 - LamA and others
- Transcription/Translation
 - Sigma factors
 - Mistranslation
- Toxin-Antitoxin Systems
 - Antibiotics targeting all redundant systems
- Biofilms
 - Overcoming reduced antibiotic accessibility
 - Further evaluating relevance in TB disease and DR strains

- Metabolism
 - TCA Cycle and related; respiration
 - TAG and Lipid Droplets (new clinical endpoints?)*
 - Is carbon metabolism different in drug resistant TB?*
- Macrophage Activation
 - Are there specific differences with DR strains?
 - Host-directed therapies
- Differentially Culturable Tubercle Bacteria
 - Appropriate testing for all possible bacteria present in the lungs
 - Better definitions of sterilising cure endpoints
- Host Factors
 - Immunometabolism
 - Specific changes in immune responses with DR strains*

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