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A Systemic Review On Abdominal Tuberculosis On Lymph , Peritoneum , Gi Tract

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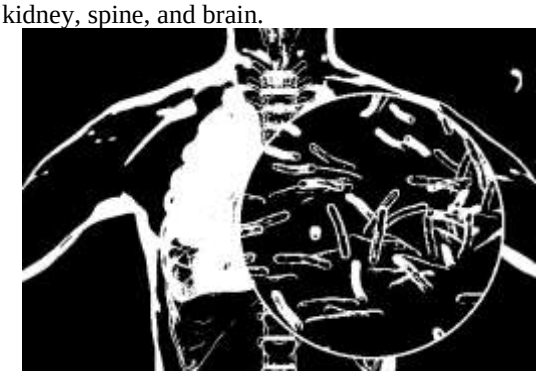
I. INTRODUCTION:

Infection of the gastrointestinal tract, peritoneum, abdominal solid organs, and abdominal lymph nodes are all arbitrary inclusions in the definition of abdominal TB. Among all abdominal tuberculous illnesses, gastrointestinal TB is the mostoften involved site it is difficult to identify gastrointestinal TB because of the varied or non-specific clinical presentation. This causes a delay in diagnosis and significant morbidity as a result. We give a current overview of the epidemiology, aetiology, clinical characteristics, diagnosis, and management of gastrointestinal TB because of its significance and the necessity to identify this long-standing infectious adversary.Due to the fact that it affects an estimated one-fourth of the world's population, tuberculosis (TB) is significant. [1] Although latent TB (LTB) is on the rise in wealthy countries as a result of immunosuppressive disorders, biological use, and migration, TB incidence is highest on the Asian and African continents

1.1 DEFINITION:

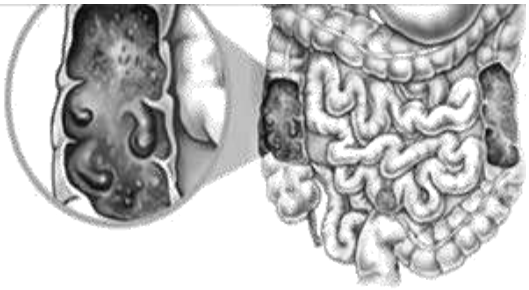
TUBERCULOSIS:

Mycobacterium tuberculosis is the bacteria that cause tuberculosis (TB). Although the TB germs typically assault the lungs, they can also affect the kidney, spine, and brain.



ABDOMINAL TUBERCULOSIS:

Involvement of the gastrointestinal tract, peritoneum, lymph nodes, and/or solid organs is all examples of abdominal tuberculosis (TB) [1-4]. Around 5% of all TB cases globally are abdominal TB infections.

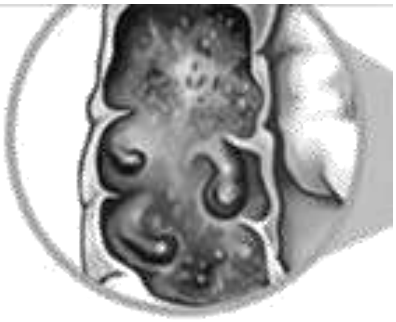


GASTROINTESTINAL TUBERCULOSIS:

1% to 3% of tuberculosis (TB) cases globally are due to gastrointestinal (GI) TB. It can happen as a primary infection without lung involvement or in the context of an active pulmonary illness.

PERITONEUM TUBERCULOSIS:

Particularly in women who come with ascites and increased CA125 values, peritoneal tuberculosis can resemble cancer. Although the differential diagnosis should always take it into account, the diagnosis is rarely straightforward for professionals.



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LYMPH NODE TUBERCULOSIS:

One or more lymph nodes are often painfully swollen as a result of the lymph node TB. Most frequently, the illness affects the supraclavicular region or the anterior or posterior cervical chains (70–90%). It can affect non-contiguous lymph nodes and is frequently bilateral.

RISK ELEMENTS:

Cirrhosis, human immunodeficiency virus (HIV) infection, diabetes mellitus, underlying malignancy, malnutrition, therapy with antitumor necrosis factor drugs [6], corticosteroids, and use of continuous ambulatory peritoneal dialysis are risk factors for the development of abdominal TB. The epidemiology of TB-related issues is covered in more detail separately.

1.2 Etiology

There are five ways that mycobacteria can infect the GI tract:

6. Mycobacterium tuberculosis from sputum intake by a patient with active pulmonary illness
7. Hematogenous dissemination from a far-off focus
8. Through diseased nodes, lymphatic dissemination occurs.
9. Extension directly from a nearby location
10. Consumption of milk products contaminated with Mycobacterium bovis, which is most common while drinking raw milk

A primary form of abdominal TB caused by ingesting M. bovis directly and a secondary form caused by the spread of human bacillus from an active lung illness are the two forms of TB that some writers have identified.

The most often affected portions are found to be the terminal ileum and ileocaecal valve. [6][7] This happens as a result of a number of things in this area. Among them include a small lumen and a comparatively elevated physiological stasis. (Allowing for the organism's absorption), little digestion occurs, and M cells, which can take up tubercle bacilli, are present in the lymphatic tissue. [8]

Mycobacteria have a lipid capsule that is difficult to digest and prevents their early GIT release. As a result, proximal GIT lesions were considered to be uncommon. [9] But it can also impact the proximal GIT.

1.3 HISTORY AND CAUSES:

The following symptoms are frequently reported by patients with gastrointestinal tuberculosis

- Continent pain
- Anorexia \sFever
- Changes in bowel habits: constipation less prevalent than diarrhea
- nausea and diarrhea
- Melena

Some individuals, however, might not have any GI TB symptoms

When examined, they frequently exhibit the following symptoms:

- Loss of weight
- Anemia and pallor
- bodily bleeding
- Ascites and a distended abdomen
- Hepatomegaly
- Splenomegaly
- Lymphadenopathy
- stomach mass

It's possible that not all patients have a clear family history of TB. Therefore, even in the absence of a family history, GI TB must be taken into account. Similar to this, a small number of individuals may also have concurrent pulmonary TB or a TB-related prior medical history.

1.4 PRECAUTIONS:

- For the duration of the house visit, put on the appropriate personal protective equipment (PPE), such as a powered air-purifying respirator (PAPR) or a N95 respirator that has been fit-tested and approved by NIOSH. Inform family members about the dangers of TB transmission and contact tracing.
- Since microscopic particles carry germs in the air, airborne precautions are utilised for illnesses like TB (usually dust). Depending on the airflow in the room, these particles may linger in the air for some time.
- A few straightforward steps can lower the risk of infection: TB may hang in the air for several hours without ventilation, thus it is important to have excellent ventilation. UV light: UV light destroys the TB bacteria naturally. Good hygiene: when coughing or sneezing, cover your mouth and nose to stop the transmission of TB bacteria.

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II. HOW WE DETECT TUBERCULOSIS:

1.1 MRI SCAN (MAGNECTIC RESONANCE IMAGING)
1.2 CT SCAN (COMPUTER TOMOGRAPHY)

2.1 MRI SCAN:

A magnetic field and radio waves produced by a computer are used in the medical imaging procedure known as magnetic resonance imaging (MRI), which produces precise pictures of your body's organs and tissues. Most MRI scanners include enormous magnets in the form of tubes.

Different pathogenic phases of TB were linked to MR results. T1-weighted imaging revealed low signal intensity in the early and middle stages of granuloma with or without caseation or liquefaction necrosis and high signal intensity at those.

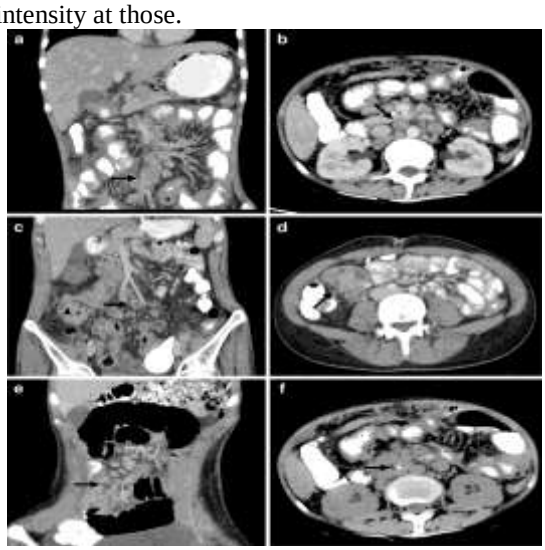
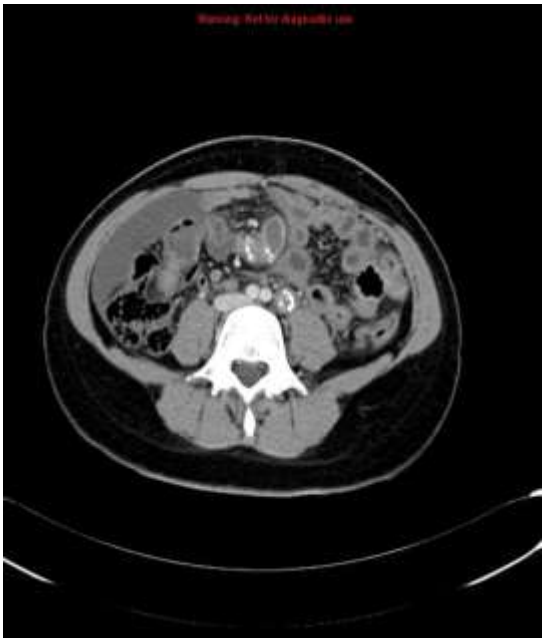


Image show the presence of tb in abd

2.2 COMPUTER TOMOGRAPHY:

The imaging process known as computed tomography (CT) employs specialised x-ray equipment to produce in-depth images, or scans, of various body regions. It is also known as computerised axial tomography and computerised tomography (CAT)

Abdominal lymph node involvement. (a) Multiple enlarged retroperitoneal and mesentericlymph nodes with characteristic hypodense centres andperipheral hyperdense rims.heterogeneous mixeddensity lymph node mass (arrows) in the mesenteric compartment. (c) An increased number of normal sizedsoft tissue density mesenteric nodes (arrows).



III. DRUGS USED IN THE TREATMENT OF ABDOMINAL TUBERCULOSIS

Isoniazid INH is frequently used in conjunction with the medications rifampin, pyrazinamide, and ethambutol to treat active TB.

Second-line injectable antibiotics are Kanamycin, Capreomycin, and Amikacin. Delamanid and Bedaquiline are recent medications. The potential efficacy of Ethambutol, Pyrazinamide, Thioamides, Cycloserine, Para-aminosalicylic Acid, Streptomycin, and Clofazimine

DRUGS USED FOR A TREATMENT OF ABDOMINAL TUBERCULOSIS

- **ISONIAZID**
- **RIFAMPICIN**
- **PYRAZINAMIDE**
- **BEDAQUINE**
- **CEFITOXIME**

3.1 ISONIAZID:

3.1.1. DEFINITION:

The antibiotic isoniazid, often referred to as isonicotinic acid hydrazide, is used to treat TB. It is frequently used with rifampicin, pyrazinamide, and either streptomycin or ethambutol to treat active TB. It is frequently used alone to treat latent TB.

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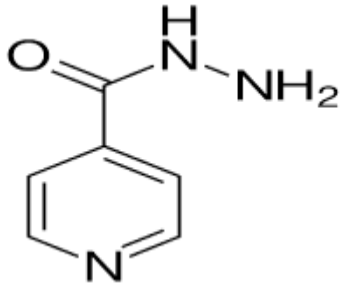
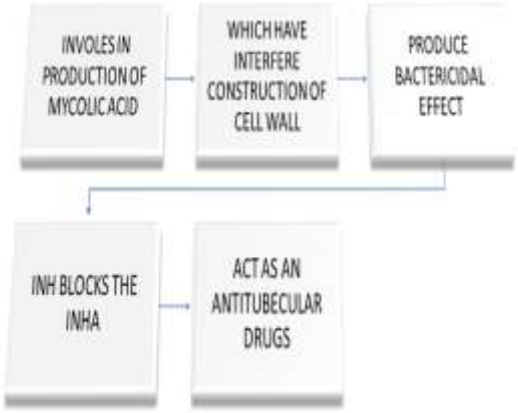
5.1.2 STRUCTURE:



3.1.3 MECHANISM OF ACTION:

Due to its capacity to prevent the production of mycolic acid, which interferes with the construction of cell walls and has a bactericidal effect, INH's antibacterial action is specific for mycobacteria.

Isoniazid (INH) blocks the activity of a particular enzyme called InhA in the production of mycolic acid,

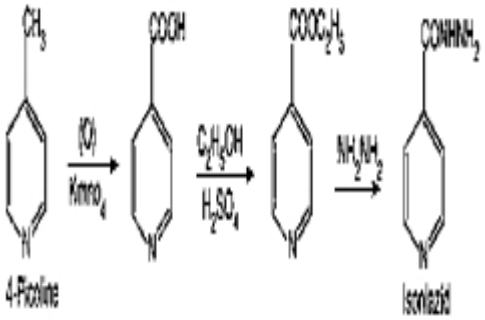


3.1.4SAR OF ISONIAZID:

- Pyridine ring is essential for activity
- Subsitutuion of R1 R2 AND N 2 are important for activity
- INH is an most active derivative

- Isopropyl group at R2 position may leads to loss of anti tubercular activity and but psychomotor act as a stmulant to maintain the drug activity

3.1.5 SYNTHESIS OF ISONIAZID:



- ✓ 4-picoline act as an starting derivative
- ✓ And its react with catalyst of potassium permagnate kmno4
- ✓ Ethyl alcohol and hydrogen sulphate have further act to produce carboxy ethylene
- ✓ And diammine act as an catalyst to form the isoniazid

3.1.6 ADR:

- numbness and tingling in the extremities,
- hepatitis (symptoms include loss of appetite, nausea, vomiting, fatigue, malaise, and weakness),
- nausea,
- vomiting,
- upset stomach,
- Fever, or.
- rash

3.1.7 ROLE OF ISONIAZID IN TUBERCULOSIS:

It functions by eradicating the disease-causing germs. Isoniazid's specific mode of action is uncertain, although it is believed to work by preventing the TB bacterium from producing mycolic acids, which are essential for the formation of the bacteria's cell walls.

INH is a pro-drug that binds to and blocks InhA, an enzyme necessary for the manufacture of mycolic acids, a component of the mycobacterial cell wall, causing mycobacterial cell death.

3.2. RIFAMPICIN:

- Rifampin is **in a class of medications called antimycobacterials**. It works by killing the bacteria that cause infection. Antibiotics such as rifampin will not work for colds, flu, or other viral infections
- **Rifampin is a common medicine used to treat LTBI**. It kills the sleeping TB germs before they make you sick. It can take many

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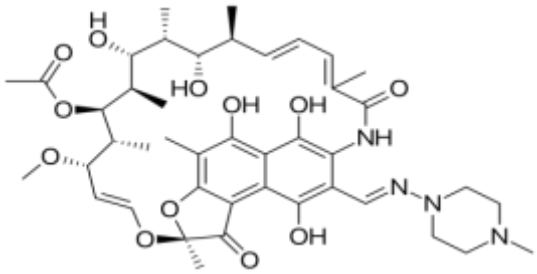
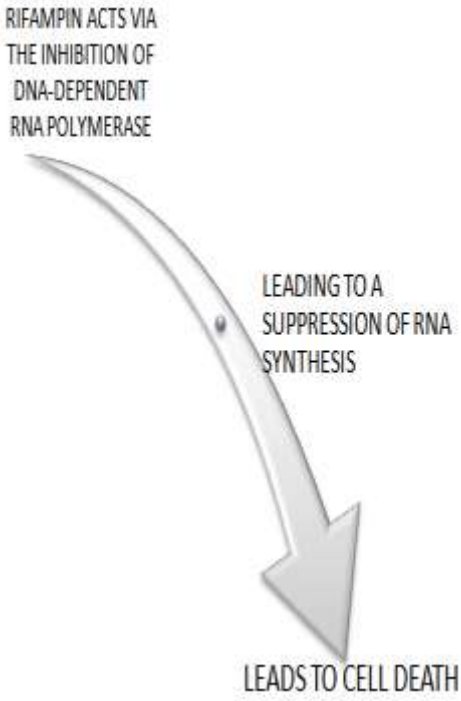
months for the medicine to kill the TB germs because they are strong.

3.2.1 STRUCTURE:



3.2.2 MECHANISM OF ACTION:

- RIFAMPIN ACTS VIA THE INHIBITION OF DNA-DEPENDENT RNA POLYMERASE
- LEADING TO A SUPPRESSION OF RNA SYNTHESIS
- LEADS TO CELL DEATH



3.2.3 ROLE OF RIFAMPICIN AT TUBERCULOSIS:

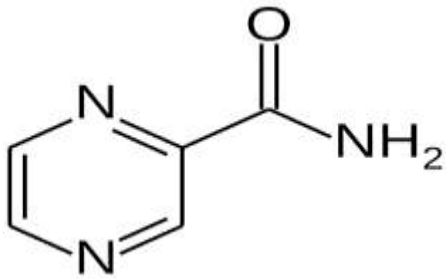
You can take medicine to prevent getting active TB disease. Rifampin is a common medicine used to treat LTBI. It kills the sleeping TB germs before they make you sick. It can take many months for the medicine to kill the TB germs because they are strong.

Take your Rifampin as often and as long as your doctor or nurse tells you. Taking your Rifampin without food is best. If your stomach is upset, it is okay to take your Rifampin with a small amount of food or try taking it at bedtime

3.3 PYRAZINAMIDE:

Pyrazinamide is a medication used to treat tuberculosis. [2] For active tuberculosis, it is often used with rifampicin, isoniazid, and either streptomycin or ethambutol.

3.3.1 STRUCTURE:



3.3.2 MECHANISN OF ACTION:

- Pyrazinamide diffuses into active M. tuberculosis that express pyrazinamidase enzyme that converts pyrazinamide to the active form pyrazinoic acid
- Pyrazinoic acid can leak out under acidic conditions to be converted to the protonated conjugate acid, which is readily diffused back into the bacilli and accumulate intracellularly
- Pyrazinoic acid has also been shown to bind to the ribosomal protein S1 (RpsA) and inhibit trans-translation. This may explain the ability of the drug to kill dormant mycobacteria

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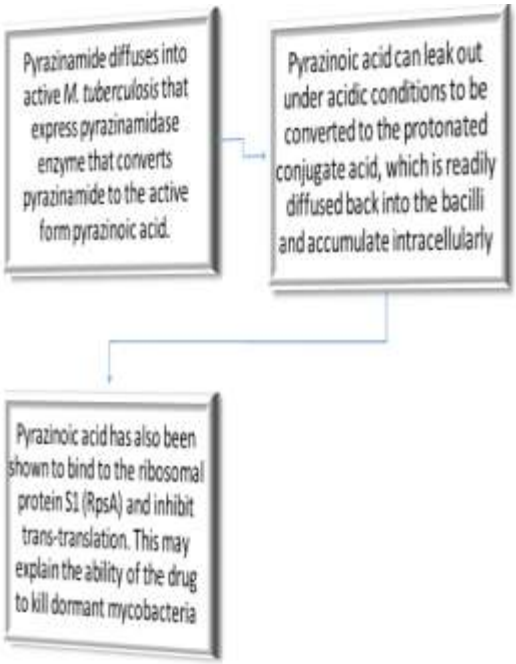


3.3.4 ROLE OF PYRAZINAMIDE IN TUBERCULOSIS:

- Pyrazinamide is an antibiotic that fights bacteria. Pyrazinamide is used to treat tuberculosis (TB) in adults and children. Pyrazinamide must be used with other TB medicines. Tuberculosis can become resistant to treatment if pyrazinamide is used alone.
- The global control and management of tuberculosis (TB) is faced with the formidable challenge of worsening scenarios of drug-resistant disease. Pyrazinamide (PZA) is an indispensable first-line drug used for the treatment of TB. It plays a key role in reducing TB relapse rates, shortening the course of the disease treatment from 9-12 months to 6 months, and the treatment of patients infected with bacillary strains that are resistant to at least isoniazid and rifampicin.

IV. UNAPPROVED DRUGS FOR TUBERCULOSIS:

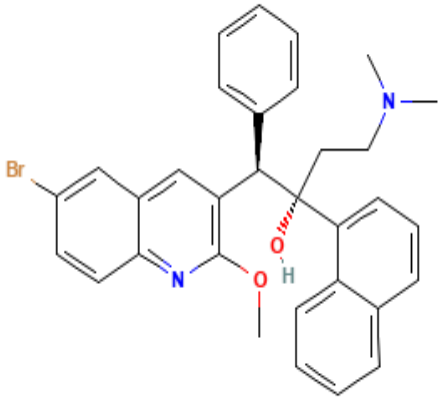
4.1 BEDAQUINILINE:

Bedaquiline, sold under the brand name Sirturo, is a medication used to treat active tuberculosis. Specifically, it is used to treat multi-drug-resistant tuberculosis (MDR-TB) along with other medications for tuberculosis. It is used by mouth. Common side effects include nausea, joint pains, headaches, and chest pain

- Formula: $C_{32}H_{31}BrN_2O_2$
- Trade names: Sirturo
- Routes of administration: By mouth
- Metabolism: Liver

Bedaquiline is a quinoline-based antimycobacterial drug used (as its fumarate salt) for the treatment of pulmonary multi-drug resistant tuberculosis by inhibition of ATP synthase, an enzyme essential for the replication of the mycobacteria. It has a role as an antitubercular agent and an ATP synthase inhibitor. It is a member of quinolines, a member of naphthalenes, an organobromine compound, aromatic ether, a tertiary alcohol and a tertiary amino compound. It is a conjugate base of a bedaquiline

STRUCTURE:



BEDAQUINLINE

REASON FOR BEING UNAPPROVED DRUG:

The emergence of bedaquiline resistance is alarming, as it may result in the rapid loss of this new drug

The most common side-effects reported with bedaquiline therapy are
Nausea (30%),
Arthralgia (26%),
Headache (22%),
Hemoptysis (14%),
Chest pain (9%),

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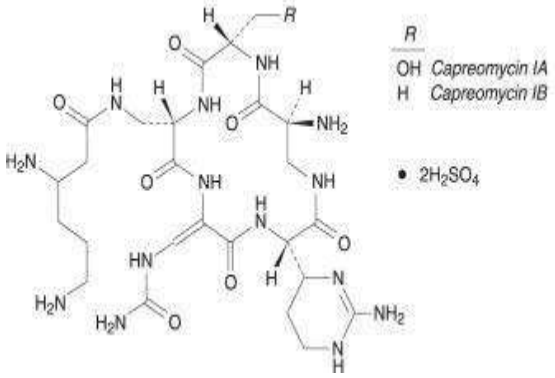
Anorexia (7%), and
Rash (6%).
Important cardiovascular adverse effect is QT prolongation.
Due to prolong time of drug medication these medication was not still approved by fda but ita have been available in market

4.2 CAPREOMYCIN:
Capreomycin is an antibiotic which is given in combination with other antibiotics for the treatment of tuberculosis. Specifically it is a second line treatment used for active drug resistant tuberculosis. It is given by injection into a vein or muscle
Capreomycin is usually given after other tuberculosis medications have been tried without success.
Genericname: capreomycin
Brandname: CapastatSulfate
Dosageform: intramuscularpowder (1g)
Drug class: Streptomyces derivatives
STRUCTURE:



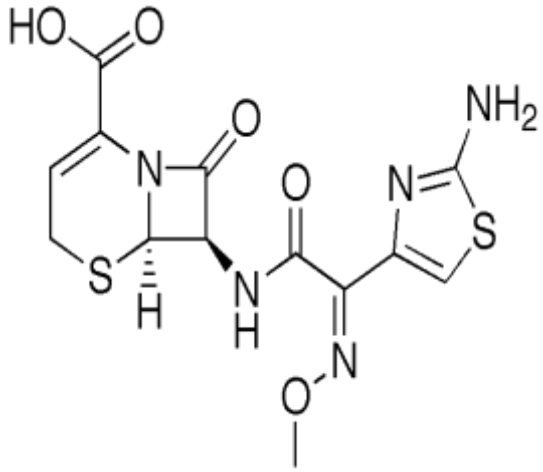
REASON FOR UNAPPROVAL:
Capreomycin can harm your kidneys or damage the nerve that controls your hearing.
To make sure capreomycin is safe for you, tell your doctor if you have:
Kidney disease
Hearing problems.
FDA pregnancy category C. It is not known whether capreomycin will harm an unborn baby. Tell your doctor if you are pregnant or plan to become pregnant while using this medicine.
It is not known whether capreomycin passes into breast milk or if it could harm a nursing baby. Tell your doctor if you are breast-feeding a baby.
Do not give this medication to anyone under 18 years old without medical advice.

It have unapproved for nan reason of causing over side effect to pregnant ladies and also verry dangerous for kidney so these drugs are not approved by an fda but these drugs also been available in market
6.3 Ceftizoxime:
Ceftizoxime is in a group of drugs called cephalosporin (SEF a low spor in) antibiotics. It works by fighting bacteria in your body.

Ceftizoxime is a broad-spectrum antibiotic used to treat a variety of bacterial infections including urinary tract infections

Genericname: ceftizoxime
Brandname: Cefizox
Drug class: Third generation cephalosporins

STRUCTURE:



Ceftizoxime

REASON FOR UNAPPROVAL OF CEFTIZOXIME :

Before using this medication, tell your doctor if you are allergic to any drugs (especially penicillin). Also tell your doctor if you have liver or kidney disease, a stomach or intestinal disorder, or if you are malnourished.

Use this medication for the entire length of time prescribed by your doctor. Your symptoms may get better before the infection is completely treated. Ceftizoxime will not treat a viral infection such as the common cold or flu.

Antibiotic medicines can cause diarrhea, which may be a sign of a new infection. If you have diarrhea that is watery or has blood in it, call your doctor. Do not use any medicine to stop the diarrhea unless your doctor has told you to.

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This medication can cause you to have unusual results with certain lab tests to check for glucose (sugar) in the urine. Tell any doctor who treats you that you are using ceftizoxime.

V. CLINICAL TRIALS :

Recent advances in the development of new drugs and regimens provide hope that well tolerated, effective, and shorter-duration treatments for tuberculosis (TB) will become available. This review covers the recent trials of new TB drugs and regimens.

Recent advances in the development of new drugs and regimens provide hope that well tolerated, effective, and shorter-duration treatments for tuberculosis (TB) will become available. This review covers the recent trials of new TB drugs and regimens.

5.1 CHALLENGES WHEN TUBERCULOSIS OCCURS TO TB PATIENT :

The COVID-19 pandemic has caused unforeseen and extreme changes in societal and health system functioning not previously experienced in most countries in a lifetime [1]. The disruptions have been dynamic-varying by time and geography-which adds to their unpredictable effect. The negative impact of COVID-19 on tuberculosis (TB) programs has recently been reported with models predicting 126,100 excess TB deaths over the next five years for every one month of COVID-related lockdown [2]. Clinical trial implementation is especially challenging in this pandemic environment, requiring sponsors to adhere to trial protocols and regulatory requirements as closely as possible while ensuring the safety of trial participants and staff.

Tuberculosis clinical trials carry inherent challenges at the best of times. Locations with the highest tuberculosis burden often have less resilient regulatory infrastructure, complex operational environments and more limited clinical trial experience [3]. During an unexpected and large-scale disruption like COVID-19, the impact of these weaknesses becomes more magnified.

STREAM is the largest multi-country trial for multidrug-resistant tuberculosis (MDR-TB) ever conducted. Conceived by the Union and global partners with initial funding from USAID, the trial has recruited over 1000 patients to two distinct stages. Results from STREAM Stage 1 were published in 2019 and 2020 [4,5], and recruitment was recently completed for the second stage in January, 2020. As of March 31, 2020, 126 participants remain on MDR-TB treatment with 21 of those in the intensive phase of treatment and 312 participants remain in active follow-up.

Stage 2 of STREAM is a registration trial [6], which adds complexity to implementation. It incorporates central safety and microbiology testing, requiring regular export of biological samples. In addition, a contract research organization (CRO) is employed to conduct onsite monitoring and source data verification to ensure data quality.

The COVID-19 pandemic has had an important impact on the implementation of STREAM. Key challenges faced by STREAM (and similar trials) together with the responses of the trial team to date, are outlined in this commentary.

Study Type :	**Interventional (Clinical Trial)**
Actual Enrollment :	**40 participants**
Allocation:	**Randomized**
Intervention Model:	**Parallel Assignment**
Masking:	**Quadruple (Participant, Care Provider, Outcomes Assessor)**
Primary Purpose:	**Treatment**
Official Title:	**Phase 2 Study of Orally Formulated Heat-killed Mycobacterium Vaccae Study in TB Patients**

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5.2 PHASE II
Study Description
Brief Summary:
This is a phase II, randomized, placebo-controlled trial, aimed to seek the therapeutic benefit of V7 in combination with standard of care anti-Tuberculosis (TB) therapy (ATT) among Mycobacterium tuberculosis-infected sputum smear positive subjects. The results will be compared to placebo combined with standard ATT therapy. The trial will consist of one stage with sputum evaluation at months 1 and 2.

Condition or disease	Intervention/treatment	Phase
Tuberculosis	Biological: V7Other: placebo	Phase 2

5.3 **PHASE III:**
Study Description

Brief Summary:

Mycobacterium Vaccae for Injection (Trade Name "Vaccae") is a kind of bio-products developed by Anhui Zhifei Longcom Biopharmaceutical Co.,Ltd.,and got "The New Drug Certificate "in 1999. Vaccae has been approved for adjuvant therapy of tuberculosis(TB), and is also the only recommended drug in TB immunotherapy by WHO. It was approved for production and sale by Anhui Zhifei Longcom Biopharmaceutical Co.,Ltd. in 2001, and got favourable comment in therapy of tuberculosis.

The purpose of this study is to add new indications for Vaccae, mainly to prevent Tuberculosis for high risk groups of Tuberculosis Infection . In December 2012, China Food and Drug Administration approved of the plan "Phase III Clinical Study of Efficacy and Safety of Mycobacterium Vaccae to Prevent Tuberculosis in high risk groups of Tuberculosis Infection". In the test, 10,000 cases whose skin tests of PPD are strongly positive are enrolled. Using random, double-blind, and placebo-controlled methods, the study is carried out to evaluate the efficacy and safety of Vaccae in preventing Tuberculosis. Meanwhile, in this test, TB incidence and degree of pathological changes of experimental group are lower than that of control group, and no drug-related SAEs are reported in treatment groups.

Condition or disease	Intervention/treatment	Phase
Tuberculosis	Drug: VaccaeDrug: placebo	Phase 3

Detailed Description:
The Main Purpose of the Study:
- Evaluation of efficacy of Vaccae to prevent Tuberculosis in high risk groups of Tuberculosis Infection.
The Secondary Purpose of the Study:

- Evaluation of Lesion Degree (Bacteriology Indicators, Cavity) of patients and its relationship with Skin Test results of TB-PPD after Injection of Vaccae into the high risk groups.
- Evaluation of Changes in Humoral Immunity and Cellular Immunologic Response Before and After Injection of Vaccae

Test Hypothesis:
In the test, TB incidence and degree of pathological changes of experimental group are lower than that of control group, and no drug-related SAEs are reported in treatment groups

Blinding and Random:

Using random, double-blind, and placebo-controlled methods, evaluation of the efficacy and safety of Vaccae.
Using block randomization method, a random sequence was generated by the statistics personnel in Fourth Military Medical University Clinical Evaluation Center using SAS9.1.3 statistical software
The Unblinding includes the first time of Unblinding and the second time of Unblinding. The first time of Unblinding only distinguish groups , and the second time of Unblinding will uncover the final Blind Codes.

VI. RESULT AND CONCLUSION :

In the world the most common form of disease was been tuberculosis many people have dies daily there is an perment source of therphy but there also been some indeed to take drugs rather then surgery and such kind of drugs have been taken for prolonged time some drugs like isoniazid are more effective on killing the mycobacterium cells and also been take for prolonged time cure out the disease

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There also some clinical trials have been done to estimate the good quality products on research purposes and development process have continuously done for future treatment over tb and several advancements must have been accomplished over an treatment of abdominal tuberculosis

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