Incursion of infected *Culicoides obsoletus* midges from northern Europe in 2007 is thought to have been the cause of the UK bluetongue outbreak. Recognition and reporting of suspect bluetongue cases is an important component of surveillance to monitor for the re-emergence and spread of bluetongue infection in 2008. Picture, Institute for Animal Health, Pirbright

Differential diagnosis of bluetongue in cattle and sheep

SUSANNA WILLIAMSON, NICK WOODGER AND KARIN DARPEL

IN 2006, bluetongue virus serotype 8 (BTV-8) caused the first recorded bluetongue outbreak in northern Europe. This occurred in countries with no previous history of bluetongue virus incursion, including the Netherlands, Belgium and Germany. Following a halt to disease transmission over the winter, the virus re-emerged in 2007, spreading throughout northern Europe and eventually reaching the UK in September 2007. The chances that BTV-8 will emerge again in the UK in 2008 are considered to be very high. Due to the wide spectrum of clinical signs and variation in severity of disease seen in cattle and sheep with bluetongue, a variety of diseases may resemble some or all features of bluetongue infection. This article describes the main differential diagnoses of bluetongue in cattle and sheep, and summarises the distinguishing features and laboratory tests that can assist in their differentiation.

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BLUETONGUE

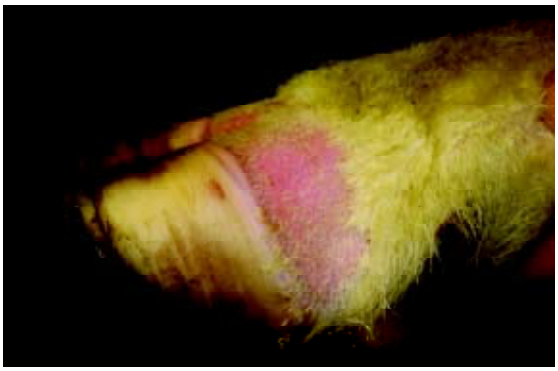
Bluetongue virus can infect all ruminants, although clinical disease in endemic regions is mainly associated with certain breeds of sheep, while cattle remain subclinically infected. The severity of disease is influenced by factors such as the virulence of the bluetongue strain, the livestock breed and individual susceptibility. Disease caused by the BTV-8 strain implicated in the recent outbreak in northern Europe is characterised by unusually severe clinical signs in cattle. However, a proportion of infected animals, especially cattle, do not show clinical signs. The spectrum of clinical disease seen in the recent northern European outbreak is wide, ranging from animals expressing one or two clinical signs to severely ill animals.

Erythema above, and exudation and crusting at, the coronary band of a cow with bluetongue. Picture, VLA – Bury St Edmunds

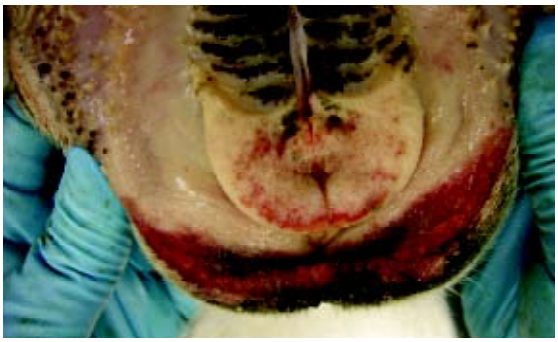
Bluetongue virus replicates primarily in endothelial cells of capillaries and small blood vessels. The degenerative, necrotic and hyperplastic changes induced by the virus cause vascular occlusion, stasis and exudation. Ultimately, these changes lead to oedema and haemorrhage with secondary tissue changes, particularly in associated epithelial surfaces. Endothelial cell damage is a major trigger for disseminated intravascular coagulation through the release of tissue thromboplastin, promotion of platelet aggregation and activation of the intrinsic clotting pathway following exposure of endothelial basement membrane col-

Suspicion of notifiable diseases including bluetongue must be reported to the Divisional Veterinary Manager (DVM) of the local Animal Health Divisional Office (AHDO) in Great Britain. Details of procedures relating to notifiable diseases are available on DEFRA's website at www.defra.gov.uk/animalh/diseases/notifiable/index.htm

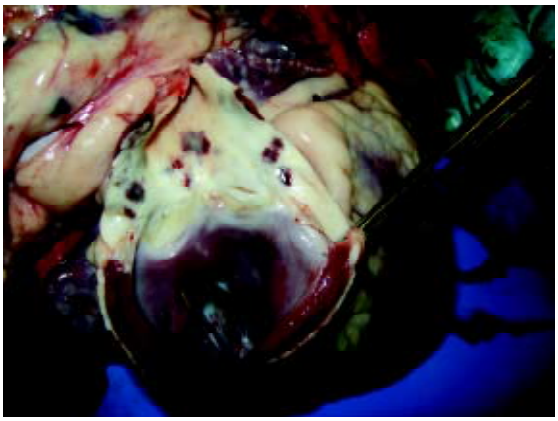
Erosion and crusting of the muzzle of a cow with bluetongue. Picture, VLA – Bury St Edmunds



Reddening at, and above, the coronary band in a sheep with bluetongue. Picture, Arbovirology, Institute for Animal Health, Pirbright



Reddening and poorly demarcated erosions of the dental pad and lip of a ram with bluetongue. Picture, VLA – Bury St Edmunds



Intramural haemorrhages at the base of the pulmonary artery in a sheep with bluetongue. Picture, VLA – Bury St Edmunds

lagens. The resulting coagulopathy contributes to the haemorrhagic diathesis seen with bluetongue infection. The early phase of clinical disease is non-specific, and resembles signs associated with many other infectious diseases characterised by pyrexia, malaise, inappetence and milk drop.

Bluetongue virus is transmitted via the bites of blood-feeding *Culicoides* species (biting midges), with infection being introduced into herds and flocks by the incursion of infected midges dispersed from another infected holding or via the movements of viraemic ruminants. As subsequent spread of bluetongue virus within

Clinical signs of bluetongue in cattle and sheep

Many animals with bluetongue (especially cattle) remain subclinically infected. When clinical disease does occur, the signs are non-specific in the early stages, and resemble those of many infectious diseases. They include pyrexia, malaise, inappetence and milk drop in lactating animals.

Sheep

The first signs of disease, which often coincide with the onset of fever (>40°C), include:

- Hyperaemia and congestion of nasal, buccal and gingival mucosae;
- Conjunctivitis and lacrimation;
- Oedema of the face and lips.

These signs can remain mild, but often progress to:

- Mucopurulent, sometimes bloodstained, nasal discharge;
- Erosions, ulceration and haemorrhages on the nose, lips, buccal mucosa and tongue;
- Severe facial oedema, which may present as 'bottle jaw';
- Salivation. Animals may be reluctant or have difficulty eating and drinking.

Occasionally:

- Swelling of the tongue leads to cyanosis, giving the disease its name;
- Pharyngeal and/or oesophageal paresis can lead to excessive salivation and aspiration pneumonia if food is inhaled into the lungs;
- Respiratory signs, including hyperpnoea, dyspnoea and respiratory distress, may occur in cases of severe bluetongue.

Coronitis develops in most sheep, usually between eight and 14 days after infection, and presents as:

- Lameness of variable severity affecting more than one limb;
- Warm lower limbs and feet;
- Generalised reddening of the skin above the coronary band;
- Serosanguineous exudate around the coronary band in severe cases;
- Hunched appearance or sheep may kneel, or be reluctant to rise and move;

Skeletal muscle necrosis also occurs and contributes to a stilted gait and stiffness.

Cattle

All or some of the following signs may be seen:

- Conjunctivitis and lacrimation;
- Excess salivation and nasal discharge (serous to mucopurulent);
- Hyperaemia and haemorrhages on oral, nasal and ocular mucosal surfaces;
- Erosions and ulceration of oral and nasal mucosal surfaces;
- Crusting and shedding of the mucosa of the muzzle;
- Petechiation of the udder and teat skin;
- Reddening and ulceration of the teats.

Coronitis is less consistent than in sheep but may cause:

- Lameness or reluctance to move and tender, warm feet;
- Reddening of the skin above the coronary band;
- Serous crusting at the level of the coronary band.

Bluetongue-infected cattle often only express one or two of these signs together with non-specific features such as pyrexia, malaise and inappetence.

Chronic effects of bluetongue in sheep and cattle

- Secondary bacterial infections of bluetongue virus-induced lesions are common, affecting ulcerated areas and the lungs
- May manifest as aspiration pneumonia due to dysphagia
- Pressure points, including joints, may become infected in animals with severe coronitis and lameness
- Economic losses may include reduced milk production, loss of condition, reduced weight gain and severe wool break

The effects of bluetongue virus infection on reproduction are poorly understood, but are believed to include:

- Temporal infertility (azoospermia) in rams and bulls;
- Reduced conception rates in cows.

The ability of BTV-8 to cross the placenta and infect the fetus is currently being investigated, with the outcome likely to depend on the stage of pregnancy. Abortion, fetal deformity, stillbirth, birth of weak calves or the birth of healthy viraemic calves could all occur.

cattle herds and sheep flocks relies on newly initiated insect transmissions, infection rates are less predictable than for some contagious (aerosol or contact) diseases, which may progressively infect an increasing proportion of a herd or flock. Whether further infections occur depends on many factors, including the density and activity of local midge populations (which are mainly temperature and humidity dependent), the vector competence of the local midge population and biting rates on host ruminants. In UK bluetongue-infected herds or flocks in which serosurveillance was carried out, the number of infected animals ranged from a single animal in a flock of 2120 sheep to 34 animals in a herd of 130 cattle. During autumn 2007, 82 per cent of cattle herds and 75 per cent of sheep flocks reporting clinical bluetongue had single clinical cases, which is likely to reflect a combination of low infection rates within herds and a proportion of infected ruminants, especially cattle, not showing any clinical signs (Institute for Animal Health, Pirbright, unpublished data).

The differential diagnoses for bluetongue relate mainly to similarities in all or some of the basic presentations of oedema, haemorrhages and epithelial damage.

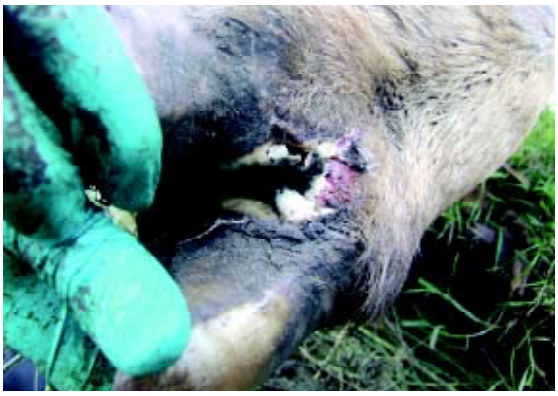
Images of the lesions in the first cases of bluetongue in UK cattle and sheep are available at www.defra.gov.uk/corporate/vla/science/science-viral-bluetongue.htm. Further images and information about the bluetongue virus can be viewed at www.iah.ac.uk/bluetongue

NOTIFIABLE DISEASES OF CATTLE AND SHEEP

The table below describes the general characteristics assisting differentiation between bluetongue and other notifiable diseases of cattle and sheep.

Foot-and-mouth disease

The first case of bovine bluetongue in the UK was reported to the local DVM as a suspected case of foot-and-mouth disease (FMD). Early clinical signs of FMD are non-specific and indistinguishable from developing



Ruptured vesicle on the foot of a cow with foot-and-mouth disease. Picture, Ryan Waters

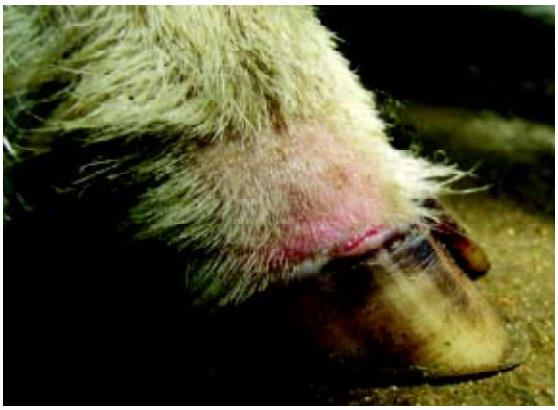
CLINICAL CHARACTERISTICS TO DIFFERENTIATE BLUETONGUE FROM OTHER NOTIFIABLE DISEASES OF CATTLE AND SHEEP

Disease	*Domesticated livestock species affected*	*Morbidity**	*Mortality*	*Transmission by direct animal contact*	*Distribution of oral lesions*	*Distribution of other lesions*	*Nature of lesions*
Bluetongue	Cattle Sheep and goats Camelids	Variable in sheep and goats, low in cattle	Variable in sheep and goats, very low in cattle	None	Mucocutaneous junctions of the lips, dental pad, inner surfaces of the lips, cranial half and lateral aspects of the tongue	Muzzle/nares, eyes, udder, feet, alimentary and respiratory tracts, musculoskeletal, systemic	Haemorrhagic, erosive and oedematous
Foot-and-mouth disease	Cattle Sheep and goats Camelids Pigs	High in cattle and pigs, variable in sheep and goats	Only young animals	Efficient	Dental pad, inner lips and upper gum, tip and dorsum of the tongue	Muzzle/nares, teats, feet, (rarely eyes). Myocarditis in young animals	Vesicular and erosive
Vesicular stomatitis	Cattle Sheep and goats Pigs Horses	Variable	Negligible	Possible, but also insect vector-borne	As for foot-and-mouth disease	Teats and feet	Vesicular and erosive
Rinderpest	Cattle Sheep and goats (Pigs rarely – some virus strains)	High	High	Efficient	Lips, gums, ventral, lateral and caudal parts of the dorsum of the tongue, hard palate, buccal mucosa	Muzzle/nares, eyes, skin, alimentary and respiratory tracts, systemic	Erosive, necrotic and haemorrhagic
Peste des petits ruminants	Sheep and goats (Camelids rarely)	High	High	Efficient	Gums, buccal mucosa, hard palate, dental pad, dorsum of the tongue	Nares, eyes, alimentary and respiratory tracts, systemic	Erosive, necrotic and haemorrhagic
Lumpy skin disease	Cattle	Variable 5 to 45%	Up to 10%	Poorly efficient	Inner lips, gums, dental pad	Skin including udder, muzzle, eyes, upper respiratory tract, reproductive tract, lymphoid	Proliferative, nodular and necrotic
Sheeppox and goatpox	Sheep and goats	Medium to high	Over 80% in young animals	Main method, but variable efficiency	Lips, gums, dental pad, hard and soft palates	Skin including udder, nose, eyes, alimentary and respiratory tracts, lymphoid	Hyperaemia then proliferative, papular and pustular

*Proportion of animals in a naive population showing clinical disease

Ulceration on the tongue and muzzle of a cow with foot-and-mouth disease. Picture, Ryan Waters

Ruptured vesicle with epithelial flap on the dental pad of a sheep with foot-and-mouth disease. Picture, Phil Watson



Ruptured vesicle at the coronary band of a sheep with foot-and-mouth disease. Picture, Ryan Waters

bluetongue, but the rapid development and progression of vesicular lesions in individuals, and of disease within a group of animals distinguish FMD from bluetongue. In bovine FMD, blanched foci rapidly develop into fluid-filled vesicles that rupture to leave well-demarcated focal lesions. Bluetongue lesions are less well demarcated, are more diffuse and never vesicular in nature. Haemorrhage is unusual in FMD and only occurs in erosions left by recently ruptured vesicles, whereas mucosal haemorrhages and petechiation that occur in cases of bluetongue are not necessarily associated with erosions. In both diseases, lesions develop in areas subject to wear and tear; however, focal FMD lesions are often found on the tip and dorsal aspect of the tongue in the mouth of cattle, whereas bluetongue lesions are commonly seen on the lateral aspects of the tongue, adjacent to the lingual aspects of cheek teeth.

FMD lesions are not associated with oedema and are unlikely to involve the muzzle except as an extension of oral lesions. Clinical cases of bluetongue in cattle have often involved significant crusting, exudation and erosion of the muzzle. Ruptured or healing FMD vesicles could resemble focal bluetongue erosions in the mouth (especially on the dental pad and inner lips) and on the coronary band, particularly in sheep where the vesicular stage of FMD lesions may be missed and lesions can be mild. In these cases, DEFRA officials may request testing for FMD to rule out the disease. Unlike FMD, oral lesions in sheep with bluetongue commonly present together with swelling of the lips; nasal and ocular discharges, and crusting around the nares and medial canthus may be seen, with panting and dyspnoea in more severe cases. Lameness and reluctance to rise are seen in both diseases, although coronary band lesions are discrete vesicles and erosions in FMD compared with more generalised hyperaemia and haemorrhage in bluetongue that results in warm painful feet.

Mortality in sheep with FMD is unlikely unless very young animals are involved in which sudden deaths due to myocarditis have been described; in contrast, bluetongue can cause the death of sheep of all ages. Unlike FMD, bluetongue does not affect pigs.

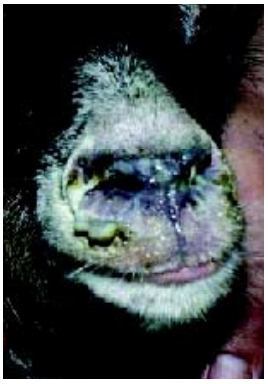
Vesicular stomatitis

Vesicular stomatitis causes vesicular disease clinically indistinguishable from FMD, although generally milder in cattle. It can also affect pigs, horses and, occasionally, sheep. The disease occurs in North, Central and South America.

Rinderpest and peste des petits ruminants

Both rinderpest and peste des petits ruminants (PPR) are caused by morbilliviruses that replicate in lymphoid and epithelial cells, especially those in the alimentary tract. An extensive eradication programme has eliminated rinderpest from all but occasional pockets of infection in East Africa and the Middle East.

Several features help differentiate infections with rinderpest or PPR from bluetongue. First, high morbidity and mortality would occur should either disease enter the UK's naive livestock. Secondly, the severity of alimentary tract disease results in a necrotic malodorous stomatitis and gastroenteritis with diarrhoea. Although diarrhoea is described in cases of bluetongue, the widespread alimentary mucosal lesions found in animals dying of rinderpest or PPR are striking and may be concentrated on lymphoid tissue such as Peyer's patches.



Mucopurulent nasal discharge in a goat with peste des petits ruminants. Picture, Tom Barrett. Reprinted, with permission, from Wohlsein and Saliki (2006)

Capripox viruses

In bovine lumpy skin disease, sheeppox and goatpox, capripox viruses replicate in cells of the dermis and other tissues and disseminate around the body in macrophages. Pyrexia and lymph node enlargement are accompanied by characteristic skin nodules in cases of lumpy skin disease, and by papular followed by pustular crusting skin lesions in animals with sheeppox or goatpox. Necrotic plaques can also develop on the mucosa of the oral cavity and respiratory and digestive tracts. Although cattle affected with lumpy skin disease may show lacrimation, nasal discharge and salivation, the wide distribution and proliferative, rather than erosive, nature of the lesions, especially in the skin of affected animals, are helpful distinguishing features. Morbidity and mortality vary with virus strain and host immunity, but are generally higher than expected for bluetongue, and mortality in young lambs may be very high.

DIAGNOSTIC FEATURES AND TESTS AVAILABLE TO DIFFERENTIATE BLUETONGUE FROM OTHER ENDEMIC INFECTIOUS DISEASES OF CATTLE

Disease	*Gross findings*	*Histopathological findings*
Malignant catarrhal fever	Multifocal ulceration, erosion, haemorrhage and necrosis of the alimentary tract from the oral cavity distally. Gastroenteritis. Peripheral keratitis and corneal opacity. Lymph node enlargement	Lymphoid hyperplasia and infiltrates, fibrinoid vasculitis, perivascular lymphoid cuffing. Keratitis, uveitis, interstitial nephritis and hypopyon
Mucosal disease	Multifocal ulceration, erosion and necrosis of the alimentary tract from the oral cavity distally. Gastroenteritis. Peripheral lymph node enlargement. Thymic atrophy. Interdigital/coronary band erosions	Mucosal epithelial ulceration/necrosis. Crypt dysplasia and loss in the small and large intestines, especially overlying the Peyer's patches. Lymphoid necrosis and depletion and herniation of crypts into the Peyer's patches. Hyaline degeneration and fibrinoid necrosis of submucosal and mesenteric arterioles. Ulcerative and parakeratotic dermatitis
Acute bovine viral diarrhoea	No lesions or, occasionally, erosions and shallow ulcers on the muzzle and nares. Epithelial erosion on the palate and tips of the buccal papillae. Similar, but milder, lesions to those described for mucosal disease. There may be haemorrhages in the presence of thrombocytopenia	As for mucosal disease, but milder
Infectious bovine rhinotracheitis	Hyperaemia and necrosis of the upper respiratory tract. Conjunctivitis. Rhinitis, laryngitis, pharyngitis and tracheobronchitis (may be diphtheritic). Bronchopneumonia	Fibrinonecrotic tracheobronchitis. Occasional rafts of epithelial cells with intranuclear inclusions may be seen where cells remain. Secondary bronchointerstitial pneumonia may be present
Bovine papular stomatitis and pseudocowpox	Focal proliferative papular and pustular or erosive lesions. Lesions on the teats form a dark brown ring or horseshoe scabs. Brownish spots persist for several weeks	Marked epithelial hyperplasia, with hyperkeratosis and focal necrosis. Ballooning degeneration of cells in deeper epidermal layers. Large eosinophilic inclusions may sometimes be seen, surrounded by a clear halo in keratinocytes
Bovine herpes mammillitis	More severe lesions than pseudocowpox. Painful, swollen oedematous teats, with fragile vesicles that rupture exposing the inflamed dermis. Lesions form scabs and may coallesce	Severe intercellular oedema of the epidermis, with prominent perivascular infiltrate of mononuclear cells in the dermis. Intranuclear eosinophilic inclusions may be present in rafts of syncytial epidermal cells
***Actinobacillus lignieresii* granulomatous dermatitis**	Enlargement of the draining lymph node(s). Firm, focal skin swellings with oedema. Discharging sinuses may be present in the mouth or on the skin. Alopecia over lesions	Pyogranulomatous inflammation surrounding characteristic eosinophilic aggregates associated with bacteria (Splendore–Hoeppli bodies)

ENDEMIC DISEASES OF CATTLE IN THE UK

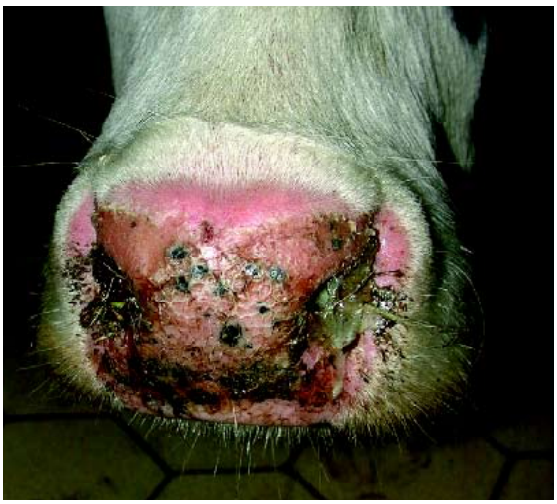
The table above summarises the features that distinguish bluetongue from other endemic diseases of cattle, and indicates what laboratory tests to use to provide evidence of these.

Malignant catarrhal fever

Malignant catarrhal fever (MCF) in the UK is due to infection with the gammaherpesvirus, ovine herpesvirus type 2 (OHV-2). Some of the first cases of bluetongue in northern Europe were initially mistaken for MCF due to its similarity with typical bluetongue. MCF generally presents as individual cases and is nearly always, ultimately, fatal. There is usually a history of contact with sheep, although this may be indirect and months before signs develop. Disease is considered to be mediated immunologically, leading to severe pathological changes characterised by T cell lymphoproliferation, vasculitis of medium-sized blood vessels (small blood vessels are primarily affected in bluetongue cases examined pathologically to date) and erosive to ulcerative mucosal and cutaneous lesions. Bexiga and others (2007) analysed clinical signs of MCF and bluetongue and showed that more cases of MCF than bluetongue present with a dull demeanour, reduced appetite, abnormal faeces (diarrhoeic, bloody and/or reduced volume) and bilateral superficial lymph node enlargement. The alimentary and neurological signs, keratitis and corneal opacity, and halitosis, which may develop in cases of MCF, also help differentiate the two diseases.

Mucosal disease

Bovine viral diarrhoea (BVD) virus infection of pregnant cattle in the first trimester (first 100 days) can result in the birth of calves immunotolerant of, and persistently infected with, BVD virus. These animals are often ill-thriven or small for their age, and are at risk of developing mucosal disease when BVD virus causes progressive and severe depletion of lymphoid tissue accompanied



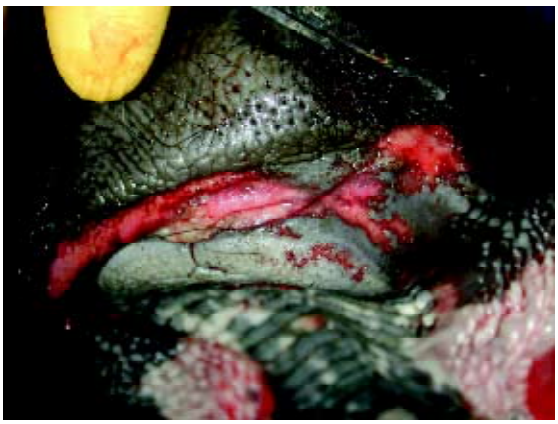
Crusting and erosion of the muzzle of a cow with malignant catarrhal fever. Picture, Andrew Holliman

Corneal opacity, lacrimation and nasal discharge in a cow with malignant catarrhal fever. Picture, Andrew Holliman

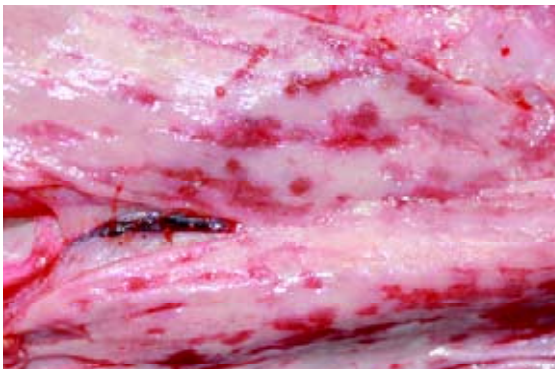
Confirmatory diagnostic tests
Serology – indirect fluorescent antibody test (IFAT) Virology – PCR on heparin blood or spleen Histopathology (brain, eye, kidney and lymph nodes)
Virology – BVD antigen ELISA or PCR on heparin blood (can be repeated after 14 days to prove persistent infection). PCR on thymus. Virus isolation Serology – BVD antibody ELISA negative or low Marked leucopenia Histopathology with immunohistochemistry (brain, ileum)
Virology – BVD antigen ELISA or PCR on heparin blood (acute stages only). PCR on tissues. Virus isolation Paired serology (ELISA) on acute/convalescent sera collected two weeks apart Histopathology with immunohistochemistry
Virology – fluorescent antibody test (FAT) on ocular/nasal/nasopharyngeal swabs, bronchoalveolar lavage fluid or trachea/lung tissues. Virus isolation Paired serology (ELISA) on acute/convalescent sera collected two weeks apart Histopathology with immunohistochemistry (lung, trachea)
Electron microscopy on scab to detect parapoxvirus Histopathology (skin biopsy samples)
Virus isolation in cell culture of scabs from early lesions. (Histopathology of skin biopsy samples may not be definitive)
Bacteriological culture from biopsies or pus/swabs from discharging lesions Histopathology (skin biopsy samples)

by necrosis of mucosae, which results in oral and nasal lesions not dissimilar to those of bluetongue. Bexiga and others (2007) included an analysis of the clinical signs of mucosal disease with those of MCF and bluetongue, and found that dull demeanour, reduced appetite and abnormal faeces were identified more frequently in cases of mucosal disease and MCF than in bluetongue. Interdigital ulceration and abnormal lung sounds also featured more in animals with mucosal disease.

Mucosal disease usually occurs sporadically in animals aged six to 24 months or, occasionally, can present as small outbreaks. It is invariably fatal, although disease may become protracted over several months; postmortem examination often reveals characteristic pathology (see table on the left).



Ulceration inside the upper lip of a cow with mucosal disease. Picture, Andrew Holliman



Linear oesophageal ulceration due to mucosal disease. Picture, Mark Wessels

Acute bovine viral diarrhoea

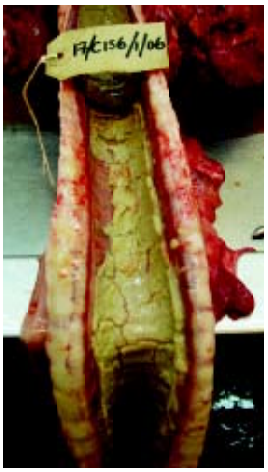
Postnatal acute BVD virus infections do not usually resemble bluetongue. However, there are reports of unusually severe outbreaks of acute BVD, mostly associated with BVD virus type 2, in which depression, pyrexia, milk drop and diarrhoea develop together with salivation, nasal discharge and oral ulceration. Haemorrhagic disease may also occur, with dysentery, epistaxis and widespread haemorrhages, increasing the similarity with bluetongue. Morbidity (up to 40 per cent) and mortality (up to 25 per cent) are both more likely to be higher than that associated with bluetongue.

Infectious bovine rhinotracheitis

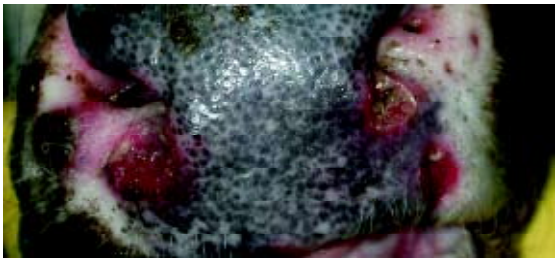
Infectious bovine rhinotracheitis (IBR) is a highly contagious disease caused by bovine herpesvirus type 1 (BHV-1). Replication in epithelial cells of the respiratory tract and conjunctivae is followed by clinical signs which, if disease is mild, include lacrimation and a serous nasal discharge with reddening of the conjunctivae and nasal passages and could be mistaken for bluetongue. However, in an affected group, it is likely that some animals will have more severe disease, and although excessive salivation, mucopurulent nasal discharges and patches of necrosis on nasal epithelia may be present in these, respiratory signs become dominant, with coughing, tracheitis and bronchitis and secondary pneumonia. The introduction of new animals or the mixing of different groups or ages frequently precedes outbreaks. Morbidity is high in susceptible groups; however, as IBR becomes latent and can recrudesce and be excreted, individual primary infections can occur if single naive animals are introduced into established, previously infected groups. Mortality is variable.

Bovine papular stomatitis/pseudocowpox

Bovine papular stomatitis and pseudocowpox are caused by a similar, if not identical, parapoxvirus, which is spread by direct contact and, in cows, by the milking process. The former results in lesions on the muzzle, lips, mouth and inside the nostrils of younger cattle, while the latter affects the teats and udders of cows. It is also zoonotic causing 'milker's nodule'. The lesions are papular and proliferative and form scabs, but may raise concern regarding bluetongue if they become eroded or as they heal and regress. It is uncommon for systemic illness to occur.



Diphtheritic tracheitis in a cow with infectious bovine rhinotracheitis. Picture, Mark Wessels

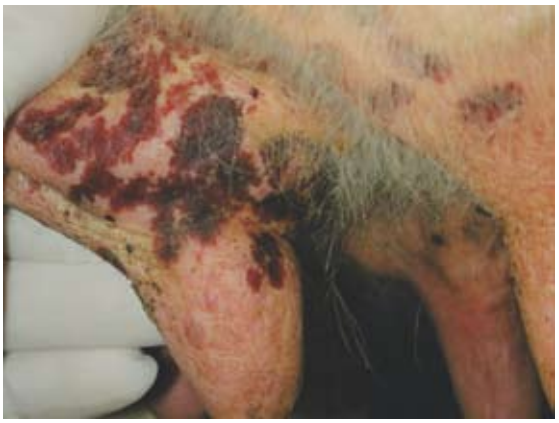


Circumscribed scabs and erosions on the muzzle of a cow with bovine papular stomatitis. Picture, VLA – Winchester

Bovine herpes mammillitis

Bovine herpes mammillitis (BHM) is caused by bovine herpesvirus type 2 (BHV-2). Lesions are restricted to the teats and udders of cows and, like pseudocowpox (but more rarely), can affect the muzzle and mouth of calves. In the UK, BHM is more common in late summer and early autumn, which coincides with the seasonal occurrence of bluetongue. However, while increased vigilance for bluetongue at such times may detect BHM lesions, their restriction to the mammary gland serves to distinguish between the two diseases. Pyrexia is absent or mild.

The seasonality of BHM may be partly due to the increased numbers of biting insects that are thought important in the mechanical transmission of the virus, and partly because the virus replicates better in cool skin.



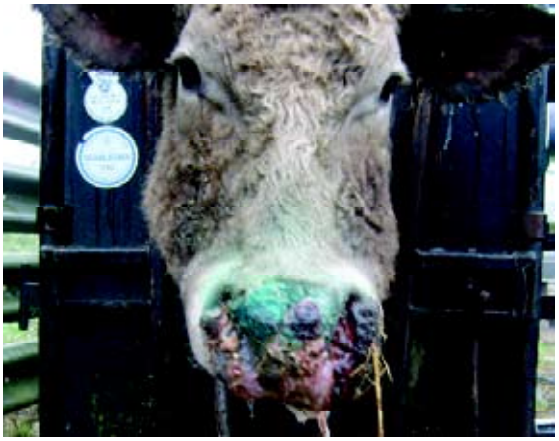
Coallescing scabs confined to the teats and body of the udder of a cow with bovine herpes mammillitis. Picture, Andrew Holliman

Miscellaneous conditions

Idiopathic necrotising enteritis of beef suckler calves may occasionally feature erosive and crusting lesions of the muzzle (Penny and others 1994) that could be mistaken for bluetongue, although cases of idiopathic necrotising enteritis usually present with diarrhoea and depression. There is progression to death in seven to 10 days, and it almost exclusively affects beef suckler calves aged two to four months.

Occasional cases of allergic reaction to insect stings or accidental exposure to corrosive agents (which young cattle, being curious, may lick) can cause damage to the oral epithelium and could produce signs similar to those of bluetongue. In the former, signs often resolve quickly following anti-inflammatory treatment; in the latter, identification of the corrosive material and the localisation of lesions may assist differentiation.

Facial swelling in individual cattle, and occasionally small outbreaks in groups on rough grazing, has been reported due to cutaneous infection with *Actinobacillus lignieresii*. This can superficially resemble bluetongue when lesions involve the cheeks, nostrils or lips. Palpation reveals firm granulomas in the soft tissues of the face and draining lymph nodes, and discharging sinuses may be present. Lesions are usually chronic and may be accompanied by illthrift.



Firm swelling of the face and crusting lesions on the muzzle of a cow with cutaneous actinobacillosis. Picture, Joe Sprinz

ENDEMIC DISEASES CAUSING ORAL LESIONS AND/OR FACIAL OEDEMA RESEMBLING BLUETONGUE IN SHEEP

Disease	*Oral lesions*	*Facial oedema*	*Confirmatory tests*
Orf	+	±	Parapoxvirus detection in scabs by electron microscopy Histopathology
Idiopathic oral ulceration	+	–	None available
Systemic pasteurellosis	±	–	Postmortem examination and bacteriological culture on internal viscera
Photosensitisation	–	+	See box on page 251
Cobalt deficiency	–	±	Low liver and serum vitamin B_{12} concentrations Histopathology and postmortem examination
Haemonchosis	–	±	Faecal worm egg counts Total worm counts Postmortem examination
Fasciolosis	–	±	Faecal fluke egg examination Postmortem examination

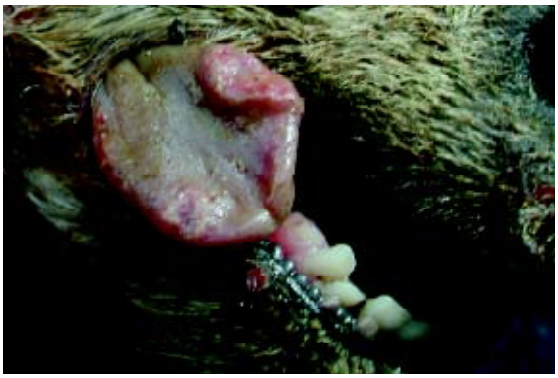
+ Present, – Absent, ± Sometimes

ENDEMIC DISEASES OF SHEEP IN THE UK

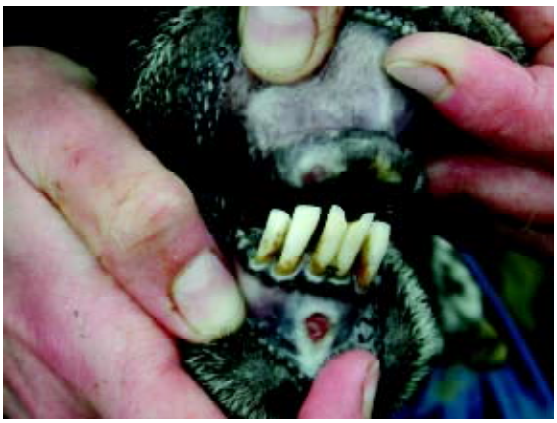
Orf

Contagious pustular dermatitis or orf is a contagious zoonotic disease of sheep in which proliferative parapoxvirus lesions develop in and around the mouth, and on the head, lower limbs, teats and udder. It may be confused with bluetongue when severe lesions cause oedematous swelling of the soft tissues of the face, including the lips and muzzle (Casey and others 2007), or if the slightly raised oral lesions become necrotic and slough to form ulcers on the tongue, lips, dental pad, palate and gingivae. In such cases, examination of other parts of the body of the affected individual may reveal more typical firm, raised papular or crusting and scabbed lesions. If

Proliferative crusting lesions around the lips of a lamb with orf. Picture, Phil Watson



Raised lesions along the margins of the tongue of a lamb with orf. Picture, Phil Watson



Focal ulceration of the gingiva and dental pad in a sheep with idiopathic oral ulceration. Picture, Phil Watson

Facial oedema in a sheep with hypoalbuminaemia due to haemonchosis. Note the poor body condition. Picture, Edward Mackley

ulcers are carefully inspected, their rims may show remnants of raised proliferative tissue.

Morbidity in outbreaks may be high and involve sheep of any age, although it is most common in young lambs. As orf is zoonotic, care should be taken handling sheep with suspected orf lesions.

Idiopathic oral ulceration

During the 2001 FMD epidemic in the UK, ovine mucosal and gum obscure disease (OMAGOD) was used to describe a variety of oral lesions in sheep that were thought to have a traumatic aetiology to reflect the concern they caused when present in flocks (Watson 2004). These are primarily focal ulcerative and healing lesions confined to the mouth and are not associated with the oedema, haemorrhage and more diffuse hyperaemia and erosion seen in bluetongue. They are most commonly found on the lower lip and gingiva; however, when they occur on the dental pad and coalesce to form large areas of ulceration, the lesions could resemble the dental pad erosion and necrosis seen in cases of bluetongue, except that they are not accompanied by lesions elsewhere or systemic illness. Morbidity varies greatly.

Conditions causing oedema

A frequent sign of bluetongue in sheep is oedema, particularly around the face, cheeks, lips and muzzle. Conditions that cause oedema (see table on page 248) may mimic this feature, especially when the face and lower limbs are affected. Peripheral oedema occurs in animals with hypoproteinaemia due to liver or kidney disease, and due to enteric conditions causing malabsorption or protein loss (eg, fasciolosis and haemonchosis). Increased central venous pressure, which occurs in cases of heart failure, is another cause. Clinical examination will reveal the presence of features associated with the various causes of peripheral oedema and the absence of other lesions associated with bluetongue. Thus, there may be illthrift and:

- Abnormal faeces in enteric conditions;
- Pale mucous membranes with parasitism;
- Jaundice with liver disease;
- Tachycardia and abnormal heart sounds in heart failure.

As in cattle, facial swelling is also a feature of allergic reactions.

Conditions causing ocular discharge

Common causes of ocular discharge are listed in the table on the right, and do not cause lesions elsewhere in the body. Cobalt deficiency in sheep results in signs of vitamin B_{12} deficiency. This disease is insidious in onset and is associated with illthrift and anaemia. However, facial oedema and an excessive watery discharge from the eyes may occur in cobalt-deficient growing lambs and show some similarity to bluetongue. Foot and oral lesions do not occur, and an unusually pale liver may be seen at postmortem examination.

Conditions causing nasal discharge and respiratory distress

Nasal discharges can occur as a flock problem due to nasal bot fly (*Oestrus ovis*) infestation. Incidence is greatest in the summer months and is often accompanied by

ENDEMIC DISEASES CAUSING OCULAR AND NASAL DISCHARGES AND RESPIRATORY DISTRESS RESEMBLING BLUETONGUE IN SHEEP

Disease	*Ocular discharge*	*Nasal discharge*	*Respiratory distress*	*Confirmatory tests*
Cobalt deficiency	+	–	–	Low liver and serum vitamin B_{12} concentrations Histopathology and postmortem examination
Listerial keratoconjunctivitis	+	–	–	Bacteriological culture from conjunctival swabs
Infectious ovine keratoconjunctivitis	+	–	–	PCR to detect *Mycoplasma conjunctivae* on conjunctival swabs
Nasal myiasis	–	+	±	Expulsion of nasal bot fly larvae Postmortem examination
Ovine pulmonary adenocarcinoma	–	+	+	Histopathology and postmortem examination
Laryngeal chondritis	–	–	+	Characteristic lesions and postmortem examination
Pneumonia (eg, pasteurellosis, lungworm)	–	+	+	Detection of lungworm Bacteriological culture Postmortem examination

+ Present, – Absent, ± Sometimes

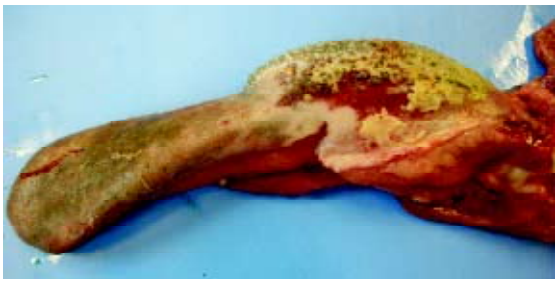
signs of irritation, including sneezing, head shaking, snorting and nose rubbing. More copious fluid discharges occur in sheep affected with ovine pulmonary adenocarcinoma. Sheep are not usually affected before two years of age. The condition occurs as sporadic cases in endemically infected flocks, and presents as chronic dyspnoea and weight loss. Individual cases of nasal discharge associated with tumours, fungal or bacterial rhinitis, maxillary tooth abscesses or foreign bodies may be seen occasionally.

Respiratory distress is a feature of bluetongue if pulmonary oedema or inhalational pneumonia develop, and may also be seen with the conditions causing nasal discharge. Pneumonia due to bacterial infections (*Pasteurella multocida*, *Mannheimia* species, *Mycoplasma ovipneumoniae*) or lungworm (*Dictyocaulus filaria*) present with respiratory distress and, in chronic cases, weight loss, or as sudden deaths.

Suspicion of bluetongue could also arise in cases of laryngeal chondritis in Texel sheep. This is an obstructive upper respiratory tract disease characterised by severe dyspnoea and death. It is caused by necrosis of the arytenoid cartilages and results in swelling and occlusion of the laryngeal lumen.

Conditions causing haemorrhages

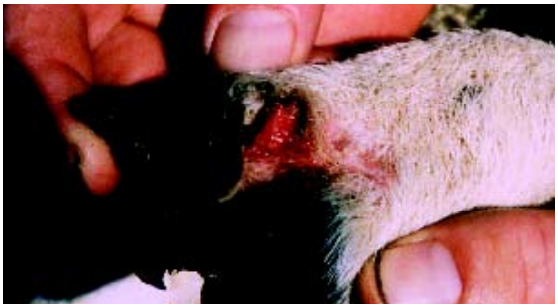
The haemorrhages seen in cases of in bluetongue may be widespread and involve mucosal and serosal surfaces and internal organs. The presence of intramural haemorrhages at the base of the pulmonary artery is very characteristic of, but not exclusive to, bluetongue; they may be a feature of other diseases involving endothelial damage such as Gram-negative septicaemias (eg, systemic pasteurellosis), pulpy kidney, Rift Valley fever and heartwater, the last two of which do not occur in the UK. Petechiation and ecchymoses are non-specific indicators of vascular damage or clotting disorders. They occur in many conditions (see table, below left) in which vasculitis, thrombocytopenia, septicaemia, toxaemia, hypoxia or disseminated intravascular coagulation occur and are, therefore, often seen during postmortem examination, particularly subepicardial haemorrhages on the heart. Of these many conditions, systemic pasteurellosis due to *Bibersteinia* (formerly *Pasteurella*) *trehalosi* or *Mannheimia* species infection causes widespread haemorrhages and oedema and, sometimes, erosions and ulceration of the lateral aspects of the tongue, pharynx and oesophagus, and mimics fatal bluetongue infection. This autumnal disease is distinguished by its typical history of sudden deaths of several six- to nine-month-old sheep in a flock within a few days after a move, or a change in feed or climate. Diagnosis is confirmed by bacteriology.



Ulceration on the lateral aspects of the tongue from a lamb with systemic pasteurellosis. Picture, VLA – Bury St Edmunds

Conditions causing lameness

Lameness is often seen in sheep flocks due to a number of causes, which may coexist (see table, bottom left). Conditions resulting in lesions of the coronary band are most likely to be confused with bluetongue and include contagious ovine digital dermatitis (CODD), orf and strawberry footrot. In general, the hyperaemic and diffuse nature of coronary band lesions in bluetongue, together with the presence of lesions elsewhere, help to distinguish it from other diseases of the feet. Rapid progression of disease and high morbidity are the hallmarks of CODD, and the early ulcerative lesion affecting the skin at or just above the coronary band is usually only present on one claw of one foot. Strawberry footrot is caused by the bacterium *Dermatophilus congolensis* (alone or in combination with orf virus), its name deriving from the raw, bleeding tissue exposed at and above the coronary band when the heaped scabs that have developed are subject to trauma. Despite these lesions, lameness is mild compared with lesions of similar severity in cases of bluetongue.



Ulceration at the coronary band of a sheep with contagious ovine digital dermatitis. Note the hoof is starting to separate. Picture, Phil Watson

ENDEMIC DISEASES CAUSING HAEMORRHAGES AND DEATH RESEMBLING BLUETONGUE IN SHEEP

Disease	*Confirmatory tests*
Systemic and pneumonic pasteurellosis	Postmortem examination and bacteriological culture on internal viscera
Other bacterial septicaemias (eg, listeriosis, salmonellosis)	Postmortem examination and bacteriological culture on internal viscera
Clostridial enterotoxaemia (pulpy kidney)	Detection of clostridial toxins in small intestinal contents by ELISA. Histopathology on brain and kidney
Bracken poisoning	Bone marrow depression indicated by histopathology (bone marrow) and haematology (pancytopenia), retinal atrophy (eye) Postmortem examination and detection of bracken in the rumen

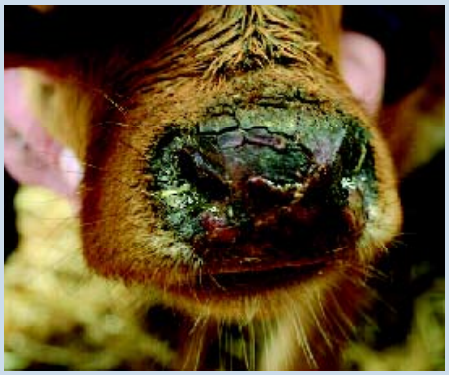
ENDEMIC DISEASES CAUSING LAMENESS AND/OR FOOT LESIONS RESEMBLING BLUETONGUE IN SHEEP

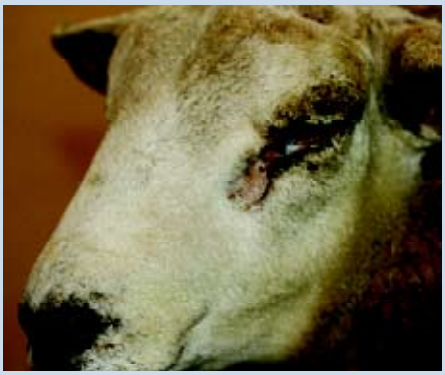
Disease	*Confirmatory tests*
Contagious ovine digital dermatitis	None available – characteristic appearance
Footrot	Characteristic appearance and microscopy/culture
Interdigital dermatitis	Characteristic appearance and microscopy/culture
Laminitis	Postmortem examination, may follow grain engorgement
Strawberry footrot	Microscopy and bacteriology on scabs
Orf	Parapoxvirus detection in scabs by electron microscopy Histopathology
Arthritis	Postmortem examination and bacteriology on joints
White muscle disease	Elevated muscle enzymes (CK and AST). Low serum vitamin E and GSH-Px (selenium) concentrations – heparin and clotted bloods. Postmortem examination and histopathology

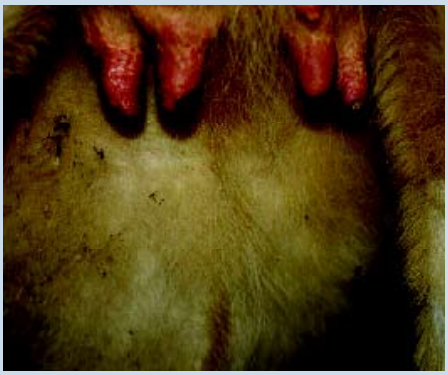
CK Creatine kinase, AST Aspartate aminotransferase, GSH-Px Glutathione peroxidase

Photosensitisation in cattle and sheep

Photosensitisation was another diagnosis attributed to the first cases of bluetongue in northern Europe, especially as the lesions frequently involve the muzzle, eyelids and udder. Photosensitivity occurs when an animal becomes hypersensitive to sunlight, and exposure leads to non-pigmented skin damage, with hyperaemia, oedema and swelling developing. As the muzzle, lips and eyelids are often involved and oedema causes the ears to droop, it is this stage of photosensitivity that most resembles bluetongue. Serum exudation follows, forming a crust and scabs, with ulceration and necrosis and, often, secondary infection. The absence of haemorrhages, a lack of erosions within the mouth, and the generalised nature of the skin lesions, in addition to an association with non-pigmented areas of the skin, may assist differentiation.







(left) Necrosis of the muzzle skin in a calf with photosensitisation. Picture, Andrew Holliman. **(middle) Thickening and crusting of the skin around the eyes, nostrils and ears in a sheep with copper poisoning.** Picture, Mark Wessels. **(right) Erythema and necrosis of the skin of all four teats of cow caused by photosensitisation.** Picture, Andrew Holliman

TYPES OF PHOTOSENSITISATION

Type	*Cause*	*Gross findings*	*Confirmatory diagnostic tests*
I	Exposure to photosensitising agents either by ingestion of toxic plants (eg, St John's wort) or skin contact with the juice of leafy parts of Umbelliferae plants (eg, parsnip, parsley)	Erythema, oedema, crusting and scab formation on white areas of skin, muzzle, ears, udder. Conjunctivitis	Identify plant exposure
II (porphyria)	Rare hereditary disorder associated with inbreeding and carried by recessive genes. Defective haemoglobin formation results in the build-up of porphyrin	Erythema, oedema, crusting and scab formation on white areas of skin, muzzle, ears, udder. Conjunctivitis. Red to brown tinge to teeth, urine, bones. Discoloration in lung, spleen and kidney and other tissues	Excess coproporphyrin I and uroporphyrin I in urine. Normochromic haemolytic anaemia. Bones, urine and teeth (especially the deciduous teeth) fluoresce pink when irradiated with near-ultraviolet light
III (hepatogenous) Most common	Accumulation of phylloerythrin (a byproduct of plant chlorophyll) due to liver damage from chronic copper toxicity or toxic plants (eg, ragwort, bog asphodel)	Erythema, oedema, crusting and scab formation on white areas of skin, muzzle, ears, udder. Conjunctivitis. Chronic hepatitis with hepatocyte necrosis and cirrhotic changes	Biochemistry reveals jaundice and liver damage/failure. Elevated liver enzymes (AST, GLDH, GGT), hypoalbuminaemia, raised bilirubin. Copper toxicity – kidney/liver copper estimation, plasma copper. Histopathology of liver and skin samples

AST Aspartate aminotransferase, GLDH Glutamate dehydrogenase, GGT Gamma-glutamyl transferase

White muscle disease, polyarthritis, postdipping lameness and acute laminitis (eg, following grain engorgement) all cause lameness in several limbs and, in animals with acute laminitis and postdipping lameness, the feet may feel hot, which is also a feature of bluetongue. Joints affected by polyarthritis are not always palpably swollen and specific clinical signs in each of the above conditions may not be evident. Clinical history and the restriction of lesions to the limbs, together with diagnostic tests including postmortem examination, are therefore important for differential diagnosis.

SUMMARY

The wide spectrum of clinical signs and the variation in severity of disease in cattle and sheep with bluetongue mean that a number of conditions may resemble some or all features of the disease. A complete history and a full clinical or postmortem examination are required for differentiation. If this provides evidence of an alternative diagnosis, the use of appropriate laboratory tests to substantiate and, if possible, confirm the diagnosis is appropriate. Where the clinical presentation cannot be distinguished from bluetongue, or where other notifiable diseases are suspected, the case must be reported to the DVM at the local AHDO.

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