Although most appendage tumors are benign, malignant variants do exist. Apocrine tumors are unusual in that malignant forms seem to be more common than benign forms. *Sebaceous carcinoma* arises from the meibomian glands of the eyelid and may follow an aggressive course replete with systemic metastases. *Eccrine* and *apocrine carcinomas* can be confused with metastatic adenocarcinoma because of their tendency to form gland-like structures.

Premalignant and Malignant Epidermal Tumors

Actinic Keratosis

Actinic keratoses; as the name implies, usually occur in sun-damaged skin and exhibit hyperkeratosis. As expected, they occur with particularly high incidence in lightly pigmented individuals. Exposure to ionizing radiation, industrial hydrocarbons, and arsenicals may induce similar lesions. These lesions may show progressively worsening dysplastic changes that culminate in cutaneous squamous cell carcinoma, and are analogous in this regard to the precursor lesions that give rise to squamous carcinomas of the uterine cervix (Chapter 22).

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Actinic keratoses are usually less than 1 cm in diameter. They are typically tan-brown, red, or skin-colored and have a rough, sandpaper-like consistency. Some lesions produce so much keratin that a "cutaneous horn" develops (Fig. 25-12*A*), which in extreme cases may become so prominent that they resemble the actual horns of animals! Sun-exposed sites (face, arms, dorsum of hands) are most frequently affected. The lips may also develop similar lesions (termed **actinic cheilitis**).

Cytologic atypia is seen in the lowermost layers of the epidermis and may be associated with hyperplasia of basal cells (Fig. 25-12*B*) or, alternatively, with atrophy that results in thinning of the epidermis. The atypical basal cells usually have pink or reddish cytoplasm due to dyskeratosis. Intercellular bridges are present, in contrast to basal cell carcinoma, in which they are not visible. The superficial dermis contains thickened, blue-gray elastic fibers (**elastosis**), a probable result of abnormal elastic fiber synthesis by sun-damaged fibroblasts. The stratum corneum is thickened, and unlike normal skin, the cells in this layer often retain their nuclei (**parakeratosis**).

Whether all actinic keratoses progress to skin cancer (usually squamous cell carcinoma) if given enough time is conjectural. Lesions may regress or remain stable during a normal life span, but enough do become malignant that local eradication is warranted. This can usually be accomplished by gentle curettage, freezing, or topical application of chemotherapeutic agents. Of interest, topical administration of imiquimod, a drug that activates Toll-like receptors (TLRs), eradicates up to 50% of lesions, a rate considerably higher than the spontaneous regression rate of approximately 5%. By stimulating TLR signaling, imiquimod activates cutaneous innate immune cells, which may recognize and eradicate precancerous lesions. Direct pro-apoptotic effects of the imiquimod on lesional keratinocytes have also been proposed, but these are poorly understood at present.

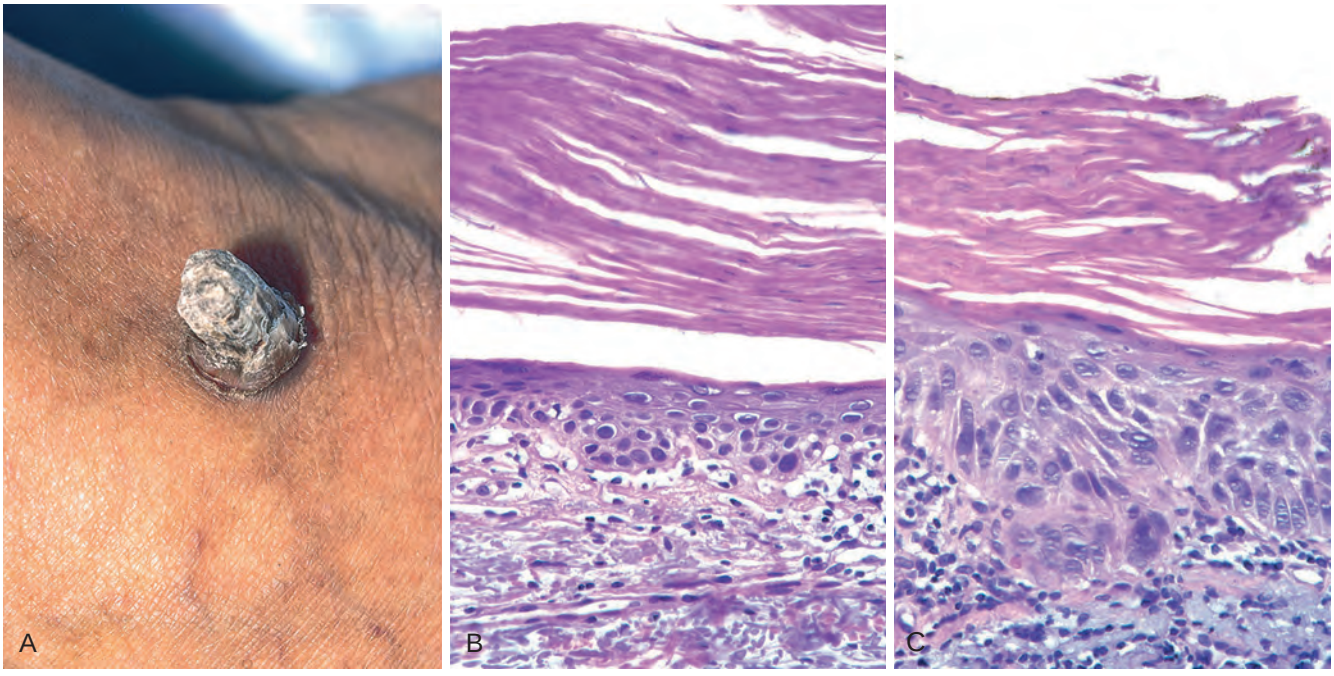

Figure 25-12 Actinic keratosis. **A,** Excessive keratotic scale in this lesion has produced a "cutaneous horn." **B,** Basal cell layer atypia (dysplasia) is associated with marked hyperkeratosis and parakeratosis. **C,** Progression to full-thickness nuclear atypia, with or without the presence of superficial epidermal maturation, heralds the development of squamous cell carcinoma in situ.