TABLE 2. Summary of vaccinia-related adverse events*

Adverse event	Description	Risk factor or predisposition	Treatment
Eczema vaccinatum (EV)	• High fever • Generalized lymphadenopathy with extensive vesicular and pustular eruption • Onset: concurrently or shortly after local vaccinial lesion in vaccinee, or in contacts, 5–19 days after suspected exposure • Risk for secondary bacterial or fungal infections • Virus recovered from lesions • High morality rate with poor prognosis	• History of eczema or atopic dermatitis irrespective of disease activity or severity • Less frequently, persons without a history of dermatological conditions	• Prompt evaluation and diagnosis • Infection-control precautions • Might require multiple doses of vaccinia immune globulin (VIG) (cidofovir, second-line therapy) • Hemodynamic support • Volume and electrolyte repletion • Observe for secondary skin infections
Progressive vaccinia (PV)	• Nonhealing vaccination site • Painless progressive (central) necrosis at the vaccination site • Occasional metastatic lesions in skin, bones, and viscera • No inflammation initially • Absence of inflammatory cells on histopathological examination • Inflammation weeks later • Bacterial infection might develop • Differential diagnosis: severe bacterial infection, severe chickenpox, disseminated herpes simplex, and other necrotic conditions • Prognosis: poor, despite therapy	• Humoral and cellular immunocompromise (e.g., malignancy, human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), severe combined immunodeficiency syndrome (SCIDS), or hypogammaglobulinemia) • Protective level of T-cell count or humoral immunity unknown	• Prompt evaluation and diagnosis • Infection-control precautions • Might require multiple doses of VIG (cidofovir second-line therapy) • Surgical debridement of progressive necrotic lesions not proven useful
Postvaccinial encephalitis (PVE) or encephalomyelitis (PVEM)	• Diagnosis of exclusion • Appears similar to postinfectious encephalomyelitis or toxic encephalopathy caused by other agents • Abrupt onset of symptoms: fever, headache, malaise, lethargy, vomiting, meningeal signs, seizures, paralysis, drowsiness, altered mental status, or coma • Age <2 years (encephalopathy): cerebral vascular changes occurring 6–10 days postvaccination • Age ≥2 years (encephalomyelitis): demyelinating changes occurring 11–15 days postvaccination • Cerebral spinal fluid (CSF): normal or nonspecific; monocytosis, lymphocytosis, or elevated protein • Prognosis: mortality, 25%; neurological sequelae, 25%; complete recovery, 50%	• Age <1 year	• Intensive supportive care • Anticonvulsants as needed • VIG not recommended • Antiviral role unclear • Use of modern imaging studies has not been evaluated
Fetal vaccinia (FV)	• Incidence: rare (<50 reported cases) • Route of transmission: unknown • Outcomes: premature birth, fetal loss, high mortality • Not associated with congenital anomalies	• Cases in all trimesters of pregnancy • Greatest risk, third trimester	• Efficacy of VIG unknown • Antivirals not recommended
Generalized vaccinia (GV)	• Maculopapular or vesicular rash • Onset: 6–9 days postvaccination • Nontoxic, with or without fever • Differential diagnosis: erythema multiforme (EM), varicella, inadvertent inoculation, progressive vaccinia (PV), and smallpox	• Hematogenous spread • Lesions contain vaccinia • More serious among immunocompromised persons	• Usually self-limited in immunocompetent person • Infection-control precautions • VIG usually not indicated • Anti-inflammatory medications • Antipruritic medications • Antivirals usually not indicated

* See text for details.

TABLE 2. (*Continued*) Summary of vaccinia-related adverse events*

Adverse event	Description	Risk factor or predisposition	Treatment
Inadvertent inoculation	• Most common complication • Physical transfer of vaccinia virus from a vaccination site to second site on the vaccinee or to a close contact of vaccinee	• Manipulation of vaccination site • Children aged <4 years • Conditions that disrupt the epidermis (e.g., burns, severe acne, or psoriasis)	• Usually self-limited • Resolution in 3 weeks • Infection-control precautions • VIG if extensive body surface involved or severe ocular disease (cidofovir, second-line therapy)
Ocular vaccinia Inadvertent periocular or ocular implantation with vaccinia virus Can range from mild to severe	Keratitis • Marginal infiltration or ulceration with or without stromal haze/infiltration Conjunctivitis • Hyperemia, edema, membranes, focal lesions, fever, lymphadenopathy Blepharitis • Lid pustules on or near the lid margin, edema, hyperemia, lymphadenopathy, cellulitis, fever	• Manipulation of vaccination site, followed by eye rubbing • More likely with conditions that cause eye itching and scratching (conjunctivitis, corneal abrasion/ulceration)	• Ophthalmologic consultation • Certain ophthalmologists consider off-label topical antiviral medications • Topical prophylactic antibacterial medications for keratitis • VIG for severe blepharitis and blepharoconjunctivitis (without keratitis) • VIG not indicated for isolated keratitis • VIG considered for keratitis with vision-threatening conditions • VIG indicated for keratitis with life-threatening conditions that require VIG
Erythema multiforme (EM) and Stevens-Johnson Syndrome (SJS)	• Typical bull's eye (target) lesions • Hypersensitivity reaction • Pruritis • Onset: 10 days postvaccination • Can progress to SJS	• No known risk factors	• Antipruritic medications • VIG not indicated • Hospitalization and supportive care for SJS • Steroid use for SJS is controversial
Pyogenic infections of vaccination site	• Uncommon • Onset: 5 days postvaccination • Fever not specific for bacterial infection • Fluctuance at vaccination site	• More frequent in children (touching vaccination site)	• Gram stain • Bacterial culture • Antibacterial medications, if clinically indicated • No topical medications
Robust take (RT)	• >7.5 cm with swelling, warmth, and pain at vaccination site • Fluctuant lymph nodes not expected • Peak symptoms: 8–10 days postvaccination • Nonprogressive • Improvement in 24–72 hours	• Might be more likely among first-time vaccinees	• Observation most important • Antibacterial medications not indicated • Rest affected limb • Antipruritic medications • Anti-inflammatory medications • No salves or ointments
Tape adhesive reactions	• Sharply demarcated raised lines of erythema that correspond to adhesive placement • Local pruritis • No systemic illness	• Sensitivity to adhesives	• No salves, ointments, or topical/oral steroids • Frequent bandage changes • Periodic bandage removal

* See text for details.