Microbiology summary

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- *1.Villi covered by enterocytes (Intestinal epithelial cells IECs)*
- *2.Crypts of Lieberkuhn that shield stem cells: give rise to all the IEC lineages , and include*
- *mucus-producing goblet cell and*
- *Paneth cells: secrete antimicrobial molecules & lysosomes*
- *3.Peyer's patches*
- *4.Microfold (M) cells : allow luminal contents to pass through and encounter antigen presenting cells (APCs) below & engulf microbes & have discontinuous BM & initiate immune response*
- *5.Intraepithelial lymphocytes (IELs) include T cells 90% & 80% CD8*
- *6. other immune cells(macrophages and dendritic cells)*

- *The mucosal immune system comprises the internal body surfaces*
- *that are lined by a mucus-secreting epithelium— they are:*
- *1. the gastrointestinal tract.*
- *2. the upper and lower respiratory tract.*
- *3. the urogenital tract, and the middle ear.*
- *4. It also includes the exocrine glands associated with these organs, such as the conjunctivae.and lacrimal glandsofthe eye, the salivary glands,and the lactating breast*

- *The (GALT) include:*
- *the tonsils, appendix, Peyer's patches and isolated follicle*

- *Mucus functions:*
- *Mucus holds the IgA (which is predominant in the GI tract) at the epithelial surface of the gut*
- *trapped molecules*
- *Uptake and transport of antigen by M cells*

- *Nature of IgA :*
- *1. Monomer (in the blood)*
- *2. Dimer or polymers (in mucosal secretions)*
- *the two monomers are linked by J chains*

- *Because M cells lack a glycocalyx and so are much more accessible than enterocytes.*

- *Microbiota*

- *On body surface, not inside (blood, deep sterile tissue)*
- *However, bacterial density increases in the distal small intestine, and in the large intestine rises to an estimated 10^11–10^12*

- *What can influence micrbiota:*
- *Environment : (way of birth!)*
- *Nutrition*
- *Hormones*
- *Genetic constitution*
- *Antibiotics*
- *Foreign objects*

- *Bifidobacterium Spp. Are the primary faeces inhabitants shortly after birth.*
- *As child shifts from mother's milk to solid foodthe microbiota shifts to a more mix population – other anaerobic bacteria Cl.difficil spp.*

- *What microbiota do for us:*
- *Stimulate and enhance host defenses*
- *Nutritional benefits*
- *Microbial antagonism*

- *Microbiota and disease 1*
- *Obesity*
- *Increased proportion of Firmicutes*
- *Related to ability of microbiota to harness energy from food?*

- *Inflammatory Bowel Diseases IBD*
- *Microbial community imbalances*
- *increased Proteobacter, depleted Firmicutes and Bacteroidetes*

- *Microbiota and disease 2*
- *Type I Diabetes*
- *Interaction of intestinal microbes with innate immune system*
- *GI Cancers*
- *H. pylori*
- *Association of various species with colorectal cancer*

- *Oral diseases*
- *Cavities and gingivitis disease*
- *Most common infectious disease worldwide*

- *Microbiota and disease 3*

- *Allergy-like (atopic) diseases*
- *Eczema, allergies, asthma*
- *Hygiene hypothesis*
- *Induction of tolerance (early exposure)*
- *Antibiotic treatment, C section increase rates of asthma*

- *Pseudomembranous colitis*
- *Follows antibiotic treatment (which alters gut microbiota) Caused by*
- *Clostridium difficile*
- *Fecal transplants shown to improve outcome*

- *Microbiota and the immune system*

- *Recently realized microbiota plays a key role in immune system development*

- *Germ free (microbiota free) animals have poorly developed immune system .*
- *Activation of Toll-like rececptors(TLRs) needed for development .*
- *Segmented Filamentous Bacteria (SFB) are needed for Th17 cells .*
- *Critical T cell lineage.*
- *Germ free mice lack Th17 cells.*
- *Antibiotics affect Th17 levels.*
- *Very recently shown that Treg cells affected by microbiota.*

- *To manipulate Microbiota 1*
- *Probiotics*
- *Live bacteria such as Lactobacilli consumed orally Some protective benefits*

- *Prebiotics*
- *Sugars and other foodstuffs used to alter microbiota*

- *Immunemodulators*
- *Inflammation affects microbiota*

- *Antibiotics*
- *Would increase resistance*

- *To manipulate Microbiota 2*

- *Phage therapy*
- *Target specific population (resistance rapidly)*

- *Fecal transplants*
- *Used in C. difficile infections*
- *May need to deplete current microbiota*

- *Use microbiota products*

- *A bacterial polysaccharide from Bacteroides fragilis affects T cell population and Th1/Th2 balance*

Lecture 2

	Bacillus cereus	Bacillus anthrax
Structure under microscope	Square ends. Spores are usually in the middle of the bacillus	Colony morphology. The colonies of bacillus anthracis are large and dry. They are called medusa-head (important)
Based on hemolysis	Cereus produces hemolysis	No hemolysis
Motility	Motile	Not motile
Production of lecithinase	Strong lecithinase activity	Absent
Antimicrobial susceptibility (penicillin and cephalosporins)	Not susceptible (Even though it's considered usually weaker than anthrax)	Susceptible

	Vomiting type	Diarrheal type
Chief complaint	Vomiting and abdominal cramps with NO diarrhea	Diarrhea and abdominal cramps with NO vomiting
What is found in food ingested	An already preformed toxin*[1]	Contains bacillus cereus*[4]
Incubation period*[2]	Short (usually half an hour or one hour)	Longer (6 hours+)
Toxin usually associated	Heat stable enterotoxin called **cerulide (can survive flash frying*[3])**	heat-labile toxin
Food usually associated	Always associated with food like rice and cereal (Chinese food)	Meat dishes and sauces

- *Clostridium Species*
- *Clostridium tetani -tetanus, Rigid paralysis.*
- *Clostridium botulinum-botulism, flaccid paralysis.*
- *Clostridium perfringens-gas gangrene and food poisoning.*
- *Clostridium difficile -pseudomembranous colitis.*

- *Characteristic:*
- *1. All are motile with EXCEPT of C.perfringens.*
- *2. All are Anaerobic.*
- *3. All are Gram positive bacteria.*

▸ *C.botulinum*

- *Botulism is characterized by symmetrical, descending, flaccid paralysis of motor and autonomic nerves usually beginning with cranial nerves (Blocks release of acetylcholine at the myo-neuronal junction resulting in a reversible flaccid paralysis)*

- *it is found in the soil, it may contaminate vegetables.*

- *Offennders: spiced, smoked, vacuum packed, or canned alkaline foods that are eaten without cooking.*

- *Botulinum toxin:*
- *Highly toxic neurotoxin-Coded for by a prophage-Seven*
- *Serotypes (A-G) based on the antigenicity of the botulinum toxin produced.*
- *Most common cause illness in humans are A,B,E while G didn't.*

- *There are five clinical categories of botulism*
- *1. Foodborne botulism. (with an already toxin & it's the most common)*
- *2. Wound botulism. (Most common by bite)*
- *3. Infant botulism. (most common vehicle is honey)*
- *4. Adult infectious botulism.*
- *5. Inadvertent, following botulinum IM toxin injection.*

- *the earliest neurologic symptoms: Dry mouth ,blurred vision, and diplopia.*
- *In infants signs of paralysis (floppy baby).*
- *In severe cases, cause respiratory muscle paralysis.*
- *Mouse bioassay, a lethal assay, is the gold standard for C.botulinum.*
- *Dx: PCR or ELISA*

▸ *C. Perfrigens*

- *An Invasive clostridium that rarely form spores.*
- *Characteristics:*
- *non-motile ,"stormy fermentation" in milk media*
- *Double zone of hemolysis (alpha and beta)*
- *Reservoir : soil and human colon*
- *Transmission: foodborne and traumatic implantation*
- *Enterotoxins secreted by C.perfringens are two types:*
- ➢ *Type A → classical food poisoning*
- ➢ *Type C → Necrotising enterocilitis (pigbel disease)*
- *Dx by neglar test.*

C. Difficle

- *A major cause of healthcare-associated infection; patients taking antibiotics, e.g.cephalosporins, clindamycin are at increased risk of developing C. difficile antibiotic associated diarrhea.*
- *➢Produces two major toxins:*
- *Toxin A (enterotoxin).➢induces cytokine production with hypersecretion of fluid.*
- *Toxin B (cytotoxin).➢ induces depolymerisation of actin with loss of cytoskeleton*
- *Diseases:*

1. *Antibiotic associated diarrhoea, Mild to moderate.*
2. *Pseudomembranous colitis (PMC), fulminant colitis, Severe forms.*

- *Dx: diarrhea with no cause , toxin A or B detected in the stool, pseudomembranes seen in the colon.*

Lecture 3

- *Enterobacteriaceae*

- *Features shared by all:*
- *All are Gram negative rods*
- *Either Motile with peritrichous flagella(most) or Non-motile such as shigella, klebseilla, and yerisenia*
- *All are Facultative anaerobes*
- *All ferment glucose , some are lactose ferment such as E.coli*
- *Reduce nitrates to nitrite*
- *All are Oxidase -ve with Excpet of plesimonas, aeromonas*
- *All are Catlase +ve*
- *Grow well on macConkey, EMB*
- *Many of them produce colicin which inhibit growth of similar Bacteria*

- *Virulence factores:*
- *➢ Endotoxin (LPs) which is O antigen*
- *➢ Capsular which is heat labile K antigen,In s.typhi the capsular antigen is VI which is resistant to serum killing*
- *➢ flagellar which is H antigen*

- *E.coli:*
- *Cause endogenous infection such as UTI.*
- *Cause exogenous infection such as meningitis, gastroenteritis..etc.*
- *Give green colonies on EMB*

- *EPEC*
- *major cause of infantile diarrhea associated with outbreaks of diarrhea in nurseries.*
- *Require two main factors:*
- *➢ Attachement: EAF which encode the bundle forming pilus to attach colon mucosa through plasmid*
- *➢Effacement: LEE which cause loss of microvilli causing explosive diarrhea.*
- *Diarrhea type: watery diarrhea*
- *Treatment: antibiotic treatment*

- *ETEC*
- *Common cause of diarrhea Travelers & in infants in developing countries.*
- *Pathogenicity started through CAF in humans to promote adherence of ETEC epithelial cells of small bowel.*
- *has two toxins:*
- ➢ *heat stable: promote cGMP*
- ➢ *heat labile: promote cAMP*
- *Diarrhea type: watery diarrhea*
- *Prevention: ingestion of Bismuth subalicylate suspension*

- *STEC/EHEC*
- *Offenders: undercooked ground beef (hamburgers),consumption of fresh products such as lettuce, Spanich, sprouts.*
- *Has 2 toxins affecting 60s ribosomal disruption which is*
- *1. SHIGA-like toxin 1*
- *2. SHIGA-like toxin 2*
- *Associated with hemorrhagic colitis.*
- *Have specific antigen called O157:H7 Cause HUS*
- *H: for hemolytic anemia*
- *U: for renal failure*
- *S. For thrombocytopenia*
- *Cause bloody diarrhea without NO fever which is Lead to IBD*
- *Antibiotics are contraindicated cuz we will have risk of HUS*
- *Dx: EIAs*

- *EIEC*
- *Produce illness by invasion of intestinal epithelial cells.*
- *Cause bloody diarrhea with Fever.*
- *Similar to shigella/ Non motile, Non lactose fermenter (late).*
- *Unlike shigella/ require large inoculum CFU*

- *EAEC*
- *cause acute & chronic diarrhea associated also with travelers, in patients with HIV infection*
- *The reasons for its name is: it's appear like Stacked-brick.*
- *Has 3 toxins:*
- ➢ *Shiga toxin like toxin (EAST)*
- ➢ *hemolysin*
- ➢ *enterotoxin*
- *Diarrhea type: watery diarrhea*
- *Treatment: multiple therapy such as sulfonamides, ampicillin,& Aminoglycosides.*

- *shigella*

- *Produce bacillary desentery.*
- *Facultative anaerobes but grow bestly aerobic*
- *All fermnter glucose with excpet of s.sonnie*
- *Non motile, do not produce H2s, produce colorless on EMB*
- *At any age but primarily children, occur in warm weather, rainy seasons*
- *most common in industrial area 1. S.sonnie 2. S. Flexes*
- *Transmission: feco oral, PTP, contaminated food*
- *NOTE: Low number are required to cause disease*
- *Highly communicable, but limited to Gi tract*
- *Pathogensis: invasion of mucosal epithelial cells e.g M cells*
- *Complications: Ulcer& PMC. Has 2 toxins:*
- *➢ endotoxin which contribute to irritation of bowel*
- *➢ exotoxin HT(shigella desentery) type1, which is neurotoxic, cytotoxic and entrotoxin*

- *After a short incubation period (1–2 days), there is a sudden onset of abdominal pain, fever, and watery diarrhea. The diarrhea has been attributed to an exotoxin (shiga toxin) acting in the small intestine. A day or so later, as the infection involves the ileum and colon (invasion starts), the number of stools increases; they are less liquid but often contain mucus and blood (bloody diarrhea).*

- *Etiology Group*
- *Group A shigella desenteriae ➢ most severe AND most potent producer of shiga toxin.*
- *Group B shigella flexeri ➢ mild severity & most common among developing countries.*
- *Group C shigella boyodiii.*
- *Group D shigella sonnei ➢ intermediate severity disease, most common among developed countries.*

Lecture 4

- *Salmonella*

- *from animal or animal products to humans where cause gastroenteritis, systemic infections, eneteric fever.*
- *It's motile with perictrichous flagella, glucose fermenter, produce h2s.*
- *Can survive in freezing water for long periods, and it's resistant to certain Chemicals.*
- *1. S. Typhi and S. Paratyphi are the causative agents of typhoid fever.*
- *2. S. Enteritidis and S. Typhimurium are most commonly isolated and they cause gastroenteritis/ enterocolitis.*
- *3. S. Cholerasuis cause bacteremia and focal lesions, they are the most common cause of osteomyelitis in sicklers.*
- *4. S. Dublin in children.*
- *Most common manifestation & chief copmlement is enterocolitis.*
- *Note: Blood cultures in typhoid/enteric fever are positive in week one, following that in week two stool cultures become positive, but enterocolitis, the stools yield positive results during the first week.*

- *Typhoid fever is systemic disease presented with*
- *➢ febrile illness (fever)*
- *➢ GI manifestation*
- *Humans are natural reservoir, cuz salmonella apis strictly to human pathogen.*
- *Chronic carrier often harbor the pathogen in their gallbladder.*
- *Symptoms: rose spots , rash in 2nd week / Intestinal hemorrhage, perforation in 3rd week.*
- *Also Bacteremia with focal lesions associated mainly with s.cholerasuis, but any type also can cause them.*
- *Typhoid salmonella modes of transmission:*
- *➢ food, water contamination with feaces so (feco-oral)*
- *➢ vertical transmission*
- *Dx: widal test*
- *Treatment: ampicillin, cholecystectomy*
- *(sickle cell trait) may be more susceptible than normal individuals (those with A/A hemoglobin).*
- *Note: Large dose required to cause disease*

- *Yerisenia*

- *It's motile at 25C, but Non motile at 37C.*
- *It's zoonotic*
- *Y.enterocolitica is associated with terminal ileitis*
- *Y.pseudotuberculosis with mesenteric adenitis,*
- *both organisms may cause mesenteric adenitis and symptoms of abdominal pain and tenderness that result in pseudoappendicitis.*

- *Consumption or preparation of raw meat , products milk (pasteurized, unpasteurized, and chocolate-flavored) and various foods (oral)contaminated with spring water products are linked with infection.*

- *initial replication in the small intestine is followed by invasion of Peyer's patches of the distal ileum via M cells, with onward spread to mesenteric lymph nodes.*
- *Virulence factors:*
- *Yeresinia outer membrane proteins (yomps)*
- *They have type III secretion*
- *pathogenicity island (PAI)*

- *Self-limiting diarrhea is the most common reported presentation in infection with pathogenic Y. enterocolitica*

- *yersinia infection is one of those infections which have a post infectious sequelae which is called REITER SYNDROM*

- *Dx: CIN agar*

- *Common sign: bull's eye appearance*

Lecture 5

The vibrio gram negative bacteria

- *Most common bacteria in water surface worldwide*
- *Serogroups:*
- ➢ ***O1 cause 6th pandemic, don't have capsule***
- ➢ ***O139 cause 7th pandemic, have capsule***
- *V. parahaemolyticus ➢ the most common cause of Sea-foodborne (raw fish or shellfish) gastroenteritisin Asia*
- *V. vulnificus ➢ cause of severe sepsis(septicemia) in patients with cirrhosis and primary wound infection (Vulnificusis Latin for "wound maker.")*
- *V. alginolyticus occasionally ➢cause eye, ear, and wound infections.*

- *It's comma shaped, motile by polar flagella, grow ate high ph, killed by acid.*
- *Need high dose to cause infection*
- *Grow well on TCBS, give yellow colonies*
- *has ability to ferment sucrose*
- *It's oxidase positive*

- *Vibrio species are sensitive to O/129*
- *These is an:*
- *halotolerant ➢ need certain conc of NACl to stimulate their growth*
- *halophillic ➢ require presence of NACl to grow*

- *V. cholera enterotoxin (it's important to attach mucosa)*
- *Has 2 subunit:*
- *➢ subunit A: increase cAMP chase dramatic diarrhea*
- *➢ subunit b: has a ganglion GM1 receptor on mucosal in Small intestine, which increases promote entry of subunit A into a cell*
- *We need TCP to cause the infection.*

- *The genes for V cholerae enterotoxin are on the bacterial chromosome*

- *We find in the stool: rice water appearance with floating mucus*
- *mortality rate without treatment is 50%*
- *50% of infections are asymptomatic*
- *treatment :*
  - *water & electrolytes replacement*
  - *Oral tetracycline and doxycyclin ,in children and pregnant women we replace the tetracycline by erythromycin*

Campylobacter

- *It's motile, Non-spore forming, curved and gram -ve*
- *Cause bloody diarrhea & systemic disease*
- *The most common cause of bacterial gastroenteritis in developed world*
- *Reservoir: in GI tract of animals & housing pets*

- *Other organisms that cause diarrheal disease include Campylobacter coli, Campylobacter lari (mostly isolated from seagulls), Campylobacter upsaliensis (from dogs),Campylobacter hyointestinalis, Campylobacter fetus, Arcobacterbutzleri, Arcobacter cryaerophilus,Helicobactercinaedi, and Helicobacterfennellia.*

- *Species that cause extraintestinal disease include Campylobacter ➢ fetus and venerealis*

- *Campylobacter Jejuni*
- *Gull wing shaped*
- *Are microaerophillic , best grow at 42 C°*

- *Transmission: oral route*
- *The main pathogenesis is the invasion of the mucous & submucosa of the small intestine (intracellular infection) which will lead to bloody diarrhea (like salmonella & shigella).*
- *C.jejuni have been associated with post-diarrheal Guillain-Barré syndrome.*
- *Culture on the selective media agar (Skirrow's, Butzler's, Blaser's, Campy-BAP and Preston media).*

- *H.pylori*

- *H.pylori is a curved or spiral-shaped gram-negative rod/bacilli*
- *It has multiple flagella at one pole and is actively motile.*
- *most notably a highly expressed urease that catalyzes urea to produce ammonia*
- *microaerophilic*

- *Humans are the only important reservoir of H. pylori.*
- *Children may acquire the organism from their parents.*
- *The transmission is believed to be feco-oral*
- *Diagnosis: Urea breath test+stool antigen test*

- *Treatment: Triple therapy combination of a proton pump inhibitor (e.g., omeprazole), a macrolide (e.g., clarithromycin), and a β-lactam (e.g.,amoxicillin)*

Lecture 6

The BRUCELLAE

- *Brucella is a non-spore forming, gram negative, non-motile, unencapsulated obligate intracellular.*
- *They are relatively inactive metabolically. Brucella melitensis typically infects goats; Brucella suis, swine; Brucella abortus, cattle; and Brucella canis, dogs. Other species are found only in animals.*

- *Brucella melitensis is the most pathogenic one, responsible for most clinical cases. Mainly transmitted from goats, sheep or camels.*
- *It is a very infectious zoonotic disease.*

- *The disease in humans, brucellosis (undulant fever, Malta fever), is characterized by an acute bacteremic phase followed by a chronic stage.*

- *The Only one Microderophilic: B.abortus*

- *They are killed by boiling and pasteurization but are resistant to freezing and drying*
- *The common sources of infection for humans are unpasteurized milk*
- *modes of transmission:*
- *1. ingestion inhalation*
- *2. mucosal*
- *3. percutaneous exposure*
- *Main target of this pathogen: RES ➢ spleen+liver+BM*
- *Osteomyelitis, meningitis, or cholecystitis also occasionally occurs.*
- *The main histologic reaction in brucellosis consists of proliferation of mononuclear cells, exudation of fibrin, coagulation necrosis, and fibrosis.*
- *The granulomas form and consist of epithelioid and giant cells, with central necrosis and peripheral fibrosis.*

Clinical Findings

- *Acute presentation of Brucellosis:*
- *The incubation period ranges from 1-4 weeks. The onset is insidious, with malaise, fever, undulant in nature which may be associated with profuse sweats, weakness, aches,.*
- *The fever usually rises in the afternoon; its fall during the night is accompanied by drenching sweat, associated with musculoskeletal symptoms.*
- *There may be gastrointestinal and nervous symptoms. Lymph nodes enlarge, and the spleen becomes palpable. Hepatitis may be accompanied by jaundice.*

- *After the initial infection, a chronic stage may develop, characterized by weakness, aches and pains, low-grade fever, nervousness.*

- *Selective culture for Brucella ➢ Brucella agar.*
- *Type of colony ➢ smooth, transparent colony.*
- *Cattle are examined by means of agglutination tests (Since they are the most common route of transmission).*

▸ *Leptospira*

- *Leptospira is motile and grows best under aerobic conditions*
- *Skin exposure is the most common route, followed by mucosal and rarely ingestion*
- *the genus Leptospira comprised two species:*
- *➢the pathogenic L. interrogans*
- *➢the free-living L. biflexa*
- *Leptospirosis; The disease is caused by pathogenic Leptospira, Human urine also may contain spirochetes in the second and third weeks of disease.*
- *Most cases are asymptomatic, some are mild, and around 1% can be severe which can lead to Weil's Syndrome.*
- *Weil's Syndrome is characterized by bleeding, blood urea nitrogen retention*
- *most commonly in the tropics and subtropics because the climate and occasionally poor hygienic conditions*

- *They then establish themselves in the parenchymatous organs (particularly liver and kidneys), producing hemorrhage and necrosis of tissue and resulting in dysfunction of those organs (jaundice, hemorrhage, nitrogen retention), Most common is hemorrhage is*
- *pulmonary hemorrhage.*

- *The diagnosis of leptospirosis in most cases is confirmed serologically with microscopic agglutination test (MAT) and ELISA.*
- *Dx by Giemsa technique.*

▸ *Mycobacterium tuberculosis*

- *Mtb is a slow growing, obligate aerobe, facultative intra- cellular bacterium.*
- *Non-spore forming, non-motile acid fast bacilli.*

- *The family mycobacterium tuberculosis complex(MTC) can cause Tuberculosis mainly the pulmonary.*

- *It includes M. tuberculosis (Mb), Mycobacterium africanum, Mycobacterium bovis, Mycobacterium microti, Mycobacterium caprae, Mycobacterium pinnipedii, Mycobacterium suricate, Mycobacterium mungi, Mycobacterium dassie, Mycobacterium oryx and Mycobacterium Canetti.*

- *M.Bovis was responsible for 6 % of tuberculosis cases before the introduction of milk pasteurization and development of BCG vaccine*

- *Mycobacterium Tuberculosis (Mtb) Staining: Acid-Fast Bacteria- Ziehl- Neelsen Stain*

- *TB is considered an airborne infectious disease although M. tuberculosis complex organisms can be spread through un-pasteurized milk, direct inoculation and other means.*

- *The primary site of TB is usually lung* 🫁
- *The abdominal TB usually occurs in four forms: tuberculous lymphadenopathy, peritoneal tuberculosis, gastrointestinal (GI) tuberculosis and visceral tuberculosis involving the solid organs*

- *palpable mass in the abdomen are common findings at presentation , Fever, weight loss, anorexia, and night sweats are also common.*

- *Dx: (Lowenstein-Jensen or Middlebrook 7H10), Radiometric broth culture (BACTEC radiometric system). mycobacterial growth indicator tube (MGIT).*
- **A nucleic acid amplification test (NAAT), Tuberculin skin tests (TSTs), Interferon-gamma release assays (IGRAs) are commonly used.*

- *Mycobacterium bovis Bacillus Calmette-Guérin (BCG), an attenuated vaccine derived from M. bovis, is the only licensed vaccine against tuberculosis (TB).*

The END