



TB: Implications for Elephant Management in Asia



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Human TB: “Ebola with Wings”

- 30 million deaths in 10 years
- Two billion infected
- 33% of cases in SE Asia
- Highest mortality in Africa
- 10-15 million in U.S. infected
- MDR-TB a growing concern

In an age when HIV, Ebola virus, cancer, and heart disease command the health news headlines, TB is an often forgotten disease. Yet, worldwide it is one of the leading causes of death from a single infectious agent. One observer has designated TB “Ebola with wings” to depict the ease with which it can spread across the globe.

Thirty million people have died from TB in the last decade (1995-2005). A startling two billion people – one-third of the earth’s population have TB bacilli in their bodies, but the disease tends to remain latent (inactive). About 4-10 percent of those will develop active disease (transmissible to others).

TB is endemic in southeast Asia and 33% of all cases occur in this region. The highest mortality occurs in Africa due to co-infection with HIV and also to a lack of resources for surveillance and drugs for treatment. TB has been reported in every state in the United States - between 10 and 15 million Americans are infected.

Multi-drug resistant TB – defined as resistance to at least INH and rifampin – the two most important anti-TB drugs is a growing concern world-wide.

ELEPHANT CARE INTERNATIONAL

A Global Human Crisis

- The Global Plan to Stop TB
↓ deaths by 50% by 2015
- Stop TB Partnership – www.stoptb.org

**THE GLOBAL PLAN
TO STOP TB
2006 - 2015**

Stop TB Partnership

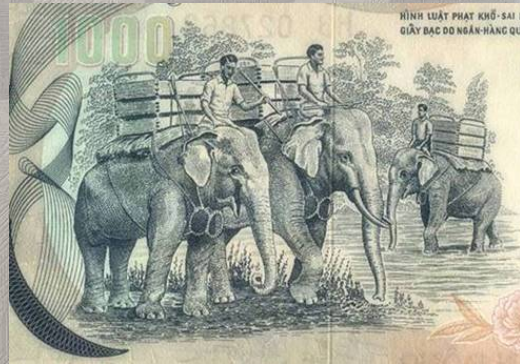
TB has been designated a “global crisis” by the World Health Organization and there is a major initiative underway - The Global Plan to Stop TB which aims to cut TB deaths in half by 2015 compared to 1990 levels (See the Stop TB Partnership www.stoptb.org/globalplan/ for more information).



Human TB in Asia*

Prevalence / 100,000

Indonesia	569
India	287
Nepal	258
Myanmar	155
Sri Lanka	72
USA	3



* (WHO 2003)

The overall prevalence of TB among humans in SE Asia is 304 / 100,000 (WHO 2004). Cambodia, Indonesia, Bangladesh, and Lao have the highest prevalence followed by India, Nepal, Malaysia, and Sri Lanka



Total Asian Elephants: ~ 60,000



So what does this mean for elephants? An estimated 60,000 Asian elephants remain on earth.



Captive Asian elephants: ~ 15,000



About one-fourth of the remaining 60,000 elephants are in captivity. The vast majority of these elephants are in Asia.



TB and Elephants

- Only captive elephants?
- A threat to wild elephants?
- A reservoir for human disease?



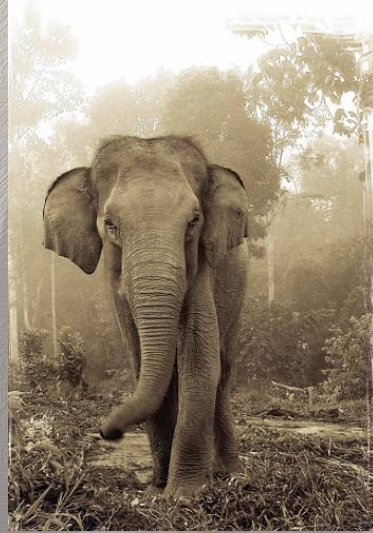
There are many questions about TB and elephants. How serious of a problem is it? Is it only a problem for captive elephants or are wild elephants at risk? Could elephants be a reservoir for humans to become infected? The following slides may not answer all of these questions but will attempt to put these issues into perspective.



Elephant TB in the U.S. (1994-2006)

36 culture positive:

- *33 Asian (M.tb)*
- *2 African (M.tb)*
- *1 African M.bovis)*

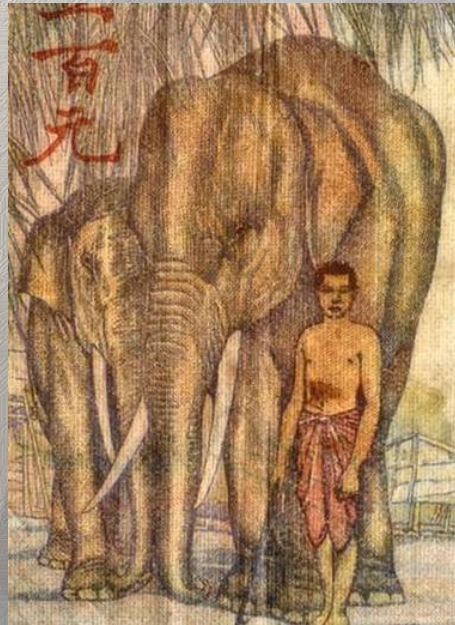


First let's look at what we know about TB in elephants in the U.S. Since 1994 there have been at least 38 known and confirmed cases. *Mycobacterium tuberculosis* has been the predominant isolate and most cases have occurred in Asian elephants. When we look at this from the perspective of the population, over this period of time, TB has been diagnosed in about 12% of the Asian elephants in the U.S. It is not known whether Asian elephants are more susceptible or if this simply reflects a closer physical contact with humans. There have been 3 cases of *M. bovis*. There have also been 2 cases (not listed above) associated with an unusual mycobacterium – *M. szulgai*.



Elephant TB in Asia

- True prevalence unknown
- Sporadic reports in literature
- Anecdotal reports suggest a problem



TB has been recognized as a disease of elephants since ancient times and has been described in Asian documents over 2000 years old. In more recent times, published reports began to appear in the 1920s (Narayanan 1925; Bopayya 1928). However, the current prevalence is unknown. Post-mortem examinations of captive elephants in southern India, as reported by colleagues, indicate that tuberculosis is present in the captive population.



Current Diagnostics

- Trunk wash culture the gold standard
- Poor sensitivity; time lag to reporting
- Important for speciation and antibiotic sensitivity testing

Culture of trunk wash samples is the currently accepted method to diagnose elephant TB. While it lacks sensitivity and requires weeks to reporting it will remain an important diagnostic tool to identify the mycobacterial species and facilitate antibiotic sensitivity testing.



Emerging TB Diagnostics

- ELISA
- Elephant TB StatPak®
- MAPIA
- Breath sampling



Elephant
TB
StatPak®



**Breathalyser detects
tuberculosis**

A number of ancillary diagnostic tests have been under investigation for the past several years.. The ELISA, Elephant TB StatPak®, and MAPIA are indirect serological tests that detect antibody rather than the TB organism. Breath sampling methods are being used experimentally in humans to detect TB antigen and may have application for elephants. We are currently investigating this possibility.



Indirect Tests

- Early predictors
- Evaluate response to treatment
- Quicker reporting time
- May or may not identify active cases
- Still experimental
- Do not replace culture

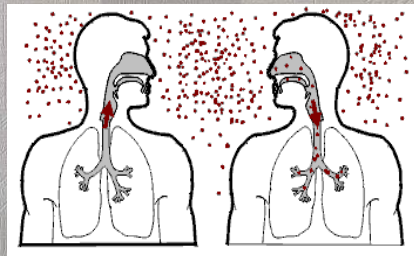


Serological tests have both advantages and disadvantages. Preliminary data shows that they may be early predictors with serological conversion occurring sometimes years in advance of a positive culture. They may therefore provide a tool for risk assessment and management prior to organism shedding and disease spread. Reporting time is greatly reduced compared to culture and sample collection is less challenging. In the case of the Elephant TB StatPak[®], results can be obtained in 20 minutes although at this time, laboratory confirmation by MAPIA is recommended. Despite these advantages, culture is still essential to detect actively shedding cases and determine antibiotic sensitivity. If validated, breath analyzers could be useful to detect shedding.



Active vs Latent TB

- 4-10% of infected humans will develop active TB
- What about elephants?
- Can latent vs active be differentiated?
- Should latent TB be treated?



TB can remain latent for decades. Of the 2 billion latently infected humans, it is estimated that between 4 and 10% will develop active disease in their lifetime. Because the majority of active cases results from re-activation of latent disease these infected individuals are an enormous reservoir of potential cases. We don't know enough about the pathophysiology to really understand the implications of latent disease in elephants but it is probably wise that we err on the side of caution with elephants that appear to be latently infected.



Nepal Project – 120 elephants

- Trunk wash culture
- ELISA
- MAPIA / Elephant TB StatPak®
- Immunoblot
- Immune profile
- CBC / Chem panel



In January 2006 we evaluated 120 captive elephants in Nepal using most of the diagnostic tests previously described. To our knowledge this is the first comprehensive surveillance of elephants in Asia for TB. The results are being evaluated and will be reported at a later date.



Nepal Project Collaborators

- Institute of Agriculture and Animal Science – Nepal (IAAS)
- Department of National Parks and Wildlife Conservation Nepal (special thanks to Mr. Giri)
- Tufts Center for Conservation Medicine
- Elephant Care International
- National Veterinary Services Laboratories
- Many researchers in Nepal and U.S.

The Nepal Project was a collaboration between IAAS – the veterinary school in Nepal, the Department of National Parks and Wildlife Conservation, Tufts Center for Conservation Medicine, Elephant Care International, NVSL, and the researchers in Nepal and the U.S.



Management Issues

- Cultural concerns
 - Protected species
 - Worshipped in some areas
 - Of national importance
- Legal and other concerns
 - Economically important (tourism)
 - Private vs government
 - Treatment vs euthanasia



Numerous issues confront the management of TB in Asia. Elephants are an integral part of the history and culture of most range countries. They are protected by national and international laws. They are essential to tourism – especially in India, Nepal, and Thailand but in other countries as well. Management and tracking of privately-owned elephants may be more difficult than government-owned elephants and management strategies may differ for these two groups.



Management Issues

- Treatment is expensive
- Resources limited in Asia
- Perception of treating elephants vs humans
- MDR- TB



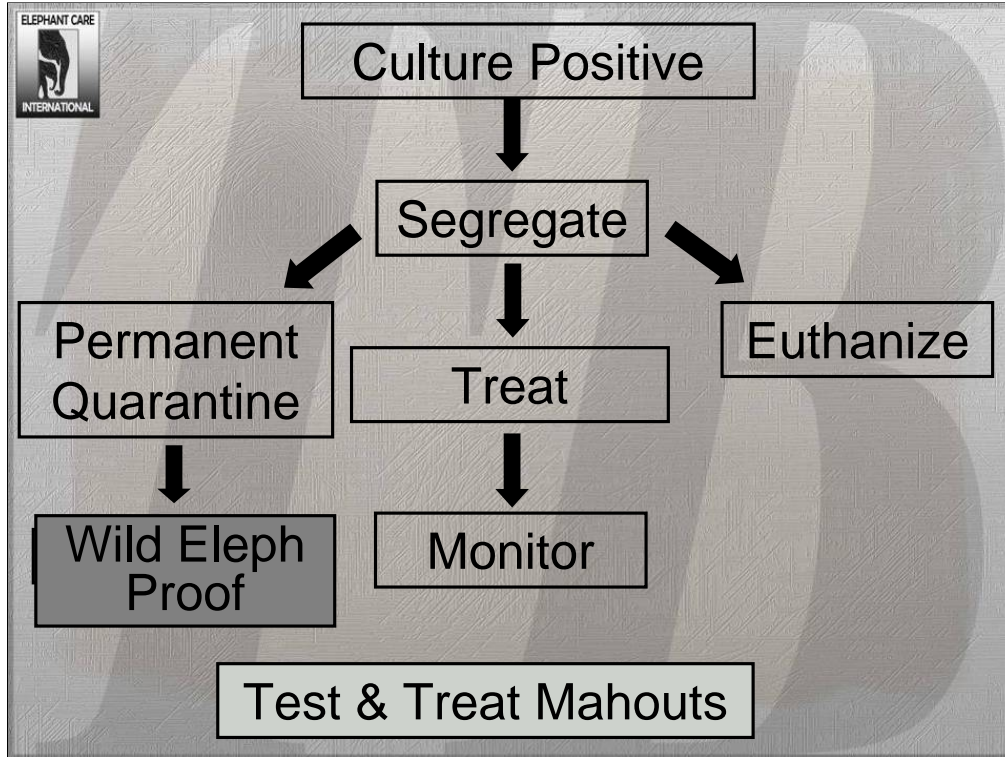
Treatment is expensive. We know in the U.S. the drugs alone may cost up to \$50,000 to treat one elephant for one year. We can only hope that we can find more inexpensive sources in Asia – but even if this is possible it will still be costly. Can funds be found? Will people rally to help the elephants or will there be a negative perception given the scope of the human TB problem in Asia? Is there a potential that MDR-TB is present in elephants in Asia? Cases have already been found in elephants in the U.S.



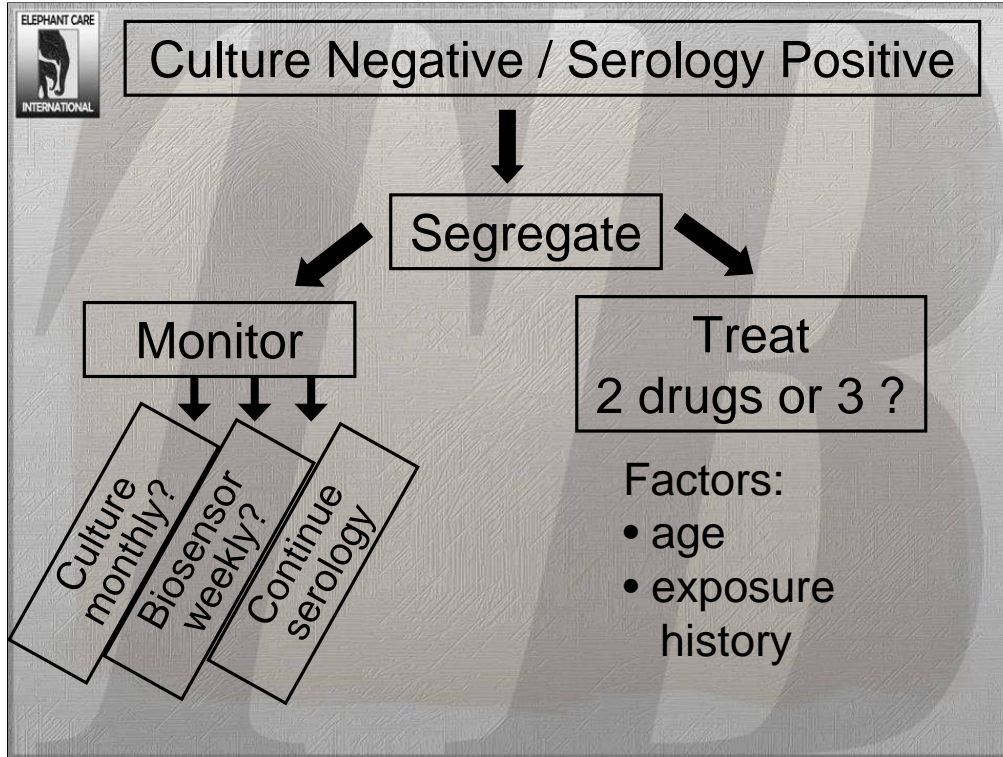
Management Options

- Active (culture positive)
 - Treat
 - Segregate
 - Euthanize (least acceptable)
- Latent (culture negative, serology positive)
 - Treat
 - Segregate and re-test
 - Euthanize (least acceptable)

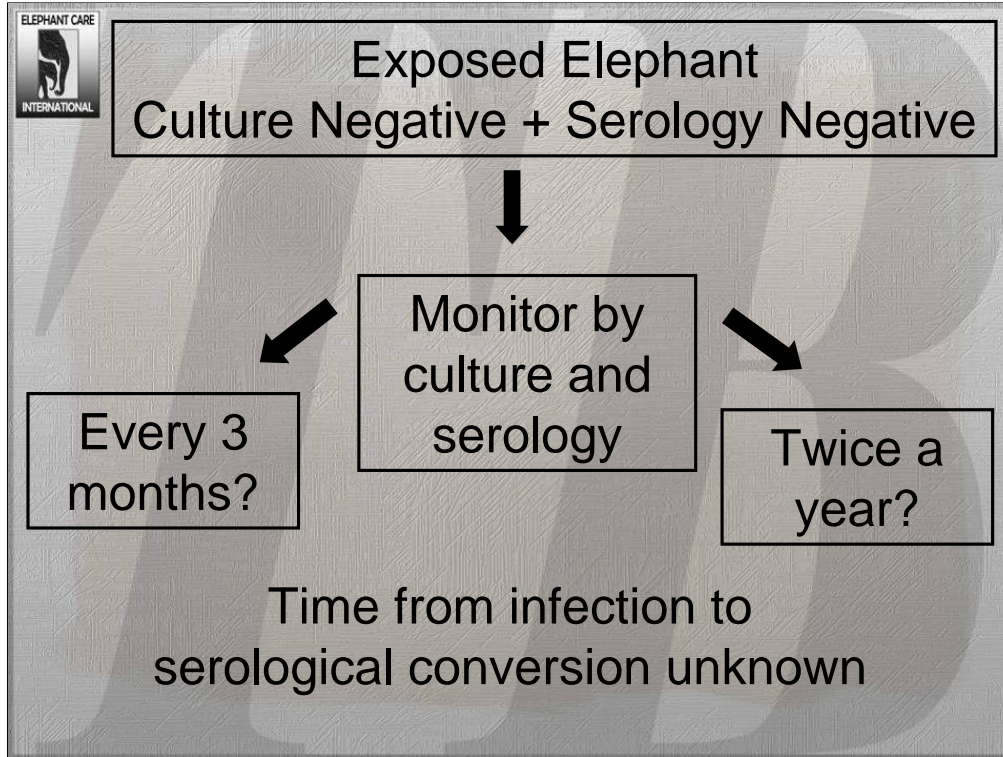
There are two broad groups to consider – those elephants that are culture positive and actively infected and those that are culture negative but serologically positive. This latter group may represent latent disease but it may not be easy to prove these are not really active cases that we have failed to detect because of the limitations of our diagnostic toolbox.



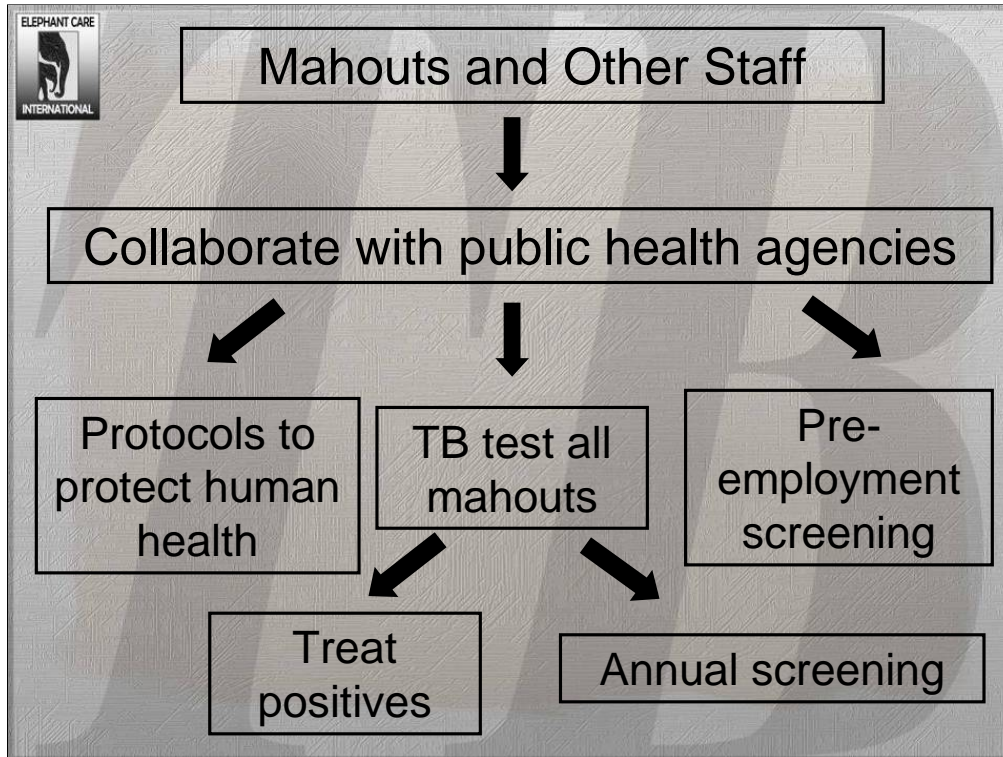
This is a simplistic flow chart to indicate possible options for culture positive elephants. Segregation may be the most effective and efficient tool and a reasonable first step. A permanent quarantine situation with protective barriers to prevent the intermingling of wild elephants may be possible. Detailed protocols for the protection of human health would be essential. Treatment may be an option if there are only a few cases and funds can be found to pay for the drugs. Euthanasia is undesirable for an endangered species but perhaps should be considered in cases of MDR-TB given the difficulty of treatment and the increased risk to humans.



The management of elephants that are culture-negative, but serologically positive is more complex. Certainly prophylactic treatment is an option - again depending on the number of cases and available funds. Whereas prophylactic treatment in humans utilizes one drug, the U.S. elephant protocol calls for two or three drug therapy. This is based on the assumption that some elephants in this group may have active disease. Elephants should be re-cultured immediately before beginning prophylactic treatment. Age and exposure history are considerations. Monitoring for active disease is also an option. Protocols will need to be established to determine the frequency of culture and continued research on other ways to detect shedding are to be encouraged. The current lack of an accurate and expedient method to determine shedding is a major drawback.



What about elephants that are culture negative and serologically negative but have had known exposure to TB positive elephants?. This group should be placed on an enhanced surveillance schedule because we do not yet know the time interval from infection to serological conversion.



A protocol to address the TB health status of mahouts and other staff is a critical component of the overall strategy to manage TB in elephants. Collaboration with public health agencies that already have TB screening programs in place will be helpful. All mahouts should be tested to initiate the program and infected individuals treated. Pre-employment screening, annual testing, education, and establishing protocols to protect human health are all essential. Elephants cared for by infected mahouts should undergo increased monitoring.



TB and Wild Elephants...?

- Not yet documented in wild
- Intermingling of captive/wild in Myanmar, Laos, Nepal, India...
- Intermingling of humans & elephants
- Systematic testing needed



TB has not yet been diagnosed in wild elephants. What are the risks that this disease will cross into wild elephants or that it may already be there? Could TB become as devastating a problem for elephants as it is for humans? The risks are greater where captive and wild elephants intermingle during grazing or breeding – Nepal and Myanmar for example. Human TB will continue to be a source of exposure for elephants. Until adequate studies of both captive and wild elephants are conducted we won't know the answers to these questions.




Other Implications

Are elephants an overlooked reservoir for human TB in Asia?




Certainly infected elephants pose a risk to mahouts and handlers who live in close association. The degree of risk to humans (or elephants) in other situations where there is close but brief contact - such as the large festivals that are held in India is believed to be minimal.



Infection can be easy — or perhaps not...

- WHO says...(see notes below)
- CDC says...(see notes below)
- Example: Only one documented instance of an air passenger infecting others and no active infections resulted
- Perhaps some species more susceptible?



Despite the potential for infection, it is estimated that an actively infected human only infects about 12-14 others per year, often even family members do not become infected.

The World Health Organization says

When infectious people cough, sneeze, talk or spit, they propel TB germs into the air. A person needs only to inhale a small number of these to be infected.

However, people infected with TB bacilli will not necessarily become sick with the disease. The immune system "walls off" the TB bacilli which, protected by a thick waxy coat, can lie dormant for years. When someone's immune system is weakened, the chances of becoming sick are greater.

CDC, Center for Disease Control says

To become infected, a person usually has to spend a relatively long time in a closed environment where the air was contaminated by a person with untreated tuberculosis who was coughing and who had numerous *M. tuberculosis* organisms (or tubercle bacilli) in secretions from the lungs or voice box (larynx).

Infection is generally transmitted through the air; therefore, there is virtually no danger of its being spread by dishes, linens, and items that are touched, or by most food products. However, it can be transmitted through unpasteurized milk or milk products obtained from infected cattle.

Travelers who anticipate possible prolonged exposure to tuberculosis (e.g., those who could be expected to come in contact routinely with hospital, prison, or homeless shelter populations) should be advised to have a tuberculin skin test before leaving the United States.

If the reaction is negative, they should have a repeat test approximately 12 weeks after returning. Because persons with HIV infection are more likely to have an impaired response to the tuberculin skin test, travelers who are HIV positive should be advised to inform their physicians about their HIV infection status.

Except for travelers with impaired immunity, travelers who already have a positive tuberculin reaction are unlikely to be reinfected. Travelers who anticipate repeated travel with possible prolonged exposure or an extended stay over a period of years in an endemic country should be advised to have two-step baseline testing and, if the reaction is negative, annual screening, including a tuberculin skin test.



Summary

- Management strategies needed now
- Nepal leading research and planning in Asia
- Support from international agencies will be needed
- Elephant Care International TB Initiative:
www.ElephantCare.org/projects.htm#Initiative

In conclusion, management strategies are needed and are under development in Nepal. These may well serve as a model for other countries as it is likely that TB is as endemic in captive elephants as it is in humans. Support from international agencies will be needed to help fund additional surveys and initiate treatment. Elephant Care International will continue to address the problem of elephant TB both from a research standpoint and from a clinical standpoint. If you would like more information about our TB Initiative and the Nepal research project, please visit our website.



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