Tuberculosis treatment protocols and complications for elephants

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Mycobacteria tuberculosis complex

- M. tuberculosis (M.tb)
- M. bovis
- M. microti
- M. africanum
- M. kinetti
- M. caprae
- M. pinnipedi
- Any species not in the M. tb complex is not truly tuberculosis.
- Infection from these are classified as mycobacteriosis.
- In people and elephants the most frequently identified tuberculosis causing agent is M. tuberculosis.
Elephant management options

- Isolation
- Euthanasia
- Treatment
Most Effective Therapy

- Prompt diagnosis
- Culture and Sensitivity
- 3-4 first line agents
- Adequate plasma drug levels
- Adequate length of treatment
- Close monitoring of hemogram and organ function.

- Close monitoring of the patient
Routes of administration

- Over the feed – not recommended, poorly accepted, poorly effective
- Directly oral – preferred, best absorption
- Rectally – good alternative to direct oral for some meds
Direct oral

- Deposit in back of throat behind base of tongue
- Use large 400 cc syringe with modified extended tip or stiff tubing.
- Train to take a bite block
Rectally

- Large animal syringe 400cc - multiple
- Flexible tubing
- Suppositories
- Lecithin – may increase absorption, increases volume
Guidelines

- First developed in 1998
- Modified several times to reflect experience and investigational results
First line drugs

- Isoniazid (INH)
- Pyrazinamide (PZA)
- Rifampin (RIF)
- Ethambutol (ETH)
- Streptomycin (STR)
INH

- Peripheral neuropathy
- Optic nerve toxicity
- Nausea, vomiting, anorexia
- *Pica*, epigastric distress
- *Elevated liver enzymes*, hepatitis.
- Agranulocytosis, *anemia*
- Skin eruptions, fever, vasculitis
- Pyridoxine deficiency, Rheumatic syndrome
- Systemic lupus erythematosis-like syndrome
PZA

- Hyperuricemia $\rightarrow$ gouty arthritis
- *Hepatocellular damage, elevated enzymes*
- Nausea, vomiting, *anorexia*
- *Arthralgia, myalgia*
- *Photosensitivity*
- Porphyria, fever
RIF

- Anorexia, nausea, vomiting
- Thrombocytopenia
- Muscle weakness, ataxia, limb pain
- Headaches, visual disturbances
- Elevated BUN and serum uric acid
- Pruritis, urticaria, rash
- Conjunctivitis
ETH

- Optic neuropathy
- Acute renal failure
PZA/Enrofloxacin

- Group of female Asians
- Varying degrees excessive epiphora, blepharitis.
- Some with stiffness/soreness of one or more limbs.
Multi-drug resistance

- MDR TB
- Typically resistance to INH and RIF
- Employ second line drugs for therapy
- Some second line drugs more toxic than first line agents.
Second line drugs

- Amikacín
- Ethionamide
- Quinolones
- Capreomycin
Aminoglycosides

- Amikacin, Capreomycin
- Potential side effects
  - Ototoxicity
  - *Nephrotoxicity*
Ethionamide

- Digestive problems
- Psychotic disturbance
- Dizziness
- Liver problems
- Photosensitivity
- Thrombocytopenia
Quinolones

- Nausea, abdominal pain
- Vomiting, diarrhea
- Dizziness, seizures
- Rash
- Crystalluria
- *Phototoxicity*, tendinopathy
Literature

- Physicians’ Desk Reference, 2006..., 60th ed. Thomson PDR, Montvale, New Jersey 07643-1742, USA


Altered regimen

- Diminishing side effects in elephants
- Withdraw medications 1-2 days a week
- Give double the dose of meds on every other day schedule = Pulse therapy
Success of treatment ------
Not 100%.
Many elephants “apparently” treated successfully to date. (rectal, oral, suppositories)
Some have not had infection successfully eliminated. (based on necropsy findings)
One Asian euthanized due to MDR and drug toxicity.
Other Aspects

- Cost of treatment $50,000 + US
- Labor intensive
- Additional costs: Blood work, serum drug level monitoring, employee time, extra materials, isolation.
- Limitations of drug availability
- Success depends on all animal care staff.
Early Detection

- Cultures take up to 8 weeks for results
  - Additional time for sensitivities
  - Contamination of samples
  - Quality of sample collection
- Serological tests are rapid in comparison
Early detection cont’

- Rapid test – screening test (ElephantTB STAT-PAK® Assay)
- Mutiantigen Print Immunoassay (MAPIA)
- DNA extractions
- Immunologic markers
- Other technology
Resources

Most recently available guidelines
Veterinarians who have experience with this disease in elephants
State Veterinarian
USDA Animal Care/ Elephant Specialist
Infectious disease/ tuberculosis specialists (MD, DVM, VMD)
Thanks to all who contributed information to this effort

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