We Herd You had TB

ND Public Health Nursing Conference
July 16, 2015

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North Dakota Department of Health
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Custer Health

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Objectives

- Describe the transmission of *Mycobacterium bovis* in humans and in animals.
- Explain methods used in testing for *Mycobacterium bovis* in humans vs. animals.
- Explain what genotyping is and the important role it plays in understanding tuberculosis transmission modes.

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THE ORGANISM

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What is *Mycobacterium bovis*?

- In the United States, the majority of tuberculosis (TB) cases in people are caused by *Mycobacterium tuberculosis (M. tuberculosis). Mycobacterium bovis (M. bovis)* is another mycobacterium that can cause TB disease in people.
- *M. bovis* is most commonly found in cattle and other animals such as bison, elk, and deer. In people, *M. bovis* causes TB disease that can affect the lungs, lymph nodes, and other parts of the body.

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The Organism

- *Mycobacterium bovis*
  - Gram positive bacterium
  - Acid fast
  - *M. tuberculosis* complex
- Persists in the environment
  - Cold, dark, moist conditions

***M. tuberculosis* complex**

- *M. tuberculosis*
- *M. africanum*
- *M. canettii*
- *M. caprae*
- *M. bovis*
- *M. pinnipedii*
- *M. microti*

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HISTORY

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History

- 1898
  - *M. bovis, M. tuberculosis* differentiated
- Early 1900s
  - TB was leading cause of death in U.S.
  - 10% of cases likely caused by *M. bovis*
- 1917
  - State-Federal Cooperative Bovine TB Program established

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EPIDEMIOLOGY

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How Common is *M. bovis*?

- *M. bovis* causes a relatively small proportion, less than 2%, of the total number of cases of TB disease in the United States.
  - Less than 230 human TB cases per year
- *M. bovis* transmission from cattle to people was once common in the United States. This has been greatly reduced by decades of disease control in cattle and by routine pasteurization of cow's milk

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TRANSMISSION

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How are people infected with *M. bovis?*

- People are most commonly infected with *M. bovis* by eating or drinking contaminated, ***unpasteurized*** dairy products. The pasteurization process, which destroys disease-causing organisms in milk by rapidly heating and then cooling the milk, eliminates *M. bovis* from milk products.
- Infection can also occur from direct contact with a wound, such as what might occur during slaughter or hunting, or by inhaling the bacteria in air exhaled by animals infected with *M. bovis.*

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Transmission in Humans

- Ingestion
  - Unpasteurized dairy products
    - 145º F for 30 minutes, 161º F for 15 seconds to kill bacteria
  - Raw or undercooked meat
    - Cook meat to 149º F for 12-18 seconds to kill bacteria
- Aerosol
- Breaks in the skin
- Person-to-person
  - Rarely
  - Immunosuppressed

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DISEASE IN ANIMALS

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Species Affected

- Maintenance hosts
  - Cattle
  - Opossums, ferrets
  - Badgers
  - Bison, elk
  - Kudu, African buffalo
  - White-tailed deer
- Spillover hosts
  - Sheep, goats, horses, pigs, dogs, others

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Disease in Cattle

- Clinical signs
  - Develop over months
  - May become dormant, reactivate
- Early stage may be asymptomatic
- Late stage
  - Progressive emaciation
  - Fever, weakness, lack of appetite
  - Moist cough
  - Enlarged, draining lymph nodes

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Disease in Other Animals

- Cats
  - Weight loss, fever, dehydration, vomiting, diarrhea, dough
  - Enlarged lymph nodes, skin infections
  - Deformity of forehead/bridge of nose
  - Blindness, retinal detachment
- Brush-tailed opossums, badgers
  - Pulmonary disease

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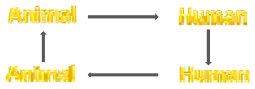
Mycobacteria

- Both *M tuberculosis* and *M bovis* cause disease in humans and in animals
- The disease can be spread from:



- Direct transmission from animals to humans through the air is thought to be rare, but *M. bovis* can be spread directly from person to person when people with the disease in their lungs cough or sneeze.

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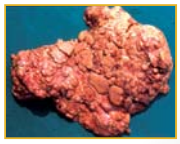
Post Mortem Lesions

- Granulomas (tubercles)
  - Appearance
    - Yellow
    - Caseous
    - Calcified
    - May resemble abscesses
  - Found in lymph nodes and organs



Photos courtesy of the CDC

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A Case of *Mycobacterium bovis*

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July 2013

- Dairy Worker
- Presented to local Nurse Practitioner
  - Cold/Flu symptom
  - Lab tests done
    - Elevated glucose
      - 15% of adult TB cases worldwide also have diabetes
      - Diabetes triples the chances of developing TB
- Referred to Infectious Disease Physician

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Why was TB Suspected?

- Classic TB Symptoms
  - Cold-like symptoms
  - Coughing
  - Fever
  - Chills
  - Unexplained weight loss
  - Sputum production

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Testing

- Sputum samples X 2 collected
  - 1+ AFB Smear
  - NAAT (nucleic acid amplification test) positive for MTB
  - CXR and CT revealed cavitation with infiltrates
  - Culture MTB positive

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CONTRACT WITH COAL COUNTRY

Direct Observed Therapy

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- **DOT**
  - Isoniazid (INH) 1 tablet
  - Rifampin (RIF) 2 tablets
  - Ethambutol (EMB) 3 tablets
  - Pyrazinamide (PZA) 3 tablets
  - B6 1 tablet

  INH, RIF, EMB and PZA given for 2 months
  INH, RIF and B6 given for 4-7 months

  Nurse M-Th, Pharm Tech Friday

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Contact Investigation

- Custer Health – Mandan, NDDoH
- HIPPA Concerns –
  - Non-English
  - BOAH
  - Employer
- Met with worker who signed a release allowing us to share information with his employer and the North Dakota Board of Animal Health

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Patient Interview

- Dairy hand acted as interpreter to translated questions
- Reported he has been working at the same farm in North Dakota for the past 5 years
- Spends 10 months working on the dairy farm/2 months at his home in Mexico
- Living with 3 other guys in a small mobile home
- Job description includes milking 150 cows twice a day

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End of July 2013 Contact Investigation/Screening

- Tested 13 named contacts
  - 11 QFT, 2 positive
  - 2TST, no reactors
  - Family in Mexico was screened, all negative

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August

- 8-6-13, new sputum samples collected to check for conversion
- Still has a productive cough
- No chills or fever
- Appetite is improving
- AFB smear negative

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October

- Notified the North Dakota Department of Agriculture-Animal Health Division and Board of Animal Health (NDDoA-AHD and BoAH)
  - **One Health** approach – a combined approach to animal, human and environmental health, and the idea that we can all benefit from working together to value and solve the health problems of the world and reduce the risk of the next pandemic.
- Dr. Susan Keller, Dr. Larry Schuler and the NDDoH visited the dairy farm to educate the owner of the dairy farm the importance of testing his herd
- Screened 11 negative contacts
  - No new reactors

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November

- Difficulty in identifying the causative agent lead to a delay in appropriate treatment. Culture results confirming *M.bovis* were not available until mid-November.
- Too late to test for *M. bovis* in urine
- Have since found out media used to identify *M. bovis* requires the addition of pyruvate to facilitate growth
- Sensitivity results showed the expected pyrazinamide resistance but also a low level resistance to INH.

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December

- Consult with Mayo
- Medications changed
  - RIF, EMB, and B6; added a second line drug -Moxifloxicin
- Treatment extended an additional 5 months (basically starting over)

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EDUCATION OPPORTUNITY

Drinking unpasteurized milk and milk products

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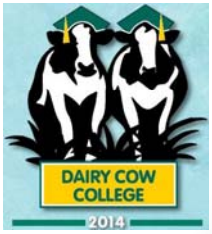
Cow College

- Dairy Cow College is a joint educational effort of the North Dakota State University Extension Service and Midwest Dairy Association (MDA) in cooperation with the NDSU Animal Sciences Department and the Extension offices in Barnes, Dunn, Emmons, McIntosh, Morton, Oliver, Stark/Billings and Stutsman counties.
  - Linton
  - Dickinson
  - New Salem
  - Jamestown



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January

- Notified ***Cure TB***
  - Helped line up services once he returned to Mexico
- Worked with provider to ensure medication compliance
- Medications provided to patient (3 month supply)
- Letter written from health department for "proof of need"

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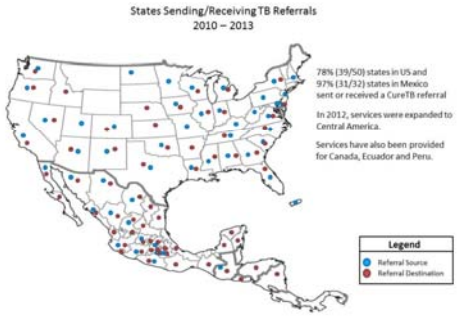
CURE TB



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February –March 2014

- Cure TB provided DOT and care while he was in Mexico with his family

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April 2014

- Returned to US
- Continued to work on dairy farm
- DOT resumes
- Patient completed treatment in September 2014

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Genotype Results

Spoligotype	MIRU	MIRU2	GENType	PCRType
703377400001771	227425113434	423-44223245	G06137	PCR00044
777776777760601	224325153323	244434423433	G24585	PCR00015
777000377760771	226125113322	143134423327	G23961	PCR08238
2640737777777600	232224253322	253472453214	G02290	PCR01217

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CATTLE INVESTIGATION

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North Dakota Tuberculosis Free -since 1976

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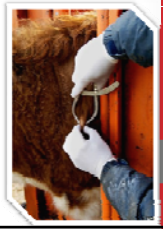
TB tests

- Caudal Fold Test (CFT)
  - Screening Test
  - Injected in caudal fold of tail, read 72 hours later
- Comparative Cervical Test (CCT)
  - Only certified state and federal regulatory veterinarians conduct the CCT test.
  - Follow-up Test
  - Avian (non-pathogenic) and Bovine (pathogenic) TB injected in two areas on neck
  - Skin thickness measured before and 72 hours later
- Bovigam/Gamma Interferon
  - Blood Test
  - Also used as a follow-up test



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ND Dairy Investigation

- Notified by ND Dept. of Health in October regarding TB positive worker at an Oliver County Dairy
  - Later identified as M. bovis infection
- Initiated communication with owner who voluntarily agreed to a whole herd test

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Testing Begins

- 11-5-13 Tested all dairy cattle 6 months of age and older
  - 319 CF tests
    - 11 CF (caudal fold) responders
      - 1 CCT (Comparative Cervical Test) suspect heifer
      - Quarantine issued 11-12-13
  - Suspect heifer slaughtered and necropsied on 11-11-13
    - NGL (no gross lesions) on necropsy
    - Lesion noted in mediastinal LN (lymph node) on Histopathology
    - PCR positive on 11-18-13
    - Culture positive on 12-16-13

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ND Dairy Investigation

- Remaining 10 CF responders (CCT negative) sent to slaughter on 12-11-13
  - A 2nd cow was found PCR + on 12-18-13, culture -
  - A 3rd cow was PCR -, culture + on 1-24-14
- Three CF negative cull cows sent to slaughter on 12-11-13
  - No gross lesions

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Additional Testing

- Producer also has beef cattle
  - Some contact between beef and dairy herds
  - First test of beef cattle completed on 1-13-14
  - All cattle ≥ 60 days of age (161 head)
    - No CF responders

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Herd Testing

- 1-17-14 Second Dairy Herd test completed
  - All dairy cattle ≥60 days of age
    - 360 head
  - 6 CF responders
    - Shipped to slaughter 2-5-14
    - No gross lesions, not histopath compatible
    - Cultures negative 4-8-14
- **This is the first negative herd test**

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Additional testing

- 16 CF negative cull cattle shipped to slaughter with responders
  - 1 Dairy cow
  - 15 Beef cattle
- All NGL (no gross lesions)

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Herd Testing

- 4-28-14 WHT completed
  - All dairy and beef cattle ≥60 days of age
  - 562 head
  - 4 CF responders
    - 3 dairy, 1 beef
- 5-7-14 TB ELISA sample collected
  - All dairy animals which had calved at least once
  - 172 head
  - 4 positive results
    - One of these was also a CF responder

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Herd Testing

- 7 Suspects from CF and ELISA testing were sent to slaughter on 5-21-14
  - NGL, histo negative
  - Cultures negative on July 21, 2014
- 12 CF negative cull cattle sent on the same load
  - One abnormal lymph node
    - Histo negative, cultures negative on July 21, 2014
- Second negative whole herd test

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Additional Testing

- July 24, 2014
  - 31 CF negative cattle shipped to slaughter on VS-127
    - 25 steers, 6 cull cows
  - All NGL
- September 5, 2014
  - 29 CF negative cattle shipped to slaughter on VS-127
    - 18 steers, 3 heifers, 8 cull cows
  - All NGL

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Herd Testing

- 10-31-14 Herd test of all beef and dairy cattle
  - All dairy and beef cattle 6 months of age
  - 494 head
  - 5 CF responders
    - Dairy cattle
- 11-3-14 CCT completed on responders
  - All negative

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Herd Update

- Quarantine released on 11-4-14
- Herd plan requires annual tests for 5 years

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Summary

- 24 suspects identified in three herd tests via CFT or ELISA
  - 1 PCR positive, culture positive from 1st herd test
  - 1 PCR positive, culture negative from 1st herd test
  - 1 PCR negative, culture positive from 1st herd test
- 91 test negative cattle shipped to slaughter on VS-127

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Epidemiology

- Positive worker originated from TB-endemic region
- Worker had direct contact with cattle
- Cattle that were confirmed positive were born in the ND herd
- No history of contact with rodeo or roping cattle
- Limited herd introductions

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Epidemiology

- Contact herd A test completed 4-7-14
  - Fenceline contact
  - 41 head (≥12 months of age)
    - 3 CF responders
    - 1 CCT suspect
      - Slaughtered 4-15-14
      - NGL, histo negative, cultures negative 6-10-14
- Contact herd B test completed 5-16-14
  - Fenceline contact
  - 199 head (≥12 months of age)
    - 7 CF responders, all CCT negative

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Surveillance

- USDA-Wildlife Services assisting with surveillance
  - 4 Feral barn cats removed, all tests negative
  - Limited wildlife in area
  - Surveillance will continue
- ND Game and Fish Department
  - Surveillance planned in wild deer during fall season

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NATIONAL VETERINARY SERVICES LABORATORIES

Suelee Robbe-Austerman, DVM PhD

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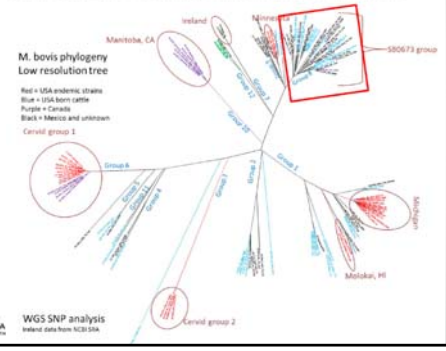
National Veterinary Services Laboratories

SNP Table detailing the SNP differences between the most closely related isolates. An in depth analysis of the 3 ND isolates show no evidence the 14 SNPs that are divergent (in positions 1264009 through 517735) exist in any of the isolates at low levels as a mixed population, consequently direction of transmission cannot be resolved by these data.

	1264009	1264383	1264789	1265429	1265502	1327987	1759059	2469082	3156270	3211060	3417058	3517522	3798860	4095660	4762227	4898204	4918024	5156269	5164183	5167171	5167243	5555374	4455081	681503	1729142	1762103	1848	2264614	3432760	4992258	517735
reference_pos																															
reference_call	G	A	A	C	T	G	G	G	G	C	C	G	G	C	A	G	C	A	T	T	T	G	C	A	A	C	G	G	G	G	A
12-037a_ZAC_TX_Fed	A	G	G	T	G	A	A	A	A	T	G	A	C	T	C	G	C	C	T	T	T	G	C	A	A	C	G	G	G	A	C
12-800U_ZAC_NB_Fed	A	G	G	T	C	A	A	A	A	T	G	A	C	T	A	G	G	T	T	T	G	C	A	A	C	G	G	G	G	A	C
11-7341a_ND_Dairy_13-6-1	A	G	G	T	C	G	G	G	G	C	C	G	G	C	A	G	C	A	G	T	C	A	G	G	A	C	G	G	G	A	C
11-7341a_ND_Human	A	G	G	T	C	G	G	G	G	C	C	G	G	C	A	G	C	A	G	T	C	A	G	G	A	C	G	G	G	A	C
11-800U_ND_Dairy_13-6-2	A	G	G	T	G	G	G	G	G	C	C	G	G	C	A	G	C	G	T	T	T	G	C	A	G	G	A	A	G	G	G

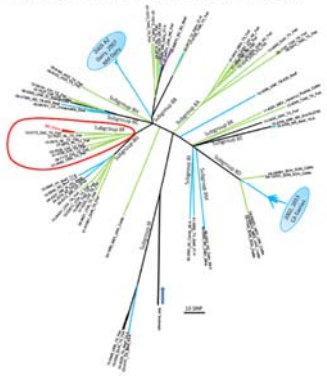
Genotype Results

Low resolution tree of M. bovis isolates. The isolate of interest is located in group 8 which is within the red box.

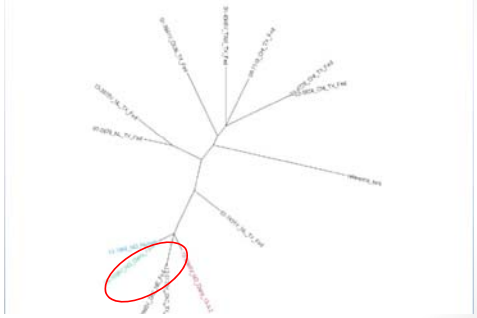


WGS SNP analysis
Ireland data from NCBI SRA

Low resolution phylogenetic tree of Group 8. USA origin cattle are blue, and Mexican origin cattle are in green. The isolates from the 2013 ND Dairy and the human associated with this dairy are located in subgroup 8F.



High resolution tree of subgroup 8F. The isolate from the human associated with the 2013 ND dairy matches one of the cattle isolates recovered from this dairy. The other isolate recovered from the 2013 ND Dairy-A contains 7 additional SNPs from the common ancestor. The Zacatecas isolates are 10- 12 SNPs from this node.



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reference_pos	2614651	2710978	4439978	450424	900102	1327787	1719053	2403082	3116273	3211263	3437558	3517522	3708363	605260	952237	1008259	1098204	1364259	1414911	1547971	2873242	3533174	4019286	4233503	1729543	1762102	18898	2054614	3332263	4002258	517735
reference_call	G	A	A	C	T	G	G	G	G	C	C	G	G	C	A	G	C	A	T	T	T	G	C	A	A	C	G	G	G	A	C
12-0171v_ZAC_TX_Feel	A	G	G	C	C	A	A	A	A	G	A	C	C	G	C	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C
12-0980v_ZAC_NB_Feel	A	G	A	C	C	A	A	A	A	G	A	C	C	A	A	C	G	T	T	T	G	C	A	A	C	G	G	G	A	C
13-7964v_ND_Dairy_13-A-1	A	G	G	C	C	G	G	G	G	C	C	G	G	C	A	G	C	A	G	C	C	A	G	G	A	C	G	G	A	C
13-7994_NCI_human	A	G	G	C	C	G	G	G	G	C	C	G	G	C	A	G	C	A	G	C	C	A	G	G	A	C	G	G	A	C
13-8366v_ND_Dairy_13-A-2	A	G	G	C	C	G	G	G	G	C	C	G	G	C	A	G	C	A	T	T	T	G	C	A	G	C	A	A	G	C

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Recent events in North Dakota have reminded us that TB remains an important public health threat.

The 2012-13 outbreak of tuberculosis in Grand Forks county moved North Dakota from being ranked 44th in the nation in 2011 to 7th in the nation in 2012 in the rate of TB disease within the human population.

In 2012, a case of bovine TB in a foreign-born farm worker resulted in an investigation in which several cows with which this worker was in contact were found to have tuberculosis.

These events highlight the need for North Dakotans, including farmers and ranchers, to be better informed about TB in order to make informed decisions to protect their own health, the health of their employees, and to avoid potential impact on their livelihood.

TB poses a special concern for livestock and dairy producers in that both types of TB bacteria that infect humans can also infect cattle and vice versa.

TB is most likely introduced into a cattle herd through two routes: first, by introducing an infected animal into a TB-free herd; and second, by exposing a herd to a person with active TB disease. Likewise people may become infected if exposed to animals infected with TB or unpasteurized products from TB infected animals.

For more information contact:

North Dakota Department of Agriculture
Division of Animal Health
701.328.2655
http://www.nd.gov/ndda/program/animal-health

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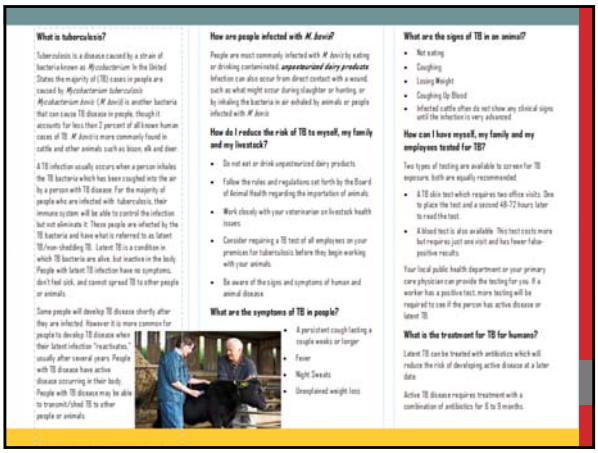
North Dakota Department of Health
Division of Disease Control
701.328.2378
http://www.ndhealth.gov/disease

Bovine Tuberculosis in Humans and Animals

>> Information for Livestock Producers

Get informed about tuberculosis. It's up to you to be aware of the symptoms of tuberculosis disease in people and what signs to look for in cattle.



What is tuberculosis?

Tuberculosis is a disease caused by a strain of bacteria known as *Mycobacterium*. In the United States the majority of (TB) cases in people are caused by *Mycobacterium tuberculosis*. *Mycobacterium bovis* (*M. bovis*) is another bacteria that can cause TB disease in people, though it accounts for less than 2 percent of all known human cases of TB. *M. bovis* is more commonly found in cattle and other animals such as bison, elk and deer.

A TB infection usually occurs when a person inhales the TB bacteria which has been coughed into the air by a person with TB disease. For the majority of people who are infected with tuberculosis, their immune system will be able to control the infection but not eliminate it. These people are infected by the TB bacteria and have what is referred to as latent TB/non-shedding TB. Latent TB is a condition in which TB bacteria are alive, but inactive in the body. People with latent TB infection have no symptoms, don't feel sick, and cannot spread TB to other people or animals.

Some people will develop TB disease shortly after they are infected. However it is more common for people to develop TB disease when their latent infection "reactivates," usually after several years. People with TB disease have active disease occurring in their body. People with TB disease may be able to transmit/shed TB to other people or animals.

How are people infected with *M. bovis*?

People are most commonly infected with *M. bovis* by eating or drinking contaminated, ***unpasteurized dairy products***. Infection can also occur from direct contact with a wound, such as what might occur during slaughter or hunting, or by inhaling the bacteria in air exhaled by animals or people infected with *M. bovis*.

How do I reduce the risk of TB to myself, my family and my livestock?

- Do not eat or drink unpasteurized dairy products
- Follow the rules and regulations set forth by the Board of Animal Health regarding the importation of animals
- Work closely with your veterinarian on livestock health issues
- Consider requiring a TB test of all employees on your premises for tuberculosis before they begin working with your animals
- Be aware of the signs and symptoms of human and animal disease

What are the symptoms of TB in people?

- A persistent cough lasting a couple weeks or longer
- Fever
- Night Sweats
- Unexplained weight loss

What are the signs of TB in an animal?

- Not eating
- Coughing
- Losing Weight
- Coughing Up Blood
- Infected cattle often do not show any clinical signs until the infection is very advanced

How can I have myself, my family and my employees tested for TB?

Two types of testing are available to screen for TB exposure, both are equally recommended.

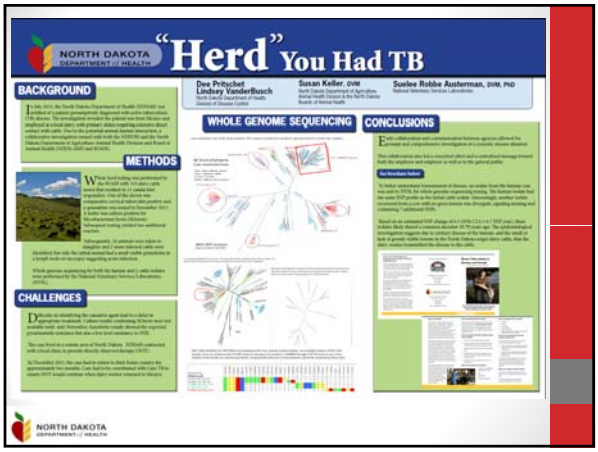
- A TB skin test which requires two office visits. One to place the test and a second 48-72 hours later to read the test.
- A blood test is also available. This test costs more but requires just one visit and has fewer false-positive results.

Your local public health department or your primary care physician can provide the testing for you. If a worker has a positive test, more testing will be required to see if the person has active disease or latent TB.

What is the treatment for TB for humans?

Latent TB can be treated with antibiotics which will reduce the risk of developing active disease at a later date.

Active TB disease requires treatment with a combination of antibiotics for 6 to 9 months.



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"Herd" You Had TB

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BACKGROUND

METHODS

CHALLENGES

WHOLE GENOME SEQUENCING

CONCLUSIONS

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Challenges

- Language barrier
- QFT testing
- Delay in organism identification
- Public Health 40 miles one way for DOT
- Work VISA
- Low Level Drug Resistance identified
  - Added length of treatment
  - Added cost

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Credits

Custer Health – Mandan
http://www.co.morton.nd.us/

Coal Country Community Health Center - Center
http://coalcountryhealth.com/

North Dakota Department of Agriculture-Animal Health Division and Board of Animal Health
http://www.nd.gov/ndda/program/animal-health

Veterinary Services – North Dakota Area Office
http://nvap.aphis.usda.gov/animal_health/area_offices/states/northdakota_info.html

National Veterinary Services Laboratories
http://www.aphis.usda.gov/wps/portal/aphis/ourfocus/animalhealth?1dmy&urile=wcm%3Apath%3A/aphis_content_library/sa_our_focus/sa_animal_health/sa_lab_information_services/sa_about_nvsl/ct_about_nvsl

Cure TB
http://www.sdcounty.ca.gov/hhsa/programs/phs/cure_tb

Center for Food Security and Public Health
Iowa State University
http://www.cfsph.iastate.edu/

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- Dr. Beth Carlson – Deputy State Veterinarian, BOAH

- Custer Health – Mandan
- Coal Country Community Health Center
- North Dakota Department of Agriculture-Animal Health Division and Board of Animal Health
- Veterinary Services – North Dakota Area Office
- National Veterinary Services Laboratories
- Cure TB

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Thank You!

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Questions???

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