Contagious Ecthyma (Orf): Advances in Epidemiology, Immunopathogenesis, and Vaccine Development for Small Ruminants

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Contagious ecthyma, also known as Orf or sore mouth, is a highly contagious, zoonotic viral disease of sheep and goats caused by Orf virus, a member of the genus Parapoxvirus within the family *Poxviridae*. The disease is characterized by proliferative and crusting lesions at mucocutaneous junctions, especially around the lips, muzzle, nostrils, teats, and feet, and may also involve the oral cavity, leading to pain, anorexia, impaired suckling, weight loss, and economic loss. The infection is of major concern in young lambs and kids, where morbidity may be high and secondary bacterial infection can worsen clinical outcomes. Factors influencing the incidence of disease are age, management practices, seasonal factors, environmental contamination and direct or indirect contact with infected animals or fomites. Diagnosis is often suspected on clinical grounds, but confirmation may require histopathology, serology, virus isolation, electron microscopy or most importantly molecular detection by polymerase chain reaction. Control of contagious ecthyma is based on supportive care, isolation of affected animals, prevention of secondary infections, vaccination in endemic areas, and strong biosecurity measures as contagious ecthyma is self-limited and has no specific antiviral therapy.

Keywords: *Contagious ecthyma, Orf virus, Zoonotic disease, small ruminants, Skin lesion, Vaccination*

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The fact that the infection is zoonotic also necessitates that farmers, veterinarians and animal handlers take personal protective measures. This chapter reviews the etiology, epidemiology,

pathogenesis, clinical signs, diagnosis, treatment, control for cosntagious ecthyma of sheep and goats, with emphasis on the current problems in diagnosis, prevention and vaccine design.

Introduction

Contagious ecthyma, commonly referred as "Orf" or "sore mouth", is a widespread highly contagious viral skin disease affecting sheep and goats. It is caused by the Orf virus belonging to the genus *Parapoxvirus* within *Poxviridae* family (Delano et al., 2007). The virus primarily affects sheep and goats, with the disease being more severe in goats than in sheep. It also affects other animals, including alpacas, camels, reindeer, deer, pronghorn antelope, wapiti, and seals and squirrels (Nagarajan et al., 2019). The disease is characterized by proliferative lesions at the muco-cutaneous junctions of the lips and nose, extending to the oesophagus. In some cases, it progresses to affect the hooves, causing strawberry foot rot. Additionally, the udder and teats of milking ewes can also be affected (Onyango et al., 2014; Cargnelutti et al., 2011). Contagious ecthyma is a zoonotic disease that primarily affects people who work with sheep and goats. The virus can be transmitted to human through direct or indirect contact, for instance, during slaughter of animal or handling infected animals (Bergqvist et al.,2017; Hosamani et al., 2009). This disease is widespread in regions that raise sheep and goats and is more common during the summer and spring seasons (Robinson and Balassu et al., 1988). The incidence of disease is lower in older animals because of the developed immunity from previous infections or vaccinations. In contrast, young animals experience a high mortality rate due to oral lesions and secondary infections that lead to anorexia, preventing them from feeding (Hosamani et al., 2009; Robinson and Balassu et al., 1988). High prevalences have been documented in Ethiopia, Iran, Bangladesh, Nigeria, Bulgaria and China, with many flocks affected and substantial morbidity and mortality (Kaya et al.,2025; Tedla et al., 2018; Alam et al., 2024; Ivanov et al., 2025).

Etiology

The Orf virus (ORFV), a causative agent of contagious ecthyma, is a prototypic member of the genus *Parapoxvirus*, subfamily Chordopoxvirinae, within *Poxviridae* family. It is a linear double-stranded DNA virus approximately 134-139 kb in size with a GC content of 66%. The virions are characterized by long, ball-shaped membrane tubules that resemble elongated threads, measuring 260 nm in length and 160 nm in width (Bhagawati et al., 2025; Ewies et al., 2024; Karki et al., 2019). This ovoid enveloped virus genome consists of core and variable regions. Most poxvirus members possess a conserved core region that encodes essential proteins involved in nucleotide biosynthesis, replication transcription, assembly. In contrast, the variable regions are located at the 5′ and 3′ terminal ends. The proteins encoded by these terminal genes are the primary factors that influence host range and viral pathogenicity (Mangga et al., 2022). *Bovine papular stomatitis virus* (BPSV) virus, *Parapoxvirus* of red deer in New Zealand (PVNZ), *pseudocowpox virus* (PCPV), *Parapoxvirus* of the grey seal, are the other members under the genus *Parapoxvirus* (Karki et al., 2019; Delhon et al., 2004; Graf et al., 2024). The terminal variable regions encode major structural and immunogenic proteins, notably the B2L gene (ORFV011, encoding the envelope protein) and the F1L gene (ORFV020, encoding the immunogenic envelope protein), which serve as key targets for diagnostic PCR, restriction fragment length polymorphism (RFLP), and molecular phylogenetic studies.

Epidemiology

Contagious ecthyma in sheep and goats is globally prevalent, especially where small ruminants are widely raised, affects sheep and goats across most sheep and goat raising countries (Spyrou et al.,2015). The disease

is severe among young animals with oral lesions impairing suckling and feeding and increasing emaciation, secondary infection, and death (Pang et al., 2026; Kaya et al., 2025; Al-Mubarak et al., 2022). Older animals can still be infected, but they generally show lower morbidity or partial protection from prior exposure rather than complete resistance (Karki et al., 2019; Khalafalla et al., 2020; Bala et al., 2019).

Global Distribution

The Disease is endemic to various regions, including Asia (notably India, China, Pakistan, Bangladesh, Palestine, and Iraq), Africa (such as Nigeria, Ethiopia, Sudan, and Egypt), Europe (specifically Italy and Norway), the Americas (including the USA, Brazil, and Argentina), and Oceania (New Zealand) (Kumar et al.,2022; Mansour et al.,2022). In India, the infection is particularly prevalent across Uttarakhand, Assam, Meghalaya, Haryana, Uttar Pradesh, Rajasthan, Tripura, Kashmir, Tamil Nadu, and Odisha states (Kumar et al.,2022).

Seasonal Pattern and Temporal Distribution

The condition demonstrates predictable seasonal cycling in both sheep and goat population with distinct periodic rhythmicity (Mansour et al.,2022).

Table1. Seasonal Prevalence Distribution

Season	Percentage of Cases
Spring	29.33% (peak occurrence) (Mansour et al.,2022)
Winter	3.05% (lowest occurrence) (Mansour et al.,2022)
Late Summer/Autumn	Elevated prevalence (Spyrou et al.,2015; Nazir et al.,2023)

Table2: Monthly Case Distribution

Month	Case Percentage
February	2.0% (minimum) (Mansour et al.,2022)
March	23.2% (Mansour et al.,2022)
April	56.1% (Peak) (Mansour et al.,2022)

Outbreak investigations indicate that disease initiation occurs during July and august coiniciding with the monsoon and late summer periods (Spyrou et al.,2015). The environmental conditions during this time appears to facilitate viral transmission (Spyrou et al.,2015; Mansour et al.,2022). As death rates increase in colder months, this situation necessitates heightened vigilance (Nazir et al.,2023). The higher prevalence of disease in spring compared to winter may be attributed to several factors. These include environmental conditions that favour pathogen survival, an increased risk of mucosal injury resulting from grazing activities, and physiological stress caused by cold weather. Additionally, Parapoxvirus is known to be resilient in the environment, capable of surviving for months under cooler conditions, while being sensitive to high and very low temperatures (Mansour et al.,2022).

Transmission

Orf virus (ORFV) can effectively spread among sheep and goat flocks primarily by direct contact with lesions and contagious crusts, both of which remain in the environment for a long duration. Close flock contact favors infection spread either by proximity of animals under intensive housing or by sharing of grazing areas

where slight lesions resulting from prickles, stubs of straw or hard feed may serve as routes of infection; thus, fomites such as feed and water troughs, feed pails, bedding and farming equipment greatly contribute to the perpetuation of infection within the herd (Bala et al., 2019; Sanders et al., 2017).

Non-Traditional Sources: Saliva and Milk

Very recent studies have unveiled new yet previously poorly recognized routes for ORFV transmission: saliva and milk. Live and virulent ORFV has been detected and isolated from the oral cavity and secretions as well as milk of dairy goats thus representing direct infectious sources. For young lambs and kids, suckling of infected dam's milk is believed to be one of the principal causes of rapid newborn outbreaks while saliva droplets, in turn, may promote within-herd spread in highly dense animal population (Ma et al., 2022). Both oral and lactational transmission routes are important for risk assessment and control measures.

Vertical Transmission

Goats have been shown to transmit ORFV vertically from dam to foetus suggesting an important route of infection in early life. At the molecular scale, the detection of the ORFV B2L gene at the maternal–foetal interface strongly suggests transplacental passage. In a study, the ORFV-positive rate was 90% in non-vaccinated dams, and dropped to 56.14% in vaccinated dams. The virus detection in umbilical cord blood also declined from 71.43% to 14.29% and no kids born to vaccinated dams were ORFV-positive, compared to 36.67% in non-vaccinated groups. This highlights the effectiveness of maternal vaccination in reducing vertical transmission and protecting newborns (Pang et al., 2026).

Zoonotic Transmission

Humans commonly contract the disease via direct contact of infected animals or animal products, mainly on areas of broken skin from which the live virus can pass into skin crevices (Sanders et al., 2017; Efridi et al., 2023). The infection is usually occupational or domestic when either handlers, veterinarians, butchers come into contact with lesions or scab materials. In humans, infection usually takes place in a part of the hands or fingers having had a small abrasion (Sanders et al., 2017; Efridi et al., 2023), but rare case report describes a possible route of transmission via the ingestion of the contents of lesion, thus causing lesions in the mouth and on other body parts by self-inoculation (Estela et al., 2016). Fomites also play a role in maintaining within-herd infection and transmission to humans (Sanders et al., 2017; Efridi et al., 2023).

Human-to-Human Transmission

Human-to-human spread has been documented in rare occasions primarily within families through close contact with an infected subject (e.g. Mother to child), or by a nurse caring the infected patient during dressing changes (Estela et al., 2016; Rajkomar et al., 2016). These reports suggest that some close contact might cause an infected subject to acquire secondary cases by direct skin-to-skin contact with actively lesioned patients under appropriate precautionary and care conditions (Estela et al., 2016; Rajkomar et al., 2016).



Figure 1.Transmission network of ORF virus

Pathogenesis

Orf virus (ORFV) is an epitheliotropic parapoxvirus, which infects epithelial cells of skin and mucous membranes and predominantly keratinocytes from the walls of wool follicles and growing epidermis (Pang et al., 2026). Infection requires damaged integrity of the integumentary system such as abrasions or minor wounds because normal intact skin inhibits entry of virus into the body (Pang et al., 2026; Fleming et al., 2015).

Viral Entry and Tropism

Entry of ORFV into susceptible cells occur primarily via clathrin-mediated endocytosis and macropinocytosis, although to a much lesser extent, via caveolae-dependent pathway. Both pathways are dynamin-dependent and require an acidic intracellular environment (Pang et al., 2026). An important host factor to facilitate internalisation of ORFV is the subunit of host potassium channel-KCNE4. ORFV typically infect epidermal keratinocytes and dermal fibroblasts in the mouth and skin, hence leading a site-specific replication focus (Pang et al., 2026; Li et al., 2018).

Replication Cycle

Orf, like all poxviruses, replicate in the cytoplasm, independently of host nucleus (Pang et al., 2026). The virus possesses its own polymerase and transcriptional machinery which replicates the viral genome, a linear ds DNA of approximately 138 kbp, into progeny virions (Pang et al., 2026; Fleming et al., 2015). During the early stages of replication, it actively inhibits apoptosis of infected cell by several of its viral proteins (e.g., viral protein ORFV119) in order to gain enough time to replicate (Pang et al., 2026; Li et al., 2018).

Lesion Development and Progression of Disease

In natural infection, incubation period generally ranges from 3-7 days, but experimental and some field data showed 12-14 days, depending on the dose of virus and other factors. Inoculation site of ORFV lesions

develops sequentially as follow after 3-7 days from infection (Santiago et al., 2019; Duffill et al., 2017; Kumar et al., 2022).

Maculo-Papular Stage (3-7 days): An area of erythematous macules or papules appear at inoculation site (Santiago et al., 2019).

Target Stage (7-14 days): An area of central necrosis is observed surrounded by a red outer halo, giving a target like appearance (Santiago et al., 2019).

Acute/Weeping Stage (14-21 days): Hyperplastic nodules and exudative areas are observed and may weep serum or serosanguinous fluid (Santiago et al., 2019).

Regenerative Stage (21-28 days): Scabs form and dry over the necrotic lesions (Santiago et al., 2019).

Papilloma Stage (28-35 days): Some papules may develop hyperplastic papillomatous aspect covered with a thickened dry crust and finally resolved (Santiago et al., 2019). Typical clinical lesions and disease progression involve vesicular-papular eruption around the lip, nostril, eyes, buccal and inner mucosa, tongue, teat, external genitalia and coronary band in all domestic animals. These then progress to pustules and proliferate exuberant proliferative and exudative crusts. Skin reaction involves necrosis and loss of affected epidermis and the dermal stratum papillae, with marked inflammation (Efridi et al., 2023).

Immune Response and Lesion Resolution

ORFV expresses several immunomodulatory proteins to evade immune response of hosts, which include suppression of interferon production, complement pathway and apoptosis. It implies that the lesions are localized infection, and subsequent reinfection can be expected, although repeated previous infection may confer some degrees of immunity to re-infection. Lesions usually undergo spontaneous resolution 4-6 weeks by cell-mediated immune response while secondary bacterial infection is complicated for healing the wounds (Pang et al., 2026; Duffill et al., 2017).

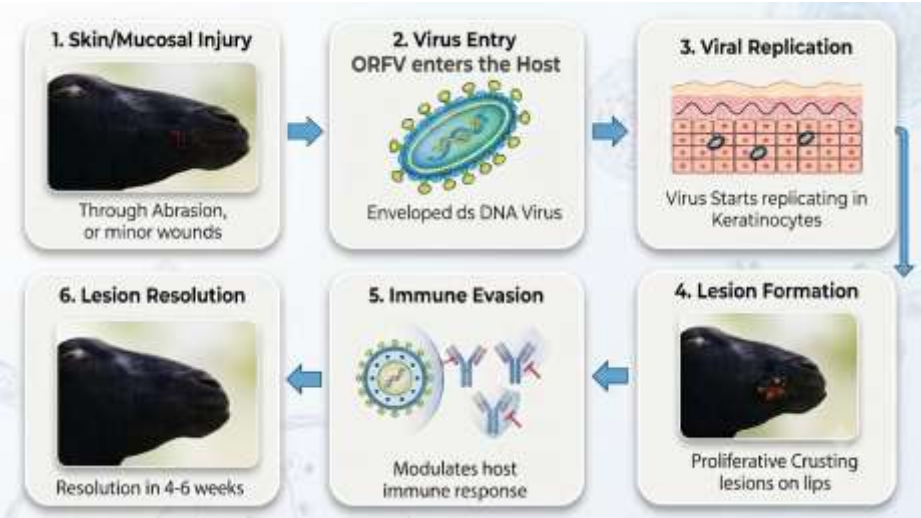


Figure 2. **Pathogenesis Of ORF virus**

Clinical Features

Sheep and goats are infected with the orf virus with proliferative, cauliflower-like lesions occurring most frequently on the skin and mucocutaneous junctions of the lips, muzzle, nostrils, gums and sometimes the tongue and udder in lactating animals, and on ears, eyelids, forehead and other cutaneous areas in severe or generalized infections (Pang et al., 2026; Kumar et al., 2022; Bennett et al., 2026; Mayenga et al., 2026).

Lesion Morphology and Distribution

Tightly packed, proliferative lesions around the mouths, originating as erythematous macules/papules, progressing to vesicles and pustules and then leading to thick, dark brown, granulating scabs (figure-1), that are friable and readily bleed when removed (Kumar et al., 2022; Mayenga et al., 2026). Exophytic lesions develop into papillomatous or angiomatous growths of the gingival mucosa around erupting incisor teeth. Lesions on the feet and extending to the coronary band or hoof-horn junction, can result in severe lameness (Kumar et al., 2022; Mayenga et al., 2026).

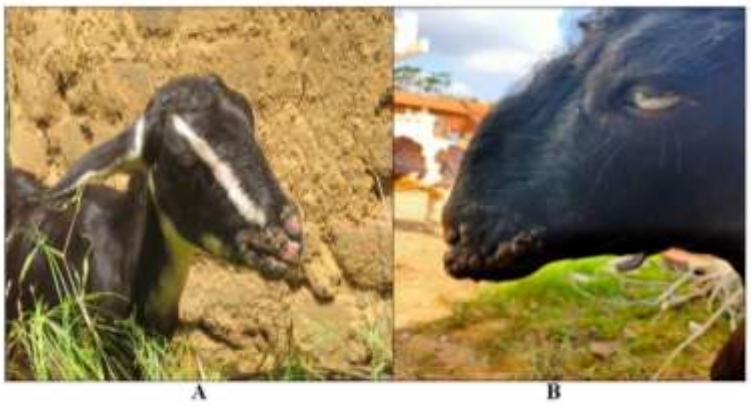


Figure 3. **Clinical Signs of Contagious Ecthyma**
(A- B) Proliferative, nodular, and crusted lesions of lips, muzzle and perioral region of affected animals

Systemic Clinical Features

Systemic signs include anorexia, depression, dullness, weakness, and reduced growth rates due to pain and reluctance to consume food (Kumar et al., 2022; De et al., 2003). Enlarged regional lymph nodes, arthritis, pneumonia and emaciation have been recorded in severe or complicated cases of Orf (Kumar et al., 2022; Nazir et al., 2021). Gross necropsy findings can include liver congestion, intestinal ballooning, consolidated pneumonia with lung adhesions and Cauliflower-like proliferations in the mouth (Nazir et al., 2021).

Diagnosis

Though Orf can be diagnosed based on clinical signs, several techniques enable accurate identification of the disease without misdiagnosis. Laboratory methods such as polymerase chain reaction (PCR), histopathology of affected tissues, enzyme-linked immunosorbent assays (ELISAs), complement fixation tests (CFTs), electron microscopy, virus neutralization tests, and cell culture isolation are used for diagnosis (Hosamani et al., 2009; Bhagawati et al., 2025; Shivaraju et al., 2021, Reddy et al., 2024, Manjunatha et al., 2025).



Figure 4. Schematic representation of methods used in disease diagnosis

Histopathology

Histopathological examination of skin biopsies can aid in diagnosis. Epidermal hyperplasia, acanthosis, ballooning degeneration, keratinocyte vacuolation, parakeratosis, and inflammatory cell infiltration in the dermis are typical abnormalities. In some cases, proliferative changes in hair follicles and adnexal tissues are associated with necrosis and ulceration (Mohammed et al., 2022). These findings are helpful but not always specific. So, histopathology is best interpreted together with lesion pattern and molecular testing (Mohammed et al., 2022; Pang et al., 2023).

Virus Isolation and Electron Microscopy

A diagnosis may be confirmed using virus isolation; however, this technique is impractical as it needs to be performed on specific ovine and bovine cell cultures in the laboratory (Pang et al., 2023; Torfason et al., 2002). Parapoxvirus particles may be detected by electron microscopy, which has in the past, proved to be a useful technique when virus isolation or culture was not possible (Torfason et al., 2002). In most laboratories today, both techniques have been superseded by molecular assays, as they are relatively difficult and time consuming to perform (Pang et al., 2023; Torfason et al., 2002).

Serological Tests

Orf diagnosis and surveillance have been carried out using serological tests including virus neutralization test, immunohistochemistry, immunofluorescence assay, and ELISA. These techniques can be utilized to investigate outbreak Epidemiology and monitor the immune response, but they are generally considered less

reliable for diagnosis of acute orf since the immune response to the virus can be delayed from the time of infection (Pang et al., 2023). For flock evaluations serology is a reliable method to assess the potential of animal exposure, particularly in conjunction with PCR and physical examination (Kumar et al., 2022; Pang et al., 2023).

Molecular Diagnosis

A confirmed method of choice for virus identification, PCR is the most accurate and popular confirmation method available. Laboratory-diagnosed PCR identified Orf with excellent specificity in the majority of scab and swab specimens that were investigated (Torfason et al., 2002). In recent days, PCR is still being used to confirm infections in sheep and goats, including the detection of ORFV037 and ORFV039 in some samples (Kumar et al., 2022; Mohammed et al., 2022). PCR can detect ORFV directly from scab material without the need to be confirmed with virus isolation, which provides the greatest advantage (Pang et al., 2023; Torfason et al., 2002). Modern molecular diagnostics include the following: Conventional PCR, real-time PCR, loop-mediated isothermal amplification, recombinase polymerase amplification, and recombinase-aided amplification. These assays improve speed, sensitivity, and field applicability, making them useful for outbreak confirmation and surveillance (Pang et al., 2023).

Differential Diagnosis

There is some overlap between Orf lesions and those of several other infectious dermatoses, and hence, differential diagnosis is essential. Differentials include foot-and-mouth disease, bluetongue, lesions associated with contagious caprine pleuropneumonia, dermatophytosis, bacterial dermatitis, and other pox virus infections (Pang et al., 2023; Torfason et al., 2002). Clinical diagnosis can be difficult, and laboratory confirmation is recommended if the clinical signs are atypical, particularly in endemic areas where several different skin diseases are prevalent (Kumar et al., 2022; Pang et al., 2023). Sheeppox and Goatpox (Capripoxvirus): Generalized papules/nodules on unfeathered skin, systemic involvement, high mortality, and internal organ lesions (Reddy et al 2015).

Table 3: Showing Clinical Features of Different Diseases.

Disease	Etiologic Agent	Key Clinical Features	Distinguishing Lesion Characteristics
Contagious Ecthyma (Orf)	Orf virus (*Parapoxvirus*)	Localized to muzzle, lips, teats, feet; low mortality in adults	Proliferative, cauliflower-like, thick brown crusts & target lesions
Foot-and-Mouth Disease (FMD)	FMD virus (*Aphthovirus*)	High fever, severe lameness, profuse salivation	Vesicles and erosions on tongue, dental pad & interdigital space (no thick crusting)
Sheeppox / Goatpox	Capripoxviruses	Generalized systemic disease, high mortality in young	Nodular skin lesions over entire body, systemic edema, internal organ lesions
Bluetongue	Bluetongue virus (*Orbivirus*)	Facial edema, fever, nasal discharge, coronitis	Cyanosis of oral mucosa ("blue tongue"), hyperemic coronary band without proliferative crusts

Control and Treatment of Contagious Ecthyma

The disease has no known antiviral treatment and therefore is best treated by supportive therapy, the prevention of secondary bacterial infection, and flock treatment (Bennett et al., 2026). Treatment aims at alleviating pain and providing comfort to infected animals, supporting their food intake and managing secondary bacterial infection, as it is otherwise usually self-limiting and can prolong recovery by exacerbating lesion size (Bennett et al., 2026; Ortin et al., 2025).



Figure 5. **Schematic representation of Control and treatment measures**

Supportive Treatment

Affected animals should be isolated from the healthy stock to reduce transmission and the lesions should be handled carefully as the virus can spread through contact and contaminated materials (Bennett et al., 2026; Walzer et al., 2008). Soft palatable feed, along with adequate hydration, helps animals with oral lesions to maintain adequate feed intake, particularly lambs and kids that may have difficulty suckling (Bennett et al., 2026). In severe cases topical antiseptics may be used to keep lesions clean. Systemic antibiotics are sometimes given only when secondary bacterial infection is suspected (Ortín et al., 2025; Ayaz et al., 1999).

Vaccination

The primary means of prevention when contagious ecthyma is found in the herd or flock is vaccination (Reichen et al., 2025; Büttner et al., 1985). The use of live attenuated vaccines has a long history and the older literature suggests flock wide vaccination at regular intervals, typically every 6 to 8 months in endemic settings (Büttner et al., 1985). However, vaccine efficacy can vary between host species and viral strains, and sheep vaccines may not reliably protect goats against wild-type ORFV adapted to goats (Reichen et al., 2025; Walzer et al., 2008).

Biosecurity and Farm Management

A key component of control includes preventing the introduction of the virus into the herd. New animals should be quarantined and examined before entering the herd, and contact with infected animals, contaminated equipment, common feeding stations and auction or market environments should be minimized (Bennett et al., 2026; Walzer et al., 2008). Orf is zoonotic so affected animals should be segregated and gloves and hygiene measures have to be adopted by personnel during outbreaks (Reichen et al., 2025; Bennett et al., 2026).

Environmental Control

Unlike the self-limiting lesions of Orf in individual animals, the virus can persist in the environment and continue to circulate within flocks, particularly where skin injuries are common (Bennett et al., 2026; Walzer et al., 2008). Cleaning and disinfecting feeding equipment, shearing tools and handling devices reduces the chance of indirect transmission (Walzer et al., 2008). Good pasture management is also useful as thorny or rough forage can cause skin abrasions which facilitate infection (Bennett et al., 2026).

Outbreak Management

Control is often based on a combination of isolation, vaccination of susceptible animals, sanitation, and careful handling of infected stock on endemic farms (Reichen et al., 2025; Walzer et al., 2008, Bayyappa et al.,2025). Lambs and kids are often more severely affected than adults and therefore monitoring of young animals should also form part of the outbreak response (Reichen et al., 2025). Where outbreaks are recurrent, it may be more practical to vaccinate replacement stock strategically than to try to achieve total eradication (Walzer et al., 2008).

Conclusion

Contagious ecthyma remains an important and often underestimated disease of sheep and goats, combining high morbidity, recurrent infections, reduced productivity and zoonotic risk. Although the disease is generally self- limiting, its impact on young animals, lactating females and herd performance can be significant, particularly in endemic production system. Diagnosis is now aided by clinical assessment supported by histopathological and molecular methods but effective long-term control still depends on better vaccines improved biosecurity and earlier recognition in the field. Future work should focus on developing safer, more effective, and strain-specific vaccines, because currently available live vaccines provide only partial protection and raise safety concerns. Improved field-friendly diagnostics increased molecular surveillance, and more region-specific epidemiological studies are also required to identify outbreaks early and better understand the circulating virus diversity.

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