TMP–SMX, resulting in a PCP rate of 7.2% compared with 0.37% for TMP–SMX (Souza *et al.,* 1999). There is no evidence that the addition of pyrimethamine to dapsone increases its prophylactic effect against PCP in this group (Rodriguez and Fishman, 2004). A meta-analysis of PCP prophylaxis trials in non-HIV immunosuppressed patients in 2008 concluded that prophylaxis was effective and that the number needed to prevent a single case of PCP when prophylaxis was given for a mean of 3 years was 15. It also concluded that prophylaxis should be offered to those groups represented in the reported trials in which PCP prophylaxis was found to be effective and in which the incidence of PCP without prophylaxis was greater than 3%. These were, in both children and adults, as follows: solid organ transplant recipients in the first 6 months after transplantation; patients undergoing allogeneic bone marrow transplantation during the first 6 months after transplantation and continuing if immune suppression is continued beyond that time; patients with Wegener's granulomatosis during the first year after diagnosis; and patients with acute lymphoblastic leukemia (Green *et al.,* 2007).

7e. *Toxoplasma gondii* infection

Dapsone is active against *T. gondii;* however, there have been limited clinical trials of treatment with dapsone or dapsone-containing combinations (Yan *et al.,* 2013). This is because its activity in animal models was significantly inferior to that of pyrimethamine and other antimicrobials. Isolated case reports of its success have been published (Derouin *et al.,* 1991). Dapsone is regarded as effective prophylaxis against reactivation of *T. gondii* encephalitis in HIV-infected patients with significant immunodeficiency. When given in combination for PCP prophylaxis with pyrimethamine and leucovorin, there is a significant protective effect against the development of *T. gondii* encephalitis (Clotet *et al.,* 1991; Girard *et al.,* 1993; Mariuz *et al.,* 1994; Opravil *et al.,* 1995a; Podzamczer *et al.,* 1995). Current guidelines recommend pyrimethamine plus dapsone plus leucovorin as alternative primary prophylaxis for patients with HIV and a CD4+ count of < 200 cells/μl who are intolerant of TMP–SMX. Dapsone alone or in combination is not recommended as therapy or for secondary prophylaxis (NIH, 2015). Further discussion on the treatment and prophylaxis of *T. gondii* infection can be found in Chapter 93, Pyrimethamine.

7f. Use as an anti-inflammatory agent

Dapsone has found a role in the therapy of many noninfectious inflammatory disorders—in particular, with a number of rare dermatoses (Wozel and Blasum, 2014). It was first observed in the late 1940s that dapsone was effective in the management of dermatitis herpetiformis (Esteves and Brandao, 1950). This has been subsequently confirmed and dapsone is now regarded as the treatment of choice for the dermatologic manifestations of this rare condition. Dermatitis herpetiformis is a chronic disorder manifesting with a blistering dermatosis and subtotal villous atrophy with consequent malabsorption. IgA deposits in the dermis are pathognomonic, and it appears that the pathogenesis relates to autoimmune cross-reactivity of IgA antibodies to a gut transglutaminase enzyme that is also present in the dermis in a similar form (Karpati, 2004). The disease cannot be cured but can be controlled by strict adherence to a gluten-free diet. Dapsone is particularly effective in controlling the dermatologic manifestations of the disease, but does not have any effect as a disease-modifying agent or on the gastrointestinal manifestations. Doses as high as 300–400 mg/day have been used to maximize the anti-inflammatory effect, but are often limited by dose-related toxicity, such as methemoglobinemia and hemolysis (see section 6, Adverse Reactions and Toxicity). Strategies to minimize these effects, such as the co-administration of cimetidine, have been moderately successful in improving the drug's tolerability (Coleman *et al.,* 1992). Strict adherence to a gluten-free diet allows the dose of dapsone to be reduced and, in some cases, ceased altogether (Fry, 1988; Egan *et al.,* 1997).

Subcorneal pustular dermatosis is a rare condition of the eye that is associated with the IgA form of pemphigus, a blistering skin disease (Huff *et al.,* 1985). Often termed the "Sneddon–Wilkinson" syndrome after the clinicians who first reported that dapsone was active against this disease of the eye (Sneddon and Wilkinson, 1956), the disease responds well to dapsone therapy, although other forms of immunosuppression are sometimes required to control the manifestations of the disease outside the eye. The broad spectrum of IgA pemphigus disease in general responds well to dapsone and, accordingly, it remains the drug of first choice (Ongenae *et al.,* 1999; Chaudhari and Marinkovich, 2007). Dapsone has been found to be a useful steroid-sparing agent in patients with pemphigus vulgaris (Rosenberg *et al.,* 1976), although more modern approaches to steroid-sparing immunosuppression, such as co-administration with mycophenolate or the use of rituximab, are now used in preference to dapsone (Piette and Werth, 2012).

Pyoderma gangrenosum, another neutrophilic dermatosis, often seen in association with inflammatory bowel disease, is usually treated with corticosteroids, although more resistant cases may respond to other forms of immune suppression such as cyclosporine, methotrexate, or thalidomide. Dapsone in combination with prednisolone has been reported as being successful in controlling this condition (Galun *et al.,* 1986).

The role of dapsone in the effective treatment of bullous systemic lupus erythematosus (SLE) has recently been reviewed (Duan *et al.,* 2015).

When dapsone was first used to treat leprosy in the 1940s, it was noticed that the patients who also had acne vulgaris experienced a significant improvement in their condition. Since that time, dapsone has been used to treat the more severe forms of acne vulgaris, its anti-inflammatory properties thought to be the mechanism by which it acts (Ross, 1961; Prendiville *et al.,* 1988). Doses ranged from 25 mg/day to 300 mg/week. Dapsone's reputation for side effects meant, however, that systemic therapy fell out of favor as it was replaced by other therapies (Thiboutot *et al.,* 2007). It was