Answers to Frequently Asked Questions on TB preventive treatment (TPT)

associated with the 2020 WHO TPT guidance [1]

1) What is tuberculosis preventive treatment?

Tuberculosis (TB) preventive treatment (or TPT) consists of a course of one or more anti-tuberculosis medicines given with the intention of preventing the development of TB disease. TPT is only given to people who are infected with TB bacteria or have been exposed to it and are at a higher risk of developing TB disease than the general population. TPT is considered one of the most critical public health measures to protect both individuals and the community from TB.

2) How does TPT work?

TPT is intended to eliminate TB bacteria that have infected the body before they can damage the organs and cause illness TPT will only work if given when there are is no evidence of active TB disease. It is estimated that about one fourth of the world's population is infected with TB bacteria and most of them will not have disease. However, some of these individuals have a higher risk of developing active disease and effective TPT can reduce that risk substantially. Once active TB disease develops, other forms of treatment will be required.

3) Who should take TPT?

TPT is offered to people who were in contact with someone with active TB, or who have HIV or other conditions that weaken their immunity. This includes people of all ages in close contact with TB patients; people of all ages living with HIV; people who will start anti-TNF treatment, who will receive dialysis, or who are preparing for organ or haematological transplantation; and prisoners, health-workers, immigrants from high TB burden countries, homeless persons and people who use drugs. The conditions under which treatment is given in these different populations is described in more detail in the new WHO guidelines.

4) Why should I take treatment when I do not feel ill?

If your healthcare worker has offered you TPT, it is because you have an increased chance of developing active TB disease or risk a poor outcome should you fall ill. When taken regularly for the time prescribed TPT will treat the TB infection early on and can prevent the bacteria from multiplying and causing disease. These medicines are well-tolerated by most people and any adverse drug reactions that emerge usually settle down by themselves.

5) What TPT options are available? Can I take whichever one suits me?

Isoniazid given daily for 6 to 9 months has been the most widely used TPT regimen worldwide. It has a long-standing history of use, good tolerance in most people and a lot of evidence for effectiveness. Rifampicin and rifapentine (known as rifamycins) are medicines that can reduce the length of TPT significantly, an important advantage for any treatment. Rifampicin can be given alone for 4 months ("4R") or with isoniazid for 3 months ("3HR"). The availability of dispersible tablets of HR makes this an attractive option for children. Rifapentine can be given together with isoniazid in a weekly dose for three months ("3HP") or daily for one month ("1HP"). More details on the best suited circumstances in which to give one regimen over another may be found in the WHO guidelines and operational handbook on TPT released in 2020.

[1] WHO consolidated guidelines on tuberculosis: tuberculosis preventive treatment. Geneva, World Health Organization. 2020. https://apps.who.int/iris/bitstream/handle/10665/331170/9789240001503-eng.pdf

6) What should I do if I develop adverse drug reactions?

If you are receiving TPT and think you may have an adverse drug reaction ("side-effect"), such as loss of appetite, nausea, vomiting, abdominal discomfort, persistent fatigue or weakness, dark-coloured urine, pale stools or yellowish discolouration you should immediately contact the healthcare worker looking after you. If a healthcare professional cannot be reached immediately you should stop your treatment until you can get expert advice.

7) Should I also get vitamin B6 with my TPT?

Vitamin B6 (pyridoxine) supplementation is not a routine requirement in individuals who are otherwise healthy and who receive isoniazid at the dose recommended for TPT. However, even low doses of isoniazid can lead to nerve injury among malnourished people or those who metabolise isoniazid slowly. Other conditions that can predispose to isoniazid-related nerve damage are chronic alcohol dependence, HIV infection, kidney failure or diabetes, or in women who are pregnant or breastfeeding. Concurrent administration of vitamin B6 with isoniazid protects against the development of nerve damage in these individuals. If signs of nerve toxicity develop - often starting with "needles and pins" or burning sensation in the feet or hands – then contact your healthcare worker to discuss if TPT needs to be changed and if treatment with vitamin B6 at a higher dose is necessary.

8) Is it necessary to test for liver function before starting TPT?

There is insufficient evidence to support routine testing of liver function before starting TPT. However, where feasible, baseline testing is encouraged for individuals with the following risk factors: history of liver disease, regular use of alcohol, chronic liver disease, HIV infection, age > 35 years, pregnancy or in the immediate postpartum period (within 3 months of delivery). For individuals with abnormal baseline test results, sound clinical judgement is required to ensure that the benefit of TPT outweighs the potential risk of damaging the liver. In individuals at risk who have been prescribed TPT testing may be needed at follow-up visits. Laboratory testing for liver and other functions should be performed in individuals who become symptomatic while on treatment.

9) Do I need to take TPT if I am living with HIV and receiving antiretroviral treatment (ART), and have a high CD4 cell count?

PLHIV are at risk of developing active TB. All PLHIV aged 10 years or older (i.e. adults and adolescents) should take TPT as part of a comprehensive package of HIV care in addition to their antiretroviral treatment (ART). This is regardless of their CD4 cell count. While regular ART reduces the overall risk of developing TB, this risk remains higher than in HIV-negative people, especially where background rates of TB are higher. Combined use of TB preventive treatment and ART significantly reduces the risk of TB.

10) Should PLHIV on ART receive rifapentine?

Regimens containing rifampicin and rifapentine should be prescribed with caution to PLHIV who are on ART because of potential drug-drug interactions. These regimens should not be administered to people receiving protease inhibitors or nevirapine. The 3HP or 1HP regimens can be administered to people on efavirenz-based ART without dose adjustment. Administration of rifapentine with raltegravir and dolutegravir was found to be safe and well tolerated and dose adjustment is not usually needed.

11) How can we rule-out active TB in PLHIV prior to TPT?

PLHIV aged 10 years or older (i.e. adults and adolescents) who report any of the symptoms of current cough, fever, weight loss or night sweats may have active TB and should be evaluated for TB. Those who do not have any of these symptoms are unlikely to have active TB and should be offered TPT, regardless of their ART status. Chest radiography (chest X-ray), if available, may be offered to PLHIV who are receiving ART and TPT given to those with normal findings. However, chest radiography should not be considered a mandatory requirement or be a barrier to initiating TPT in PLHIV.

12) Should pregnant women living with HIV take TPT?

Pregnant women living with HIV are at risk for TB, which can have devastating consequences for both the mother and their unborn child. Pregnancy should not disqualify women living with HIV from receiving preventive treatment. Isoniazid is the medicine that has been used most frequently in such a situation and, while more research is needed, there is no strong evidence to suggest that it is dangerous to the mother or baby.

13) Should TPT be given if someone in the household has multidrug-resistant TB?

TPT for contacts of people with TB strains resistant to both isoniazid and rifampicin (multidrug-resistant TB or MDR-TB) may still be possible but different medicines are used. MDR-TB is a serious form of TB and is less easy to treat than other types of TB disease. Your healthcare worker can help you make the decision about taking TPT in such a situation.

14) Can TPT worsen the TB drug-resistance problem in the world?

There is no evidence of a significant association between TB drug resistance and the TPT given to protect people at risk. Nonetheless, active TB disease must be excluded before TPT is prescribed, and regular follow-up is required to ensure that people who develop active TB while receiving TPT be identified early. TPT should not be given indiscriminately to people without an assessment of risk and presence of active TB. Countries should establish national surveillance systems for resistance to TB medicines.

15) How do I know if I have TB disease?

TB disease typically causes cough, sputum (sometimes with blood), fever, night sweats and loss of appetite. If you develop any of these while you are on TPT, or after you finish it, you should contact your healthcare provider immediately. These symptoms may be due to conditions other than TB, like colds or pneumonia. Special attention is also necessary to exclude infection with COVID-19 during the current pandemic: this needs to be confirmed using other diagnostics than the ones for TB infection.

16) How can you test for TB infection?

Either a tuberculin skin test (TST) or interferon gamma release assays (IGRA) can be used to test for TB infection. The choice will depend on test availability, previous BCG vaccination, cost and the health infrastructure. Each of the two tests has its advantages and disadvantages, but there are no solid grounds to prefer one test over the other when it comes to predicting whether infection will progress to active TB disease in an individual. Neither the TST nor IGRA can be used to diagnose *active TB disease* nor for the diagnostic workup of adults suspected of having active TB. Testing with TST or IGRA is desirable to avoid giving TPT to people who are not infected but is not a requirement for initiating preventive treatment in PLHIV or household contacts aged < 5years.

17) How is TST done?

TST is administered by intradermal injection of purified protein derivative (PPD-S) or PPD RT23, which give similar reactions in individuals infected with *M. tuberculosis*. For standardization of readings and interpretation of results, 5 tuberculin units (TU) of PPD RT23 is widely used. Administration is generally done on the inner surface of the forearm. A discrete wheal (6–10 mm) should be produced when the injection is given correctly. A note in the record should indicate the site chosen for the test. The person tested should be instructed to keep the test site clean, uncovered and not to scratch or rub it. A second visit is needed to read the reaction and it is extremely important that this is done within 48–72 hours of administration: readings outside this time range may lead to incorrect conclusions.

18) How are IGRAs done?

IGRAs detect interferon-gamma produced by white blood cells in individuals infected with M. tuberculosis. For IGRAs to measure this response accurately, a fresh blood specimen taken by phlebotomy containing viable white blood cells needs to be transported to a specially equipped

laboratory. There are currently two assays in widespread use and that have been endorsed by WHO: QuantiFERON®–TB Gold In-Tube test (QFT–GIT) and T-SPOTTB test (T–Spot). IGRAs assess response to synthetic overlapping peptides that represent specific *M. tuberculosis* proteins, such as early secretory antigenic target-6 (ESAT-6) and culture filtrate protein 10 (CFP-10). These proteins are present in all *M. tuberculosis* complex but are absent from BCG vaccine strains and from most nontuberculous mycobacteria, making IGRAs more specific to infection by TB bacilli pathogenic to man.

19) Should TPT be provided under direct observation (DOT)?

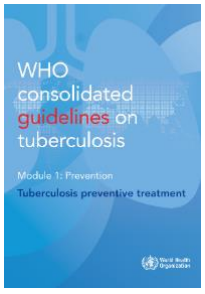
All TPT options can be self-administered. The selection of treatment options by programmes and clinicians should consider the best modality for treatment provision and support to the people taking treatment, considering their preference and their need for information (especially if adverse drug reactions emerge). It is important that people are helped to take TPT regularly and until the end.

20) What can be done to encourage treatment adherence and support completion of TPT?

Interventions should be tailored to the specific needs of the individual and to the local context to ensure adherence and completion of treatment. Akin to the treatment of active TB, such interventions could include peer support, coaching and educational interventions and regular contact (e.g. via mobile phone). Shorter TPT regimens are associated with better adherence and higher treatment completion. Concerns about adherence should, however, not be a barrier to the nationwide scale-up of TB preventive treatment.

21) Should a course of TPT be repeated?

TPT can halt progression to TB very effectively for many years, but re-infection with TB bacilli after completing treatment may reverse this protection. Studies of the benefit of repeated TPT are ongoing. In settings with high TB transmission, isoniazid for at least 36 months is recommended for PLHIV. PLHIV who have successfully completed treatment for TB disease may also receive a TPT course.



For more information please consult the …

WHO consolidated guidelines on tuberculosis:
Tuberculosis preventive treatment

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