include pleural biopsy/aspirate, lymph node biopsy, transbronchial needle aspiration and endoscopic ultrasound needle aspiration.

**Other clinical specimens**
Specimens are usually obtained to diagnose non-pulmonary TB, depending on the suspected site of infection. These commonly include: biopsies of the affected site (such as lymph nodes, skin or bowel); examination of cerebrospinal fluid; and aspiration of fluid (such as ascites). Early morning urine specimens are also examined to assist with the diagnosis of genitourinary TB.

It is vital specimens are sent to microbiology so they can be examined for AFBs and placed into culture. This is crucial to identify mycobacteria and drug resistance.

**TREATING TB**
TB treatment is highly evidence based, and is becoming standardised across the world. As outlined in part 1, the basic principle of TB control is to establish a diagnosis and initiate treatment rapidly (Hopewell et al, 2008).

While the search for a cure for TB lasted for centuries, the discovery of streptomycin in 1948 began the modern era of chemotherapy for treating TB. Today, the treatment of TB requires combination therapy of a number of antibiotics (Peloquin, 2008). The anti-TB drugs used today include those only used for mycobacterial infections, such as isoniazid and pyrazinamide, or those with broader application, such as rifampicin and streptomycin (Box 1).

NICE (2006) provides guidance on the length and components of treatment for active pulmonary and non-pulmonary TB that has been found to be fully sensitive to all first-line medication (that is, no drug resistance). Treatment for pulmonary TB consists of a six-month course of rifampicin and isoniazid, supplemented in the first two months by pyrazinamide and ethambutol. There are therefore two stages to what is known as the standard recommended regimen (NICE, 2006). The first stage consists of two months’ “quadruple therapy”, followed by four months of “dual therapy” (rifampicin and isoniazid). For full details, practitioners should consult the British National Formulary (2009) and NICE (2006).

**Non-pulmonary TB**
People with TB meningitis are given a 12-month course of treatment consisting of two months’ “quadruple therapy”, followed by isoniazid and rifampicin for the rest of the treatment. The use of glucocorticoids (such as prednisolone) is also recommended for the first 2-3 weeks of treatment, followed by gradual withdrawal (NICE, 2006).

People with peripheral lymph node, genitourinary, disseminated (including miliary), joint and bone TB or TB at any other site are recommended to take the standard treatment regimen. Those with pericardial TB are also given glucocorticoids for the first 2-3 weeks, followed by gradual withdrawal. Steroids are advocated in certain situations to minimise the inflammation and tissue damage caused by the immune response to the mycobacterial infection (Humphries et al, 1994).

For specific details on the care of each group with non-pulmonary TB, see NICE (2006).

**Possible adverse reactions**
All anti-TB drugs can cause adverse reactions. These can occur in 10% of patients, with a substantial proportion requiring modification of drug therapy (Joint Tuberculosis Committee of the British Thoracic Society, 1998). Some of the reactions are:

- **Peripheral neuropathy** – caused by isoniazid. This is preventable by giving prophylactic pyridoxine to those at high risk (such as those with diabetes, alcohol dependence, chronic renal failure, HIV infection or malnutrition) (BNF, 2009).
- **Hepatotoxicity** – may be caused by rifampicin, isoniazid and pyrazinamide (BNF, 2009). Liver function should be checked at the start of treatment and at two weeks, and then if clinically indicated (Joint Tuberculosis Committee of the BTS, 1998). Patients should be advised about the potential symptoms of hepatotoxicity:
  - **Optic neuritis** – this is rare but a recognised toxic effect of ethambutol (Joint Tuberculosis Committee of the BTS, 1998). Baseline visual acuity should be measured, and the drug only prescribed to those who will be able to report any changes in vision or eye symptoms. Patients should be advised to discontinue therapy immediately if they develop deterioration in vision and promptly seek further advice. Early discontinuation of the drug is almost always followed by recovery of eyesight (BNF, 2009).

- **Rare reactions to rifampicin, isoniazid and pyrazinamide include nausea and vomiting:**

- **Peripheral neuropathy** – caused by isoniazid. This is preventable by giving prophylactic pyridoxine to those at high risk (such as those with diabetes, alcohol dependence, chronic renal failure, HIV infection or malnutrition) (BNF, 2009).

- **Hepatotoxicity** – may be caused by rifampicin, isoniazid and pyrazinamide (BNF, 2009). Liver function should be checked at the start of treatment and at two weeks, and then if clinically indicated (Joint Tuberculosis Committee of the BTS, 1998). Patients should be advised about the potential symptoms of hepatotoxicity:
  - **Optic neuritis** – this is rare but a recognised toxic effect of ethambutol (Joint Tuberculosis Committee of the BTS, 1998). Baseline visual acuity should be measured, and the drug only prescribed to those who will be able to report any changes in vision or eye symptoms. Patients should be advised to discontinue therapy immediately if they develop deterioration in vision and promptly seek further advice. Early discontinuation of the drug is almost always followed by recovery of eyesight (BNF, 2009).

- **Rare reactions to rifampicin include shock, acute renal failure and thrombocytopenic purpura:** In these cases the drug should be withdrawn and not reintroduced (Joint Tuberculosis Committee of the BTS, 1998).

Patients should have baseline blood tests (urea and electrolytes, full blood count, liver function and HIV) and visual acuity recorded. Liver function tests should be repeated at two weeks and then if clinically indicated. Patients should be advised about possible adverse reactions and symptoms of concern that should be reported to their clinician. It is a recommendation that all patients with TB have an HIV test, and patients need to give their consent to this as with any other medical investigation (British HIV Association, 2008).

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**BOX 1. ANTI-TB DRUGS IN THE NICE (2006) STANDARD RECOMMENDED REGIMEN**

- **Rifampicin** introduced in 1967, is one of the most important anti-TB drugs. It is bactericidal against *M. tuberculosis* and is metabolised in the liver.
- **Pyrazinamide** has a bactericidal action and is metabolised in the liver.
- **Isoniazid** has a sterilising effect for use in the first two months of treatment, or for longer if drug resistance is established. It is useful in treating TB meningitis due to good meningeal penetration. It is metabolised in the liver, and serious liver toxicity may occasionally occur (BNF, 2009).
- **Ethambutol** is bacteriostatic and is the fourth anti-TB drug used in quadruple therapy. Introduced in 1982, it inhibits synthesis of the mycobacterial cell wall. The dose is reduced in people with renal disease (BNF, 2009).