



13. Bastones Acido- Alcohol Resistentes

- ✓ *Mycobacterium*
- ✓ *Nocardia*

Mycobacterium

Dominio: *Bacteria*

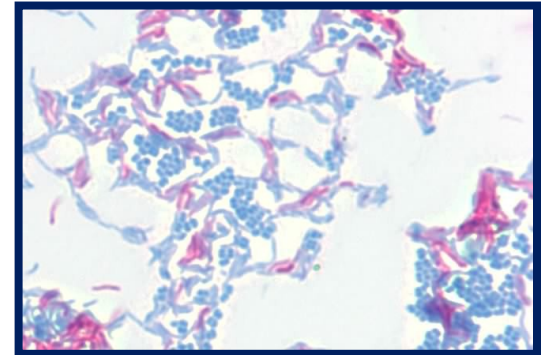
Phylum: *Actinobacteria*

Clase: *Actinobacteria*

Orden: *Actinomycetales*

Familia: *Mycobacteriaceae*

Género: *Mycobacterium*





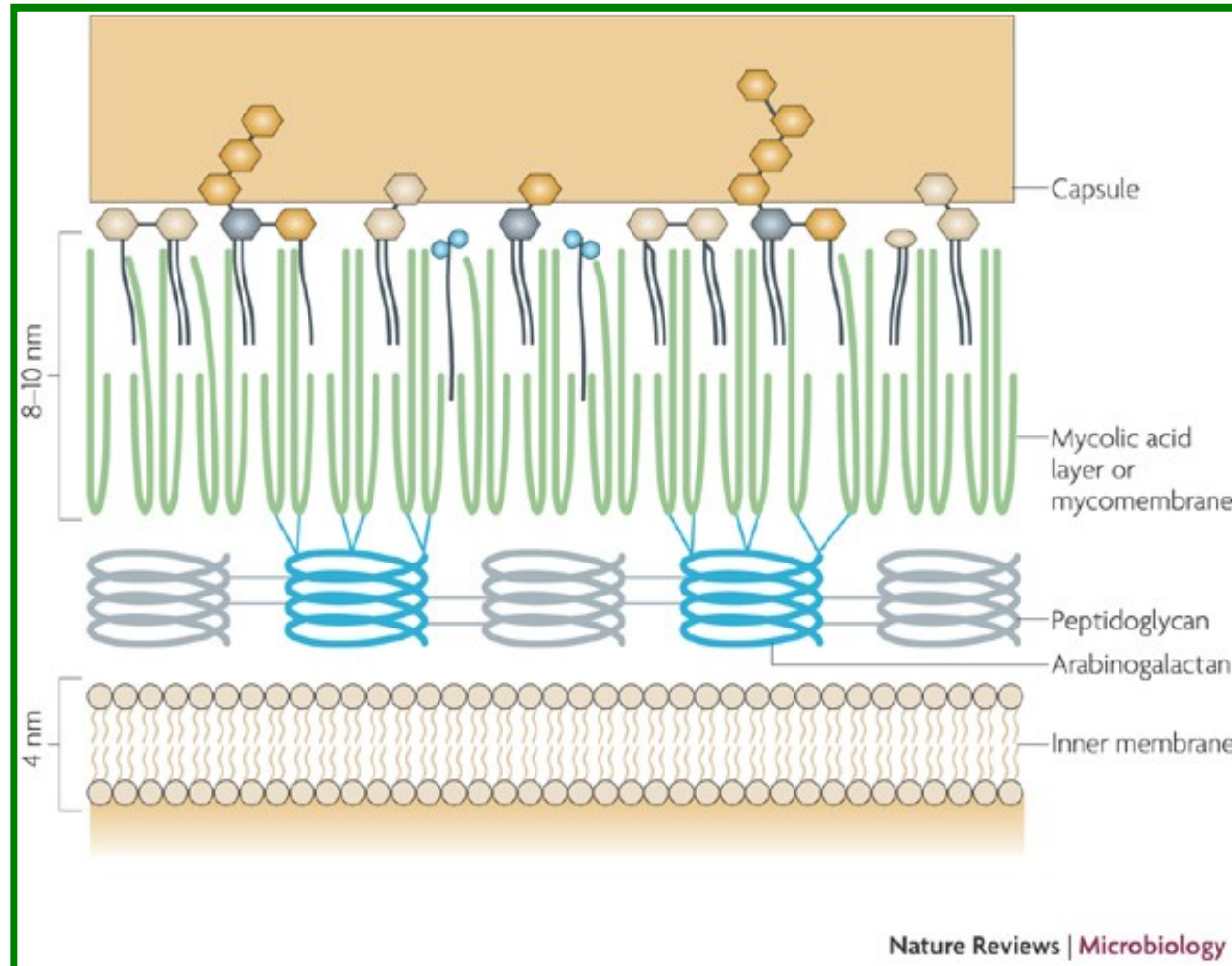
Mycobacterium

- Son bastones aerobios e inmóviles.
- Las micobacterias incluyen especies saprófitas y patógenas.
- Las especies patógenas son de crecimiento lento en el laboratorio, las colonias se hacen visibles después de semanas de cultivo.
- Las micobacterias patógenas son facultativas intracelulares, y producen infecciones crónicas granulomatosas.

Mycobacterium: Pared celular

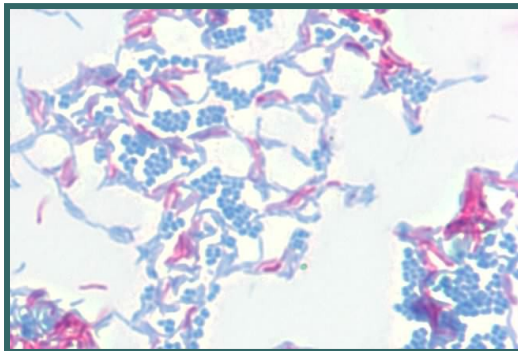
- Las micobacterias poseen un contenido alto de lípidos (20-40% en peso seco) en su pared celular. Esto las hace resistentes a factores humorales y celulares de defensa, a desinfectantes y a factores ambientales adversos.
- Entre éstos lípidos se encuentran:
 1. **Ácidos micólicos**: Son ácidos grasos que hacen a la célula hidrofóbica e impermeable a las tinciones acuosas en frío. De aquí se deriva la propiedad de ácido-alcohol resistentes (tinción de Ziehl-Neelsen).
 2. **Glicolípidos** (lipoarabinomano; factor de cuerda): Contribuyen a la formación de los granulomas, a la sobrevivencia de la bacteria en el interior del fagocito, a la reacción de hipersensibilidad (tuberculina), y al efecto adyuvante.

Pared celular de bacterias ácido-alcohol resistentes



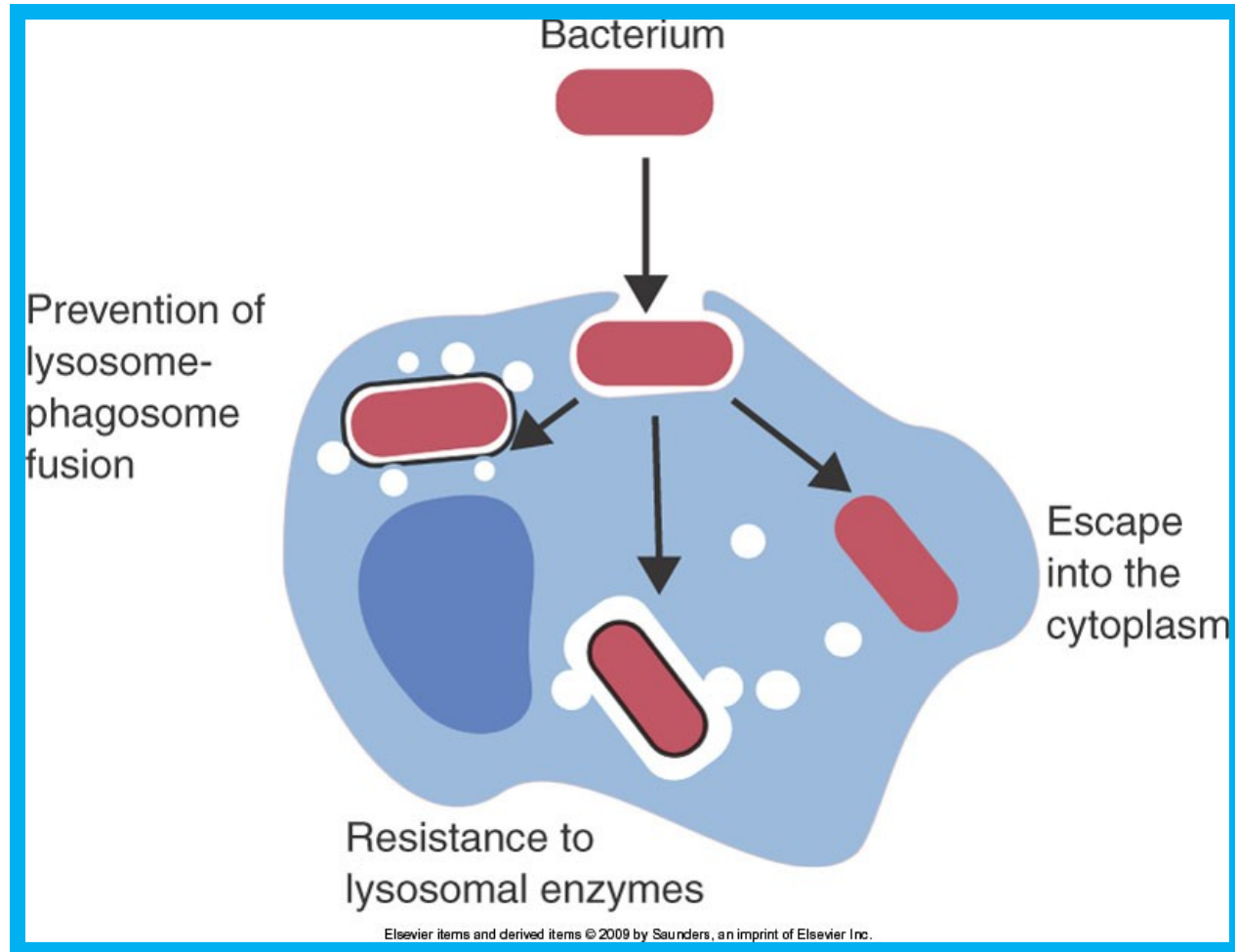
Tinción de Ziehl-Neelsen

- Fue desarrollada por Franz Ziehl (1859-1926) y Friedrich Neelsen (1854-1894)
- **Procedimiento:**
 1. Agregar carbol-fucsina al frotis durante cinco minutos en una platina caliente.
 2. Lavar con agua para enfriar el portaobjetos.
 3. Agregar la mezcla de ácido-alcohol (alcohol etílico con un 3% de HCl) para decolorar.
 4. Lavar nuevamente con agua y contrateñir con azul de metileno por dos minutos.
 5. Las bacterias ácido-alcohol resistentes mantienen el color rojo de la fucsina.



Mycobacterium smegmatis
(rojo-rosa) y *Micrococcus*
luteus (azúl) a 1000x

Mycobacterium: Prototipo de los facultativos intracelulares

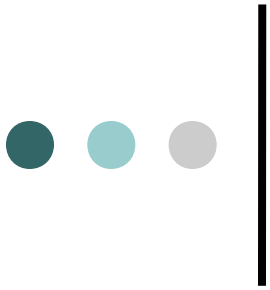




Mycobacterium

Las principales especies de interés veterinario son:

- ❖ *M. bovis*: Tuberculosis bovina
- ❖ *M. avium* subsp. *paratuberculosis*: Paratuberculosis (bovinos, ovinos, caprinos)
- ❖ *M. avium* subsp *avium*: Tuberculosis en aves
- ❖ *M. lepraemurium*: Lepra felina

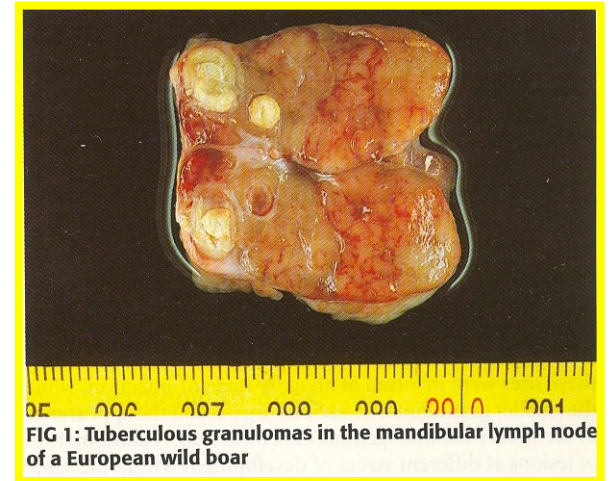


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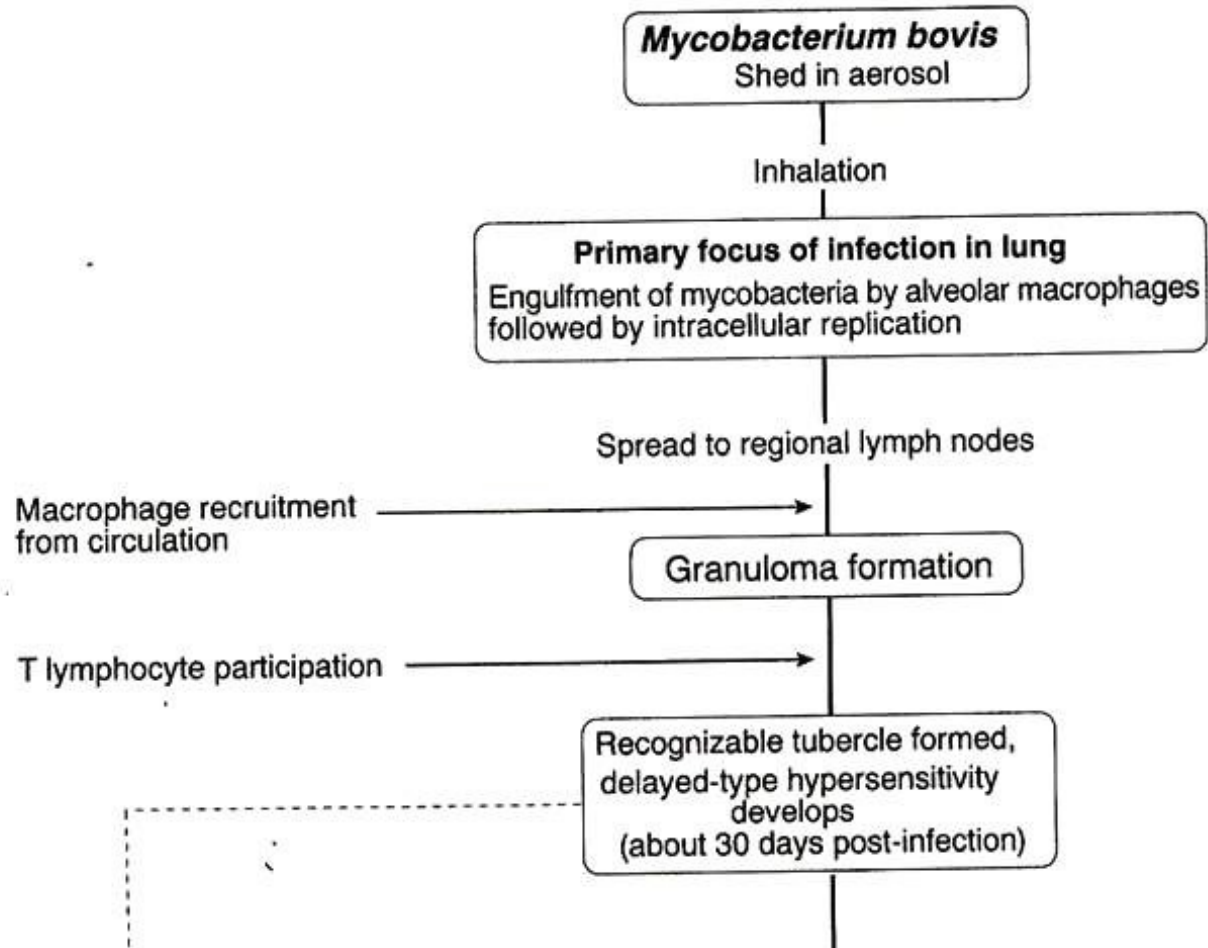
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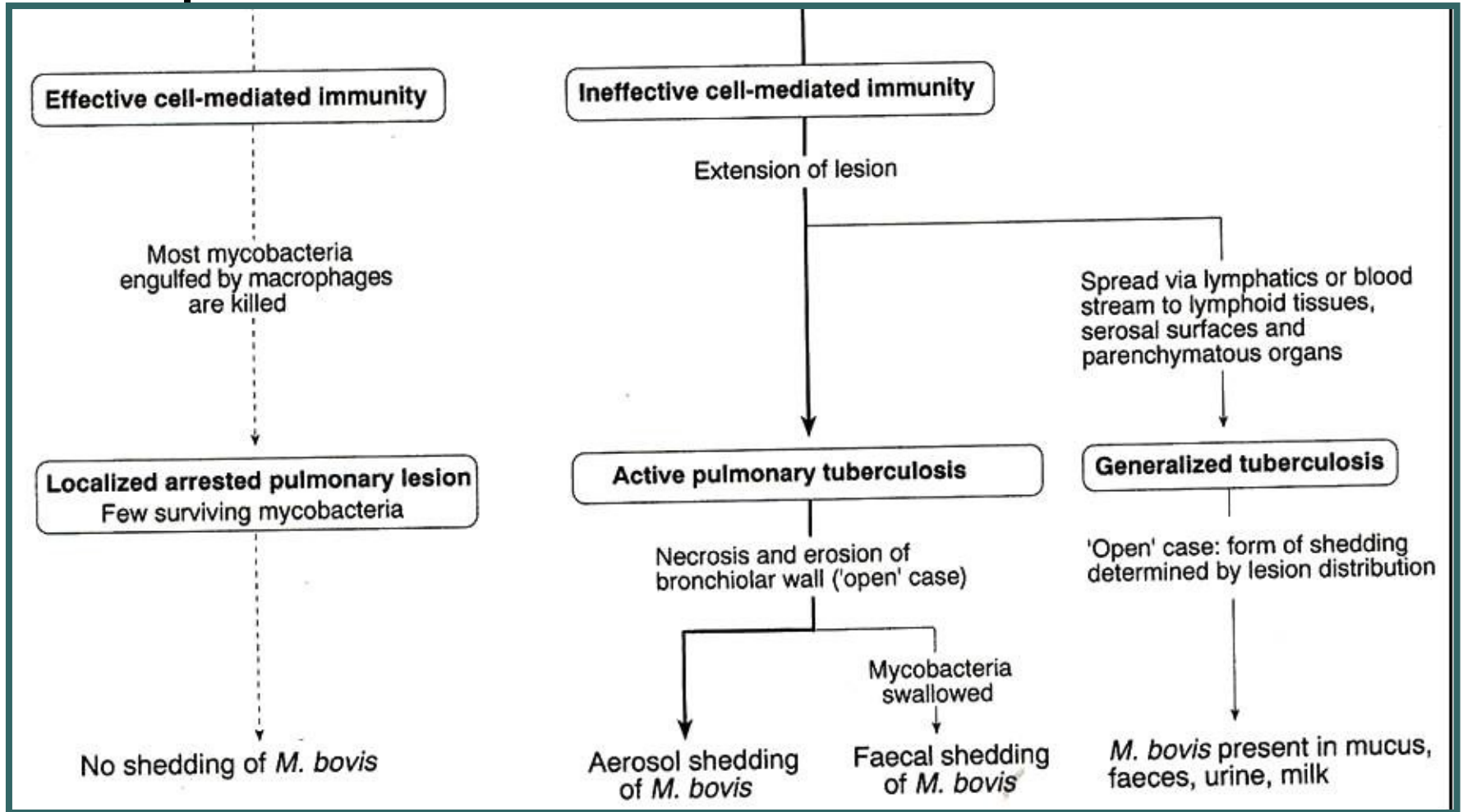
M. bovis : Tuberculosis

- El bovino es el hospedero principal; también puede presentarse la infección en cerdos, equinos, ovinos, perros, gatos, conejos, cuyes, fauna silvestre y el humano .
- En los bovinos se presenta tuberculosis pulmonar que incluye a los ganglios linfáticos de la zona. La lesión característica es el **granuloma (tubérculo)**.
- Se puede presentar una forma diseminada denominada **tuberculosis miliar**, en la que se observan pequeños granulomas en diversas vísceras.



The possible consequences of *Mycobacterium bovis* infection in cattle, acquired via aerosols

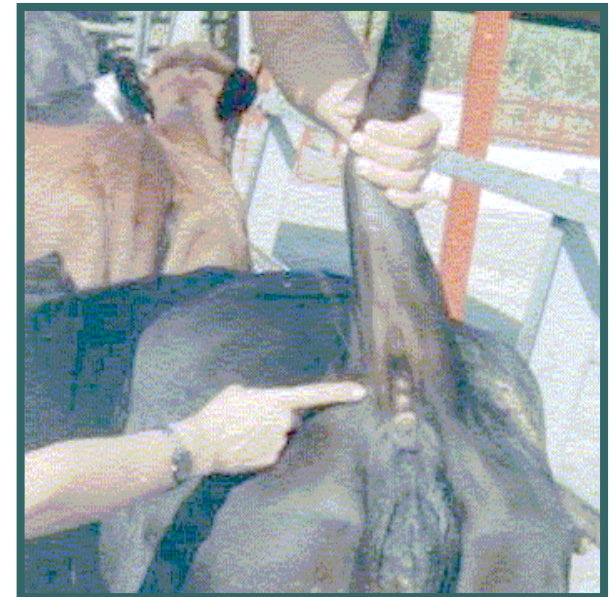




M. bovis

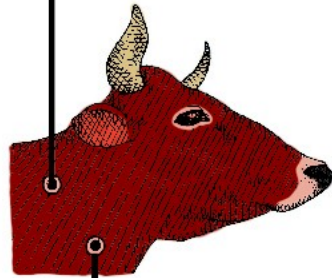


- o Diagnóstico *in vivo*: Prueba de Tuberculina:
- a) Simple: En el maslo de la cola.
- b) Comparativa: PPD bovino vs PPD aviar (aumento > a 4 mm)





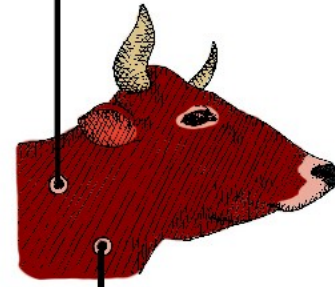
PPD bovino



PAD aviar

48 - 72 hrs.

>6 mm

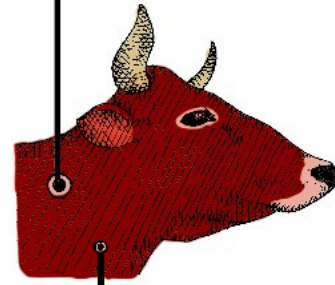


= negativo

>6 mm

48 - 72 hrs.

>7 mm

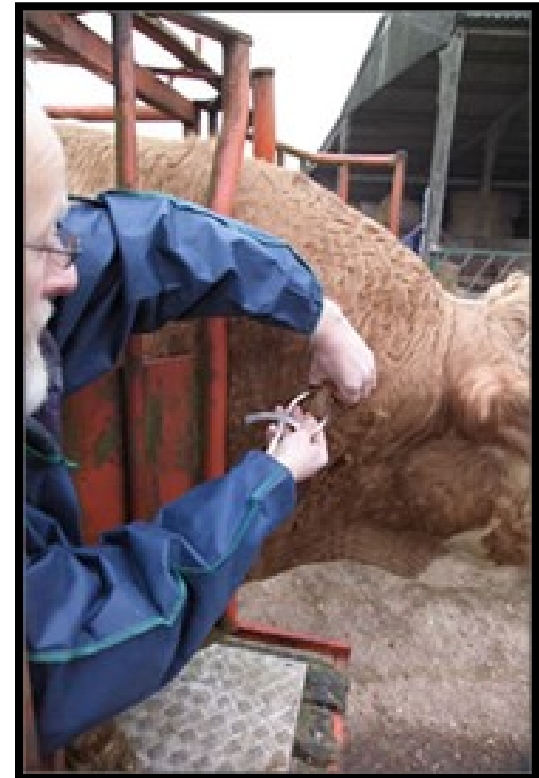


= positivo

>2 mm

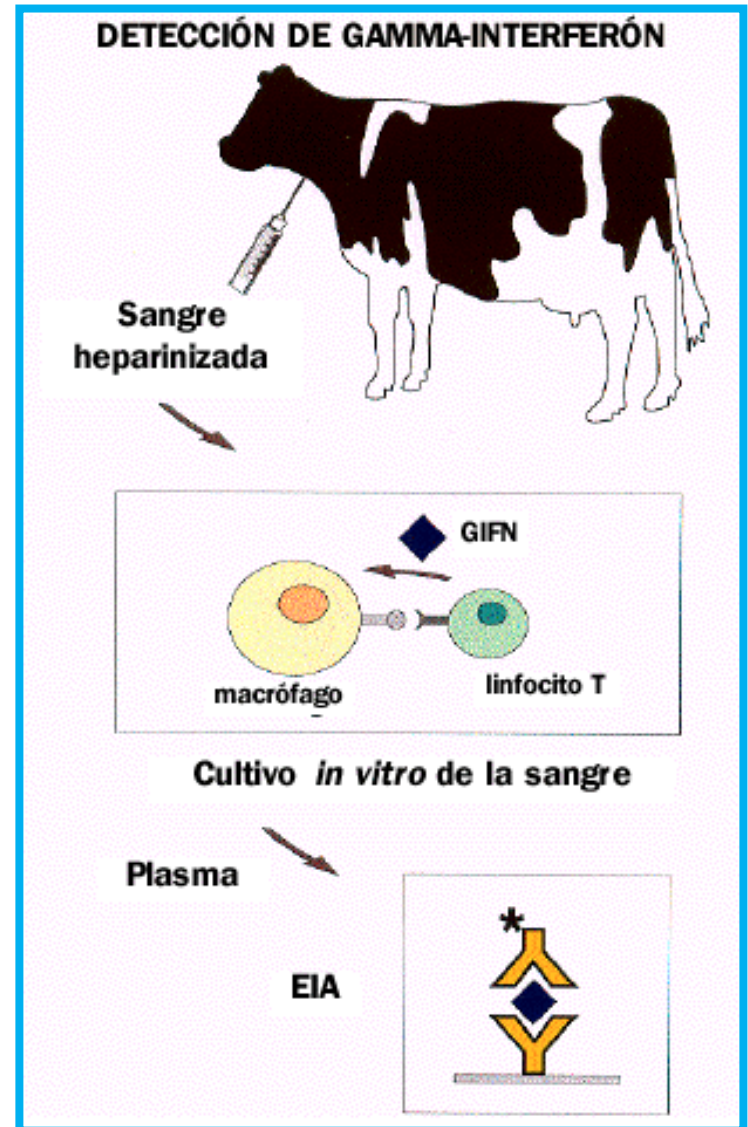


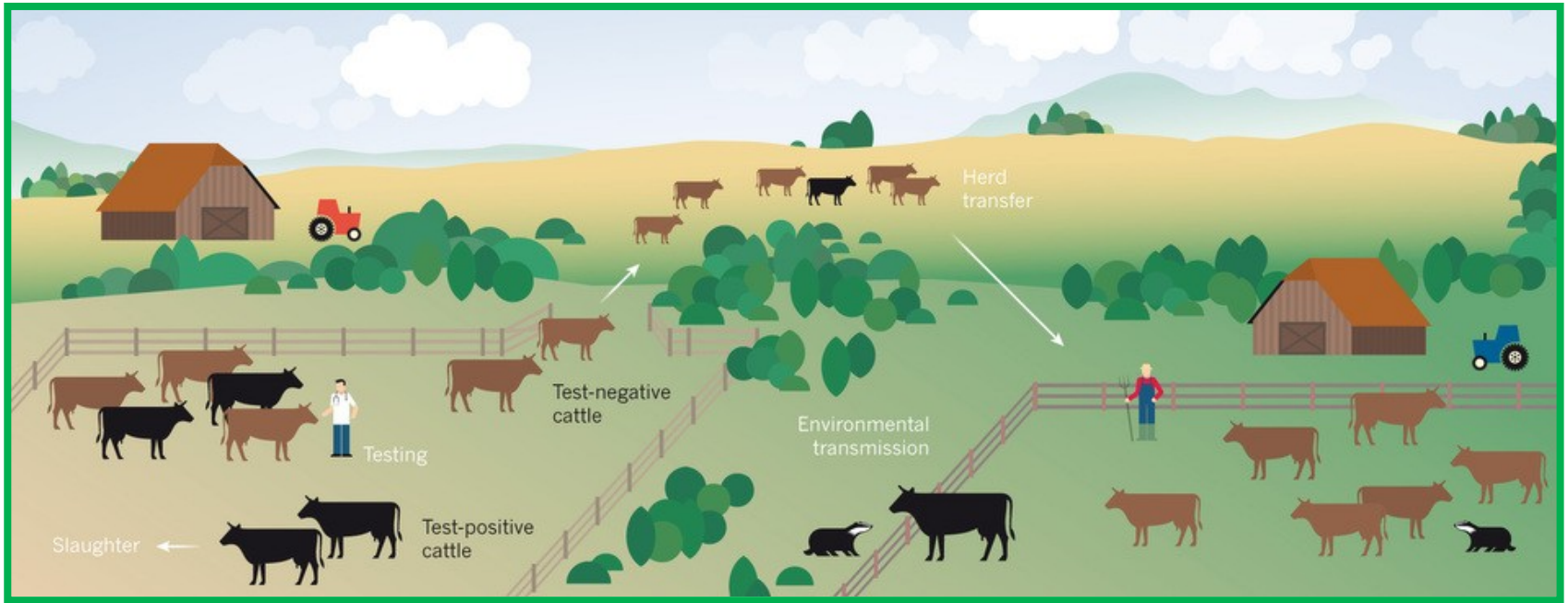
Figure 11.13 A reactor to the single intradermal comparative tuberculin test. There is no reaction to the avian PPD at the upper site but a marked reaction has occurred to the bovine tuberculin (lower site). Photographed 72 hours after injection.



M. bovis

- ✓ Diagnóstico *post mortem*: Identificación de las lesiones características (granulomas)
- ✓ Diagnóstico *in vitro*:
 - a) Cultivo en medio Lowenstein-Jensen.
 - b) Identificación de IF γ









The infection can be spread between badgers, cats, deer, humans and cattle



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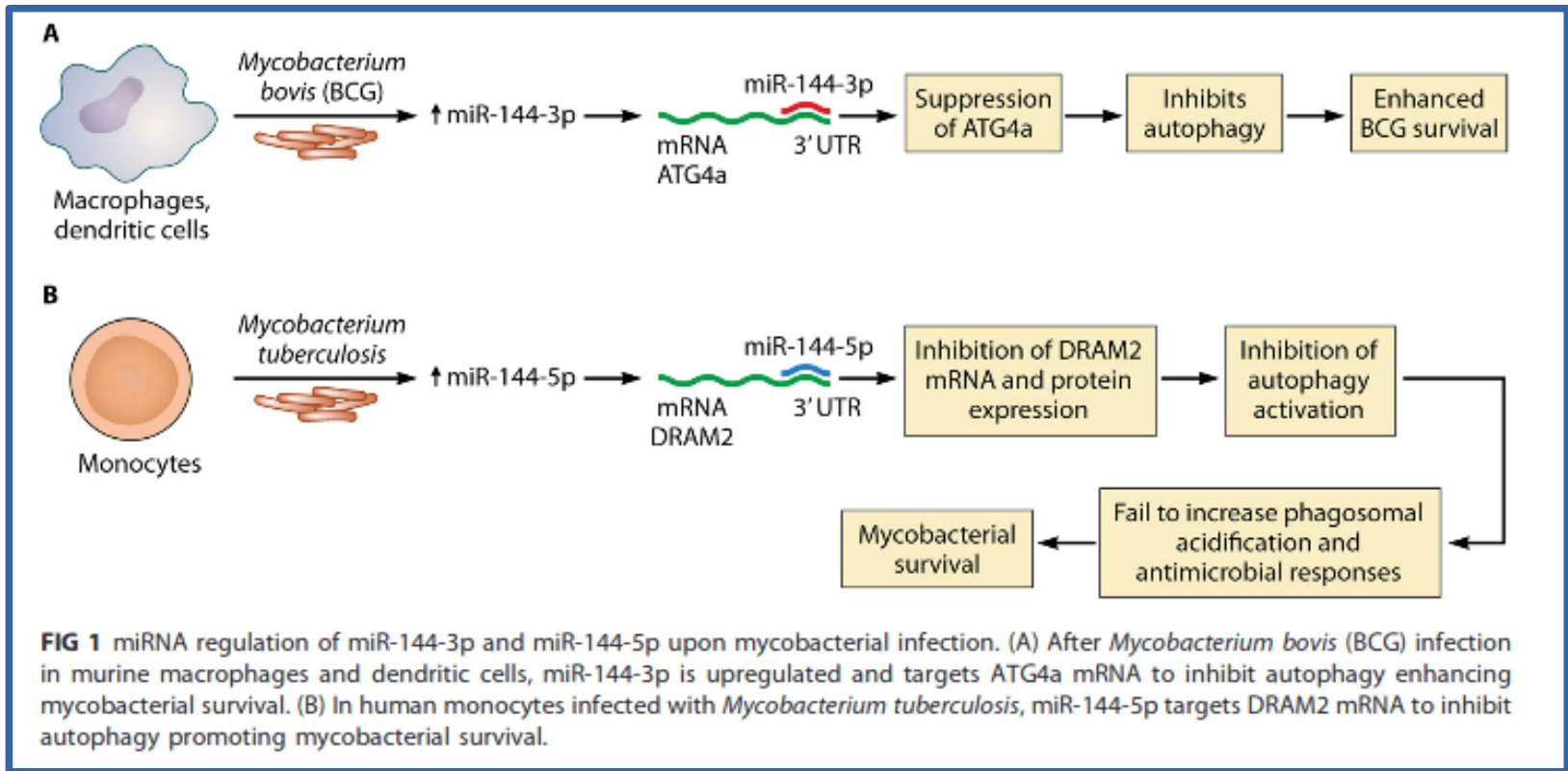
Unraveling the Role of MicroRNAs in *Mycobacterium tuberculosis* Infection and Disease: Advances and Pitfalls

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^aDepartamento de Enfermedades Infecciosas del Adulto, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

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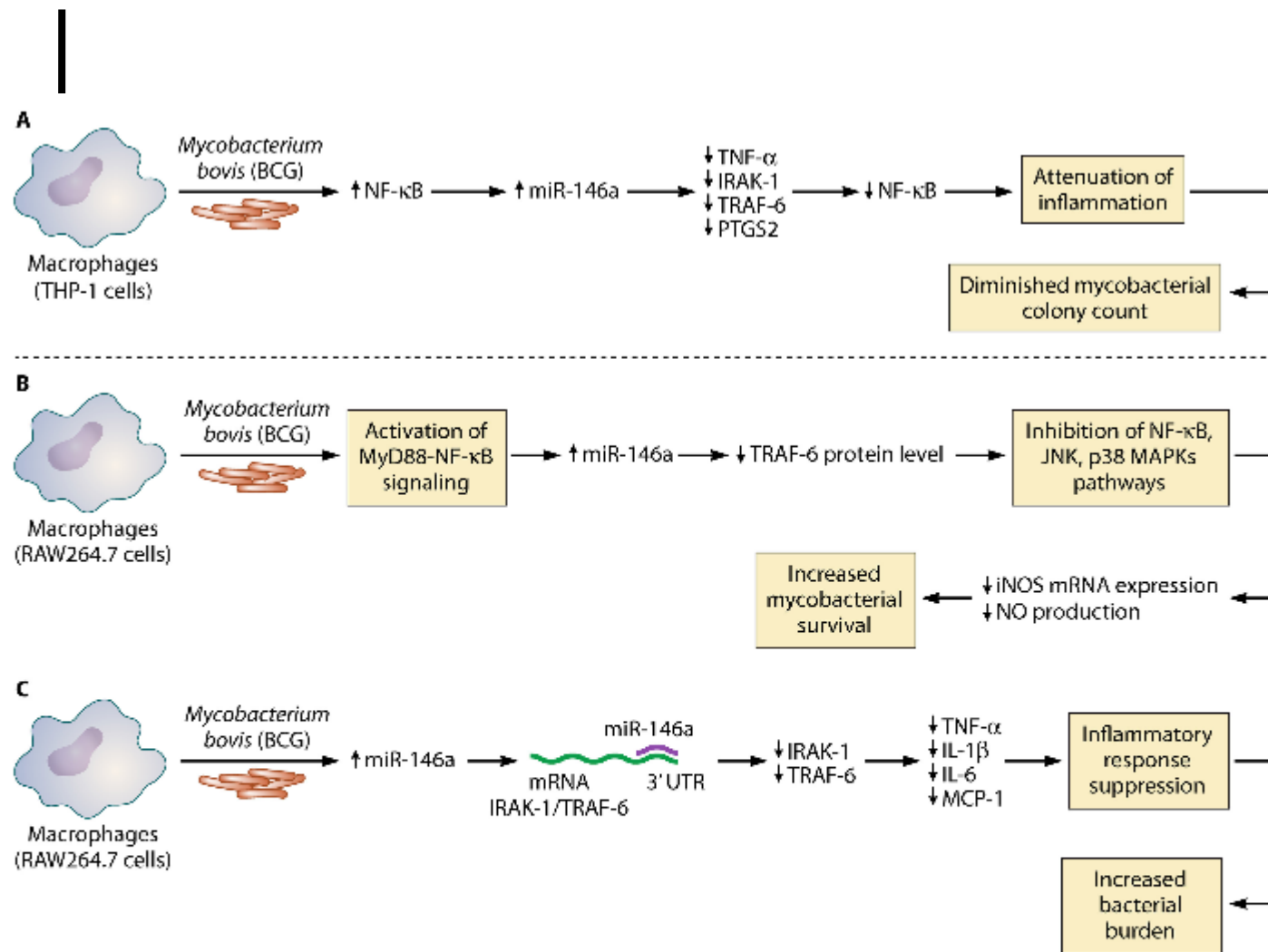


FIG 2 Dual role of miR-146a in the survival of mycobacteria. (A) Upon *Mycobacterium bovis* (BCG) infection in macrophages differentiated from human THP-1 cells, miR-146a increases its expression and downregulates transcription factors to suppress the inflammatory response leading to a reduction in mycobacterial survival. (B and C) After BCG infection in murine macrophages, miR-146a increases its expression and downregulates transcription factors and cytokines to suppress the inflammatory response leading to an increase in mycobacterial survival.



M. bovis como zoonosis

- En 1998 la WHO reportó que el 3.1% de casos de Tuberculosis en el humano eran atribuibles a *M. bovis*.
- En México un estudio de 2008 reporta aislamiento de *Mb* en 13.8% de pacientes sintomáticos.
- La transmisión de *Mb* del bovino al humano ocurre por el consumo de leche bronca, o por contacto estrecho con animales infectados.

In summary, short-course (3- to 4-month) rifamycin-based treatment regimens are preferred over longer-course (6–9 month) isoniazid monotherapy for treatment of LTBI. These updated guidelines can be used by clinicians, public health officials, policymakers, health care organizations, and other state and local stakeholders who might need to adapt them to fit individual clinical circumstances.



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Review

Mycobacterium bovis at the animal–human interface: A problem, or not?

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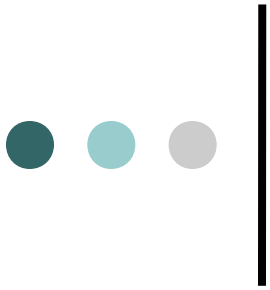
Mycobacterium bovis

Livestock/human interface

Wildlife tuberculosis

ABSTRACT

Mycobacterium bovis is a pathogen of significant importance in livestock and a wide range of wild animal species worldwide. It is also known to cause tuberculosis disease in humans, a fact which has raised renewed concerns regarding the zoonotic risk for humans, especially those living at the animal–human interface. This review consolidates recent reports in the literature mainly on animal and zoonotic tuberculosis with an emphasis on evolution, epidemiology, treatment and diagnosis. The information presented reveals the fundamental differences in the complexity and level at which the disease affects the economy, ecosystem and human population of regions where animal tuberculosis control is achieved and regions where little or no control is implemented. In conclusion the review suggests that bovine tuberculosis has essentially been reduced to a disease of economic importance in the developed world, while low-income countries are facing a multifaceted impact which potentially affects the health of livestock, humans and ecosystems and which is likely to increase in the presence of debilitating diseases such as HIV/AIDS and other factors which negatively affect human livelihoods.

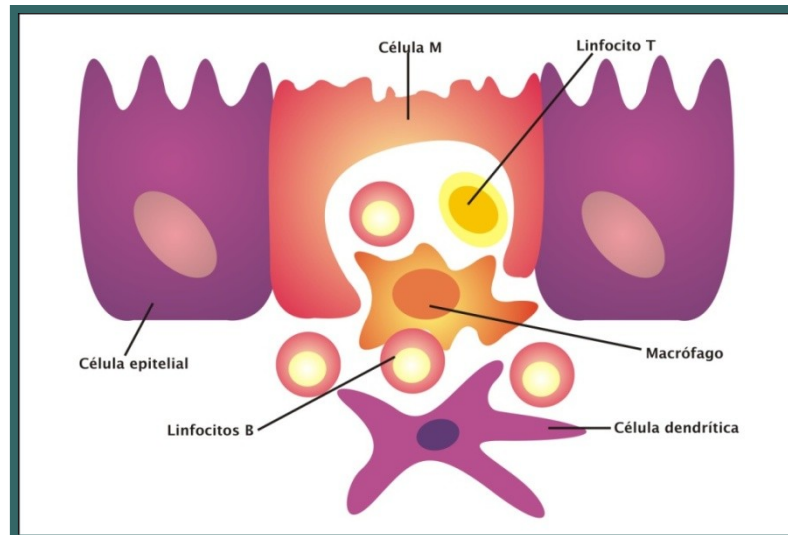


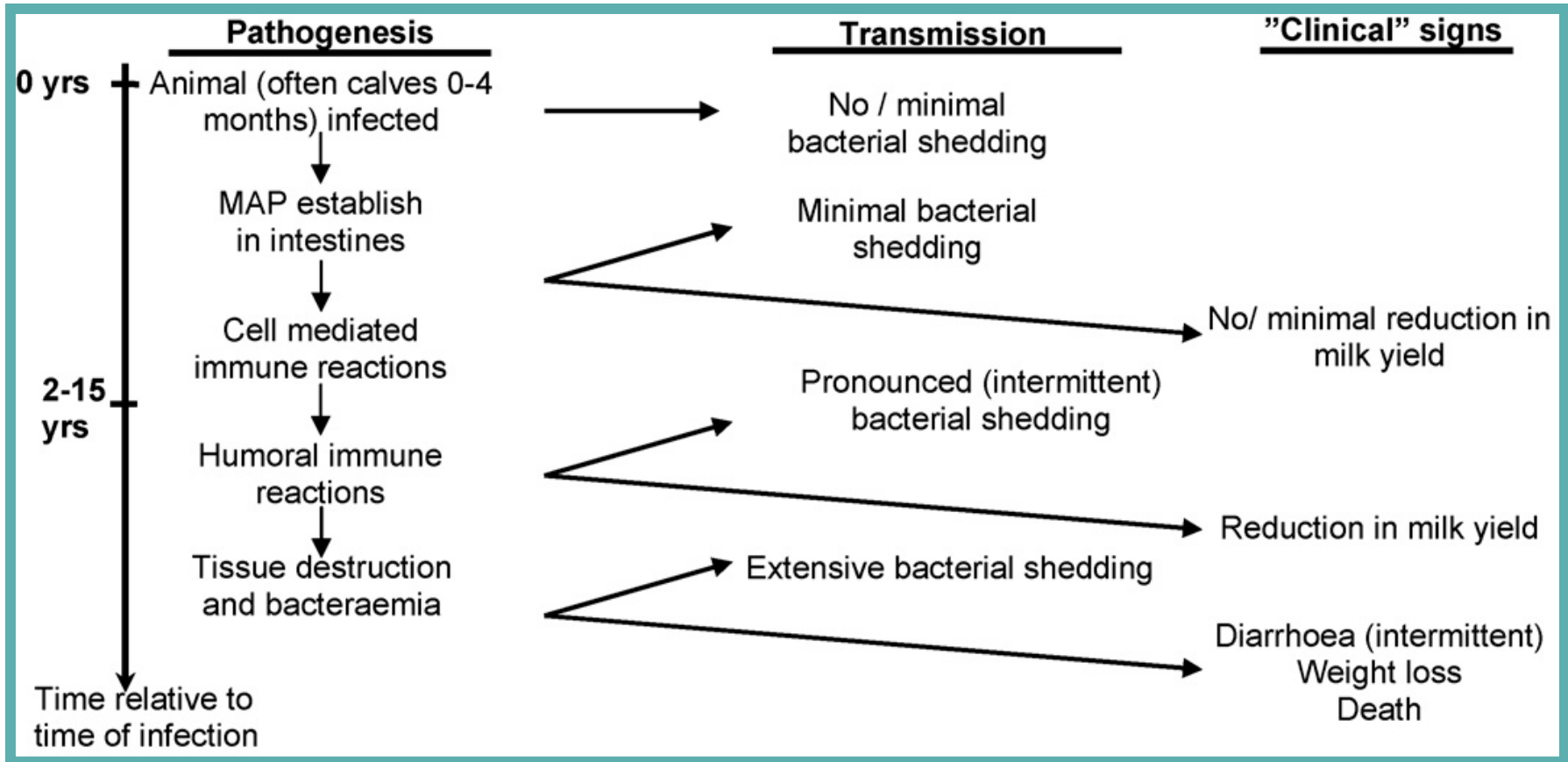
/media/juan/Clases y Ar/Bacter Enero 20/Gram + 2020-2/MYCOBACTERIUM AVIUM sbsp PARATUBERCULOSIS.pdf

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M. avium subespecie *paratuberculosis* (*M. paratuberculosis*)

- Agente etiológico de **Paratuberculosis o Enfermedad de Johne** que se presenta en bovinos, ovinos, caprinos y rumiantes salvajes.
- Los animales usualmente se infectan durante los primeros días o semanas de vidas por ingestión de leche (u otro alimento) contaminado.
- El punto de entrada al organismo es el tejido linfoide del intestino delgado (Placas de Peyer).





M. avium subsp. *paratuberculosis* (*M. paratuberculosis*)

- En bovinos se observa una enteritis crónica, con diarrea severa. La enfermedad es usualmente progresiva, desembocando en emaciación y muerte.
- Es característico el engrosamiento de la mucosa intestinal.
- En ovinos y caprinos no se observa diarrea; el principal signo es la pérdida de peso corporal.

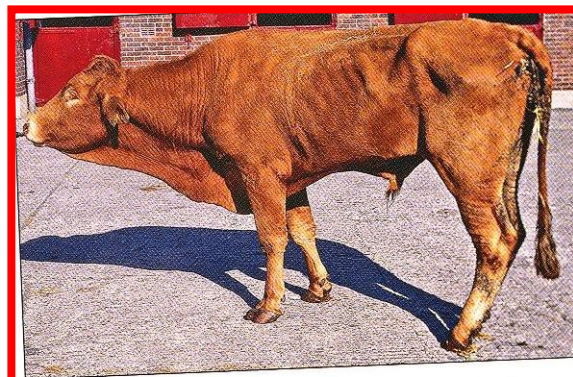
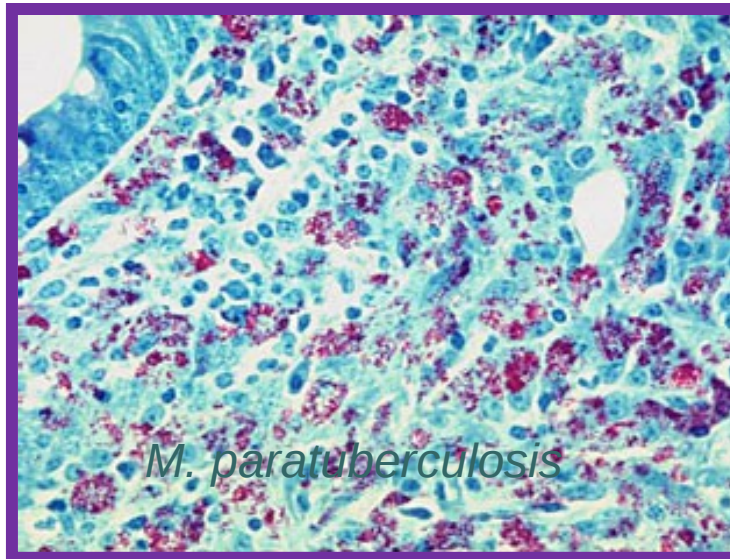


Figure 11.15 A South Devon bull with advanced Johne's disease (*M. avium* subspecies *paratuberculosis*). There is pronounced diarrhoea, emaciation and muscle atrophy.



M. avium subsp. *paratuberculosis* (*M. paratuberculosis*)

- En raspados de mucosa rectal teñidos con la tinción de Ziehl-Neelsen pueden observarse los bacilos.
- El cultivo bacteriológico a partir de las heces (micobactina dependiente) es el estándar de oro; las colonias bacterianas pueden tardar hasta ocho semanas en ser visibles.
- Serología-ELISA (comercial o casera)



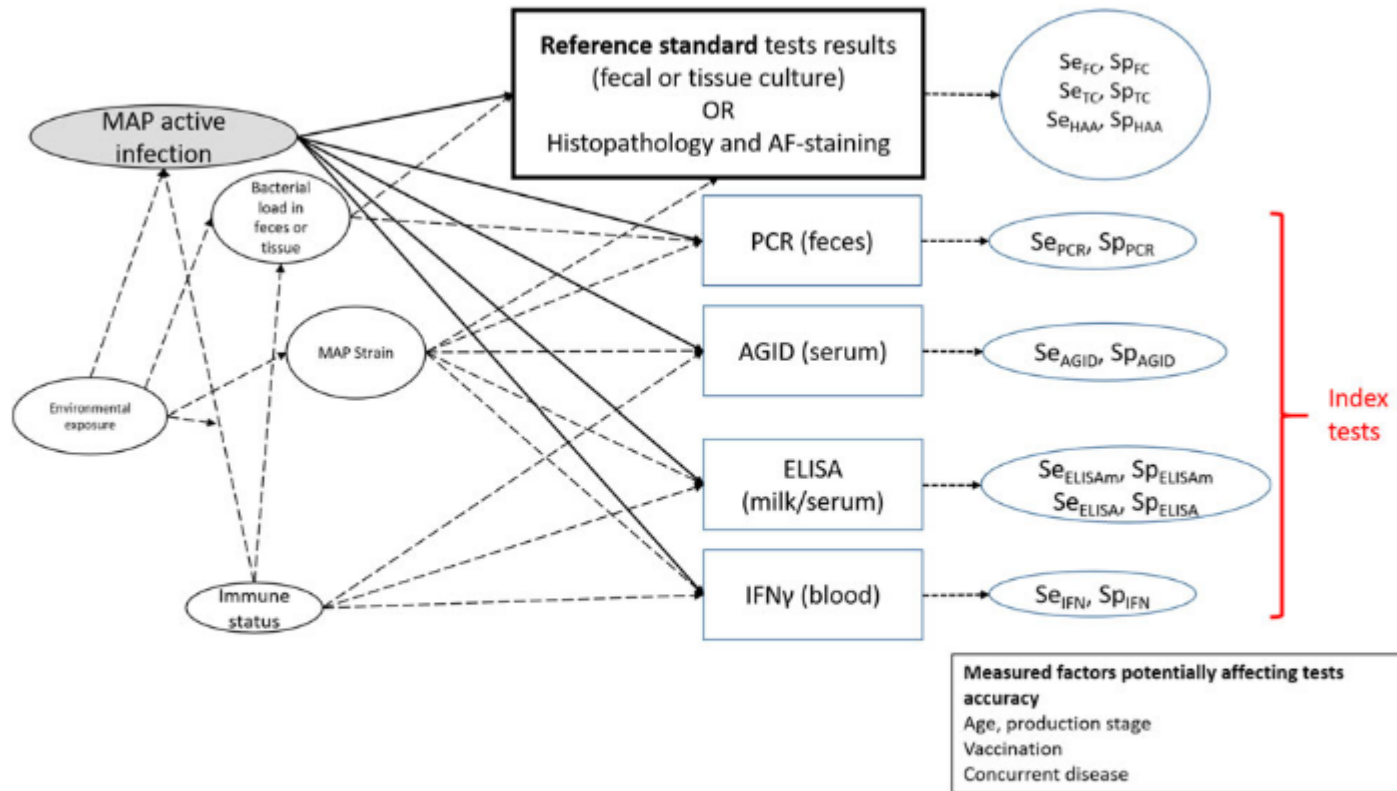


Fig. 1. Model specifying prior beliefs of relations between latent and observed variables for diagnostic test accuracy in small ruminant paratuberculosis. The latent variable in the grey oval is MAP active infection status of the animal. Other latent variables that may impact test accuracy (indicated as dotted lines) are environmental exposure, bacterial load in the feces, or tissue as well as the MAP strain ('C' versus 'S' strain). The immune status of the animal may also interfere with indirect and direct tests. The variables of interest are the index test accuracy (which is determined by the bivariate Se (sensitivity) and Sp (specificity)). The measured covariates that may impact test accuracy are detailed in a specific box. FC, fecal culture; TC, tissue culture; HAA, histopathology and acid-fast staining; Em, ELISA on milk; E, ELISA on serum; AGID, Agar Gelose ImmunoDiffusion; A, AGID on serum; PCR, polymerase chain reaction; IFN, interferon γ .

Table 1:

Sensitivity and specificity of tests available for the identification of *Mycobacterium avium* subspecies *paratuberculosis* infection in cattle

Diagnostic test	Sample	Sensitivity	Specificity
Culture (liquid media)	Faeces	24 per cent using Bayesian latent class analysis (Fosgate and others 2009) 23 per cent (Nielsen and Toft 2008) 25 to 42 per cent compared to findings at slaughter (Whitlock and others 2000)	Assumed to be 100 per cent unless bacteria consumed, excreted and infection not established (Nielsen and Toft 2008) 99 per cent using Bayesian latent class analysis (Fosgate and others 2009)
Culture (solid media)	Faeces	25 to 29 per cent (infected), 74 per cent (infectious) (Nielsen and Toft 2008)	100 per cent unless bacteria consumed, excreted and infection not established (Sweeney and others 1992, Nielsen and Toft 2008)
PCR	Faeces	Limited information available. 100 per cent (1600 colony-forming units [cfu]/g faeces), 60 per cent (160 to 480 cfu/g faeces), 20 per cent (<112 cfu/g faeces) (Collins and others 1993)	100 per cent unless bacteria consumed, excreted and infection not established (Sweeney and others 1992, Nielsen and Toft 2008), and if designed and validated to not identify other species of <i>Mycobacterium</i>
ELISA (healthy animals – screening)	Serum	30 to 32 per cent (Collins and others 2006, Fosgate and others 2009) 7 to 18 per cent (Nielsen and Toft 2008) 67 per cent (IDEXX 2010). These estimates were mainly made compared to animals thought to be positive on clinical examination or shown to be positive on the culture of lymph nodes at slaughter (eg, Sweeney and others 1995)	98 to 99 per cent (Collins and others 2006, Fosgate and others 2009) 91 to 98 per cent (Nielsen and Toft 2008) 99 per cent (IDEXX 2010). 98.9 per cent in animals that had three negative faecal culture results, 99.8 per cent from testing in Western Australia where the disease is not present in certified negative herds (discussed in Whitlock and others 2000)

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Box 1: Essential and discretionary actions relating to the control of Johne's disease that should be detailed in the health plan of herds participating in the CHeCS programme

Essential actions

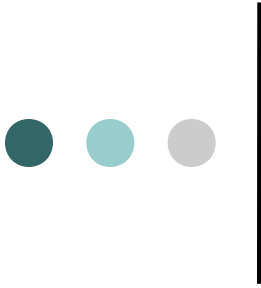
- Annual testing must be carried out in accordance with the CHeCS technical document
- Added animals other than from sources with level 1 status must be tested before entering participating herds. Both blood and faecal testing are required, regardless of age
- All seropositive animals must be separated from young calves, seronegative animals and animals intended for breeding until follow-up testing is carried out
- Blood- and/or faecal-positive animals must be removed from the herd as soon as is practical. While they are retained, they must remain isolated and their faeces must be kept away from other cattle. When a positive animal is retained, the pasture it is held on should not be used for grazing cattle for 12 months. Disposal direct to slaughter is advised
- Any calf at foot of a positive animal must not be retained or sold as a replacement

Discretionary actions

- While Johne's disease can be transferred between adult animals, young calves are considered to be

the most susceptible to infection. Herd-specific instructions should be in place to reduce stock exposure to faecal contamination and this should be focused on the calving period. The calving area and young calf accommodation should be kept as clean as possible

- Ideally there should be a gap of at least 12 months between spreading slurry/ manure on pasture and using it for grazing young calves
- Faecal contamination of feed and water sources should be reduced if possible
- It is advised that mains water is provided for grazing cattle where possible to reduce the potential for faecal contamination
- Non-flowing natural water sources should be fenced off to prevent access, again to reduce the potential for faecal contamination
- Co-grazing with other ruminants is not recommended as they may act as a reservoir of infection
- The last two calves born to a positive female are considered to have a higher risk of being infected than other calves. It is advised that these are not retained for breeding or sold as breeding animals



M. avium subespecie *paratuberculosis*
(*M. paratuberculosis*)

- *M. paratuberculosis* se ha aislado de humanos que padecen Enfermedad de Crohn o Ileitis, enfermedad muy parecida a Paratuberculosis.

M. avium subespecie *avium*

- ❖ Es el agente etiológico de la Tuberculosis en aves domésticas (criadas generalmente al aire libre) y silvestres; los signos clínicos son poco específicos y los granulomas pueden observarse en mo, hígado, bazo, intestino.
- ❖ El diagnóstico *in vivo* puede hacerse inyectando PPD aviar en las barbillas; alternativamente se haría postmortem buscando lesiones granulomatosas.
- ❖ Puede infectar a cerdos alimentados con alimento contaminado; la infección suele no manifestarse clínicamente, y se restringe a lesiones granulomatosas en los ganglios linfáticos.
- ❖ Se ha aislado de pacientes con SIDA.



7. Bone lesion in *Mycobacterium avium*-infected chicken. (Raymor



FIGURE 11-6 Positive skin test in a *Mycobacterium avium*-infected pig. (Courtesy J. Glenn Songer.)



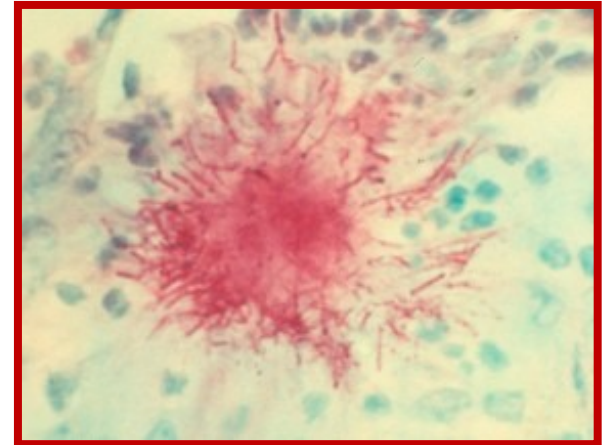
M. lepraemurium

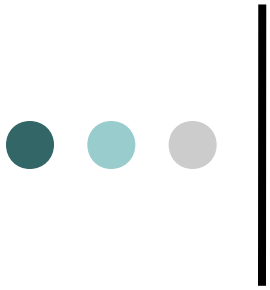
- ❖ Es el agente etiológico de Lepra en las ratas.
- ❖ Los gatos se infectan a través de éstos roedores.
- ❖ La Lepra Felina es una infección cutánea caracterizada por lesiones granulomatosas o ulcerativas (algunas no producen dolor).
- ❖ Las lesiones pueden removerse quirúrgicamente.



Nocardia

Dominio: *Bacteria*
Phylum: *Actinobacteria*
Clase: *Actinobacteria*
Orden: *Actinomycetales*
Familia: *Nocardiaceae*
Género: *Nocardia*



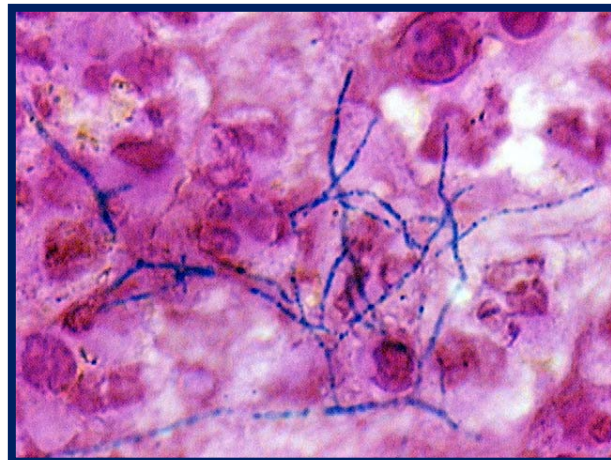


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Nocardia

- Son bastones débilmente ácido-alcohol resistentes; aerobios, inmóviles.
- En frotis de exudados de animales infectados se observan formaciones filamentosas.
- *N. asteroides* es la principal especie patógena para las especies domésticas. Se le encuentra ampliamente diseminada en el medio ambiente (suelo).
- *In vivo* se comporta como facultativo intracelular.



N. asteroides

- Nocardiosis es una enfermedad crónica progresiva, caracterizada por lesiones granulomatosas.
- La infección se adquiere por inhalación o infección de heridas.
- Las lesiones pueden ser localizadas (en la piel) o sistémicas.
 - 1) Bovinos: Mastitis crónica granulomatosa.
 - 2) Equinos: Nocardiosis respiratoria o sistémica.
 - 3) Perros: Piel y ganglios linfáticos superficiales; o presentación sistémica.
 - 4) Gatos: Piel y ganglios linfáticos superficiales.





Cuestionario Capítulo 13

1. Que quiere decir la frase “ácido-alcohol-resistente”.
2. A que se le llama “patógeno facultativo intracelular”.
3. ¿Las bacterias del género *Mycobacterium* son Gram positivas?
Si/No (explica tu respuesta).
4. Qué es un granuloma (investigar).
5. Diapositivas 11 y 12: ¿Por qué es efectiva la inmunidad celular en la defensa contra *M. bovis*? (investigar)
6. Que ventajas representa la prueba de tuberculina comparativa con respecto a la prueba de tuberculina simple.
7. Diapositiva 17: ¿qué nos dice este dibujo?
8. Diapositiva 27: Haz una versión en español de esta diapositiva.
9. Diapositiva 29: ¿qué significa la frase “estándar de oro”?