

1 **In Practice**

2

3 Caseous Lymphadenitis (CLA) in Sheep: An Update

4 Emily Gascoigne^{1*}, Nicky Ogden², Dr Fiona Lovatt^{2,3}, Dr Peers Davies⁴

5

6 ¹Synergy Farm Health LTD, West Hill Barns, Evershot, DT2 0LD

7 ²Summerleaze Vets Ltd., Gammons Hill, Kilmington, EX13 7RA

8 ³Flock Health Ltd, Eggesburn Farm, Eggleston, Barnard Castle, Co Durham, DL12 0BD, UK

9 ⁴Department of Epidemiology and Population Health, University of Liverpool, CH64 7TE

10

11 *Corresponding Author

12 *Email address:* (E. Gascoigne) emily.gascoigne@synergyfarmhealth.com

13

14 **Caseous lymphadenitis (CLA) caused by the Gram Positive bacteria *Corynebacterium***
15 ***pseudotuberculosis* has been present in the UK since the 1980s and is now considered**
16 **endemic. CLA is considered to be an iceberg disease i.e. production limiting disease,**
17 **characterised by slow insidious onset, and production limiting effects in a larger**
18 **proportion of the flock than that exhibiting clinical signs at any given point in time. The**
19 **disease was previously reviewed in *InPractice* by Baird (2003) so we will consider updates**
20 **in our understanding of the pathology, risk factors for flocks and the challenges of**
21 **initiating control where the cost of the disease is still relatively unquantified.**

22

23 **Pathogenesis**

24 Animals become infected by either inhalation or via skin abrasions where the bacteria
25 releases the exotoxin phospholipase D (PLD) and mycolic acid resulting in surface necrosis;
26 increased vascular permeability, resulting in infection of phagocytes. Phospholipase D is a
27 chemotaxonomic factor which impairs chemotaxis of neutrophils (Baird and Fontaine,
28 2007). Whilst these lesions may be confined to superficial lesions, migration of infected
29 phagocytes to regional lymph nodes can result in lymph node destruction and further
30 infection of phagocytes. CLA infection results in chronic granulomatous lesions known
31 commonly as “cheesy gland” due to accumulation of infected phagocytes, eosinophils and
32 cellular debris forming distinct abscesses with multi-centric layers (see figure 1).

33 **Figure 1:** A mesenteric lymph node with CLA showing concentric rings (source Delia Lacasta,
34 University of Faculty of Veterinary Medicine, University of Zaragoza)

35

36 Lesions fistulate permitting bacterial dissemination i.e. through the skin allowing abscesses
37 to drain or mediastinal abscesses fistulating into the bronchi to permit aerosolisation.

38

39 Both visceral and superficial lymph nodes can be affected with the anatomical location
40 apparently linked to the geographical location of the animals. UK lesions tend to be
41 associated with superficial lymph nodes around the head and neck with Australian lesions
42 more commonly linked with the torso, popliteal, prescapular and prefemoral lymph nodes
43 (Binns, Bailey and Green, 2002; Baird, 2007). Additional locations described include the
44 udder, upper respiratory tract (see figure 2) and kidneys (Ferrer et al., 2009) (see figure 3).
45 Remnants of superficial lesions which have healed may be visible as scarring (figure 4).

46

47 Figure 2: A mediastinal lymph node with CLA (source Delia Lacasta, University of Faculty of
48 Veterinary Medicine, University of Zaragoza)

49

50 Figure 3: Renal invasion with CLA (source Delia Lacasta, University of Faculty of Veterinary
51 Medicine, University of Zaragoza)

52

53 Figure 4: A ewe with evidence of old CLA lesions i.e. scarring over lymph node site

54

55 **Risk factors for transmission**

56 Spread of the infection can be direct i.e. close contact with neighbouring animals or indirect
57 contact via fomites. There is evidence that risk of abscess development is likely to be
58 proportional to the inoculating dose and that some animals will clear infections but still be
59 seropositive on screening (Batey, 1986).

60

61 Risk factors for spread are largely related to the large volumes of infectious material yielded
62 from ruptured abscesses and inhalation as a consequence of aerosolisation of internal
63 lesions.

64

65

66 Baird (2000) found that rams were significantly more likely to be seropositive than ewes in
67 the same flock and it has been suggested that this may reflect behaviour within ram mobs
68 i.e. fighting leading to ruptured abscesses and infection spread. With regards to fomites,
69 *Corynebacterium pseudotuberculosis* has been reported to survive in the environment for 55
70 days in organic materials and that low environmental temperatures favour survival.

71 Furthermore Windsor (2011) demonstrated the pathogen can survive in sheep dip for 2
72 hours post inoculation. Shearing sheep with abscesses or plunge dipping of sheep with
73 draining tracts along with non-infected flock mates are known to be risk factors.

74

75

76

77 Clearly, buying in infected animals with an unknown status is a risk factor for introducing
78 CLA into naïve flocks and given the stratified system of flocks within the UK, movements are
79 a significant risk factor for the UK. The work from Baird et al., (2004) suggests that rams
80 therefore have an important role as sentinels for appraising flock health status and
81 screening rams at purchase is important for reducing the risk of introducing infected
82 animals.

83

84 *Corynebacterium pseudotuberculosis* infections have been reported in humans where there
85 is a high exposure to infected sheep or they are employed in high risk occupations such as
86 livestock workers and butchers (Peel et al., 1997, Bregenzer et al., 1997) but these are often
87 isolated incidents.

88

89

90 **Prevalence**

91 At a national level VIDA (Veterinary Investigation Diagnosis Analysis) data based on
92 diagnoses is available (See figure 5), but this is likely to be an underestimate of the national
93 situation. Small studies have been published which provide an indication of prevalence.
94 Baird et al., (2004) looked at terminal sire flocks and found that >18% of flocks had at least
95 one seropositive ram on screening. The overall population prevalence was found to be
96 9.93% prevalence (95% CI 8.76-11.1 per cent) (Baird et al., 2004) with 18% of flocks having
97 at least one positive animal and 36% flocks of these having more than one positive animal.

98

99 More recent work in the UK suggested a flock prevalence of 4% based upon the
100 identification of macroscopic CLA lesions (superficial and visceral) detected during post-
101 mortem examination and confirmed by culture (P Davies, *unpublished data*). The sampling
102 frame from which this data was derived involved a convenience sample of 56 flocks from
103 England, Scotland and Wales. Each flock supplied between 12- 25 cull ewes for post-mortem
104 examination by Farm Animal Post Mortems Ltd. The flocks represented a wide variety of
105 breeds with a bias towards lowland breeds and were distributed throughout the high sheep
106 density areas of the mainland UK. However, the Davies et al data required farmer
107 cooperation in the participation and submission of cull ewes. Therefore, this data cannot be
108 regarded necessarily as a representative sample of UK flocks. Furthermore, the diagnosis of
109 CLA was based upon presence of lesions visible to the pathologist conducting the
110 examination. This contrasts with the serological approach adopted by previous studies. This
111 contracting methodology would be expected to be less sensitive but more specific than
112 serological studies. This complements data collected in a fallen stock survey which found
113 <1% of carcasses positive for CLA lesions on gross post-mortem (Lovatt and Strugnell.,
114 2013). However, when uncontrolled in flocks, 60% of adults can become seropositive (Binns
115 et al., 2002). To date in the UK, no CLA prevalence study has been conducted using a truly
116 randomised sampling frame.

117

118 Figure 5: Graph to show VIDA diagnoses submitted through APHA

119

120

121 **Productivity losses**

122 CLA is often listed as an “iceberg disease” along with Maedi Visna and Ovine Pulmonary
123 Adenomatosis causing prematurely thin ewe syndrome i.e. emaciation in absence of other
124 pathology and with normal nutrition. The iceberg nature i.e. clinical cases being an indicator
125 of many more subclinical cases, makes identification and eradication of subclinical infected
126 animals important for disease management on farm. Thin ewes with CLA are more
127 commonly associated with the visceral form of CLA. Arsenault et al., (2003) showed that
128 38.5% of animals with superficial lesions had visceral lesions on post-mortem inspection at
129 the abattoir in Canada.

130

131 Where CLA is endemic in flocks, economic costs are associated with premature culling,
132 reduced milk yields, and documented reductions in wool yields. Whilst all the of work done
133 looking at reduced wool crops is Australian, the reductions of 0.2-0.25kg per head and
134 overall reduction by 4-7% (Windsor, 2011) of clean fleece are likely to indicate the
135 physiological impact of CLA on individual sheep that may well be correlated with reduced
136 production in other areas such as milk yield and fecundity. More research is required to
137 understand the significance of these physiological impacts in the context of the UK sheep
138 sector.

139

140 CLA is a challenge for the processing sector as documented in Canada and Australia
141 (Arsenault et al., 2003, Windsor and Bush, 2016) with lesions at risk of rupturing whilst on

142 the line resulting in carcass contamination in addition to trimming due to the presence of a
143 lesion.

144

145 At the low prevalence suspected in the UK, the economic impact of CLA is poorly
146 understood. However, CLA infection within a flock and particularly the presence of CLA
147 lesions is detrimental to profitability of pedigree flocks due to the inability to sell affected
148 animals through public sales. It will restrict export opportunities in some cases.

149

150 **Differential diagnoses**

151 When approaching individuals with a suspected abscess in the region of lymph nodes, other
152 differential diagnoses should be considered. Investigation should be with care given the
153 highly infectious nature of the purulent materials i.e. lesions should not be lanced to
154 minimise the risk of spreading CLA. Fine needle aspiration of lesions is recommended before
155 draining. Key differentials could include the following:

156

157 Actinobacillosis i.e. granulomatous lesions infected with *Actinobacillus lignieresii* that results
158 in a suppurative adenitis in the regional lymph nodes. This gram negative bacteria would be
159 differentiable on fine needle aspirate and gram stain.

160

161 Salivary mucocoele are less common in sheep but may be an important differential in goats.
162 The contents of these cysts will initially mimic saliva and be sterile but may become
163 inspissated over time (Linklater and Smith, 1993).

164

165 Actinomyces pyogenes: Lumpy jaw secondary to primary dental lesions or drench gun
166 injuries may result in mandibular swelling with regional lymph node involvement. The
167 involvement of the bone in the mandible or maxilla would move this up the differential list
168 (see figure 6).

169

170 Figure 6: *Actinomyces pyogenes* infection of the jaw.

171

172 Morel's disease: *Staphylococcus aureus subsp. Anaerobius* has been found to produce
173 similar abscesses to CLA on the head and neck of goats and be reported at high prevalences
174 within flocks. However, in contrast to CLA, Morel's typically affects young goats, has a
175 shorter incubation periods (<3 weeks) and lesions are not always located near lymph nodes
176 (Szaluś-Jordanow et al., 2010) (see figure 7)).

177 Figure 7: Morel's disease in a goat (source Jaroslaw Kaba, Faculty of Veterinary Medicine,
178 Warsaw University of Live Sciences).

179 Other differentials could include trauma, haematoma, healing fractures, granulomas or
180 dermal cysts.

181

182 **Diagnosis**

183 There are a range of ways in which CLA can be diagnosed. Lesions can be identified on
184 clinical examination or post-mortem examination and bacteriology with isolation of the
185 bacteria is considered gold standard. However, this proves challenging where internal
186 abscesses are of concern or in live animals where lesions may take up to 6 months to
187 appear. Furthermore, direct microscopy can be limited especially when sampling old and
188 calcified lesions. Haematology changes were described by Scott et al., (1997) in affected
189 animals i.e. neutrophilia and lymphocytosis but these are non-specific changes.

190

191 Serology

192 The most common test currently used in the live animal is the ELISA, however clear
193 communication of sensitivities and specificities to the farmer prior to tests being conducted
194 is important. CLA stimulates both the humoral and cellular immunities and therefore IgG or
195 IFN- γ can be measured as indicators of each respectively. Serology against exotoxin
196 phospholipase D is the most commonly used test because of its cost efficacy and acceptable
197 test performance (Sn 87%, Sp 98%, Voigt et al., 2012, ELLITEST CLA Hyphen, France). The
198 low sensitivity is likely to be a reflection of the intracellular nature of the bacteria. The low
199 specificity will reflect the potential confusion with other *Corynebacterium* and potentially
200 vaccination (Oreiby, 2015). It is also recommended that only lambs over 6 months old
201 should be tested using serology (Williamson, 2001). Furthermore, serological tests are not
202 able to distinguish animals who have cleared infections and those with active lesions.
203 Western Blot testing is often used as a confirmatory test to improve the specificity of results

204 found. Currently the only available vaccination (Glanvac; Zoetis) cannot be differentiated
205 from natural infection on serology.

206 Bulk milk tank testing has been developed for goats in Norway (Nagel-Alne et al., 2015) with
207 sensitivity of 72.7% and specificity of 88.6% with respect to identified prevalences >2%.

208

209

210 Interferon Gamma Testing

211 Interferon Gamma testing is in development (Sunil et al., 2008) with early sensitivities of
212 91% and specificities of 98% demonstrated *in vivo*. A major advantage of IFN- γ testing is the
213 increased sensitivity and being unaffected by the vaccinal status of the sheep. In addition, it
214 has early diagnostic capability being able to detect animals 5 days post infection (in
215 comparison with between 6-11 days post infection with the ELISA Paule et al., 2003). There
216 is no correlation between the severity of lesion and either the level of sero-positivity or the
217 level of IFN- γ positivity

218

219 **Box 1: An approach to CLA diagnosis in a commercial flock**

220

221 Flocks may trigger screening for multiple reasons. Flocks may be interested in pursuing high
222 health status, may have been requested to demonstrate freedom from CLA pre-sale of animals
223 or may be concerned after finding evidence of suspicious lesions.

224

225 Gold standard diagnosis of CLA on farm would be isolation and culture of *Corynebacterium*
226 *pseudotuberculosis* from lesions of affected animals. Abscesses should be conservatively
227 aspirated to avoid further spread whilst diagnosis pending, an impression smear made, and
228 the bacteria submitted on a plain swab. This approach can be applied to both live animal and
229 post-mortem samples

230

231 When lesions are largely resolved i.e. scarred or where calcified serology should be
232 considered. The ELISA with Western Blot to confirm infection in animals with a positive
233 ELISA result for the identification of CLA positive animals.
234

235 *Cull ewe screening*

236 When trying to establish status for a flock with no history of lesions a cull animal screen with
237 both physical and serological examination could be considered as is common practice with
238 the other iceberg diseases. However we know that rams are valuable sentinels for flock and
239 therefore annual tup screening could also be considered.
240

241 *Screening suspect clinical cases*

242 For all flocks, recommending isolation of any animals with suspicious lesions prior to
243 sampling for culture is prudent. Ewes are most likely to be examined for CLA as single/small
244 groups of incidental animals i.e. in an outbreak situation or as part of thin ewe screens post-
245 weaning at culling.
246

247 *Screening at introduction and biosecurity*

248 Where there is an absence of a history of CLA on farm and where a farm wants to preclude
249 its introduction into a flock, screening on new animals on arrival and whilst in isolation is
250 recommended. Due to the delays in seroconversion, repeat testing at a 12 week interval and
251 whilst in isolation should be considered. A single sample may miss recently infected animals.
252 Vaccination status should be established prior to sampling as false positives may occur where
253 there has been a history of vaccination.
254

255 Whilst movement of animals is the most obvious risk factor, fomites and persons should not
256 be forgotten. Shearing equipment, shared handling facilities or handling infected animals and
257 then clean ones subsequently may spread CLA. Where CLA is present in a flock, shearing
258 older animals or those with lesions later on may reduce the risk of “nicking” abscesses and
259 spreading infection to younger animals. All equipment including that of contractors should be
260 thoroughly cleaned prior to use on all flocks.
261

262 Crucially, abscesses should not be lanced as they release highly infectious material
263 contaminating the environment and potentially increasing the risk of further cases.
264

265

266 End of Box 1

267

268 **Treatment**

269

270 Given the highly infectious nature of CLA, the risk of multi-systemic involvement and the
271 inability to entirely eradicate infection, animals are not conventionally treated. Whilst in the
272 literature there are references to the relatively high susceptibility of *Corynebacterium*
273 *pseudotuberculosis* to antibiotics including penicillin, the thick nature of the abscess wall
274 make treatment prohibitive Senturk and Temizel, 2006, Washburn et al., 2009, Selera et al.,
275 2016).

276

277 Senturk and Temizel, (2006) attempted to treat animals with draining abscesses with
278 Rifamycin and Oxytetracycline. Whilst the 10 day combined courses resolved gross lesions,
279 bacteriological cure was not demonstrated and we must be mindful that it is not
280 appropriate to use Rifamycin as it is not licensed in the UK and it is listed as a critically
281 important antibiotic given its role in treating *Mycobacterium tuberculosis* and leprosy.

282

283 Selera et al., (2016) attempted photodynamic therapy post-operatively after surgical
284 draining of lymph nodes. There was no evidence of recurrence within the treated lymph
285 nodes within 6 months of the procedure. Whilst this does not involve antibiotic therapy, this
286 treatment by definition will not access internal abscesses.

287

288 Given the good efficacy of vaccination for CLA compared to the very poor efficacy of
289 antibiotic treatment, the authors do not consider it justifiable or prudent antibiotic
290 stewardship to treat cases with antibiotics and would encourage an emphasis of flock level
291 control and prevention measures.

292

293 **Management**

294 Following initial diagnosis and investigation (see box 1), there are two main strategies
295 described for management of CLA in commercial flocks: vaccination and test-and-cull.

296

297

298 The vaccine available is a formalin inactivated exotoxin vaccine for PLD Glanvac 6 (Zoetis,
299 Australia) with field trial results showing rates of protection from 25-90%. The vaccination is
300 also a clostridial vaccination requiring annual boosting pre-lambing. It can be imported into
301 the UK under license via the Veterinary Medicines Directorate as it is not commercially
302 available in the UK. Vaccination has resulted in the near elimination of overt clinical signs
303 associated with CLA in flocks using the vaccine correctly in Australia (Windsor, 2014).

304

305 The advantages of using vaccination include that it reduces the number of animals with lung
306 and skin lesions thus reducing challenge in the flock and rate of new infections. It will
307 therefore reduce spread in a flock but is not able to eradicate disease entirely. Sustained
308 vaccination is therefore required to reduce bacterial load within the flock i.e. protecting
309 younger animals whilst older infected animals are progressively culled. However, we need
310 to be mindful and communicate the limitations of our understanding of the efficacy of *Glanvac*
311 programmes in the absence of epidemiological trials conducted under UK management
312 conditions, pathogen strain, host genetic susceptibility and transmission dynamics/infection
313 pressure. It should also be clearly communicated to flocks that at the moment there is no

314 DIVA vaccine available. Whilst this may be of little importance in commercial flocks, this may
315 be of imperative significance in those considering future export and informed consent
316 should be sought. Vaccination can be used in adult animals to reduce infection burden
317 permitting the serological screening of young animals pre-sale and may be most appropriate
318 for flocks with confirmed disease wishing to reduce infectious load within the flock with an
319 aspiration to sell either pre-vaccinated or pre-screened animals for sale.

320

321 The protocol for vaccination is two doses, 4 weeks apart with an annual booster at least a
322 month before lambing or shearing. Strategies for application of vaccination are described in
323 box 2. The vaccination experience in Australia has been that prior to vaccination
324 introduction, flock prevalence was as high as 97% flocks (New South Wales) with the flock
325 level prevalence 29% in 1995. Abattoir screening and recording was subsequently
326 introduced and found to be as low as 17% of consignments had at least one lesion positive
327 animal and 1.3% of all animals were lesion positive (Windsor, 2011). These results have
328 been achieved despite a further piece of work demonstrated that just 12% of flocks used
329 the vaccines as recommended (Paton et al., 2003). The prevalence was demonstrated to be
330 lower when vaccines were used correctly.

331

332 'Test and cull' has been used for control in commercial suckler sheep flocks using individual
333 antibody ELISA (Baird and Malone (2010), Voigt et al., (2012)) and coupled with bulk milk
334 tank serology in goat herds in Norway (Nagel-Alne et al (2015). This requires repeated
335 serological testing of the adult flock with subsequent removal of any positive animals.

336

337 Voigt et al., (2012) demonstrated that they achieved flock sero-positivity reduction from
338 10% to 0.4% within two years by blood sampling every three months and culling any
339 seropositive or culture positive animals.

340

341 However, there is a huge cost associated with this strategy (see table 1) (Baird and Malone
342 (2010). There may be a premium obtainable for CLA negative flocks, however, in the
343 absence of an accreditation scheme in the UK, there is no formal recognition,
344 standardisation or quality control available. The test characteristics needs to be clearly
345 explained as it is highly likely that false negatives will occur, prolonging the testing period
346 and extending time to eradication and furthermore false positives will be taken which in
347 itself may have consequences for the economic value of the flock. Additionally, as
348 prevalence reduces, the relative proportion of false positives increased (which may be
349 equally detrimental for flocks with high value individuals). We must also remember that
350 prevalence is not static, and animals with false negative results or those only recently
351 infected may propagate infection during the testing interval. CLA common in inguinal &
352 scrotal lymph nodes of rams at breeding soundness exam but semen quality was normal & no
353 organism excreted in semen (Gouletsou & Fthenakis, 2010) so CLA positive animals could be
354 considered for semen collection or embryo flushing.

355

356 Table 1: Examples of costs for a 300 ewe flock, with 60 replacements and 5 rams testing and
357 removing after sequential rounds of testing. We have made the assumption that the starting

358 prevalence of CLA is 10% before the onset of testing and that given the sensitivity some
 359 animals will be missed at each round of testing.

Testing round	Blood sampling cost	Time to bleed animals	Animals identified (87%) sensitivity (98% specificity)	CLA positive animals remaining in the flock
>12 weeks intervals	(£5.80 per sample, SAC 2018, >40 samples)	(£100 per hour)		10% starting prevalence
0				37 animals
1	£2117	£500	32 animals true positive, 1 false positive	5 animals
2	As above	As above	4 animal true positive, <1 false positive	1 animal
3	As above	As above	87% chance of finding the remaining 1 animal	
Total	£6351	£1500		
Total	£7851			

360

361

362

Box 2: Application of vaccination in sheep flocks

363

Glanvac 6 (Zoetis, Australia) is a multi-valent vaccine licensed for the use in flocks for control of caseous lymphadenitis in addition to clostridial management. The protocol requires 1ml of vaccine injected under the skin near the neck. The primary course is completed with a second vaccine four weeks later with recommended annual booster doses to control CLA. Injection site reactions are not uncommon with the vaccine.

364

365

How the vaccine is applied within flocks requires clear communication and informed decision making between vets and farmers.

366

367

- Whole flock vaccination with initial vaccination when replacements recruited to the flock

368

- Rams have been shown to be high risk for becoming and propagating infection. Therefore some commercial flocks may choose to vaccinate rams to reduce propagation within ram mobs and reduce infection risk to the ewe mob. This will not limit the impact of CLA within the ewe flock

369

- Flocks wishing to control CLA but sell stock which could be demonstrated to be free from disease may choose to vaccinate the adult flocks and retained replacements, leaving for young-stock for sale unvaccinated in the absence of a DIVA vaccination. These animals should be in strict isolation and ideally blood sampled twice 12 weeks apart as per the former SAC health scheme. This may

370

371

372

373

374

375

376 **Implications for flocks**

377 Although the suspected UK flock-level prevalence is low and the economic implications for
378 CLA infection are not fully understood, sheep movements between infected and non-infected
379 flocks means that the spread of CLA is very likely. The impact of this is described in
380 Norwegian literature where test and cull had to begin after an outbreak of CLA in a “ram
381 breeding circle” (Hektoen et al., 2012).

382

383 A positive diagnosis of CLA on a farm may preclude the premises from exporting and
384 furthermore preclude them from sales where “clear” animals are required. Formerly, there
385 was an accreditation scheme available in the UK through the Scottish Agricultural College.
386 The scheme was abandoned due to low uptake and difficulties in isolating new animals for
387 long periods post-purchase to complete quarantine testing and the cost of two veterinary
388 visits, 12 weeks apart to accredit a small number of rams.

389

390 There are limitations with all strategies of management for CLA. Whilst vaccination has been
391 highly efficacious in the Australian situation, this has not been repeated in the UK and for
392 those flocks who may require sero-negative status to permit export or because this is
393 required from their customers, the lack of DIVA vaccine available may preclude this option.
394 Test and cull may be a costly strategy given the sensitivity of the test and even after
395 apparent “clearance of reactors” positive animals may still be found. The lack of a strategy
396 which is practical with clear cost benefit is compounded by the apparent inertness of CLA in
397 the UK commercial market in contrast with MV, OPA, infectious lameness, resistance
398 parasites etc and the difficulty in defining the cost of the disease. Whilst motivators in the
399 UK have not been studied with regards to attitudes towards CLA, in the authors’
400 experiences, desire to sell “clean” stock, the visual nature of the disease in prized stock,
401 avoiding comeback, protecting the breed brand and pride in the stock they sell are
402 motivators for implementing any strategy. For some farmers the emotional/reputational
403 cost of this disease may drive their decision making above the cost benefit.

404

405 **Summary**

406 Further work is needed to understand the economic impact and prevalence of CLA in the UK
407 sheep flock and goat herd but initial work suggests that the prevalence of infected flocks is
408 much lower than observed in Australia. Vaccination has been demonstrated to be highly
409 efficacious in reducing prevalence of disease within infected flocks but this requires a period
410 of sustained vaccination, client compliance and clear communication. If a declared ‘CLA-free
411 status’ is the aim, other routes such as test and cull should be considered. The relatively low
412 sensitivity of serological testing presents its own challenges and informed consent should be

413 sought before commencing whole flock testing as this may be a long and costly process.
414 Whilst we suspect the national prevalence is low, there is also evidence that prevalence is
415 high among ram breeders and terminal sire flocks in particular and therefore the role of
416 rams in the spread of CLA should not be underestimated. Discussions can be initially
417 triggered by vets at cull ewe screens or of rams at point of purchase but as described, the
418 next step for flocks as to investigation and implementation of control can be a tricky
419 decision. Often there are bigger, clearer threats to production but for businesses built on a
420 reputation of higher health, elite stock, this may be just as damaging to their business.
421 Ultimately in the absence of clear cost-benefit analysis based on observational data from
422 the UK, CLA management should be a clearly communicated undertaking with defined,
423 costed outcomes.

424 **Acknowledgements**

425 This paper was produced as a result of a literature review generated as part on a project
426 funded by the Agricultural and Horticultural Development Board (AHDB) looking at iceberg
427 diseases on commercial sheep flocks.

428

429

430 **References**

431 Arsenault, J., Girard, C., Dubreuil, P., Daignault, D., Galarneau, J.R., Boisclair, J., Simard, C.
432 and Bélanger, D., 2003. Prevalence of and carcass condemnation from maedi–visna,
433 paratuberculosis and caseous lymphadenitis in culled sheep from Quebec,
434 Canada. *Preventive veterinary medicine*, 59(1-2), pp.67-81.

435

436 Baird, G., 2000. Differential diagnosis of non-parasitic skin conditions in sheep. *In Practice*, 22(2),
437 pp.72-7

438

439 Baird, G., Synge, B. and Dercksen, D., 2004. Survey of caseous lymphadenitis seroprevalence
440 in British terminal sire sheep breeds.

441

442 Baird, G.J. and Fontaine, M.C., 2007. *Corynebacterium pseudotuberculosis* and its role in
443 ovine caseous lymphadenitis. *Journal of comparative pathology*, 137(4), pp.179-210.

444

445 Batey, R.G., 1986. Pathogenesis of caseous lymphadenitis in sheep and goats. *Australian*
446 *veterinary journal*, 63(9), pp.269-272.

447

448 Binns, S.H., Green, L.E. and Bailey, M., 2002. Postal survey of ovine caseous lymphadenitis in
449 the United Kingdom between 1990 and 1999. *Veterinary Record*, 150(9), pp.263-268

450

451 Bregenzer, T., Frei, R., Ohnacker, H. and Zimmerli, W., 1997. *Corynebacterium*
452 *pseudotuberculosis* infection in a butcher. *Clinical Microbiology and Infection*, 3(6), pp.696-
453 698.

454

455 Bush, R.D., Barnett, R., Links, I.J. and Windsor, P.A., 2012. Using abattoir surveillance and
456 producer surveys to investigate the prevalence and current preventative management of
457 Caseous lymphadenitis in Merino flocks in Australia. *Animal production science*, 52(7),
458 pp.675-679.

459

460 Ferrer, L.M., Lacasta, D., Chacón, G., Ramos, J.J., Villa, A., Gómez, P. and Latre, M.V., 2009.
461 Clinical diagnosis of visceral caseous lymphadenitis in a Salz ewe. *Small ruminant*
462 *research*, 87(1), pp.126-127.

463

464 Gouletsou, P.G. and Fthenakis, G.C., 2010. Clinical evaluation of reproductive ability of rams. *Small*
465 *ruminant research*, 92(1-3), pp.45-51

466

467 Hektoen, L., 2012. An outbreak of caseous lymphadenitis in a Norwegian ram circle and
468 attempts to eliminate the disease. *Small ruminant research*, 106(1), pp.25-26.

469

470 Linklater, K.A. and Smith, M.C., 1993. *Color atlas diseases and disorders of the sheep and*
471 *goat*. Wolfe Publishing Ltd.

472

473 Lovatt, F.M. and Strugnell, B.W., 2013. An observational study involving ewe postmortem
474 examination at a fallen stock collection centre to inform flock health
475 interventions. *Veterinary Record*, 172(19), pp.504-504.

476

477 Nagel-Alne, G.E., Valle, P.S., Krøntveit, R. and Sølverød, L.S., 2015. Caprine arthritis
478 encephalitis and caseous lymphadenitis in goats: use of bulk tank milk ELISAs for herd-level
479 surveillance. *The Veterinary record*, 176(7), pp.173-173.

480

481 Oreiby, A.F., 2015. Diagnosis of caseous lymphadenitis in sheep and goat. *Small Ruminant*
482 *Research*, 123(1), pp.160-166.

483

484 Paton, M.W., Walker, S.B., Rose, I.R. and Watt, G.F., 2003. Prevalence of caseous
485 lymphadenitis and usage of caseous lymphadenitis vaccines in sheep flocks. *Australian*
486 *veterinary journal*, 81(1-2), pp.91-95.

487

488

489 Paule, B.J.A., Azevedo, V., Regis, L.F., Carminati, R., Bahia, C.R., Vale, V.L.C., Moura-Costa, L.F.,
490 Freire, S.M., Nascimento, I., Schaer, R. and Goes, A.M., 2003. Experimental *Corynebacterium*
491 *pseudotuberculosis* primary infection in goats: kinetics of IgG and interferon- γ production, IgG avidity
492 and antigen recognition by Western blotting. *Veterinary immunology and immunopathology*, 96(3-4),
493 pp.129-139.

494 Experimental *Corynebacterium pseudotuberculosis* primary infection in goats: kinetics of
495 IgG and interferon- γ production, IgG avidity and antigen recognition by Western
496 blotting. *Veterinary immunology and immunopathology*, 96(3-4), pp.129-139.

497

498 Peel, M.M., Palmer, G.G., Stacpoole, A.M. and Kerr, T.G., 1997. Human lymphadenitis due to
499 *Corynebacterium pseudotuberculosis*: report of ten cases from Australia and review. *Clinical*
500 *Infectious Diseases*, 24(2), pp.185-191

501

502 Scott, P.R., Collie, D.D.S. and Hume, L.H., 1997. Caseous lymphadenitis in a commercial ram
503 stud in Scotland. *Veterinary record*, 141(21), pp.548-549.

504

505 Szalus-Jordanow, O., Kaba, J., Czopowicz, M., Witkowski, L., Nowicki, M., Nowicka, D.,
506 Stefanska, I., Rzewuska, M., Sobczak-Filipiak, M., Binek, M. and Frymus, T., 2010.
507 Epidemiological features of Morel's disease in goats. *Polish journal of veterinary*
508 *sciences*, 13(3), p.437.

509

510 Sellera, F.P., Gargano, R.G., Della Libera, A.M.M.P., Benesi, F.J., Azedo, M.R., de Sá, L.R.M.,
511 Ribeiro, M.S., da Silva Baptista, M. and Pogliani, F.C., 2016. Antimicrobial photodynamic
512 therapy for caseous lymphadenitis abscesses in sheep: report of ten cases. *Photodiagnosis*
513 *and photodynamic therapy*, 13, pp.120-122.

514

515 Sunil, V., Menzies, P.I., Shewen, P.E. and Prescott, J.F., 2008. Performance of a whole blood
516 interferon-gamma assay for detection and eradication of caseous lymphadenitis in
517 sheep. *Veterinary microbiology*, 128(3-4), pp.288-297.

518

519 Senturk, S. and Temizel, M., 2006. Clinical efficacy of rifamycin SV combined with
520 oxytetracycline in the treatment of caseous lymphadenitis in sheep.
521

522 Voigt, K., Baird, G.J., Munro, F., Murray, F. and Brülisauer, F., 2012. Eradication of caseous
523 lymphadenitis under extensive management conditions on a Scottish hill farm. *Small*
524 *ruminant research*, 106(1), pp.21-24.
525

526 Washburn, K.E., Bissett, W.T., Fajt, V.R., Libal, M.C., Fosgate, G.T., Miga, J.A. and Rockey, K.M.,
527 2009. Comparison of three treatment regimens for sheep and goats with caseous
528 lymphadenitis. *Journal of the American Veterinary Medical Association*, 234(9), pp.1162-1166.
529

530 Williamson, L.H., 2001. Caseous lymphadenitis in small ruminants. *Veterinary Clinics: Food*
531 *Animal Practice*, 17(2), pp.359-371.
532

533 Windsor, P.A., 2011. Control of caseous lymphadenitis. *Veterinary Clinics: Food Animal*
534 *Practice*, 27(1), pp.193-202.
535

536 Windsor, P.A., 2014. Managing control programs for ovine caseous lymphadenitis and
537 paratuberculosis in Australia, and the need for persistent vaccination. *Veterinary Medicine:*
538 *Research and Reports*, 5, pp.11-22.
539

540 Windsor, P.A. and Bush, R.D., 2016. Caseous lymphadenitis: Present and near forgotten
541 from persistent vaccination?. *Small Ruminant Research*, 142, pp.6-10.