1978; Klotz *et al*., 1980). Additionally, Campieri *et al.* (1981) showed that treatment with 5-ASA, 4 g daily given by retention enema, was superior to similar treatment with hydrocortisone, 100 mg daily. Resin-coated tablets containing 5-ASA are now available commercially, which after oral administration remain intact until they reach the colon. The mechanism by which 5-ASA (generic name mesalazine) is beneficial in inflammatory bowel disease remains unclear (Peppercorn, 1984). It has been combined with carrier agents other than sulfapyridine, including the combination of two molecules of mesalazine together (olsalazine). All these preparations (e.g. olsalazine, ipsalazide, balsalazide) deliver 40–60% of available mesalazine to the feces and appear to have a similar therapeutic response but without the toxicity, including male infertility (Editorial, 1987; Raimundo *et al*., 1991).

For adults, a dosage of 4 g daily is the maximum tolerated by many patients, but a few will tolerate and respond better to dosages of 6 g per day. Similarly, some patients tolerate and respond to a higher maintenance dosage than 2 g per day (Peppercorn, 1984). The side effects of sulfasalazine include those of the sulfonamide and those peculiar to sulfasalazine. Apart from the side effects described in preceding sections (see section 6, Adverse reactions and toxicity), sulfasalazine can also cause an increased heart rate and a bluish skin discoloration; the anionic exchange resin cholestyramine and antibiotics may prevent the breakdown in the gut of sulfasalazine, whereas sulfasalazine can interfere with the bioavailability of digoxin (Cowan *et al*., 1977; Peppercorn, 1984). The role of sulfasalazine and 5-ASA in inflammatory bowel disease has recently been reviewed (Dhaneshwar, 2014; Hauso *et al*., 2015).

7n. Inflammatory arthritis

Sulfasalazine is an effective drug for treatment of rheumatoid arthritis (Neumann *et al*., 1983; Pullar *et al*., 1983; Nuver-Zwart *et al*., 1989; van der Heijde *et al*., 1989), and in this disease sulfapyridine seems to be the active moiety (Pullar *et al*., 1985). In a double-blind randomized trial comparing the outcome of treatment with sulfasalazine vs. hydroxychloroquine in patients with rheumatoid arthritis, sulfasalazine resulted in a clinical response 8 weeks earlier than in the hydroxychloroquine-treated group, although the overall effect at 48 weeks was not significantly different (Nuver-Zwart *et al*., 1989). Radiographical evidence of erosions was significantly less in the sulfasalazine-treated group after both 24 and 48 weeks of treatment (van der Heijde *et al*., 1989). It has been used with success in radiation bowel disease, scleroderma, and dermatitis herpetiformis (Peppercorn, 1984). Sulfasalazine also has activity in the management of juvenile idiopathic arthritis (Hashkes and Laxer, 2005). In a Cochrane review, sulfasalazine was beneficial in ankylosing spondylitis with improvement in erythrocyte sedimentation rate and symptoms of early-morning stiffness, although there was no change in pain, spinal mobility, or enthesitis (Chen and Liu, 2005).

7o. Burns

Certain sulfonamides applied topically are of benefit in the management of burns. Mafenide (sulfamylon) was used in Germany for the topical therapy of war wounds in the 1940s. Because this topical therapy was effective in suppressing *P. aeruginosa* infection in burned rats, it was used with similar results for the treatment of burns in humans (Lindberg *et al*., 1965). Many studies have since confirmed that an 11.2% cream of mafenide can significantly reduce sepsis in burned patients (Lowbury *et al*., 1971; Pegg, 1972). These applications are usually painful, and mafenide is absorbed through burned areas. Mafenide and its breakdown products are strong acids and also carbonic anhydrase inhibitors, so that if large quantities of the drug are used, metabolic acidosis may result, but this is usually compensated for by hyperventilation (Pegg, 1972). Silver nitrate in a 0.5% solution was another popular topical application for burned patients (Lowbury *et al*., 1971). Mafenide 5% was compared with 10% povidone, 0.25% sodium hypochlorite, 3% hydrogen peroxide, and 0.25% acetic acid in the management of contaminated wounds (Bennett *et al*., 2001). Mafenide was superior in maintaining an aseptic environment and increasing angiogenesis, fibroblast proliferation, and dermal thickness. Topical 5% mafenide also inhibits DNA and protein synthesis in wounds (Zhang *et al*., 2006). Mafenide 2.5% has been used in a pediatric burn hospital without increased rates of bacteremia or wound infection compared with mafenide 5% (Ibrahim *et al*., 2014).

The topical use of the compound SSD (see section 2a, Routine susceptibility) has also been very effective for the prevention and treatment of sepsis in burn wounds (Stanford *et al*., 1969; Lowbury *et al*., 1971; McDougall, 1972; Clarke, 1975; Sawhney *et al*., 1989; Monafo and West, 1990; Masterton, 1992). Sawhney *et al*. (1989) found that whereas *S. aureus* had been the predominant surface organism isolated from burn patients treated with 1% SSD cream in the early 1980s, *Pseudomonas* and *Klebsiella* species became more commonly isolated from such patients in the late 1980s. They found that the incidence of invasive infection and overall mortality was significantly reduced with the use of SSD cream. Controlled trials have indicated that 0.5% silver nitrate compresses, 1% SSD cream, and a cream containing 0.5% silver nitrate and 0.2% chlorhexidine digluconate are all about equally effective in protecting burns from infection. Silver nitrate was, however, less active than the other two preparations against less common Gram-negative bacilli (Lowbury *et al*., 1976). In one burn unit, sulfonamide-resistant Gram-negative bacilli became predominant during a trial of SSD cream, and the effectiveness of the preparation was reduced such that it became necessary to suspend SSD usage and replace it with silver nitrate and chlorhexidine cream (Lowbury *et al*., 1976; Bridges and Lowbury, 1977). In another burn unit, *in vitro* tests suggested that extensive use of parenteral gentamicin and replacement of topical mafenide ointments with SSD cream favored the emergence of *Providencia stuartii* over *P. aeruginosa* as the predominant colonizing organism (Wenzel *et al*.,