

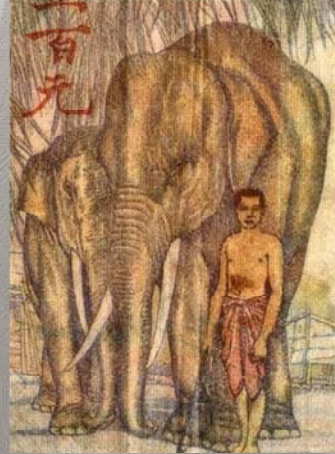
# A Brief History of TB in Elephants

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## Overview

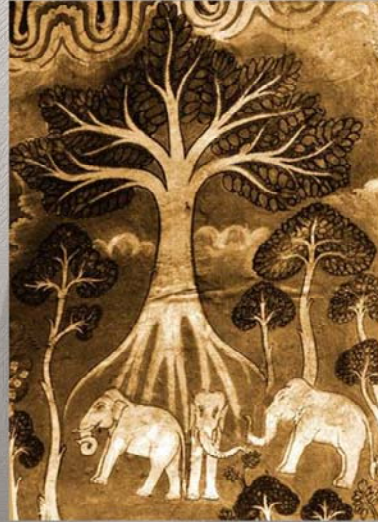
- Complex disease
- Much unknown
- TB in humans > 100 years
- TB in elephants < 15 years



TB is a complex disease about which there are many unknowns. In contrast to humans where TB has been studied for over 100 years, TB in elephants has been under investigation for only the last 15 years. The history of elephant TB that I will present today is a synopsis of the literature and will introduce you to many of the scientists who will be presenting details on their work later in this conference.

## TB in Elephants

- 2000 years ago
- Hastayurveda  
(Sanskrit document)



TB has been recognized in elephants for millennia although not by the name we use today. A disease clearly resembling TB was observed in elephants in ancient times and was described in Sanskrit documents over 2000 years ago.

## TB in Mastodons

(*Mammot americanum*)

- TB in 59 of 113 of skeletons
- A “hyperdisease”
- Possible role in extinction



Rothschild B.M. and Laub R.  
2006. Hyperdisease in the late  
Pleistocene: validation of an early 20th  
century hypothesis. *Naturwissenschaften*  
93: 557-564.

While somewhat controversial, TB has been implicated as a possible causative factor in the extinction of the mastodon. In this 2006 study, Rothschild found lesions typical of TB in the foot bones and ribs of 52% of 113 mastodon skeletons. Recognizing that only a portion of animals infected by TB develop bone involvement, the high frequency of the pathology in the mastodons suggested that TB may have been a hyperdisease that contributed to the mastodon's demise.

## 19th Century ....

London 1875 ... one case

Garrod, A.H. 1875. Report on the Indian elephant which died in the society's gardens on July 7th, 1875. Proc. Zool. Soc. Lond. 1875 542-543.



Jumping forward in history, the first report of tuberculosis in an elephant in more recent times was a case at the London Zoo in 1875.

## Early 20<sup>th</sup> century ...

- Damman 1909
- Thieringer 1911
- Narayanan 1925
- Baldrey 1930 ...
- And others ...



Sporadic case reports of TB in captive Asian elephants appeared in the early part of the 20<sup>th</sup> century by these authors and others...

## Mid 20th century ....

Gorovitz, C. 1962.  
Tuberculosis in an  
African elephant.  
Nord Vet Med 14:  
351-352.



... and in 1962 the first case in an African elephant was reported.

## Late 20<sup>th</sup> century...

- Gutter 1981 – M. tb in an Asian elephant ...
- Devine 1983 – Isoniazid therapy ...
- Mikota 1994 – Medical Management of the Elephant.



In the latter part of the 20<sup>th</sup> century Gutter reported on TB in a circus elephant and the first anti-TB drug study on isoniazid levels in a single elephant was published. In a retrospective study of 379 zoo elephants by Mikota, Sargent, and Ranglack, only 8 elephants died of TB between 1908 and 1994. This study preceded routine diagnostic testing for TB and did not include privately owned elephants. As we will see later TB is more common than this study revealed.



## Late 20<sup>th</sup> century cont....

Saunders, G. 1983. Pulmonary *Mycobacterium tuberculosis* infection in a circus elephant. J. Am. Vet. Med. Assoc. 183, 1311-1312.



No one knew it at the time but this report of TB in a circus elephant that appeared in the AVMA journal in 1983 foreshadowed a nationwide problem for captive elephants in North America and Europe that would not become apparent until more than a decade later. This was an elephant from what is now considered the index herd.

## Elephant TB References

- Elephant Care International Bibliographic Database
  - ~ 4000 references
  - many TB references
- [www.elephantcare.org](http://www.elephantcare.org)



As I continue this tour of the elephant TB literature I will be citing some full references. For the most part though, I've abbreviated the references and included only the first author's name. Full citations for all the publications in this presentation will be available in the conference proceedings. Elephant Care International maintains a bibliographic database of elephant healthcare and conservation articles. There are currently about 4000 citations in the database, many of which are about TB. You can access this database at the Elephant Care International website. We have just posted an updated list of TB articles and the link is on our home page under "What's New."

## 1996: Elephant TB “Emerges”

- 2 elephants from Illinois herd die
- TB Advisory Panel formed by USDA



1996 is usually considered the year that TB emerged or more accurately “re-emerged” in elephants in the U.S. The death of these two circus elephants three days apart raised a great deal public concern. As a result USDA consulted with the American Association of Zoo Veterinarians to form a TB Advisory Panel to decide what to do with the remaining elephants in the herd.

## The Index Herd



Following the death of the two elephants in the preceding slide 18 elephants remained in the index herd. This is an image of 6 of the elephants at the barn where they were housed in Illinois. The initial diagnostic work-up revealed one additional culture-positive elephant.



The death of the two traveling elephants raised public concern and resulted in media coverage about TB in elephants that continues to this day.

## 1997 ...

- Binkley – TB in captive elephants
- Ryan – TB in circus elephants
- Maslow – TB as zoonoses
- Mikota, Maslow – Diagnostic TB techniques

**5 new culture-confirmed cases!**

There were a number of publications in 1997 pertaining to the index herd or to broader aspects of TB in elephants. But the most significant event in 1997 was the diagnosis of 5 new culture-positive cases at 4 separate facilities.

1997 ...

- Data from 5 herds
- 87 humans tested
- 11 PPD pos
  - All from one herd
  - 3 PPD conversions
  - 8 unknown (+ at first testing)
  - 1 active TB case



Michalak et al. 1997; Emerg Inf Dis 4:283-7

Also in 1997 Michalak and colleagues documented transmission of TB between humans and elephants. 87 people from the original 5 TB-infected herds were tested. 11 were skin test positive – all from the index herd. Three were known to be conversions - the other 8 were positive at first testing so there was no way to know whether the source of their exposure was the Illinois facility or if they had been previously exposed. There was one active case of human TB and the handler and the elephant shared the same strain, although it is not known who was infected first.

## Guidelines for the Control of TB in Elephants

- TB Advisory Panel → NTB WGZWS
- 1st Elephant TB Guidelines 1998
- Testing, surveillance, treatment
- Administered by USDA
- Revised in 2000, 2003, 2008, 2010



As it became obvious that TB was a more wide-spread problem, the original TB Advisory Panel merged with the National TB Working Group for Zoo and Wildlife Species that was formed by AAZV in 1997 to address TB in zoo mammals. The Elephant Subcommittee of this group produced the 1<sup>st</sup> Guidelines for the Control of TB in Elephants in 1998. They have been revised over the years, most recently in 2010 as more scientific information has become available. The guidelines are currently under the auspices of the USAHA but USDA is responsible for compliance. You will hear more about the history of the Working Group and the Guidelines in later presentations.



1998 ...

Dunker – Management and treatment of an  
M. tb positive elephant at the San Francisco  
Zoo...

Rectal dosing method  
reported



One of the 5 new cases that I mentioned above was an elephant at the San Francisco Zoo and Dr. Freeland Dunker reported on his experiences with rectal dosing methods in 1998.

1999...



Isaza – A Trunk Wash Technique for the Diagnosis of TB in Elephants



The following year the trunk wash procedure that was in wide use was formally described and published by Dr. Ramiro Isaza. The procedure is comparable to obtaining a sputum sample from a human. 60 cc of sterile saline is instilled into the trunk, the trunk is elevated and then lowered and the sample collected in a plastic bag, transferred to a secure tube, and submitted for culture. Ideally the elephant will forcibly exhale so that the sample is from the lower respiratory tract. However, not all elephants comply..

## 2000 ...

- Aug 1996 - June 2000
- 17 culture pos eleph
- 8 herds
  - Ill; CA; FL; ARK; MO
  - 3 zoo; 14 private-owned
- 5 M.tb strains
- Estimated prevalence ~ 3.0 %



Mikota, S.K., Larsen, R.S., and Montali, R.J. 2000.  
Tuberculosis in elephants in North America. *Zoo Biology*  
19: 393-403.

The first review paper published in 2000 summarized the events that had occurred since 1996. 17 culture positive elephants were identified from 8 different herds in Illinois, California, Florida, Arkansas, and Missouri. Three elephants originated from zoos and 14 were privately owned. Five distinct TB strains were identified. At this time the estimated prevalence of TB among elephants in North America was about 3%.

2000 ...

Lyashchenko, K., M. Singh, R. Colangeli and M.L. Gennaro. 2000. **A multi-antigen print immunoassay for the development of serological diagnosis of infectious disease.** J Immunol Methods 242: 91-100.



There were two publications in 2000 on the serological diagnosis of TB. This paper by Lyashchenko described a multi-antigen print immunoassay technique. And...

2000 ...

Larsen, R.S., M.D. Salman, S.K. Mikota, R. Isaza, R.J. Montali and J. Triantis. 2000. **Evaluation of a multiple-antigen ELISA for detection of *M. tb* infection in captive elephants.** J. Zoo Wildl. Med. 31: 291-302.



Larsen's investigation sought to validate a multiple-antigen ELISA. Infection status of each animal was determined by culture of trunk washes. The assay showed 100% sensitivity and specificity however the sample size was limited. This ELISA is not currently available to my knowledge.

## 2001 ...

- 118 elephants in 6 herds
- Aug 1996 – Sept 1999
- 12 culture-positive
- ELISA, BTB
- Intradermal tuberculin test
  - Sensitivity – 16.7%
  - Specificity – 74.2%



In 2001 an article in the Journal of Zoo and Wildlife Medicine reported on 6 infected elephant herds. The period studied was 1996-1999. Out of a total of 118 elephants, 12 were culture positive for M.tb. The clinical course of the 12 elephants was reviewed and culture results were compared with indirect methods of TB diagnosis such as intradermal tuberculin testing, ELISA, and the BTB, a lymphocyte stimulation assay that is no longer available. This study demonstrated the poor sensitivity and specificity of the intradermal tuberculin test, a finding confirmed in subsequent studies.

2001 ...

Mikota, S.K., Peddie, L., Peddie, J., Isaza, R., Dunker, F., West, G., Lindsay, W., Larsen, R.S., Salman, M.D., Chatterjee, D., Payeur, J., Whipple, D., Thoen, C., Davis, S., Sedgwick, C., Montali, R.J., Ziccardi, M., and Maslow, J. 2001. **Epidemiology and diagnosis of M. tb in captive Asian elephants.** J. Zoo Wildl. Med. 32: 1-16.



This is the full citation for the study in the previous slide. I would like you to note that there are 17 authors. This was emblematic of the level of cooperation that existed in 2001 to evaluate this challenging problem of TB. I feel that this level of collaboration has been lost in recent years but I hope that this conference will serve to break down whatever obstacles have caused this to occur.

2001 ...

- Harr – Clinicopathological findings in M.tb culture-positive elephants
- Davis – M.tb risk for elephant handlers and veterinarians



Also in 2001 Harr published a study correlating clinical pathology with culture status and Davis reported on the zoonotic risk of TB for elephant handlers and veterinarians.



2002 ...

Oh – Human exposure following *M.tb* infection of multiple species in a Metropolitan Zoo



The next year saw further information on the zoonotic aspects of TB with Oh's article on human exposure that occurred as a sequelae to *M. tb* infections in several zoo animals including 2 Asian elephants. No active cases were identified in humans but tuberculin skin test conversions were associated with training elephants and attending an elephant necropsy.

2002 ...

Payeur – Mycobacterial isolations  
in captive elephants in the U.S.

- 539 elephants; 5100 samples
- 24 culture positive; 11 herds
- 17 pre-mortem; 7 postmortem



Dr. Janet Payeur reported in 2002 on the results of 5100 samples that were submitted to NVSL. There were now a total of 24 culture-confirmed cases from 11 different herds. 17 cases were diagnosed pre-mortem and 7 postmortem.

## 2005 ...

- Maslow – Population pk of INH
- Maslow – Pk of ethambutol
- Zhu – Pk of pyrazinamide
- Lewerin – Outbreak of M.tb  
in a Swedish zoo



The next two years were quiet in terms of publications. Then in 2005 there were 3 studies on the pharmacokinetics of isoniazid, ethambutol, and pyrazinamide. We also learned of an M.tb outbreak in elephants at a zoo in Sweden.

2006 ...

Peloquin – Dose selection and pk of rifampin in elephants J Vet Pharm Ther 29: 581-585.

Dumonceaux – TB treatment protocols and complications for elephants. Proc Intl Eleph Conserv / Res Symp 84-85.



A 4<sup>th</sup> pharmacokinetic paper on rifampin appeared the following year along with a paper addressing complications of treatment. I'll mention this again later when I discuss future research needs but we still need additional pharmacokinetic studies. The data in these 4 reports was generated retrospectively from multiple sources. And while we have learned that we can achieve serum TB drug levels in elephants known to be curative in humans, not all elephants can tolerate these doses. It would be useful to conduct prospective studies and to include some of the second-line Tb drugs.

2006 ...

**Lyashchenko – TB in elephants: ab responses to defined antigens of M.tb, potential for early diagnosis, and monitoring of treatment** Clin. Vaccine Immunol. 13(7): 722-732.



Also in 2006, it was demonstrated that two serological assays, the Multi-antigen print immunoassay or MAPIA and a Rapid Test could detect TB 3.5-4 years prior to detection by a positive culture. In 4 elephants the MAPIA declined with treatment suggesting that it might be a means to monitor therapeutic response.

2006 ...

**Ball – Comparison of trunk wash results matched to MAPIA in a group of captive Asian elephants.** Proc Amer Assoc Zoo Vet 303-304.



Dr. Ball and colleagues conducted a study to determine if NTM affected serological results.

<b>Mycobacterium culture</b>	<b>Stat-Pak</b>	<b>MAPIA</b>
<i>M. avium</i> complex (5)	-	-
<i>M. asiaticum</i> (1)	-	-
<i>M. fortuitum</i> (2)	-	-
<i>M. terrae</i> (1)	-	-
<i>M. abscessus</i> (1)	-	-
<i>M. intracellulare</i> (2)	-	-
<i>M. flavescens</i> (1)	-	-
<i>M. mucogenicum</i> (1)	-	-
<i>M. nonchromogenicum</i> (1)	-	-
<i>M. Gordonae</i> (2)	-	-
<i>M. chelonae</i> (1)	-	-
<i>M. simiae</i> (1)	-	-

In Dr. Balls study there were 19 TW samples from 4 healthy elephants that were positive for a variety of NTM. Serum collected at the same time was non-reactive on both the Stat-Pak and MAPIA tests.

## ElephantTB STAT-PAK® Kit (U.S. Veterinary License No. 645)



In 2007 the Rapid Test which had been under research and development for several years was licensed by the USDA as the Elephant TB Stat-Pak® Assay. The Stat-Pak is a screening test for the detection of antibodies to *M.tb* and *M.bovis* in serum, plasma, or whole blood from Asian and African elephants. Later presentations will discuss the immunological basis and supporting data for the Stat-Pak assay.



2007...

Lacasse – **Two cases of atypical mycobacteriosis caused by *M. szulgai* associated with mortality in captive African.** J. Zoo. Wildl. Med. 38: 101-107.



That same year we learned of two African elephants that succumbed to an unusual NTM - *M. szulgai*. Both elephants were reactive on the Stat-Pak and MAPIA assays although the MAPIA pattern was unusual. This was reported in the J of Zoo and Wildlife Medicine.

2009 ...

Greenwald, R., Lyashchenko, O., Esfandiari, J., Miller, M., Mikota, S., Olsen, J., Ball, R., Dumonceaux, D., Schmitt, D., Moller T., and Lyashchenko, K. 2009. **Highly accurate antibody assays for early and rapid detection of TB in African and Asian elephants.** *Clinical and Vaccine Immunology* 16(5):605-612.



In 2009 Greenwald and colleagues published this study describing the results of the Elephant TB Stat-Pak, MAPIA and DPP VetTB tests. The DPP or Dual Path Platform is a point of care test that is a field version of the MAPIA.

## Greenwald 2009

Status	# Eleph	Stat-Pak reactive	MAPIA reactive	DPP reactive
Culture pos	26	26	26	26
Exposed	63	22	10	10
Non-exposed	147	7*	0	0

In this study 26 culture positive elephants were also reactive on the Stat-Pak, MAPIA, and DPP. Of 63 exposed elephants, 22 were Stat-Pak reactive (35%) and 10 (16%) were also reactive on MAPIA and DPP. There are several reasons that the Stat-Pak and the MAPIA/DPP might not agree: it may be that the Stat-Pak is showing a false pos reactions, however, the Stat-Pak detects all immunoglobulin classes and it may be more sensitive. We also know that in cases where an elephant has been treated the MAPIA will decline but the Stat-Pak tends to stay reactive. In group of 147 elephants with no known exposure there were 7 Stat-Pak reactors; 3 of these were elephants infected with NTM.

## Sensitivity and Specificity

Elephant TBStat-Pak      MAPIA and DPP VetTB

- Sensitivity 100%
- Specificity 95%
- Sensitivity 100%
- Specificity 100%



The Greenwald study reported a sensitivity of 100% and a specificity of 95% for the Eleph TB Stat-Pak NS 100% sensitivity and specificity for the MAPIA and DPP. The methodology, immunology, and further data on these assays will be presented later in the conference.

2009 ...

Landolfi, J.A., S.A. Schultz,  
S.K. Mikota and K.A. Terio. 2009.  
**Development and validation  
of cytokine quantitative, real  
time RT-PCR assays for  
characterization of Asian  
elephant immune responses.**  
Vet. Immunol. Immunopathol.  
131: 73-78.



Dr. Jennifer Landolfi developed a real-time PCR assay in 2009 as a tool to begin to evaluate the immune response of elephants to infectious diseases including TB.

2010 ...

Landolfi, J.A., Mikota, S.K.,  
Chosy, J., Lyashchenko, K.P., Giri,  
K., Gairhe, K., and Terio, K.A.

**Comparison of systemic cytokine  
levels in *Mycobacterium* spp.  
seropositive and seronegative  
Asian elephants** . J Zoo and  
Wildlife Med 41(3): 445–455.



She continued this work applying the assay to sero-positive and sero-negative elephants. Dr. Landolfi will be presenting her work later in the conference.

2010 ...

Kay, M.K., Linke, L., Triantis, J., Salman, M.D., Larsen, R.S. **Evaluation of DNA extraction techniques for detecting MTB complex organisms in Asian elephant trunk washes.** J Clin Microbiol. Dec 15.



This recent publication that will also be presented here looked at the sensitivity and specificity of 3 DNA extraction methods to detect MTB complex in trunk wash samples from Asian elephants.

2011...

Murphree R, Warkentin JV, Dunn JR, Schaffner W, Jones TF. **Elephant-to-human transmission of tuberculosis, 2009.** Emerg Infect Dis. Mar 2011.



Just this past March an article appeared in Emerging Infectious Diseases on elephant to human transmission of TB and Dr. Murphree will be presenting her work later in this conference as well.



2011...

Mikota SK, Maslow JN. **TB at the human-animal interface: An emerging disease of elephants.** *Tuberculosis* 2011 Mar 10. [Epub ahead of print]



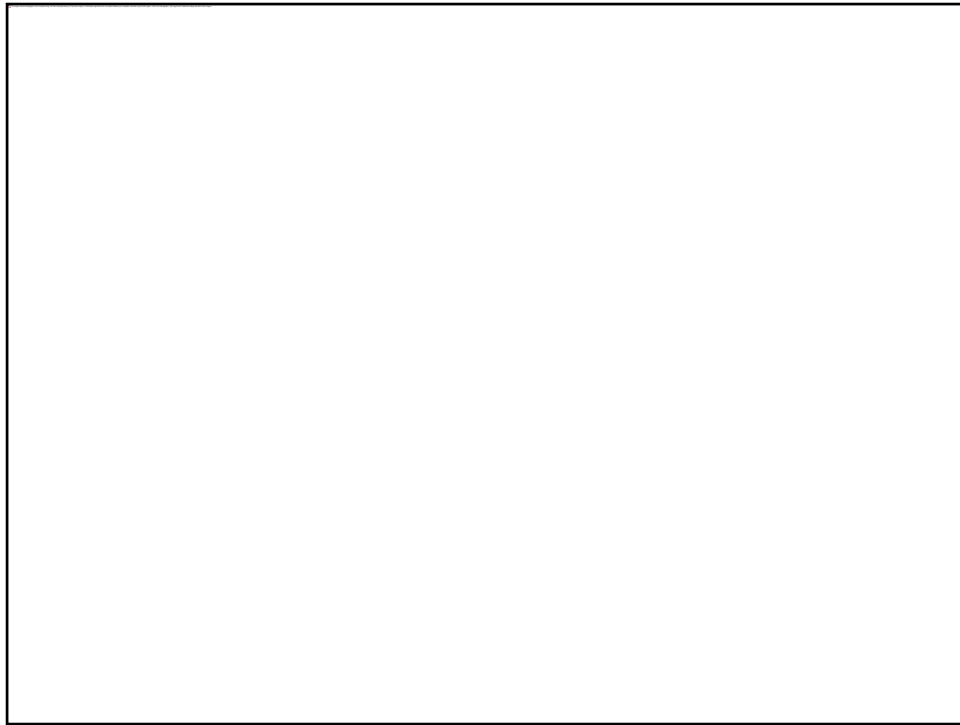
Also recently published is this review article by Mikota and Maslow that will appear in the journal *Tuberculosis*.

## The Index Herd

- 1994 - 2003 (n=22)
  - 5 TB cases at home facility (4 deaths)
  - 4 deaths other / unknown causes
- 2003-2006 – herd dispersed
  - 14 elephants to 3 facilities
- 3 additional TB cases identified
- 9 of 22 TB positive = 41%



Regarding the status of the index herd – 5 culture-confirmed cases of TB were identified between 1994 and 2003, 4 of which died. Four other deaths occurred due to other or unknown causes. Between 2003 and 2004 the herd was dispersed and the 14 remaining elephants moved to 3 separate facilities. Three additional culture positive cases have since been identified. So based on culture alone 41% of the known elephants from this herd were TB-infected.



If we look at the data for all of the U.S. there are 51 known culture-confirmed cases of TB in elephants that were identified between 1994 and 2011. 45 Asian and 5 African elephants had *M.tb* and there was one case of *M.bovis* in an African elephant. We don't know if Asian elephants are more susceptible; the higher # of cases may just reflect their closer association with humans. 31 cases were dx antemortem and 20 at PM. The majority of cases were not associated with clinical signs indicative of TB. In addition, there were the 2 cases of *M.szulgai* that I mentioned before that were associated with the death of 2 African elephants.

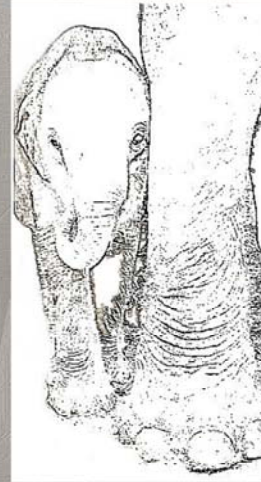


So what have we learned?

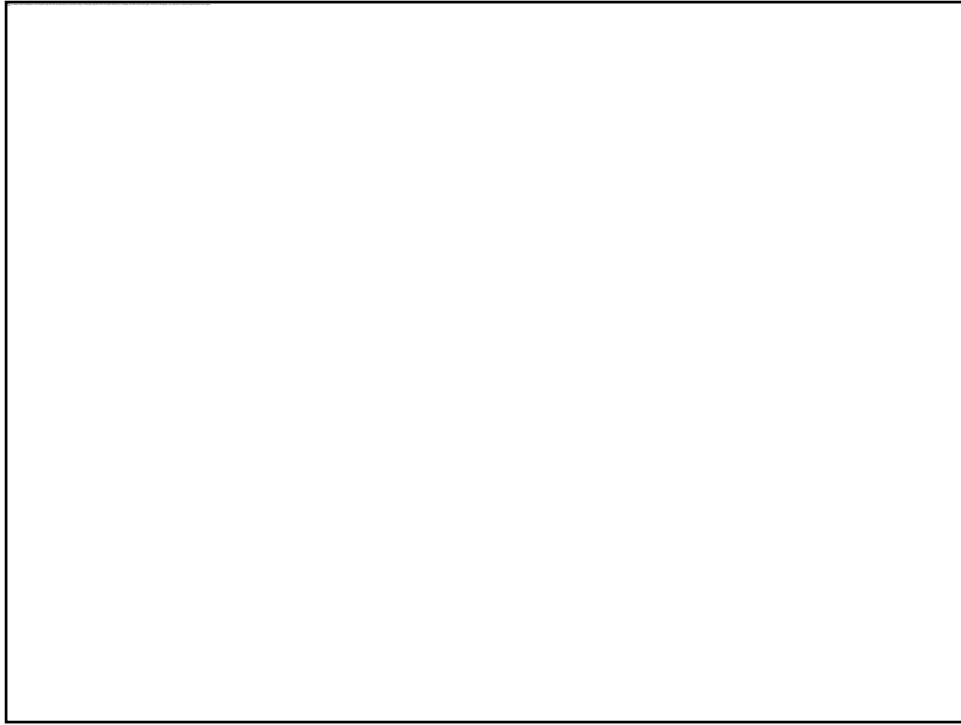
## 1. The # of detected TB cases has increased

- 2000: 17 culture pos ~ 3%
- 2002: 24 culture pos ~ 4%
- 2005: 33 culture pos ~ 6%
- 2011: 51 culture pos ~ 11.3%
  - Asian elephants ~ 18 %

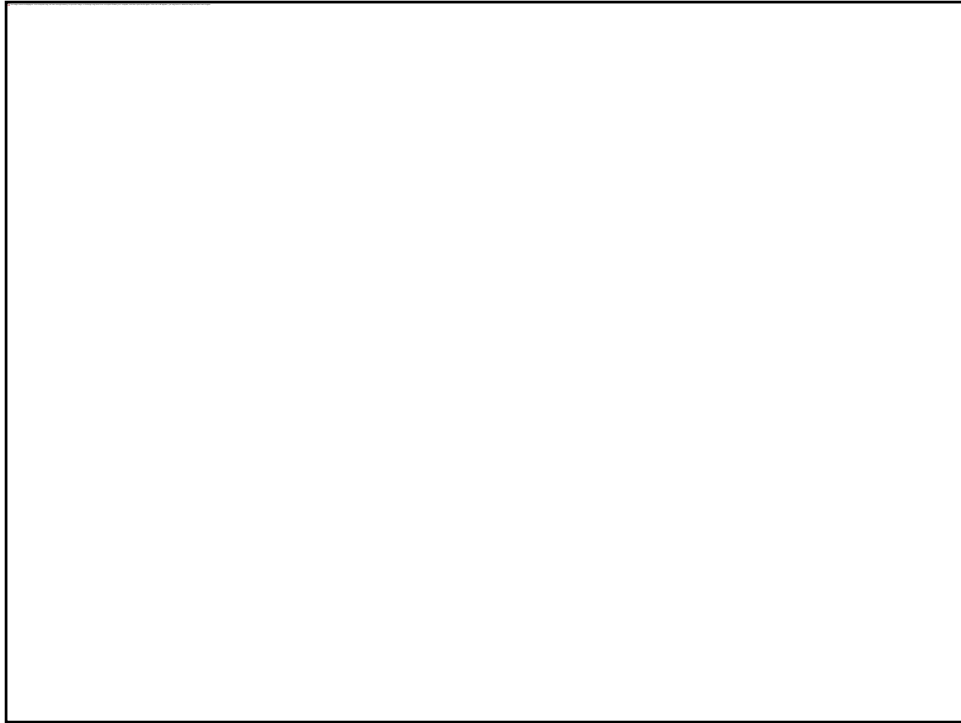
Elephant population in U.S. = ~ 451  
250 Asians  
201 Africans



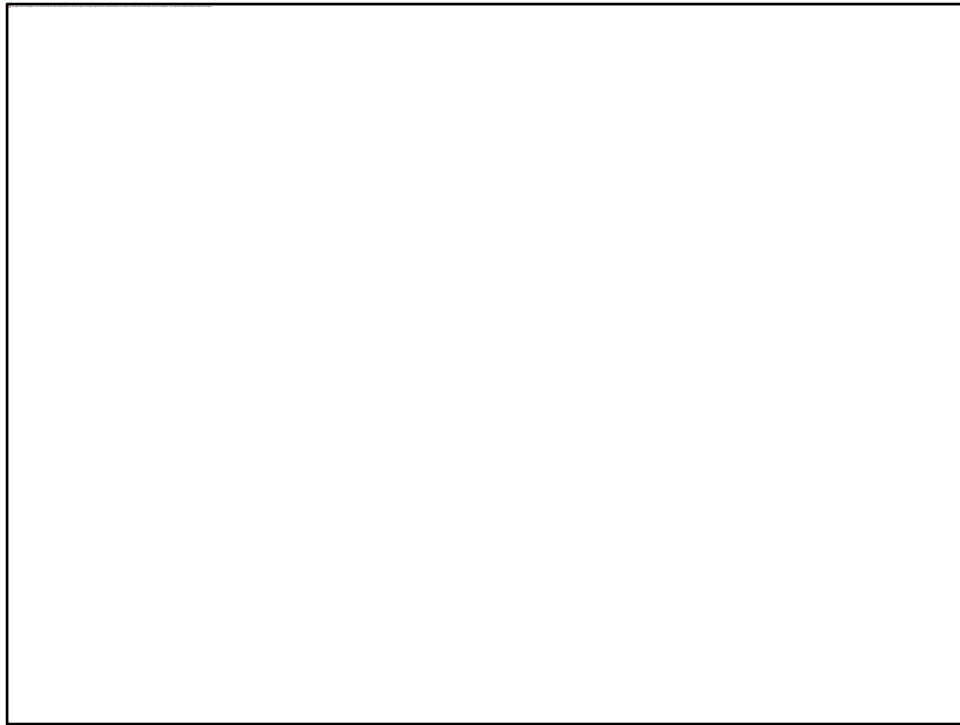
The first thing we have learned is that we have seen an increasing number of TB cases since we first began systematic surveillance in 1998. In 2000 there were 17 culture positive cases. The total number has now jumped to 51. The population of elephants has changed somewhat over time so these percentages are estimates but the trend is clear. To date we have identified culture-confirmed TB in over 11% of the elephants in the U.S. based on the current population of about 451. If we consider only Asian elephants in which the majority of cases have occurred the percentage among this group is even higher – 18 %.



Clinical signs, such as those that occur in humans may also be seen in elephants, however, most infected elephants have not shown any signs.

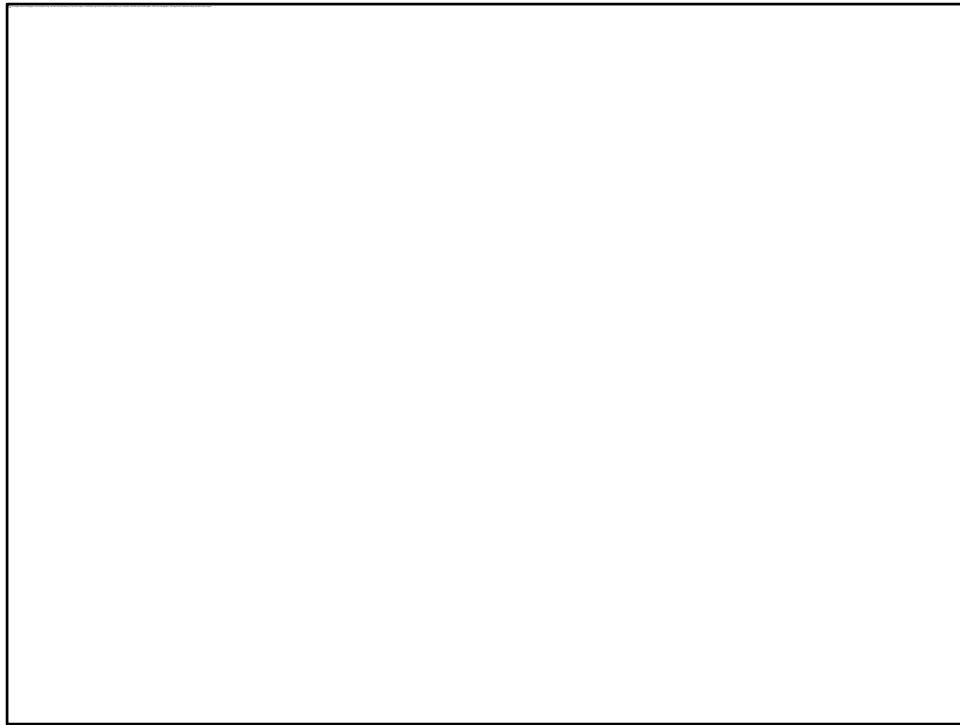


Here is the image again of the 2 elephants that died of TB 3 days apart. One elephant is clearly emaciated but the general body condition of the other elephant is normal. In some cases TB may be found at postmortem but may not be the immediate cause of death. Nonetheless these elephants may still be shedding TB organisms.

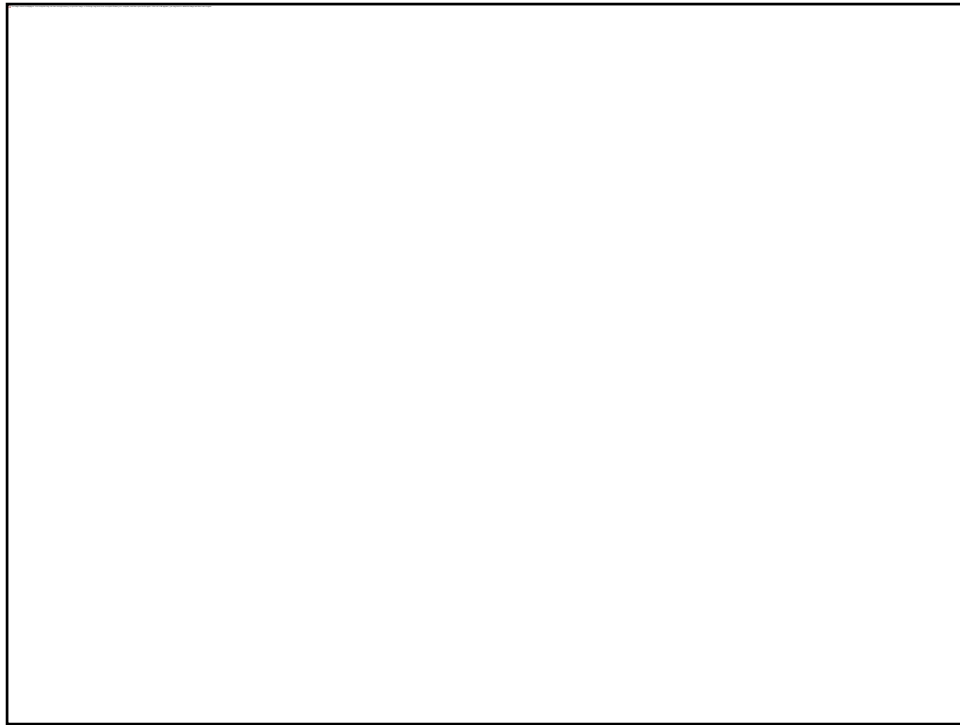


Although isolation of the organism is the “gold standard” to diagnose TB, culture has inherent limitations as a primary diagnostic technique: 1) Failure to isolate the organism does not rule out infection as intermittent shedding is characteristic and provides the potential for false-negative results. 2) Elephants use their trunks for a variety of functions and contamination is a common problem. If the sample is overgrown by other bacteria then the results are non-diagnostic. 3) 3 samples are required and reporting time is slow, typically 6-8 weeks. Infected elephants that are shedding while culture results are pending pose a risk to other elephants and humans.

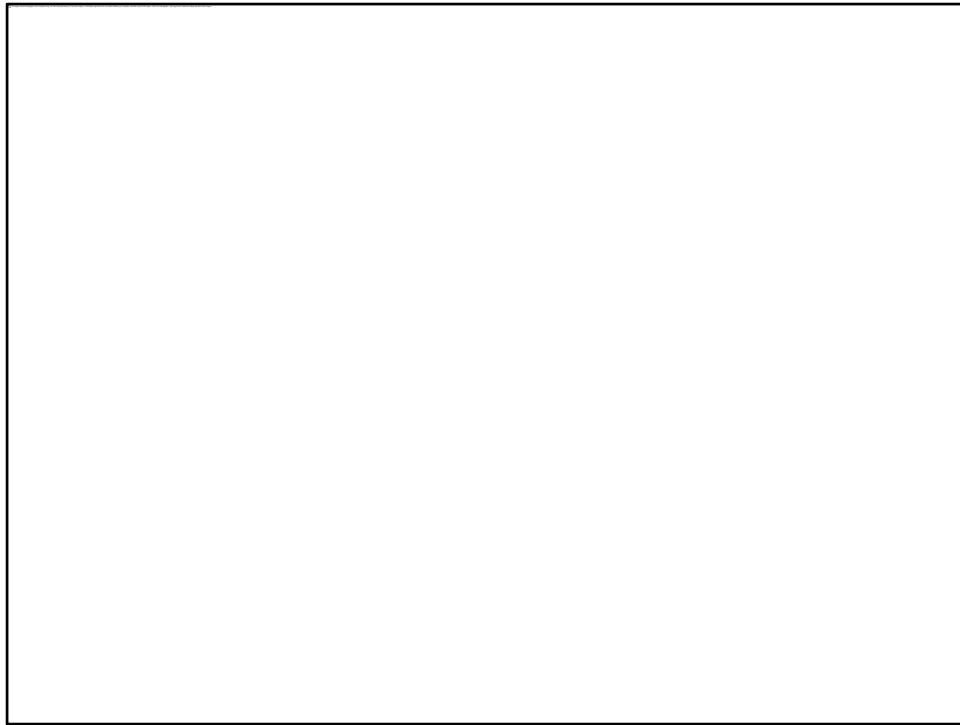




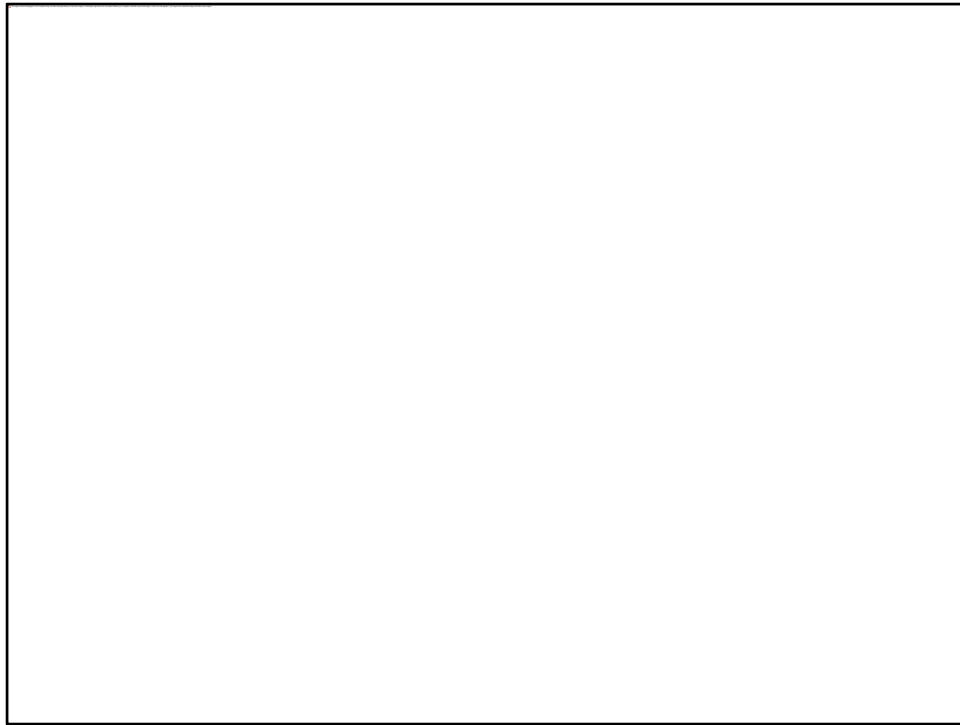
Referring to the Greenwald study again - only 58% of the elephants w necropsy-confirmed TB had positive ante-mortem TW cultures – the other 42% may have been shedding undetected. Further, we know that humans w sputum negative pulmonary TB can transmit disease.



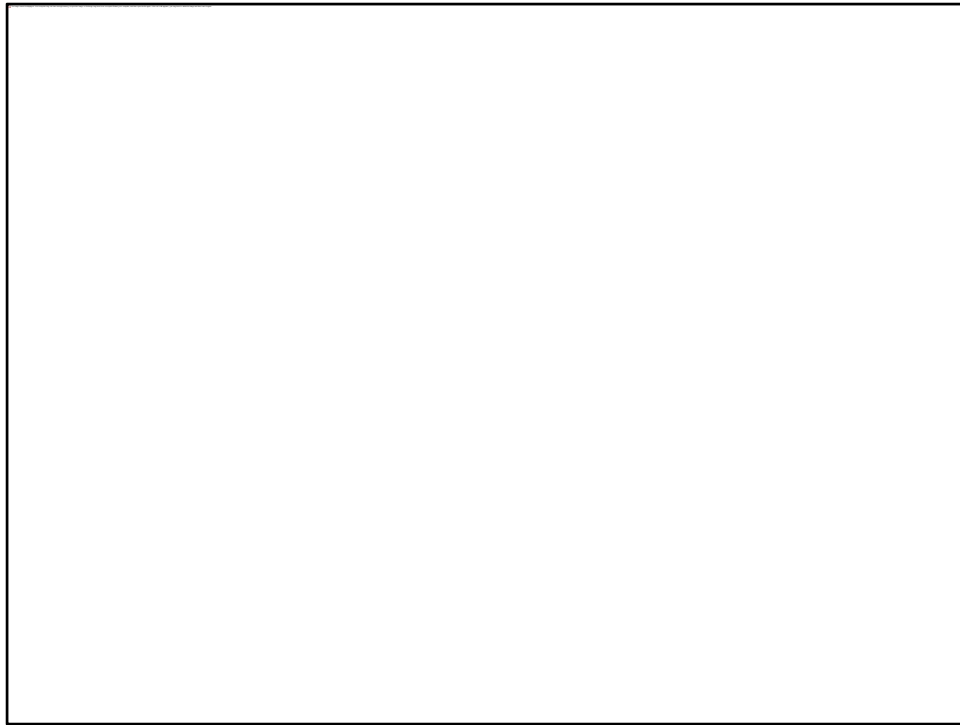
These two studies illustrate that while a positive TW is diagnostic, a negative TW does not rule out disease. In the Swedish study, TB was isolated from only 7 of 189 TW samples collected from 5 elephants that were confirmed infected at postmortem. In Thailand, only 2 of 60 TW samples collected from 4 infected elephants were positive.



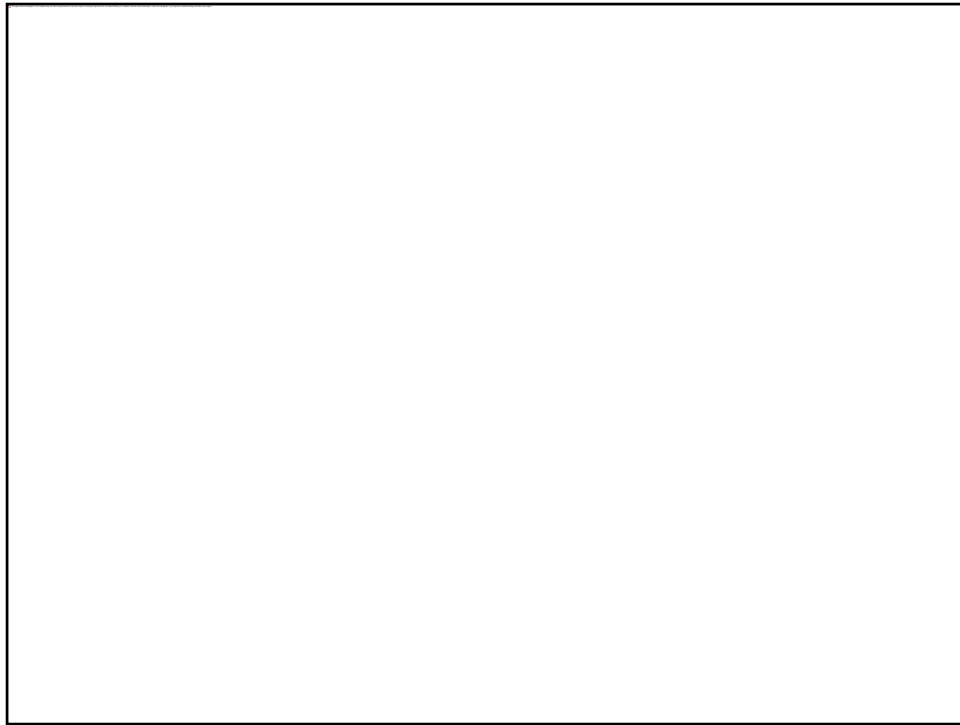
The currently available serological tests which you will hear about in greater detail later have given us a tool for the early diagnosis of TB in elephants. As with any test there are advantages and disadvantages. Serological tests provide a rapid, affordable, 1<sup>st</sup> line tool to screen elephants that provide a means to diagnose and treat TB before it spreads to other animals or humans. Serological tests are indirect – measuring antibodies rather than directly detecting the organism and lab confirmation of the Stat-Pak by the MAPIA is necessary. We will always need culture but studies have shown it's limited value as a primary diagnostic test. Culture is useful for antibiotic sensitivity testing and for genotyping which contributes to our understanding of the epidemiology of TB in elephants.



There was no precedent for treating TB in animals when TB emerged in elephants so humans became the model. The basic protocol is to administer 3 drugs for 2 months followed by two drugs for 10 months. Direct or rectal administration is used depending on the selected drugs. Serum drug levels are monitored and dosages adjusted accordingly to achieve target levels.

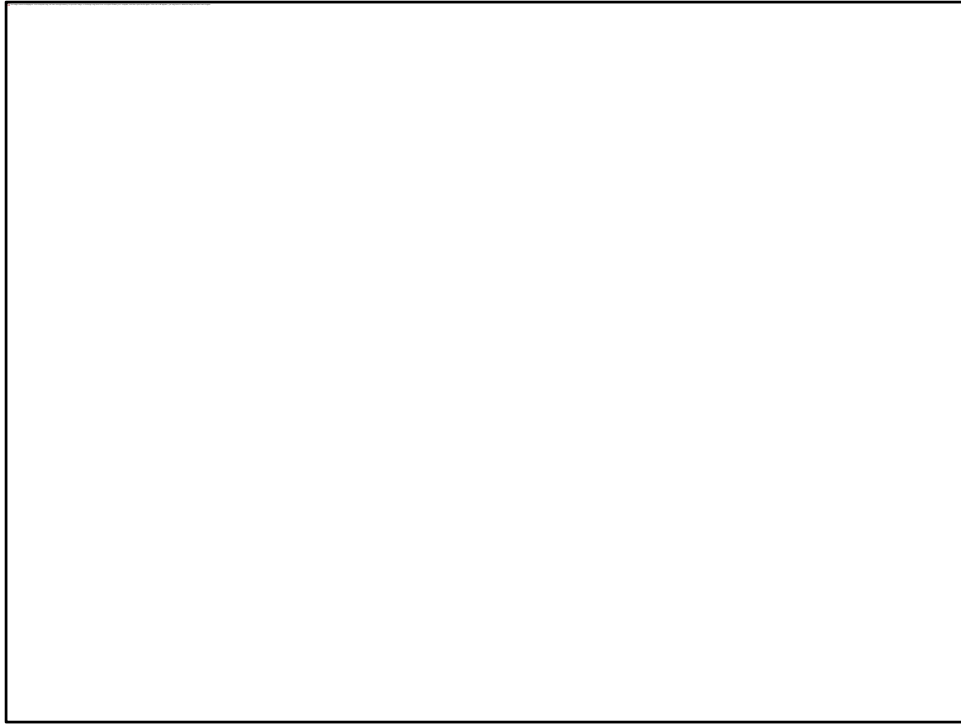


Elephants are notorious for refusing medications and many food items have been tried – apples, twinkies and beer to name a few. On the right is a peanut butter, jelly, and isoniazid sandwich. Many food items will work for a time but few will work for the entire year of treatment. We learned from the index herd that adequate blood levels cannot be achieved by simply putting medications over food. The drugs must be administered directly.

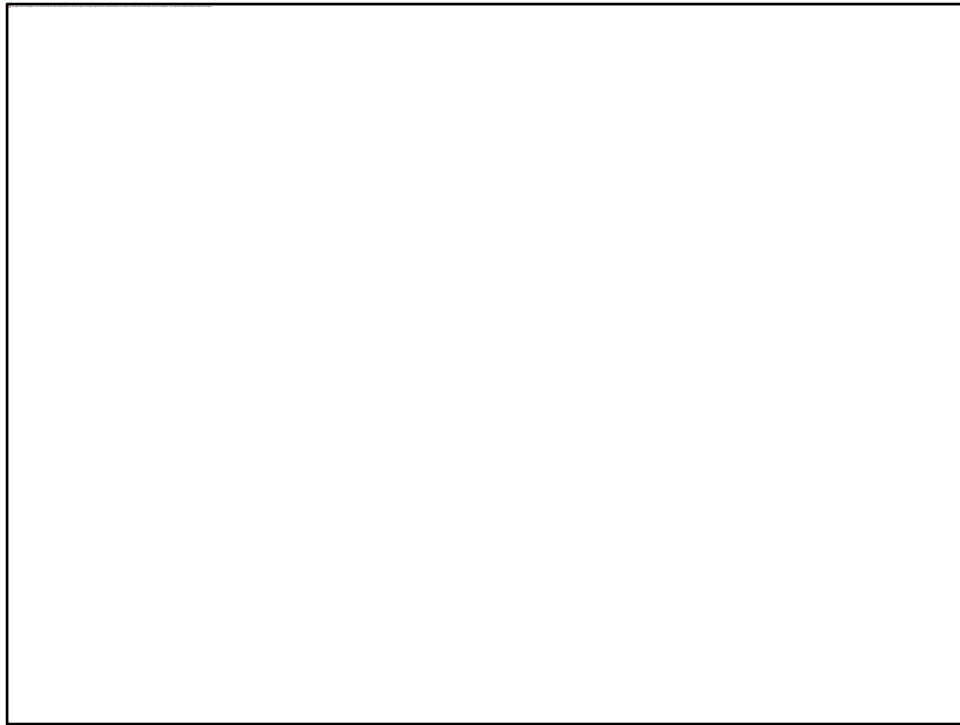


While we know we can achieve blood levels in elephants comparable to those in humans we don't really know if these levels are adequate to cure the disease. We may not be able to cure long-standing infections in older elephants with advanced lesions. Some elephants do experience side effects. In my experience, loss of appetite is the most common and if drugs are withdrawn for a few days and then increased to full dose gradually, the problem usually resolves.

The new serological tests may help us to identify infected elephants earlier and initiate treatment. I believe that early treatment can be effective. We can use the MAPIA to monitor response to treatment but we lack a test that confirms cure. A few treated elephants in the U.S. have gone to necropsy and no lesions were found but we still need to follow a large cohort and perform thorough postmortem examinations to know for sure which were cured and how they were treated. Drug resistance is another concern and there have been a few cases of drug resistant TB in the U.S.



We have learned a great deal about TB in elephants over the past 15 years, clearly more research is needed.

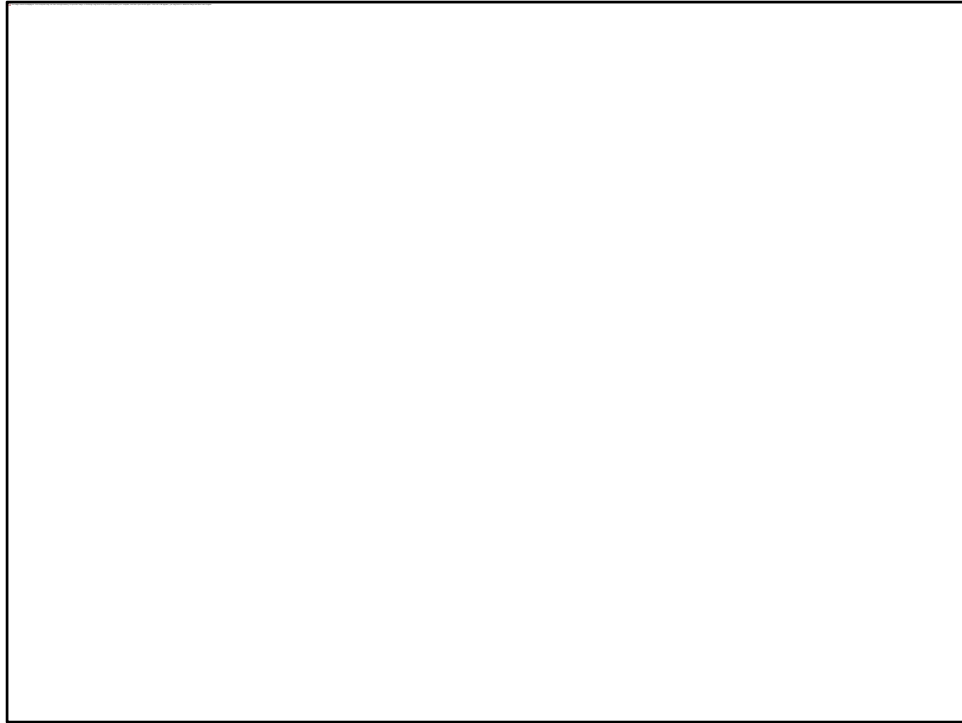


From a diagnostic standpoint we need more options. Culture of trunk wash samples is less than ideal but perhaps we would get better results if we had a different collection procedure that gave us a sample from deeper in the respiratory tract. A rapid method to detect shedding like this TB breathalyser would be extremely useful and could allow suspect elephants to be sampled daily.

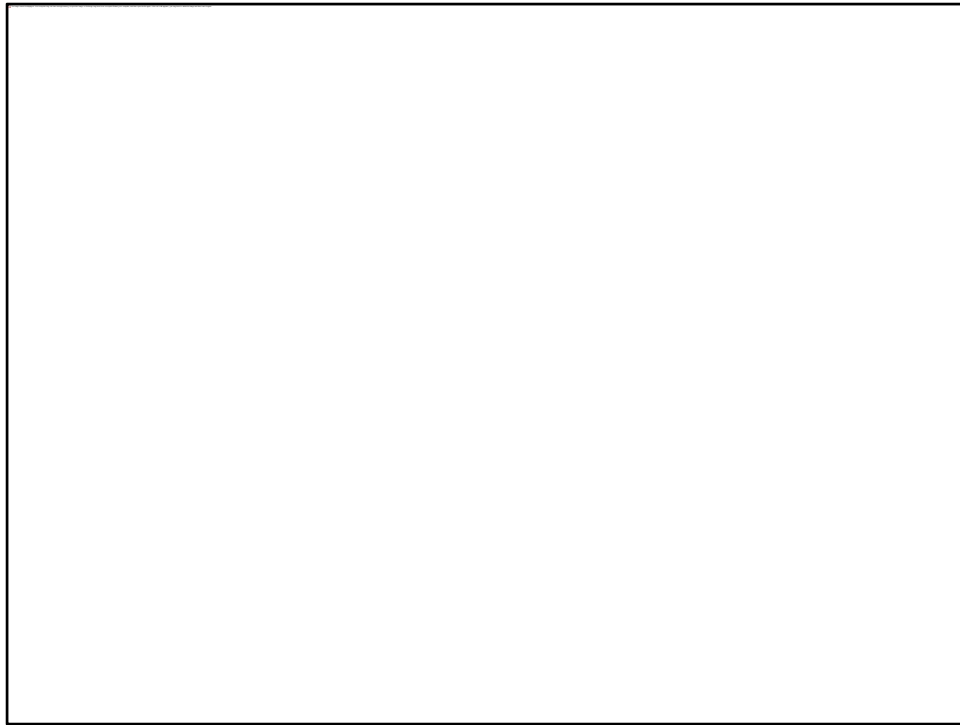
We don't really know if elephants get latent TB or if our current diagnostics just fail to detect active disease so this is another avenue for research. It would be great if there was a way to xray or otherwise image eleph chests but so far that has not been possible.

In elephants that are not showing overt clinical signs we don't have a way to determine the stage of disease. Elephants are wild animals in captivity – they have not really been domesticated. In this regard they are like other wild animals that tend to hide signs until the disease is very advanced. Perhaps developing pulmonary function tests for eleph could be useful. And we need further studies on the immune system.





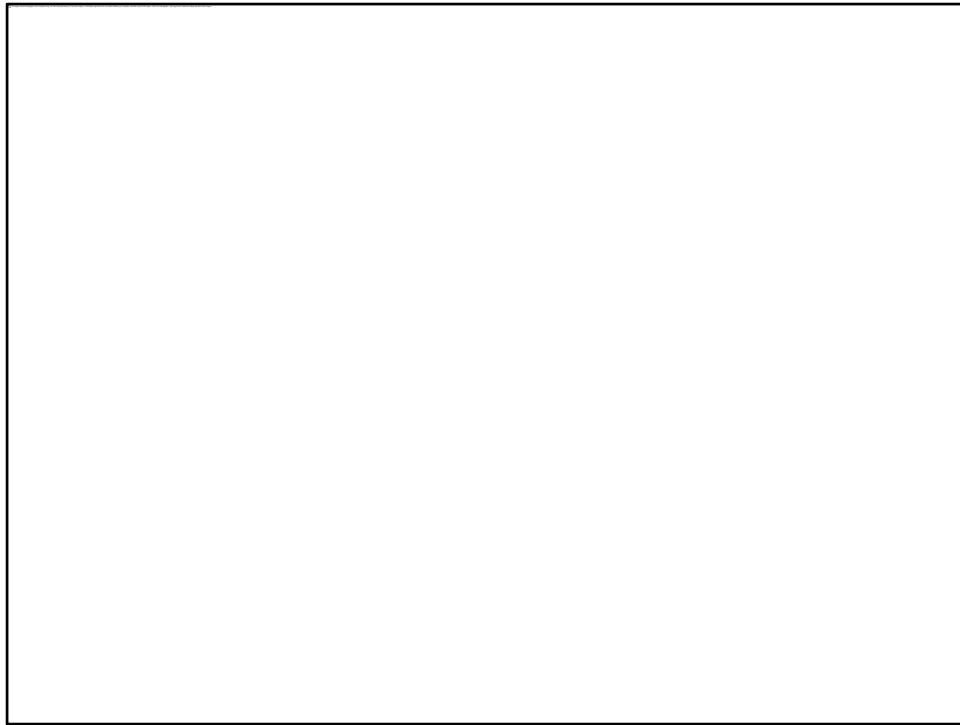
Trained Gambian rats have been used to diagnose TB with greater accuracy than humans looking at smears. Using volatiles to diagnose TB and other diseases is being explored in humans and may one day have application to elephants.



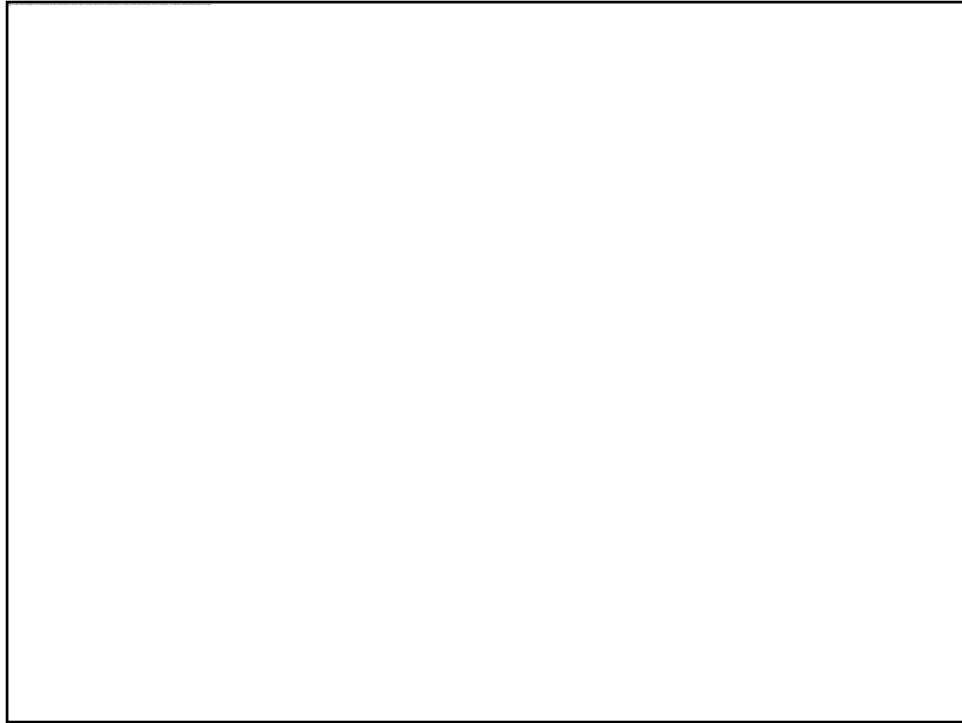
In the area of treatment one of our most urgent needs is better tasting medications or better ways to disguise the taste of the drugs some of which are very bitter. Right now we can give medications orally and rectally but what about inhalation therapy or transdermal application?

We need more PK studies. The studies we have published so far pooled existing data but we really need well designed prospective studies.

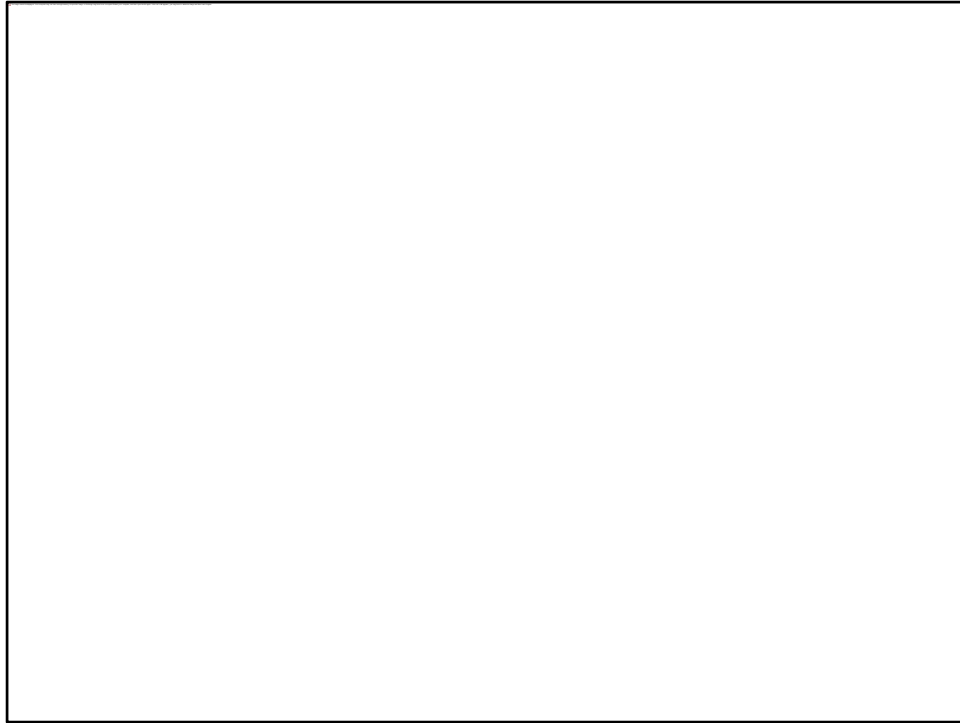
We also need additional tests to monitor response to treatment.



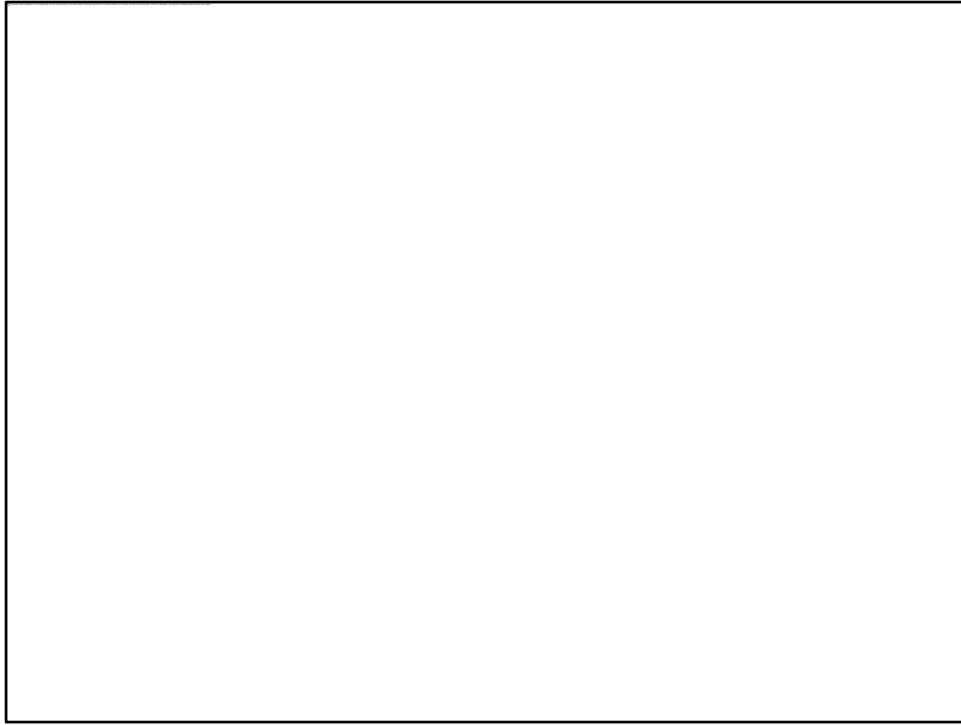
TB is the perfect example of the trend in veterinary and human medicine to look at disease from a One-Health standpoint. TB impacts humans, domestic livestock, and wildlife in an ever-narrowing interface. Addressing a disease of this nature requires a multi-disciplinary effort.



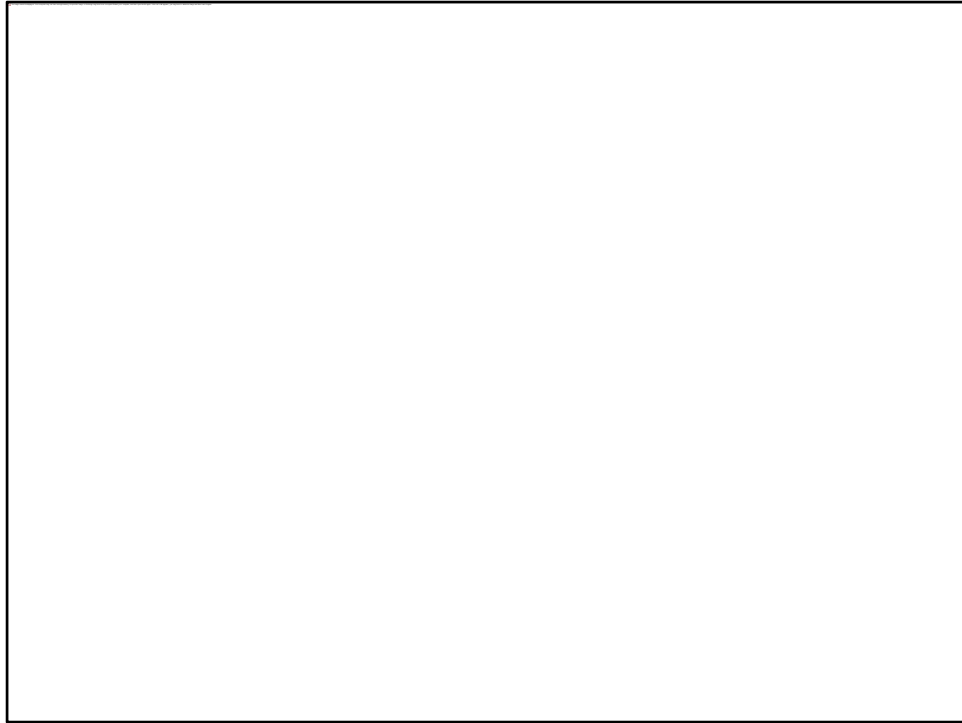
I would like to acknowledge the organizations and zoos that that have helped to support Elephant Care International's TB work in the U.S and in Asia. I would especially like to thank the USFWS Asian Elephant Conservation Fund that has supported much of our work in Nepal.



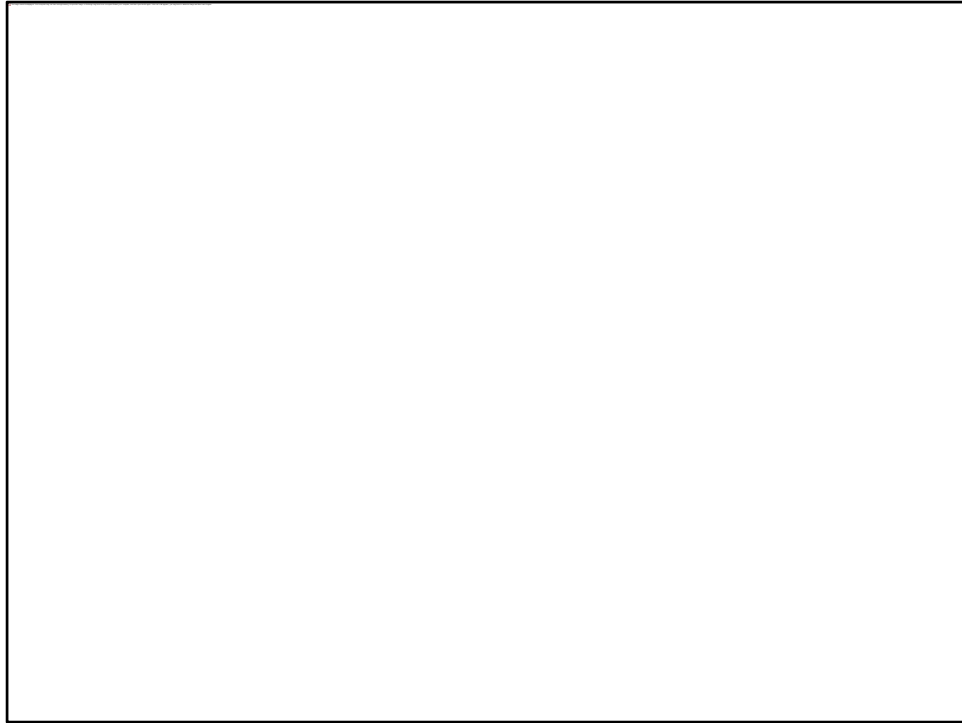
I would also like to acknowledge all of the individuals that have contributed to our knowledge of TB in elephants over the years. I generated this list from the many publications that I mentioned today. There are a lot of names here and I apologize if I have overlooked anyone.



Here are more individuals. I think you can see by this list that a tremendous effort has gone into this issue.

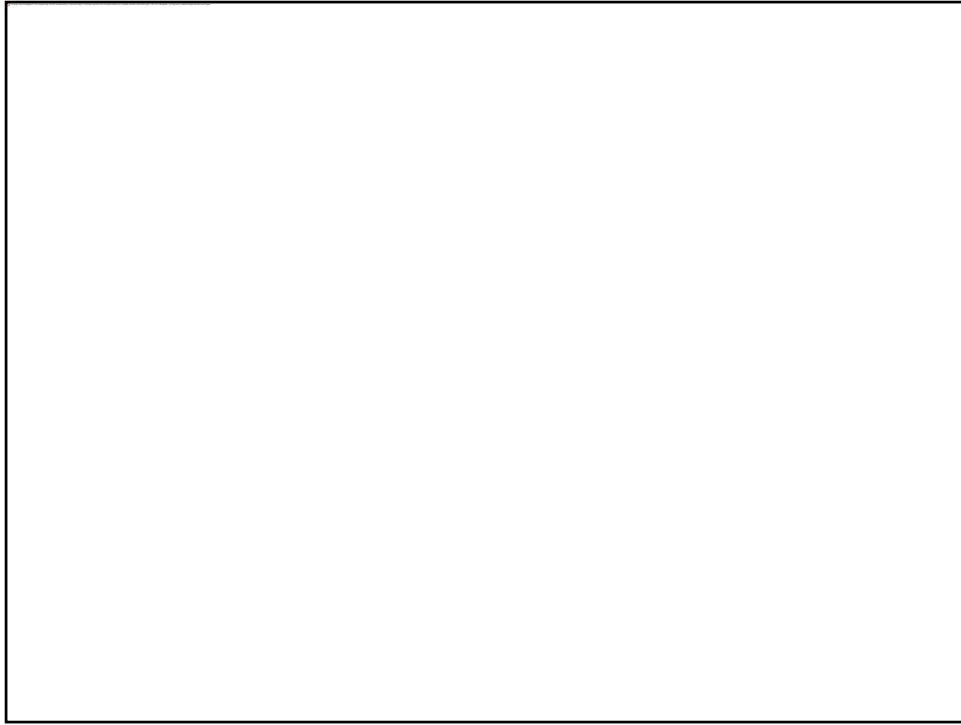


I would also like to acknowledge facilities. When TB emerged in 1996 many of the individuals on the preceding slide and many of the facilities listed on this slide and the next worked collaboratively to address the problem of TB. New collaborations have formed but many have dissolved.

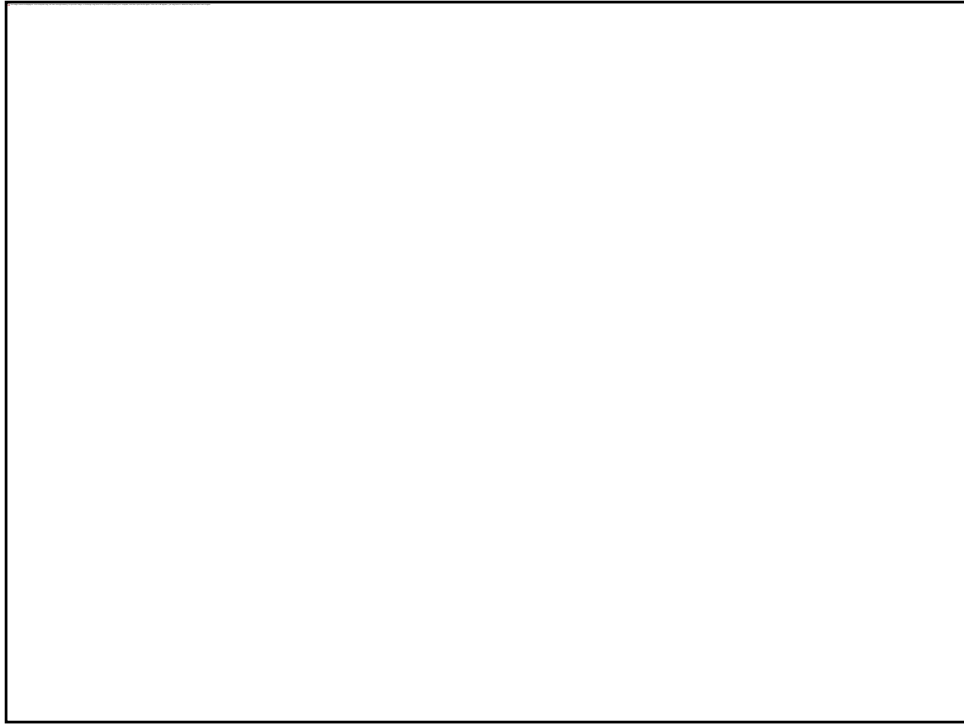


It is my sincere hope that this conference will inspire us to all work together again. Only by doing so can we hope to move forward on this issue and truly be of service to the elephants that we collectively care for.





If you have any questions please hold them for the panel at the end of the day.



Thank-you for your attention!