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[1] ANSES, Laboratoire de Sophia Antipolis, Unité Fièvre Q animale, Sophia Antipolis, France (*French RNL for Q fever*)

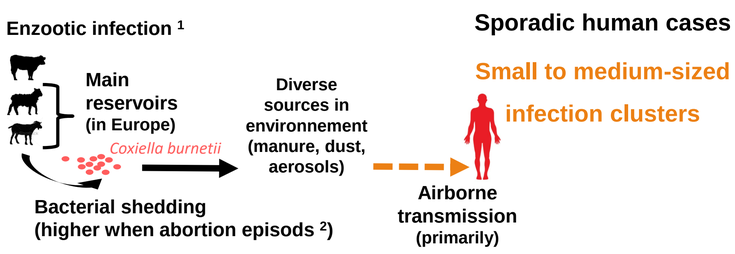
[2] Exploitation agricole d'Oloron, Lycée des Métiers de la Montagne, Oloron Sainte Marie, France

[3] Clinique Vétérinaire du Haut-Béarn, Oloron Sainte Marie, France

[4] GDS France, Fédération Nationale des Groupements de Défense Sanitaire, Paris, France

[5] Université Clermont Auvergne, INRAE, VetAgro Sup, UMR EPIA, Saint-Genès-Champanelle, France

A major gap in Q fever knowledge is to understand transmission risks to humans on the field (see also # 150)



Great variability of situations at-risk for transmission to humans

Importance of describing and learning from these situations

- ✓ **Underdiagnosed disease**
  - o non-specific symptoms, little-known by Medical Doctors
- ✓ **More or less serious disorders**
  - o ranging from flu-like syndrome to organ injury (eg. cardiac, hepatic, pulmonary)
  - o clinical manifestations may appear several years after the infection occurs and include disabling disorders (chronic organ damage, chronic fatigue syndrome)
- ✓ **Importance of early diagnosis**
  - o necessity of a long-lasting antibiotic treatment when infection is installed
- ✓ **Disease visibility only from emergence of clustered cases**
  - o alert by Medical Doctors to health authorities (notification is not mandatory in France but diagnosis of an abnormal number of cases is of concern)
  - o increased vigilance for Q fever in the local population (short and long term)

Background

1/ Medical Doctors reports human cases

Jan 2019

12 suspected cases

➔ 5 confirmed by the NRC (French National Reference Center)

2/ Source quickly identified

=> sheep farm of an agricultural school

Sept 2018 | Oct | Nov | Dec | Jan 2019 | Feb

First abortions (adult ewes)

Q fever suspected

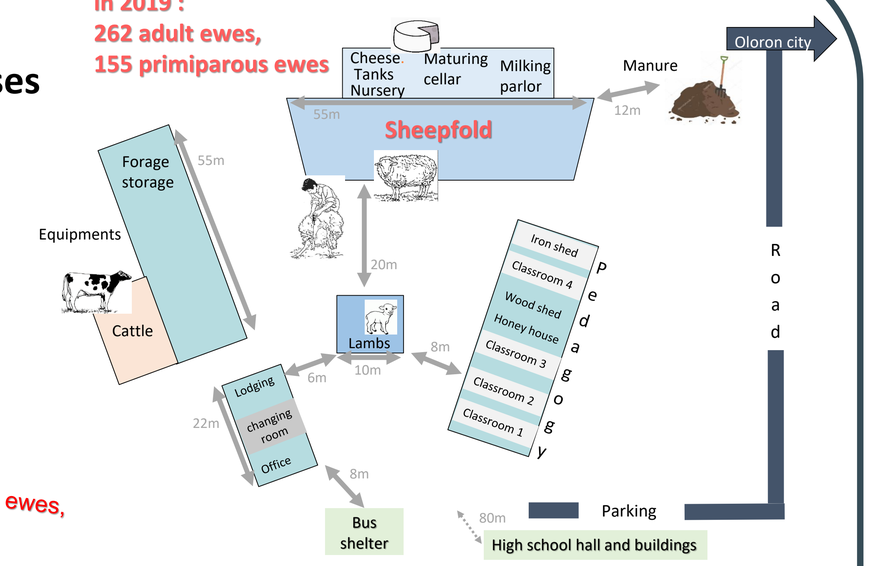
Second strong aborting wave on primiparous ewes

Abortion rate: 11%
- 24% among primiparous ewes,
- 3% among adult ewes

Diagnostic confirmation

=> Exposure period from December

in 2019 :
262 adult ewes,
155 primiparous ewes



Strong concern about a risk of exposure for:
200 students and 60 school staffs
Visitors of the school Open Day (held in March)

Objectives

- ❑ to recommend management measures
- ❑ to conduct a veterinary and environmental investigation for 2 years

Methods

- ❑ **1st year: main undertaken sanitary measures**
  - ▪ Interruption of farm-related visits and scholar activities
  - ▪ Vaccination of all sheep including new lambs
  - ▪ Composting of manure removed from the sheepfold
  - ▪ Two cleanings and disinfections (C/D), the last one using sporicide after animals' departure for summer pasture
- ❑ **2nd year: vaccination** (booster and primovaccination)
- ❑ **Both years: veterinary & environmental monitoring**

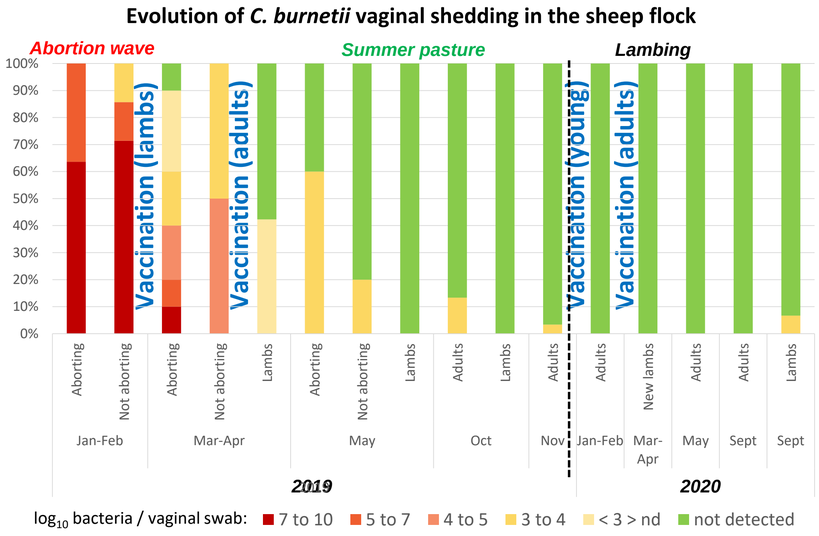
Sampling : - Vaginal swabs and wool from random ewes
- Dust repeatedly from the same relevant sites[2]

qPCR analysis with a difference of 2 $\log_{10}$ set as significant

Results

Animal shedding

Evolution of *C. burnetii* vaginal shedding in the sheep flock



$\log_{10}$ bacteria / vaginal swab: 7 to 10 | 5 to 7 | 4 to 5 | 3 to 4 | < 3 > nd | not detected

Up to 2 months post-abortion wave:

✓ massive vaginal shedding by both aborting and non-aborting ewes

Months 4-10:

✓ bacterial loads in vaginal swabs significantly lower or undetected

2nd year:

✓ sporadic shedding and low abortion rate (1%)

Environmental contamination

- ✓ **Farm (areas with animals):** persistence of a high bacterial load (both dust and wool) for several months despite intensive C/D during the first year
- ✓ **Cheese factory and school:** widespread initial environmental contamination with progressive decrease after intensive C/D using routine methods

Distribution and evolution of *C. burnetii* quantities detected in dust from the farm and the school sites ($\log_{10}$ bacteria per swab for air vents or per cloth for large surfaces)

	SAMPLE SITES	TYPES	FEB 19		MAR 19		MAY 19		JUL 19	OCT 19	MAY 20		JUL 20	SEPT 20
Cheese factory	Cheese factory / Tanks	Cloth	7.50	C / D	6.36		5.77	C / D	4.76	4.30	6.02	C / D	4.73	nd
	Cheese fact. (wall air vent)	Swab	6.17	C / D	4.29		2.27	C / D	2.07	nd	2.75	C / D	nd	nd
	Cheese factory (air vent)	Swab	6.34	C / D	4.05		2.20	C / D	nd	nd	nd	C / D	nd	nd
	Tanks (ceiling air vent)	Swab	6.55	C / D	5.55		5.31	C / D	4.71	nd	2.76	C / D	4.74	nd
	Bulk Tank Milk (wall air vent)	Swab	6.24	C / D	4.20		3.07	C / D	nd	nd	nd	C / D	nd	4.12
	Nursery (air vent)	Swab	5.99	C / D	5.70		4.81	C / D	4.75	5.19	2.40	C / D	3.14	4.09
	Maturing cellar (air vent)	Swab	5.43				4.77		4.08	5.07	nd		3.99	4.39
	Milking parlor	Cloth	8.01				7.34		7.20	5.80	6.46		5.75	5.09
Farm	Sheepfold (adults)	Cloth	8.92				9.08	KD*/L	7.28	6.77	6.87	L	7.30	6.95
	Sheepfold maternity area	Cloth	10.2					KD*/L	6.90	7.60	5.08	L	6.32	4.85
	Lambs farm	Cloth	8.50				7.97	KD*/L	5.10	5.55	3.90	L	5.77	5.60
	Iron shed	Cloth	8.34						5.16	6.11	5.23		4.65	5.49
	Classroom (1 and 2)	Cloth			7.57		7.24	C+	6.09	nd	4.61	C / D	nd	4.49
	Classroom (3 and 4)	Cloth			6.59			C+	5.56	5.25	5.25	C / D	nd	4.80
	Changing room	Cloth	7.17	C / D	7.07		5.94	C+	4.96	7.30	5.30	C / D	5.39	5.12
	Cattle farm	Cloth	7.25				6.93	KD*/L	4.71	4.97	5.45	C / D	nd	4.80
School	High school hall	Cloth			6.29	C+	5.78							
	High school hall (hall1)	Cloth			6.67	C+			3.61	4.63	3.91		5.04	nd
	High school hall (hall2)	Cloth			5.67	C+			nd	nd	nd		nd	nd
	Student cafeteria	Cloth			5.25	C+			3.31	nd	4.36		4.12	4,00
	Bus shelter	Cloth			5.63				3.63	nd	3.75		nd	3.96
	School classroom	Cloth			5.04	C+			3.58	nd	nd		nd	4.41

Manure clear out ♦; C: Cleaning; D: Disinfection; K: Karcher; **+: reinforced** ; L: liming

Conclusions and discussion

- ❖ This "One Health" investigation reports an episode of 45 aborting ewes with massive *C. burnetii* shedding and persistent high level of environmental contamination that lead to 5 confirmed clinical cases among at least 300 individuals exposes.
- ❖ Many questions raised regarding both the impact of management measures and the risk factors for human clinical infection.

☞ Was shedding reduction a result of the normal within-flock bacterial circulation dynamics? Was it a result of vaccination? If yes, of which animals (all females or only those that were recently infected)?

☞ Should C/D be recommended for farm buildings? Does it facilitate bacterial resuspension? Does it have an impact on bacterial infectiousness even if bacterial loads remain high? Are the bacteria sensitive to the present conditions without C/D?

☞ Which ambient dose is effective for human transmission? For human clinical disease? How virulent is the circulating strain for humans? Has natural immunization been acquired in this agricultural population? Have all cases been diagnosed?

Aknowledgements

We thank all the actors involved in the initial survey led by the health authorities (DGAL, DGS): "Q fever interventions group" of the French Platform for animal health surveillance (including SPF and NRC), ARS-NA, DDPP64 and GDS64. Thanks also to Antoine Bechamp for this famous sentence "The microbe is nothing, the terrain is everything."

References

[1] Gache K, Rousset E, Perrin JB, DE Cremoux R, Hosteing S, Jourdain E, Guatteo R, Nicollet P, Touratier A, Calavas D, Sala C. Estimation of the frequency of Q fever in sheep, goat and cattle herds in France: results of a 3-year study of the seroprevalence of Q fever and excretion level of *Coxiella burnetii* in abortive episodes. Epidemiol Infect. 2017 Nov;145(15):3131-3142.

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