

# Paratuberculosis - prehľad

---

Slovakia, March 6, 2012

Michael T. Collins, DVM, PhD  
Professor of Microbiology  
University of Wisconsin-Madison



**SCHOOL OF  
VETERINARY MEDICINE**  
University of Wisconsin-Madison

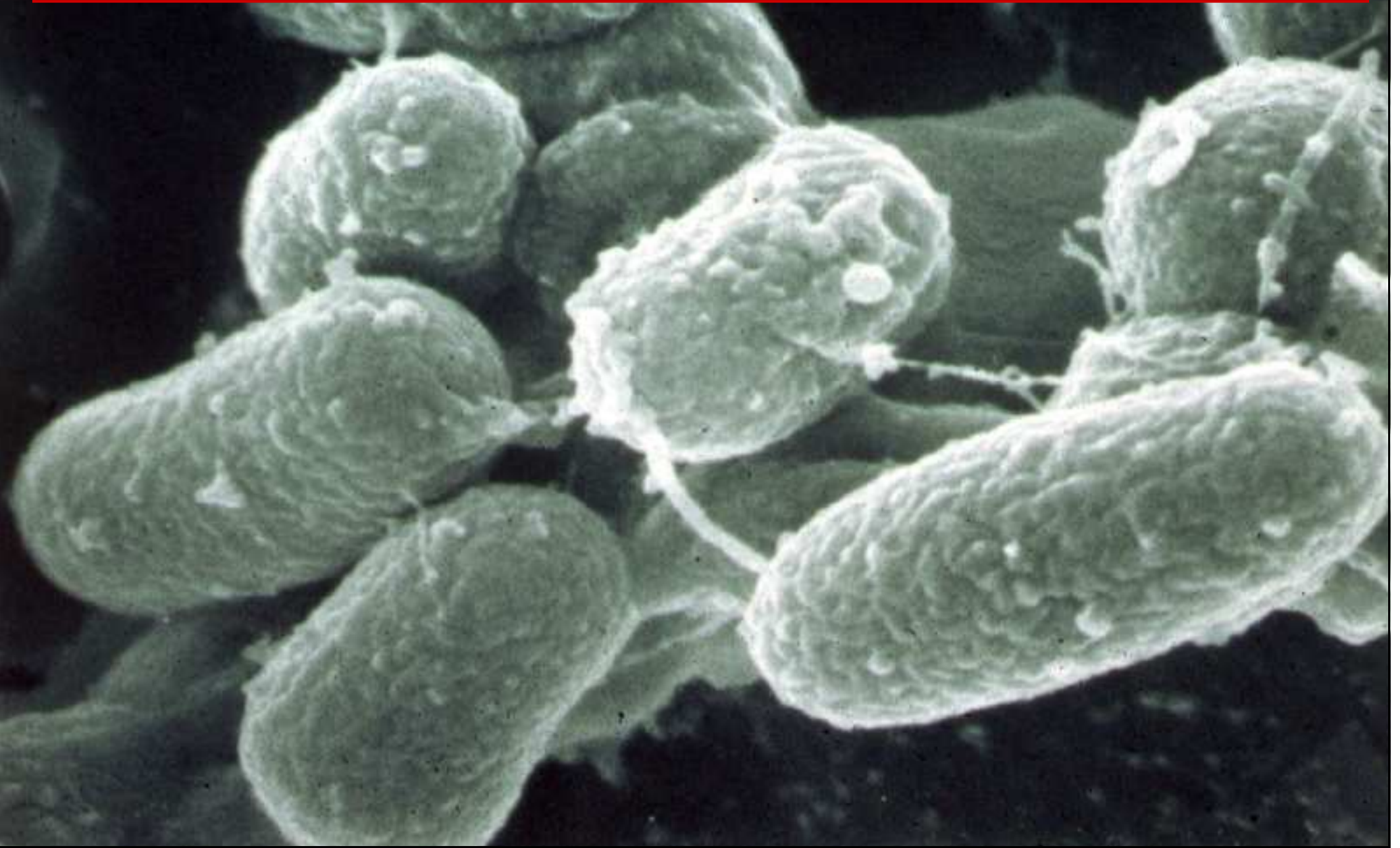
# Paratuberculosis (Johne's disease)



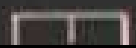
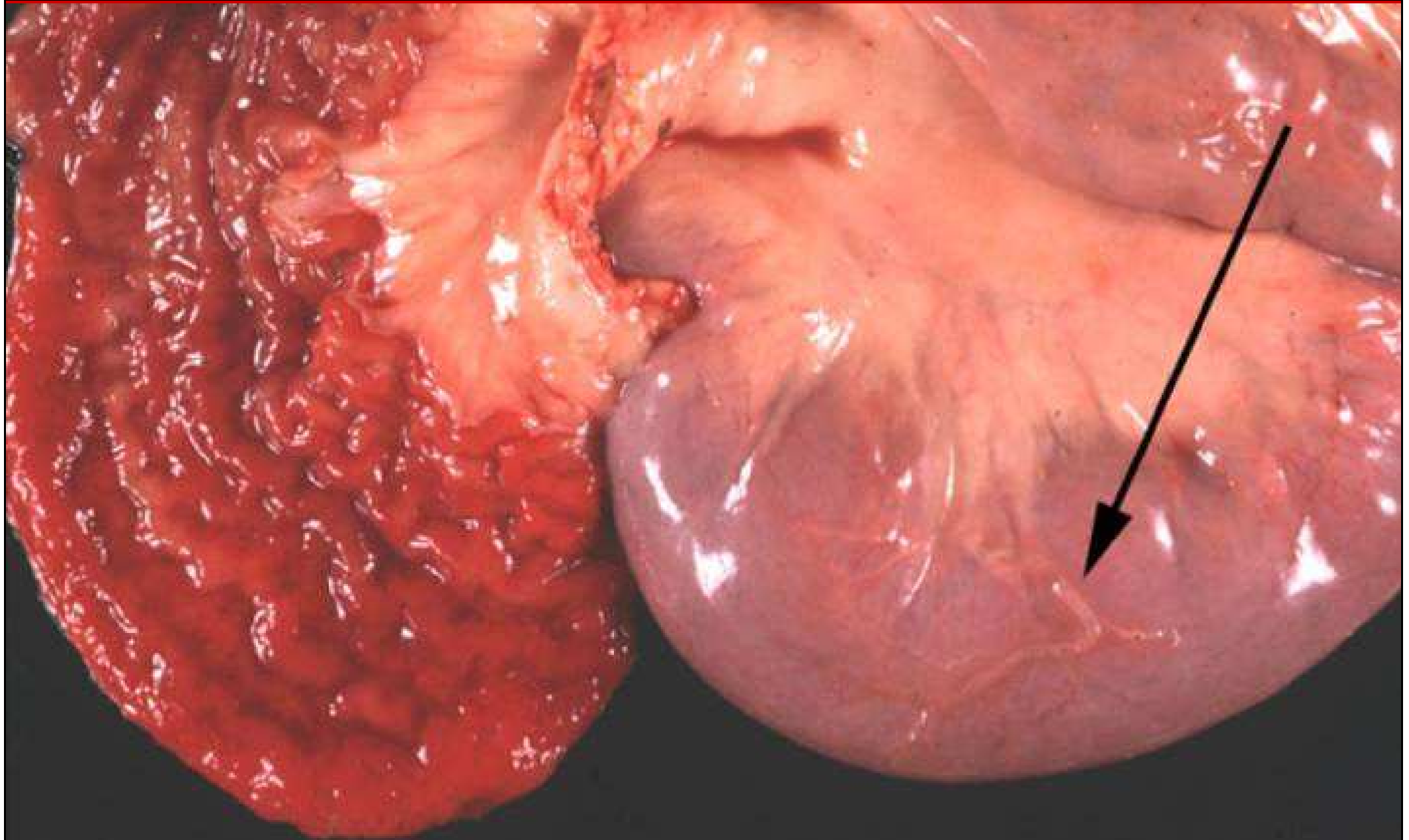


Pôvodca:

*Mycobacterium avium paratuberculosis*



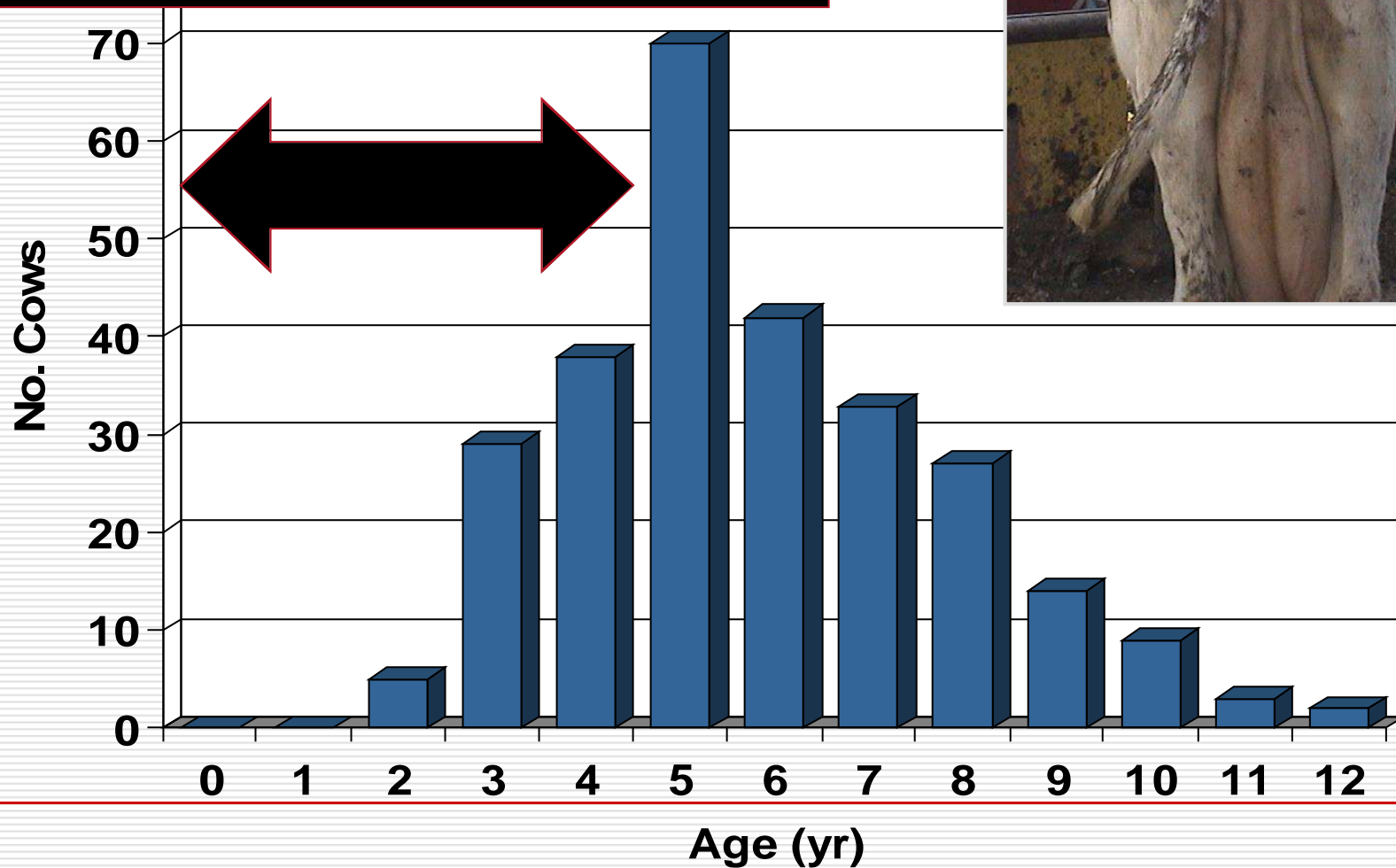
# Výsledek: poškodené črevo



# Clinical Johne's disease

Austrálske údaje zo 179 stád

**stredná inkubačná doba = 5 rokov**





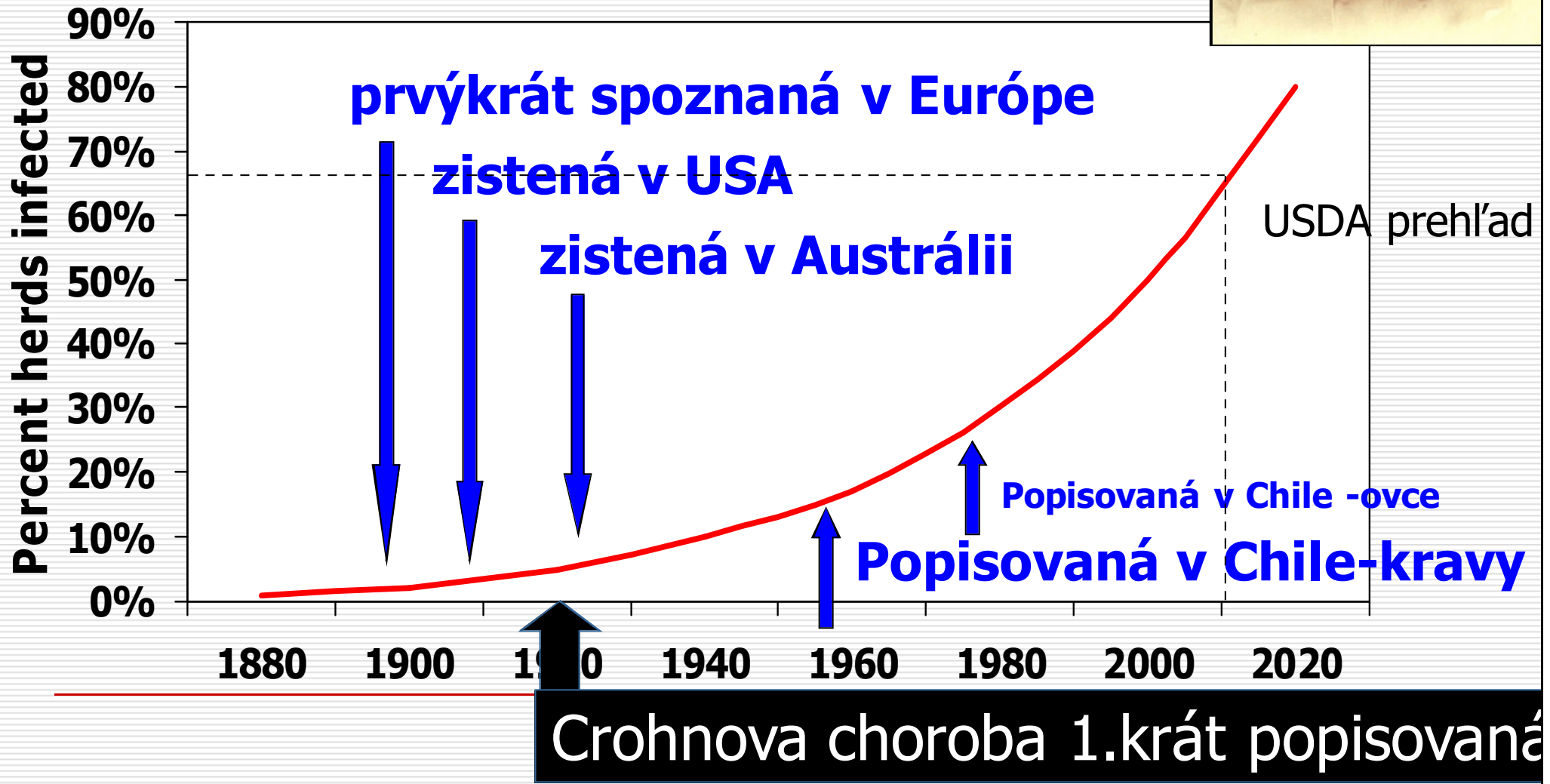
# Fľašková sánka- klasický príznak (tiež názov „submandibulárny edém“)

---



**Paratuberculosis je  
bežná & prenosná**

# Global Epidemic



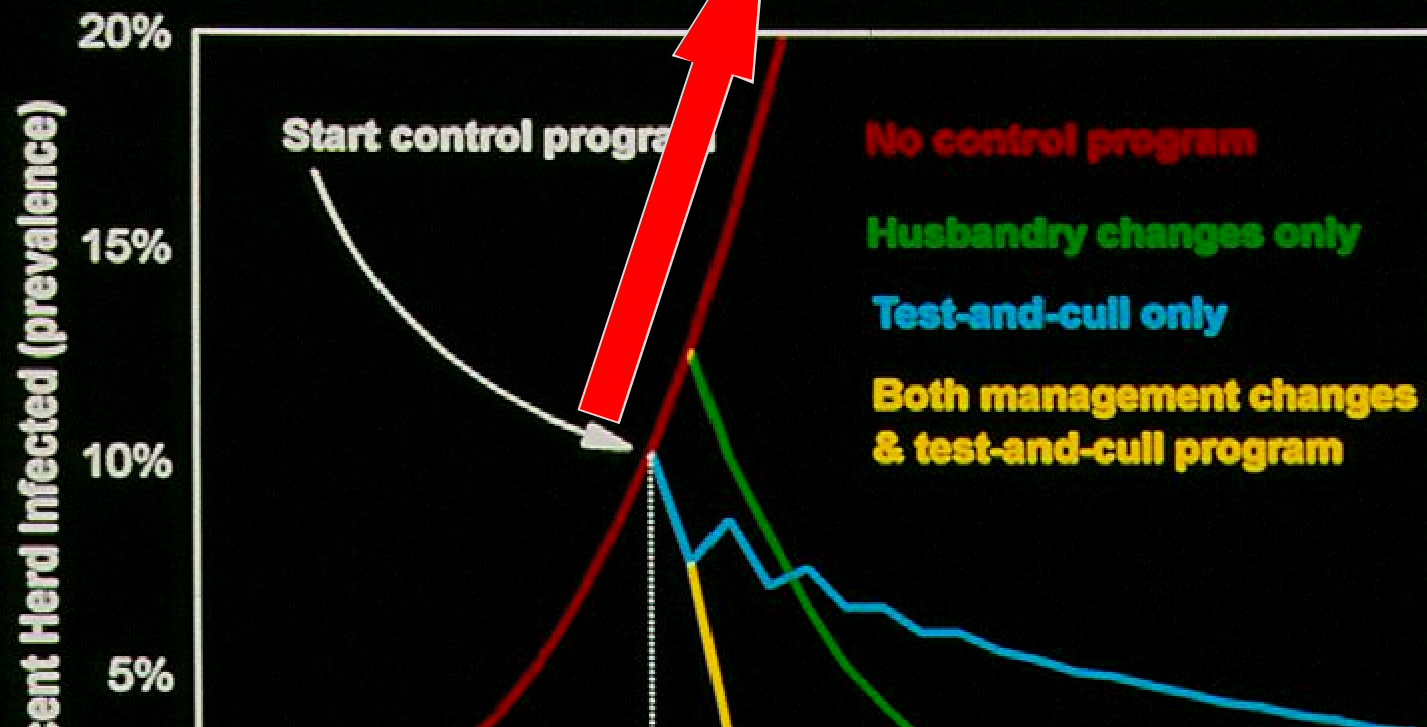




Johne's disease je globálny problém.

# Johne's šírenie v stáde!

Computer simulation of different Johne's control programs



Poučenie:

Máte na výber čo robiť, ale **NIEČO** robiť musíte!

# Paratuberculosis

Znižuje mliečnu produkciu



# Paratuberculosis znižuje produkciu

Produčný Parameter	ELISA výsledok		
	Negatívny, nízko-pozitívny Pozitívny	vysoký (Silne) Pozitívny	
ME305 MILK	21,327 lb <sup>a</sup> (9,694 Kg)	18,631 lb <sup>b</sup> (8,467 Kg)	<b>-2,696 lb</b> <b>-1,225 Kg</b>
Laktačné dni	344 <sup>a</sup>	290 <sup>b</sup>	<b>-54 DIM</b>

Hodnoty s inými označeniami sú signifikantné odlišné p<0.05

Možná

Zoonóza?

# MAP križovatky

Je to zoonotické ochorenie?

Yes

No

**Mandatory testing**  
**Agresívna kontrola**  
**Public subsidies**

Dobrovoľné testovanie  
kontrola vychádza z ekonomiky  
Limited public subsidies



# Johne's disease – Crohn's disease

## **podobné klinické prejavy**

---

Objavenie sa pri pohlavnom dospievaní

Diarrhea

Strata hmotnosti

Abdominálne bolesti

Chronicita

Debilitating

Progresivita

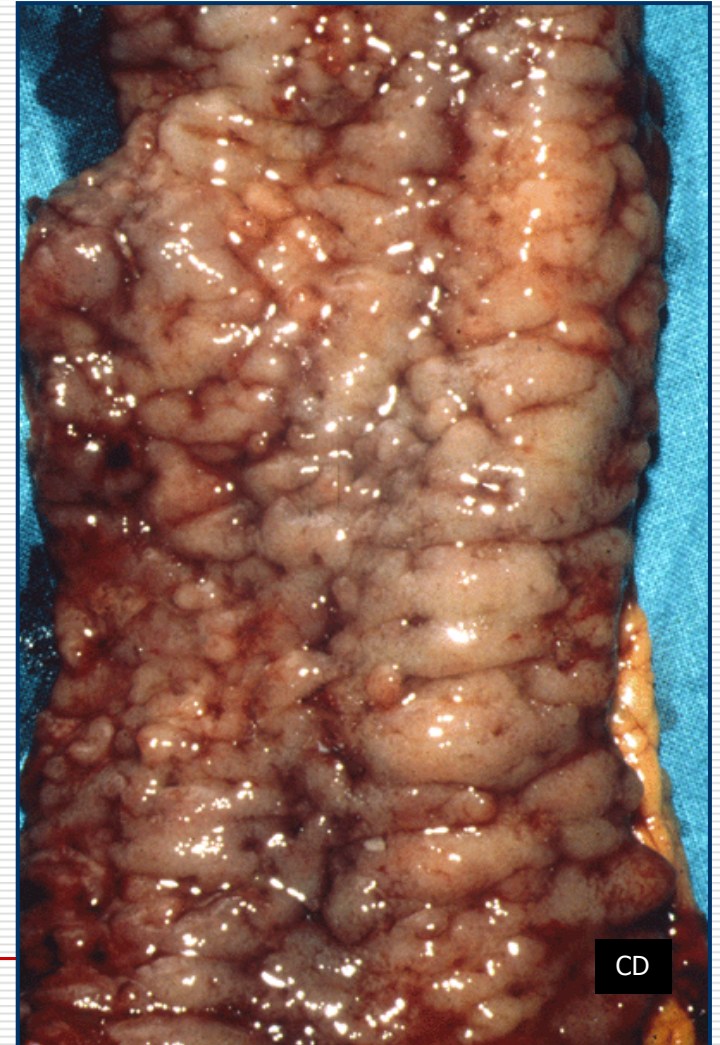
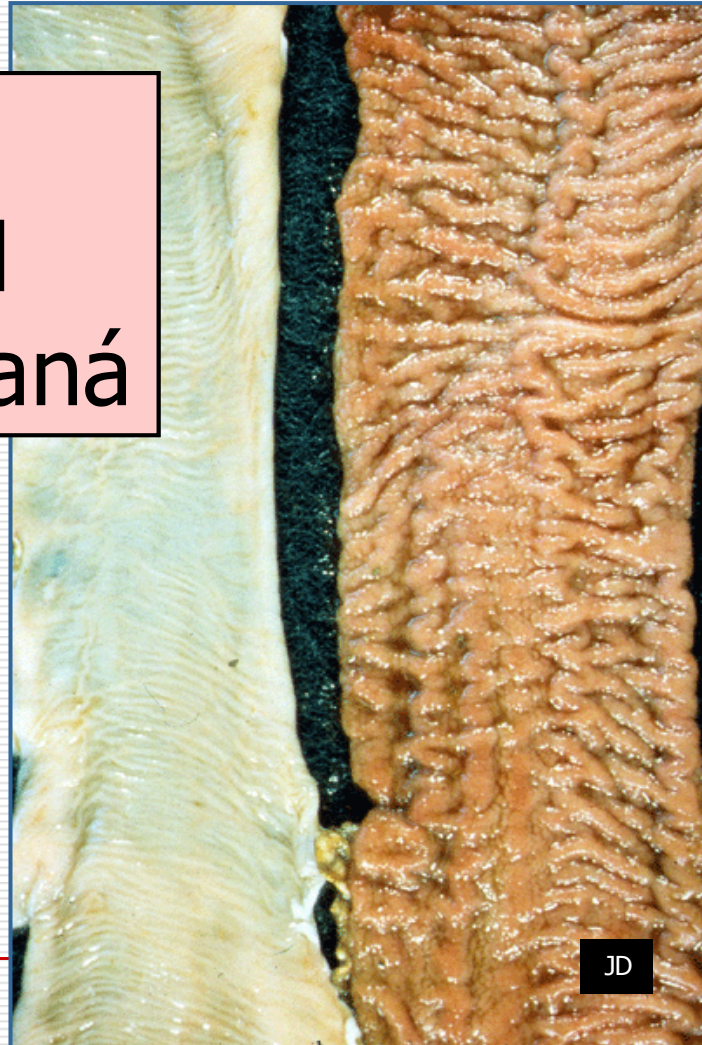


# Johne's disease – Crohn's disease

## **podobná hrubá patológia**

---

zhrubnutá  
Corrugated  
ne-ulcerovaná

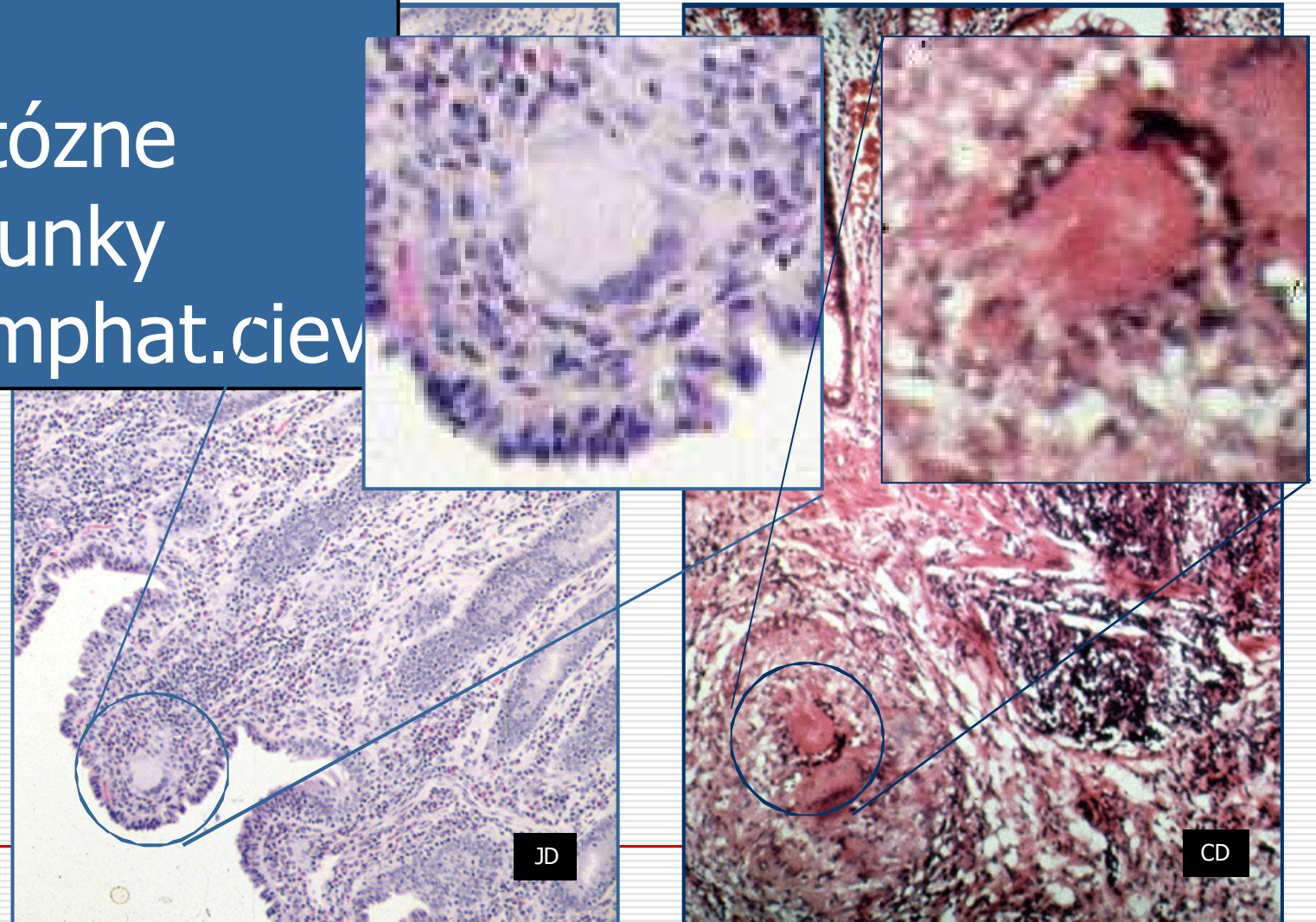




# Johne's disease – Crohn's disease **podobná histopatológia**

---

Diffúzne  
Granulomatózne  
Obrovské bunky  
Dilatácia lymfatických ciev



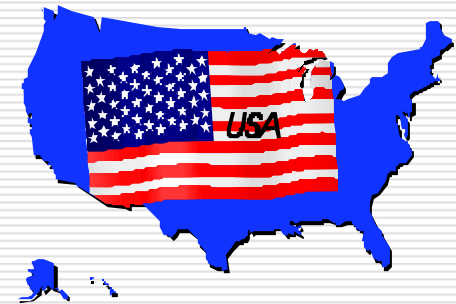


# Prevalence of Crohn's Disease in No. America

Incidence (8-10/100,000) is misleading

---

- ❖ USA: 133 per 100,000
- ❖ **1 in 752 people**

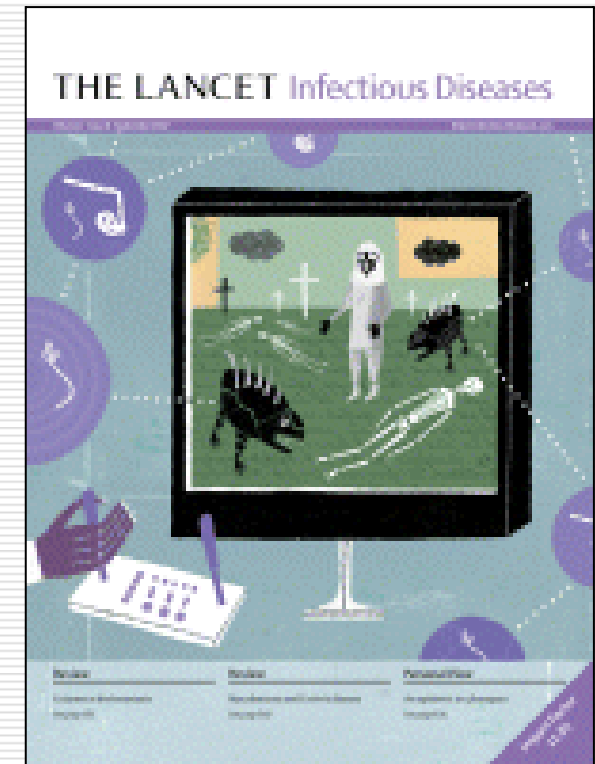
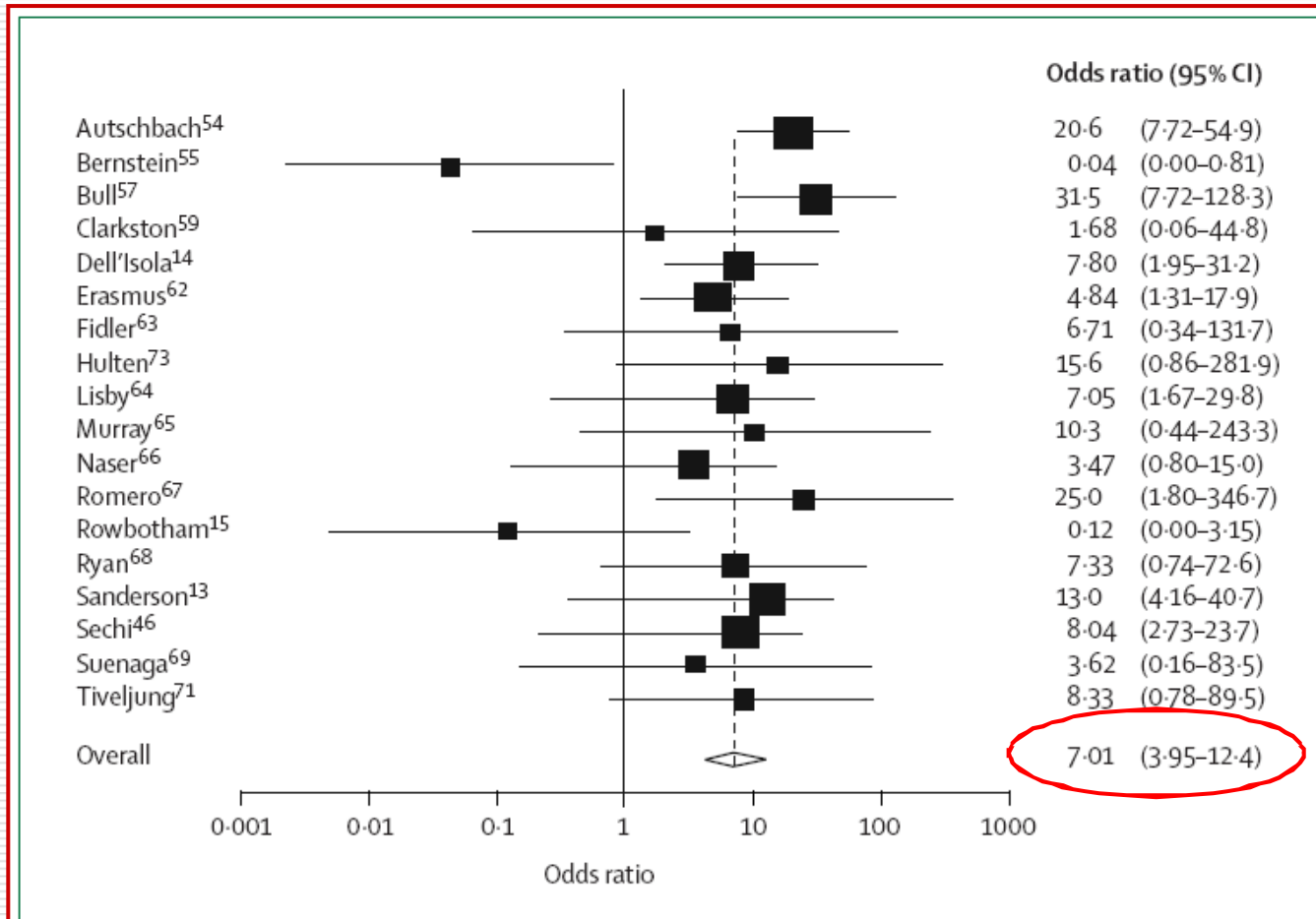


Loftus et al., *Gastroenterology*, 114:1161-1168, 1998.

MAYO  
CLINIC



“Prepojenie *MAP* a Crohn-ovej choroby, zistené podľa PCR V ELISA testov, je zjavné a pochybujeme, že nové významné zistenia môžu byť získané z ďalších štúdií....”



## *Mycobacterium avium* subspecies *paratuberculosis* and Crohn's disease: a systematic review and meta-analysis

Martin Feller, Karin Huwiler, Roger Stephan, Ekkehardt Altpeter, Aijing Shang, Hansjakob Furrer, Gaby E Pfyffer, Thomas Jemmi, Andreas Baumgartner, Matthias Egger

September, 2007

## High prevalence of viable *paratuberculosis* in Crohn's disease

30/30 (100%) CD pacientov MAP-pozitívnych  
Všetci majú spheroplasty v kultúrach – vid' foto

Juan L. Mendoza, Amparo San-Pedro, Esther Culebras, Raquel Cies, Carlos Taxonera, Raquel Lana, Elena Urcelay, Fernando de la Torre, Juan J Picazo, Manuel Díaz-Rubio

September 2010

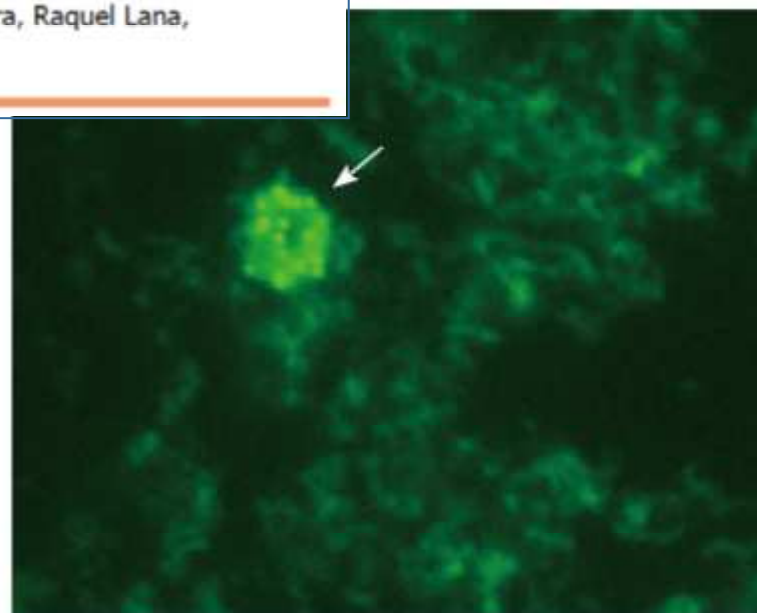


Figure 1 Microscopic examination of *Mycobacterium avium* subspecies *paratuberculosis* cultures isolated from blood of patients with Crohn's disease. Phenolic-acridine orange techniques to detect cell-wall-deficient *Mycobacterium avium* subspecies *paratuberculosis* [spheroplasts (arrow)].





# Association of *Mycobacterium avium* subspecies *paratuberculosis* With Crohn Disease in Pediatric Patients

\*Adrienne Lee, \*Tanya A. Griffiths, \*Rohan S. Parab, §Robin K. King, ||Marla C. Dubinsky, †Stefan J. Urbanski, ‡Iwona Wrobel, and \*Kevin P. Rioux

Terminal ileum		
CD	7/20	35%
UC	1/20	5%
Control	1/19	5.2%

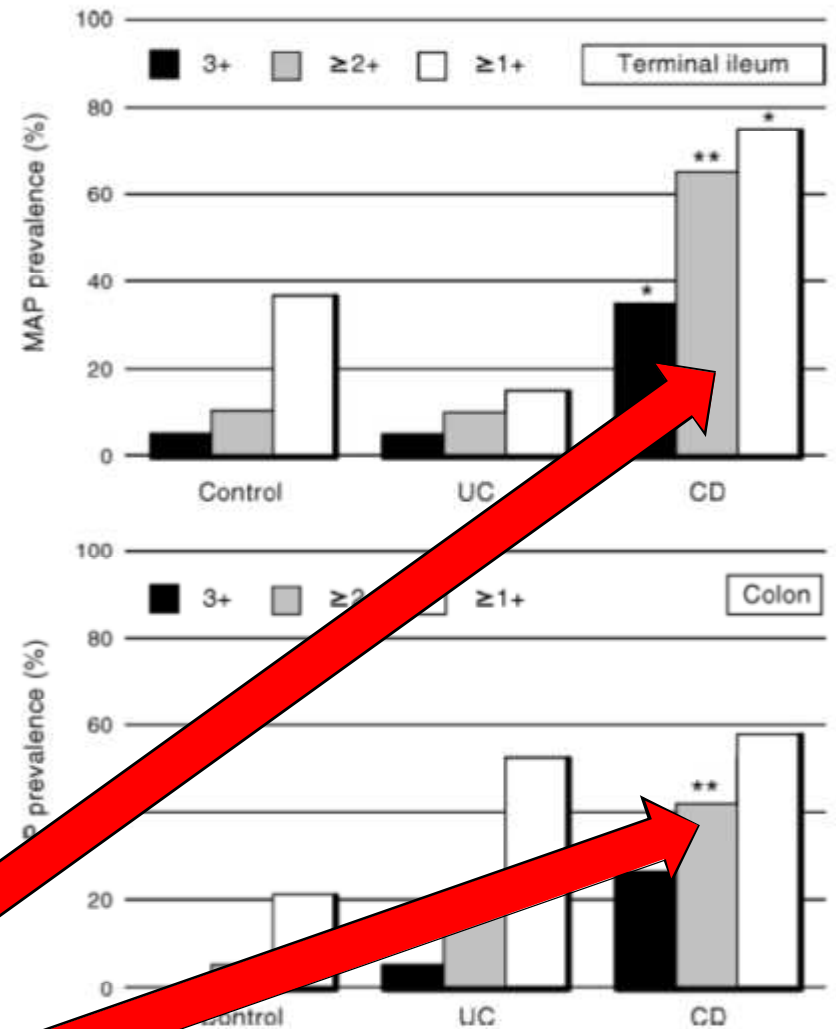
*P* < 0.05 (CD vs UC), *P* = NS (UC vs Control), *P* < 0.05 (CD vs Control)

Colon		
CD	5/9	26.3%
UC	1/19	5.2%
Control	0/19	0%

*P* < 0.05 (CD vs UC), *P* = NS (UC vs Control), *P* = NS (CD vs Control)

**FIGURE 1.** Summary of MAP prevalence in pediatric granulomatous CD. MAP *IS900* was detected in about one-third of ileal and one-fourth of colonic biopsies in patients with CD, which was significantly greater than MAP prevalence in control subjects. Prevalence of MAP in UC was not significantly different from controls. This analysis used the most stringent criteria to define MAP positivity (triplicate PCR reactions were positive for *IS900*, which was confirmed by sequencing). Specimens in which PCR failed to amplify the *APC* gene were excluded. CD = Crohn disease; MAP = *Mycobacterium avium* subsp *paratuberculosis*; PCR = polymerase chain reaction; UC = ulcerative colitis.



**FIGURE 2.** MAP *IS900* prevalence stratified by stringency of PCR replicates. Nested *IS900* PCR reactions were carried out in triplicate. The primary analysis defined MAP prevalence based on all three replicates showing the presence of *IS900*. If less stringent criteria were applied, MAP detection could be defined on the basis of  $\geq 2/3$  or  $\geq 1/3$  PCR positive for *IS900*. Regardless of the level of stringency, the association between pediatric CD and MAP *IS900* detection in ileum (top panel) or colon (bottom panel) remained intact. \**P* < 0.05, \*\**P* < 0.01 vs respective control samples. CD = Crohn disease; MAP = *Mycobacterium avium* subsp *paratuberculosis*; PCR = polymerase chain reaction.

**Paratuberculosis**  
**je potenciální**  
**problém potravinové**  
**bezpečnosti**

2009

REVIEW ARTICLE

**Contamination of food products with *Mycobacterium avium paratuberculosis*: a systematic review**

M.M. Eltholth, V.R. Marsh, S. Van Winden and F.J. Guitian

Department of Veterinary Clinical Sciences, Royal Veterinary College, London, UK

Súčasné dostupné dáta naznačujú že pravdepodobnosť kontaminácie mliečnych a mäsových produktov MAP by nemala byť prehliadaná.

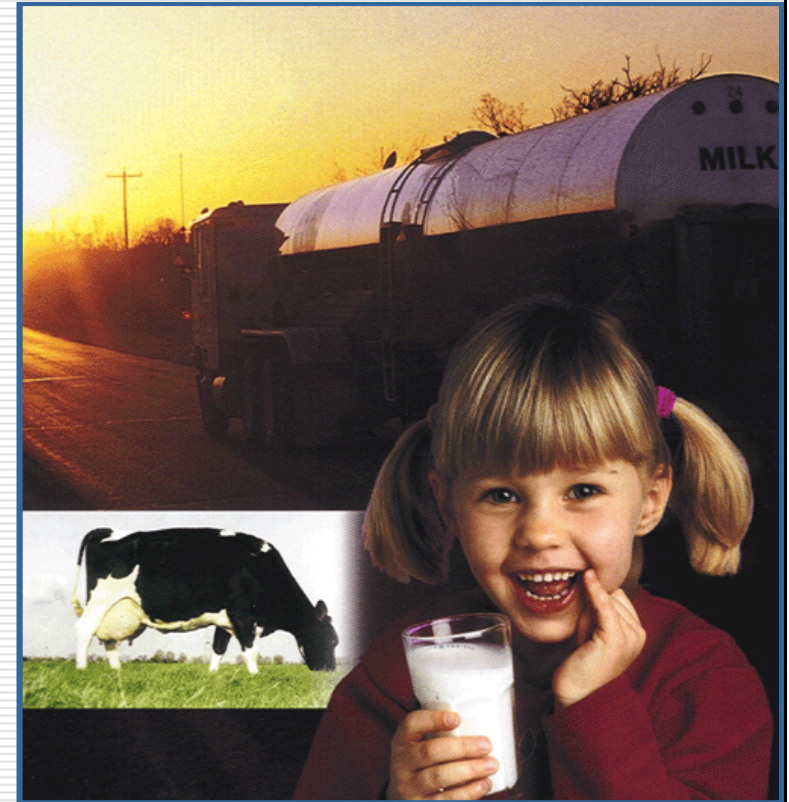




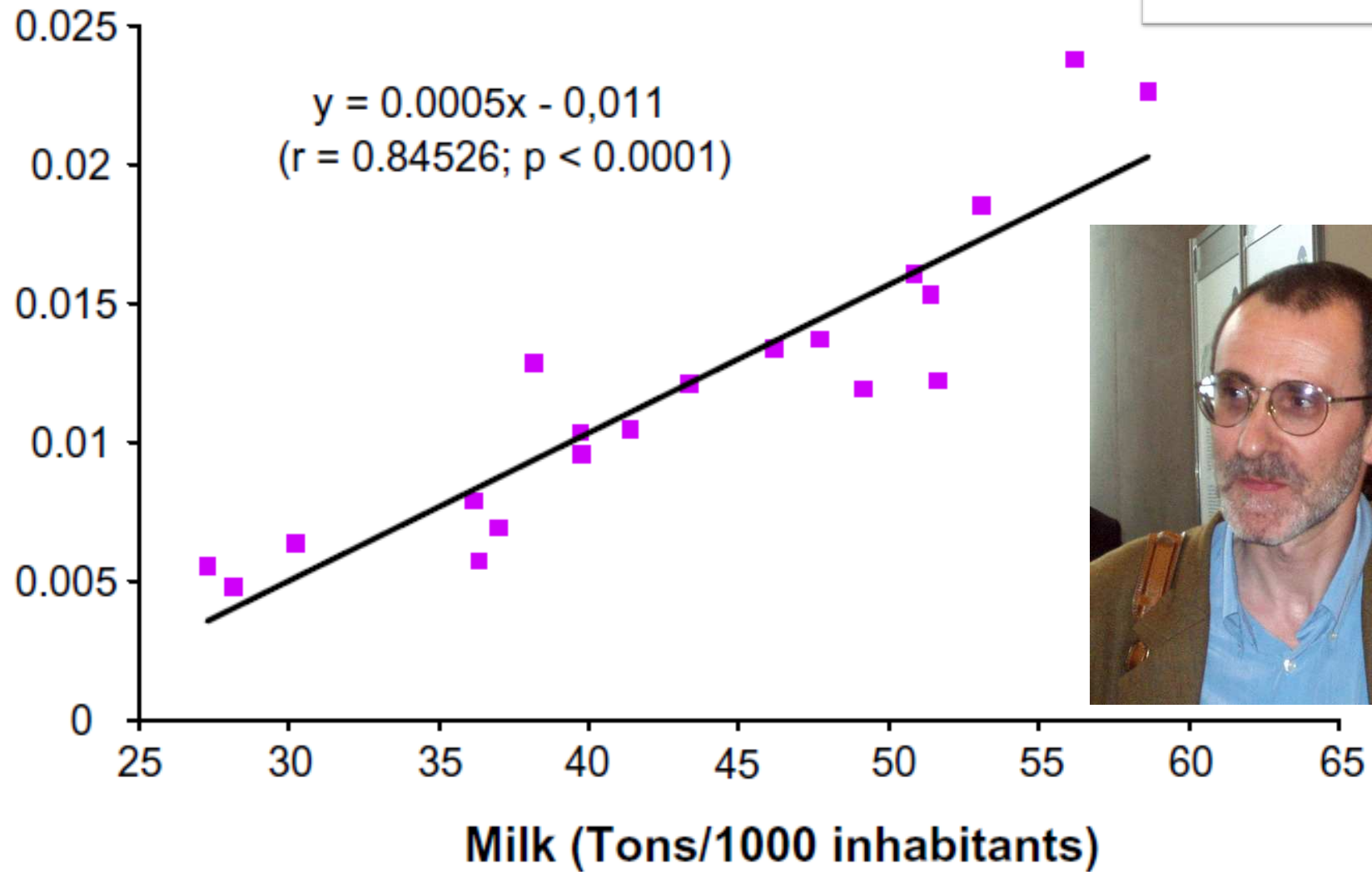
# Pasterizácia nie je na 100% efektívna

---

- *MAP*: najviac tepelne-odolné *Mycobacterium sp.* (lab studies):
  - U.S., U.K., Germany
  
- *MAP*: kultivované z predajného HTST pasterizovaného mlieka
  - 1.8% in U.K. (AEM May 2002)
  - 1.6% in Czech Rep. (AEM March 2005)
  - 2.8% in U.S. (J. Food. Protect. May 2005)
  - 67% in India (Int. J. Infect. Dis. Feb. 2010)
  
- 2.7% in Brazil (11-ICP, Carvalho et al., 2012)



CD yearly incidence (arc sinus square root)



**Fig. 4.** Association between milk consumption and Crohn's disease incidence in Japan during the period 1966–1985.



# MAP v práškových mliečnych produktoch pre dojčatá



Krajina	Veľkosť štúdie	% PCR positive	% Culture positive	Reference
---------	----------------	----------------	--------------------	-----------

## Botsaris et al. 11-ICP

35 vzoriek; 11 producentov

9.4% MAP culture-positive

21.9% PCR-positive



Epidemiologické štúdie: kojenie znižuje riziko Crohnovej choroby.

# Identification and Characterization of a Spore-Like Morphotype in Chronically Starved *Mycobacterium avium* Subsp. *Paratuberculosis* Cultures

Elise A. Lamont<sup>1</sup>, John P. Bannantine<sup>4</sup>, Anibal Armien<sup>1</sup>, Don Sanjiv Ariyakumar<sup>3</sup>, Srinand Sreevatsan<sup>1,2\*</sup>

<sup>1</sup> Veterinary Population Medicine, University of Minnesota, St. Paul, Minnesota, United States of America, <sup>2</sup> Department of Veterinary Biomedical Sciences, University of

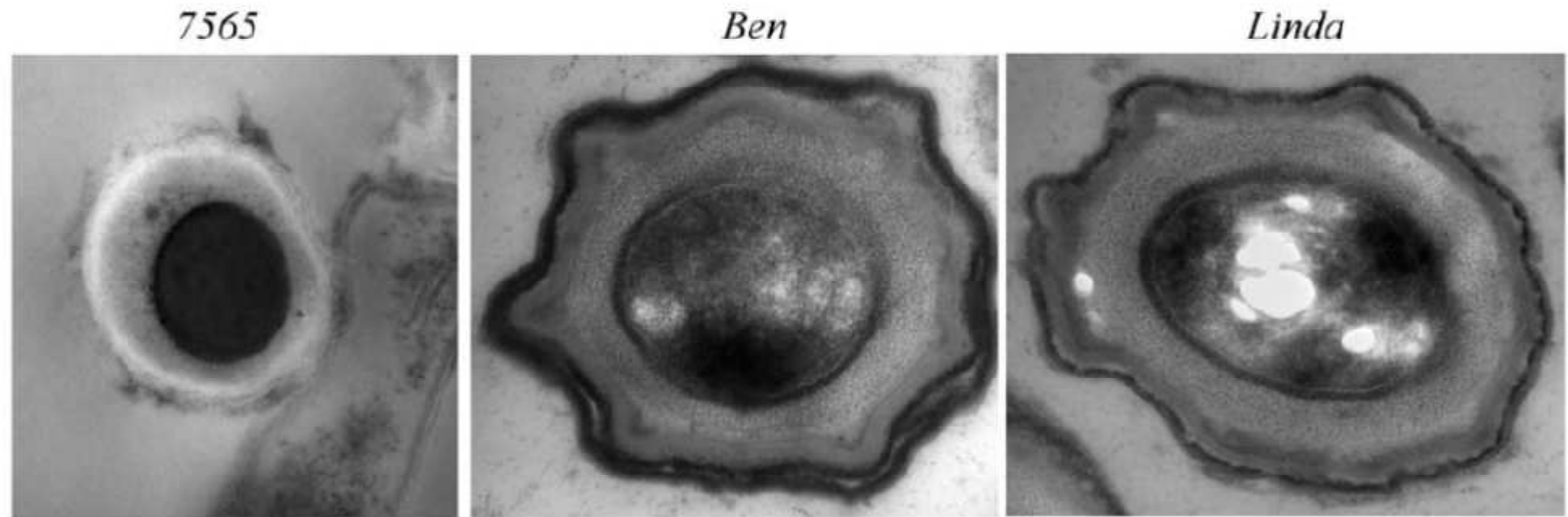
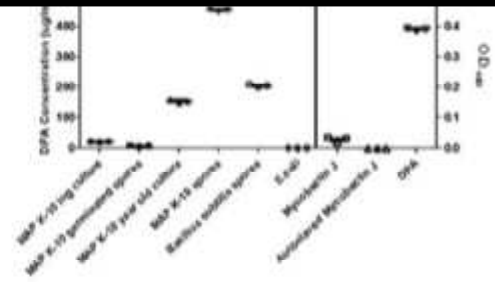
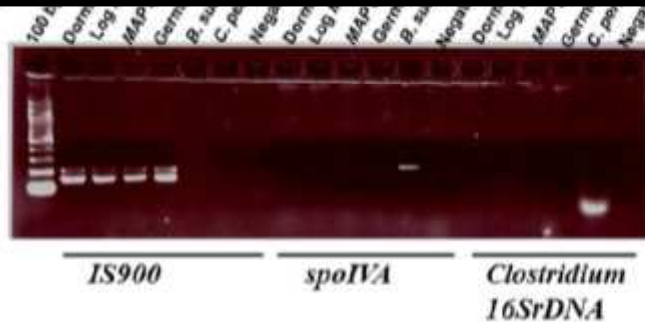


Figure 4. Sporulation occurs in multiple *MAP* strains.







# Microbiological characterisation of artisanal farmhouse cheeses manufactured in Scotland

ALAN G WILLIAMS\* and SUSAN E WITHERS

*Department of Biological and Biomedical Sciences, Glasgow Caledonian University, Glasgow G4 0BA, Scotland*

August, 2010

*Twenty-eight Scottish artisanal farmhouse cheeses were examined in respect of 16 microbial groups of significance for food safety and cheese character development. Microbial populations were diverse and although *Escherichia coli* O157 and *Salmonella* spp. were not detected the occurrence of potential food-borne pathogens was confirmed in 86% of the samples analysed. *Mycobacterium avium* subsp. *paratuberculosis* was detected in 25% of the cheeses tested and some *Staphylococcus aureus* and the *Bacillus cereus* isolates were enterotoxigenic. Resistance to methicillin and vancomycin and other clinically important antibiotics was detected in some *S. aureus* and *Enterococcus* strains. The inappropriate labelling of some raw milk cheeses and the consequences of the complexity of the microbial population on isolation media specificity is discussed.*

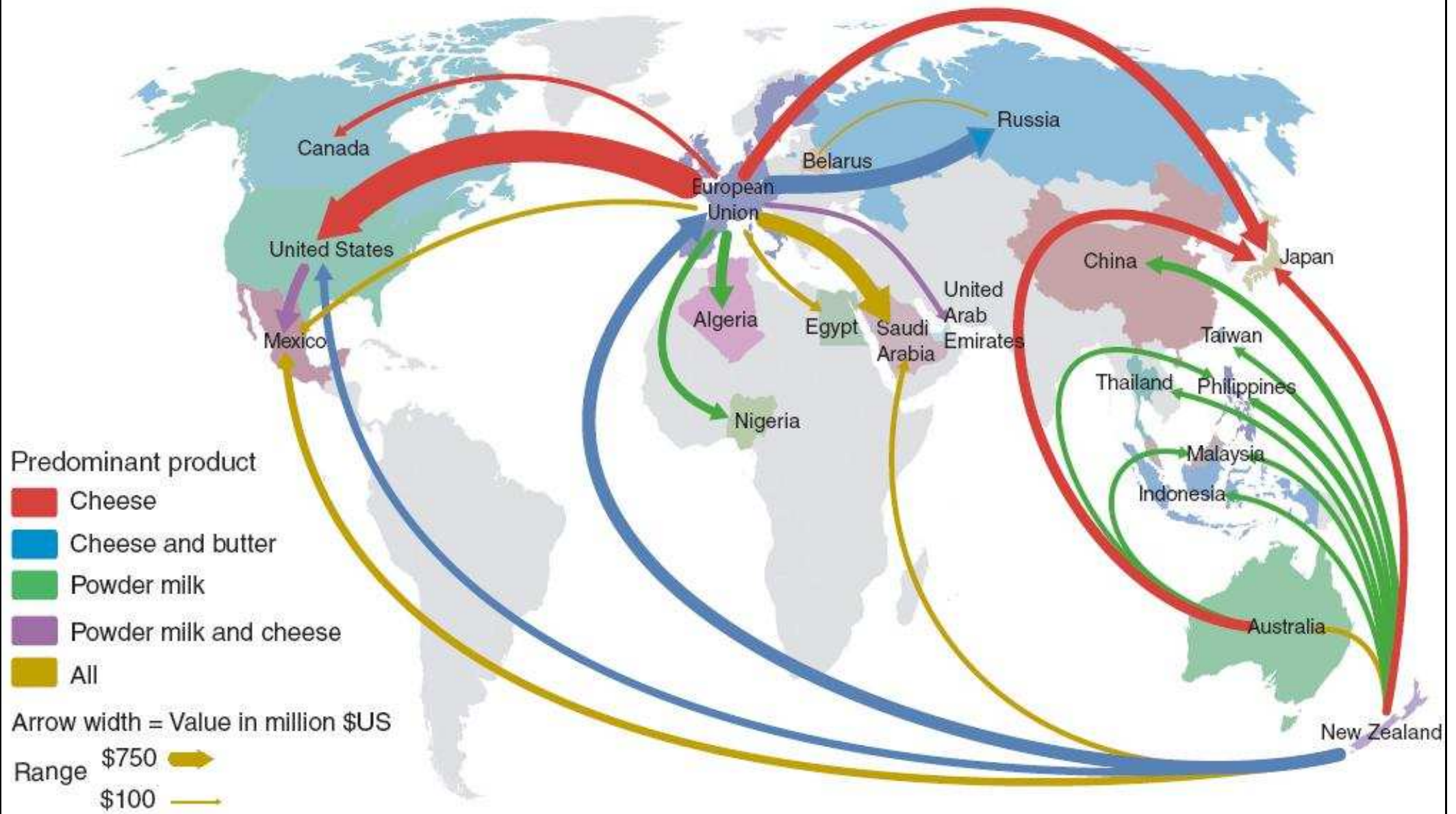
MAP detekované kultiváciou  
u 25% testovaných syrov

*rium avium* subsp.

Mliečne produkty sú mobilné



# Major Global Trade Flows of Dairy Products in 2003







# Kravy s Paratuberkulózou sú zabíjané & konzumované

- ❑ Prejdú ante-mortem veterinárnou inšpekciou
- ❑ Prejdú post-mortem veterinárnou inšpekciou
- ❑ Často majú diseminované MAP infekcie



**Test-and-cull JD kontrolné programy sú v základe test-and-feed-to-the-public.**

**Relationships between clinical signs,  
pathological changes and tissue distribution  
of *Mycobacterium avium* subspecies  
*paratuberculosis* in 21 cows from herds  
affected by Johne's disease**

C. BRADY, D. O'GRADY, F. O'MEARA, J. EGAN, H. BASSETT

**TABLE 3: Distribution of *Mycobacterium avium* subspecies *paratuberculosis* (MAP) in the 11 pooled samples of tissues from 21 cows from eight herds affected by Johne's disease**

Animal*	Head LNs	Thoracic organs	Terminal ileum	Mesenteric LN	Ileocaecal LN	Caecal contents	Small intestine	Large intestine	Abdominal organs	Prescapular and popliteal LN	Supramammary LN and mammary gland
A1	+	+	+	+	+	+	+	+	+	+	+
A2	CT	+	+	+	+	+	+	+	CT	+	CT
A3	+	+	+	+	+	+	+	+	+	+	+
A4	+	-	+	+	-	+	+	+	-	+	-
A5	+	+	NR	+	NR	+	NR	NR	+	-	NR
A6	-	+	+	+	+	+	-	+	-	+	+
A7	+	+	+	+	+	+	+	+	+	-	-
B1	-	+	+	+	+	+	+	+	-	-	-
B2	-	+	+	+	NR	-	-	-	-	-	-
B3	CT	+	+	NR	+	+	+	+	+	+	NR
B4	+	+	+	+	+	CT	+	+	+	+	+
B5	+	+	+	+	+	+	+	+	+	+	+
B6	CT	-	+	-	+	+	+	-	-	-	-
C1	+	+	+	+	+	NR	+	+	+	+	+
C2	+	-	+	-	+	+	NR	-	NR	NR	NR
C3	-	-	ELISA-positive; klinicky normálne					-	+	NR	
C4	-	-	+	+	+	+	+	+	-	-	-
D1	+	+	+	+	+	NR	-	+	CT	+	+
D2	-	+	+	+	NR	NR	+	-	-	+	+
D3	-	-	+	-	+	CT	+	-	-	NR	-
D4	+	-	+	+	+	+	+	-	-	+	-

\* Group A Persistent diarrhoea, Group B Intermittent diarrhoea, Group C No diarrhoea but illthriven, Group D Clinically normal  
 LN Lymph node, + MAP cultured, CT Contaminated, - MAP not cultured, NR No result

# Nie všetky Johne's kravy sú chudé

IDEXX ELISA S/P = 2.0 = Strong-positive



CSU study: 12 of 21 (57%) zabitých dojníc potvrdených s MAP-infekciou nemalo nijaké klinické príznaky Johne's disease.



## Isolation of *Mycobacterium avium* subsp. *paratuberculosis* from Muscle Tissue of Naturally Infected Cattle

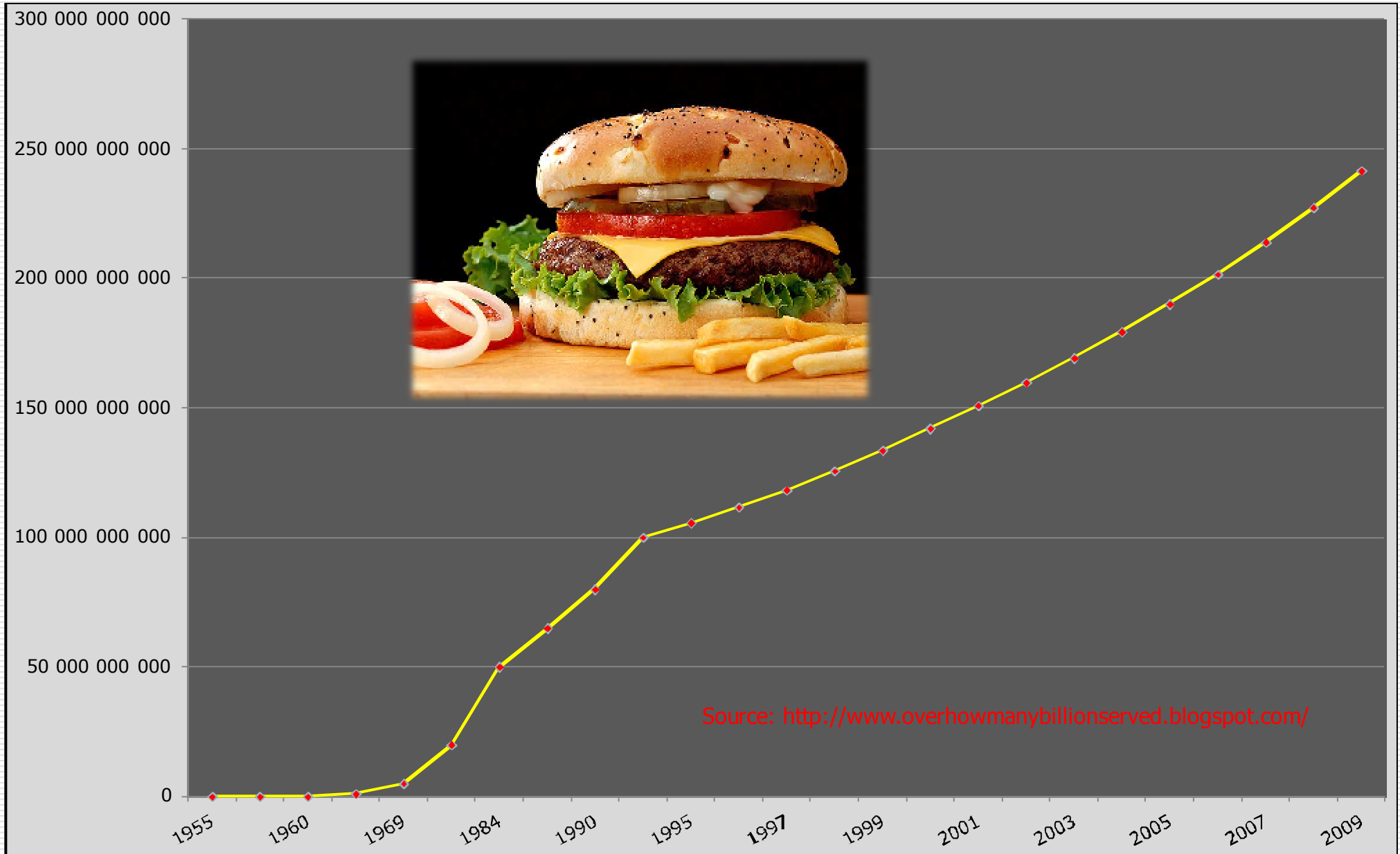
Marta Alonso-Hearn, Elena Molina, Marivi Geijo, Patricia Vazquez, Iker Sevilla, Joseba M. Garrido, and Ramon A. Juste



Type	Breed	# Animals	% clinical signs of pTB	% culture-positive muscle
Dairy	Jersey	11	45%	9%
Dairy	Friesian	31	22%	10%
Beef	Limousin	5	0	40%
Total		47	26%	13%

# Billions and Billions of Burgers!

Logos of retail hamburger chains removed for liability concerns



Epidemiológia je komplexná

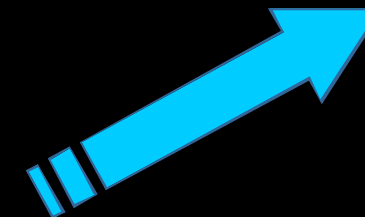
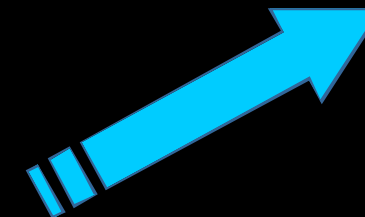
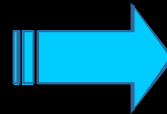
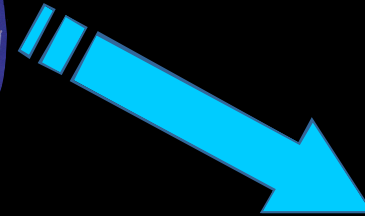
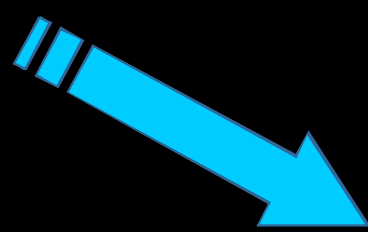
ale

zrozumiteľná

„nosiče“

zdroj

vnímavý  
hostitel'







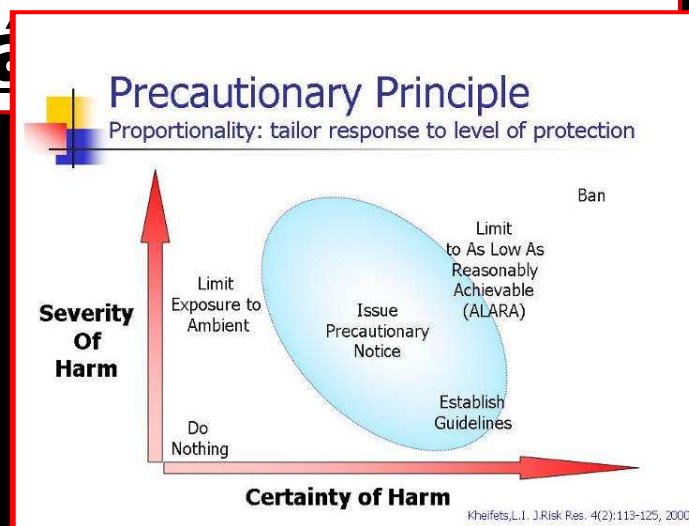
# TAFS

INTERNATIONAL FORUM FOR

TRANSMISSIBLE ANIMAL DISEASES & FOOD SAFETY

TAFS odporúča MAP kontrolu na farme, národnej a nadnárodnej úrovni, aby sa takým spôsobom limitovala MAP kontaminácia potravín na preventívnom princípe aby surové mlieko a mäso pochádzalo z **test-negatívnych** sta

<http://www.tseandfoodsafety.org/>



## **Jednoduchý koncept:**

**Zdravé potraviny pochádzajú zo zdravých zvierat.**

## **Jednoduchý fakt:**

**Zvieratá s paratuberkulózou nie sú zdravé.**

**Producenti a ich veterinárni lekári majú vedomosti a nástroje ako produkovať surové produkty s nízkym rizikom *MAP* kontaminácie.**

# **5 dôvodov prečo kontrolovať pTB**

---

- 1. pTB znižuje mliečnu produkciu.**
  - 2. pTB je infekčné ochorenie (šíriace sa).**
  - 3. pTB testy sú presné a cenovo dostupné.**
  - 4. pTB kontrola zlepšuje celkové zdravie stáda.**
  - 5. vedecky založený program postavený na mliečnom ELISA je ľahký, dostupný, a tým pravým, čo je treba robiť pre konzumentov.**
-

- Použi HACCP Princípy –  
Umiestniť početné prekážky medzi *MAP* zdroj  
a  
telatá či konzumentov

---

- ☑ Predchádzať infikovaniu stád
- ☑ Zabrániť šíreniu infekcie na farmách
- ☑ Testovať stáda a vyradovať pozitívne jedince
- ☑ držať mäso a mlieko hygienicky
- ☑ Pasterizovať všetky mliečne produkty

Potravinová bezpečnosť:  
“teat to tongue” or “moo to you”

---



# Jeden Svet – Jeden Štandard Bezpečnosti Potravín



---

Praktická skúsenosť naznačuje, že  
paratuberculosis **môže byť**  
**kontrolovaná** ale nie iba  
zmenami manažmentu  
samotnými.

**TESTOVANIE JE  
ZÁKLADOM**

---



Otázky?