United States Tuberculosis Zone Status

USDA Classification by Prevalence

TB Status as of October 2011:

- **TB Free**
- **Modified Accredited Advance**
- **Modified Accredited**

MAA

5.4MM cattle, 1.8MM milking

Eradication Program Started in 1917

**242 TB-affected herds from 1987 through June 30, 2014
AFFECTED HERDS, BY STATE, FY1998-2014**

Without Michigan’s 63 Herds

EIGHT states had TB affected herds since 1998

*Eight states detected TB in 2007 or later for the first time in many years

**65 herds 1998 to June 30, 2014: 49% beef, 37% dairy, 11% captive cervid, 3% mixed
Bovine TB Surveillance in California

A. Slaughter Surveillance

- Had four of top 40 US adult packing plants (95% of adults)
- Submit granulomas to CA lab (FY12-13) = 1,866 total
  - And split sample to NVLS
- Adults slaughtered in CA (FY12-13) = 875,333
  Rate = 4.4 submissions per 2,000 adults
- “Fat” cattle slaughtered in CA (FY12-13) = 834,852

B. Live Cattle TB Surveillance

- Private Veterinarians: 122,794 CFTs (1,413 accessions)
  Suspects = 1,346  Response Rate 1.1%
- Regulatory Veterinarians: 145,762 CFTs (105 herds)
  Suspects = 3,437  Response Rate 2.40%
California Bovine TB: 1999-2014

- 1999: Gain Bovine TB “Free Status”
- April 2003: Downgraded to “Mod. Accredited Advanced” (MAA) - bovine TB in 3 dairy herds
- April 2005: Regained “Free Status”
- Sept 2008: Downgraded to MAA - bovine TB in 3 dairy herds
- Jan 2009: 4th affected dairy herd
- Eligible for “Free” in 2012 but ...
- 2011-12: 3 affected dairy herds
- Feb 2013: 1 affected dairy herd

11 affected dairy herds in 11 years
## Eleven Bovine Tuberculosis Affected Herds Detected in California During the Last Eleven Years

<table>
<thead>
<tr>
<th>Premises</th>
<th>Date Herd Detected</th>
<th>How Detected</th>
<th>Approximate Herd Size</th>
<th># Infected Animals</th>
<th>Resolution</th>
<th>Epidemiology</th>
<th>Strain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dairy A Tulare Co.</td>
<td>May 2002</td>
<td>Slaughter trace</td>
<td>3,600 adults</td>
<td>53</td>
<td>Depopulated ~6,500 in November 2002; restocked</td>
<td>Unknown source; bulls from local breeders; replacements from out of state</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy B Tulare Co.</td>
<td>October 2007</td>
<td>Traces into and out of Dairy A (owner also a dealer)</td>
<td>2,000 adults</td>
<td>1</td>
<td>Depopulated ~5,000 in March 2003; restocked</td>
<td>Exposed to Dairy A</td>
<td>Genotype matched Dairy A</td>
</tr>
<tr>
<td>Dairy C Kings Co.</td>
<td>December 2002</td>
<td>Slaughter trace</td>
<td>400 adults</td>
<td>35</td>
<td>Depopulated ~600 in April 2003; restocked</td>
<td>Unknown source; purebred herd, imported ~60% of cattle from &quot;TB Free&quot; states</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy D Fresno Co.</td>
<td>December 2007</td>
<td>Slaughter trace</td>
<td>2,600 adults</td>
<td>5</td>
<td>Depopulated ~5,000 in August 2008; restocked</td>
<td>Unknown source; purebred herd, few trace-ins</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy E Fresno Co.</td>
<td>May 2008</td>
<td>Trace out of Dairy D</td>
<td>400 adults</td>
<td>1</td>
<td>Depopulated ~1,000 in August 2008; restocked on different premises</td>
<td>Infected cow moved from Dairy D (infected animal was CFT negative)</td>
<td>Genotype matched Dairy D</td>
</tr>
<tr>
<td>Dairy F Fresno Co.</td>
<td>May 2008</td>
<td>Trace into Dairy D</td>
<td>2,500 on one premises, 9,500 at other</td>
<td>1</td>
<td>Test and removal program; released from quarantine December 2009</td>
<td>Unknown source; purebred herd, very few trace-ins</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy G San Bernardino Co.</td>
<td>January 2009</td>
<td>Trace out of Dairy F</td>
<td>1,300 adults</td>
<td>1</td>
<td>Test and removal program; released from quarantine June 2010</td>
<td>Unknown source</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy H San Bernardino Co.</td>
<td>April 2011</td>
<td>Slaughter trace</td>
<td>6,000 (total)</td>
<td>9</td>
<td>Test and removal program; released from quarantine February 2013</td>
<td>Unknown source</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy I San Bernardino Co.</td>
<td>October 2011</td>
<td>Slaughter trace</td>
<td>1,500 adults</td>
<td>65</td>
<td>Depopulated ~3,300 in June 2012; not restocked</td>
<td>Unknown source; shared equipment with M-branded cattle in the past</td>
<td>New strain type</td>
</tr>
<tr>
<td>Dairy J San Bernardino Co.</td>
<td>December 2011</td>
<td>Contact with Dairy I</td>
<td>2,000 (total)</td>
<td>1</td>
<td>Test and removal program; released from quarantine November 2012</td>
<td>Exposed to Dairy I</td>
<td>Genotype matched Dairy I</td>
</tr>
<tr>
<td>Dairy K Tulare Co.</td>
<td>February 2013</td>
<td>Slaughter trace</td>
<td>2,200 adults</td>
<td>14</td>
<td>On test and removal program; anticipate release June 2014</td>
<td>Potentially exposed to Dairy A</td>
<td>Genotype matched Dairy A</td>
</tr>
</tbody>
</table>
11 Affected Dairy Herds in 11 years

- 6 detected by slaughter surveillance
- 5 detected by trace testing (2 were new strains!)

7 different *M. bovis* strain types =
7 introductions of bovine TB in California’s dairies

- Never found source of the 7 introductions
- Minimal spread from herds (4 w/same strain-type)
- CA is only MAA State in nation

How is *M. bovis* entering CA dairies?
Direct: Cattle (legal/illegal), wildlife, people, etc?
Fomite: Foodborne, airborne, environment, etc?
How can we mitigate these introductions?
February 2013 TB-Affected Herd

- Granuloma at AZ packing plant, September 2012
- NVSL “not compatible”: *M. bovis* cultured October 2012
- Trace: No individual ID collected, 1 of 151 rebranded cattle, 117 from CA (72 CA herds) 34 from other states
  - Breed DNA = Holstein female (62 CA herds)
  - *M. bovis* genotype matched strain from 2002 CA herd
- Focus “trace & 2002 related” affected herd
  - 2,200 cow dairy: test & removal plan (USDA model)
    - 14 TB-infected cattle removed (on first two tests)
  - Anticipate release July 2014 (after 5 whole herd tests)
  - Annual tests for 5 years after release quarantine
Investigation of 2013 Affected Herd

5 years: brand records + sale-yard records + private sales
• 11 dairy herds assoc. at calf ranch
• Trace ~4,400 cattle sold 2008-2013
• Epi investigated 99 herds
• Examined 36 herds for “brands from affected herd”
• Tested 65 trace herds (approx 106,000 cows)
• No spread of bovine TB detected
• Wildlife surveillance: negative
• Two USDA/APHIS/VS IMT assisted with investigation
• Public Health and OSHA oversight of dairy personnel

How did infection “hide” for 10 yrs (only ~1 SNP change)?
April 2013: Slaughter Trace

- Granuloma at California plant
- PCR positive; *M. bovis* cultured
  
  Inadequate ID to confidently trace
- Breed DNA: Jersey female
  
  Most likely: 3 yr old cow
From dispersed 500 cow San Diego Co dairy
  
  To California Jan 2012 from Pennsylvania dealer (origin untraceable)
- *M. bovis* genotype: unique strain (8th)
- Most closely resembles Mexican steer in TX in 2001 (26 SNPs difference)
- Investigations complete
September 2013: Slaughter Trace

- Granuloma at California plant (during TB-review)
- PCR positive; *M. bovis* cultured
- *M. bovis* genotype: same strain as April 2013 cow
- Trace (backtag): 12 year-old home raised beef cow
- Granuloma DNA matched to ½ sibling in herd
- Herd ~150 pairs quarantined: TB tested neg. twice
- Retest herd in 12 months
- Contacts & wildlife tested neg
- Herd was exposed to dairy (source of April 2013 sample)
- Which infected first?
November 2013: Slaughter Trace

- *M. bovis* cultured Dec 26, 2013
- Granuloma collected at California plant Nov 2013
- Trace: Utah backtag, but hair DNA not match TB-tissue DNA
- Female; Holstein
- *M. bovis* genotype: Unique strain (9th)
- Test: herds of origin of index and cattle on either side on packing-plant rail
- Utah tested 3 “most likely” herds: neg
- California tested two herds: neg
- Additional herds scheduled

52 adults (12%), 87 US fed (20%) & 295 Mexican origin (68%)

434 positive cases

52 adults (12%), 87 US fed (20%) & 295 Mexican origin (68%)
Percentage of Human TB cases Attributable to *M. bovis*, California, 2003-2011

*M. bovis* accounts for ~4% of all culture-positive TB cases in CA, compared to 1-2% nationally\(^1\)

Cases occurred in 32 counties, concentrated in southern California

In San Diego, 10% of TB cases are attributable to *M. bovis*

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\(^1\) Hlavsa, Clin Infect Disease, 2008
Human TB cases attributable to *M. bovis* by age group, California, 2003-2012

Count

% M. bovis

- <15 yrs
- 15-64 yrs
- 65+ yrs
- % M. bovis

## Spoligotype and 24 MIRU-VNTR Genotyping Results

<table>
<thead>
<tr>
<th>Year</th>
<th>Bovine M. bovis Case</th>
<th># Bovine Isolates Genotyped</th>
<th># CA Human Cases with Genotype</th>
<th>Any Epi Links?</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>Dairy D: Fresno</td>
<td>6</td>
<td>5</td>
<td>0 reside in affected counties, 2 recent US arrivals, 2/3 interviewed/no link accurate search neg</td>
</tr>
<tr>
<td>2007</td>
<td>Dairy F: Fresno</td>
<td>1</td>
<td>3</td>
<td>0 reside in county, 2 interviewed, no epi link accurate search neg</td>
</tr>
<tr>
<td>2009</td>
<td>Dairy G: San Bernardino</td>
<td>1</td>
<td>4</td>
<td>Accurate search neg</td>
</tr>
<tr>
<td>2011</td>
<td>Dairy H: San Bernardino</td>
<td>4</td>
<td>2</td>
<td>0 reside in county, accurate and DMV searches, no links</td>
</tr>
<tr>
<td>2011</td>
<td>Dairy H: San Bernardino</td>
<td>1*</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>2011</td>
<td>Dairy I: San Bernardino</td>
<td>23</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>2011</td>
<td>Dairy I: San Bernardino</td>
<td>1*</td>
<td>2</td>
<td>0 reside in county, accurate and DMV searches, no links</td>
</tr>
</tbody>
</table>

* 1-off MIRU-VNTR

16 people infected with strains that match 5 herd strains
Whole Genome Sequencing SNP Analysis

Red = USA endemic strains
Blue = USA born cattle
Purple = Canada
Black = Mexico and unknown

6,300 SNPs total
316 SNPs within MI

Cervid group 1
Cervid group 2

M. bovis phylogeny in US: low resolution tree

Matching results mean isolates are part of the same outbreak; temporal relationships can be better understood
Conclusions

1. New strains of *M. bovis* continue to be introduced into US cattle with no definitive source

2. Lack of individual cattle identification hinders tracing

3. Need active surveillance of adult and fed cattle

4. Need accurate & rapid tests to detect infection

5. *M. bovis* is a significant disease in people in California

6. Genotyping is helping us recognize disease relationships

7. Need more data to understand the epidemiology and mitigate the introduction of disease