Caseous lymphadenitis (CLA) in sheep and goats

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CLA – presentation outline

- Introducing CLA
- Control of disease
- Prevalence of disease
- Diagnosis
- Flock eradication by serology
- CLA study in 4 culled flocks



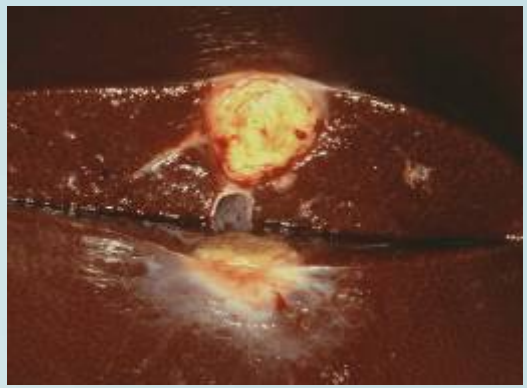


Caseous Lymphadenitis (CLA)

- *Corynebacterium pseudotuberculosis*
- First diagnosed in GB sheep in 1991 (goats 1990)
  - NI in 1999
  - RoI in 1998
- Mainly terminal sire breeds
- Prevalence in Britain may be as high as 18% of flocks
- Prevalence of > 25% within some affected flocks

CLA infection

- Infection enters through wounds
  - Abscesses in lymph nodes
  - Lung and viscera abscesses
- Spreads rapidly within flock
- Losses
  - Culling affected sheep
  - Affected parts of carcase condemned
    - downgrading of carcase
  - Trade implications
- Human infection - uncommon

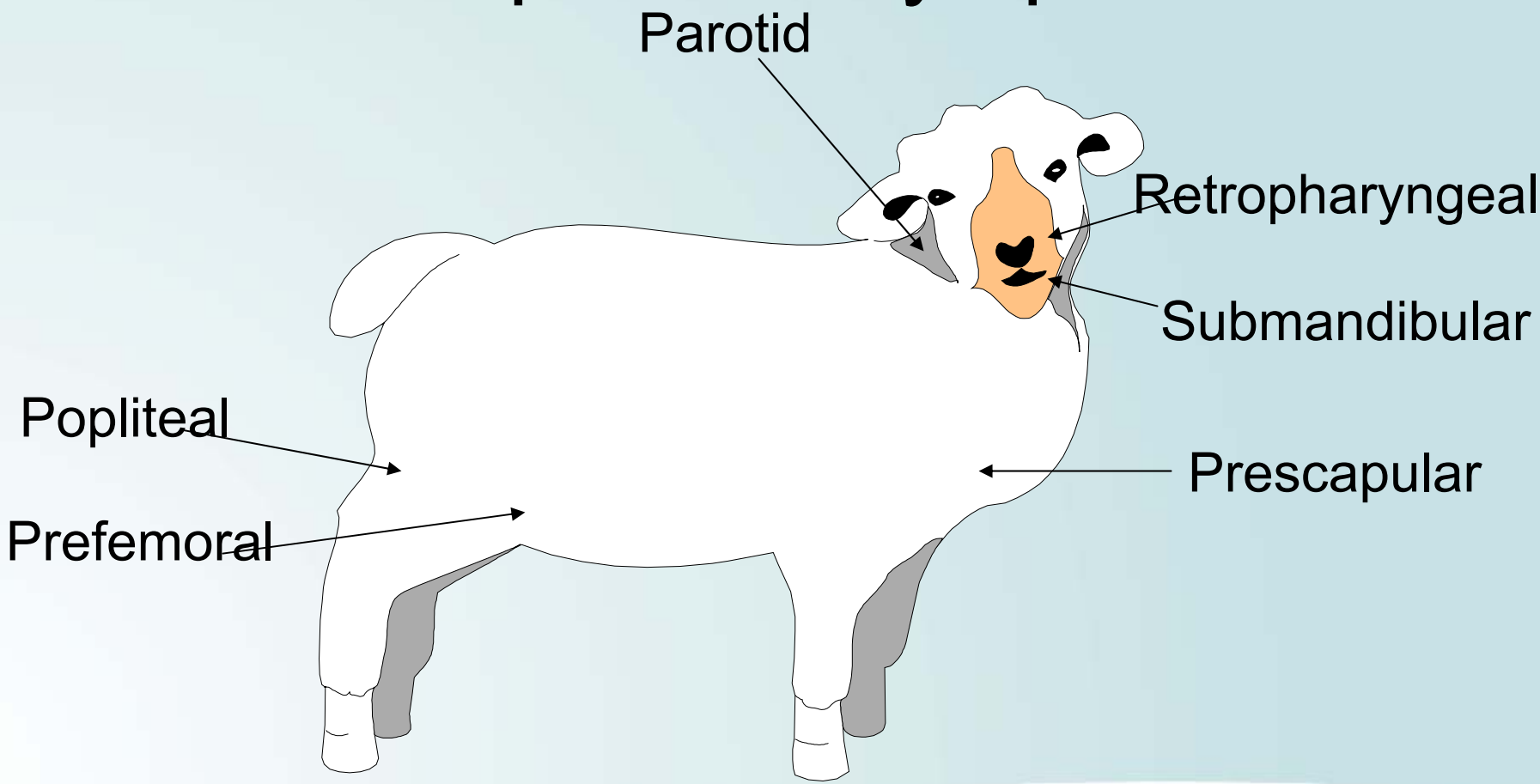


CLA in goats

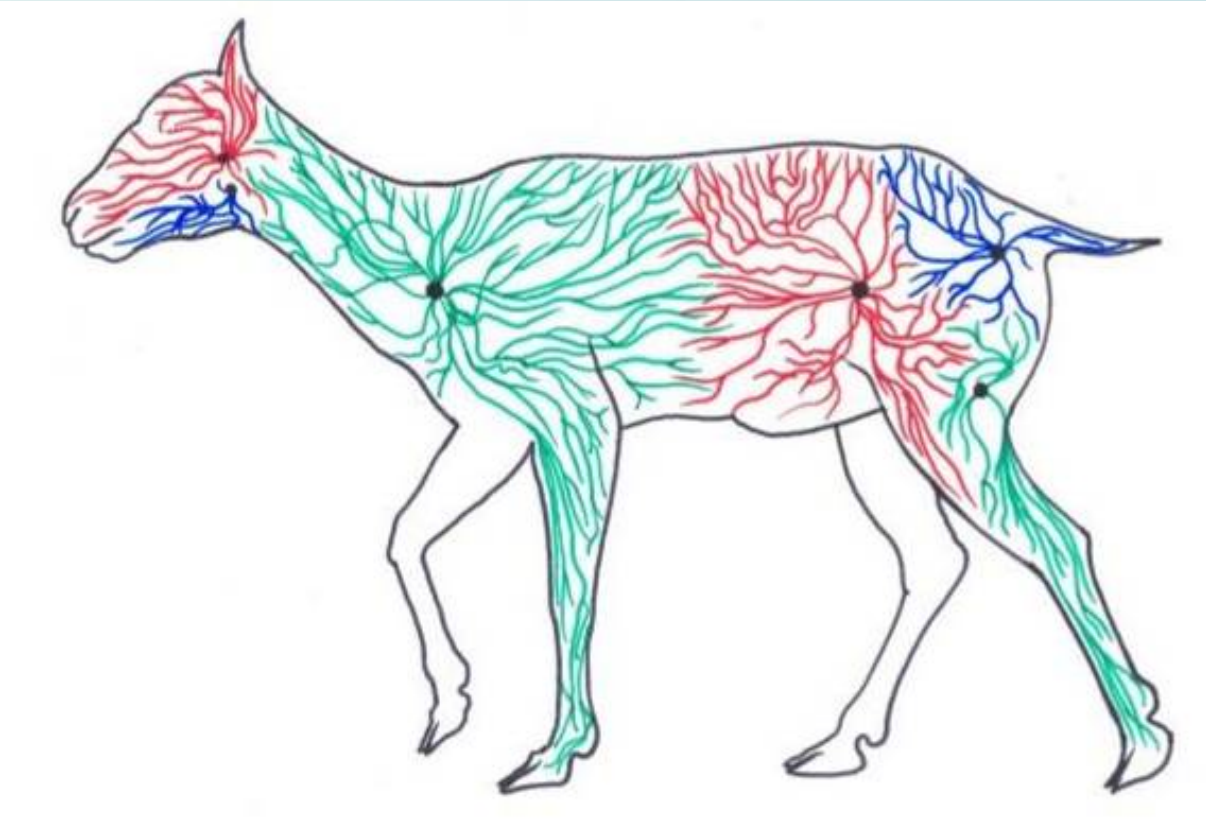
- Natural infection similar to sheep
- Same biotype of *C. pseudotuberculosis*
- Clinical presentation
  - Superficial lymph nodes
    - Mainly head and neck
- Main route of infection
  - via oral cavity
  - Skin abrasions face and head
- Visceral lesions more common in sheep



CLA in Superficial Lymph Nodes



CLA – lymphatic drainage



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CLA in Parotid Lymph Node



CLA in Parotid Lymph Node



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CLA in Parotid Lymph Node



CLA abscesses in LNs





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CLA Abscesses in Lungs



Differential diagnosis

- *Arcanobacterium pyogenes*
- *Actinobacillus lignieresi* (cruels)
- Staphlococcal dermatitis



CLA

- problems with control

- Carrier animals
  - Incubation period up to four months
- Many cases – only visceral lesions
- Organism survives long periods in environment
- Antibiotic treatment ineffective
- Definitive diagnosis only by culture

Preventing CLA

- Avoid introducing infected sheep
- New cases associated with the purchase or loan of infected sheep
- Examine sheep thoroughly before purchase
- SAC CLA monitoring scheme
- Consider a quarantine period
- Ensure high levels of biosecurity especially during visits by shearing contractors

Managing CLA

- Regular examination of the flock
  - every two to three months
- Separation of sheep showing suspicious lesions
- Cull affected sheep
- Alternatively operate a “clean” and “dirty” flock policy
- Attention to hygiene especially when dealing with pus discharge

Managing CLA

- At shearing time
  - Shear younger animals first, known infected animals last
  - Personal hygiene and disinfection of cutters and combs is important
  - Flock owners should ensure adequate washing facilities & provide disposable protective clothing
- Avoid dipping within 2 weeks of shearing

Managing CLA

- Spread of infection before weaning is low
  - rearing weaned lambs as an entirely separate group should maintain this status
  - this can then form the nucleus of a “cleaner” flock
  - possible to sell from such a group with some degree of assurance that infection is not being passed on to purchaser

Vaccination

- Early vaccines – inactivated whole cell preparations
- Recent formalin-killed virulent UK isolate in alhydrogel
- Toxoid vaccines – Phospholipase D (PLD) formalin inactivated
- Glanvac™ - Australian combined clostridial/CLA vaccine
- Offers significant protection in sheep and goats
  - not authorised for use in Britain or Ireland
- Moredun recombinant PLD vaccine

CLA in Europe

- Czech Republic
- France
- Germany
- Great Britain
- Netherlands
- Italy
- Ireland
- Norway
- Poland
- Portugal
- Romania
- Spain

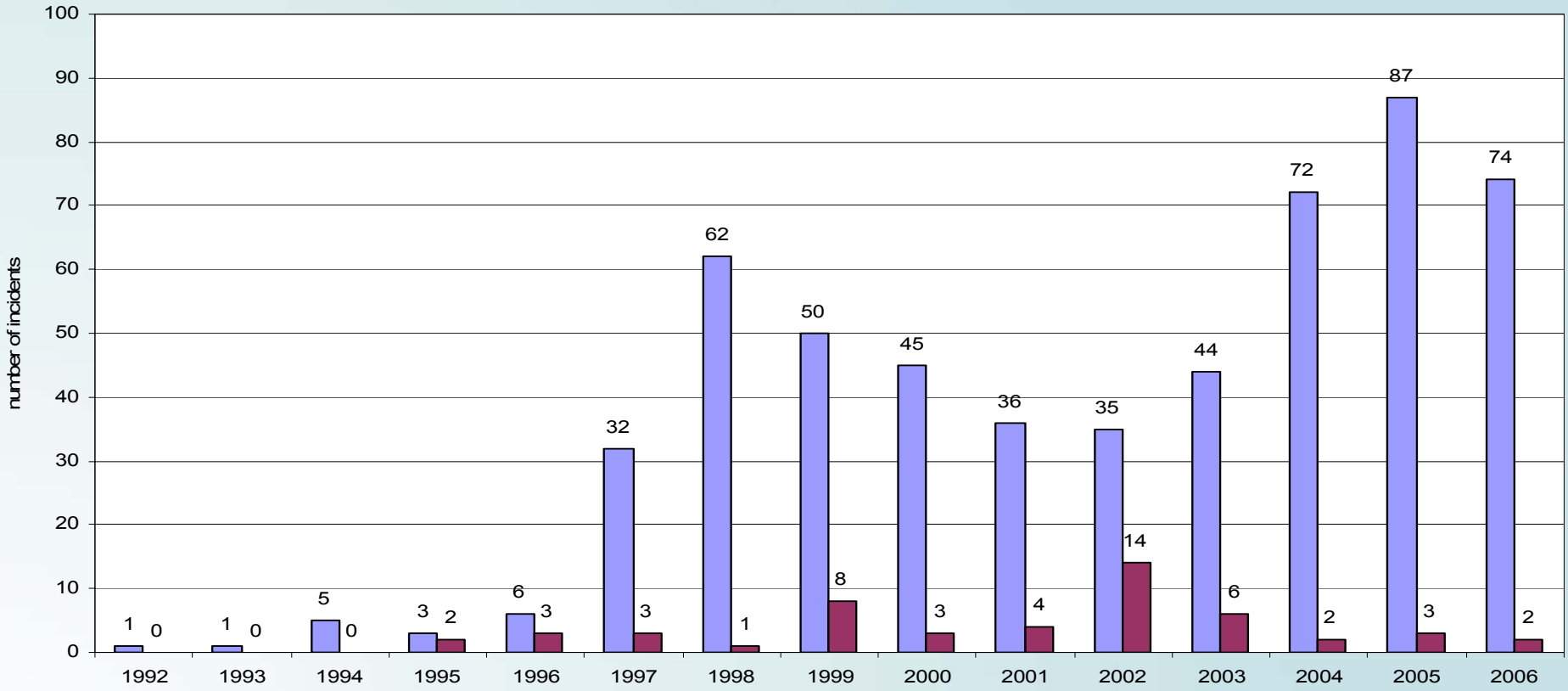
Global prevalence of CLA

- Worldwide distribution – small ruminants
- Present in majority of sheep rearing countries
- Abattoir-based prevalence studies
  - Australia (>50% adult sheep in 1984
    > 20% in 2002)
  - New Zealand (7.1% adult sheep in 1986-7)
  - Western USA (42.5% adult sheep in 1984)
  - Alberta, Canada (13% adult sheep in 1998)
  - Quebec, Canada (21-36% adult sheep in 2003)

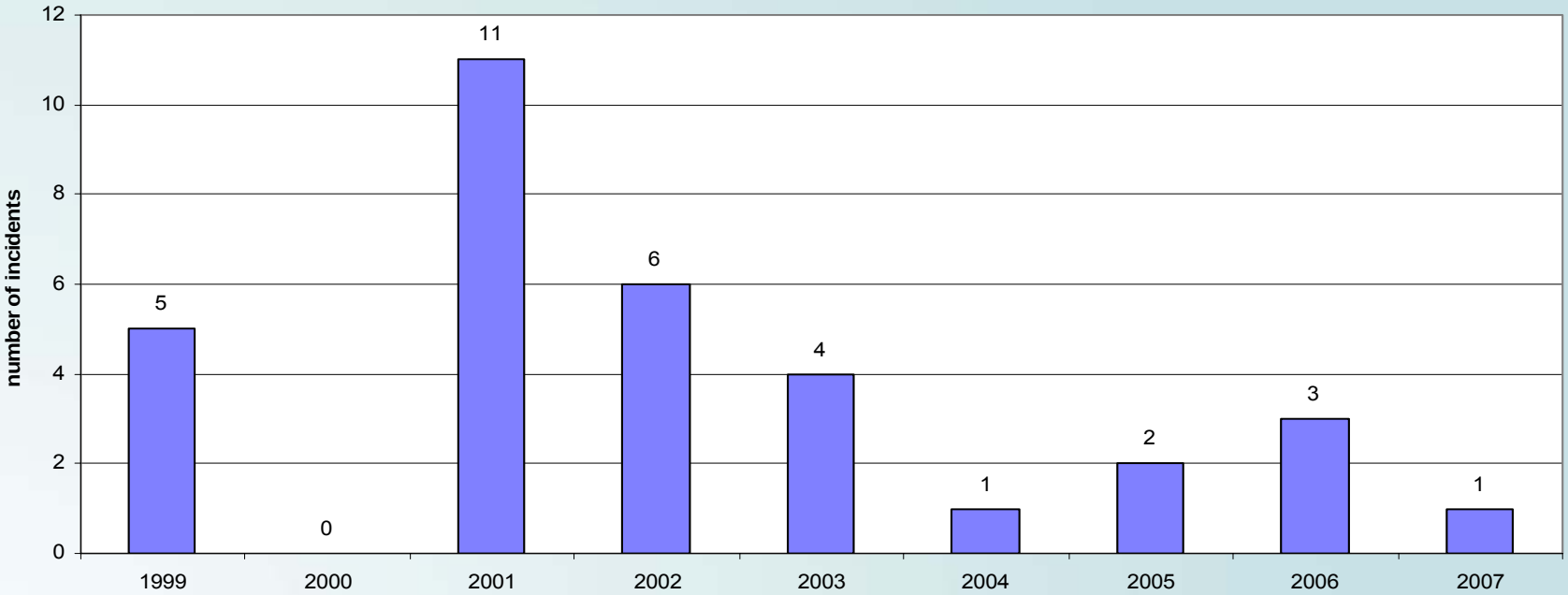
Prevalence of CLA in GB

- Serological survey in 2000
  - 2538 samples from rams in 745 flocks
  - 9.93% of sheep seropositive
  - 18% of flocks had one or more positive animals
- Postal survey in 2000
  - vets in Sheep Veterinary Society
    - 18% had diagnosed CLA
  - sheep farmers
    - 56% reported abscesses in sheep
    - 13% had CLA diagnosed

CLA incidents GB

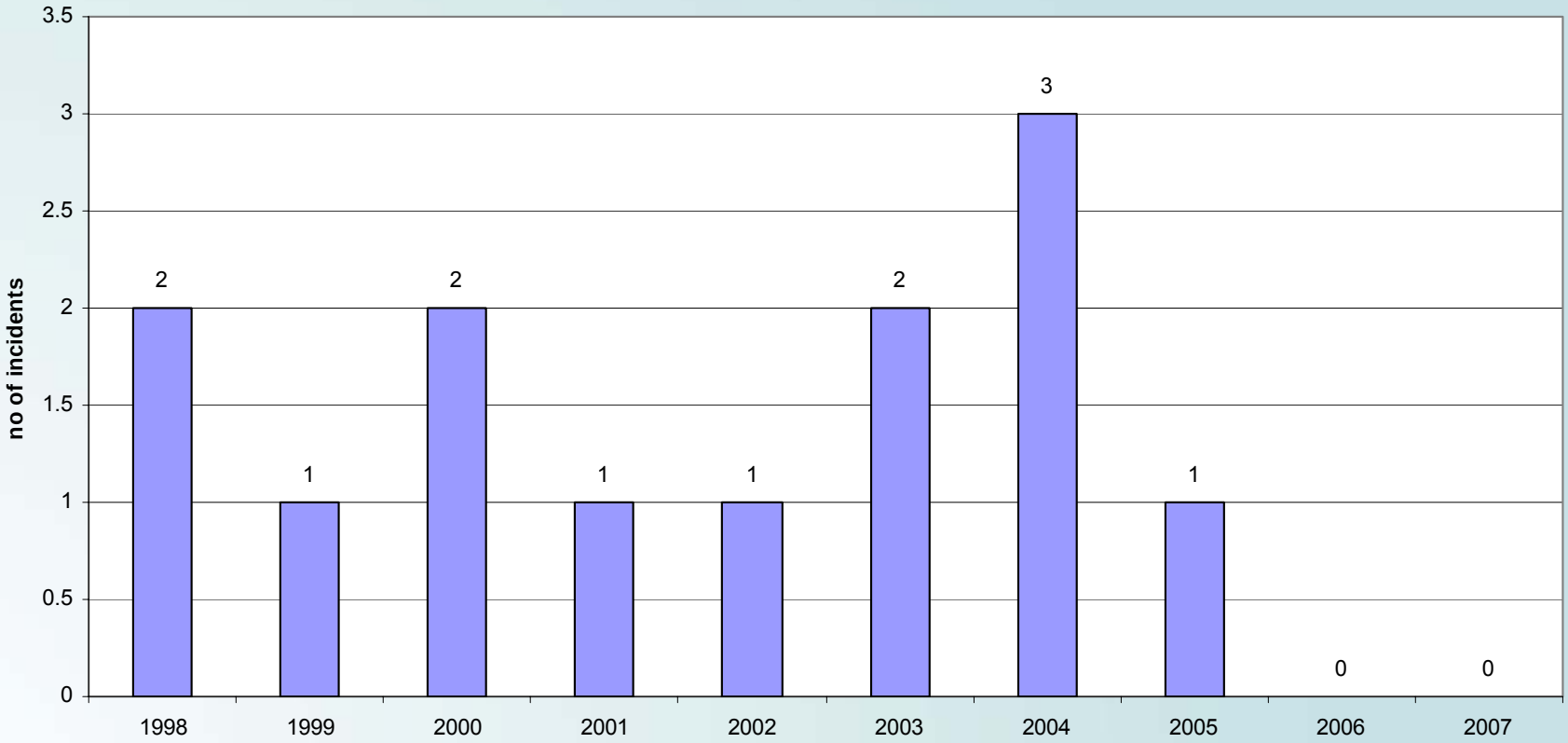


CLA incidents NI



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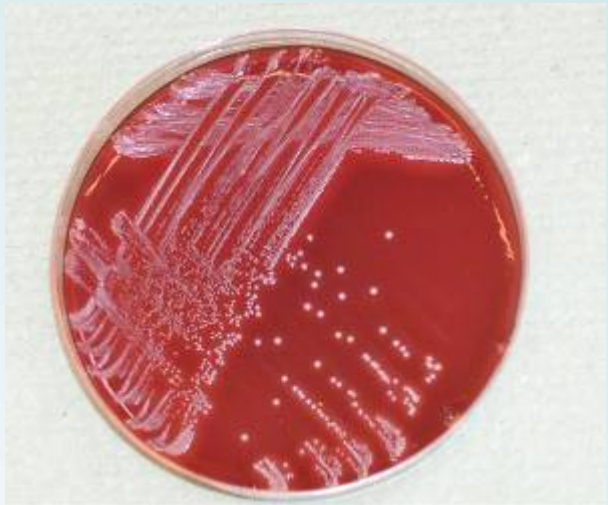
CLA incidents in RoI

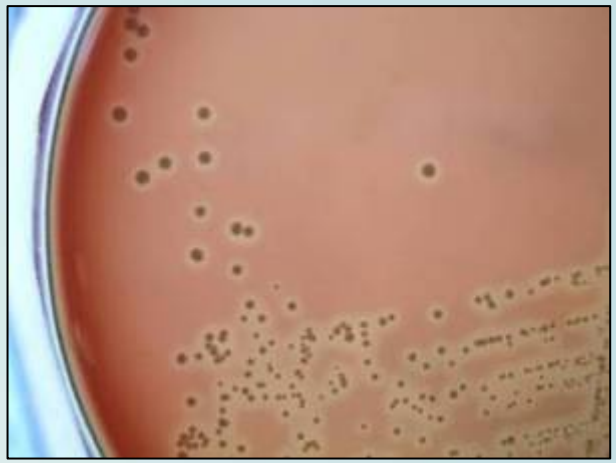


PFGE of isolates

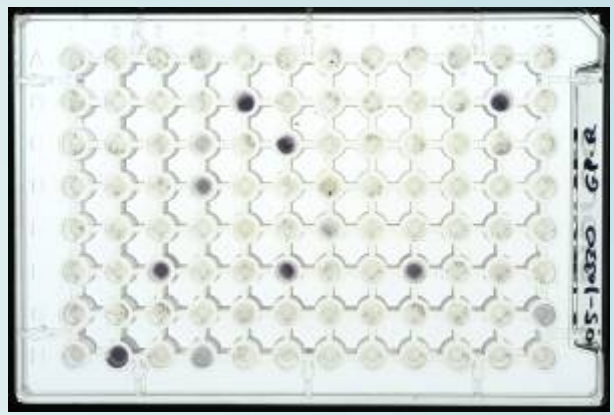
- Biotypes (S+G; C+H)
- 49 UK *C. pseudotuberculosis* isolates tested by PFGE
- 43/46 sheep isolates and 2/3 goat – P2.
  - single P3, P5, P6 isolates in sheep
  - single P4 isolate in goats
- All clonally related
- Goat isolates were from the original UK outbreak
- 2/2 equine isolates – P1 (not clonally related)
- 42 global isolates – Australia, Canada, Netherlands, NI and RoI.
  - sheep and goat isolates clonally related – irrespective of country of origin

Culture









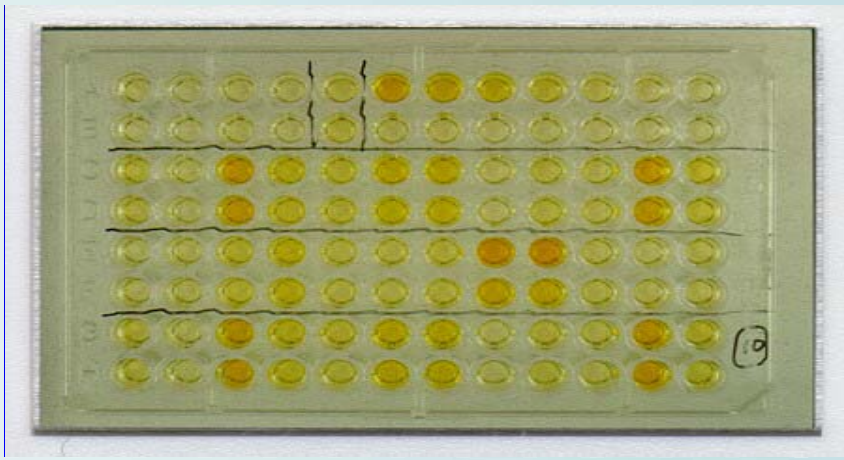
CLA in the Netherlands

- Sheep: 1978 first isolation in the Netherlands of *C. pseudotuberculosis* from a lung
- Goats: 1984 CLA described as clinical entity (imported with French goats)
- Indirect double antibody sandwich ELISA
  - Ter Laak *et al*. (1992)
- Plates coated with immunoglobulins from a rabbit hyperimmune serum raised against a crude exotoxin preparation of *C. pseudotuberculosis*
- Test and cull in NL goats

Eradication in goats - NL







Modified ELISA

	ELISA A	ELISA B	ELISA C	ELISA D
Goat				
Sensitivity (%)	72±5	94±3	61±3	56±6
Specificity (%)	99±1	98±1	86±3	97±1
Sheep				
Sensitivity (%)	51±6	79±5	75±5	59±6
Specificity (%)	97±2	99±1	69±4	92±3

Sensitivity = % animals with CLA with a positive test result

Specificity = % of CLA negative animals with a negative test result

CLA ELISA - Trial Flocks

- Total of six flocks chosen
  - Three in Scotland
  - Two in Northern Ireland
  - One in Northern England

- All 6 flocks had established CLA
  - Confirmed by bacterial culture

ELISA test for CLA

- Developed at the ID-DLO in Lelystad
- A refinement of the test used in Dutch goat CLA health scheme – ELISA B

- Lab trials in sheep established ELISA B
  - Sensitivity of 79% ± 5%
  - Specificity of 99% ± 1%

The Trial Flocks

- Visits at ~ 6-monthly intervals
  - Summer 1999
  - Clinical examination and blood sampling of all sheep 6 months of age
- Isolation and bacteriological sampling of all animals with clinical signs of CLA
- Removal or effective separation of CLA-positive animals
  - Culture or antibody ELISA

The Trial Flocks

- Testing began in summer of 1999
  - effectively suspended for a year due to FMD outbreak
- Post-mortem examinations of both seronegative and seropositive animals
- One flock sold during first year of trial
- Second flock-owner failed to remove sheep testing positive
  - Incidence of CLA increased in this flock

The Trial Flocks - Results

- 4 flocks
  - Considerable reduction in disease
- ELISA blood test
  - All 4 flocks negative for CLA
- Clinical examination
  - No new cases in last 6 months of trial

Results

Flock	Initial seroprevalence	Final seroprevalence
A	13%	0%
B	63%	0%
C	29%	67%
D	8%	0%
E	5%*	2%
F	0%**	0%

* Flock withdrawn from trial after six months
** Second flock test at 9% seroprevalence

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Flock B results

- July 1999
  - 68/108 animals were ELISA positive
  - 30/108 animals clinical signs of CLA
- Flock divided into “infected” and “non-infected” parts on basis of test
- Only one further case of clinical disease within “non-infected” part of flock
- March 2002
  - No new seropositive animals detected in “non-infected” group

Conclusions

- "Test & cull" policy can dramatically reduce flock CLA
  - Changes in management practice
- Incidence of new clinical cases is very low within ELISA-negative group
- ELISA test for CLA may be of use in controlling and/or eradicating disease

Post-mortem and serological examinations of sheep in four flocks affected with caseous lymphadenitis

4 flocks - A

- July 2001 - 104 sheep - 3 groups
  - 4 stock rams, 62 ewes & 38 lambs
- 25 sheep slaughtered as clinical CLA
  - CLA confirmed in 9 ewes, 4 rams & ram lamb
    - 6 ewes - lung lesions, one ewe ~30 abscesses both lungs, abscesses mediastinal & prescapular LN
- remaining ewes purchased
- source of infection
  - 2 rams imported from Scotland in August 2000

4 flocks - B

- June 2001 - 148 sheep - 5 groups
  - 2 stock rams, 88 ewes, 25 shearlings, 18 ewe lambs & 15 ram lambs
- 49 sheep slaughtered as clinical CLA
  - CLA confirmed at PME
    - extensive lesions - 35 carcases condemned
- remainder of flock purchased
- source of infection
  - ram from flock A in late October 2000

4 flocks - C

- August 2001 - 101 sheep in 6 groups
  - groups had mixed
- CLA confirmed at PME in 21/28 suspect ewes
  - 7 lung lesions
- rest of flock purchased in batches
- source of infection
  - ewe purchased November 1999
  - from same flock in Scotland as flock A

4 flocks - D

- August 2001 – 75 sheep in groups
  - groups not mixed
- 3 ewes clinically suspect CLA
  - these 3 + 2 others in group positive at PME
- Further 6 ewes positive CLA at PME
- Remainder of flock clinically negative until de-restricted in March 2002
- Source of infection
  - 5 ewes from flock A in December 2000

CLA ELISA

- Dercksen and others (2000)
  - false negatives in sheep flocks
    - modified ELISA B
- ELISA evaluated in:
  - healthy sheep from CLA-free flocks
  - sheep with culture confirmed CLA abscesses
    - specificity 99 $\pm$ 1%, sensitivity 79 $\pm$ 5%
- present study evaluates ELISA within 4 affected flocks

4 affected flocks

- 329 sheep (63 male, 266 female)
  - A (n=98), B (n=95), C (n=100), D (n=36)
  - blood sampled for ELISA
  - subsequently examined *post mortem*
- 133 sheep
  - CLA lesions at post-mortem examination
  - confirmed on culture
- 196 sheep
  - CLA not confirmed *post mortem*

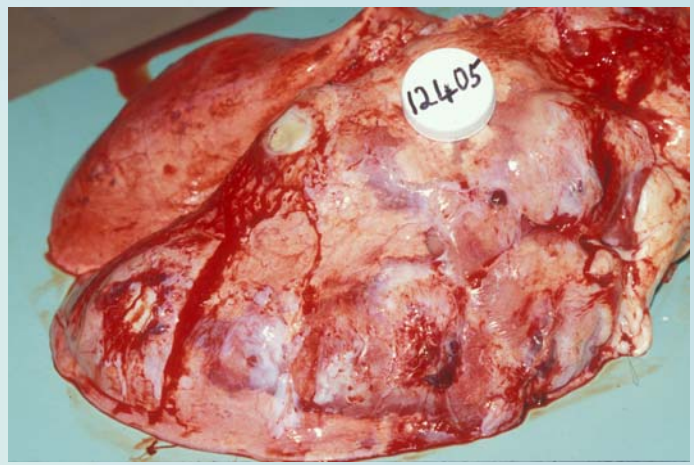
ELISA sensitivity and specificity

	ELISA				
CLA lesion	Positive	Negative	Total	Sensitivity	0.88
Positive	117	16	133	Specificity	0.55
Negative	88	108	196		
Total	205	124	329		

CLA lesions

- 133 sheep
  - CLA-confirmed lesions
- lungs – 46 (35%)
- parotid LN – 44 (33%)
- prescapular LN – 38 (29%)
  mediastinal LN – 30 (23%)
- retropharyngeal LN – 11 (8%)





CLA lesions

- 133 sheep
  - CLA-confirmed lesions
- prefemoral LN – 10 (8%)
- bronchial LN – 9 (7%)
- submandibular LN- 8 (6%)
- liver – 5 (4%)
- mesenteric LN – 4 (3%)
- mammary LN – 4 (3%)
- other sites – 11 (8%)



CLA lesions

- CLA lesions (133 sheep)
  - multiple sites
- Superficial LN or

  S/C lesions only - 69
- Internal lesions (lungs and visceral LN) only – 32
  - 28 ELISA-positive
- Visceral lesions in ~ 24%





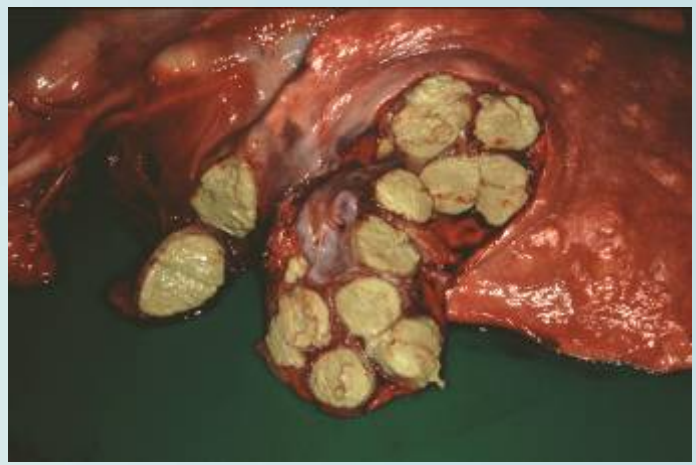
Conclusions

- Visceral lesions only - approx 24% of cases
  - clinical exam will not remove all CLA cases
  - ELISA detects non-apparent cases
- ELISA high sensitivity (0.88), low specificity (0.55)
  - low specificity
    - infected sheep eliminating disease - no lesions

Conclusions

High number of respiratory tract lesions

- intensive husbandry
- rapid spread of disease



Mathematical model of *C. pseudotuberculosis* in sheep

Model examined 3 possible routes of transmission

I. Overt to overt

II. Respiratory to overt

III. Respiratory to respiratory

Dynamics of infection in flocks

- Using lesion and culling data from 4 flocks
  - Overt to overt most frequent route of transmission
- Initial epidemic of overt abscesses
  - followed by gradual increase in respiratory abscesses
- Approximately 25% of sheep with overt abscesses were predicted to develop respiratory abscesses

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