Disclosures

No financial/industry conflicts
Learning objectives

At the end of this program, participants will be able to:

1. Understand the global burden of tuberculosis
2. Describe the current status of TB diagnostics
3. Describe the current status of TB therapeutics
In 2015, there were an estimated 10.4 million new (incident) TB cases:

- 5.9 million (56%) among men
- 3.5 million (34%) among women
- 1.0 million (10%) among children
TB Diagnostics
TB Diagnostics 1900

TB Diagnostics 2017
TB Diagnostic Algorithm: Mayo Clinic

Pulmonary TB Suspects

Sputum AFB Microscopy
CXR

PCR

Culture

Identification (molecular)

Susceptibility Testing
TB Diagnostic Algorithm: WHO

Pulmonary TB Suspects

Sputum AFB Microscopy

Any smear +

2 smears -

Rx: Non TB antibiotics. Improvement?

Repeat AFB CXR

Positive results

Rx: TB

Negative results

CXR, molecular tests, clinical suspicion and judgment

No TB
1. Upgrade to established, more effective technologies

Molecular tests for identification of tuberculosis and drug-susceptibility testing

2. Digital radiography

3. Biomarkers

Strategies to Improve TB Diagnostics
<table>
<thead>
<tr>
<th>Conventional Ziehl-Neelsen light Microscopy</th>
<th>Conventional Fluorescent Microscopy (CFM)</th>
<th>Light-emitting diode Fluorescent Microscopy (LED-FM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most cost-efficient</td>
<td>• 10% higher sensitivity</td>
<td>• Performance = CFM</td>
</tr>
<tr>
<td>• Rapid</td>
<td>• More efficient - 25% of the time</td>
<td>• Less expensive</td>
</tr>
<tr>
<td>• Inexpensive</td>
<td>• High cost</td>
<td>• Lower maintenance</td>
</tr>
<tr>
<td>• Low and variable sensitivity</td>
<td>• Short life of lamp</td>
<td>• No warm-up time</td>
</tr>
<tr>
<td>• 30-70%</td>
<td>• Lamp warm-up time</td>
<td>• No toxic products</td>
</tr>
<tr>
<td>• Lower in HIV</td>
<td>• Maintenance needs</td>
<td>• No need for darkroom</td>
</tr>
<tr>
<td>• Lower in children</td>
<td>• Need for darkroom</td>
<td></td>
</tr>
</tbody>
</table>

- Performance = CFM
- Less expensive
- Lower maintenance
- No warm-up time
- No toxic products
- No need for darkroom
Upgrade to established, more effective technologies

Molecular tests for identification of tuberculosis and drug-susceptibility testing

Digital radiography

Biomarkers
Xpert® MTB/RIF

1. Sputum liquefaction and inactivation with 2:1 sample reagent
2. Transfer of 2 ml material into test cartridge
3. Cartridge inserted into MTB-RIF test platform (end of hands-on work)
4. Sample automatically filtered and washed
5. Ultrasonic lysis of filter-captured organisms to release DNA
6. DNA molecules mixed with dry PCR reagents
7. Seminested real-time amplification and detection in integrated reaction tube
8. Printable test result

Pulmonary TB:
Sensitivity, Smear positive disease – 98.7%
Specificity - 98.2%

Time to result, 1 hour 45 minutes
Line Probe Assays

*M. tuberculosis* complex detection and INH/RIF resistance

Source: http://www.hain-lifescience.de
Comparison of *TB* Diagnostic Modalities

Proportion of TB Cases Detected by Each Method

![Graph showing the proportion of TB cases detected by each method](image)

While lab turnaround time is <1 day with Xpert, treatment is started after 17 days!
1. Upgrade to established, more effective technologies

2. Molecular tests for identification of tuberculosis and drug-susceptibility testing

3. Digital radiography

4. Biomarkers
Digital Radiology for TB

- Convergence of:
  - X-ray detector technology
  - Image acquisition
    - High diagnostic quality
    - Consistency of images
  - Digital image storage
  - Computer-aided detection (CAD)
- High cost an issue
- Variable performance
Upgraded to established, more effective technologies

Molecular tests for identification of tuberculosis and drug-susceptibility testing

Digital radiography

Biomarkers
Biomarkers for Diagnosing Tuberculosis

- Adenosine deaminase (ADA)
- lipoarabinomannan (LAM)
- BlaC
- Decoy receptor (DcR) 3
- Prostaglandin E2 (PGE2)
- TNF-α Mtb-specific CD4+ T cells
- Serum cytokines: IL-2, IL-9, IL-13, IL-17, and TNF-α

- Urease
- TB stearic acid (TBSA)
- Pleural IFN-γ
- IFN-induced protein 10 (IP-10)
- Soluble FasL
- PCT
- Lipoxin/PGE2
Diagnostic Accuracy of a Rapid Urine Lipoarabinomannan Test for Tuberculosis in HIV-Infected Adults

Lydia Nakiyingi, MBChB,* Vineshree Mischka Moodley, MBChB,† Yukari C. Manabe, MD,*‡§ Mark P. Nicol, PhD,† Molly Holshouser, MPH,‡ Derek T. Armstrong, MHS,‡ Widaad Zemanay, PhD,† Welile Sikhondze, MBChB,† Olive Mbabazi, BA,* Bareng A.S. Nonyane, PhD,§ Maunank Shah, MD,‡ Moses L. Joloba, PhD,¶ David Alland, MD,‖ Jerrold J. Ellner, MD,# and Susan E. Dorman, MD,‡§ J Acquir Immune Defic Syndr 2014;66:270–279

Rapid point-of-care detection of the tuberculosis pathogen using a BlaC-specific fluorogenic probe

Hexin Xie†, Joseph Mire‡, Ying Kong†, MiHee Chang‡, Hany A. Hassounah‡, Chris N. Thornton4, James C. Sacchettini2, Jeffrey D. Cirillo3 and Jianghong Rao1*
<table>
<thead>
<tr>
<th>Gene</th>
<th>Function</th>
<th>Diagnostic evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>apa</td>
<td>Unknown (could mediate bacterial attachment to host cells).</td>
<td>Tested in sputum and serum of active smear-positive TB patients (Chanteau et al., 2000).</td>
</tr>
<tr>
<td>esxA</td>
<td>Elicits high level of IFN-gamma from memory effector cells during first phase of a protective immune response.</td>
<td>Detected in cerebrospinal fluid (CSF) of tuberculous meningitis patients (Kashyap et al., 2009).</td>
</tr>
<tr>
<td>fbpA</td>
<td>Involved in cell wall mycolylation.</td>
<td>Antigen 85 complex proteins have been detected in sputum (Wallis et al., 1998) and serum (Kashyap et al., 2007) specimens of TB patients.</td>
</tr>
<tr>
<td>glcB</td>
<td>Involved in glyoxylate bypass, an alternative to the tricarboxylic acid cycle.</td>
<td>Assayed with promising results in CSF in tuberculous meningitis (Haldar et al., 2012).</td>
</tr>
<tr>
<td>groEL2</td>
<td>Prevents misfolding and promotes folding and proper assembly of unfolded polypeptides.</td>
<td>Showed a good diagnostic performance in ELISA of serum samples of TB patients (Rajan et al., 2007).</td>
</tr>
<tr>
<td>hspX</td>
<td>Stress protein induced by anoxia. HSPX has a proposed role in maintenance of long-term viability during latent, asymptomatic infections, as well as in replication during initial infection.</td>
<td>Assayed with promising results in CSF in tuberculous meningitis (Haldar et al., 2012).</td>
</tr>
<tr>
<td>moeX</td>
<td>Involved in molybdopterin cofactor biosynthesis.</td>
<td>Identified by mass spectrometry in urine from active tuberculosis patients (Pollock et al., 2013).</td>
</tr>
<tr>
<td>mpt64</td>
<td>Secreted protein of unknown function specific for M. tuberculosis complex. Highly secreted during initial phases of bacterial growth.</td>
<td>A lateral flow assay was developed for the identification of M. tuberculosis complex in liquid culture media by using anti-MPB64 monoclonal antibodies (Akyar et al., 2010).</td>
</tr>
<tr>
<td>pstS1</td>
<td>Involved in active transport of inorganic phosphate across the membrane (Chang et al., 1994).</td>
<td>Assayed in CSF in tuberculous meningitis (Haldar et al., 2012).</td>
</tr>
<tr>
<td>TB31.7</td>
<td>Regulates mycobacterial growth and is required for the entry of tubercle bacillus into the chronic phase of infection (Drumm et al., 2009).</td>
<td>Potential biomarker for the diagnosis of latent as well as active tuberculous meningitis infection. Assayed in CSF (Jain et al., 2013).</td>
</tr>
<tr>
<td>apa</td>
<td>Unknown (could mediate bacterial attachment to host cells).</td>
<td>Tested in sputum and serum of active smear-positive TB patients (Chanteau et al., 2000).</td>
</tr>
</tbody>
</table>
VOC: A Nose for Disease

Caenorhabditis elegans

T-Bee

Caenorhabditis elegans
The Tuberculosis Diagnostics Pipeline
Albert Schatz and Selman Waksman

H. Corwin Hinshaw and William Feldman
TB Therapeutics
Anti-Tuberculous Drugs

Group 1
- Isoniazid
- Rifampin
- Pyrazinamide
- Ethambutol

Group 2
- Amikacin
- Capreomycin
- Kanamycin
- Streptomycin

Group 3
- Levofloxacin
- Moxifloxacin
- Gatifloxacin
- Ofloxacin

Group 4
- Ethionamide
- Prothionamide
- Cycloserine
- Terizidone
- PAS

Group 5
- Linezolid
- Clofazimine
- High-dose Isoniazid
- Amoxicillin/Clavulanate
- Imipenem
- Clarithromycin
- Thiacetazone
- Bedaquiline

First line  Second-line  Third-line
### WHO Classification of Drugs for the Treatment of DR TB

<table>
<thead>
<tr>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D1</th>
<th>Group D2</th>
<th>Group D3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin</td>
<td>Amikacin</td>
<td>Ethionamide</td>
<td>PZA</td>
<td>Bedaquiline</td>
<td>PAS</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>Capreomycin</td>
<td>Prothionamide</td>
<td>EMB</td>
<td>Delamanid</td>
<td>Imipenem</td>
</tr>
<tr>
<td>Gatifloxacin</td>
<td>Kanamycin</td>
<td>Linezolid</td>
<td>High-dose</td>
<td>Amoxicillin/Clavulanate</td>
<td></td>
</tr>
<tr>
<td>Streptomycin</td>
<td>Cycloserine</td>
<td>Terizidone</td>
<td>INH</td>
<td>Clarithromycin</td>
<td></td>
</tr>
<tr>
<td>Clofazimine</td>
<td></td>
<td></td>
<td></td>
<td>Thiacetazone</td>
<td></td>
</tr>
</tbody>
</table>
TB Regimens and Duration of Tuberculosis Treatment

**Drug-Susceptible**
- First-line drugs
  - INH/RIF/EMB/PZA X 2 months
  - INH/RIF X 4 months

**MDR**
- 2nd and 3rd Line drugs
  - A minimum of 4 (preferably 5 or 6) active drugs
  - 18+ months

**XDR**
- 2nd and 3rd Line drugs
  - A minimum of 4 (preferably 5 or 6) active drugs
  - Consider surgery
  - 24+ months
Potency and Tolerability of TB Drugs

Increasing potency, reliability, reproducibility of susceptibility testing

First-line Drugs
- Rifampin
- Isoniazid
- Pyrazinamide
- Ethambutol

Fluoroquinolones
(moxifloxacin, gatifloxacin, levofloxacin)

Injectable agents
Aminoglycosides (streptomycin, amikacin, kanamycin)
Polypeptides (capreomycin)

Oral bacteriostatic agents
(ethionamide, protonamide, cycloserine/terizidone, p-aminosalicylic acid, thiacetazone)

Agents with unclear efficacy (clofazimine, amoxicillin-clavulanate, clarithromycin, linezolid)

Decreasing tolerability

Disposition of Patients with Drug-Resistant TB

- 73% Hospitalized
- 27% Home isolation
- 9% Die during treatment

Centers for Disease Control and Prevention
Depression/psychosis: 13%
Hearing impairment: 13%
Hepatitis: 11%
Kidney impairment: 8%
Loss of mobility: 7%
Vision impairment: 1%
Seizures: 1%
Centers for Disease Control and Prevention

Average Treatment Costs, Per Case (2010 dollars)

- **Productivity loss during treatment**
- **Direct treatment costs, including:**
  - Drugs & diagnostics
  - Case management & social work
  - Housing & transportation
  - Hospitalization

<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment Duration</th>
<th>Direct Costs</th>
<th>Productivity Loss</th>
<th>Total Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB</td>
<td>6-9 mo.</td>
<td>$17,000</td>
<td>$134,000</td>
<td>$151,000</td>
</tr>
<tr>
<td>MDR TB</td>
<td>20-26 mo.</td>
<td>$260,000</td>
<td>$126,000</td>
<td>$386,000</td>
</tr>
<tr>
<td>XDR TB</td>
<td>32 mo.</td>
<td>$554,000</td>
<td>$124,000</td>
<td>$678,000</td>
</tr>
</tbody>
</table>
Optimization of Current Anti-Tuberculous Drugs

Repurposing of Drugs with Other Indications

New Drugs

New Regimens

Host-Directed Therapy

Strategies to Improve TB Therapeutics
## Optimization of Current TB Drugs

<table>
<thead>
<tr>
<th>INH</th>
<th>Rifamycins</th>
<th>PZA</th>
<th>Quinolones</th>
</tr>
</thead>
</table>
| Genetic variability in INH metabolism  
  • N-acetyltransferase 2 (NAT2)  
  Phenotypic-guided dosing  
  Genotypic-guidance of dosing | **Rifampin**: Cost was basis for 600 mg  
  Close to nadir of dose-response  
  Higher doses used elsewhere  
  **Rifapentine**: no plateau with dose escalation from 450 mg to 1,800  
  Highest RPNT exposures associated with greatest efficacy | PZA activity is dose-dependent  
  AUC/MIC >11.3 best associated with PZA sterilizing activity.  
  Higher PZA doses would be needed to achieve this target  
  Higher doses may improve treatment outcomes | Higher doses may improve outcomes  
  27% reduction in MOXI AUC with rifampin  
  Higher doses could increase toxicity, QTc interval prolongation.  
  Levofloxacin relatively safer in this regard as compared to MOXI |
Optimization of Current Anti-Tuberculous Drugs

Repurposing of Drugs with Other Indications

New Drugs

New Regimens

Host-Directed Therapy
## Candidate Drugs for Repurposing Against TB

<table>
<thead>
<tr>
<th>Name</th>
<th>Class</th>
<th>Current Use</th>
<th>In vitro MIC Against H₃₇Rv</th>
<th>Stage of Repurposing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ivermectin</td>
<td>Avermectin</td>
<td>Anti-helminthic</td>
<td>6.8 μM</td>
<td>In vitro MTT assay</td>
</tr>
<tr>
<td>Carprofen</td>
<td>2-Arylpropanoid acid</td>
<td>Analgesic</td>
<td>146 μM</td>
<td>In vitro HT-SPOTi</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Phenothiazine</td>
<td>Anti-psychotic</td>
<td>47 μM</td>
<td>Mouse model</td>
</tr>
<tr>
<td>Disulfiram</td>
<td>Thiocarbamate</td>
<td>Alcohol withdrawal drug</td>
<td>5.3 μM</td>
<td>broth dilution tests</td>
</tr>
<tr>
<td>Entacapone</td>
<td>Nitrocatechol</td>
<td>Anti-Parkinson's drug</td>
<td>205 μM</td>
<td>broth dilution</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Nitroimidazole</td>
<td>Broad-spectrum antibiotic</td>
<td>&gt;1.4 mM</td>
<td>Phase II</td>
</tr>
<tr>
<td>Meropenem/clavulanic acid</td>
<td>ß-Lactams</td>
<td>Antibiotic</td>
<td>1.7 μM</td>
<td>In vivo and small-scale human patient studies</td>
</tr>
<tr>
<td>Nitazoxanide</td>
<td>Nitrothiazole</td>
<td>Anti-protozoal</td>
<td>52 μM</td>
<td>In vitro</td>
</tr>
<tr>
<td>Oxyphenbutazone</td>
<td>Pyrazolidinedione</td>
<td>Analgesic</td>
<td>200 μM</td>
<td>In vitro</td>
</tr>
<tr>
<td>Pyrvinium pamoate</td>
<td>Methylquinolinium</td>
<td>Anti-helminthic</td>
<td>310 nM</td>
<td>Alamar blue assay</td>
</tr>
<tr>
<td>Tebipenem/clavulanic acid</td>
<td>ß-Lactams</td>
<td>Antibiotic</td>
<td>2.9 μM</td>
<td>Enzyme inhibition studies</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>Phenothiazine</td>
<td>Anti-psychotic</td>
<td>27 μM</td>
<td>BACTEC 460-TB</td>
</tr>
<tr>
<td>Tolcapone</td>
<td>Nitrocatechol</td>
<td>Anti-Parkinson's drug</td>
<td>457 μM</td>
<td>Systems biology</td>
</tr>
</tbody>
</table>
Optimization of Current Anti-Tuberculous Drugs

Repurposing of Drugs with Other Indications

New Drugs

New Regimens

Host-Directed Therapy
The Global TB Drug Pipeline includes early stage development and clinical development phases. Preclinical development includes compounds such as Riminophenazine TBI-166, Caprazene nucleoside CPZEN-45, Capuramycin SQ609, Spectinamide 1599, and Macrolide SEQ-9*. Clinical development phases include Phase I with compounds like Sutezolid (PNU-100480) and Linezolid EBA, Phase II with Bedaquiline (TMC-207) and Delamanid (OPC-67683), and Phase III with Pretomanid-Moxifloxacin-Pyrazinamide Regimen and Bedaquiline-Pretomanid-Linezolid NiX-TB Regimen.
Optimization of Current Anti-Tuberculous Drugs

Repurposing of Drugs with Other Indications

New Drugs

New Regimens

Host-Directed Therapy
Early Bactericidal Activity of Novel TB Regimens

Log CFU Change From Baseline

Day

0 2 4 6 8 10 12 14

-3.0 -2.5 -2.0 -1.5 -1.0 -0.5 0 0.5

Standard-of-care regimen

Novel PA-824/ PZA/moxifloxacin regimen

- Bedaquiline - RHEZ
- Bedaquiline + PZA - PA-824 + PZA
- Bedaquiline + PA-824 - PA-824 + PZA + moxifloxacin

Studies of Fluoroquinolones in Treatment-Shortening Regimens for Pulmonary Tuberculosis

Successful ‘9-month Bangladesh regimen’ for multidrug-resistant tuberculosis among over 500 consecutive patients


515 patients→
84.5% cure!
5.6% death
Stream Study

**Regimen A**

- Clofazimine
- Ethambutol
- Moxifloxacin
- Pyrazinamide
- Isoniazid
- Kanamycin
- Prothionamide

**Regimen B**

*(Stage 1 study regimen)*

- 16 weeks
- 40 weeks

**Regimen C**

*(modified Stage 1 study regimen, all oral)*

- Bedaquiline added
- Moxifloxacin replaced by levofloxacin
- Kanamycin dropped

**Regimen D**

*(modified Stage 1 study regimen, shortened)*

- Bedaquiline added
- Moxifloxacin replaced by levofloxacin
- Prothionamide dropped
- Ethambutol dropped
Nix-TB

Participants are required to have documented XDR-TB, or MDR TB treatment intolerance or failure (TI or Fr)

Follow up for relapse-free cure over 24 months

6 months of treatment

Additional 3 months if sputum culture positive at 4 months

Conradie F, et al. CROI2017
Nix-TB

51% HIV+
65% XDR

Conradie F, et al. CROI2017
Nix-TB Preliminary Results

Primary Endpoint

31 patients have reached 6 months since completion of treatment
Two relapses/reinfection
– XDR TB on LPA- Genome sequencing will determine whether relapse or new infection
– DS-TB on LPA -appears at this stage to be a reinfection.
Four patients have died (all in the first 8 weeks)
– 3 had multi-organ TB on autopsy
– 1 had a GI bleed due to erosive esophagitis.

Time to Culture Conversion

• All surviving patients were culture negative at 4 months.
• 26 (74%) negative at 8 weeks as of December 2016.

Conradie F, et al. CROI2017
Optimization of Current Anti-Tuberculous Drugs

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New Drugs

New Regimens

Host-Directed Therapy
Potential Targets of Host-directed Therapy Against Mycobacterium Tuberculosis

- **Phagocytosis**
  - ESX-1-mediated phagosome permeabilization
  - Inhibition of phagolysosome fusion by ManLAM
- **Phagosome**
  - Promote phagolysosome fusion (metformin), and phagosome acidification and maturation (imatinib)
- **Inflammatory pathways**
  - Cytokine production (e.g., TNF)
  - Inflammasome activation
  - Immune receptor expression
  - Immune signalling pathways
  - ROS production
  - MMP production
  - Leukotriene and prostaglandin production
- **Inhibit inflammation**
  - Corticosteroids
  - TNF blockers
  - PDE4 inhibitors
  - Leukotriene inhibitors
  - Statins
  - PPARy agonists
  - COX inhibitors
  - Prevent lung damage
  - MMP inhibitors

- **Autophagy**
  - Induce autophagy
    - Gefitinib
    - Vitamin D
    - mTOR inhibitors
- **Induce cathelicidin and other antimicrobial peptides**
  - Vitamin D
  - HDAC inhibitors

Nature Reviews | Immunology
## Potential Candidates for Host-directed Therapy Against Mycobacterium Tuberculosis

<table>
<thead>
<tr>
<th>Suitability and clinical readiness</th>
<th>Augmenting macrophage effector mechanisms</th>
<th>Reducing inflammation and/or preventing lung damage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitable for Phase II clinical trials</td>
<td>Metformin</td>
<td>TNF inhibitors (including adalimumab)</td>
</tr>
<tr>
<td></td>
<td>High-dose immunoglobulin</td>
<td>Statins (including rosuvastatin)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>COX inhibitors (including ibuprofen)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doxycycline (MMP inhibitor)</td>
</tr>
<tr>
<td>Clinical optimization required</td>
<td>Phenylbutyrate plus vitamin D3*</td>
<td>CC-10050+ (PDE4 inhibitor)</td>
</tr>
<tr>
<td></td>
<td>Imatinib*† (tyrosine kinase inhibitor)</td>
<td>Various statins†</td>
</tr>
<tr>
<td>Preclinical research and development required</td>
<td>Gefitinib (autophagy inducer)</td>
<td>Various PDE inhibitors</td>
</tr>
<tr>
<td></td>
<td>Various tyrosine kinase inhibitors</td>
<td>PPARγ agonists (including rosiglitazone and telmisartan)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Zileuton (leukotriene inhibitor)</td>
</tr>
<tr>
<td>Discovery of new agents required</td>
<td>Protein kinase R inhibitors</td>
<td>MMP inhibitors</td>
</tr>
<tr>
<td></td>
<td>Autophagy inducers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PPARγ antagonists</td>
<td></td>
</tr>
</tbody>
</table>

COX, cyclooxygenase; MMP, matrix metalloproteinase; PDE4, phosphodiesterase isozyme 4; PPARγ, peroxisome proliferator-activated receptor-γ; TNF, tumour necrosis factor. *A dose-selection study is needed. †A pharmacokinetic drug–drug interaction study with rifamycins is needed.
Tuberculosis represents a considerable disease burden.

Current TB Diagnostics and therapeutics is suboptimal.

Pace of TB diagnostics has escalated but remains a challenge.

Renewed interest in TB therapeutics; but pace not meeting needs.
Call for Papers

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

A NEW ONLINE OPEN ACCESS, PEER-REVIEWED JOURNAL

“We believe that this journal fills an unmet need by providing a platform for the dissemination of the results of clinically relevant research; the sharing of clinical observations that illustrate important points, highlight complexities, generate discussions, and provide impetus for further clinical research; and presenting opinions from experts with in depth experience in the management of mycobacterial diseases on topics for which clinical trial-based evidence to direct clinical management is not available.”

Editor-in-Chief
Zelalem Temesgen, MD

Associate Editors
Stacey A. Rizza, MD • John W. Wilson

All from Mayo Clinic Center for Tuberculosis
Rochester, Minnesota, USA

Journal of Clinical Tuberculosis and Mycobacterial Diseases aims to provide a forum for clinically relevant articles on all aspects of tuberculosis and other mycobacterial infections, including (but not limited to) epidemiology, clinical investigation, transmission, diagnosis, treatment, drug-resistance and public policy, and encourages the submission of clinical studies, thematic reviews and case reports.

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UNITE TO END TB

TOGETHER WE WILL MAKE IT HAPPEN

World Health Organization