**Introduction**

1. Tuberculosis (TB) is a curable condition but requires prolonged treatment for its cure. During last 3 decades tremendous advances have been made in the diagnosis and treatment of tuberculosis. Though the incidence in the Armed Forces have remained almost static, added dimension to this problem have cropped up in the form for entry of women officers to the services, prolonged survival of service personnel following treatment of malignant diseases and increasing number of clientele with solid organ transplant.

**Objective**

2. This DG Memorandum is being brought out to give a guideline to treating doctors in diagnosis and management of tuberculosis in Armed Forces keeping in mind the existing National and International protocols on the subject.

3. The diagnosis of TB refers to the recognition of an active case, i.e. detection of a patient with symptomatic disease due to lesions caused by M. tuberculosis. Beyond making the diagnosis of TB, it is also necessary to define the type of TB case, i.e. to make a case definition. This applies to all TB patients, adults and children.

4. **Pulmonary TB** refers to disease involving the Lung parenchyma. Therefore tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitute a case of extra-pulmonary TB. A patient with both pulmonary and extra-pulmonary TB constitutes a case of pulmonary TB. (ICD-011)

The case definition of an extra-pulmonary case depends upon the site of involvement. Involvement of two non-contiguous organs with tubercular disease will be termed as **disseminated TB**. Thus involvement of pulmonary parenchyma with
any other non-contiguous extra pulmonary site by tubercular process will be considered as pulm TB with extra pulmonary dissemination. A patient having pulmonary and meningeal TB will be labeled as Pulmonary TB with meningeal dissemination.

5. **Severity of TB diseases**

Bacillary load extent of disease and anatomical site are considerations in determining TB disease severity and therefore the appropriate treatment. Involvement of an anatomical site results in classification as severe disease if there is either a significant acute threat to life (i.e. pericardial TB) or a risk of subsequent severe handicap (i.e. spinal TB), or both (e. o. meningeal TB).

The following forms of extra-pulmonary TB are classified as **severe**: -

(a) Meningitis  
(b) Miliary  
(c) Pericarditis  
(d) Peritonitis  
(e) Bilateral or extensive pleural effusion.  
(f) Spinal TB (with neurological defect)  
(g) Intestinal  
(h) Genito-urinary

The following forms of extra-pulmonary TB are classified as **less severe**: -

(a) Lymph node  
(b) Pleural effusion (unilateral).  
(c) Bone (excluding spine).  
(d) Spinal (without neurological involvement)  
(e) Peripheral joint  
(f) Skin

6. **Bacteriology (result of sputum smear)**

The importance of defining the smear result in pulmonary cases is for the following: -
(a) the identification of smear-positive cases (because they are the most infectious cases and they have an increased mortality).

(b) recording and reporting (smear-positive cases are the only cases for which bacteriological monitoring of cure is available).

7. **Diagnosis of Tuberculosis**

On clinical suspicion of tuberculosis with systemic features like fever, night sweat, anorexia and weight loss, pulmonary manifestation of cough of more than 2 weeks duration or haemoptysis, the patient must be examined for any sign of pulmonary disease. Essential investigation will include chest x-ray (CXR) and examination of two early mornings and one overnight sputum for acid fast bacillus (AFB). Any patient showing sputum smear positive twice for AFB will be classified as sputum positive case. Those with one specimen of sputum showing positive or all specimen shown negative for AFB, with evidence of pulmonary disease on CXR will be considered x-ray positive suspects of tuberculosis. They may be offered a 7-10 days course of artibacterials (except quinolones, streptomycin and rifampicin). A repeat clinical examination of CXR may be carried out to asses clinical and radiological recovery. Similar evaluation will be carried out for household contacts of sputum positive patient.

8. All such bacteriologically positive and x-ray positive cases should be transferred to a Resp Centre for further evaluation.

(a) In accordance with WHO guidelines any patient with two sputum specimen positive for AFB or one sputum specimen positive with x-ray shadow suggestive pulm infiltrate or one smear and one sputum MTB culture being positive will be taken as a bacteriologically positive case of Pulm TB

(b) Any patient who does not show sputum to be positive for AFB but radiologically there are suspicious shadows and there is no response to broad spectrum anti-bacterials will be taken as sputum negative Pulm TB. Any other patient with suspicion of extra-pulm disease and with clinical features to suggest anti TB treatment with or without histopathological/bacteriological confirmation will be grouped as a case of extra-pulm TB. Mycobacterial culture must be put up in all cases from available sputa and/or from the tissue/serosal fluid (as the case may be),
Note: - Presence or absence of cavity and extent of pulmonary parenchymal involvement denotes the anatomical extent of lesion but it may not correlate with bacteriological status of the patient

(c) other investigation like tuberculosis positive status, polymerase chain reaction (PCR) and ELISA for tuberculosis may be complementary to diagnostic work up but they do not have definitive diagnostic value.

9. Other routine inv. includes. Blood count ESR, liver function tests, serum transaminases, alkaline phosphates, uric acid, blood sugar (fasting and post parandial) and HIV serology if facilities are available.

Treatment - Our success rate in treatment of pulmonary tuberculosis in Armed Forces during last quarter century has remained between 98-100% with relapse rate much below 1%. All efforts must be directed to maintain this record and if possible to improve upon it.

10. Aims of Treatment The aims of treatment of TB are the following :-
    (a) to cure the patient of TB :
    (b) to prevent death from active TB or its late effects:
    (c) to prevent relapse of TB:
    (g) to decrease transmission of TB to others.

It is vital to achieve these aims while preventing the selection of resistant bacilli in infectious patients.

11. The essential anti TB drugs

There are three main properties of anti-TB drugs: bactericidal ability, sterilizing ability and the ability to prevent resistance. Different anti-TB drugs possess these properties to different extents. Isoniazid and rifampicin are the most powerful bactericidal agents. Pyrazinamide is active in an acid environment against the bacilli inside macrophages. Streptomycin is active against rapidly multiplying extracellular bacilli. Ethambutol and thiacetazone are bacteriostatic drugs used in association with more powerful bactericidal drugs to prevent the emergence of resistant bacilli.

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12. **Intermittent Therapy**

Isoniazid, rifampicin, pyrazinamide and streptomycin are all as efficacious when given intermittently (2 or 3 times per week) as when given daily.

<table>
<thead>
<tr>
<th>Essential Anti TB drugs</th>
<th>Mode of action</th>
<th>Recommended Dose (mg/kg)</th>
<th>Daily</th>
<th>Intermittent (3/wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (H)</td>
<td>Bactericidal</td>
<td>5 (4-6)</td>
<td>10 (8-12)</td>
<td></td>
</tr>
<tr>
<td>Rifampicin ®</td>
<td>Bactericidal</td>
<td>10 (8-12)</td>
<td>10 (8-12)</td>
<td></td>
</tr>
<tr>
<td>Pyrazinamide (Z)</td>
<td>Bactericidal</td>
<td>25 (20-30)</td>
<td>35 (30-40)</td>
<td></td>
</tr>
<tr>
<td>Streptomycin (S)</td>
<td>Bactericidal</td>
<td>15(12-18)</td>
<td>15 (12-18)</td>
<td></td>
</tr>
<tr>
<td>Ethambutol (E)</td>
<td>Bacteriostatic</td>
<td>15</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

13. **Principle**

The basic principle of tuberculosis treatment is based on the fact that there has to be an initial intensive phase followed by a continuation phase.

(a) **Intensive Phase** is required with an aim to kill maximum number of actively multiplying organisms. This should be continued with 4 drugs S/E HRZ for 2-3 months and subsequently we only have to consolidate the recovery in the next phase.

(b) **Continuation Phase** aims at sterilizing the lesion by eliminating the intermittently multiplying bacilli or persisters among bacterial debris.

(c) **Duration of Treatment & Hospitalization** – Total duration of treatment has to be minimum six months in all cases. In deserving cases it may be extended by the specialist concerned. In cases of pulmonary TB is service personnel hospitalization to be ensured till they become sputum negative for AFB and general condition stabilizes.
14. All anti-TB drugs except the 2\textsuperscript{nd} line or reserve drugs are best absorbed on empty stomach. Philosophy of antitubercular chemotherapy aims more at peak rather than sustained serum level.

**Regimens**

15. For simple cases without much of pulmonary parenchymal destruction, intensive phase need to be continued for 2 months with SHRZ E can replace S at the dose of 20-25 mg/kg for first 2 months. This can be extended to 3 months in case of extensive/miliary/disseminated diseases & re-treatment in cases where sputum continues to be AFB positive. When attack phase is continued for 3 months, dose of ethambutol to be brought down to 15 mg/kg after initial 60 days of the drug administration.

In continuation phase rifampicin ® and isoniazid (H) are continued ordinarily for 4 months but in case of extensive organ dissemination a total of 9-12 months of treatment can be considered. It after 2 months of continuation phase, sputum for AFB remains positive, repeat sputum culture to be put up and attack phase extended to 3 months, further line of management must be guided in consultation with a specialist in the subject based on bacteriological response as well as clinical condition of the patient.

**Monitoring**

16. (a) Monthly - Sputum AFB smear. MTB culture, Blood ESR Hb, TLC

(b) Once in 2 months - x-ray Chest

(c) LFT in case of suspicion of hepatic dysfunction.

(d) Review by physician/chest physician. After completing 01 02. 04. 06 and 9 months.

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17. Treatment for Pregnant Women

It is important to ask a woman before she starts anti-TB chemotherapy if she is pregnant. In case facilities are available it will be ideal to get an ultrasound of pelvis carried out to confirm any product of conception. Most anti-TB drugs are safe for use in pregnant women except in the first trimester. The exception is streptomycin (which is ototoxic to the fetus) should not be used in pregnancy and can be replaced by ethambutol. It is important to explain to a pregnant woman that successful treatment of TB with the recommended standardized regimen is important for a successful outcome of pregnancy. It must be stated here that all first line drugs except streptomycin are being used by doctors during pregnancy without any problem.

In case of high-risk pregnancy, a specialist in tuberculosis and respiratory diseases may be consulted.

18. Treatment for Breast Feeding Women

A woman who is breastfeeding and has TB should receive a full course of anti-TB chemotherapy. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to her baby. All the anti-TB drugs are compatible with breastfeeding and a woman taking them can safely continue to breastfeed her baby. The mother and baby should stay together and the baby should continue to breastfeed in the normal way. The baby should receive isoniazid prophylaxis and BCG immunization under the guidance of a specialist in paediatric/tuberculosis. As long as the mother is sputum smear positive, facemask is advisable during feeding.

19. Treatment for Women taking the Oral Contraceptive Pills

Rifampicin interacts with the oral contraceptive pill with a risk of decreased protective efficacy against pregnancy. A woman who usually takes the oral contraceptive pill may choose:

(a) Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of estrogen (50 mcg).
(b) Alternatively she could use another form of contraception.
20. **Treatment for patients with liver disorders**

The following drugs with antitubercular properties are safe for liver. They are i) ethambutol, ii) cycloserine, iii) aminoglycosides (streptomycin, kanamycin, tobramycin and amikacin) as well as Quinolones (ofloxacin, ciprofloxacin)

The patients with the following conditions can receive the usual short-course chemotherapy regimens provided that there is no clinical evidence of chronic liver diseases: hepatitis virus carriage, a past history of acute hepatitis, excessive alcohol consumption.

(a) **Established chronic liver disease**

Isoniazid plus rifampicin plus one or two non-hepatotoxic drugs such as streptomycin, ethambutol ofloxacin/ciprofloxacin can be used for a total treatment duration of eight months. An alternative regimen is streptomycin plus isoniazid plus ethambutol ofloxacin/ciprofloxacin in the initial phase followed by isoniazid and ethambutol in the continuation phase with total treatment duration of 12 months. **Patients with liver disease should not receive pyrazinamide.** Therefore recommended regimens are the following: 2 SHRE/ 6HR or 2 SHRE/10 HE. Patient must be monitored with weekly clinical examination and monthly Liver Function Test (LFT) test (Sr Bil, transaminase), if there is no ongoing hepato cellular dysfunction. Fortnightly, LFT in case of mild biochemical degrangement (where transaminase levels are less than 3 times normal or base line).

(b) **Acute hepatitis (e.g. acute viral hepatitis)**

It is a rare eventuality that a patient has TB and also at the same time acute hepatitis unrelated to TB or anti TB treatment. In some case it is possible to defer TB treatment until the acute hepatitis has resolved. In other cases when it is necessary to treat TB during acute hepatitis, cautious use of non- hepatotoxic drugs with frequent monitoring of hepatic parameters need to be done.
21. **Extra Pulmonary Tuberculosis**

(a) **Lymph node.** It is the commonest extra pulmonary tissue to be involved. One third of cases of lymphnode tuberculosis may show apparent increase in size and aggravation of lesion while on treatment. However, they do not necessarily suggest failure of treatment. In such case while all attempts have to be made to get antibiotic susceptibility of mycobacterium, no 2nd line drug need be added unless there is definite evidence of clinical deterioration with systemic features or any evidence of radiological deterioration of the disease. An extended treatment in such cases will be beneficial. Total duration of treatment may be extended to 9-12 months in the later group.

(b) **Bone and Joint Tuberculosis.** A course of regular ATT and 9 months regime seems to be adequate in the case of spinal TB without neurological involvement.

(c) **CNS TB.** Involvement of brain parenchyma may demand prolonged treatment upto a period of one year. Drugs like isoliazid, pyrazinamide and ethionamide penetrate well into blood brain barrier and they have to be preferentially used in such cases. Systemic steroid therapy is added to reduce meningeal inflammation and prevent any obstruction to CSF flow. High dosage of steroid will be required (50 mg/kg to start with) in view of concurrent refampicin therapy.

(d) **Genito Urinary Tuberculosis.** A six month regime with present short course therapy seems to be adequate except in case where there has been involvement of prostate and seminal vesicles. In such cases treatment need to be prolonged for one year or more.
(e) **Abdominal Tuberculosis.** Gastrointestinal involvement is a fairly common occurrence. Extra pulmonary tuberculous lesions in out lumen and peritoneum may heal quickly but those involving intra-abdominal lymphnodes may take more time requiring 9-12 months of treatment. The involvement of intra abdominal lymphnodes should be monitored by ultrasonography.

(f) **HIV with Tuberculosis.** Therapeutic response in cases with dual infection seem to be good as far as tuberculosis is concerned, till such time increasing viral load has not brought down the effective T cell population. An extended short course chemotherapy, lasting upto one year will be a prudent approach. The question of continuing life long prophylaxis in such a situation has not yet been resolved.

(g) **Treatment of Tuberculosis in Solid Organ Transplant Patients**

In many such patients receiving cyclosporin, rifampicin has to be avoided. In the absence of rifampicin one of the strongest anchor of short course chemotherapy the total duration of the treatment need to be prolonged to 18-24 months i.e. a treatment programme like that of conventional (pre short course) treatment era.

22. **Disposal of cases of Pulmonary Tuberculosis**

(a) All serving officers and men suspected to be suffering from Pulmonary tuberculosis are to be hospitalised at (a) Base Hospital Delhi Cantt (b) MH (CTC) Pune (c) MH Namkum (d) MH Dehradun (d) INHS Asvini (e) Comd Hosp (AF) Bangalore. After detailed evaluation the diagnosis has to be established and an attributability Medical Board held. Treatment has to be continued as per the guidelines mentioned above.

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Note :- These hospitals are authorized Respiratory Centres. Administrative Instructions for setting up facilities for Isolation, diagnosis (AFB culture), AMB (Atributability Medical Board), referral of pulmonary tuberculosis cases to these centers and treatment will be issued by the respective service HQs. AO 150/75.

(b) **Duration of Hospitalization** – Till the condition has been stabilized and patient has been considered non-infectious. Preferably intensive phase of treatment should be under supervision and in a hospital.

(c) **Discharge from the Hospital** - Once medical authorities feel that the above criteria have been fulfilled, patient can be discharged in low medical category (P-3 Temp) provided it is felt that, prescribed domiciliary treatment can be carried out at unit level and regular drug supply also is ensured.

(d) **Subsequent categorisation.** Till such time the patient is on medication he should be observed in cat P-3 or equivalent for maximum duration of one year. Once the patient is off medication and minimum of observation period of 24 weeks have been completed he can be considered for up-gradation to P2 category. Re-categorization to be done after review by a Medical Specialist at nearest service hospital.

23. **Treatment and Disposal of Drug Resistant Cases**

(a) All cases of pulmonary tuberculosis where there are chances of drug resistance should be transferred to MH (CTC) Pune which should remain a nodal point for tuberculosis referral and research. Drug resistance has to be suspected, in case there is no clinical and radiological improvement and or sputum smear remains positive 3 months after supervised and TB treatment. All such cases should be subjected to detailed bacteriological work up and reserve drug to be used under supervision of a specialist in Tuberculosis and Resp disease.

(b) **DISPOSAL**

(i) All cases of multi drug resistant (MDR) TB i.e those having combined resistance to rifampicin and isoniazid with or without resistance to any other drug will be candidates for invalidment.

(ii) However patients showing clinical, radiological improvement and bacteriological quiscence within 6 months of start of anti TB
treatment or attributability Med board (whichever is earlier) may be considered for retention in service. However such decision has to be left to a Senior Adv in TB and Resp Disease or Consultant in Medicine.

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(iii) Patients with single drug resistance or polyresistance (ie resistance to more than one anti TB drugs other than a combined resistance to rifampicin and isoniazid) may be considered for retention in service.

(iv) Any patient not showing bacteriological quiescence 6 months after start of anti TB treatment or AMB, irrespective of type of resistance will be considered for invalidement out of service and will be permitted six month indoor treatment of MH (CTC) Pune as ex-servicemen after invalidement