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**A REVIEW OF CONTAGIOUS ECTHYMA (ORF) IN SHEEP AND GOATS AND  
THE STATUS OF DISEASE IN IRAN**

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**ABSTRACT**

Orf virus (ORFV) is a member of the genus Parapoxvirus, in the subfamily Chordopoxvirinae of Poxvir-idea family. Contagious ecthyma (Orf), an acute, debilitating, contagious and economically important sheep viral skin disease, goat and some other domesticated and occasionally other wild animals that has worldwide distribution. Animals infected with orf virus typically develop scabby sores (lesions) around their lips, muzzles, and in their mouth. It is more severe in goats compared with sheep. Contagious ecthyma is found around the world and can occur at any time. Morbidity and mortality has been reported to range from 20% to 100% and 1% to 93% respectively, and the rate of mortality depends on conditions like stress, immune system problems, etc. Financial losses are related to decline in production devaluation of meat, leather and wool in national and international markets, as well as costs related to being zoonotic. The aim of this review article is to present the latest information on the Orf disease for readers that in turn help the effective and efficient management of the disease leading to the reduction of the economic losses to a great extent.

**Keywords: contagious ecthyma, orf, zoonotic, parapoxvirus, economic losses**

## INTRODUCTION

Orf virus (OV), a member of the parapoxvirus genus in the Poxviridae family, is the etiological agent of a severe exanthematic skin disease known as contagious ecthyma. This disease, affecting small domestic ruminants and occasionally other wild animals, is spread wherever sheep and goats are farmed and usually is more severe in goats compared with sheep. Ecthyma is a non-systemic skin disease. The causative Orf virus has been extensively investigated over recent years because of its growing host-range and zoonotic importance (1).

There are 80 medical names for this disease (2, 3). The disease is also known as scabby mouth, contagious pustular dermatitis or sore mouth (4). Orf in Old English means rough and tough (5). Gourreau and et al. (1986) believe that the disease is called Orf when it occurs in humans (6, 7). The precise geographical distribution of Orf is not known, but it is thought to be present in any part of the world where goats and sheep are raised (8) with the previous outbreaks was mainly reported in the Americas and Europe, such as the United States, Germany and Greece (9-15).

The disease is manifested by proliferative lesions on the muzzle and mouth that usually resolve in 1–2 months. Primary

lesions are more severe with a clinical progression of erythematous macule, vesicle, papule, pustule and scab formation in 4–6 weeks and in young animals the risk is higher than others. Severe oral and facial lesions in lambs may interfere with suckling, the lesions on the udder may result in the abandonment of offspring and foot lesions are the cause of transient lameness. Reinfection lesions progress through the same clinical stages, but are not proliferative and are generally smaller, usually resolving rapidly within 2–3 weeks (4).

Orf is not normally fatal and is a debilitating disease but if lambs and kids are deprived from suckling or succumb to secondary bacterial or fungal infections it can be fatal. The mortality due to secondary bacterial infections may reach 15% and morbidity of the disease may reach up to 100%. Zoonoses occur most frequently during lambing, docking, shear-ing, drenching or slaughtering of affected animals. In humans most infections are localized and heal spontaneously. However, large poorly healing lesions are usually seen in immunosuppressive individuals. Financial losses are related to decline in production devaluation of meat, leather and wool in national and international markets,

as well as costs related to being zoonotic (4, 16, 17).

### **Etiology**

Orf virus belongs to the parapoxvirus genus, in the chordopoxvirinae subfamily of the poxviridae family (18). In addition to the Orf virus (parapox virus ovis) this genus includes bovine papular stomatitis (parapox virus bovis 1), pseudocowpox (parapox) virus bovis and parapox virus deer. scientist also put three viruses with the names of auzduk disease virus (contagious ecthyma virus), chamois contagious ecthyma virus and sealpox capripox in this genus tentatively (21). Parapox viruses are similar in terms of genetic and antigenic structure and shape (morphology), they have similar genomic organization and virulence, and they have too many genetic similarities to capri poxviruses ,serologically (8, 19).

Virions are cocoon shaped with about 160nm in width and 260nm in length and covered with long thread like surface tubules resembling a ball of yarn. The viral genome, one of the smallest in Poxviridae family, is composed of 140 kbp linear ds DNA with closed hairpin loop ends and genes located on both strands with a bidirectional orientation (4, 20, 21). Parapoxviruses are distinguished from other poxvirus genera by crisscross pattern on the particle surface, the relatively small

size, their ovoid shape and the high G+C content (approximately 64%) of the genome (22). Parapoxviruses are sensitive to ether, chloroform, benzene and toluene and are resistant to glycerol. The parapoxvirus is quite resistant and survives for several months in dry and cool environment but is destroyed by high and very low temperatures, wetting and UV light. The virus resists physical damage and persists through the winter months on hedges, feeding troughs and barns. It can be inactivated in 30 min at 60 °C. Orf virus on shaded ground retains infectivity for years, whereas sunlight exposed scab remains infective for longer period. The virus can retain infectivity about 15 years, at room temperature (4, 23-25).

### **Epidemiology**

The epidemiology of Orf is poorly understood. In addition to the normal manifestations of the infection, explanations are needed for the unusual forms of the disease, including outbreaks in which newborn lambs have clinical signs (26). Detailed and updated information on epidemiology of this disease would not only help in updating the knowledge of the scientific community but also would be useful for policy makers in formulating appropriate measures for eradication and control of the disease (27).

### **Hosts**

This disease affects many species like sheep, goats, camels, camels of south America, caribou, chamois, dall sheep, mountain goats and bighorn sheep, buffalo, cat, dog, wild goats, etc (4, 31). Orf is considered as a zoonotic disease. The virus can be passaged in rabbits. Mild lesions occur in chorioallantois of 9 to 12 days chick embryos. Guinea-pigs and rats are not sensitive to the virus (4). Wildlife role in the survival and transmission of the disease should not be ignored, because virus also has been separated from reindeer, seals, Squirrel and musk oxen (*Ovibos moschatus*) (30, 32).

#### **Prevalence, Morbidity and Mortality**

Contagious ecthyma is found around the world and can occur at any time (4), but often occur under conditions of drought on pasture or indoors with manual feeding (28). The disease In grassland or fattening system in late summer, autumn and winter is common (4). Orf outbreak is usually has two peaks time, one Immediately after birth and the other one is within a period of 3 to 4 months after birth (33, 34). In a two-year study in the UK herd prevalence of 25 percent, 19.5 percent in lambs and 1.8 percent in ewes have been reported (35). The disease often occurs in lambs 3 to 6 months old when in pasture. Lambs 10 to 12 days old and adult animals can also be severely affected (28).

Orf usually has been proposed as a mild disease and there are different reports about Morbidity and mortality in Outbreaks of disease in sheep herds. For example the rate of Morbidity and mortality has been reported respectively 20% to 100% and 1% to 93%, with the rate of mortality depending on conditions like Stress, immune system problems, comorbidities, malignant Orf, secondary infections and skin myiasis, however, these rates usually are higher in goats (8, 28, 36). Fatality of the disease is caused by lesions in the respiratory tract and if sufficient care is not taken, fatality rate will increase in lambs (28).

#### **Transmission**

It seems that the virus present subclinically in wild animals such as reinder (43). Survival of the disease in the herd may be due to chronic wounds that remain in infected animals for long periods. Infection can be the result of the virus existence in the environment or acquired from infected animals. Spread of the disease in a herd is very quick via direct contact with infected animals or with contaminated inanimate items such as manger. some outbursts in associated with the use of the tool for cutting off the tail is registered (28). According to separate studies, the transmission by direct contact or through

contaminated animal products have been proven (37).

It is believed that natural infection in pasture, occurs because of virus attack after skin irritation by thorny plants or stubble rubbing a viral suspension on the damaged skin which is a standard method of the disease transmission. On the other hand, an outbreak with no oral lesions occurred in a large group of lambs, collected from several farms and transported in a vehicle, within 23 hours of arrival. It has been occurred that is, while there were no oral lesions. Humans in addition to being infected can become carriers of the virus from animal to animal, so when there is a contact with sick animals great care should be taken and protective gloves should be used (38). Iatrogenic transmission of the virus can happen in large and small operations, touching, feeding liquid, etc (4, 39). Animals with immunodeficiency and chronic infection play an important role in survival of Orf in nature (40). Orf virus can also be transferred in adult animals through subclinical injuries or resistant infection and cause the disease under stress situations (26). Among slaughterhouse workers most outbreaks can be seen in group of people who deal with wool and fur (28). It is important to note that the failure to observe safety precautions when working with live vaccines may cause infections in humans.

So far, no cases of human to human transmission or mother to fetus have been reported (2, 36).

### **The Possibility of Disease Transmission to Humans**

The first recorded case of Orf in man was made by a Norwegian, Hansen, in 1879, but 58 years were to elapse before the occurrence of human Orf in the United Kingdom was reported by Peterkin of Edinburgh (41). In the United Kingdom it has been identified as one of the most frequent occupational zoonoses and is also described as a common disease in Australia. The disease was also recorded in the United States at 1939 (42).

The disease has a zoonotic potential, although it is more an occupational hazard to people working with animals (e.g. veterinarians, farmers, animal carers) (29) at the time of shearing affected sheep, administering medication, vaccination, working with live vaccines without proper protection, slaughtering infected animals and consumption of their meat, or by contact with pets in the exhibitions or zoos the disease can be transmitted (28, 41, 43). In humans, after an incubation period of 2–4 days, lesions may be observed. The duration of lesions ranges from 4 to 9 weeks. Healing takes place without scarring, but secondary infections may retard healing, or the situation may become

complicated with creation of erythema multiform and generalized papulovesicular eruption (5, 44).

Severe complications, such as regional adenitis, fever, lymphangitis, or blindness when the eye is affected, has been reported (5). Lesions are usually single and confined to the hands, arms and people's face. Itchy lesions do not respond well to topical treatments and recover themselves (4). Although large lesions are seen in patients with immune suppression (26). So far, no cases of human to human transmission or mother to fetus has been reported (2, 36). In humans, poxvirus infections are neglected zoonoses and are undoubtedly under-reported, so the true impact of these diseases remains unknown (45). True incidence and prevalence rate of Orf disease in humans are unknown (44). Parapoxvirus infections in humans can be like tularemia lesions, skin anthrax or tumor (46).

### **Risk Factors**

In recent years there have been proper studies on risk factors (1, 35, 47). The primary risk factors are the presence of the virus, the immune status of animals and vaccination. Virus infections, cross-border interference, age, stress, congestion, immunosuppressive diseases, forage weed (thorny plants), the increasing number of orphaned lambs and the duration period of

lambing are also important risk factors (28, 35, 47).

### **Economic Losses**

This information about economic losses might allow farmers and their veterinarians to make realistic cost-benefit decisions about their Orf control strategy such as whether to vaccinate or not (33). Some pundits believe that ecthyma is among the 20 viral sheep and goats diseases that affects poverty, and they believe that socio-economic damage related to the disease is estimated less than the actual amount. The most important reason is underreporting. Great losses of this disease are related to losses of lambs and yearlings, infertility, mastitis, reduced milk production, costs and side effects of vaccination, discarding the milk of infected animals, slow growth of lambs, medical expenses, compulsory costs of removal and replacement ewes, costs related to manual feeding of lambs to keep them alive, different degrees of pain, loss of efficiency, problems relating to export, the costs related to zoonotic disease, and the devaluation of meat, leather and wool in national and international markets (4, 28, 33, 48, 49). Bennett estimated direct costs of ecthyma in UK sheep population (with almost 16 million sheep) around 4 million Euros per year (50). In another study, the average annual economic losses

of the disease in Great Britain is estimated to be 10 (3.1 to 28.3) million Euros (33).

### Pathogenesis

Orf viruses tend to damaged skin epithelium for establishment of infections and lesions. Following the viral skin damage, the virus is not institutionalized in the epidermis, but deployed in the injured epidermis. Following skin damage in sheep and the contact of virus with new epidermis, virus antigen cannot be identified in the skin. seventy two hours after infection, virus is identifiable for the first time in the center of a new epidermis subtraction, just under the stratum corneum. During the eclipse stage the virus is unknown. At first, infection starts from new epidermis in outer stratum spinosum bilaterally and uniform and then spreads out in the whole depth of the epidermis (28).

Skin reactions include a cellular response to necrosis and destroyed affected epidermis and stratum papillare of derm. The cutaneous response to infection is an increase in delayed sensitivity and infiltration of inflammatory cells, including neutrophils, basophils, and probably mast cells. The usual stages of lesions are macule, papul, vesicles, pustule and scab. Pustules are seen and blow out within a few days, which causes the ulcer, then a thick skin covering or scab will be seen on top of

the lesion that will dissever within 3 to 4 weeks and no scars will be left (4). When Orf affects the teats of lactating ewes, potential changes in the local defense mechanisms can occur, and predispose the animals to mastitis. For example, interleukin-10 suppresses production of cytokines from activated macrophages. In addition, in this disease the activity of macrophages is weakened (29).

Despite the simplicity of the pathogenesis of Orf, secondary bacterial infections such as Staphylococci, alpha hemolytic Streptococci and Corynebacteria, Dermatophilus Congolensis or myiasis complicate the situation of disease (4, 51). In humans, Orf passes through six clinical stages (maculopapular, target, acute, papillomatous, reconstruction and restoration) and each stage lasts for approximately one week (43).

### Immunity

Sheep that have recovered from natural infection are highly resistant to reinfection. Despite a multiplicity of immunogenic virus strains, the presently used commercial single-strain live vaccines have produced fair immunity in all parts of the USA. Failure in vaccination may be due to the virulence of the infecting strain rather than differences in antigenicity of the vaccine (52). There is only partial protection following vaccination or clinical disease.

Recurrent infections can occur in 1 to 3 months but are less severe and heal rapidly. The cell-mediated immune response plays an important role, as passively transferred antibody from dam does not provide protection. Cell culture propagated contagious ecthyma virus preparations are less effective in eliciting immunity than propagated in sheep. Lambs without maternal antibodies that are vaccinated at the age of 1 to 4 days of age develop protective immunity against contagious ecthyma. In some animals, such as reindeer, the immune response is unknown (4, 30, 53).

In primary infections, before the host mounts an effective immune response there is a period of time, in which the virus can both replicate and produce immunomodulating and virulent proteins, so that lesions usually last for 4 to 6 weeks. Reinfection is less severe and only last for 2 to 3 weeks due to an accelerated immune response (33). Under field conditions, recovered animals are safe for 2 to 3 years, but no antibodies can be seen in 2176ingival2176s, and newborn lambs from immune ewes are more susceptible. There is a strong immunity against the disease, but it only lasts for eight months. Whereas there is a humeral immune response against the virus, the recovery is related to cell mediated immunity

mechanisms. According to experiences, reinfection after recovery compared with initial infection will be mild and faster. In the secondary challenge of the virus, pustules and scabs form earlier, injuries recover more quickly and there may not be the blister formation stage (28).

### **Clinical Findings**

Orf virus is highly epitheliotropic and gains access to tissues through wounds or abrasions. The Orf lesions appear 6 to 7 days after infection. Proliferative cauliflower lesions are usually confined to the muzzles, lips, nostrils, mucous membranes of the mouth, eyelids and ears, and teats of nursing ewes (54). McElroy et al described details of clinical lesions of the mouth (gums, tongue, palate, dental pad) in lambs with natural viral infection and reported that tongue, palates and gums lesions respectively recovered after 14, 15 and 22 days (55). There is a report from America that Orf created painful proliferative lesions in the animal's foot (38).

### **Sheep**

The incubation period of the disease varies from 4 to 8 days with an initial rise in temperature (4) At first lesions appear in a rash and pustular form, the process that usually remains hidden, these lesions then progress to the proliferative areas, moderately proliferative area of

granulation, and covered with a sweet inflammatory stiff and thick scab. The development of early lesion site is to form scabs takes approximately 6 to 7 days. New lesions are created during the first 10 days after infection. Initial lesions are created in the oral mucocutaneous junction and are usually accompanied by inflammation of lips. Lesions spread out to some parts of the muzzle and nose, hairy skin around mouth, and buccal mucosa. Lesions may appear like thick and individual scabs with a diameter of 0.5 cm or attached together as a continuous plaque. Perforation of lesions occurs, and touching of scabs is painful. These lesions are easily crushed, but hardly apart from lower granulation texture. Because of limitation in sucking and grazing affected lambs suffer from severe negative effects. In mild cases scabs dry and fall, and full recovery is achieved within 3 weeks. Affected suckled lambs may pass the virus into ewes teats (28).

In ewes, lesions are observed mainly in the body of the teat and on the udder skin, as well as around the teat orifice and, sometimes, in the inguinal area and the thigh. Affected ewes may subsequently develop mastitis caused by staphylococci or *Mannheimia haemolytica*. In adult animals, lesions can also be found in the genital organs (ewes: vulva and skin-vaginal junction, rams: preputial orifice). The

venereal form of the disease is characterized by appearance of papules, vesicles and ulcers on the skin of vulva in ewes and preputial orifice in rams (29).

In some cases, secondary skin infections occur with bacteria or larvae of flies. In ram, the lesion on scrotum is characterized by the accumulation of fluid in scrotal sac and associated with loss of libido, inability to mount the ewe, paresis of penis after mating, and myiasis in the preputial orifice may contribute to incomplete erection. Sometimes, lesions of enhanced severity, that do not resolve easily and debilitated body conditions have been reported in atypical parapoxvirus infection in sheep. Such forms of Orf causes extensive proliferative skin lesions confined to the legs above the coronary band and fore head. Rarely, systemic involvement occurs and lesions appear in the ears, around the anus, vagina, prepuce, nasal mucosa and cheeks. During systemic invasion, the infection may extend to trachea and alimentary tract leading to bronchopneumonia and severe gastroenteritis. Secondary effect of Orf infection often leads to mastitis in ewes and incidence is high in unvaccinated ewes due to infection with *Mannheimia haemolytica* and coagulase-negative staphylococci compared to vaccinated ones. The oral lesions due to Orf in sheep are most likely

to develop at sites such as tongue, dental pad, and the upper and lower gums. It is observed more often when lambs under 2 months of age are involved. These lesions do not create scabs in the oral mucosa, but these lesions which are similar to rash are also surrounded by a bulging congested area. There is also wide proliferative lesions which are very painful on the border between gums and incisors. In lambs, lesions on 2178ingival adjoining incisors, palate and tongue are characterized by single or multiple coalescing papules followed by ulceration covered with yellowish exudates. When the coronets are affected in finishing lambs, they are often granulomatous, proliferative and persistent and result from infection with *Dermatophilus congolensis* and are



Fig 1: Lesions on the tongue

### Goat

After an outbreak, persistent Orf in a boer goat has been registered. There was a classic form of the disease in most animals of the herd with a 3–4 week clinical course.

referred to as 'strawberry foot rot'. There are a number of reports of lambs with dual Orf/sheep pox virus infection and Orf/papillomavirus infection (4).

In some outbreaks skin lesions are highly proliferative without covering scabs at the top of granular lesions. This form of lesions are more common in Suffolk sheep and occur on the lips, the edges of the nose and around the eyes. In addition, some of these proliferative lesions that have involved animal legs, have been patented. The malignant form of the disease in sheep is presented with acute oral blisters and spread of lesions to gastrointestinal tract and granulomatous lesions cause falling hooves (28). Some wild animals such as musk ox, experience similar injuries like sheep (27).

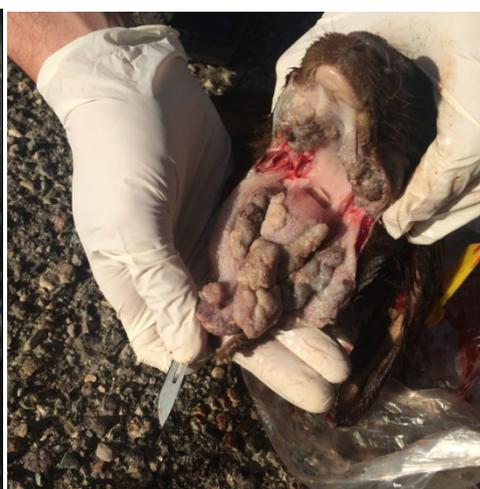


Figure 2: Oral cavity lesions

In 2% of the animals, a permanent infection occurred for several months with lesions throughout the body. The genome of viruses isolated from these animals had no difference by other Orf viruses and

permanent infection was probably the result of individual sensitivity factors of these hosts. Orf infections in Boer and Boer cross goats are manifested by multifocal, severe proliferative dermatitis accompanied by arthritis, moderate to severe lymphadenopathy and chronic pneumonia. The disease usually runs a 3–4 week course. In the mouth of affected mountain goats there are dry, brown, proliferative lesions that are prominent on the markedly edematous hyperemic lips, but the severity diminishes toward the commissures. Lesions of the oral cavity especially on the gum become moist, reddish-brown and in certain sites, intensely hyperemic (4). Severe generalized infections characterized by disseminated proliferative lesions,

arthritis and pneumonia have been described in goats. Prompted diagnosis can be complicated when there is clinical disease in goats, but sheep located on the same premises are asymptomatic (45). In Italy simultaneous infection of Orf and orthopoxviruses in goat have been reported in which the lesions were in the form of skin papillomatosis (38).

An outbreak in goat with high lethality and the presence of multifocal nodular and proliferative lesions of varying sizes which disseminated throughout the body, teats, udder, base of the tail, vulva, abdomen, around the hooves, nostrils and lips has recently been described in Northern Brazil (56).

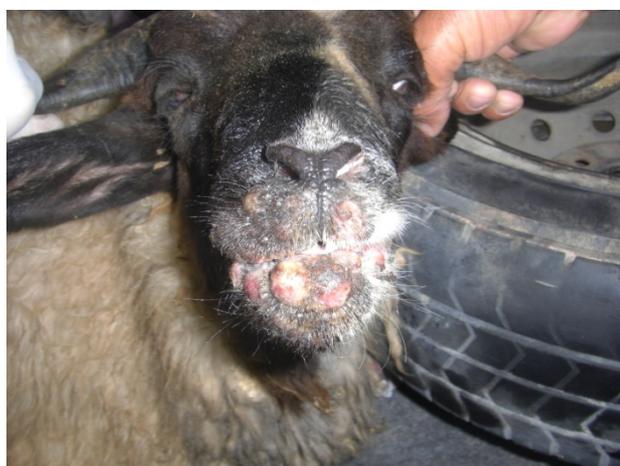


Fig 3: Lesions on lips

### Clinical Pathology

In a study in China according to site of the pathological changes of the lesions, the disease is divided to labial, udder, vaginal and mixed types (40). Traditionally laboratory detection of parapoxvirus is by

electron microscopy and the observation of an elliptical shape with a cross pattern of virion strings surface that is smaller than orthopoxviruses (36). Commonly employed laboratory tests include: electron microscopy (EM), serological tests such as

agglutination test, agar gel precipitation test (AGPT), enzyme linked immunosorbent assays (ELISAs), complement fixation test (CFT), serum neutralization test (SNT), histopathology of affected tissues, restricted fragment length polymorphism (RFLP) analysis and nucleic acid based assays including polymerase chain reaction (PCR) (4). The LAMP method for detection of Orf infections, especially in clinical practice has been also reported as an easy, rapid, accurate and sensitive method (57). Recovered animals had high level of neutralizing antibodies in their serum that is identifiable with gel diffusion and other serological tests. but it is of little clinical value (28) or unlike ELISA, AGID and CFT methods it is not suitable for the detection of serum antibodies (58).

Because of cross serological reaction between parapox virus and capripox virus, an unequivocal differentiation should be implemented with molecular techniques. Hence, PCR is used as a rapid, simple, specific and sensitive assay (47). The duplex PCR assay can be completed in five hours or less, provides significant savings in cost, time and materials. This is a significant advantage compared to the individual PCR assays or virus neutralization testing available for identification of ORFV or CPV from clinical samples. Furthermore, the duplex

PCR assay demonstrated a similar sensitivity when compared to the isolation of virus in cell cultures for direct detection of these viruses in field specimens (59). Accurate and rapid differential diagnosis is therefore essential, as early recognition of Orf not only allows for specific management strategies and institution of proper control measures for unweaned animals, but also prevents zoonotic transmission (36).

### **Necropsy Findings**

In malignant cases, lesions are observed with abnormal shapes, congested borders in the oral cavity and upper respiratory tracts, and in rare cases there are esophageal mucosa, abomasum, and small intestine involvement. Specified lesions of the disease are proliferative and after a while the central cells fall, which causes ulcer-like lesions (28). Purulent and scaly lesions in heads, udders, legs, and ulcerative lesions in the nasal cavities, erosion in the esophageal mucosa, upper respiratory tracts and inflammation of reticulum, abomasums, intestines and necrotic lesions in the lungs and the pleura may be seen (60).

Histological examination of the proliferative verrucous lesions of the affected animals revealed severe epidermal hyperkeratosis and hyperplasia. There were degenerative changes within the stratum

spinosum, with numerous swollen, vacuolated cells having pyknotic nuclei. Intraepidermal aggregates of inflammatory cells were present, and the formation of intracytoplasmic eosinophilic inclusion bodies were present in vacuolated necrotic

prickle cells typical of poxviruses. Necessarily histological samples to confirm the diagnosis include fixed lesions in formalin and obtained virology samples from bullous lesions (54).



**Figure 4: Lesions on the gingiva**

### Differential Diagnosis

In most ecthyma outbreaks, cases are so mild that there is no concerns about the diagnosis or indiscrimination. But in some stages Orf disease may be clinically similar to bluetongue disease, ulcerative dermatosis, mycotic dermatitis, facial eczema, facial warts, FMD (28), papillomatosis, staphylococcus dermatitis, sheep pox, goat pox and PPR (36). For differential diagnosis other clinical and epidemiological evidences should be considered. In a study in Shiraz 50 samples were obtained from scabby skin of sheep and goats muzzles, and molecular diagnostic test using PCR was performed which proved 50% to be orf, 4% smallpox, and 1% of them were positive for PPR.

Based on the results of this study, the role of Orf virus in the development of scabby skin on the muzzles, is higher than the two other aforementioned viruses (47). A bacteriological culture of the lesion makes it possible to discard some confounding processes such as cat scratch disease, anthrax, sporotrichosis, staphylococcal cellulitis and American blastomycosis (2).

### Therapeutic management

There is no specific treatment for the disease. Picking scabs and rubbing ointments or astringent lotions were used, but in most cases they delayed the healing of wounds. Providing warm and pleasant feed for animals is recommended. It is claimed that the combination of hot and cold compresses in the healing of

proliferative lesions of the oral cavity in young lambs, are effective (28). Specifically tailored treatments should be applied to common infections that occur concurrently with the disease. The use of systemic antibiotics and antibiotic ointments are helpful in this regard (4).

Regarding secondary bacterial infections that commonly coexist with the disease, special treatment should also be undertaken. The use of antibiotics can help and should be applied for this purpose. Locally, an antibiotic ointment can be applied whilst local application of preparations that contain boric acid and KMnO<sub>4</sub> may also be helpful. Levamisole has been proposed for use as immunostimulant. Supportive treatment of young animals in bad states due to poor feed intake should be applied by administering glucose solution through esophageal intubation. In recent years, anti-viral drugs have been applied in human and animal Orf infections and the results were satisfying (29).

The acyclic nucleoside phosphonates (ANPs) are the most potent drugs available against poxviruses, their mechanism of action is targeted at the viral DNA polymerase acting as chain terminators and, therefore preventing DNA replication. In an experimental study, results demonstrate that the topical application of cidofovir

cream can result in milder lesions that resolve more quickly than untreated lesions confirming that this antiviral molecule does offer some hope in the treatment of Orf virus lesions in goats and sheep. However it is also clear that the treatment regimen and the excipient used for healing is also critical to the outcome of the treatment (42).

In humans no specific treatment is needed except for local disinfection to avoid secondary infection. In immunocompromised cases lesions often become very large and atypical. In these cases, multiple treatments have been successfully used such as 40% topical idoxuridine application, cryotherapy and surgical excision. Cryotherapy should be tried as first choice treatment because it is easy to use and there are almost no side effects (6). In humans cidofovir and imiquimod ointments are used to treat orf lesions (45). In South Africa the use of vaseline oil or engine oil is the most common treatment. Also in some rural communities in the North West province the disease is treated by using the root of a plant called sebeta or morototshweshwe, which has been identified as *Cassia italica* (36). Thuja 30c is a kind of homeopathic drug and it has been used successfully in the treatment of orf in human, sheep and goats (61). Mombeni et al. (2012) have

claimed that in Khuzestan, Iran goat pox vaccine could cure contagious ecthyma in lambs and sheep. Therefore, they can be used in outbreaks of contagious ecthyma (62).

### **Control**

Although vaccination is an efficient and cost effective method of preventing the Orf virus infections, disinfection practices and zoo sanitary measures should also be implemented along with it. For preventing the spread of the disease, isolation of infected animals can be helpful. The new animals should be quarantined before mixing with other animals of a farm to prevent the entry of the Orf virus (4). Because of the zoonotic nature of the disease, protective gloves and face masks should be worn by farmers and veterinarians (29).

One of the most important measures of control is to avoid bringing affected animals to public places such as exhibition or animal market (41). Some apparently healthy carrier animals without any signs of the disease may spread the virus. Necessary measures should be taken to prevent the virus incidence in the farm through equipment and other fomites. Animals should not be allowed to feed on vegetation or rough straw or feed to reduce the risk of cuts on the muzzle or in the mouth, as the virus can enter through the cuts. Moreover,

particularly the migration of the infected animals from one place to another should be prohibited. However, the Orf virus once it has entered a herd or flock is difficult to eradicate, (4). In most cases, animals that have been infected or vaccinated with OV are resistant to natural infections. However, outbreaks of Orf have also been reported in Orf vaccinated animals (8).

Various programs have been suggested for vaccination in the early stages of an outbreak. Affected animals must be isolated and the rest of the animals should be vaccinated. When a large number of animals already have the disease, vaccination is not very useful. The permanent presence of the disease in a herd and grassland from one year to another is common, and in this condition lambs should be vaccinated in 6 to 8 weeks of age. To prevent the disease observed in previous years, vaccination of indoors lambs must be timely performed (28). Since antibody transferred via colostrum cannot induce protection from a CE virus challenge in one month old lambs, to protect young lambs from outbreaks of CE the lambs themselves must be vaccinated with CE virus (53). But some believe that vaccinating ewes few weeks before lambing can reduce the likelihood of disease in ewes at lambing time, thus

minimizing the risk of an epidemic in lambs (5).

Reinfection in animals recovered from the disease as well as vaccinated animals, may be seen after several years. This reinfection beside the persistence of the virus in soil and environment make the eradication of the disease difficult in herds at least for 12 years (40, 47). Considering the seasonal and self limiting nature of Orf, and the apparent low mortality and short immunity of vaccine in some places such as South Africa, only a small proportion of farmers use commercial vaccine against Orf (36). But in a study on 19 dairy sheep farms in Argentina, it was found that in 47.3% of the farms ecthyma vaccine is used (63).

During the outbreak of contagious ecthyma disease in the south of Iran a high dose of the goat pox vaccine obtained from Razi Institute (Karaj-Iran) was injected to all of the animals in three flocks. Three days after vaccination, no new cases were seen and the sick animals recovered rapidly. The cured animals will be immune for 2-3 years after the vaccination but authors such as Renshaw (1978) believe that goat pox and Orf vaccine cannot be used for cross immunogenicity (62).

### **Prevention**

There are various kinds of vaccines against Orf disease, but live attenuated vaccines are always considered superior to others and

are used in some parts of the world where the disease is endemic. An autologous vaccine can be prepared after triturating the scab material in saline followed by the addition of penicillin/streptomycin. On the other hand, live contagious ecthyma vaccines contain live virus prepared from propagated in tissue culture or dried scabs. The vaccines should be used in the farms where infections have occurred in the past. Recently vaccinated animals should be isolated from unvaccinated animals. Live attenuated tissue culture vaccine is effective in reducing the severity of the disease. However, the duration of immunity after vaccination is controversial. In the vaccinated animals the outbreaks have occurred due to break down of immunity by the virulent strain of Orf virus. However, the main disadvantage of this vaccine is that it can cause the disease by disseminating the vaccine virus so it is unable to confer solid immunity to reinfection (4).

Some researchers believe that live Orf vaccines reduce losses Only by reducing the duration and severity of clinical disease (64). According to reports of outbreaks caused by vaccine virus, routine vaccination against the Orf disease in herds where the disease was already rampant, is not recommended. (28). Recently, researchers used a wild virus strain

attenuated through a serial passages on primary chicken embryo fibroblast tissue cultures as a vaccine against the disease (29).

In a study, a single layer of sheep embryo skin tissue cells are cultured and then infected with ecthyma virus and incubated at  $36.5 \pm 5^{\circ}\text{C}$  for several days. The attenuated virus collected in 2 stages was then used for the production of vaccine (65). Sheep infection with full piece of virus in recombinant vaccines (that indicate Orf virus genes) creates significant protection against Orf virus infection in the field compared with the control group lambs that received only the vaccine virus as a vector. Vaccine containing goat strains are more effective in goats compared to vaccines derived from strains of sheep (66). The susceptibility of sheep to reinfection, possibility of a chronic disease in sheep and viral resistance to dry justify the difficulty of eradication when the herd becomes infected (5).

### **The Status Of Contagious Ecthyma And Its Perspective In Iran**

Contagious ecthyma is endemic in Iran, and it is sometimes difficult to differentiate it from similar diseases, especially sheep and goat pox and peste des petits ruminants (PPR). This disease in sheep and goats is a native infectious and zoonotic disease in some regions of Iran (47).

There are many reports of the disease specially in Southern parts of Iran like Khuzestan. This disease is not eradicated in Iran because there is no specific contagious ecthyma vaccine in this country (Iran). Therefore, the disease has occurred with a high prevalence and low mortality rate and has caused enormous economic losses each year especially in young animals. Mombeni et al. reported an orf outbreak in 2012 in Khuzestan. To control outbreaks and treat of affected animals, they used goat pox vaccine in three herds located in different districts. These herds contained lambs, kids, sheep and goats showing characteristic signs of the disease in 566 (38.2 %) of the 1481 livestock. The vaccination was successful after three to four days, and no new cases were seen and the sick animals recovered rapidly. Capripox vaccine, obtained from Razi institute (Karaj-Iran) and transported while maintaining the cold chain, was injected in infected herds using higher doses of 1 ml per sheep and goat and 0.5 ml per lamb and kid via subcutaneous injections. Therefore, Mombeni et al. found the Razi-institute goat pox vaccine effective to prevent and treat the contagious ecthyma disease in infected animals in the herds of Khuzestan province (62).

In 2014 Davari et al., after molecular analysis of extracted DNA, recorded a

strain named Orf-059-Shiraz in the GeneBank and subsequently underwent phylogenetic analysis (67). In another research by Davari et al. 50 muzzles crusts were collected from involved goats and sheep and PCR was carried out for molecular detection. Twenty-five (50%) of 50 scab specimens were Orf positive, four (8%) were pox virus positive and one (2%) was positive for PPRV. For the first time, this study demonstrated the characteristics of sheep and goat contagious ecthyma in Fars province, Iran (47).

In 2006, Nourani and Maleki performed a pathological case report of contagious ecthyma in Iran. An outbreak of camel contagious ecthyma (CCE) in dromedary and bactrian camels in Qum Province (an arid area with hot and dry climate), north of Iran, was confirmed by Barani et al. in October 2009. This report was the first CCE outbreak in Iran (68). Scabs and nodules from seven affected animals were collected for virus identification. Results showed that 27 camel calves less than one year old and one male bactrian camel were affected and no adult female camels were found to be infected. The prevalence of the disease in adult camels and camel calves was 30.33%, 1.5% and 100%, respectively. Affected animals showed the swelling of head with nodular lesions around the lips, which developed into pustules and fissured

crusts. The history of contact with sheep or goats, previous involvement with this disease, food resources and season can all have a role in epidemiology of the disease. Morbidity rate was reported to be low (10%-20%) in adult camels (69). Morbidity of 100% in calves had been described by other researchers (70). It was also reported that 98% of the cases of Orf in camel occurred in calves aged less than one year, with a mortality rate reaching 38% (71). Mombeni reports an outbreak of CCE in a herd in Southwest Iran. The infected animals exhibited an increase in body temperature, severe papules on the lips and legs, profusion of saliva, facial edema, and foul mouth smell. *Staphylococcus aureus* was identified in some samples. The morbidity and mortality rates were 70.6 and 6%, respectively. This report was the second report on the presence of CCE in Iran. There is no vaccination program against CE virus for camels in Iran, therefore establishing such a program will be helpful (72).

Parapox virus is the causative agent of Orf disease which is basically seen in sheep and goats. It can be transferred to human being by several methods like direct contact with infected animals or indirect contact with infected meat or contaminated butchery instruments like knives. The skin lesions are usually found in fingers. In 2007

Shirzadi et al. reported eleven patients infected with Orf disease in Kohgiluyeh and Boyer-Ahmad province, Iran (72). In another report by Taghipour et al. eight patients were infected with orf viruses in the northern of Iran (Mazandaran) (73). There were other human Orf disease cases in Karaj province, Iran, Kashan City, Iran and Fars province (shiraz) that were reported by Varshovi, Afzali and Nourani respectively (6, 74, 75). In Iran there is no specific contagious ecthyma vaccine, but goat pox vaccination is a part of governmental plans. This attenuated live vaccine along with Anthrax vaccine are impregnated simultaneously on kids and goats which are older than 6 months, once a year. Nevertheless, prevention of the disease would be difficult because Capripoxvirus remains viable on the hair or wool of previously infected animals for several months. Moreover, orf virus is resistant to the environmental conditions (47, 76, 77). Therefore, establishing vaccination program in Iran seems to be essential in controlling and eradicating of the disease.

## **CONCLUSION**

Contagious ecthyma is a highly contagious viral disease that is too important economically. This disease affect the skin of infected animals like goat and some other domesticated and wild ruminants and

is of zoonotic importance. The virus enters mainly into a new area or region by introduction of infected animals. To prevent introduction of contagious ecthyma, it is crucial to restrict animals and their products movements. Suitable decontamination procedures must be used for animal products before entering non endemic areas. If a new infected animal is confirmed in an area, the animal should be quarantined and infected or exposed animals should be slaughtered and the premises should be cleaned and disinfected. Susceptible animals must be vaccinated with a potent and efficacious vaccine and keeping the infected herd(s) in quarantine should be considered. If the disease has spread out over a large area, vaccination is the most effective way to control economic losses, however, feasibility of eliminating infected, exposed flocks by slaughtering, suitable disposing of animals and contaminated material, cleaning and disinfecting contaminated equipment and premises should also be considered. Some sheep and goats may act as carrier animals and they may have no symptoms of the disease. With all these measures, the virus may persist for many months in contaminated areas. To prevent the disease from spreading, the imposition of quarantines on farms and infected premises is required. Depopulation of infected and

exposed herds should be implemented if limited spreading has occurred. When the disease has spread extensively, massive vaccination and the restriction of animal movements in the infected area, is a viable and ideal strategy to control and then eradicate Orf. Orf is a zoonotic disease in nature, so these cases should be handled with care and caution and the public should be informed about the communicability of the disease to humans.

### COMPETING INTERESTS

The authors declare that they have no conflict of interests.

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