products of the culture and lysis of *Mycobacterium tuberculosis* and/or *M. bovis*. It contains a suitable preservative that does not give rise to false-positive reactions. It is a colourless or pale yellow liquid; the diluted preparation may be a freeze-dried powder which upon dissolution gives a colourless or pale yellow liquid. Protect from light.

USP 31 (Tuberculin). A sterile solution derived from the concentrated, soluble products of growth of the tubercle bacillus (*Mycobacterium tuberculosis* or *M. bovis*) prepared in a special medium. It is provided either as Old Tuberculin, a culture filtrate adjusted to the standard potency by the addition of glycerol and isotonic sodium chloride solution, or as Purified Protein Derivative (PPD), a further purified protein fraction. Store at 2° to 8°.

Adverse Effects

Pain and pruritus may occur at the injection site, occasionally with vesiculation, ulceration, or necrosis in highly sensitive persons. Granuloma has been reported.

Nausea, headache, dizziness, malaise, rash, urticaria, oedema, and pyrexia have been reported occasionally; immediate systemic hypersensitivity, including anaphylaxis, has been reported rarely. There have also been rare reports of lymphangitis.

Hypersensitivity. There are rare reports[1-4] of severe anaphylactic or anaphylactoid reactions, occasionally fatal,[1] to tuberculin.

1. DiMaio VJM, Froede RC. Allergic reactions to the tine test. *JAMA* 1975; **233:** 769.
2. Spiteri MA, *et al.* Life threatening reaction to tuberculin testing. *BMJ* 1986; **293:** 243–4.
3. Wright DN, *et al.* Systemic and local allergic reactions to the tine test purified protein derivative. *JAMA* 1989; **262:** 2999–3000.
4. Sanofi Pasteur, Canada. Risk of serious allergic reactions following TUBERSOL [Tuberculin Purified Protein Derivative (Mantoux)] administration (issued 19th May 2005). Available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/tubersol_hpc-cps-eng.pdf (accessed 08/08/08)

Lymphangitis. Lymphangitis has been reported on 5 occasions after the Mantoux test and on 7 occasions after the Heaf test.[1] However, it was noted that a tuberculin test may have been inappropriate in some of these patients, particularly older subjects and those with evidence of healed tuberculous lesions.[2]

1. Morrison JB. Lymphangitis after tuberculin tests. *BMJ* 1984; **289:** 413.
2. Festenstein F. Lymphangitis after tuberculin tests. *BMJ* 1984; **289:** 625–6.

Precautions

Tuberculin should be given with caution to patients who have, or are suspected of having, active tuberculosis; although severe local reactions may occur in patients with active tuberculosis, sensitivity may be diminished if it is particularly severe. Sensitivity to tuberculin may also be diminished in the following conditions: viral or severe bacterial infection including HIV infection and infectious mononucleosis; neoplastic disease particularly lymphoma; sarcoidosis; corticosteroid or immunosuppressive therapy; recent use of live virus vaccines; ultraviolet light treatment; chronic renal failure; dehydration; and malnutrition.

Tuberculins may be adsorbed onto the surface of syringes and should therefore be given immediately.

Uses and Administration

Tuberculin skin tests are used to detect tuberculoprotein hypersensitivity when BCG vaccination is being considered or as an aid to diagnosis of tuberculosis. A person showing a specific sensitivity to tuberculin is considered to have been infected with the tubercle bacillus, though the infection may be inactive. Tuberculin for sensitivity testing is given by intradermal injection as in the Mantoux test. Multiple-puncture devices such as the Heaf test or tine tests have also been used, although they are no longer available in the UK.

In the UK, it is recommended that tuberculin testing should always be performed when BCG vaccination is being considered, and the **Mantoux** test is recommended. For a routine Mantoux test, a diluted solution of tuberculin purified protein derivative (PPD) is given by intradermal injection and the reaction, which is graded by the degree of induration, read 48 to 72 hours later. A retest with a stronger solution of PPD may be considered if the results of the initial test are unclear. Different commercial preparations vary in labelling format and potency, and doses and interpretation of results cannot therefore be extrapolated from one preparation to another.

Individuals with no or minimal reactions who have not previously been given BCG vaccines may be offered BCG vaccination. Patients with a positive reaction are considered to be hypersensitive to tuberculoprotein and should not be vaccinated. Investigation for the presence of active tuberculosis is generally only indicated for patients showing a strongly positive reaction to a tuberculin skin test. However, there are many factors that should be considered when interpreting the results; in addition to those listed under Precautions (see above), there are the effects of previous BCG vaccination, repeated tuberculin testing, and age. In some areas, a positive reaction may be a result of cross-sensitivity of the test to non-tuberculous mycobacteria (see below).

For the **Heaf** test, a solution of PPD is applied to the forearm using a multiple-puncture gun (Heaf gun), and the reaction evaluated about a week later.

The term **tine** test is generally used for disposable multiple-puncture devices coated with dried old tuberculin or PPD. However, some consider tine tests to be unreliable.

In some other countries, the population tested, the procedures used, and grading of reactions may differ slightly from that outlined above.

Tuberculins have also been used, in conjunction with other antigens, for anergy testing to assess the status of cell-mediated immunity.

Latent tuberculosis. Full eradication of tuberculosis from developed countries requires identification of latent as well as active cases.[1] Tuberculin testing has been in use for over 100 years and, while still considered a useful diagnostic agent for tuberculosis, the problems of false-positive reactions or reduced sensitivity to the test are well recognised.[1] Use of the test to identify latent disease has evolved with experience.[2] Previous BCG vaccination is one factor that significantly increases the likelihood of a false-positive reaction to tuberculin testing, which makes the diagnosis of latent tuberculosis particularly difficult.[3] Interpretation of the skin test should therefore be made by considering the induration size in the context of the individual clinical profile, including other risk factors for infection.[2,3] Three different approaches to assess the annual risk of tuberculous infection using tuberculin testing gave different results in a study of schoolchildren who had been given BCG vaccinations early in life.[4] This led the authors to conclude that the effect of previous BCG vaccination on tuberculin reactivity may be more complex than assumed, and that the tuberculin test is a poor indicator of latent infection. It has been suggested[2] that it is not necessary for low-risk persons in the general population of the USA to receive routine tuberculin testing for tuberculosis; high-risk groups of adults and children for whom screening might be warranted have been defined, and consensus recommendations made. An opinion has also been ventured[5] that tuberculin testing before BCG vaccination is not necessary in children in the UK.

1. Lee E, Holzman RS. Evolution and current use of the tuberculin test. *Clin Infect Dis* 2002; **34:** 365–70.
2. American Thoracic Society. Targeted tuberculin testing and treatment of latent tuberculosis infection. 1999. Available at: http://www.thoracic.org/sections/publications/statements/pages/mtpi/latenttb1-27.html (accessed 14/07/06)
3. Wang L, *et al.* A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. *Thorax* 2002; **57:** 804–9. Correction: *ibid.* 2003; **58:** 188.
4. Leung CC, *et al.* Tuberculin response in BCG vaccinated schoolchildren and the estimation of annual risk of infection in Hong Kong. *Thorax* 2005; **60:** 124–9.
5. Bothamley GH, *et al.* Tuberculin testing before BCG vaccination. *BMJ* 2003; **327:** 243–4.

Malignant disease. Benefit has been reported[1] in 2 patients with adult T-cell leukaemia/lymphoma predominantly involving the skin after local treatment with tuberculin purified protein derivative.

1. Kanekura T, *et al.* Purified protein derivative treatment for skin lesions of adult T-cell leukaemia/lymphoma. *Br J Dermatol* 1999; **140:** 767–8.

Non-tuberculous mycobacterial infection. The tuberculin skin test is not specific for *Mycobacterium tuberculosis*, but can also represent a cross-reaction caused by antigens on other non-tuberculous mycobacteria. Re-examination[1] of results from children with non-tuberculous mycobacterial infection concluded that the avian Mantoux test (avian tuberculin purified protein derivative (PPD) prepared from *M. avium*) was more sensitive than the human Mantoux test (tuberculin PPD prepared from *M. tuberculosis*) in the detection of non-tuberculous mycobacteria in regions with a low incidence of tuberculosis, and may be a useful aid to differential diagnosis in areas where tuberculosis is prevalent.

1. Daley AJ, Isaacs D. Differential avian and human tuberculin skin testing in non-tuberculous mycobacterial infection. *Arch Dis Child* 1999; **80:** 377–9.

Preparations

Ph. Eur.: Old Tuberculin for Human Use; Tuberculin Purified Protein Derivative for Human Use;
USP 31: Tuberculin.

Proprietary Preparations (details are given in Part 3)
Austria: Monotest; ***Belg.:*** Monovacc-Test†; ***Canad.:*** Tubersol; ***Fr.:*** Monotest†; Tubertest; ***Ger.:*** Tubergen-Test†; ***Gr.:*** Imotest Tuberculin; ***Ital.:*** Biocine Test PPD; Monotest†; ***NZ:*** Monotest†; Tubersol; ***S.Afr.:*** Biocine Test; Japan Freeze-Dried Tuberculin; Monotest†; ***Spain:*** Tubersol PPD†; ***Swed.:*** Monotest†; ***USA:*** Aplisol; Tubersol; ***Venez.:*** Imotest Tuberculina†.

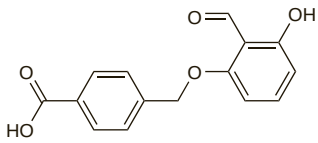
Multi-ingredient: ***Austral.:*** Multitest CMI; ***Austria:*** Multitest; ***Cz.:*** Imunoskintest†; ***Ger.:*** Multitest†; ***Israel:*** Multitest CMI; ***NZ:*** Multitest CMI†; ***S.Afr.:*** Multitest CMI†.

Tucaresol *(BAN, rINN)* ⊗

BW-589C; 589C; 589C80; Tucarésol; Tucaresolum. α-(2-Formyl-3-hydroxyphenoxy)-*p*-toluic acid.

Тукарезол

$C_{15}H_{12}O_5$ = 272.3.
CAS — 84290-27-7.



Profile

Tucaresol is reported to interact with haemoglobin to increase oxygen affinity. It has been investigated as an oral drug for the treatment of sickle-cell disease (p.1044). Tucaresol is also reported to have immunostimulant properties and is under investigation in HIV infection and hepatitis B. Hypersensitivity reactions have occurred.

◊ References.

1. Rolan PE, *et al.* The pharmacokinetics, tolerability and pharmacodynamics of tucaresol (589C80; 4[2-formyl-3-hydroxyphenoxymethyl]benzoic acid), a potential anti-sickling agent, following oral administration to healthy subjects. *Br J Clin Pharmacol* 1993; **35:** 419–25.
2. Arya R, *et al.* Tucaresol increases oxygen affinity and reduces haemolysis in subjects with sickle cell anaemia. *Br J Haematol* 1996; **93:** 817–21.
3. Peck RW, *et al.* Effect of food and gender on the pharmacokinetics of tucaresol in healthy volunteers. *Br J Clin Pharmacol* 1998; **46:** 83–6.
4. Gori A, *et al.* Immunomodulation induced by tucaresol in HIV infection: results of a 16 week pilot Phase I/II trial. *Antivir Ther* 2004; **9:** 603–14.

Javanese Turmeric

Curcuma Zanthorrhiza; Curcumae Javanicae; Curcumae xanthorrhizae rhizoma; Geltonšaknių ciberžolių šakniastiebiai; Gurkmeja, javanesisk; Jaavan kurkuma; Jávai-kurkuma gyökértörzs; Oddenek kurkumy žlutokořenné; Temoe lawacq; Temoe Lawak; Témoé-lawaq.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Turmeric, Javanese). It consists of the dried rhizome, cut in slices, of *Curcuma xanthorrhiza*. It contains not less than 5% v/w of essential oil and not less than 1% of dicinnamoyl methane derivatives expressed as curcumin, both calculated with reference to the anhydrous drug. It has an aromatic odour. Protect from light.

Profile

Javanese turmeric is an ingredient of preparations indicated for biliary and gastrointestinal disorders. It is a close relative of the spice turmeric (p.1473), which has been used similarly.

Irritable bowel syndrome. For reference to the ineffectiveness of Javanese turmeric in patients with irritable bowel syndrome see under Fumitory, p.2307.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Gallentee†; ***Ger.:*** Bilagit Mono†; Curcu-Truw; Curcumen; Infi-tract; Pankreaplex mono.

Multi-ingredient: ***Austria:*** Choleodoron; ***Fr.:*** Hepaclem; ***Ger.:*** Bilisan Duo; Cholosom SL†; Cholosom-Tee; Divalol W†; Enzym-Harongan; Gallexier; Hepaticum novo†; Infi-tract†; ***Hong Kong:*** Hepatofalk; ***Indon.:*** Curliv; Curliv Plus; Curson; Gramuno; Hepa-Q; Hepacell; Hepatofalk Planta; Hepimun; Librozym; Norflam; Verona; ***S.Afr.:*** Choleodoron; ***Singapore:*** Hepatofalk Planta; ***Switz.:*** Choleodoron†.

Turpentine Oil

Aetheroleum Terebinthinae; Esencia de Trementina; Essence de Térébenthine; Oleum Terebinthinae; Oleum Terebinthinae Depuratum; Rectified Turpentine Oil; Spirits of Turpentine; Térébenthine, huile essentielle de; Terebentin Yağı; Terebinthini aetheroleum; Terebintin Esansı; Trementina, aceite esencial de.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *Jpn*.
Ph. Eur. 6.2 (Turpentine Oil, Pinus Pinaster Type; Terebinthini Aetheroleum ab Pinum Pinastrum). An essential oil obtained by steam distillation, followed by rectification at a temperature below 180°, from the oleoresin obtained by tapping *Pinus pinaster*. A suitable antioxidant may be added. It contains 70.0 to 85.0% α-pinene, 0.5 to 1.5% camphene, 11.0 to 20.0% β-pinene, maximum 1% car-3-ene, 0.4 to 1.5% β-myrcene, 1.0 to 7.0% limonene, 0.2 to 2.5% longifolene, 0.1 to 3.0% β-caryophyllene, and maximum 1.0% caryophyllene oxide.
A clear, colourless or pale yellow liquid with a characteristic odour. Relative density 0.856 to 0.872. Store in well-filled airtight containers at a temperature not exceeding 25°. Protect from light.

Adverse Effects

In poisoning with turpentine oil there may be local burning and gastrointestinal upset, coughing and choking, pulmonary oedema, excitement, coma, fever, tachycardia, liver damage, haematuria, and albuminuria. Fatalities have occurred.