Ecthyma contagiosum (orf), a worldwide cause of the hand pus- 
tule, is caused by orf virus, a member of the genus Parapoxvirus, 
which causes an epitheliotropic zoonotic infection that spreads from rumi- 
nants to humans. Early and rapid diagnosis of this classic condition 
is critical to prevent unnecessary biopsies or extensive testing, and determination of etiology can be important in preventing reinfection or spread to other humans by the same infected animal.

A patient presenting with a hand pustule is a phe-
nomenon encountered worldwide requiring care-
ful history-taking. Some occupations, activities, 
and various religious practices (eg, Eid al-Adha, Passover, 
Easter) have been implicated worldwide in orf infection. In the United States, orf virus usually is spread from infected animal hosts to humans. Herein, we review the differential for a single hand pustule, which includes both infectious and noninfectious causes. Recognizing orf virus as the etiology of a cutaneous hand pustule in patients is important, as misdiagnosis can lead to unnecessary invasive testing and/or treatments with suboptimal clinical outcomes.

Case Series
When conducting a search for orf virus cases at our 
institution (University of Iowa Hospitals and Clinics, Iowa 
City, Iowa), 5 patient cases were identified.
Patient 1—A 27-year-old otherwise healthy woman presented to clinic with a tender red bump on the right ring finger that had been slowly growing over the course of 2 weeks and had recently started to bleed. A social history revealed that she owned several goats, which she frequently milked; 1 of the goats had a cyst on the mouth, which she popped approximately 1 to 2 weeks prior to the appearance of the lesion on the finger. She also endorsed that she owned several cattle and various other animals with which she had frequent contact. A biopsy was obtained with features consistent with orf virus.

Patient 2—A 33-year-old man presented to clinic with a lesion of concern on the left index finger. Several days prior to presentation, the patient had visited the emergency department for swelling and erythema of the same finger after cutting himself with a knife while preparing sheep meat. Radiographs were normal, and the patient was referred to dermatology. In clinic, there was a 0.5-cm fluctuant mass on the distal interphalangeal joint of the third finger. The patient declined a biopsy, and the lesion healed over 4 to 6 weeks without complication.

Patient 3—A 38-year-old man presented to clinic with 2 painless, large, round nodules on the right proximal index finger, with open friable centers noted on physical examination (Figure 1). The patient reported cutting the finger while preparing sheep meat several days prior. The nodules had been present for a few weeks and continued to grow. A punch biopsy revealed evidence of parapoxvirus infection consistent with a diagnosis of orf.

Patient 4—A 48-year-old man was referred to our dermatology clinic for evaluation of a bleeding lesion on the left middle finger. Physical examination revealed an exophytic, friable, ulcerated nodule on the dorsal aspect of the left middle finger (Figure 2). Upon further questioning, the patient mentioned that he handled raw lamb meat after cutting the finger. A punch biopsy was obtained and was consistent with orf virus infection.

Patient 5—A 43-year-old woman presented to clinic with a chronic wound on the mid lower back that was noted to drain and crust over. She thought the lesion was improving, but it had become painful over the last few weeks. A shave biopsy of the lesion was consistent with orf virus. At follow-up, the patient was unable to identify any recent contact with animals.

Comment

Transmission From Animals to Humans—Orf virus is a member of the Parapoxvirus genus of the Poxviridae family. This virus is highly contagious among animals and has been described around the globe. The resulting disease also is known as contagious pustular dermatitis, soremuzzle, echyma contagiosum of sheep, and scabby mouth. This virus most commonly infects young lambs and manifests as raw to crusty papules, pustules, or vesicles around the mouth and nose of the animal. Additional signs include excessive salivation and weight loss or starvation from the inability to suckle because of the lesions. Although echyma contagiosum infection of sheep and goats has been well known for centuries, human infection was first reported in the literature in 1934. Transmission of orf to humans can occur when direct contact with an infected animal exhibiting active lesions occurs. Orf virus also can be transmitted through fomites (eg, from knives, wool, buildings, equipment) that previously were in contact with infected animals, making it relevant to ask all farmers about any animals with pustules around the mouth, nose, udders, or other commonly affected areas. Although sanitation efforts are important for prevention, orf virus is hardy, and fomites can remain on surfaces for many months.
among animals and from animals to humans frequently occurs; however, human-to-human transmission is less common. Ecthyma contagiosum is considered an occupational hazard, with the disease being most prevalent in shepherds, veterinarians, and butchers. Disease prevalence in these occupations has been reported to be as high as 50%. Infections also are seen in patients who attend petting zoos or who slaughter goats and sheep for cultural practices.

Clinical Characteristics in Humans—The clinical diagnosis of orf is dependent on taking a thorough patient history that includes social, occupational, and religious activities. Development of a nodule or papule on a patient’s hand with recent exposure to fomites or direct contact with a goat or sheep up to 1 week prior is extremely suggestive of an orf virus infection.

Clinically, orf most often begins as an individual papule or nodule on the dorsal surface of the patient’s finger or hand and ranges from completely asymptomatic to pruritic or even painful. Depending on how the infection was inoculated, lesions can vary in size and number. Other sites that have been reported less frequently include the genitals, legs, axillae, and head. Lesions are roughly 1 cm in diameter but can vary in size. Ecthyma contagiosum is not a static disease but changes in appearance over the course of infection. Typically, lesions will appear 3 to 7 days after inoculation with the orf virus and will self-resolve 6 to 8 weeks later.

Orf lesions have been described to progress through 6 distinct phases before resolving: maculopapular (erythematous macule or papule forms), targetoid (formation of a necrotic center with red outer halo), acute (lesion begins to weep), regenerative (lesion becomes dry), papilloma (dry crust becomes papillomatous), and regression (skin returns to normal appearance). Each phase of ecthyma contagiosum is unique and will last up to 1 week before progressing. Because of this prolonged clinical course, patients can present at any stage.

Reports of systemic symptoms are uncommon but can include lymphadenopathy, fever, and malaise. Although the disease course in immunocompetent individuals is quite mild, immunocompromised patients may experience persistent orf lesions that are painful and can be much larger, with reports of several centimeters in diameter.

Dermatopathology and Molecular Studies—When a clinical diagnosis is not possible, biopsy or molecular studies can be helpful. Histopathology can vary depending on the phase of the lesion. Early stages are characterized by spongiform degeneration of the epidermis with variable vesiculation of the superficial epidermis and eosinophilic cytoplasmic inclusion bodies of keratinocytes (Figure 3). Later stages demonstrate full-thickness necrosis with epidermal balloon degeneration and dense inflammation of the dermis with edema and extravasated erythrocytes from dilated blood vessels. Both early- and late-stage disease commonly show characteristic elongated thin rete ridges.

Molecular studies are another reliable method for diagnosis, though these are not always readily available. Polymerase chain reaction can be used for sensitive and rapid diagnosis. Less commonly, electron microscopy, Western blot, or enzyme-linked immunosorbent assays are used. Laboratory studies, such as complete blood cell count with differential, erythrocyte sedimentation rate, and C-reactive protein, often are unnecessary but may be helpful in ruling out other infectious causes. Tissue culture can be considered if bacterial, fungal, or acid-fast bacilli are in the differential; however, no growth will be seen in the case of orf viral infection.

Differential Diagnosis—The differential diagnosis for patients presenting with a large pustule on the hand or fingers can depend on geographic location, as the potential etiology may vary widely around the world. Several
zoonotic viral infections other than orf can present with pustular lesions on the hands (Table). 17-24

Clinically, infection with these named viruses can be hard to distinguish; however, appropriate social history or polymerase chain reaction can be obtained to differentiate them. Other infectious entities include herpetic whitlow, giant molluscum, and anthrax (eTable).24-26 Biopsy of the lesion with bacterial tissue culture may lead to definitive diagnosis.26

**Treatment**—Because of the self-resolving nature of orf, treatment usually is not needed in immunocompetent patients with a solitary lesion. However, wound care is essential to prevent secondary infections of the lesion. If secondarily infected, topical or oral antibiotics may be prescribed. Immunocompromised individuals are at increased risk for developing large persistent lesions and sometimes require intervention for successful treatment. Several successful treatment methods have been described and include intralesional interferon injections, electrocautery, topical imiquimod, topical cidofovir, and cryotherapy.8,14,27-30 Infections that continue to be refractory to less-invasive treatment can be considered for wide local excision; however, recurrence is possible.8 Vaccinations are available for animals to prevent the spread of infection in the flock, but there are no formulations of vaccines for human use. Prevention of spread to humans can be done through animal vaccination, careful handling of animal products while wearing nonporous gloves, and proper sanitation techniques.

**Complications**—Orf has an excellent long-term prognosis in immunocompetent patients, as the virus is epitheliotropic, and inoculation does not lead to viremia.2 Although lesions typically are asymptomatic in most patients, complications can occur, especially in immunosuppressed individuals. These complications include systemic symptoms, giant persistent lesions prone to infection or scarring, erysipelas, lymphadenitis, and erythema multiforme.5,31 Common systemic symptoms of ecthyma contagiosum include fever, fatigue, and myalgia. Lymphadenitis can occur along with local swelling and lymphatic streaking. Although erythema multiforme is a rare complication occurring after initial ecthyma contagiosum infection, this hypersensitivity reaction is postulated to be in response to the immunologic clearing of the orf virus.32,33 Patients receiving systemic immunosuppressive medications are at an increased risk of developing complications from infection and may even be required to pause systemic treatment for complete resolution of orf lesions.34 Other cutaneous diseases that decrease the skin’s barrier protection, such as bullous pemphigoid or eczema, also can place patients at an increased risk for complications.35 Although human-to-human orf virus transmission is exceptionally rare, there is a case report of this phenomenon in immunosuppressed patients residing in a burn unit.36 Transplant recipients on immunosuppressive medications also can experience orf lesions with exaggerated presentations that continue to grow up to several centimeters in diameter.31 Long-term prognosis is still good in these patients with appropriate disease recognition and treatment. Reinfection is not uncommon with repeated exposure to the source, but lesions are less severe and resolve faster than with initial infection.1,8

**Conclusion**

The contagious hand pustule caused by orf virus is a distinct clinical entity that is prevalent worldwide and requires thorough evaluation of the clinical course of the lesion and the patient’s social history. Several zoonotic

### Zoonotic Infections Presenting With a Large Papule or Pustule on the Hands or Fingers

<table>
<thead>
<tr>
<th>Disease</th>
<th>Viral genus</th>
<th>Animal reservoir</th>
<th>Relevant social history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine papular stomatitis</td>
<td>Parapoxvirus</td>
<td>Cattle</td>
<td>Farmer, butcher, veterinarian</td>
</tr>
<tr>
<td>Cutaneous leishmaniasis</td>
<td>Leishmania</td>
<td>Sandflies</td>
<td>Exposure to area where sandflies are endemic</td>
</tr>
<tr>
<td>Orf</td>
<td>Parapoxvirus</td>
<td>Sheep and goats</td>
<td>Shepherd, butcher, farmer, veterinarian, petting zoos, wool-shearer</td>
</tr>
<tr>
<td>Pseudocowpox (milker’s nodule)</td>
<td>Parapoxvirus</td>
<td>Cattle</td>
<td>Cattle farmer, butcher, veterinarian</td>
</tr>
<tr>
<td>Sealpox</td>
<td>Parapoxvirus</td>
<td>Seals</td>
<td>Marine mammal technician</td>
</tr>
<tr>
<td>Tularemia (rabbit fever)</td>
<td>Francisella</td>
<td>Rabbits, ticks, deer flies</td>
<td>Exposure to animal or fomites, biting insects, contaminated food or water</td>
</tr>
<tr>
<td>Yatapoxvirus</td>
<td>Chordopoxvirus</td>
<td>Monkeys and baboons</td>
<td>Travel to Africa, animal handlers</td>
</tr>
</tbody>
</table>
viral infections have been implicated in this presentation. Although biopsy and molecular studies can be helpful, the expert diagnostician can make a clinical diagnosis with careful attention to social history, geographic location, and cultural practices.

REFERENCES
### eTABLE. Other Considerations for Patients Presenting With a Large Papule or Pustule on the Hands or Fingers

<table>
<thead>
<tr>
<th>Disease</th>
<th>Classic description</th>
<th>Relevant social history</th>
<th>Workup</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbuncles</td>
<td>Perifollicular erythematous tender nodules or abscess that can undergo necrosis</td>
<td>Adolescent or young adults (males more often than females), poor hygiene, HIV</td>
<td>Gram stain and culture</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>Erythema with poorly defined borders and swelling of the digit; possible abscess formation with necrosis</td>
<td>Immunocompromised, comorbid conditions, trauma (portal for bacterial entry), IV drug use, tinea infection</td>
<td>WBC, tissue and blood culture, radiograph if concern for osteomyelitis</td>
</tr>
<tr>
<td>Cutaneous anthrax</td>
<td>Nonpainful pruritic papules or vesicles that ulcerate and form black eschars with surrounding edema</td>
<td>Contact with animal wool, hides, or meat; can be present in soil</td>
<td>Gram stain, PCR, biopsy</td>
</tr>
<tr>
<td>Disseminated gonorrhea</td>
<td>Scattered (often necrotic) pustules, primarily located on the distal portions of the extremities</td>
<td>Sexually active patient; also may be associated with arthritis or ophthalmitis</td>
<td>Nucleic acid amplification testing, culture with Gram stain</td>
</tr>
<tr>
<td>Felon</td>
<td>Erythema and edema at the distal fingertip pad with abscess formation and possible necrosis</td>
<td>Penetrating trauma to the finger or nail, untreated paronychia</td>
<td>Gram stain and culture; radiograph if concern for osteomyelitis, foreign body, or gas formation</td>
</tr>
<tr>
<td>Giant molluscum</td>
<td>Smooth, dome-shaped, firm papule with central umbilication</td>
<td>Commonly spread through children and fomites, sexual transmission in adults</td>
<td>Clinical diagnosis; consider HIV testing in adults at higher risk</td>
</tr>
<tr>
<td>Herpetic whitlow</td>
<td>Grouped vesicles or pustules on an erythematous base that can coalesce to form a bulla</td>
<td>Dental technicians, health care exposure, children, concurrent HSV infection</td>
<td>PCR for HSV DNA, Tzanck smear, viral culture, direct fluorescent antibody</td>
</tr>
<tr>
<td>Keratoacanthoma</td>
<td>Painless, solitary, dome-shaped nodule with central keratin plug</td>
<td>Sun-exposed skin, immunosuppression</td>
<td>Skin biopsy</td>
</tr>
<tr>
<td>Mycobacterium marinum (fish tank granuloma)</td>
<td>Tender pustule or nodule that can ulcerate and undergo necrosis and lymphangitic spread</td>
<td>Exposure to contaminated fish tanks, swimming pools, or lake or ocean water</td>
<td>Biopsy with atypical mycobacteria, tissue culture, PCR, radiograph if osteomyelitis is suspected</td>
</tr>
<tr>
<td>Paronychia</td>
<td>Proximal or lateral nail fold erythema, edema, and possible abscess formation</td>
<td>Trauma to nail fold, recent pedicure, finger sucking in children</td>
<td>Tissue culture for bacteria and fungi, consider viral etiology, radiograph if concern for osteomyelitis</td>
</tr>
<tr>
<td>Pyogenic granuloma</td>
<td>Friable red papule or nodule with associated ulceration and crusting</td>
<td>Trauma, eczema dermatitis, pregnancy, retinoid use, young adults</td>
<td>Dermoscopy or biopsy</td>
</tr>
<tr>
<td>Sporotrichosis</td>
<td>Painless nodules that ulcerate and present in a lymphatic distribution; more common on hands and forearms</td>
<td>Florists, gardeners, forestry workers; more common in tropical climates with exposure to thorny plants</td>
<td>Skin biopsy with fungal culture</td>
</tr>
<tr>
<td>Tophaceous gout</td>
<td>Smooth multilobulated nodules that can ulcerate</td>
<td>Uric acid nephrolithiasis or gout attacks, renal insufficiency, alcohol consumption</td>
<td>Aspirate or biopsy with polarizing microscopy, radiograph, WBC, ESR</td>
</tr>
</tbody>
</table>

Abbreviations: ESR, erythrocyte sedimentation rate; HSV, herpes simplex virus; IV, intravenous; PCR, polymerase chain reaction; WBC, white blood cell count.