# DEPARTMENT OF MICROBIOLOGY
## INFECTIOUS DISEASE BULLETIN

VOLUME 1 ISSUE 3 MARCH 2022


## WORLD *Tuberculosis* DAY
**24th March 2022**


Each year, World TB Day is observed on March 24 to raise awareness about tuberculosis around the world. This annual event commemorates the date in 1882 when Dr. Robert Koch announced his discovery of *Mycobacterium tuberculosis*, the bacillus that causes tuberculosis (TB), which opened the way towards diagnosing and curing this disease.

Our March ID Bulletin is dedicated to the continous efforts being made to End TB.....


As per the WHO report, 27% of the global TB cases are from India. Besides the high burden, India also accounts for about one-fourth of the worldwide burden of drug-resistant tuberculosis. Multi-drug resistant tuberculosis (MDR-TB) resistance to first-line anti-TB drugs viz. Rifampicin and Isoniazid pose a serious threat to the End TB initiative. The global incidence of MDR-TB is 3.4% in new cases and 18% in previously treated cases. Indian government survey from 2014 to 2016 estimated the incidence of MDR-TB as 2.84% in new cases and 11.6% among previously treated patients.

Active case finding, rapid diagnosis using rapid molecular tests, prompt appropriate treatment, and improved airborne infection control are the cornerstone for controlling MDR-TB as endorsed by WHO. The basics of TB care are to ensure timely diagnosis and initiation of appropriate treatment, with continuous support and supervision to achieve successful treatment completion and cure; also applies to MDR-TB. Drug resistance should be considered in every patient, and an aggressive effort to collect biological specimens to detect resistance should be made. A rapid test for at least rifampicin resistance should ideally be done for every patient, followed by prompt treatment, as delays have been associated with increased transmission.

Regimens should only include drugs that the patient's isolate has documented or have a high likelihood of susceptibility. Medications known to be ineffective based on in vitro resistance or clinical and epidemiological information should not be used. Drugs should be selected based on their efficacy and the possibility that patients will tolerate them without significant toxicity. Treatment response is monitored clinically, radiographically, and bacteriologically. If sputum cultures remain positive after three months of treatment, or if there is a bacteriological reversion from negative to positive at any time, DST should be repeated, and therapy needs to be modified as per the new report.

*Dr. Sanjay Singhal, MD Pulmonary Medicine, EDRM*

TB is a type IV hypersensitivity reaction which can pathologically present at any site as a granulomatous lesion. Various other granulomatous diseases can also show similar findings on histopathology. So, a detailed clinical evaluation, and sometimes specific studies like TB GeneXpert or QuantiFERON TB Gold testing are needed. Usually in case of dilemma, empirical anti-tubercular treatment is started due to very high prevalence in India. Moreover, even after a patient has a proven tuberculosis, there should be an extensive search of any other malignant features in the biopsy as TB can manifest as an association to any malignancy including carcinoma, sarcoma or lymphoma, due to immunosuppression. Even the local draining lymph nodes in a case of any carcinoma may show not only metastases but also caseating granulomas. It may also be associated with HIV / AIDS, or any other primary or secondary immunodeficiency disorders. Any histopathological features of these associated diseases should also be searched and recognized. Hence a pathologist should not only know the morphological findings of tuberculosis, but also should consider it as just a manifestation and try to find out if any other associated disease is present.

*Dr. Garima Anandani, MD Pathology, PDF (Hematopathology)*

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## PHOTO QUIZ

A 28-year-old female G2P1 with an uneventful antenatal period delivered a full-term female child weighing 2.5 Kg by normal vaginal delivery. After 1 week of delivery, she developed intermittent high-grade fever associated with chills. There were no other complaints and no significant past history including no contact with any TB case. Physical examination revealed pallor. No enlarged lymph nodes. Systemic examination was normal. Initial laboratory investigations were as follows: haemoglobin-8.3 gm/dL, total leucocyte count-7,500/cumm with 57% polymorphs and 30% lymphocytes. Erythrocyte sedimentation rate was 45 mm fall first hour. Liver and renal function tests were within normal limits. Widal test for enteric fever, strip test for malarial parasite, urine and blood culture were not contributory. Serology for HIV, HBV and HCV was negative. Chest radiography and ultrasound abdomen done during second week of fever were normal.

Patient was initially treated as a case of viral fever and then empirically for enteric fever. She, however, continued to have low-grade fever with added night sweats. Three weeks later follow-up ultrasound abdomen revealed mild hepatosplenomegaly. Repeat chest radiograph done at this stage was normal. Mantoux test was negative. Patient was now put empirically on antimalarials but she continued to be symptomatic. Chest radiograph followed by high-resolution CT scan taken 4 weeks later are shown in Fig 1 and Fig 2.

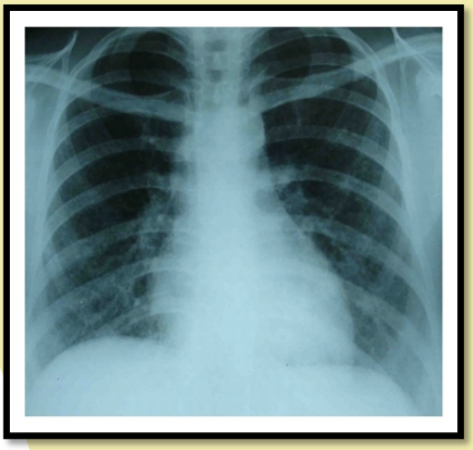

Fig 1. Chest radiograph

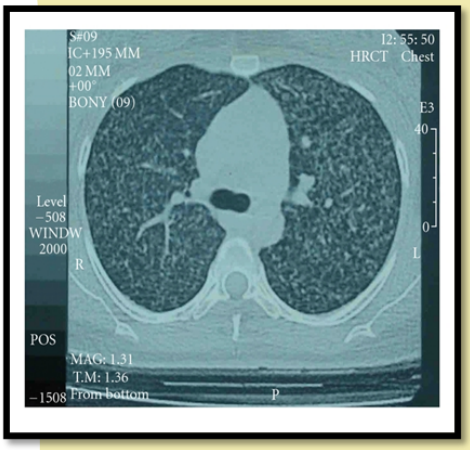


Fig 2. HRCT chest

## Top findings and messages in the Global Tuberculosis Report 2021

The COVID-19 pandemic has reversed years of progress in providing essential TB services and reducing TB disease burden. To add, Global TB targets are mostly off-track. There has been a large global drop in the number of people newly diagnosed with TB and reported, this have fell from 7.1 million in 2019 to 5.8 million in 2020, an 18% decline back to the level of 2012 and far short of approximately 10 million people who developed TB in 2020. 16 countries accounted for 93% of this reduction, with India, Indonesia and the Philippines the worst affected. Provisional data up to June 2021 show ongoing shortfalls. Reduced access to TB diagnosis and treatment has resulted in an increase in TB deaths. Declines in TB incidence (the number of people developing TB each year) achieved in previous years have slowed almost to a halt. Other impacts include reductions between 2019 and 2020 in the number of people provided with treatment for drug-resistant TB (-15%, from 177 100 to 150 359, about 1 in 3 of those in need) and TB preventive treatment (-21%, from 3.6 million to 2.8 million), and a fall in global spending on TB diagnostic, treatment and prevention services (from US$ 5.8 billion to US$ 5.3 billion, less than half of what is needed). Actions to mitigate and reverse these impacts are urgently required. The immediate priority is to restore access to and provision of essential TB services such that levels of TB case detection and treatment can recover to at least 2019 levels, especially in the most badly-affected countries.

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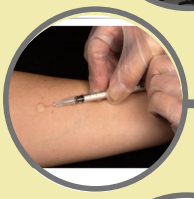
# TUBERCULOSIS CHRONICLES

**JOHANN SCHONLEIN**
coined the term Tuberculosis

**1834**

**1st research lab for TB**

**1894**

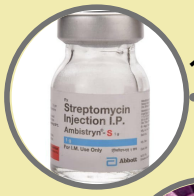


**Montoux test**

**1908**


**PPD**

**1930**

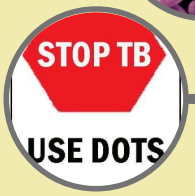



**1st antibiotic Streptomycin**

**1943**

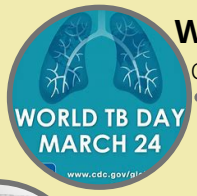
**1st outbreak of drug resistant TB**

**1970**



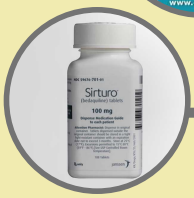

**DOTS :**New TB control Stratergy

**1995**




**World TB Day 24 March**
celebration started

**1999**



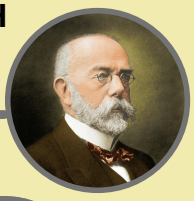

**Bedaquiline discovery**

**2004**


**RNTCP renamed as NTEP**
to eliminate TB in India by 2025

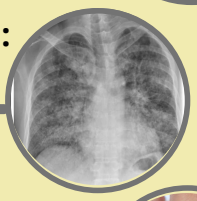
**2020**

**ROBERT KOCH**
Announced the discovery of Tuberculosis bacilli :ZN stain



**1882**

**Invention of X-ray : TB diagnosis**

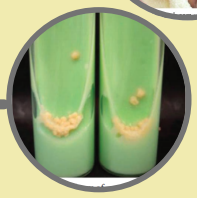


**1895**

**BCG vaccine**

**1921**

**Selective medium- LJ medium**



**1930**

**Discovery of four drugs HRZE**

**1951-66**

**WHO declared TB 'A global health emergency'**

**1993**

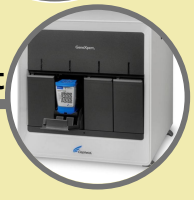
**Launch of RNTCP**


**1997**

**STOP TB partnership**
global plan to stop TB


**2001**

**Launch of Gene Xpert**



**2010**

DEPARTMENT OF MICROBIOLOGY
INFECTIOUS DISEASE BULLETIN
VOLUME 1 ISSUE 3 MARCH 2022

# KNOW YOUR DRUG

## BEDAQUILINE

### What is it ?

Diarylquinoline antibiotic
Action by inhibiting Mycobacterial ATP synthase activity which prevents the bacteria from generating ATP leading to cell death
Activity against MTB & multiple NTMs - *M. avium, M. abscessus*

### Approved for

- Initial approval-FDA (2012): MDR TB treatment, TB resistant to INH and R
- WHO- Recommends its use in MDR-TB patients who lack treatment options, commonly used for XDR-TB
- Approved for adults 18 years & older
- Approved for a total course of 6 months

### Adverse reactions

MC-Nausea, arthralgia, headache

QT interval prolongation, monitor ECG closely for patients receiving Bedaquiline together with other drug that prolong QT interval e.g., Quinolones, Macrolides, Clofazimine

Increase Liver transaminases (15-20% pts)

Black box warning

### Preparation and Dosage

- Available in tablet form - 100mg- bedaquiline fumarate base
- Administered orally as 400mg once daily with food × 14 days, followed by 200 mg thrice weekly to complete 24 weeks of therapy
- It must be given together with optimized background treatment consisting of atleast 3 or 4 other drugs to which patient's MDR -TB isolate is sensitive
- MDR-TB treatment is generally continued after the 24-week course of Bedaquiline is completed, for a total treatment duration of 12-24 Months

### Don'ts

Not approved for use in latent TB, extrapulmonary TB or drug susceptible TB
No current guidelines for pregnant and lactating mothers
Co-administration of bedaquiline & efavirenz, bedaquiline & rifamycins is not advised

### To Note

Bedaquiline activity is concentration dependent and the AUC/MIC is its main pharmacokinetics/dynamic driver
No dose adjustment for patients with mild or moderate renal & hepatic impairment

Guidelines for use of bedaquiline in RNTCP for management of DR-TB in India
https://tbcindia.gov.in/showfile.php?lid=3246

## ANSWER TO PHOTO QUIZ

### Miliary Tuberculosis Presenting as Puerperal Fever

A diagnosis of miliary tuberculosis was made based on radiological findings and the patient was started on 4-drug regimen ATT (isoniazid, rifampicin, ethambutol, and pyrazinamide) for first 3 months, followed by isoniazid and rifampicin for next six months. There was significant improvement in general condition of the patient in next few days. She became afebrile after 10 days of ATT. Follow-up imaging study done after 9 months of treatment revealed no residual activity. Newborn was vaccinated with BCG at birth and was breast fed and put on INH prophylaxis for 3 months. She had a normal chest skiagram and negative Mantoux test before and after INH therapy. Both mother and child were doing fine after one year of follow-up.

To note, the classic appearance of miliary disease on chest radiograph may become apparent days or weeks after presentation. So, HRCT chest is considered more sensitive and accurate for miliary TB than plain chest radiography in early course of disease.

Clinicians usually include TB in their differential diagnosis list when managing patients with fever of unknown origin. However, due to non-specific clinical manifestations and absence of typical chest radiographic findings, miliary tuberculosis as an etiology is usually bypassed and the diagnosis (if any) is delayed.

- Case by Dr.(Col) Ashwini Agarwal

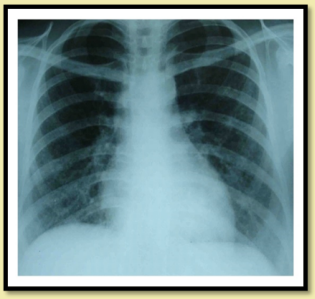


Fig 1. Chest radiograph showing bilateral diffuse miliary nodular lesions

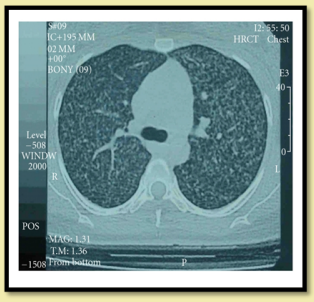


Fig 2. HRCT chest-lung window shows bilateral diffuse miliary nodular opacities having random distribution

DEPARTMENT OF MICROBIOLOGY
INFECTIOUS DISEASE BULLETIN
VOLUME 1 ISSUE 3 MARCH 2022

## IN THE NEWS

### 1.CDC recommends 4-month regimen for drug-susceptible TB

https://www.tbonline.info/posts/2022/2/25/cdc-recommends-4-month-regimen-drug-susceptible-tb/

The CDC published a recommendation and interim guidance in MMWR for a 4-month regimen to treat patients aged 12 years or older with drug-susceptible pulmonary tuberculosis. This regimen consisting of 8 weeks of daily treatment with rifapentine, isoniazid, pyrazinamide and moxifloxacin, followed by a continuation phase of 9 weeks of daily treatment with rifapentine, isoniazid, and moxifloxacin.

### 2. Detecting TB outside the lungs

https://www.tbonline.info/posts/2022/1/27/detecting-tb-outside-lungs/

A new fluorescent probe for detecting TB can now identify disease-causing bacteria in extra-pulmonary tissue for better diagnosis

### 3. New vaccine may provide better treatment for TB

https://www.tbonline.info/posts/2022/1/28/new-vaccine-may-provide-better-treatment-tb/

A new vaccine so-called H56: IC31 may also be used in tuberculosis treatment. The vaccine is safe to give to people with tuberculosis disease and strengthens the immune system's ability to attack the bacteria that cause the disease.

### 4.CROI 2022: Fewer pills plus shorter time: New way to control drug-resistant TB?

https://www.tbonline.info/posts/2022/2/17/croi-2022-fewer-pills-plus-shorter-time-new-way-co/

Three investigational drug regimens to treat drug-resistant tuberculosis (TB) were superior to standard of care, with fewer unfavourable outcomes and a shorter treatment time. (Bedaquiline, pretomanid, and linezolid (BPaL),Bedaquiline, pretomanid, linezolid, and clofazimine (BPaLC) and Bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM)

### 5.AI algorithms identify TB on lateral chest X-rays

https://www.tbonline.info/posts/2022/3/2/ai-algorithms-identify-tb-lateral-chest-x-rays/

Tuberculosis (TB) can be consistently detected on lateral chest x-rays by an ensemble of two different types of deep-learning networks.

### 6.Tuberculostearic acid, a potential parameter for scoring system construction for tuberculous meningitis diagnosis

https://www.ijmyco.org/article.asp?issn=2212-5531;year=2021;volume=10;issue=4;spage=428;epage=432;aulast=Fong

Prospective utilization of TBSA is worth combining into a scoring system for characterizing the features of MTB, showing a great potential of TBM diagnosis by TBSA in future.

# Upcoming Events

## World Malaria Day
## 25 April 2022