

The Agents

HHS SELECT AGENTS AND TOXINS

Abrin
 Botulinum neurotoxins
 Botulinum neurotoxin producing species of *Clostridium*
 Cercarial dermatitis
 Cercarial dermatitis (Herpes B virus)
Clostridium perfringens epsilon toxin
Coccidioides posadasii/Coccidioides immitis
 Conotoxins
Coxiella burnetii
 Crimean-Congo haemorrhagic fever virus
 Diacetoxyscirpenol
 Eastern Equine Encephalitis virus
 Ebola virus
Francisella tularensis
 Lassa fever virus
 Marburg virus
 Monkeypox virus
 Reconstructed replication competent forms of the 1918
 pandemic influenza virus containing any portion of the
 coding regions of all eight gene segments (Reconstructed
 1918 influenza virus)
 Ricin
Rickettsia prowazekii
Rickettsia rickettsii
 Saxitoxin
 Shiga-like ribosome inactivating proteins
 Shigatoxin
 South American Haemorrhagic Fever viruses
 Flexal
 Guanarito
 Junin
 Machupo
 Sabia
 Staphylococcal enterotoxins
 T-2 toxin
 Tetradotoxin
 Tick-borne encephalitis complex (flaviviruses)
 Central European Tick-borne encephalitis
 Far Eastern Tick-borne encephalitis
 Kyasanur Forest disease
 Omsk Hemorrhagic Fever
 Russian Spring and Summer encephalitis
 Variola major virus (Smallpox virus)
 Variola minor virus (Alastrim)
Yersinia pestis

OVERLAP SELECT AGENTS AND TOXINS

Bacillus anthracis
Brucella abortus
Brucella melitensis
Brucella suis
Burkholderia mallei (formerly *Pseudomonas mallei*)
Burkholderia pseudomallei (formerly *Pseudomonas*
pseudomallei)
 Hendra virus
 Nipah virus
 Rift Valley fever virus
 Venezuelan Equine Encephalitis virus

USDA VETERINARY SERVICES (VS) SELECT AGENTS

African horse sickness virus
 African swine fever virus
 Akabane virus
 Avian influenza virus (highly pathogenic)
 Blue tongue virus (exotic)
 Bovine spongiform encephalopathy agent
 Camel pox virus
 Classical swine fever virus
Ehrlichia ruminantium (Heartwater)
 Foot-and-mouth disease virus
 Goat pox virus
 Japanese encephalitis virus
 Lumpy skin disease virus
 Malignant catarrhal fever virus
 (Alcelaphine herpesvirus type 1)
 Menangle virus
Mycoplasma capricolum subspecies *capripneumoniae*
 (contagious caprine pleuropneumonia)
Mycoplasma mycoides subspecies *mycoides* small
 colony (*MmmSC*) (contagious bovine pleuropneumonia)
 Peste des petits ruminants virus
 Rinderpest virus
 Sheep pox virus
 Swine vesicular disease virus
 Vesicular stomatitis virus (exotic); Indiana subtypes
 VSV-IN2, VSV-IN3
 Virulent Newcastle disease virus¹

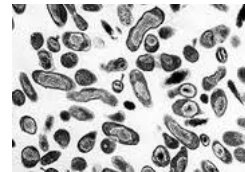
USDA PLANT PROTECTION AND QUARANTINE (PPQ) SELECT AGENTS

Peronosclerotaria philippinensis (*Peronosclerotaria*
sacchari)
Phoma glycnicola (formerly *Pyrenochaeta glycinis*)
Ralstonia solanacearum race 3, biovar 2
Rathayibacter toxicus
Sclerophthora rayssiae var. *zeae*
Synchytrium endobioticum
Xanthomonas oryzae
Xylella fastidiosa (citrus variegated chlorosis strain)

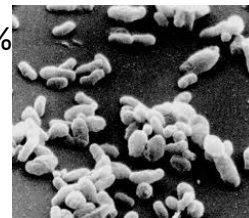
Why these organisms?

- Some cases: high mortality, no treatment, high public panic
- High morbidity, low mortality
- Easily spread from one organism to another
- Includes human, animal and plant pathogens
- Potential to cause large number of infections, economic losses from animal loss or crop loss

Coxiella burnetti

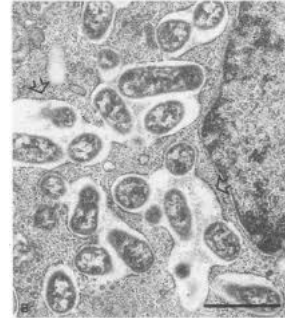


- Q fever
- Obligate intracellular bacterium, pleomorphic Gram negative coccobacillus
- Low infectious dose, resistant to desiccation, disinfectants
- Fever, malaise, endocarditis
- Inhalation, skin contact, sexual transmission
- Acute and chronic infection
 - Acute self limiting, chronic mortality 60%
- Antibiotics effective

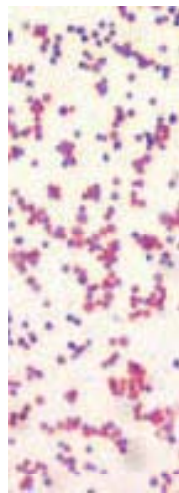


Brucella sp.

- *B. abortus*, *B. melitensis*, *B. suis*
- Gram negative
- Laboratory acquired infections
- Most often occurs due to ingestion of unpasteurized dairy products, handling infected animals
- Acute form: non specific “flu like” symptoms
- Chronic form: chronic fatigue syndrome, depression, arthritis
- Variable incubation period- can be months
- Antibiotics are effective, but must be taken for 6 months



Francisella tularensis



- Tularemia, Rabbit fever, deer fly fever
- Small, aerobic, pleomorphic, non-motile, gram-negative coccobacillus, fastidious
- Small mammals acquire through insect bites and contact with contaminated environment.
- Infectious dose: 10-50 (inoculation/ inhalation), 10^8 (ingestion) , incubation 2-10 days
- No person to person transmission
- Ulceroglandular and pneumonic
- Mortality: with antibiotics 2%, without antibiotics 5-15%, severe disease (pneumonic) 30-60%
- Susceptible to antibiotics: Streptomycin, Gentamicin, Tetracycline, and others

Burkholderia mallei

- Glanders
- Gram negative, bipolar, aerobic
- Most cases in horses, mules, and donkeys
 - Humans infected when handling infected animals
- Incubation period- 1-14 days
- Pulmonary, mucous membrane, farcy
- Untreated mortality-100%, antibiotics are effective
- Person to person transmission unlikely



Foot and Mouth Disease

- FMD is a member of the genus *Aphthovirus*, in the family *picornaviridae*.
- seven, distinct serotypes: O,A,C, SAT-1, SAT-2, SAT-3, and ASIA-1, over 60 strains.
- FMD is characterized by high fever and blisters (vesicles) on the feet and in and around the mouth.
- Spread by inhalation of aerosolized virus, ingestion of contaminated feed, or entry of virus through skin abrasions.



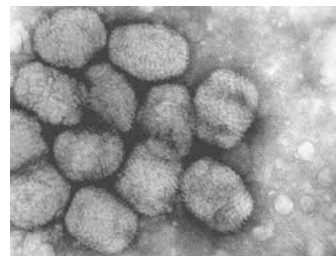
The most susceptible: cattle, swine, sheep, goats, and other farm animals. Cause great economic losses when outbreak occurs. Detrimental for export of meat; FMD present with or without vaccinations, FMD-free with vaccinations, and FMD-Free without vaccinations.

Poxviruses

- Smallpox, Monkeypox, Camel pox, Sheep pox, Goat pox, lumpy skin disease
- Poxviridae
- Different host ranges
- Smallpox- humans only
- ds DNA viruses, enveloped

smallpox

- Human virus
- 30% mortality in untreated victims
- incubation 12 days
- fever, chills, malaise, rigors, vomiting, headache, backache
- initial rash turns to lesions
- good vaccine, also used for treatment
- Transmissible human to human



Smallpox Virus (Variola Major)



Ebola

Filovirus: enveloped, non-segmented, negative stranded ssRNA virus

Linear genome

Fevers, general achiness, fatigue, progress to hemorrhaging

Transmission person to person, through bodily fluids, no evidence of respiratory transmission, except Reston strain

There are 5 subtypes of Ebola virus

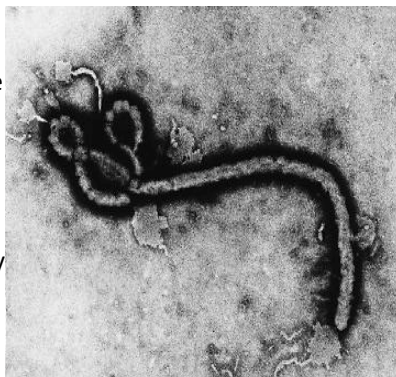
Ebola Zaire: Mortality rate 83%-90% and the most common form.

Ebola Sudan: Mortality rate between 54% and 68%

Ebola Reston: Only seen in non-human primates

Ebola Ivory Coast: Only one known human case in which the person survived.

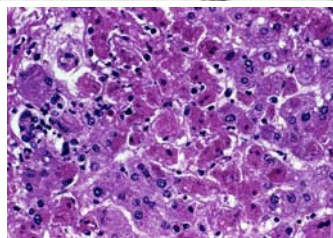
Ebola Bundibugyo: Mortality Rate 34%



Petechiae

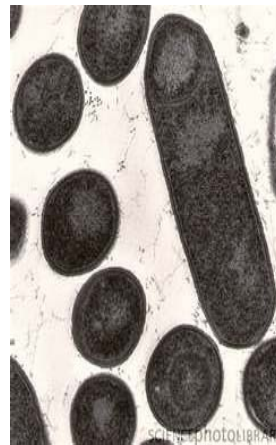
Marburg

- Filovirus: negative stranded ssRNA virus
- Low infectious dose: 1-10 virions
- Transmission not well understood: contact with body fluids, aerosolization not known
- Fever, chills, malaise, progress to hemorrhaging
- Fatality 23-90%, infects humans and nonhuman primates
- Bats are a potential reservoir
- No treatment



Botulinum Toxin

- Toxin produced by *Clostridium botulinum*
 - Anaerobic, Gram positive, spore forming, rod shaped
- 1 ng/kg is lethal
- BoNT is broken down into 7 neurotoxins (labeled as A,B,C,D,E,F, and G.)
- Ingestion, Wound, Inhalation
- Inhalation: 24-72 hr onset
- Symptoms: nausea, vomiting, dry mouth, muscle weakness, drooping eyelids, eventually muscle paralysis
- Antitoxin available



Ricin

- Castor bean plant *Ricinus communis*
- incubation 24-72 hours
- nausea, vomiting, bloody diarrhea, abdominal cramps, breathing difficulty, renal failure, circulatory collapse
- no antitoxin



Staphylococcal Enterotoxin B

- Toxin from *Staphylococcus aureus* bacterium
 - Gram positive coccus
- low concentrations to induce intoxicating symptoms
 - Incapacitating to 50% of humans at 0.0004 $\mu\text{g}/\text{kg}$ and 50% lethal dose was 0.02 $\mu\text{g}/\text{kg}$
- Toxin can be isolated from *S. aureus* culture supernatants
- Can be easily mistaken for accidental contamination
- Delay of onset of symptoms; 2-6 hours- fevers, chills, diarrhea, nausea, vomiting (if ingested), respiratory distress (if inhaled)
- Antibiotic treatment for bacteria, no effective antitoxin

Group Discussion

- If you had to remove a biological agent, which would you remove and why?
- If you had to pick a biological agent to use, which one would you pick and why?
 - If you do not know specifically which one, narrow down to a type:
 - Animal/ Human/ Plant
 - High morbidity/ High mortality
 - Target?