Review Article
Volume 6:4, 2022

Journal of Animal Health and Behavioural Science

ISSN: 2952-8097 Open Access

Review on Pathological Changes and Diagnosis Techniques of Contagious Ecthyma in Small Ruminant

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Abstract

Contagious ecthyma or alternatively called contagious pustular dermatitis is a viral disease of sheep and goat caused by contagious ecthyma virus. This disease is most commonly seen in small ruminants though camelids and rarely other ruminants can also be affected. The objective of this review is to give emphasis about pathological features (lesions) and diagnosis techniques of contagious ecthyma in sheep and goat. Contagious ecthyma is an acute, contagious, debilitating and economically important zoonotic viral skin disease that affecting sheep, goat and some other domesticated and wild ruminants. The disease initially presents itself as papules that progress to blisters or pustules before encrusting. They can spread around the outside and inside of the mouth, face, lips, ears, vulva, lets, scrotum, teats, and feet, usually in the interdigital region. Necropsy findings are scattered hemorrhagic papules, vesicles, pustules, and numerous multifocalto-coalescing proliferative and necrotizing scabs affecting haired skin at the mucocutaneous junctions (commissures) of the lips and affecting the oral papillae. A definitive diagnosis is based on viral isolation and an immunologic test. Histopathology is also helpful. Molecular identification and investigation several molecular diagnostic methods including polymerase chain reaction, serological tests such as agar gel precipitation test, agglutination test, complement fixation test. Since it is very economically important disease but it does not have effective diagnosis techniques further research should be conducted to develop its effective treatment.

Keywords: Contagious ecthyma • Diagnosis • Pathology • Small ruminant

Introduction

Small ruminants have a significant role in terms of generating income in the form of meat, hide, wool and milk to landless and small or marginal farmers particularly in arid and semi-arid regions of the country. However, health challenges deterring by infectious diseases are still hindering the productivity and causes huge economic losses [1]. Contagious ecthyma one of an acute, contagious, transferable and economically significant skin disease that puts detrimental effects on animals, principally small ruminants and other native and wild ruminants. Contagious ecthyma is caused by a parapoxvirus and results in dried spiny feed erode the tissue of lips, mouth and nostrils during grazing [2]. Gingiva and adjoining incisors, tongue, palates develop lesions and categorized by single or numerous amalgamating papules concealed with yellowish exudates [3]. Humans can be infected after contact with affected lesions.

Although the rate of morbidity is generally higher than the mortality rate, younger animals such as lambs are more susceptible for the disease and the mortality is significantly higher [4]. The disease is economically important disease, but due to insufficient review on the disease about its pathological change on the affected cells because of limited diagnosis techniques on this disease. Therefore, the objective this review paper is to giving highlights about pathological features (lesions) and the diagnosis techniques on contagious ecthyma in sheep and goat.

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Date of Submission: 13 July 2022; Manuscript No. ahbs-22-71230, **Editor assigned:** 15 July 2022, PreQC No. P-71230; **Reviewed:** 28 July 2022, QC No. Q-71230, **Revised:** 03 August 2022; Manuscript No. R-71230; **Published:** 11 August 2022, DOI: 10.37421/2952-8097.2022.6.164

Literature Review

Epidemiology

Contagious ecthyma is caused by orf virus which belongs to the family of poxviridae and based on the classification of International Committee on Taxonomy of Viruses (ICTV). Causative organism of the contagious ecthyma is a double-stranded DNA, enveloped virus. At electron microscopy, this large virus has a characteristic "basketwork" or "ball-of-wool" appearance due to genomic microtubules [5].

Contagious ecthyma is found worldwide and is more common in late summer, fall and winter on pasture and in feedlots. This seasonality is likely related to increased close contact among animals, as well as increased physiological stress from lambing or cold weather [6]. It has been reported from many countries [7]. It has been occurred from many countries. It was initially reported by Zellor in 1920 from South West Africa. Since then, it has been reported from almost all parts of world those involved in rearing sheep, goats, cattle, dogs, camel and both free living wild and captive animals. For instance, the disease outbreaks have been reported in 1992 by FAO/OIE from Norway, China, Indonesia, Iraq, Brazil, Ethiopia and [8].

Host range

Contagious ecthyma is an acute, contagious, debilitating and economically important zoonotic viral skin disease that affecting sheep, goat and some other domesticated and wild ruminants. Several countries report incidences of orf viral infections in human, among which UK reports on an average 3 cases per year from 2004- 2014 [3].

Transmission

The Orf virus is transmitted from infected animals to non-infected animals direct contact or by exposure to fomites carrying the virus [4]. Its transmission may also occur during minor or major surgical intervention, hand contact, drenching and ear tagging. Animal with immune defects and persistently infected animals play an important role in the maintenance of the orf virus in the nature [6]. The virus is highly resistant to adverse environments and can persist for many years. Human acquire the infection from contact with

infected or recently vaccinated animals and/or fomites in conjunction with skin trauma [9]. Human infection typically is associated with occupational animal contact. However, human-to-human transmission has not been reported [10]. Iatrogenic transmission of orf virus may also occur during minor or major.

Morbidity and mortality: In flocks where the disease occurs for the first time, morbidity rates can be up to 70%. Mortality however, is usually low (<1%), although increased rates (up to 90%) have been reported in lambs after secondary bacterial infections [11]. The disease is most danger in young animals which may refuse to nurse and can die of starvation [12]. Aggravating factors for Orf virus infection include; age, congestion due to increased stocking density, stress, immunosuppressive diseases, prolonged parturition and forage weed [4].

Pathogenesis

The virus enters the body through broken skin and replicates in the cytoplasm of the host epithelial cell [10]. Following an incubation period of 2-14 days, papules and vesicles develop around the margins of the lips, nostrils, eyelids, gums, tongue, or teats; skin of the genitalia; or coronary band of the feet. The viral replication leads to edematous and granulomatous inflammation of dermal cells. Typical lesions are initially erythematous spots followed by formation of papules, vesicles, pustules with a yellowish creamy appearance and scabs that finally become dry and shed with no scar remaining. This development pattern takes place in a period of one to two months. The vesicles form pustules that rupture and finally scab over. Primary skin lesions develop two to six days after infection at the portal of entry of the virus to the body and there is no detectable viremia [13].

Diagnosis

Diagnosis is based on presence of symptoms and a history of contact with infected sheep, goats, or wild ungulates, the characteristics and location of the lesions, as well as herd history of previous outbreaks. A definitive diagnosis is based on viral isolation and an immunologic test. Histopathology is also helpful. Molecular identification and investigation several molecular diagnostic methods including Polymerase Chain Reaction (PCR) and Quantitative PCR (qPCR) have been developed to detect orf virus [6]. In addition, serological tests such as Agar Gel Precipitation Test (AGPT), agglutination test, complement fixation test (CFT), Enzyme Linked Immunosorbent Assays (ELISAs), Serum Neutralization Test (SNT) could be employed [14]. The classical roles for diagnosis, which might depend on histopathological examinations and clinical manifestations were less accurate, since the isolation of the virus is thought to be the golden standard method, but its need time. Nevertheless, with the development of molecular biology, as the polymerase chain reaction technique is widely used to amplify genomic fragments from the specimens of diseased sheep and it has a strong tool in molecular diagnosis [15].

Necropsy findings significant gross necropsy findings included scattered hemorrhagic papules, vesicles, pustules, and numerous multifocalto-coalescing proliferative and necrotizing scabs affecting haired skin at the mucocutaneous junctions (commissures) of the lips, extending into and affecting the oral papillae, the medial canthus of the left eye, and the distal prepuce [16]. 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, abomasums, and small intestine involvement. Specified lesions of the disease are proliferative and after a while the central cells fall, which causes ulcer like lesions [17].

Clinical signs

The disease initially presents itself as papules (elevation of the skin) that progresses to blisters (fluid-filled pouches) or pustules before encrusting. These lesions are found in the skin of the lips, multifocal-to-coalescing necrotizing and proliferative cheilitis and dermatitis (Figure 1C). They can spread around the outside and inside of the mouth, face, lips, ears, vulva, lets, scrotum, teats, and feet, usually in the interdigital region, eye (palpebrae, medial canthus, focal hemorrhagic pustule (Figure 1D). Extensive lesions on the feet can lead to lameness in adults and young animals [15]. The infection is spread by direct and indirect contact from infected animals or by contact with infected tissue or saliva containing the virus. The diagnosis is generally based on clinical signs, which are typical. The oral lesions are usually seen in young animals born into endemic herds. Orf lesions are differentiated from oral lesions of FMD and Bluetongue by the clinical signs of crusty scabs as opposed to erosions and ulcerative lesions [10].

The Orf lesions appear 6 to 7 days after infection. Proliferative cauliflower lesions are usually confined to the muzzles (Figure 1A), lips, nostrils, mucous membranes of the mouth, eyelids and ears, and teats of nursing ewes [6]. The lesions on the udder (Figure 1B) are due to direct contamination during nursing that cause mastitis (inflammation of the mammary gland) in does and ewes. Severe to moderate enlargement of the lymphnodes, arthritis, and pneumonia

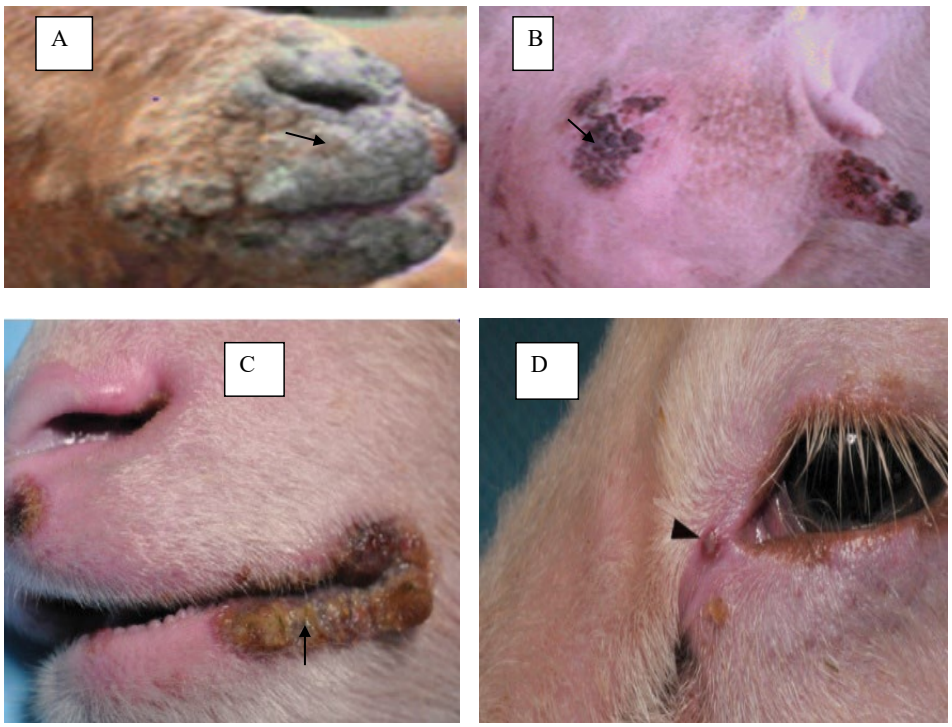

Figure 1. (A): Small ruminant with sore mouth (B): contagious ecthyma lesion on udder (C): lips and philtrum; multifocal-to-coalescing necrotizing and proliferative cheilitis and dermatitis (D): palpebrae, medial canthus and focal hemorrhagic pustule.

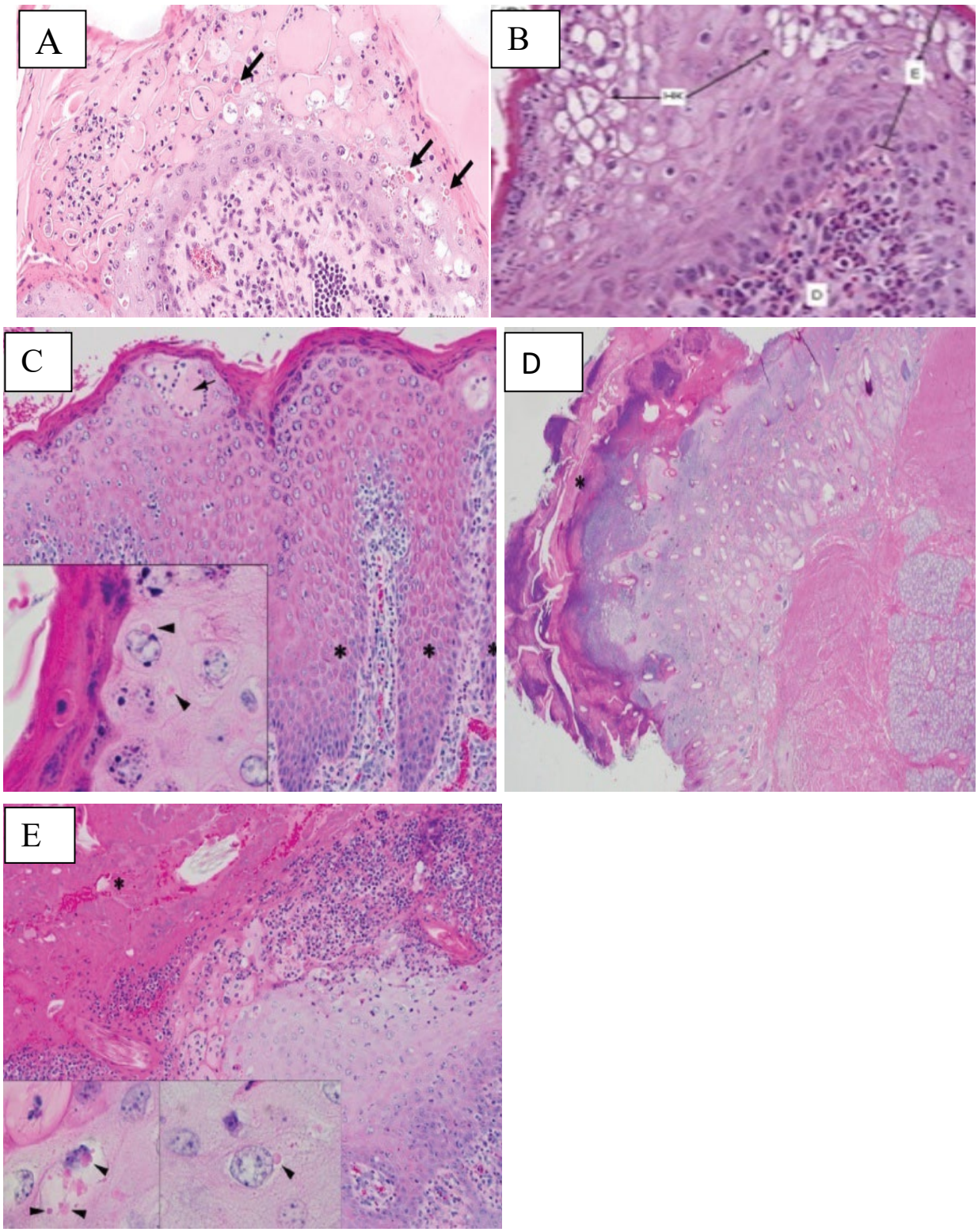

Figure 2. (A): The lip mass in goat showing epithelial cell degeneration with many intracytoplasmic viral inclusion bodies indicated with arrow. (B): Epidermal hyperplasia, keratinocyte degeneration, hyperkeratosis, and infiltration of inflammatory cells. (C): Lip commissure. Epithelial hyperplasia (arrow) with increased thickness (acanthosis) with prominent intracellular clear spaces/bridging (spongiosis), anastomosing rete ridges, and a vesicle (arrow). (D): Focally, extensive, severe, proliferative, and necrotizing dermatitis, with epithelial hyperplasia, and necrosis. (E): Epithelial hyperplasia, necrosis, and loss with overlying serocellular crust composed of keratin, proteinaceous fluid, degenerate neutrophils, and numerous mixed bacteria.

resulting from sore mouth has been reported [13]. The clinical signs in captive wild animals were like domestic sheep and goats which had poor general body condition and difficulty in feeding and loss of body weight [15].

Gross lesion: Lesions seen at necropsy generally resemble those in the live animal. Necropsy findings significant gross necropsy findings included scattered hemorrhagic papules, vesicles, pustules, and numerous multifocalto-coalescing proliferative and necrotizing scabs affecting haired skin at the mucocutaneous junctions (commissures) of the lips and affecting the oral papillae, the medial canthus of the left eye, and the distal prepuce [18].

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, abomasums, and small intestine involvement [10].

Specified lesions of the disease are proliferative and after a while the central cells fall, which causes ulcer like lesions. Numerous lesions particularly on muzzle, mouth and face region of animals are obvious. Animals of various ages have very painful erythematous macule, pustule, vesicle, papule, and then scab development [5,19].

Histopathological lesions: Histological, the development of lesions following natural infection of skin with Orf virus occurs in three separate, but confluent, phases. The separate phases can be described as cellular infiltration, tissue response and recovery. Following skin abrasion, infection with Orf virus leads to a cellular response within 24 hours that cannot be differentiated from the normal response to abrasion [20]. Thereafter, a rapid increase in the number of neutrophils peaks at around 24 hours to form a band of cells located above a layer of active fibroblasts [7]. T-cells and B-cells accumulate during the following 48-72 hours. During this period of immune cell infiltration the epidermal cells begin to vacuolate and by the fifth day after infection the typical ballooning degeneration of infected epidermal cells is evident [3].

Microscopic changes are typical of poxvirus infections, including epidermal hyperplasia, keratinocyte degeneration, hyperkeratosis, and infiltration of inflammatory cells (Figure 2B). Late in the course of the infection the epidermis expands into the underlying dermis forming an intricate epithelial network (rete pegs) that persists after macroscopic resolution of lesions [21] (Figure 2C). Also it includes ballooning degeneration of keratinocytes and eosinophilic cytoplasmic inclusions bodies (Figure 2A). Rarely, lesions have also been reported in the esophagus, rumen, omasum, lungs, heart and lower intestinal tract. In addition to skin lesions, Boer goats with severe infections had severe to moderate lymphadenopathy of the draining lymph nodes in areas of affected skin [3].

The epidermis disintegrates resulting in a necrotic, polymorphonuclear infiltrated dermis. A scab covers the lesion post-infection and comprises the necrotic stratum papillare, the infiltrated cells of the cellular immune response, wool fibres, fibrin, collagen and serum. Under the scab the epidermis continues to hypertrophy. Later, the skin surface is largely indistinguishable from that pre-infection [3]. It has been suggested that the 'papillomatous' lesions often associated with the lips may occur due to a reduced protection to viral infection afforded by the thinner epidermal layers found in the buccal tissues [4]. Epithelial hyperplasia, necrosis, and loss with overlying serocellular crust composed of keratin, proteinaceous fluid, degenerate neutrophils, and numerous mixed bacteria (Figure 2E). Extensive, severe, proliferative, and necrotizing dermatitis, with epithelial hyperplasia, and necrosis was observed (Figure 2D). The healing process may be disrupted by a concomitant bacterial infection; a mild infection may result in debris containing lymphocytes and bacteria, whereas a severe infection may disrupt the dermis itself [3].

Economic importance

Economic importance of Orf can cause welfare and economic impacts usually associated with poor growth in lambs, mastitis in ewes and death in worst case scenarios [10]. Production losses associated with reduced growth rate or weight loss in lambs may be considerable, due to a reluctance to suckle or graze. Losses due to the disease will depend upon the severity of infection and the within-flock prevalence, which may vary considerably from below 10% to all of the flock being affected [22]. Presence of contagious ecthyma in a country limits the trade of new breeds and development of intensive animal's production. The level of impact varies from country to country both qualitatively and quantitatively. Contagious ecthyma is one of the animal bioterrorist agents as it; (a) Causes high morbidity and mortality. (b) It has potential for rapid spread. (c) Potential to cause serious socioeconomic disturbances (trade limitations) or public health consequences. Factors resulting in stress or an increased transmission of virus, such as high stocking density or transport, may play a major role in determining the course of flock infection [8]. Thus a significant impact will be seen in severe outbreaks where mortality may be considerable [19].

Contagious pustular dermatitis lesions on the teats of ewes may be associated with an increased level of mastitis in the flock. In consequence, the udder half may be lost to milk production and the ewe culled as a result. Other losses associated with growing lambs may be associated with strawberry foot rot. Infected lambs show a reduced growth rate and an extended time to finishing [23]. This inevitably has a deleterious economic impact for the farm. It also causes mortality and weight loss in lambs that are reluctant to eat because of oral and peri-oral lesions. Its biosecurity is paramount importance (USDA, Agricultural bioterrorism act of 2002. United Kingdom has documented 2.167 million contagious ecthyma affected sheep, leading to £10 million loss, includes both treatment and production losses. It is reported that prevalence of Orf in UK to be 1.88% and 19.53%, in ewes and lambs respectively.

Treatments

Treatment of contagious ecthyma in sheep is usually unnecessary as the disease normally resolves without intervention within 5-7 weeks for a primary infection and within 2-3 weeks for subsequent infections. In cases where lambs are having obvious difficulty in suckling, bottle feeding to prevent severe weight loss and debilitation may be necessary [1]. The use of antiviral agents, in both sheep and goat, has been proven to be effective against Orf virus infection, although currently none of the drugs tested are licensed for such use. The antiviral drug Cidofovir has powerful anti-orf activity. Similar results have been obtained using a cream containing Imiquimod (5%) [7]. A formulation of Cidofovir that can be sprayed directly onto Orf lesions has been tested in sheep with good results. The most frequent secondary infections result from the uncontrolled growth of skin commensal *Streptococci* spp. and *Staphylococci* spp. Antibiotic use is usually unnecessary except in the most severe cases, but the topical application of antibiotic formulations or antiseptics and in some cases systemic application may be appropriate. As with any antibiotic usage, they should be used prudently and only as directed by a qualified veterinary practitioner [9,23].

Conclusion

Contagious ecthyma, caused by parapox virus, is one of the most common skin diseases of sheep, goats. The primary lesion develops at the mucocutaneous junction of the lips and around erupting incisor teeth and may extend to the mucosa of the buccal cavity. Due to contagious nature of the disease, it is easily transmitted to other animals within herd and also to animals of other herd when they come in contact with infected animals while grazing. Diagnosis of Orf based on traditional method is not accurate to identify the level of infection and as a result, we established a molecular diagnostic approach using PCR for confirmation of the virus and discriminating from other bacterial and viral pathogens. Future works will be focused on the detail phylogenetic analysis of the viral strains in all regions of the country. A definitive diagnosis is based on viral isolation and an immunologic test. Histopathological investigation was made with standard technique for fixation, dehydration, cleaning, embedding, sectioning and staining, that there was ballooning degeneration in stratum granulose. Both parenteral and topical antibiotics may help combat secondary bacterial infection of the skin lesions. In endemic areas, appropriate repellents and larvicides should be applied to the lesions to prevent myiasis.

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How to cite this article: Melkamu, Samrawit. "Review on Pathological Changes and Diagnosis Techniques of Contagious Ecthyma in Small Ruminant." J Anim Health Behav 6 (2022): 164.