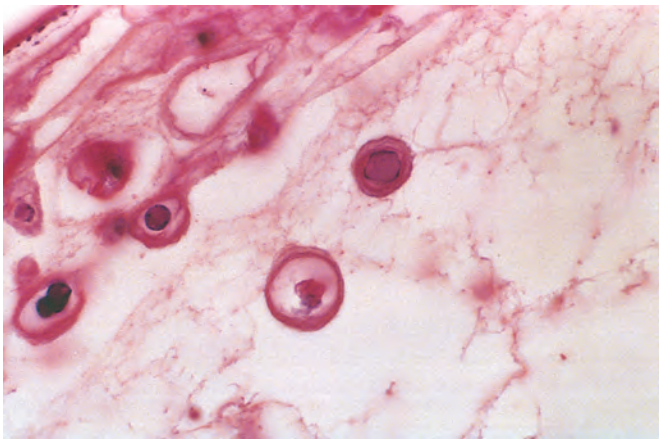

Figure 8-9 A herpesvirus blister showing glassy intranuclear viral inclusion bodies.

HSV-1 and HSV-2 cause lesions ranging from self-limited cold sores and gingivostomatitis to life-threatening disseminated visceral infections and encephalitis. **Fever blisters or cold sores** favor the facial skin around mucosal orifices (lips, nose), where their distribution is frequently bilateral and independent of skin dermatomes. Intraepithelial vesicles (blisters), which are formed by intracellular edema and ballooning degeneration of epidermal cells, frequently burst and crust over, but some may result in superficial ulcerations.

Gingivostomatitis, which is usually encountered in children, is caused by HSV-1. It is a vesicular eruption extending from the tongue to the retropharynx and causing cervical lymphadenopathy. Swollen, erythematous HSV lesions of the fingers or palm (herpetic whitlow) occur in infants and, occasionally, in health care workers.

Genital herpes is more often caused by HSV-2 than by HSV-1. It is characterized by vesicles on the genital mucous membranes as well as on the external genitalia that are rapidly converted into superficial ulcerations, rimmed by an inflammatory infiltrate (Chapter 22). Herpesvirus (usually HSV-2) can be transmitted to neonates during passage through the birth canal of infected mothers. Although HSV-2 infection in the neonate may be mild, more commonly it is fulminating with generalized lymphadenopathy, splenomegaly, and necrotic foci throughout the lungs, liver, adrenals, and CNS.

Two forms of **corneal lesions** are caused by HSV (Chapter 29). **Herpes epithelial keratitis** shows typical virus-induced cytolysis of the superficial epithelium. In contrast, **herpes stromal keratitis** is characterized by infiltrates of mononuclear cells around keratinocytes and endothelial cells, leading to neovascularization, scarring, opacification of the cornea, and eventual blindness. Here, the damage is caused by an immunologic reaction to the HSV infection, rather than the cytopathic effects of the virus itself.

Herpes simplex encephalitis is described in Chapter 28.

Disseminated skin and visceral herpes infections are usually encountered in hospitalized patients with some form of underlying cancer or immunosuppression. **Herpes esophagitis** is frequently complicated by superinfection with bacteria or fungi. **Herpes bronchopneumonia**, sometimes stemming from intubation of a patient with active oral lesions, is often necrotizing, and **herpes hepatitis** may cause liver failure.

Varicella-Zoster Virus (VZV)

Acute infection with VZV causes chickenpox and reactivation of latent VZV causes shingles (also called *herpes zoster*). Chickenpox is mild in children but more severe in adults and in immunocompromised people. Shingles is a source of morbidity in older and immunosuppressed persons. Like HSV, VZV infects mucous membranes, skin, and neurons and causes a self-limited primary infection in immunocompetent individuals. Also like HSV, VZV evades immune responses and establishes a latent infection in sensory ganglia. In contrast to HSV, VZV is transmitted in epidemic fashion by respiratory aerosols, disseminates hematogenously, and causes widespread vesicular skin lesions. Latent VZV infection is seen in neurons and/or satellite cells around neurons in the dorsal root ganglia. Reactivation and clinical recurrences causing shingles are uncommon but may occur many years after the primary infection. Localized recurrence of VZV is most frequent and painful in dermatomes innervated by the trigeminal ganglia, where the virus is most likely to be latent. VZV rarely recurs in immunocompetent individuals (in only 1-4% of infected individuals), but immunosuppressed or older persons can have multiple recurrences of VZV. For this reason, vaccination to prevent shingles is now recommended in all patients over age 60 years, and in younger adults with chronic disorders that may impair immunity. VZV infection is diagnosed by viral culture or detection of viral antigens in cells scraped from superficial lesions.

MORPHOLOGY

The **chickenpox** rash occurs approximately 2 weeks after respiratory infection. Lesions appear in multiple waves centrifugally from the torso to the head and extremities. Each lesion progresses rapidly from a macule to a vesicle, which resembles a dewdrop on a rose petal. On histologic examination, chickenpox lesions show intraepithelial vesicles (Fig. 8-10) with intranuclear inclusions in epithelial cells at the base of the vesicles. After a few days most chickenpox vesicles rupture, crust over, and heal by regeneration, leaving no scars. However, bacterial superinfection of vesicles that are ruptured by trauma may lead to destruction of the basal epidermal layer and residual scarring.

Shingles occurs when VZV that has long remained latent in the dorsal root ganglia after a previous chickenpox infection is reactivated and infects sensory nerves that carry it to one or

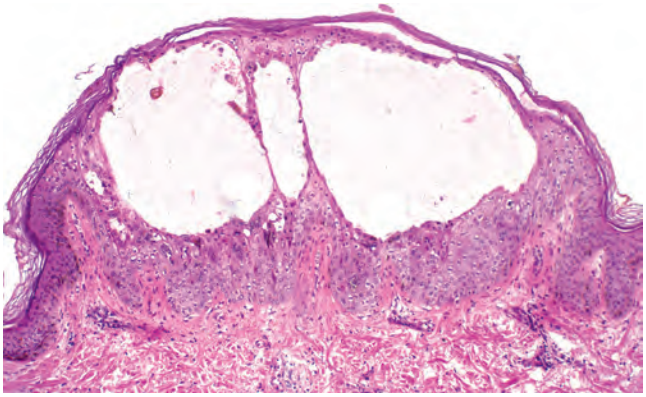

Figure 8-10 Skin lesion of chickenpox (varicella-zoster virus) with intraepithelial vesicle.