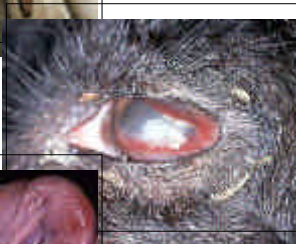




Lung pathology in cattle with special reference to CBPP and other bovine mycoplasmoses: different sides of the same coin?

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Istituto Zooprofilattico Sperimentale of Sicily (Italy)

## Pathogenic mycoplasmas of cattle



*Mycoplasma opalescens*

*Mycoplasma arginini*

*Mycoplasma bovigenitalium*

*Mycoplasma bovirhinis*

***Mycoplasma bovis***

*Mycoplasma bovoculi*

*Mycoplasma canadense*

*Mycoplasma dispar*

***Mycoplasma m. mycoides SC***

*Ureaplasma diversum*

## Economical importance of mycoplasma respiratory diseases

List A  
**CBPP**  
OIE diseases

CBPP is one of the most serious diseases of cattle in Africa, causing estimated losses of US \$ 2 billion per year, arguably making it the most important cattle disease in sub-Saharan Africa. Recognised cause of hunger in African population



BRD  
**Mycoplasma bovis**

In Europe BRD every year kill 84.5 million cattle with 576 million € relate to *M.bovis* for at least 25% of the total (Nicholas *et al.*, 2000). *M. bovis* affect USA meat industry for an estimate amount of 32 million of USD every year added to other 100 millions € lost from mastitis in dairy farms (Rosengarten and Citti, 1999)



## Mycoplasma respiratory diseases - pathology

List A  
**CBPP**  
OIE diseases

**Fibrinous pleuro-pneumonia**



BRD  
**Mycoplasma bovis**

**Chronic (broncho)-pneumonia (catarrhal, necrotic, caseonecrotic?)**

**Interstitial pneumonia ?**



## CBPP (& *M.bovis*): clinical signs



- Fever (unconstant)
- Fast, difficult or noisy breathing
- Nasal/mouth discharge
- **Coughing** after activity
- Air “gaspings”
- Body weight loss

*“It is difficult to predict the pathology on the basis of clinical symptoms...”* (H.Ball, 2009)

## Contagious Bovine Pleuropneumonia (CBPP)



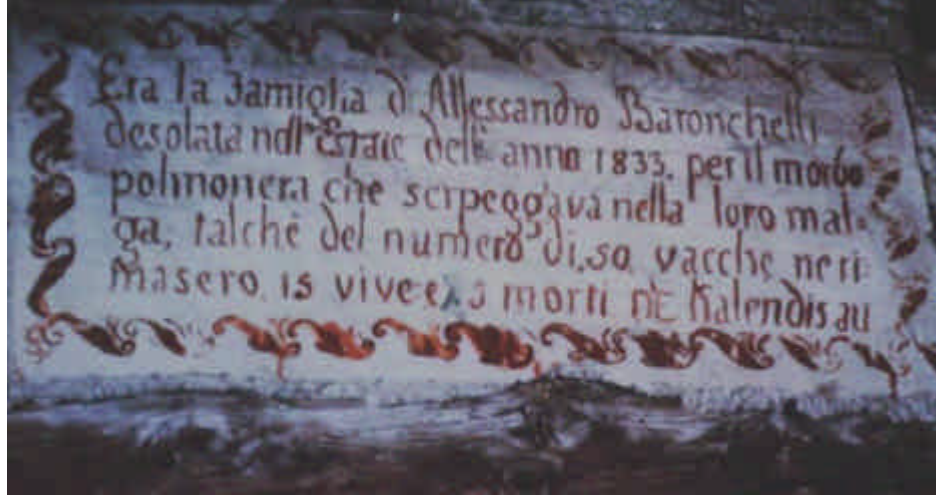
Highly contagious disease characterised by severe non-purulent, inflammatory, exudative lesions at lung and pleural membranes.

Normally with sub-acute/chronical course

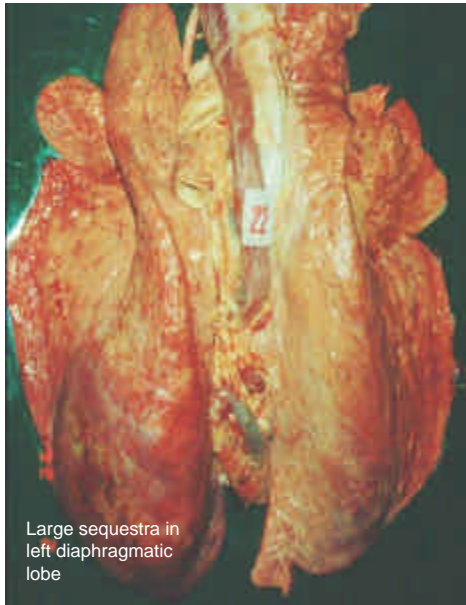




Italy: De Sanctis *et al.*, 2000; Grieco *et al.*, 2001; ...



CBPP Pathology



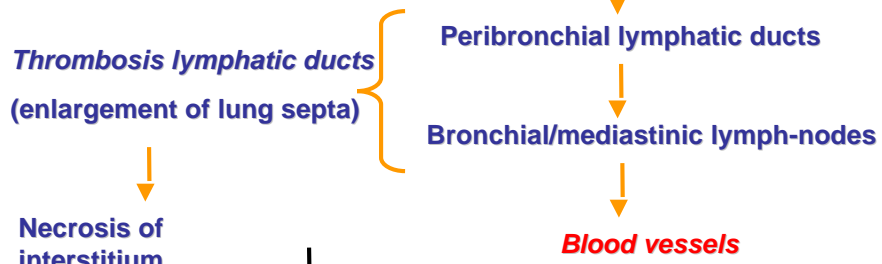
Large sequestra in  
left diaphragmatic  
lobe

Lung and pleura  
of adult cattle  
(up to 80% unilateral)

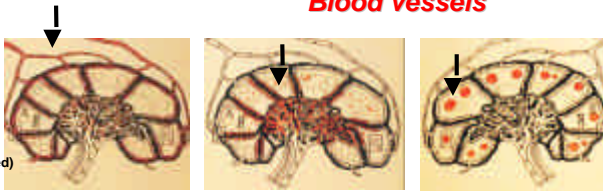
Pericardium  
Peritoneum  
Joints  
Kidney

## CBPP Pathogenesis (acute):

**M.m.m.sc** → **Bronchioli (catarrhal bronchiolitis)**

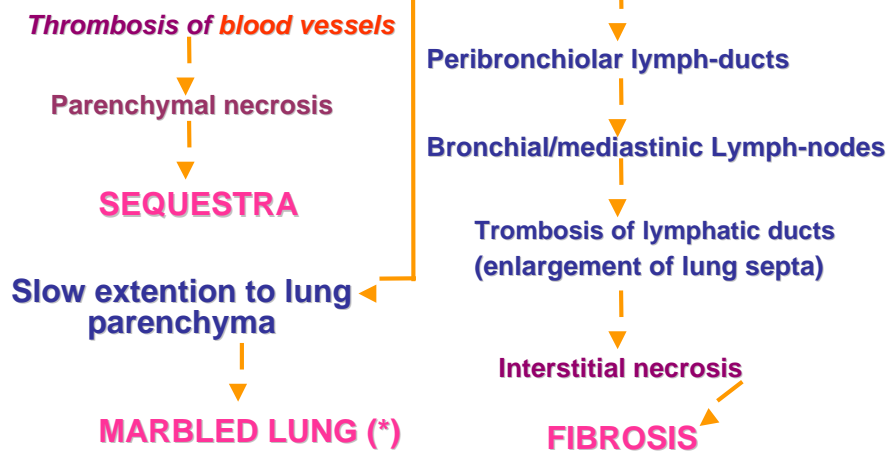


Antigen circulation in lymph-nodes (red)

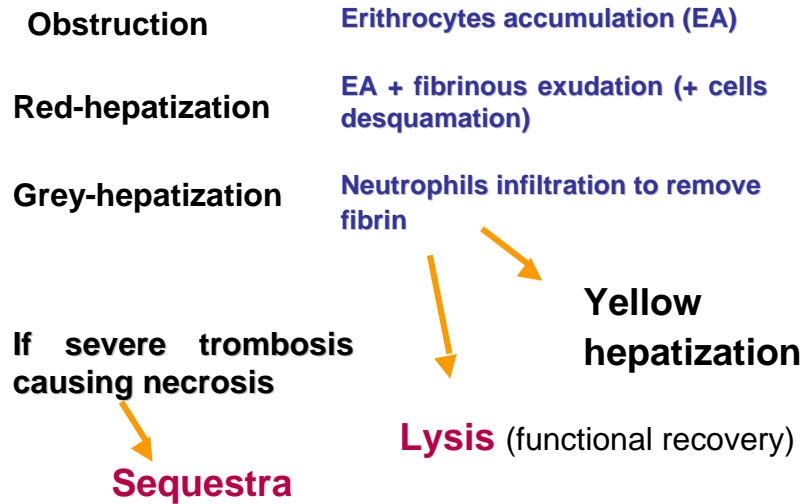


## CBPP Pathogenesis (sub-acute/chronic):

**M.m.m.sc** → **Bronchioli (catarrhal bronchiolitis)**



## CBPP Pathogenesis: (\*) “marbled” lung



## CBPP Pathogenesis: sequestra

*Mycoplasma mycoides* SC contains

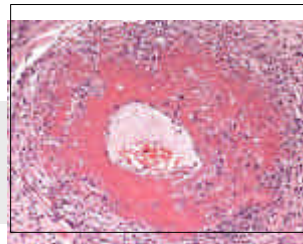
**GALACTAN**

Cross-reactivity between galactan and polysaccharides belonging lung surfactant

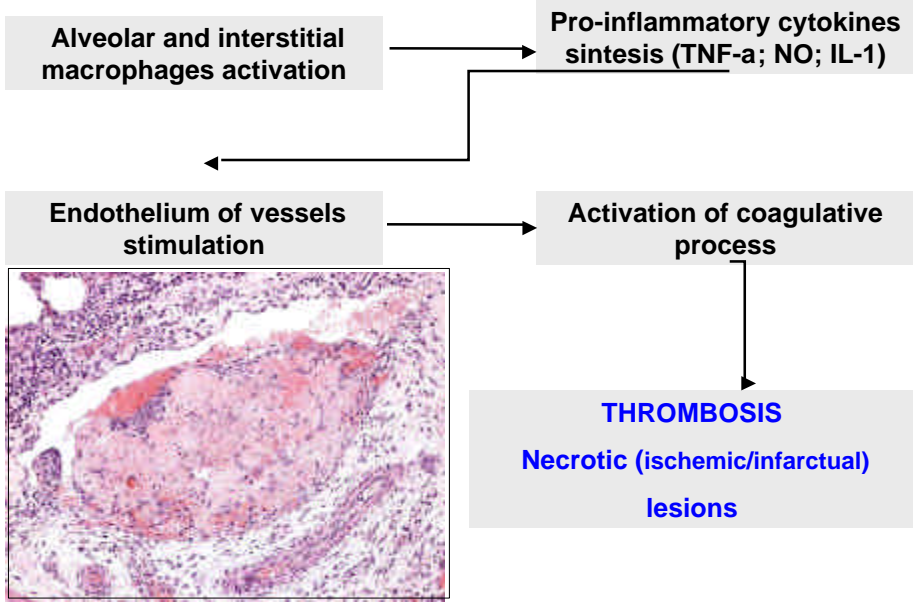
hypersensitivity of III type: immunocomplexes deposit (Ag/Ab) in vessel followed by complement activation

**Trans-mural vaculitis**

**Necrotic lesions ischemic/infarctual**



## CBPP Pathogenesis: sequestra



## CBPP Pathology – Acute form



*Most known pathological finding (pathognomonic):*  
**“Marbled”**  
lung

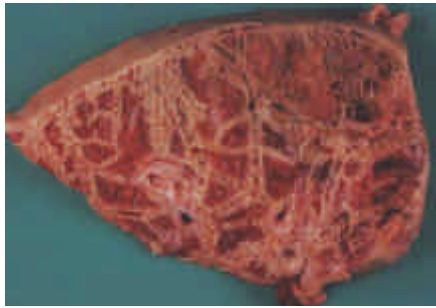




CBPP Pathology



Acute CBPP



CBPP Pathology



Sub-acute/chronic  
CBPP

CBPP Pathology



Large sequestra



Chronic CBPP

CBPP Pathology

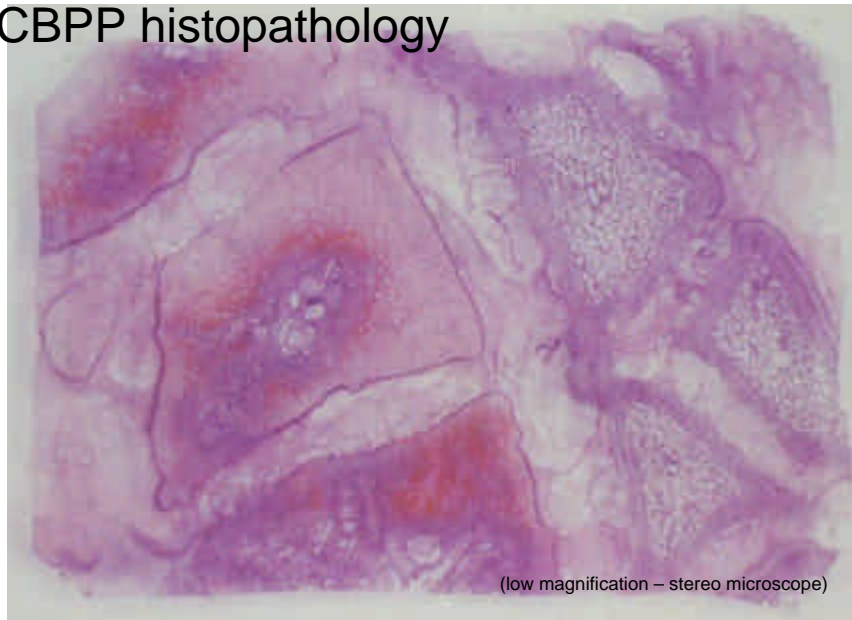


Small sequestra

Chronic CBPP  
(...temporary clinical  
recovery)

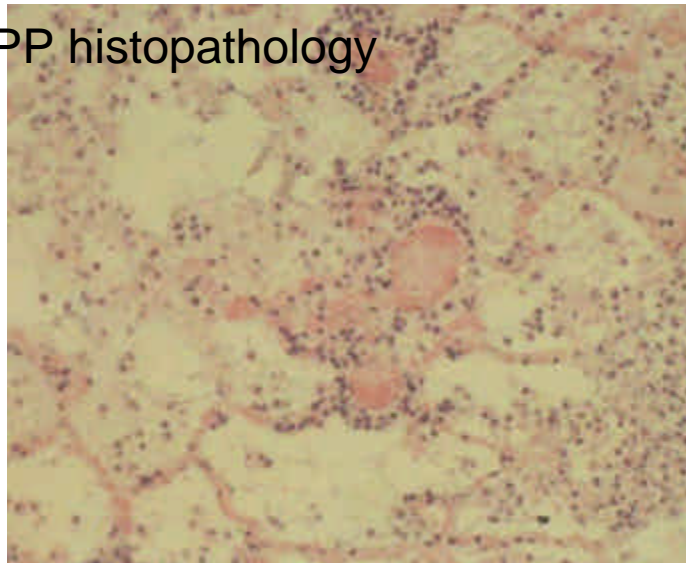


CBPP histopathology



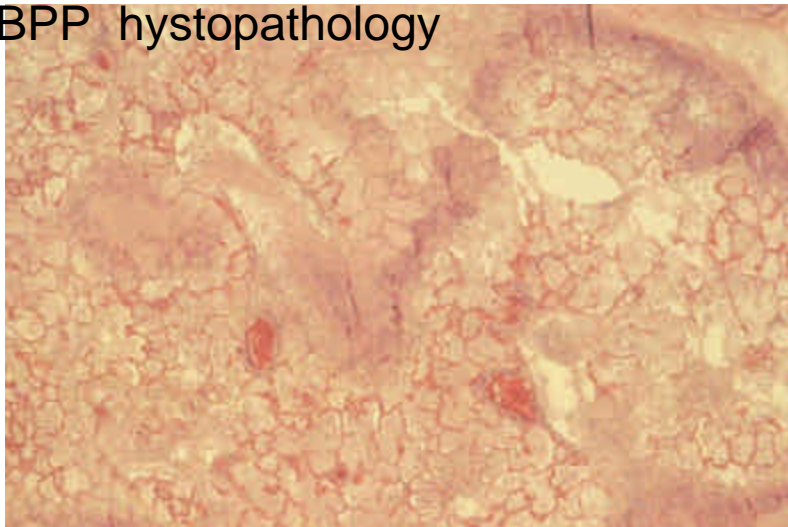
(low magnification – stereo microscope)

## CBPP histopathology



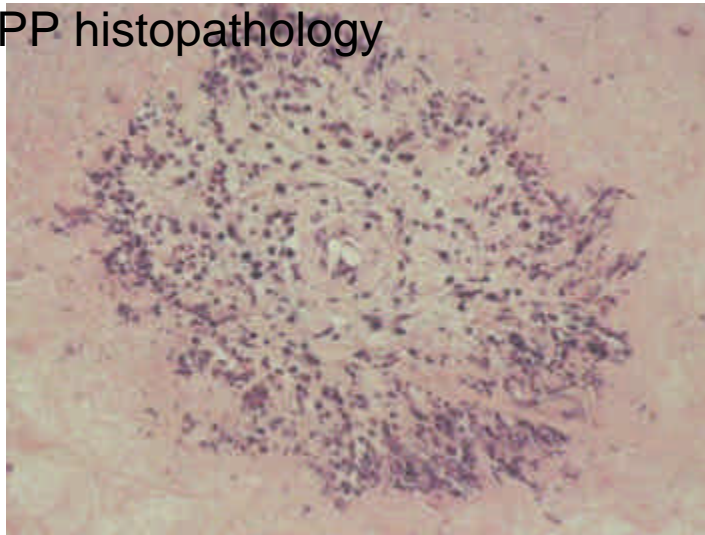
Acute CBPP: hyperaemia of septa and fibrinous exudate in the alveoli

## CBPP histopathology



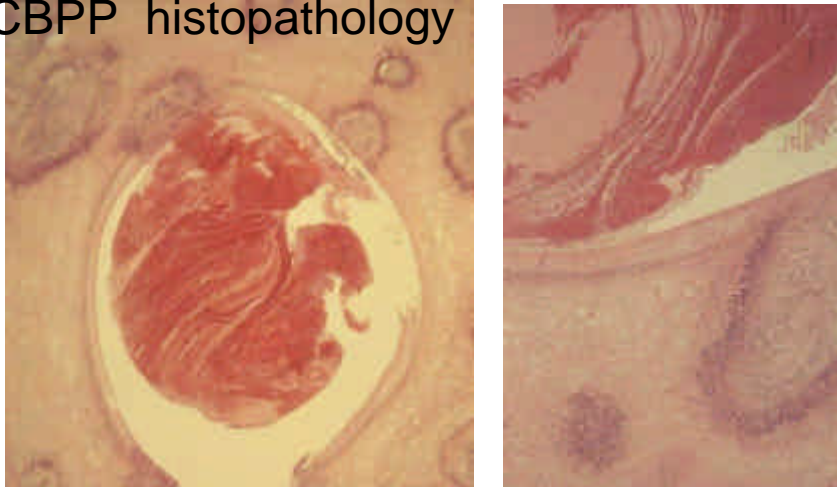
Sub-acute CBPP: hyperaemia of septa, fibrinous exudate in the alveoli, perlobular necrosis

## CBPP histopathology



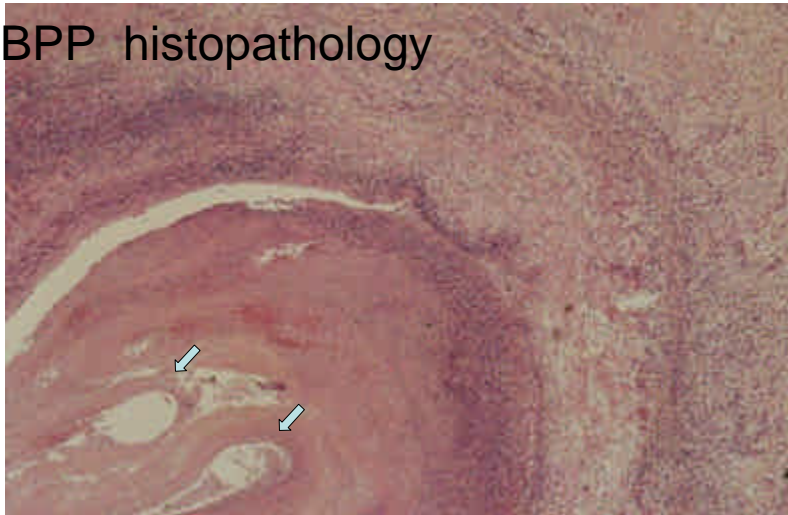
Sub-acute CBPP: perivascular organization – vasculitis

## CBPP histopathology



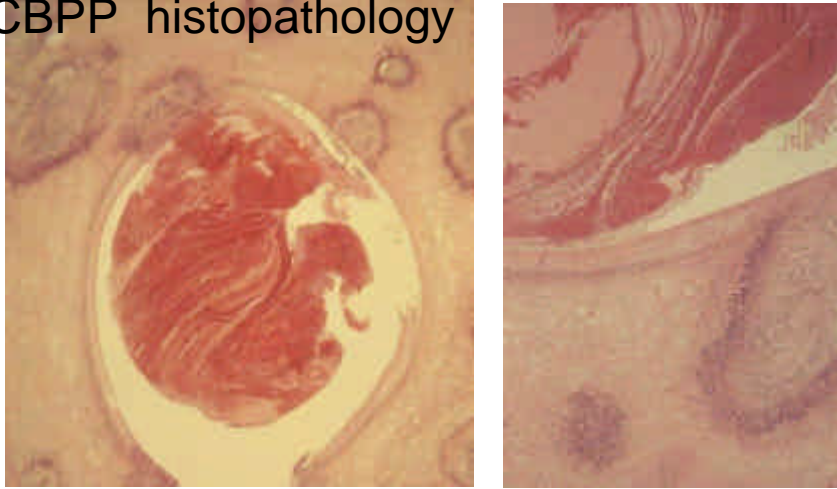
Sub-acute CBPP: perivascular organization, vasculitis, thrombosis

## CBPP histopathology



Sub-acute CBPP: perivascular organization with coagulum canalization

## CBPP histopathology

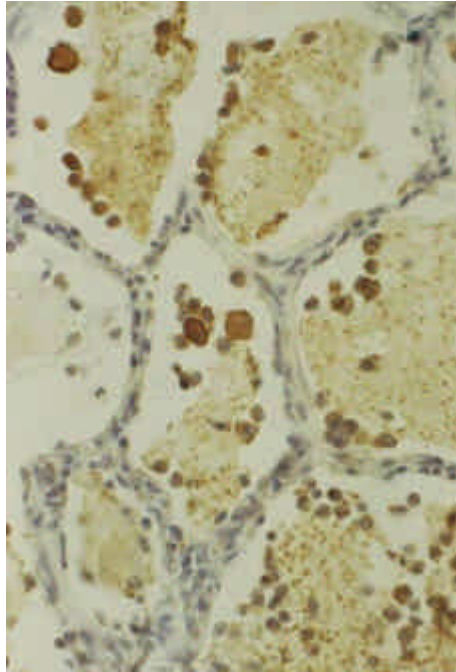


Sub-acute CBPP: perivascular organization, vasculitis, thrombosis

## CBPP histopathology



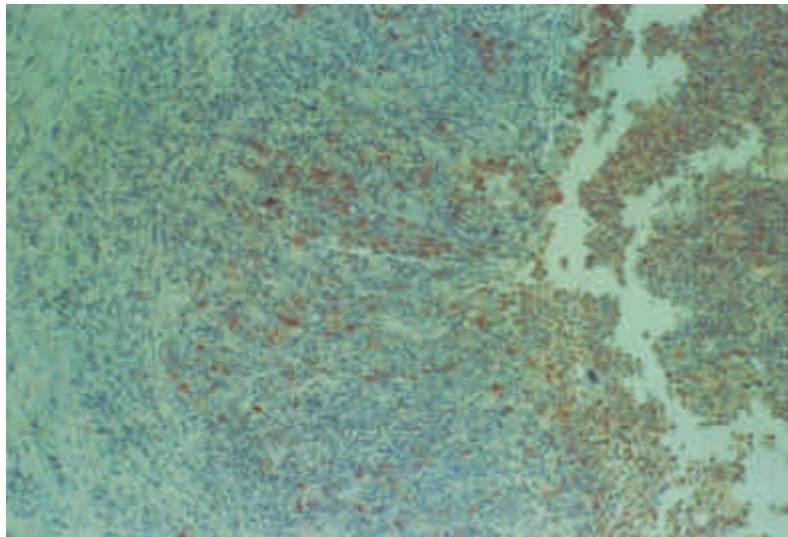
Sub-acute CBPP: perivascular organization with coagulum canalization



Acute CBPP

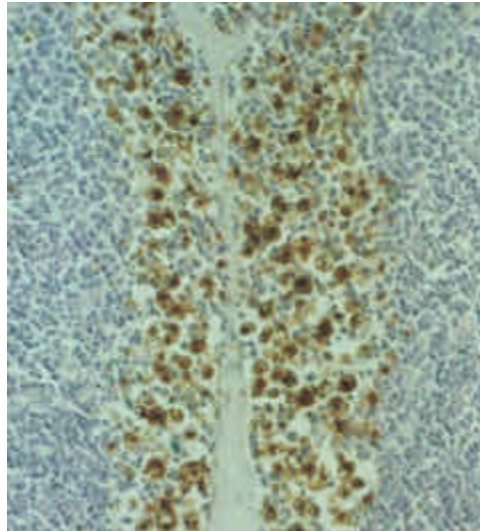
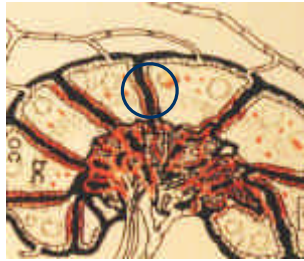
(Immunohistochemistry):

Granular positivity of  
fibrin and alveolar  
macrophages cytoplasm  
(desquamation)



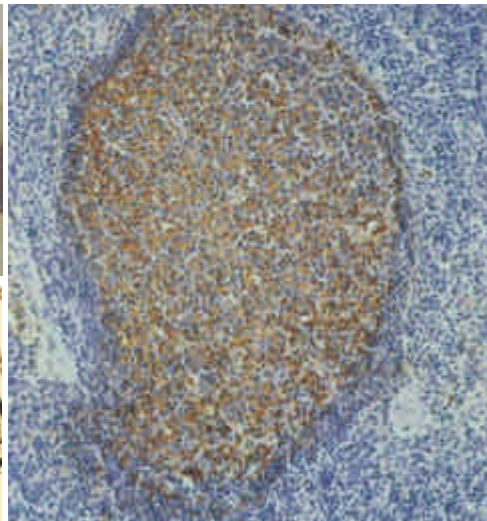
Chronic CBPP (Immunohistochemistry):

positivity in the necrotic material and sequestra wall

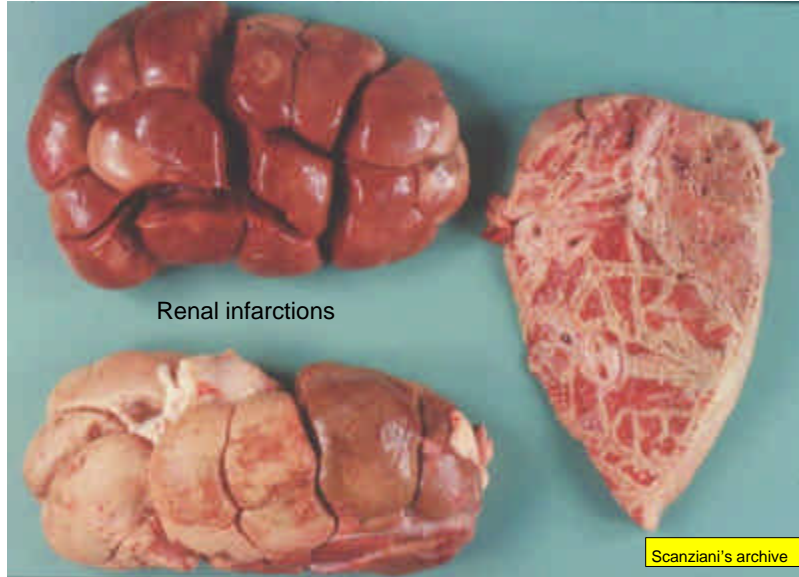


CBPP acute phase:  
lymph-node  
Immunohistochemistry  
(sub capsular sinus)

PPCB chronic phase: lymph-node immunohistochemistry  
(medullary sinus-germinal center)



CBPP it is a lung disease but often involves other organs ...



### *Mycoplasma bovis* - respiratory disease

*M. bovis* is included among BRD pathogens as "management" disease characterised by different degrees of pathologies linked to age, purpose and host immune system



*M. bovis*: different syndromes/pathologies linked to productive purpose

**Calf**

? [Respiratory syndrome](#)

? Polyarthritis



**Cow**

? [Mastitis](#)

? Genital diseases

? Otitis media (purulent)

? Keratoconjunctivitis

? Cutaneous abscesses

? Meningoencephalitis

? Myocarditis

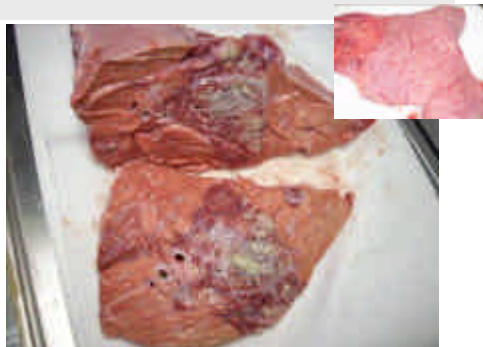
? Genital diseases



***M. Bovis* anatomo-pathological pattern**

***Mycoplasma bovis***

- ✓ Cranio-ventral progression, both lungs involved
- ✓ Moderate enlargement of interlobular septa
- ✓ Moderate pleural involvement
- ✓ Necrotic foci at (sub) lobular diffusion



***Mycoplasma mycoides SC***

- ✓ Monolateral lesion diaphragmatic lobes
- ✓ Severe enlargement of interlobular septa
- ✓ Severe and massive pleural involvement
- ✓ Necrotic foci and multilobular diffusion



## ***Mycoplasma bovis* and respiratory pathology in Italy**

**From few published reports of abbattoire monitoring *M. bovis* results to be the most frequent bacterial respiratory pathogen**

**Sicily: 27,3% - 9 / 33 ( Loria *et al.*, 2004 )**

**Veneto (North-Est): 11,6% - 60 / 517 ( Manfrin *et al.*, 1998)**

**Lombardia: 67,2% - 41 / 67 nasal swabs from meat calves ( Luini *et al.*, 2007 )**



Available online at [www.sciencedirect.com](http://www.sciencedirect.com)



Research in Veterinary Science 85 (2008) 782–790



[www.elsevier.com/locate/rvsc](http://www.elsevier.com/locate/rvsc)

Bacteriological, serological, pathological and immunohistochemical studies of *Mycoplasma bovis* respiratory infection in veal calves and adult cattle at slaughter

E. Radaelli<sup>a,\*</sup>, M. Luini<sup>b</sup>, G.R. Loria<sup>c</sup>, R.A.J. Nicholas<sup>d</sup>, E. Scanziani<sup>a</sup>

<sup>a</sup> Sezione di Anatomia Patologica Veterinaria e Patologia Aviare, Dipartimento di Patologia Animale, Igiene e Sanità Pubblica Veterinaria, Facoltà di Medicina Veterinaria, Via Celoria, 10, 20133 Milano, Italy

<sup>b</sup> Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna, Lodi, Italy

<sup>c</sup> Istituto Zooprofilattico Sperimentale della Sicilia, Palermo, Italy

<sup>d</sup> Mycoplasma Group, Veterinary Laboratories Agency, Weybridge, KT15 3NB, UK

### **Study on *Mycoplasma bovis* and related pathology in cattle farming of Lombardia e Piemonte**

**N° 140 meat cattle belonging n. 14 farms:**

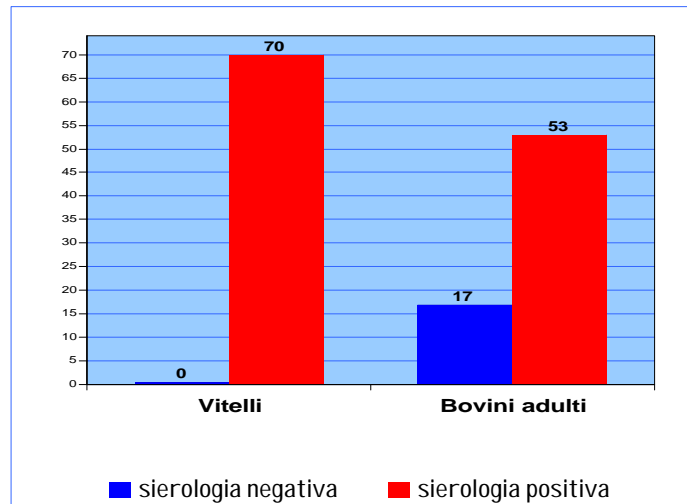
**N° 70 adult around 20 months of age**

**N° 70 calves (white meat) 6 months old**

- In consideration of their production n. 7 groups of adult and other 7 of calves have been selected
- Each group were constituted by 10 heads according:
  - N° 7 heads with visible lung lesions
  - N° 3 heads negative for lesions

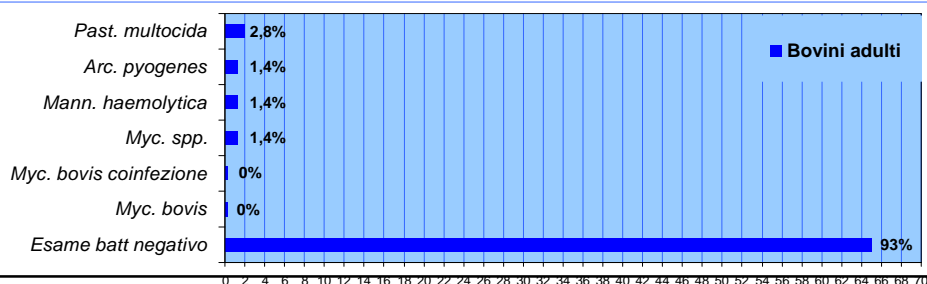
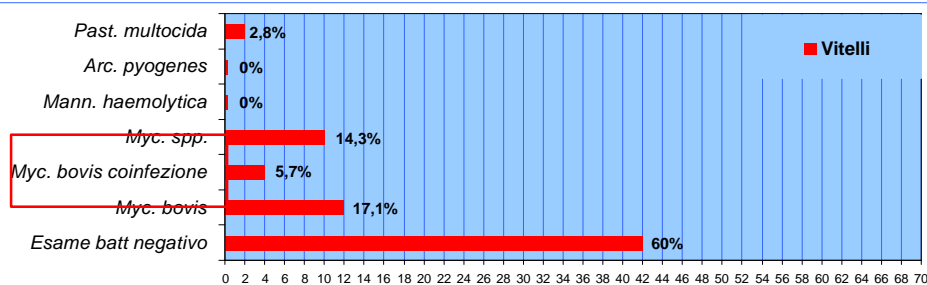
## Serological test for *Mycoplasma bovis* Ab (ELISA)

- Calves: 100% positive
- Adult cattle: 76% positive



## Results lung bacteriology

*Mycoplasma bovis* only isolated from calves: n° 16 / 70 ( 23% )  
 Higher number of respiratory pathogens found in white meat calves  
 N° 16 strains of *M.bovis* always isolated from inflammatory lesions



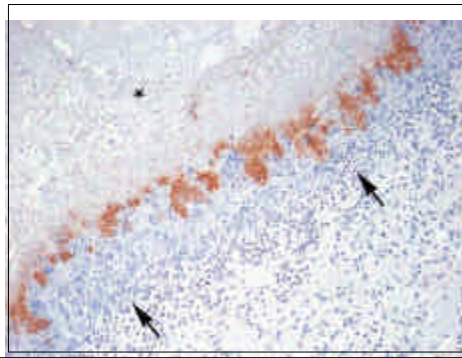
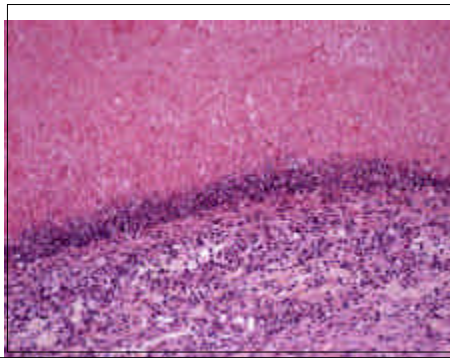
Record	IHC	Bacteriology	Degree of severity	Classification
258#06	+	<i>M. bovis</i>	Severe	Broncopneumonia (necrotic-suppurative)
258#02	+	<i>M. bovis</i>	Severe	Pneumonia fibrinous-necrotic
256#04	+	<i>M. bovis</i>	Severe	Broncopneumonia (necrotic-suppurative)
249#11	+	<i>P.M. bovis</i>	Severe	Broncopneumonia (necrotic-suppurative)
245#12	+	<i>A. pyogenes</i>	Severe	Broncopneumonia (necrotic-suppurative)
245#09	+	<i>P.M. bovis</i>	Severe	Broncopneumonia (necrotic-suppurative)
245#06	+	<i>P.M. bovis</i>	Severe	Broncopneumonia (necrotic-suppurative)
245#02	-	<i>M. bovis</i>	Moderate	Catarrhal Broncopneumonia
245#05	-	<i>M. bovis</i>	Mild	Interstitial Pneumonia
245#07	-	<i>M. bovis</i>	Mild	Interstitial Pneumonia
254#01	-	<i>M. bovis</i>	Moderate	Interstitial Pneumonia
254#02	-	<i>M. bovis</i>	Moderate	Interstitial Pneumonia
254#08	-	<i>M. bovis</i>	Mild	Interstitial Pneumonia
256#05	-	<i>M. bovis</i>	Severe	Interstitial Pneumonia
256#06	-	<i>M. bovis</i>	Severe	Catarrhal Broncopneumonia
256#07	-	<i>M. bovis</i>	Severe	Catarrhal Broncopneumonia

**Pattern n. 1 (7 cases):**

Severe necrotic-suppurative bronchopneumonia with strong IHC positivity at necrotic-suppurative foci (massive presence of *Mycoplasma bovis*)

**Pathogenesis (hypothesis):**

1. Production of necrotizing factors by *Mycoplasma bovis*.
2. Immune response characterised by exaggerate inflammatory reaction followed by severe oxidative damage of tissues.



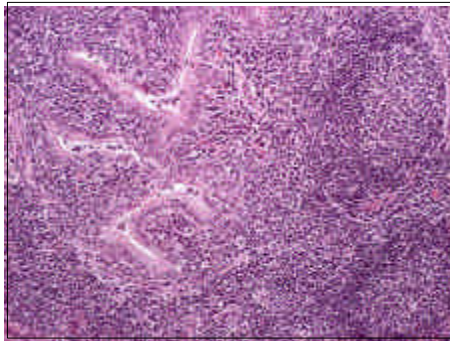
**Pattern n. 2 (9 cases):**

- Mild lesions of interstitial pneumonia or catarrhal pneumonia (**without necrotic suppurative aspects**) with low UFC values and negative IHC (scarce presence of *Mycoplasma bovis* into affected tissues)

**Pathogenesis (hypothesis):**

1. Long term, limited infection mainly ubicated in restricted foci (generally among cilia of respiratory epithelium), avoiding host immune response but causing a continuous antigenic stimulation

**1. Different in pathogenicity among *M.bovis* strains**



Stipkovits L., Hungarian Academy of Sciences  
Veterinary Medical Research Institute

SHORT PAPER

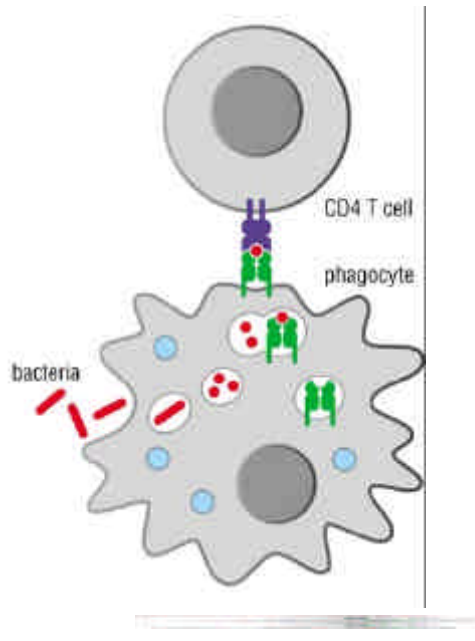
**Expression of Class II Major Histocompatibility  
Complex Molecules in Chronic Pulmonary  
*Mycoplasma bovis* Infection in Cattle**

**E. Radaelli<sup>1</sup>, M. Lugini<sup>2</sup>, C. Domeneghini<sup>3</sup>, G. R. Loria<sup>4</sup>,  
C. Recordati<sup>1</sup>, P. Radaelli<sup>1</sup> and E. Scanziani**

<sup>1</sup> Dipartimento di Patologia Animale, Igiene e Sanità Pubblica Veterinaria (Sezione di Anatomia Patologica Veterinaria e Patologia Aziendale), and <sup>2</sup> Dipartimento di Scienze e Tecnologie Veterinarie per la Sicurezza Alimentare, Facoltà di Medicina Veterinaria, Via Celoria 10, 20133 Milan, <sup>3</sup> Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna, Lodi, <sup>4</sup> Istituto Zooprofilattico Sperimentale della Sicilia, Palermo, and <sup>5</sup> Dipartimento di Metodi Quantitativi per le Scienze Economiche ed Aziendali, Università degli Studi di Milano-Bicocca, Milan, Italy

**Pathogenesis of lung lesions: which immune mechanism is related to the 2  
different pneumonic patterns due to *Mycoplasma bovis* infection ?**

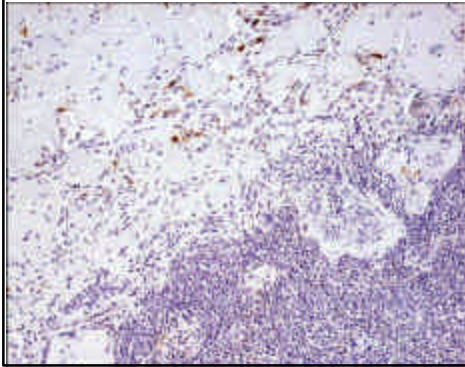
### MHC II role: ANTIGEN PRESENTATION



#### Severe necrotizing (and suppurative) Bronchopneumonia (Massive intralesional presence of *M. bovis*)

• **Scarce** MHCII expression and visible only in few infiltrative leucocytes

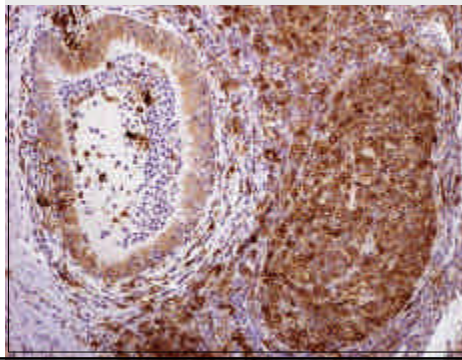
• **Reduced** activation of the antigen presentation mechanisms with massive bacterial invasion and severe pathology (necrosis)





#### Mild catarrhal pneumonia and/or bronchial-interstitial pneumonia (Scarce/absent intralesional presence of *M. bovis*)

• **Marked** expression of MHCII in leucocytes of reactive respiratory epithelium

• **Improved** activation of antigen presentation mechanisms with presence of immune response



 <b>CBPP</b>	 <b><i>M.bovis</i> RD</b>
Mainly in adult	Mainly in calves
Monolateral	Bilateral
Severe lesions	Moderate lesions
Marbling	Consolidation
Pleuritis	Rare pleuritis
Sequestra	Small/rare sequestra like-lesions
Contagious disease	"Management" disease (?)



Thanks to:

-My Institute **IZS of Sicily**

-Robin Nicholas and **VLA**  
Mycoplasma Team

-Eugenio Scanziani,  
Valeria Grieco, Enrico  
Radaelli of **University of  
Milan**



**Thank you**