

Table 1: Conditions that may mimic smallpox; (*) indicates most likely

Macule-papule stage	Comments
Drug*	Febrile prodrome + morbilliform rash; Drug history, HIV status
Measles (rubeola)*	3Cs: cough, coryza, conjunctivitis; generalized erythematous rash, itchy. Vaccination history
Rubella (German measles)	Mild; fever, erythematous rash; fades after 1-3 days Vaccination history
Secondary syphilis	Usually no fever; rapid plasma reagin (RPR)
Scabies, insect bites	Exposure history, itchy
Rickettsial pox (<i>R. akari</i>)	Exposure to mice, mites; eschar with widespread rash
Acne	Usually no fever, limited distribution
Scarlet fever	Infection, symptom history
Coxsackie virus infection	Prodromal morbilliform rash
Vesicule-pustule stage	Comments
Varicella *	Most often confused with smallpox See Table 2, Figures 12-13
Monkeypox *	Lesions similar to smallpox (Figure 14); lymphadenopathy key distinguishing feature; history animal exposure; smallpox vaccine prevents (additional comments below)
Disseminated herpes simplex (eczema herpeticum) *	Rare, severe, pre-existing skin barrier damage (eg, atopic dermatitis)
Disseminated herpes zoster *	History of varicella; HIV status; painful, burning,
Generalized vaccinia, eczema vaccinatum *	Often in atopic dermatitis; after smallpox vaccination, or accidental transmission of vaccinia virus within 7-10 days of immunization
Pustular drug reaction *	Febrile, widespread pustular rash; drug history
Erythema multiforme (including Stevens-Johnson) *	Drug, infection history
Pustular psoriasis	Little or no fever; history of psoriasis
Extensive molluscum contagiosum	HIV status
Bullous impetigo	History, lesion morphology, distribution
Contact dermatitis	Exposure history; itchy
Hand, foot and mouth disease	Mild fever; characteristic lesions focused on 3 locations

Table 2: Comparison of smallpox and varicella (chickenpox)

Smallpox			Chickenpox	
Severe	2-4 days before rash: prostration, high fever, headache, myalgias, vomiting, enanthem	Prodrome	None, or mild	Often at time of rash or 1-2 days before rash; no enanthem
Centrifugal	Face and distal extremities, lesions on palms and soles	Distribution (Figures 12-13)	Centripetal	Trunk, face and scalp; rarely palms and soles
Slow	Macule □ papule □ vesicle □ pustule; each stage 1-2 days; lesions in same stage	Evolution	Rapid	Macule □ papule □ vesicle □ pustule □ crust; each stage < 24 hours; lesions in different stages
Round	4-6 mm, deep (dermal), firm, well circumscribed	Pock	Oval	2-4 mm, superficial, "dew drop on a rose petal"
Painful	Tender on palpation	Symptoms	Itchy	Lesions may be excoriated
7-10 days	After 1 st lesion appears	Peak	3-5 days	After 1 st lesion appears
14-21 days	After 1 st lesion appears	Desquamation	6-14 days	After 1 st lesion appears