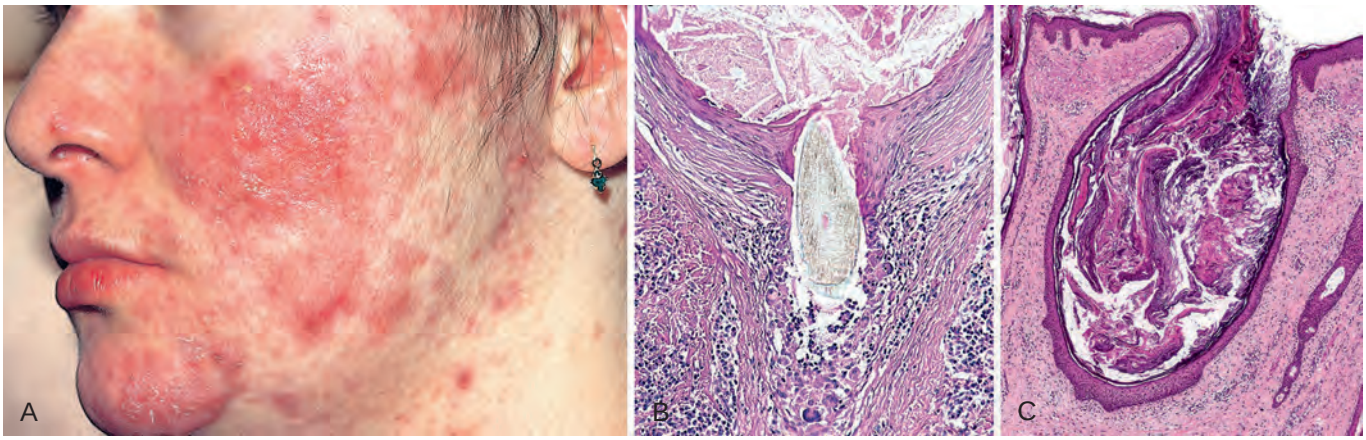

Figure 25-37 Acne. **A,** Inflammatory acne associated with erythematous papules and pustules. **B,** A hair shaft pierces the follicular epithelium, eliciting inflammation and fibrosis. **C,** An open comedone.

telangiectasia, (3) pustules and papules, and (4) rhinophyma—permanent thickening of the nasal skin by confluent erythematous papules and prominent follicles.

Pathogenesis. Individuals with rosacea have high cutaneous levels of the antimicrobial peptide cathelicidin, an important mediator of the cutaneous innate immune response. *The cathelicidin peptides present are qualitatively distinct from those seen in individuals without rosacea as a result of alternative processing by proteases such as kallikrein 5* (also known as stratum corneum tryptic enzyme). Injection of cathelicidin peptides from patients into mice induces some of the cutaneous changes seen in rosacea, including inflammation and vascular dilation. In addition, it has been noted that activation of Toll-like receptor 2 (TLR2) up-regulates kallikrein 5 expression in keratinocytes, suggesting that factors that stimulate TLR2 are involved. Several microbial triggers have been proposed, but none are proven.

MORPHOLOGY

Rosacea is characterized by a nonspecific perifollicular infiltrate composed of lymphocytes surrounded by dermal edema and telangiectasia. In the pustular phase neutrophils may colonize the follicles, and follicular rupture may cause a granulomatous dermal response. The development of rhinophyma is associated with hypertrophy of sebaceous glands and follicular plugging by keratotic debris.

Panniculitis

Erythema Nodosum and Erythema Induratum

Panniculitis is an inflammatory reaction in the subcutaneous adipose tissue that may preferentially affect (1) the lobules of fat, or (2) the connective tissue that separates fat into lobules. Panniculitis often involves the lower legs. *Erythema nodosum* is the most common form and usually has a subacute presentation. A second somewhat distinctive form, erythema induratum, also merits brief discussion.

- *Erythema nodosum* presents as poorly defined, exquisitely tender, erythematous plaques and nodules that may be more readily palpated than seen. Its occurrence is often associated with infections (β-hemolytic streptococcal infection, tuberculosis and, less commonly, coccidioidomycosis, histoplasmosis, and leprosy), drug administration (sulfonamides, oral contraceptives), sarcoidosis, inflammatory bowel disease, and certain malignant neoplasms, but many times a cause cannot be identified. Fever and malaise may accompany the cutaneous signs. It is considered to be caused by a delayed hypersensitivity reaction to microbial or drug related antigens. In some cases immune complexes have been implicated but in many cases the pathogenesis remains mysterious. Over the course of weeks, lesions usually flatten and become bruiselike, leaving no residual clinical scars, while new lesions develop. Biopsy of a deep wedge of tissue to generously sample the subcutis is usually required for histologic diagnosis.
- *Erythema induratum* is an uncommon type of panniculitis that affects primarily adolescents and menopausal women. Although the cause is not known, most observers regard this as a primary vasculitis of deep vessels supplying the fat lobules of the subcutis; the associated vascular compromise leads to fat necrosis and inflammation. Erythema induratum presents as an erythematous, slightly tender nodule that usually goes on to ulcerate. Originally considered a hypersensitivity response to tuberculosis, erythema induratum today most commonly occurs without an associated underlying disease.

MORPHOLOGY

The histopathology of **erythema nodosum** is distinctive. In early lesions, the connective tissue septae are widened by edema, fibrin exudation, and neutrophilic infiltration. Later, infiltration by lymphocytes, histiocytes, multinucleated giant cells, and occasional eosinophils is associated with septal fibrosis. Vasculitis is not present. In **erythema induratum**, on the other hand, granulomatous inflammation and zones of caseous necrosis involve the fat lobule. Early lesions show necrotizing vasculitis affecting small- to medium-sized arteries and veins in the deep dermis and subcutis.