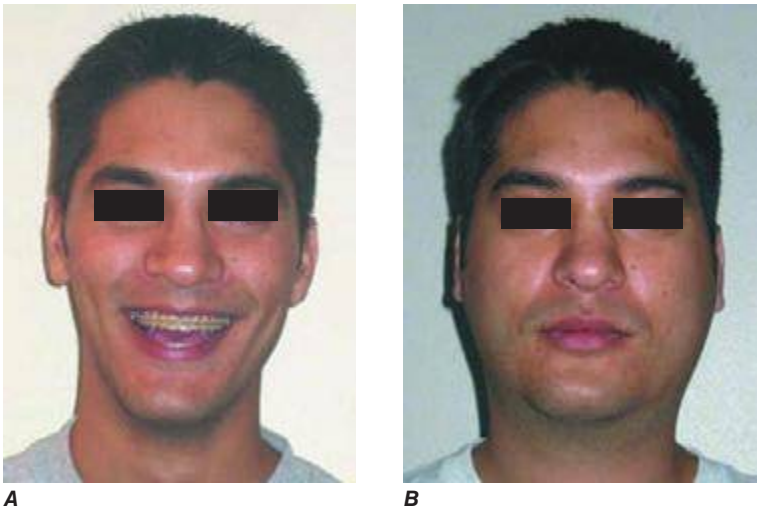
decline in mumps vaccination–induced immunity with time may be due to both declining titers and decreasing avidity of antibodies. The waning of mumps immunity over time is supported by studies suggesting that a third dose of MMR vaccine significantly reduces the mumps attack rate; however, these studies were not adequately controlled to rule out the possibility that the observed declines in mumps incidence were unrelated to the intervention. Therefore, the effectiveness of a third dose of MMR vaccine remains to be demonstrated.



A *B*

FIGURE 231e-2 A comparison of a person before acquiring mumps (*A*) and on day 3 (*B*) of acute bilateral parotitis. *(Courtesy of patient C.M. From Shanley JD. The resurgence of mumps in young adults and adolescents. Cleve Clin J Med 2007; 74:42-48. Reprinted with permission. Copyright © 2007 Cleveland Clinic Foundation. All rights reserved.)*

PATHOGENESIS

Humans are the only natural hosts for mumps virus infection. The incubation period of mumps is ~19 days (range, 7–23 days). The virus is transmitted by the respiratory route via droplets, saliva, and fomites. Mumps virus is typically shed from 1 week before to 1 week after symptom onset, although this window appears to be narrower in vaccinated individuals. Persons are most contagious 1–2 days before onset of clinical symptoms. Inference from related respiratory diseases and animal studies indicates that primary replication likely occurs in the nasal mucosa or upper respiratory mucosal epithelium. Mononuclear cells and cells within regional lymph nodes can become infected; such infection facilitates the development of viremia and poses a risk for a wide array of acute inflammatory reactions. Classic sites of mumps virus replication include the salivary glands, testes, pancreas, ovaries, mammary glands, and central nervous system (CNS).

Little is known about the pathology of mumps since the disease is rarely fatal. The virus replicates well in glandular epithelium, but classic parotitis is not a necessary component of mumps infection. Affected glands contain perivascular and interstitial mononuclear cell infiltrates and exhibit hemorrhage with prominent edema. Necrosis of acinar and epithelial duct cells is evident in the salivary glands and in the germinal epithelium of the seminiferous tubules of the testes. The virus probably enters cerebrospinal fluid (CSF) through the choroid plexus or via transiting mononuclear cells during plasma viremia. Although relevant data are limited, typical mumps encephalitis appears to be secondary to respiratory spread and is probably a parainfectious process, as suggested by perivenous demyelination, perivascular mononuclear cell inflammation, and relative sparing of neurons. Although rare, presumed primary encephalitis has been associated with mumps virus isolation from brain tissue. Evidence of placental and intrauterine spread in pregnancy has been found in both early and late gestation.

CLINICAL MANIFESTATIONS

Up to half of mumps virus infections are asymptomatic or lead to nonspecific respiratory symptoms. Inapparent infections are more common in adults than in children. The prodrome of mumps consists of low-grade fever, malaise, myalgia, headache, and anorexia. Mumps parotitis—acute-onset unilateral or bilateral swelling of the parotid or other salivary glands that lasts >2 days and has no other apparent cause—develops in 70–90% of symptomatic infections, usually within 24 h of prodromal symptoms but sometimes as long as 1 week thereafter. Parotitis is generally bilateral, although the two sides may not be involved synchronously. Unilateral involvement is documented in about one-third of cases. Swelling of the parotid is accompanied by tenderness and obliteration of the space between the earlobe and the angle of the mandible **(Figs. 231e-2 and 231e-3)**. The patient frequently reports an earache and finds it difficult to eat, swallow, or talk. The orifice of the parotid duct is commonly red and swollen. The submaxillary and sublingual glands are involved less often than the parotid gland and are almost never involved alone. Glandular swelling increases for a few days and then gradually subsides, disappearing within 1 week. Recurrent sialadenitis is a rare sequela of mumps parotitis. In ~6% of mumps cases, obstruction of lymphatic drainage secondary to bilateral salivary gland swelling may lead to presternal pitting edema, associated often with submandibular adenitis and rarely with the more life-threatening supraglottic edema.

Epididymo-orchitis is the next most common manifestation of mumps, developing in 15–30% of cases in postpubertal males, with bilateral involvement in 10–30% of those cases. Orchitis, accompanied by fever, typically occurs during the first week of parotitis but can develop up to 6 weeks after parotitis or in its absence. The testis is painful and tender and can be enlarged to several times its normal size; this condition usually resolves within 1 week. Testicular atrophy develops in one-half of affected men. Sterility after mumps is rare, although subfertility is estimated to occur in 13% of cases of unilateral orchitis and in 30–87% of cases of bilateral orchitis. Oophoritis occurs in ~5% of women with mumps and may be associated with lower abdominal pain and vomiting but has only rarely been associated with sterility or premature menopause. Mumps infection in postpubertal women may also present with mastitis.

Documented CSF pleocytosis indicates that mumps virus invades the CNS in ~50% of cases; however, symptomatic CNS disease, typically in the form of aseptic meningitis, occurs in <10% of cases, with a male predominance. CNS symptoms of aseptic meningitis (e.g., stiff neck, headache, and drowsiness) appear ~5 days after parotitis and also occur often in the absence of parotid involvement. Within the first 24 h polymorphonuclear leukocytes may predominate in CSF (1000–2000 cells/μL), but by the second day nearly all the cells are lymphocytes. The glucose level in CSF may be low and the protein

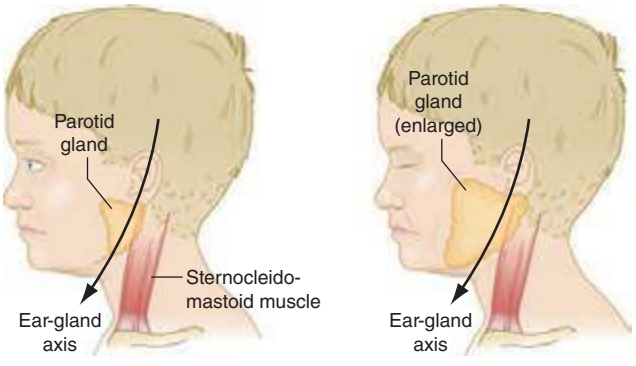


FIGURE 231e-3 Schematic drawing of a parotid gland infected with mumps virus (*right*) compared with a normal gland (*left*). An enlarged cervical lymph node is usually posterior to the imaginary line. *(Reprinted with permission from Gershon A et al: Mumps, in Krugman's Infectious Diseases of Children, 11th ed. Philadelphia, Elsevier, 2004, p 392.)*