and protozoan forms are compared, explaining the differential effects seen between species. This folate synthesis pathway does not exist in mammalian cells, hence its attractiveness as a target for the selection of novel antimicrobial agents. Dapsone competes with *p*-aminobenzoic acid for binding with DHPS (Nzila, 2006). Mammalian cells are able to use exogenous folate; however, bacteria are incapable of this, and the effects of these drugs that inhibit these bacterial or parasitic enzymes cannot, in general, be reversed by the administration of folic or folinic acid. Some strains of *P. falciparum* are, on the other hand, able to use exogenous folate, the so-called "folate effect," which is antagonized by pyrimethamine (Gregson and Plowe, 2005). Exogenous preformed folate is salvaged by energy-dependent specific transporters from the surrounding medium, bypassing the *de novo* synthesis pathway (Salcedo-Sora *et al.,* 2011).

Dapsone has an anti-inflammatory effect, but the actual mode by which this occurs is still poorly understood. Dapsone is effective in the treatment of a number of dermatoses that all have the common characteristic of abnormal neutrophil accumulation in the dermis. It interferes with neutrophil chemotactic migration, beta-2-integrin–mediated adherence of neutrophils *in vitro* and activation of the signal transduction cascade that mediates chemotaxis (Harvath *et al.,* 1986; Booth *et al.,* 1992; Debol *et al.,* 1997). It has also been shown to inhibit neutrophil myeloperoxidase- and eosinophil peroxidase–mediated cytotoxicity (Bozeman *et al.,* 1992). Dapsone has also been shown to inhibit neutrophil lysosomal enzymes and leukotriene B4–stimulated inflammation in mice, and appears to block the adherence of normal neutrophils to immunoglobulin A (IgA) and IgG on basement membranes of patients with dermatitis herpetiformis and bullous pemphigoid. It is a strong inhibitor of interleukin-8 (IL-8) release, which may explain some of its anti-inflammatory effect (Kanoh *et al,*, 2011). Despite these individual experimental findings, the most significant pathway by which dapsone exerts its anti-inflammatory effect is yet to be determined. Dapsone is thought not to be disease modifying, but rather purely anti-inflammatory in its effect (Wolf *et al.,* 2000; Zhu and Stiller, 2001). Its use as an anti-inflammatory agent has been reviewed (Wozel and Blasum, 2014).

4. MODE OF DRUG ADMINISTRATION AND DOSAGE

4a. Adults

Dapsone is available as 25-mg and 100-mg tablets, and as a 5% gel formulation (NPS MedicineWise, 2016). Recommended dapsone doses vary according to the condition being treated.

Before the initiation of dapsone therapy, all patients should be tested for glucose-6-phosphate dehydrogenase (G6PD) deficiency (see section 6, Adverse Reactions and Toxicity). In general, patients with a history of porphyria should avoid the drug. Those with moderate to severe anemia or other forms of bone marrow suppression should be administered dapsone only with caution. Regular complete blood examinations should be performed—for example, weekly for the first month, monthly for 6 months, then every 6 months thereafter (NPS MedicineWise, 2016). Concurrent administration with other folate inhibitors should be undertaken only with caution.

MYCOBACTERIUM LEPRAE

The normal adult dose is 100 mg orally once daily, but dapsone should always be combined with one or more other drugs active against *M. leprae* (WHO, 1994). The WHO-recommended regimen is as follows: in patients who have paucibacillary leprosy, dapsone is combined with monthly rifampicin 600 mg and continued for 6 months. For multibacillary leprosy, the dose is dapsone 100 mg daily plus 50 mg of clofazimine daily plus rifampicin 600 mg monthly plus clofazimine 300 mg monthly, with the treatment course lasting for a total of 12 months. A single dose of rifampicin, ofloxacin, and minocycline is recommended for single-lesion (indeterminate) paucibacillary leprosy, but at this stage is still regarded as experimental, and long-term follow-up is proceeding.

The USPHS National Hansen's Disease Program (NHDP) has continued with a more conservative form of MDT. The recommendations are as follows: for paucibacillary disease, dapsone 100 mg daily plus rifampicin 600 mg daily for 12 months; and for multibacillary disease, dapsone 100 mg daily plus rifampicin 600 mg daily plus clofazimine 50 mg daily for 24 months (Moschella, 2004; Health Resources and Services Administration [HRSA], 2016).

PLASMODIUM INFECTION

Dapsone alone should not be used as treatment for malaria, nor should the combination of dapsone and pyrimethamine (Maloprim) because they are only weakly effective (see section 7, Clinical uses of the drug). The combination of chlorproguanil with dapsone (CD, LapDap) was available in some countries in Africa for treatment of uncomplicated *P. falciparum* infection in which *P. falciparum* is resistant to sulfadoxine–pyrimethamine (Fansidar) but still susceptible to LapDap. LapDap has now been withdrawn from use by its manufacturer (WHO, 2008).

Dapsone alone or in combination with pyrimethamine (Maloprim) is now not recommended for prophylaxis of malaria (see Chapter 93, Pyrimethamine).

PNEUMOCYSTIS JIROVECI INFECTION

Dapsone is used as an alternative choice for both treatment and prophylaxis of *P. jiroveci* pneumonia (PCP), both in HIV infection and in other forms of immunosuppression. For treatment, it is used at a dose of 100 mg daily for mild to moderate disease only, in combination with trimethoprim 15 mg/kg/day in three divided doses.

Dapsone is also efficacious for both primary and secondary prophylaxis of PCP, but only as a second-line agent after combination therapy with TMP–SMX. Regimens that have proven to be effective are dapsone 50 mg orally twice daily;