Introduction

It is almost 60 years since Lever (1953), on the basis of specific clinical and histological features, recognized bullous pemphigoid (BP) as a distinct disorder within the large group of blistering disorders, including the pemphigus group. One milestone in the evolution of our understanding of BP was the demonstration by Jordon et al. (Jordon et al., 1967) that the disease was associated with in vivo bound and circulating autoantibodies directed against proteins of the basement membrane zone of stratified epithelia. Complementary DNAs for the two targeted autoantigens bullous pemphigoid antigen 230 (BP230, BPAG1-e) and bullous pemphigoid antigen 180 (BP180, BPAG2 or type XVII collagen) were subsequently isolated independently by various groups (Stanley et al., 1988, Diaz et al., 1990, Sawamura et al., 1991; Li et al., 1992; Giudice et al., 1992; Hopkinson et al., 1992). Today, BP has emerged as an example of organ-specific autoimmune disease and it represents the most frequent autoimmune blistering disorder.

In this review, we will discuss the clinical and immunopathological features of BP, its differential diagnosis and therapeutic options. We will also focus on recent progress in our understanding of the pathophysiology of this disorder and on the role of targeted autoantigens in the maintenance of epithelial-stromal adhesion.

Clinical features

In the prodromal, non-bullous phase manifestations of BP are frequently nonspecific and, thus, misleading. Patients complain of severe itch accompanied or not by excoriated, eczematous, papular and or urticated lesions that may persist for several weeks or months, or even remain the only signs of the disease.

In the bullous stage vesicles and bullae develop on apparently normal or erythematous skin together with urticated and infiltrated plaques that have occasionally an an-
nular or figurate pattern. The blisters are tense, with a clear exudate, and may persist for several days, leaving eroded and crusted areas (Fig. 1). The lesions are frequently distributed symmetrically and predominate on the flexural aspects of the limbs, and abdomen. In the intertriginous spaces, vegetating plaques can be seen. Involvement of the oral cavity is observed in 10–30% of cases. The mucosae of eyes, nose, pharynx, esophagus and ano-genital areas are more rarely affected (reviewed in Lever, 1953; Liu et al., 1986; Korman, 1987).

Several clinical variants of BP have been described (reviewed in Liu et al., 1986; Korman, 1987). Lesions remain occasionally localized, such as on the pretilial area (“pretilial pemphigoid”), around stomas, on the vulvar region (“vulvar pemphigoid”), on irradiated areas or confined to a paralyzed limb. Palmo-plantar involvement mimicking dyshidrosiform eczema (“dyshidrosiform pemphigoid”) can also be observed. Several other variants, such as a prurigo nodularis-like (“pemphigoid nodularis”), erythroderma-like form, intertrigo-like variants or forms mimicking severe bullous drug eruption have been described. These variants have all been reported with various terms: only dermatologists can afford to have so different names for the same condition!

A peculiar form of BP typically associated with pregnancy, for which a separate term appears justified, is gestational pemphigoid (also called “pemphigoid gestationis” or “herpes gestationis”) (reviewed in Shornick, 1993; Jenkins et al., 1993). This disease is also rarely