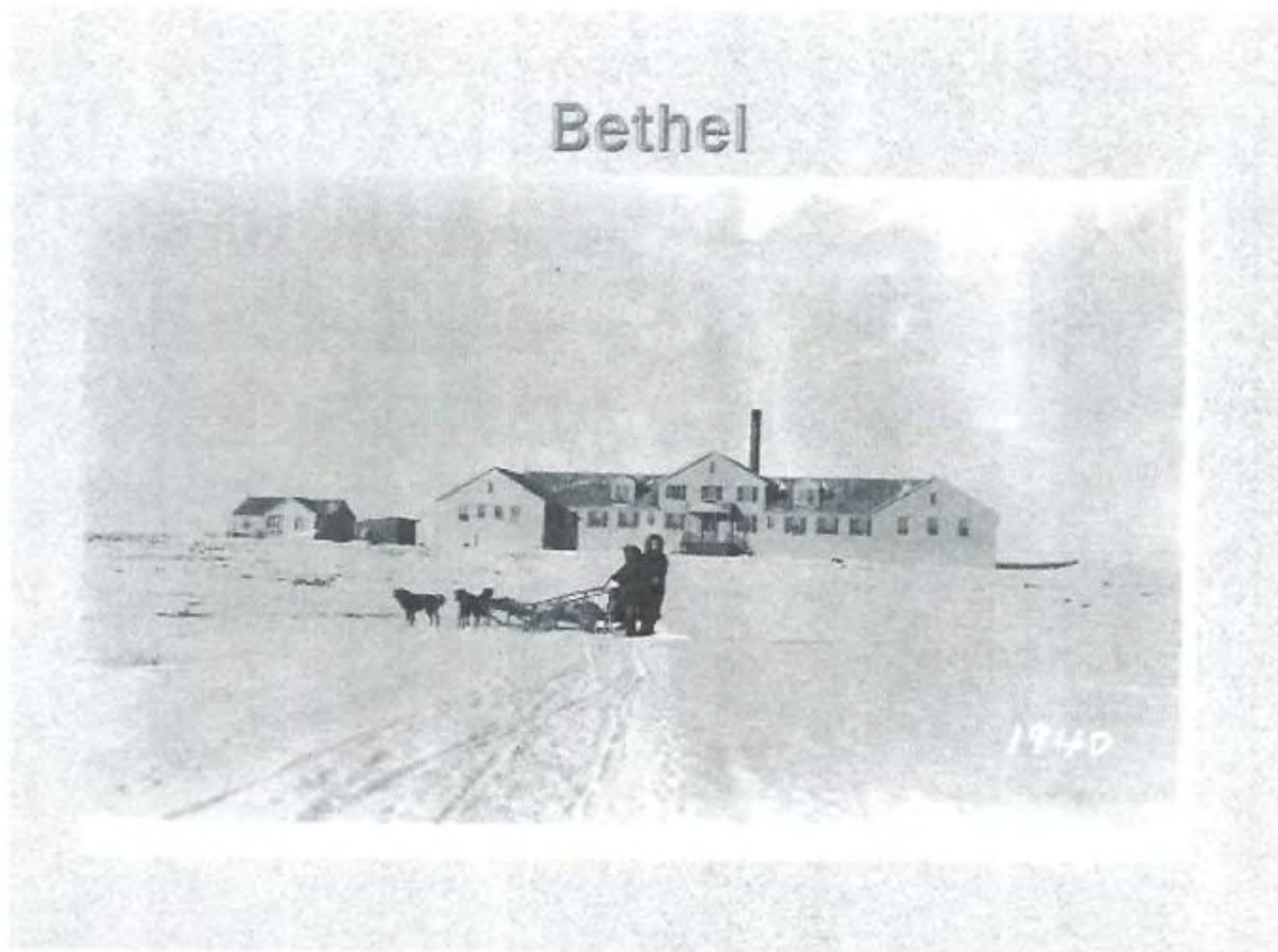


Bethel





High-tech TB in remote Alaska

rapid TB testing & what you need to know

Ron Bowerman, MD, MPH
Yukon-Kuskokwim Delta Regional Hospital
Bethel, Alaska



Disclosures: None



Lecture objectives

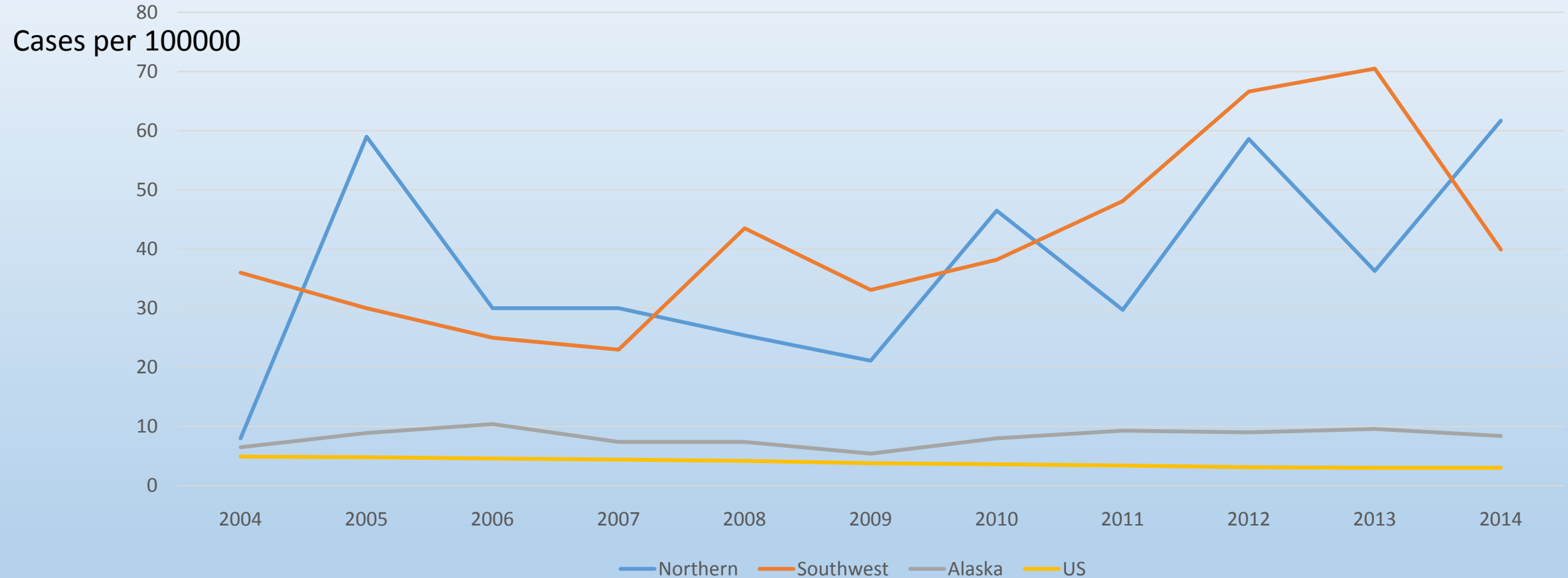
- Understand the reasons for the increased TB incidence in western Alaska
- What is the current practice of TB control in remote Alaska?
- How rapid TB testing technology might transform our current way of controlling TB in roadless Alaska and the world





Subregional Clinic Service Areas
 Emmonak
 St. Mary's
 Aniak
 Toksook Bay

Western* Alaska TB Incidence 2004-2014



*Northern+Southwest regions

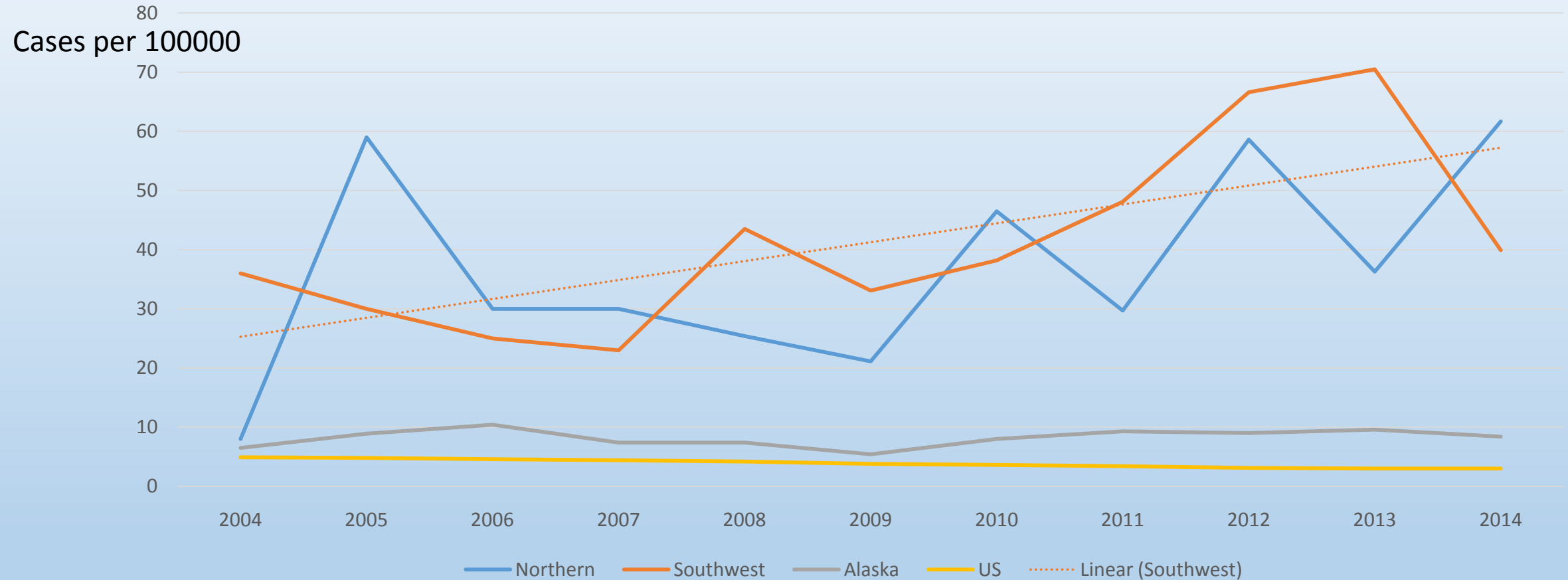
-Northern: North Slope, Maniilaq, and Norton Sound health districts

-Southwest: Y-K Delta, Bristol Bay, Eastern Aleutian, and Aleutian-Pribilof Islands health districts

Graph data from: 1. Alaska Epidemiology Bulletin No. 31; December 1, 2009. Available at: http://www.epi.alaska.gov/bulletins/docs/b2009_31.pdf

2. State of Alaska. Tuberculosis in Alaska 2013 Annual Report. Available at: http://www.epi.hss.state.ak.us/pubs/webtb/TB_Report_2013.pdf

Western* Alaska TB Incidence 2004-2014



*Northern+Southwest regions

-Northern: North Slope, Maniilaq, and Norton Sound health districts

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2. State of Alaska. Tuberculosis in Alaska 2013 Annual Report. Available at: http://www.epi.hss.state.ak.us/pubs/webtb/TB_Report_2013.pdf

Case 1: 25 y/o male cough x3 weeks

Presented to Yukon Clinic with above c/o from a coastal village



Case 1: continued

- Other Sx-purulent green sputum with streaks of blood
- Denies-fever, weight loss, night sweats, dyspnea
- Vitals: Afebrile, P 100, BP 121/78, RR 24
- PMHx-previously healthy, known +TST since 12 y/o, no LTBI tx
- CXR



RLL infiltrate, apical scarring noted

What's next?

- A. Discharge home on oral Augmentin, CXR f/u 6 wks
- B. Re-check TST and f/u in clinic 48-72hrs
- C. Admit to inpt for AFB sputum collection w/Airborne precautions
- D. Discharge home on oral Augmentin & collect AFB sputums x3

What's next?

- A. Discharge home on oral Augmentin, CXR f/u 6 wks
- B. Re-check TST and f/u in clinic 48-72hrs
- **C. Admit to inpt for AFB sputum collection w/Airborne precautions**
- D. Discharge home on oral Augmentin & collect AFB sputums x3

(actually all correct except B)

Answer is “C”

- Since active pulmonary TB is a concern, admit on airborne isolation, collect 3 AFB sputum and treat likely community acquired pneumonia (CAP)
- 6 days later due to weekend delay, State Lab reports all 3 AFB Neg, MTB cultures are pending
- The patient is sent home via plane on continued CAP treatment and fully recovers

This patient might have been DC home with surgical face as a Bethel resident with these stable vitals and reliable

A photograph of a forest scene. In the foreground, a tree with bright yellow-green leaves is prominent. The background shows a dense forest of taller trees, some with dark trunks, and a glimpse of a mountain range in the distance. The overall lighting is bright, suggesting a sunny day.

Tuberculosis

a quick review

Mycobacterium tuberculosis

Obligate aerobe

Facultative intracellular pathogen

Infects macrophages

Slow growing

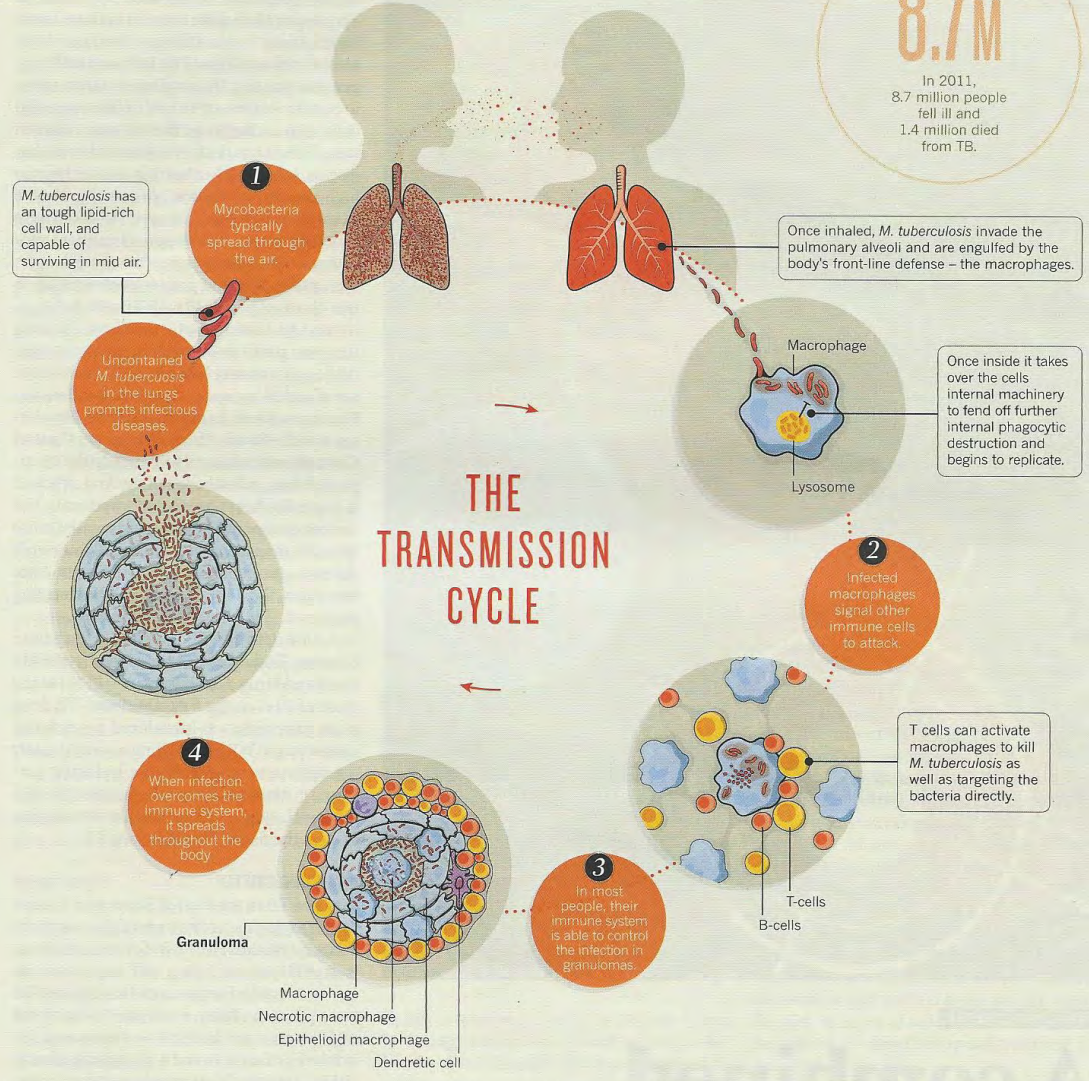
Hydrophobic → unable to gram stain

Acid-fast bacilli



8.7M

In 2011,
8.7 million people
fell ill and
1.4 million died
from TB.



1

Transmission
People with active disease develop symptoms such as a cough, which propels bacteria into the air where it can be inhaled by others. Tuberculosis must be diagnosed and treated as soon as possible to render the person non-infectious and prevent the spread of disease (see 'Control issues', page S16).

2

Immune response
The BCG vaccine offers little protection to adolescents and young adults from the form of the disease that causes most deaths. Any effective vaccine will need to harness T cells, but scientists are still looking for correlates of protection (see 'An age-old problem', page S8).

3

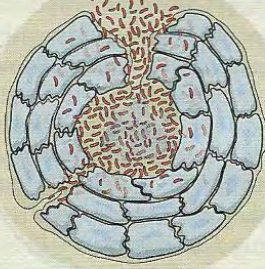
Latency
M. tuberculosis can be contained within granulomas for years. It is thought that latency may encompass a spectrum of states, from people who have completely controlled the disease, to those with undetected, subclinical disease (see 'Latency: A sleeping giant', page S14).

4

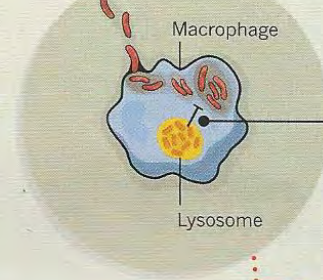
Activation
If the immune system weakens as a person ages or contracts HIV infection, for example, bacterial replication can overcome the immune system and granuloma breaks down, releasing *M. tuberculosis* into the lungs and advancing disease (see 'A combined effort', page S4).

WORLD TUBERCULOSIS REPORT 2012. LIENHARDT, C. ET AL. NATURE REVIEWS MICROBIOLOGY 10, 407-416 (2012)

Uncontained *M. tuberculosis* in the lungs prompts infectious diseases.

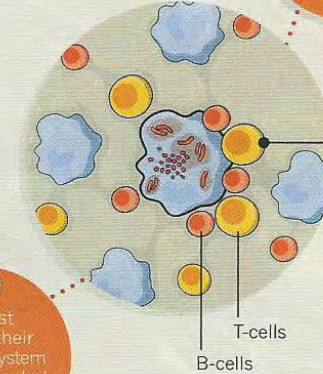


THE TRANSMISSION CYCLE



Once inside it takes over the cells internal machinery to fend off further internal phagocytic destruction and begins to replicate.

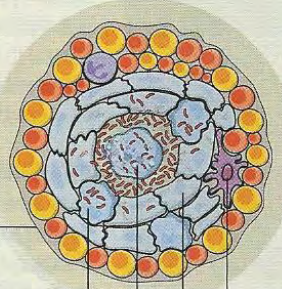
2 Infected macrophages signal other immune cells to attack.



T cells can activate macrophages to kill *M. tuberculosis* as well as targeting the bacteria directly.

3 In most people, their immune system is able to control the infection in granulomas.

4 When infection overcomes the immune system, it spreads throughout the body



Granuloma
Macrophage
Necrotic macrophage
Epithelioid macrophage
Dendritic cell

1

Transmission

People with active disease develop symptoms such as a cough, which propels bacteria into the air where it can be inhaled by others. Tuberculosis must be diagnosed and treated as soon as possible to render the person non-infectious and prevent the spread of disease (see 'Control issues', page S16).

2

Immune response

The BCG vaccine offers little protection to adolescents and young adults from the form of the disease that causes most deaths. Any effective vaccine will need to harness T cells, but scientists are still looking for correlates of protection (see 'An age-old problem', page S8).

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Latency

M. tuberculosis can be contained within granulomas for years. It is thought that latency may encompass a spectrum of states, from people who have completely controlled the disease, to those with undetected, subclinical disease (see 'Latency: A sleeping giant', page S14).

4

Activation

If the immune system weakens as a person ages or contracts HIV infection, for example, bacterial replication can overcome the immune system and granuloma breaks down, releasing *M. tuberculosis* into the lungs and advancing disease (see 'A combined effort', page S4).



Robert Koch

German physician/microbiologist

1843 (May 24) -1910

1882 discovered tubercle bacilli (also cholera, anthrax)

1896 discovered tuberculin

1905 received Nobel Prize in Medicine (for pioneering TB work)

TB, the big picture:

1/3 of the world's population is infected

-World Health Organization, 1997





HOW CONTAGIOUS IS MTB?



MTB Contagious Risk*

- LTBI: by definition no risk
- Active Extrapulmonary: no risk
- Active Pulmonary: low risk (usually)

*assumes normal immuno-competence

MTB Contagious Risk

- Most exposure is from low levels-over time
- Most people can naturally defend from at least 100 MTB molecules (without skin-test evidence)
- Non-Coughing children pose (almost) no threat
- Once a risk is known, those in contact wear N-95
- Patient should only wear normal surgical mask to prevent risk around them
- TB medications usually “sterilize” in 2 wks

Quick Alaska Tuberculosis History*

- AD 400: St. Lawrence Island, frozen remains with anatomic TB signs
- AD 1500: Barrow, frozen remains with anatomic TB signs
- 1900: most common cause of death in Alaska Natives
- 11/1953: ANMC opens in Anchorage (300 of 400 beds for TB)
- 12/1957: YK-Delta INH (controlled double-blind) field trials begin

*Fortune R. "Must we all die?"-Alaska's Enduring Struggle with Tuberculosis. 2005 University of Alaska Press

Quick Alaska Tuberculosis History

- Western Alaska is where the first major isoniazid (INH) field trials (n=7,333) were conducted 60 years ago.*
- They demonstrated drug effectiveness (68% reduction TB) while stopping a devastating TB epidemic (25% annual TST conversion rate).
- As a result, these trials guided future United States TB control strategy.

*Comstock GW. Isoniazid prophylaxis in an underdeveloped area. Am Rev Respir Dis 1962; 21: 9-27.



Current status TB Alaska

- Tuberculosis (TB) continues to be a major health concern in Alaska
- It ranks at or near the top among states, usually competing with Hawaii followed closely by either California or the District of Columbia.
- There has been no sustained decline in the last 15 years.

Tuberculosis Rank Order by States*

Rank Order	State 2014	Case Rate**	State 2013	Case Rate
1	Hawaii	9.6	Alaska	9.6
2	Alaska	8.4	Hawaii	8.2
3	California	5.5	District of Columbia	5.7
4	District of Columbia	4.9	California	5.6

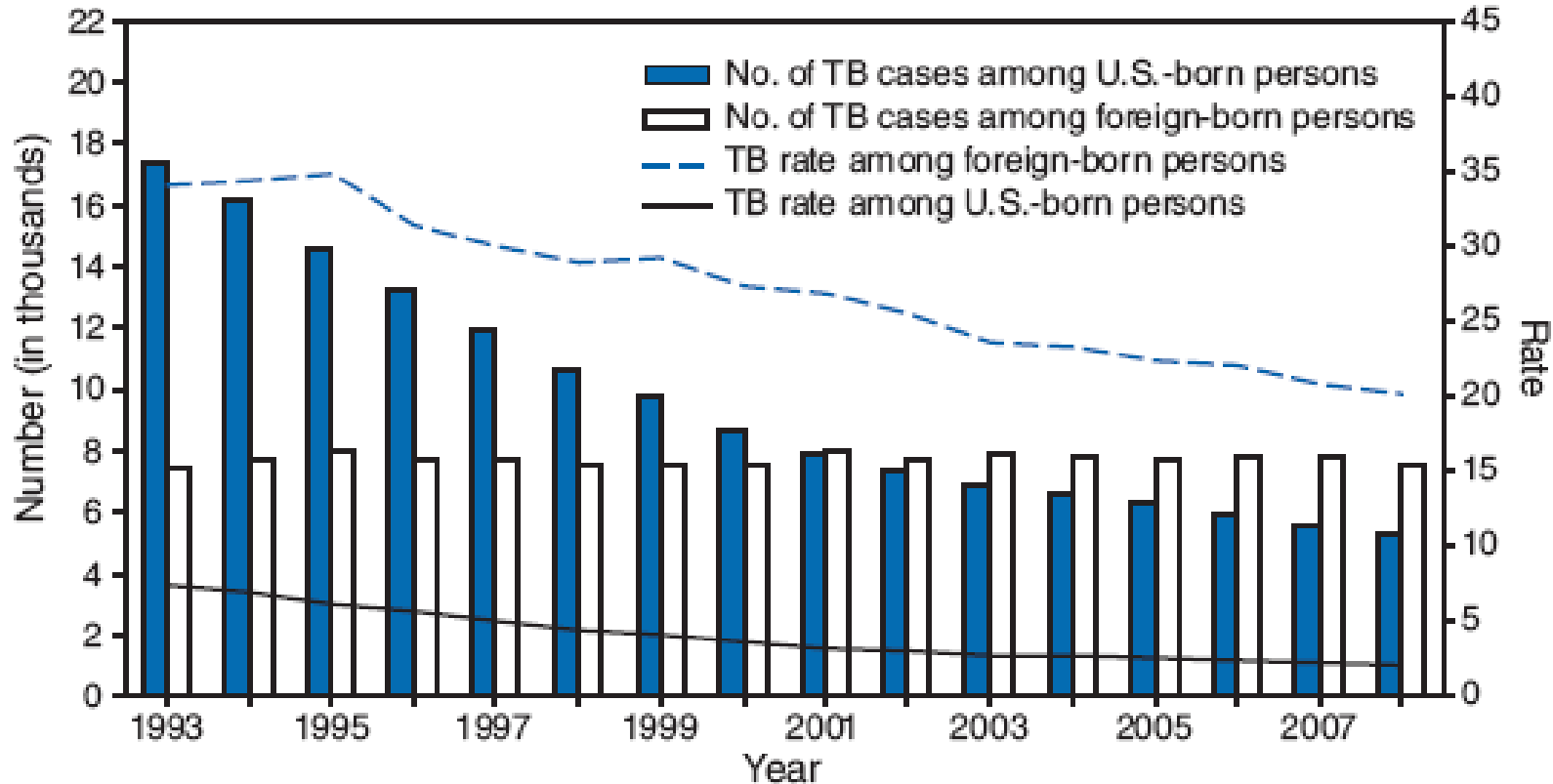
*US average case rate 3.0 both 2013 and 2014

** all case rates per 100,000

CDC. Reported Tuberculosis in the United States, 2014.

Available at: <http://www.cdc.gov/tb/statistics/reports/2014/table30.htm>

FIGURE 2. Number and rate* of tuberculosis (TB) cases among U.S.- and foreign-born persons, by year reported — United States, 1993–2008†

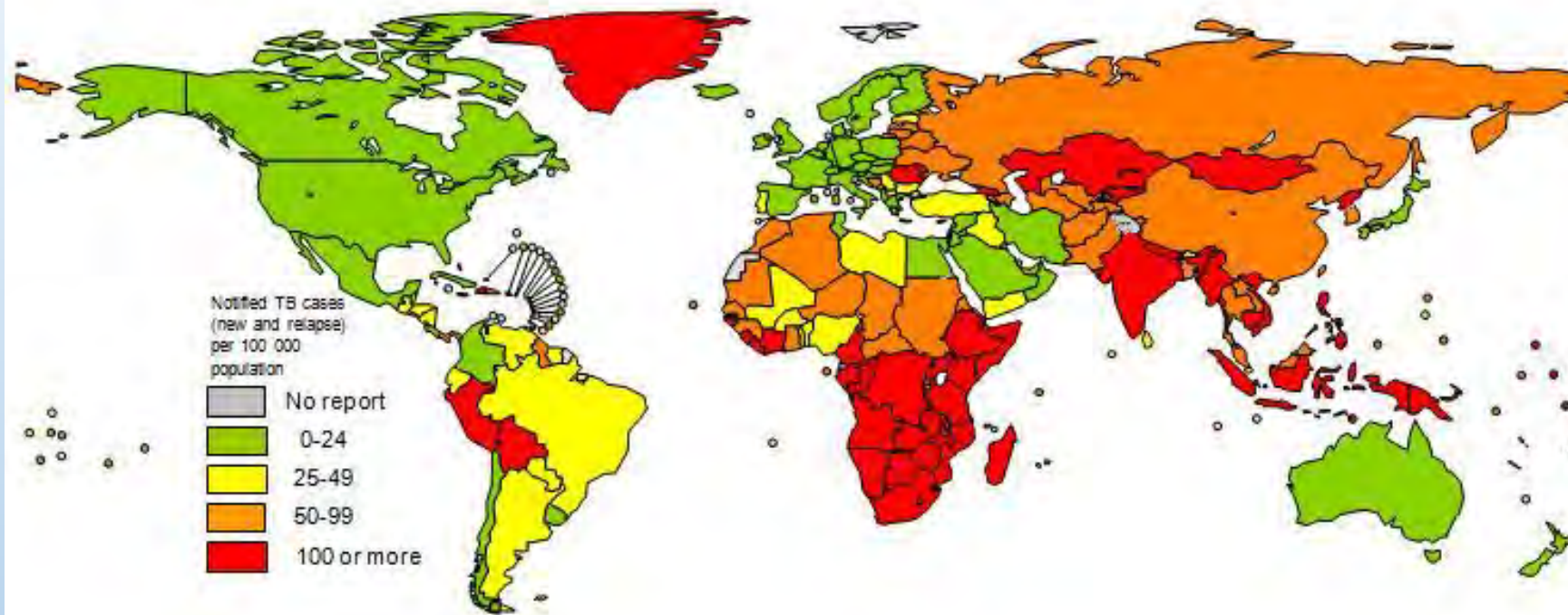


SOURCE: National TB Surveillance System.

* Per 100,000 population.

† Data are updated as of February 18, 2009. Data for 2008 are provisional.

Tuberculosis notification rates, 2005



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

© WHO 2006. All rights reserved



Current status TB Alaska

- Nowhere is this increase in TB more apparent than in rural and remote western Alaska
- This is a wide swath of land (approximating half the area of the state of Alaska) bordering both the Bering Sea on the west and the Arctic Ocean at the north
- High rates are again climbing despite the best public health practices.



Current status TB Alaska

- The process by which active pulmonary tuberculosis (TB) is detected can be tediously slow in rural and often roadless Alaska
- Several hundred air or boat miles can separate a patient from a chest x-ray and/or sputum collection.
- Additionally, the only TB reference lab in the state is many hundreds of air miles away albeit centrally located in Anchorage.

Current status TB Alaska

- Under such conditions, serial acid fast bacillus (AFB) sputum samples may take up to a week to process.
- This can result in either delayed onset of treatment or unnecessary empiric treatment calculated to both treat the patient and protect the community.
- This dilemma often results in precautionary hospital isolation of a patient who might otherwise be able to travel home by air.

Enter a new lab test from Silicon Valley

Xpert® MTB/RIF

Two-hour detection of MTB and resistance to rifampicin.

*Go from test and wait
to **test and treat.***



CE  In vitro diagnostic medical device

defining *on-demand* molecular diagnostics.

 **Cepheid.**
Bring answers to life.

Xpert MTB/RIF test

- cartridge-based, automatic diagnostic test
- detects DNA sequences specific to
 - Mycobacterium tuberculosis (& cmplx)
 - Rifampin resistance mutations

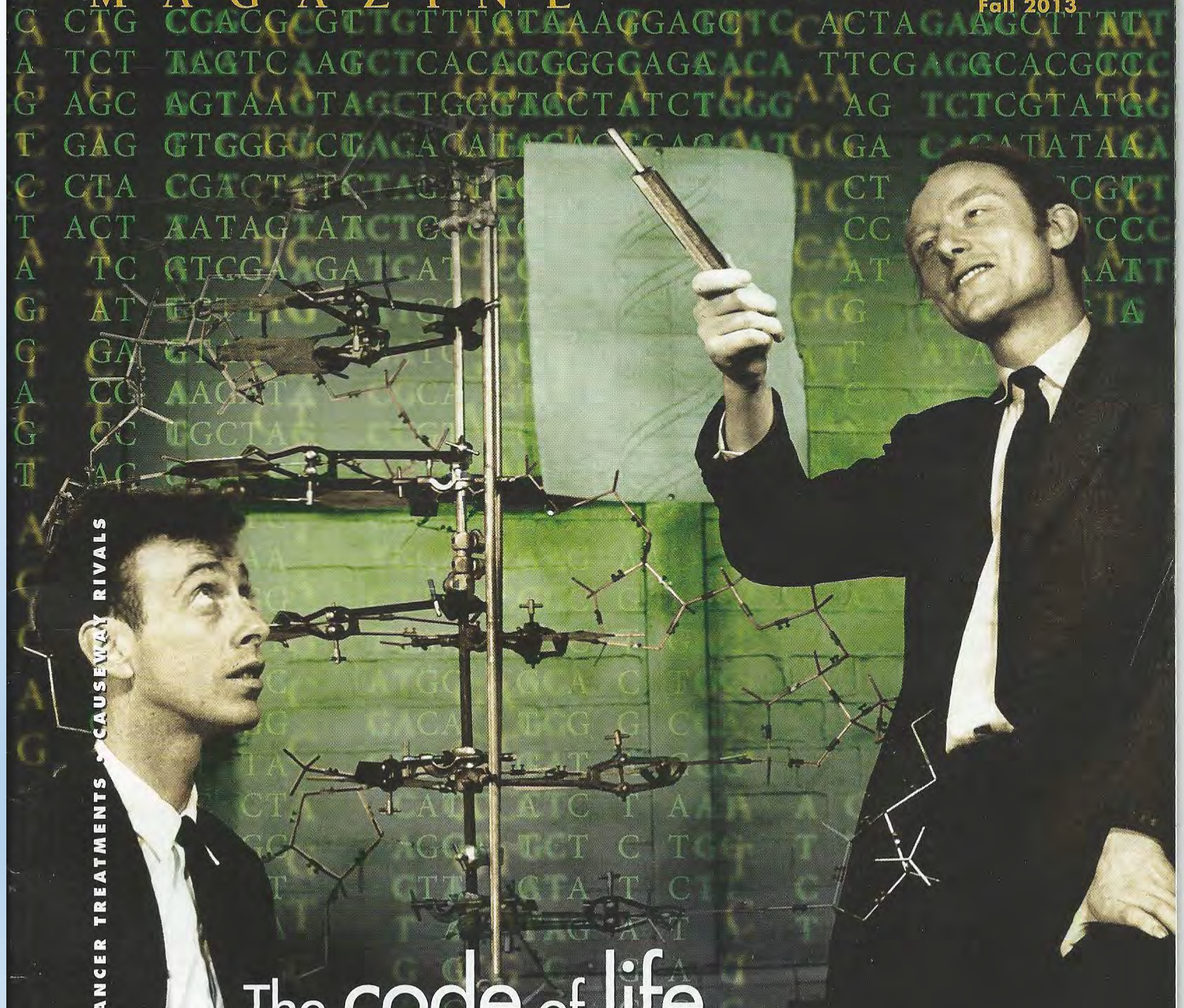
2010 endorsed by WHO for use in TB endemic areas
2013 FDA-approved & CLIA-endorsed in the US



Xpert MTB/RIF test

- Results are from an unprocessed sputum sample
- Very low level bio-hazard
- Little technical training (CLIA moderate complexity)
- Sputum → result in as soon as 90 minutes





CANCER TREATMENTS SO CAUSEWAY RIVALS

The code of life

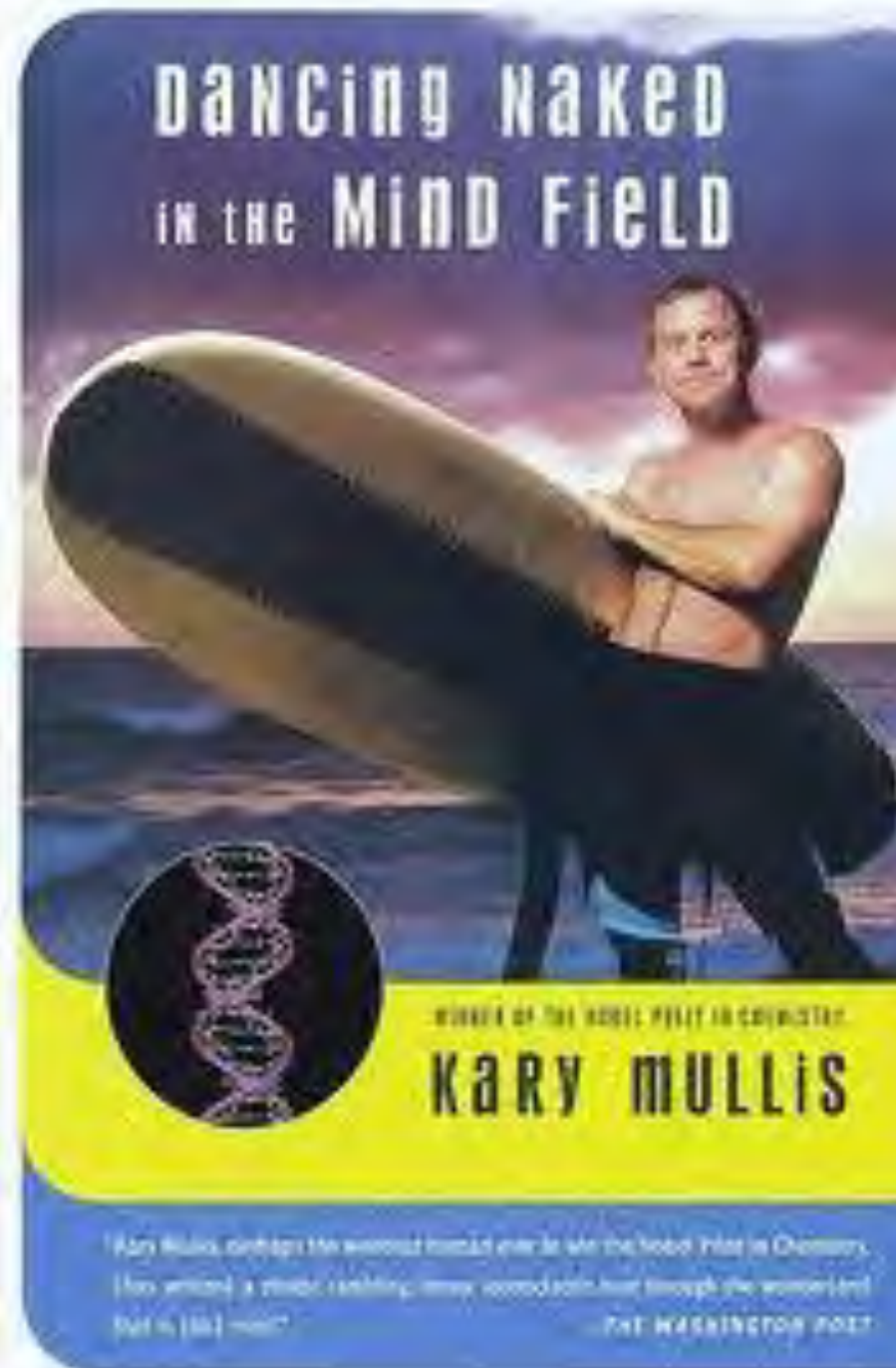
Xpert MTB/RIF test

- separation of TB and Rifampin resistant gene sequences
- amplification by PCR (polymerase chain reaction)
- ID by molecular beacons
- very QUICK and PORTABLE

Dr. Kary Mullis

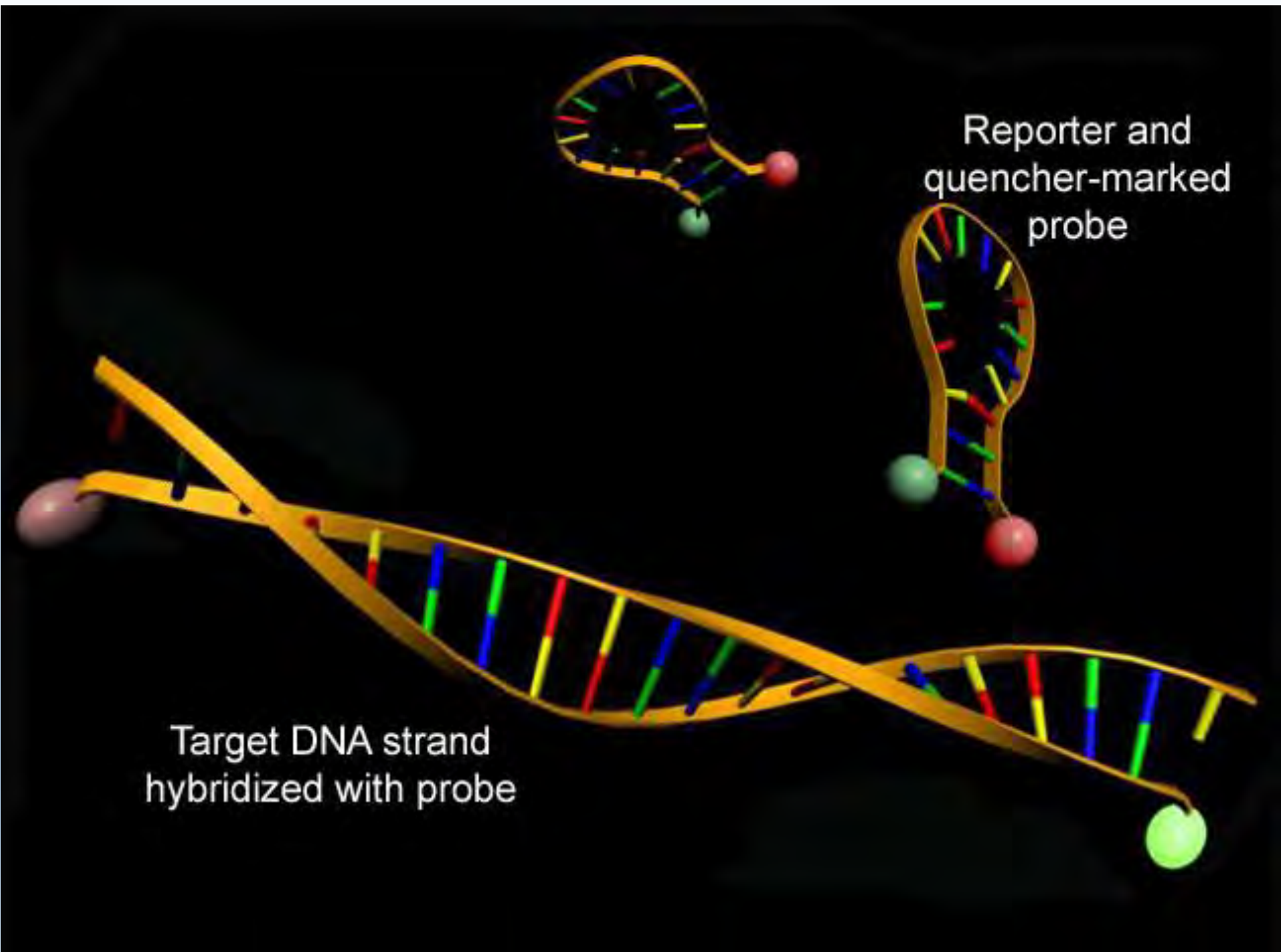
**Nobel Prize in
Chemistry 1993**

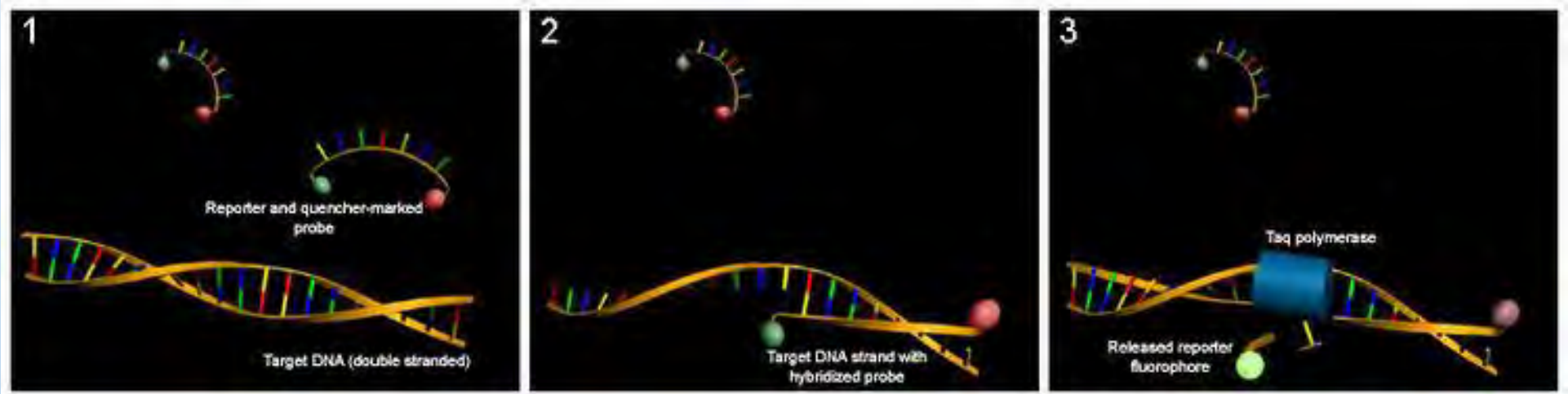
delevoped PCR process



Kary Mullis, PhD receiving Nobel prize in Stockholm







GeneXpert test platforms by Cepheid





Photo courtesy of Cepheid

1
Sputum liquefaction
and inactivation with
2:1 sample reagent



2
Transfer of
2 ml material
into test cartridge



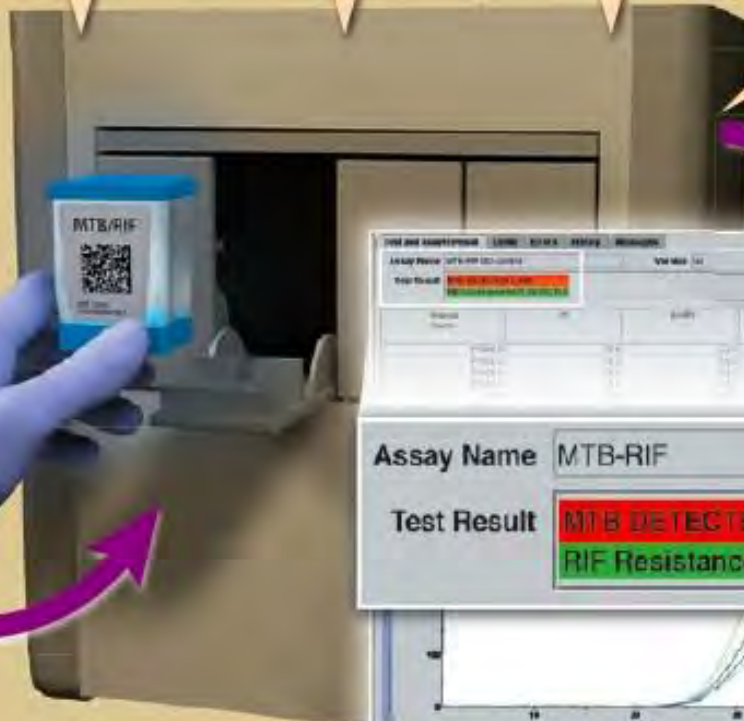
3
Cartridge inserted into
MTB-RIF test platform
(end of hands-on work)

4
Sample
automatically
filtered and
washed

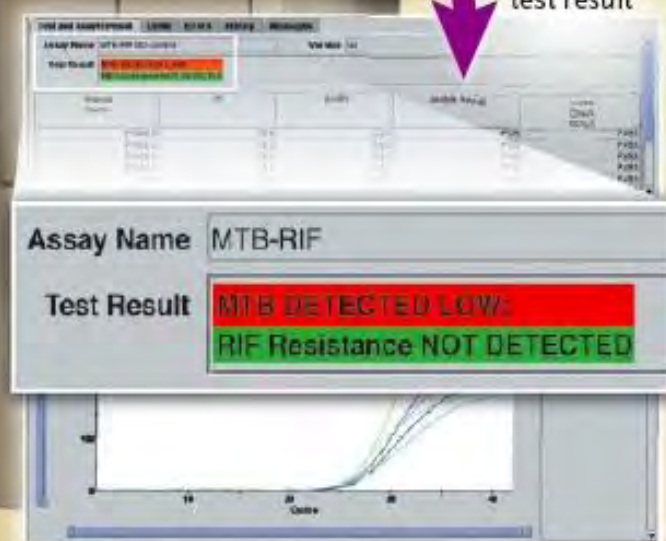
5
Ultrasonic lysis
of filter-captured
organisms to
release DNA

6
DNA molecules
mixed with dry
PCR reagents

7
Seminested
real-time
amplification
and detection
in integrated
reaction tube



8
Printable
test result



Time to result, 1 hour 45 minutes



Microfluidics Technology

is a multidisciplinary field intersecting engineering, physics, chemistry, nanotechnology and biotechnology, with practical applications to the design of systems in which small volumes of fluids will be handled. Microfluidics emerged in the beginning of the 1980s and is used in the development of inkjet printheads, DNA chips, [lab-on-a-chip](#) technology, micro-propulsion, and micro-thermal technologies.

From Wikipedia, the free encyclopedia

Current status TB Alaska: this may help

- The recently FDA-approved Xpert[®] MTB/RIF assay (Cepheid Inc., Sunnyvale, CA) is rapid (<2 hours)
- It is also highly accurate for a *single* unprocessed sputum specimen [92.2% sensitivity, 99.2% specificity for culture positive pulm TB]*
- This far exceeds AFB x3 microscopy sensitivity of 67.5%**

*Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 2010; 363: 1005-1015.

**Mathew P, Yen-Hong K, Vazirani B, et al. Are three sputum acid-fast bacillus smears necessary for discontinuing tuberculosis isolation? J Clin Microbiol 2002; 40: 3482-3484.

Current status TB Alaska: this may help

- [Xpert MTB/RIF may be] a roadmap for remote healthcare settings in Alaska that might bridge our current TB diagnostic ability with a better way in the future.*

*Bowerman RJ. The promise of rapid detection of active pulmonary tuberculosis in rural Alaska. Alaska Med 2015; 56:24-28.

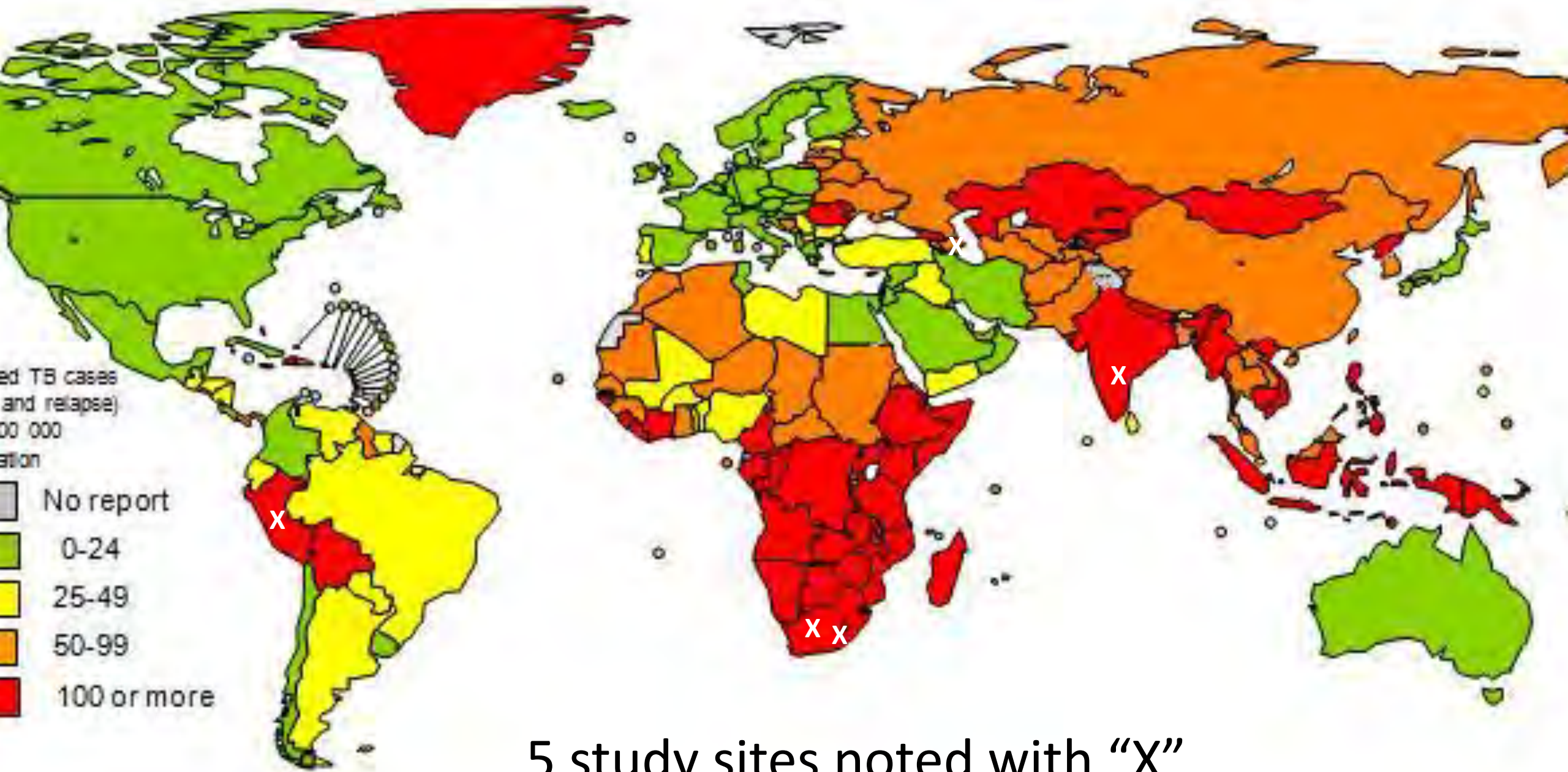
Xpert MTB/RIF test accuracy for pulmonary TB

for single sputum samples

- Sensitivity of combined smear (+) & smear (-) *culture-confirmed* TB patients: 92.2%
- Sensitivity of smear (+) TB patients : 98.2%
- Sensitivity of smear (-) TB patients: 72.5%
- Specificity (i.e. true neg result): 99.2%

Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 2010; 363: 1005-1015.

(n=1730 suspected TB patients from five (5) centers S.Africa(2), Peru, Azerbaijan, and India)



5 study sites noted with "X"

Sensitivity & Specificity

- Sensitivity*: the ability of a test to find cases
- Specificity: The ability of a test **avoid** false-positives & r/o Dz
- <not effected by Dz prevalence>

*the current healthcare standard for initial testing for active PulmTB, *AFB* x3, has a sensitivity = **67.5%**[^]

[^]Mathew P, Yen-Hong K, Vazirani B, et al. Are three sputum acid-fast bacillus smears necessary for discontinuing tuberculosis isolation? J Clin Microbiol 2002; 40: 3482-3484.

Calculations for sensitivity/specificity

*single sputum for the 1341 suspected TB patients not excluded**

	Dz**	no Dz	totals
Xpt (+)	675	5	680
Xpt (-)	57	604	661
Totals	732	609	1341



Sensitivity: measures Xpert MTB/RIF assay ability to correctly identify Active PulmTB cases $[675 / 675 + 57] = 92.2\%$

Specificity: measures Xpert MTB/RIF assay ability to correctly **exclude** those w/o Dz $[604 / 609] = 99.2\%$

*Includes MDR-under tx, insufficient sample number or volume size, indeterminant dx, pt death`

**includes both AFB smear (+) and smear (-) who had sputum culture-confirmed active pulmTB

Calculations for sensitivity/specificity

*single sputum for the 1341 suspected TB patients not excluded**

	Dz**	no Dz	totals
Xpt (+)	675	5	680
Xpt (-)	57	604	661
Totals	732	609	1341

Sensitivity: measures Xpert MTB/RIF assay ability to correctly identify Active PulmTB cases $[675 / 675 + 57] = 92.2\%$

Specificity: measures Xpert MTB/RIF assay ability to correctly **exclude** those w/o Dz $[604 / 609] = 99.2\%$

*Includes MDR-under tx, insufficient sample number or volume size, indeterminant dx, pt death

**includes both AFB smear (+) and smear (-) who had sputum culture-confirmed active pulmTB

Negative Predictive Value

- Ability of the test to correctly label people who test Neg

The current healthcare standard for ruling-out active PulmTB using

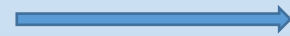
AFB x3, has a NPV = **98.2%**

<a decrease in Dz Prevalence will Raise the Negative Predictive Value>

Calculation for Negative Predictive Value

*single sputum for 1170 suspected TB patients not otherwise excluded**

	Dz**	no Dz	totals
Xpt (+)	551	5	556
Xpt (-)	10	604	614
Totals	561	609	1170



Negative Predictive Value (NPV)

NPV: ability of Xpert MTB/RIF assay to correctly label those who test NEG [604/614] = **98.4%**

*Includes AFB-Neg-Sputum Cx-positive, MDR-under tx, insufficient sample number or volume size, indeterminant dx, pt death

****includes only AFB smear (+) who had sputum culture-confirmed active pulmTB**

Boehme CC, Nabeta P, Hillemann D, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med 2010; 363: 1005-1015.

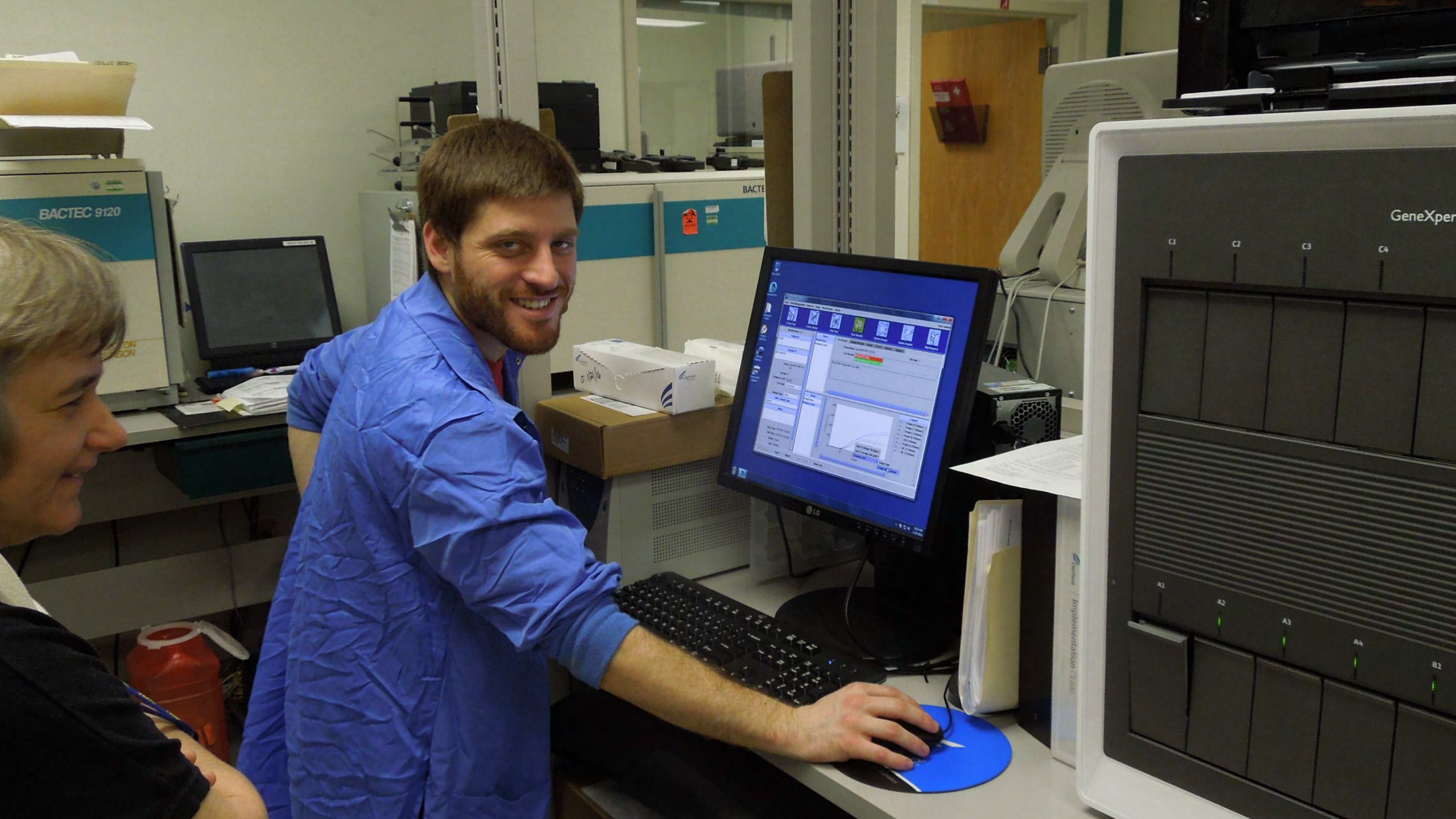
Key Findings for Xpert MTB/RIF assay

- Ability to diagnose suspected TB patients
 - Sensitivity of a single sputum Xpert MTB/RIF assay (<2hrs): **92.2%**
 - Sensitivity of sputum AFB x3 (1-3 days): **67.5%**
- Ability to rule-out Active PulmTB
 - NPV* of a single sputum Xpert MTB/RIF assay: **98.4%**
 - NPV of sputum AFB x3: **98.2%**

*NPV (Negative Predictive Value) will be higher if TB prevalence is lower than the study population

GeneXpert assay platform in Alaska

- Presently YKHC-Bethel is the only regional hospital with this test
- 2 other local hospitals (road system) are capable of running the test.



BACTEC 9120

BACTEC

GeneXper

C1 C2 C3 C4

A1 A2 A3 A4 B1

Our pathway from desire to “go live”

- Realization
- Political will + funds to purchase assay platform
- Installation
- Training personnel + test validation
- EMR build
- Go Live!

YKHC Lab Validation of Xpert MTB/RIF

State Lab sample	Mycobacterium	Drug Resistance	MTB result	RIF result
A	tuberculosis cmplx	SIRE & PZA	detected	resistant
B	tuberculosis cmplx	IR	detected	resistant
C	tuberculosis cmplx	SIRE	detected	resistant
D	tuberculosis cmplx	SIRE	detected	resistant
E	tuberculosis cmplx	SIRE	detected	resistant
F	tuberculosis	none	detected	Not resistant
G	avium		Not detected	-
H	avium/intrcell cmplx		Not detected	-
I	gordonae		Not detected	-

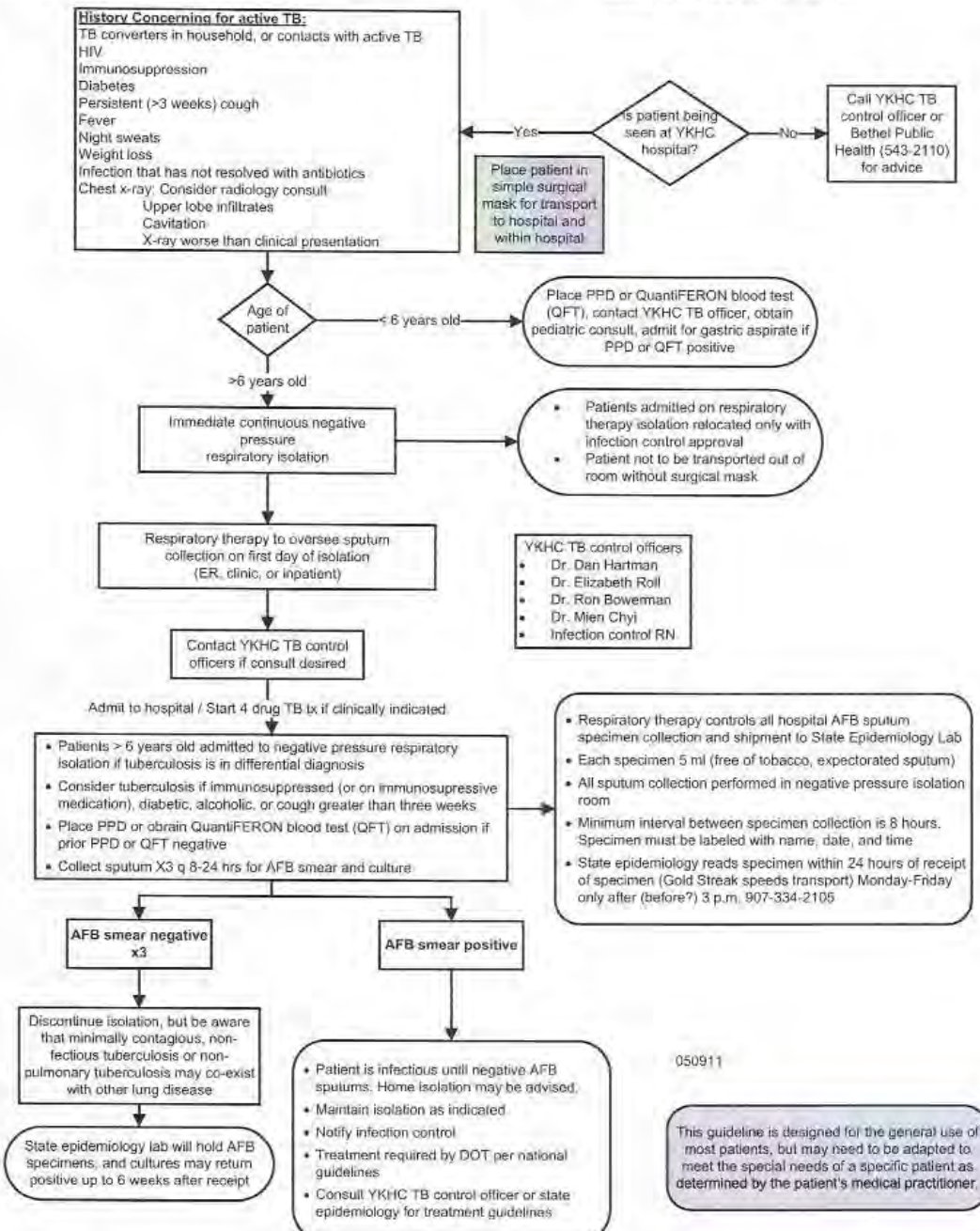
YKHC guideline for rapid TB assay

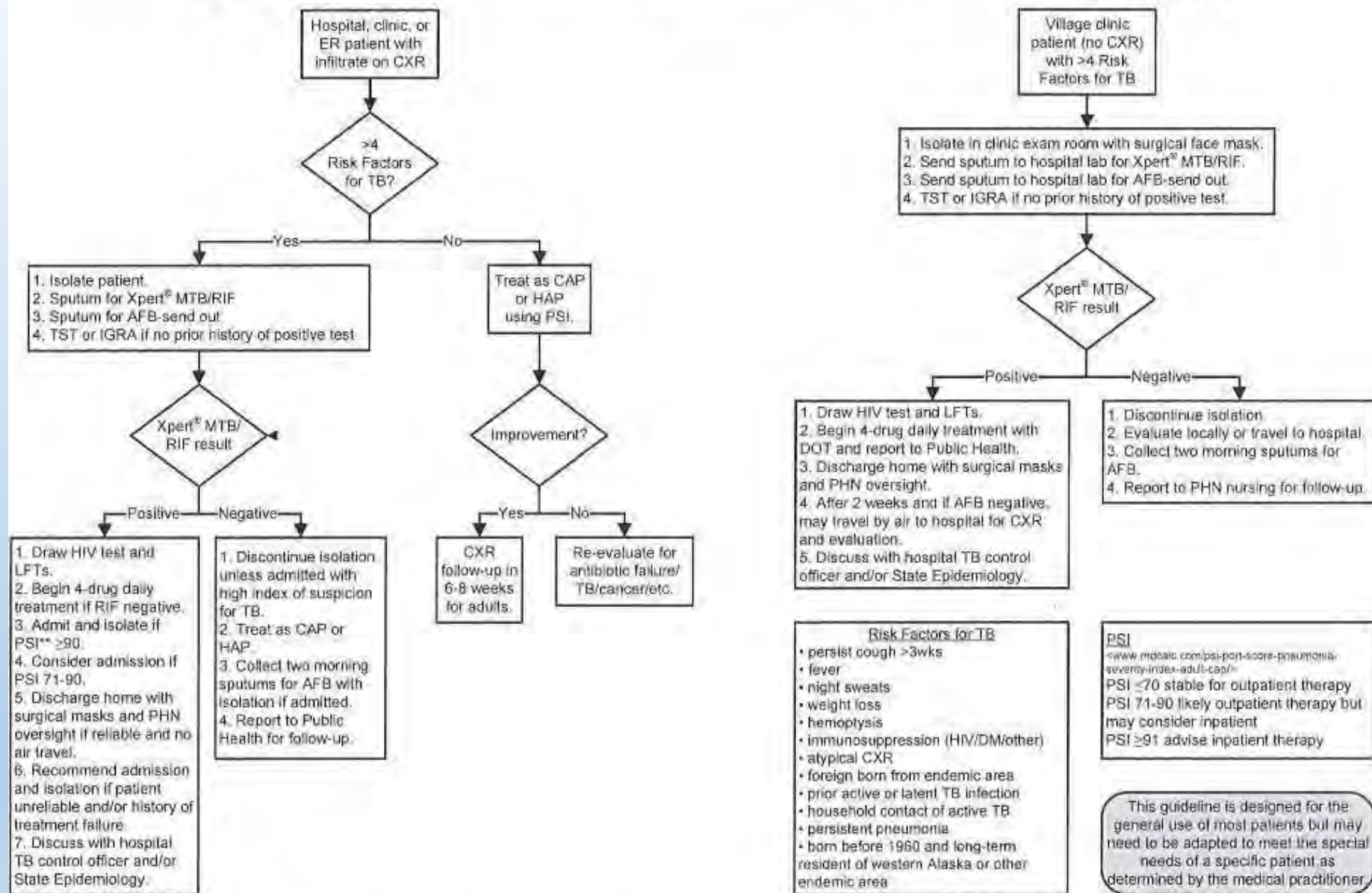
- The TB diagnostic guideline for our area (Yukon-Kuskokwim Delta) was reviewed for integration of the Xpert[®] MTB/RIF assay
- Our purpose was to improve TB healthcare while emphasizing patient benefits and cost savings.

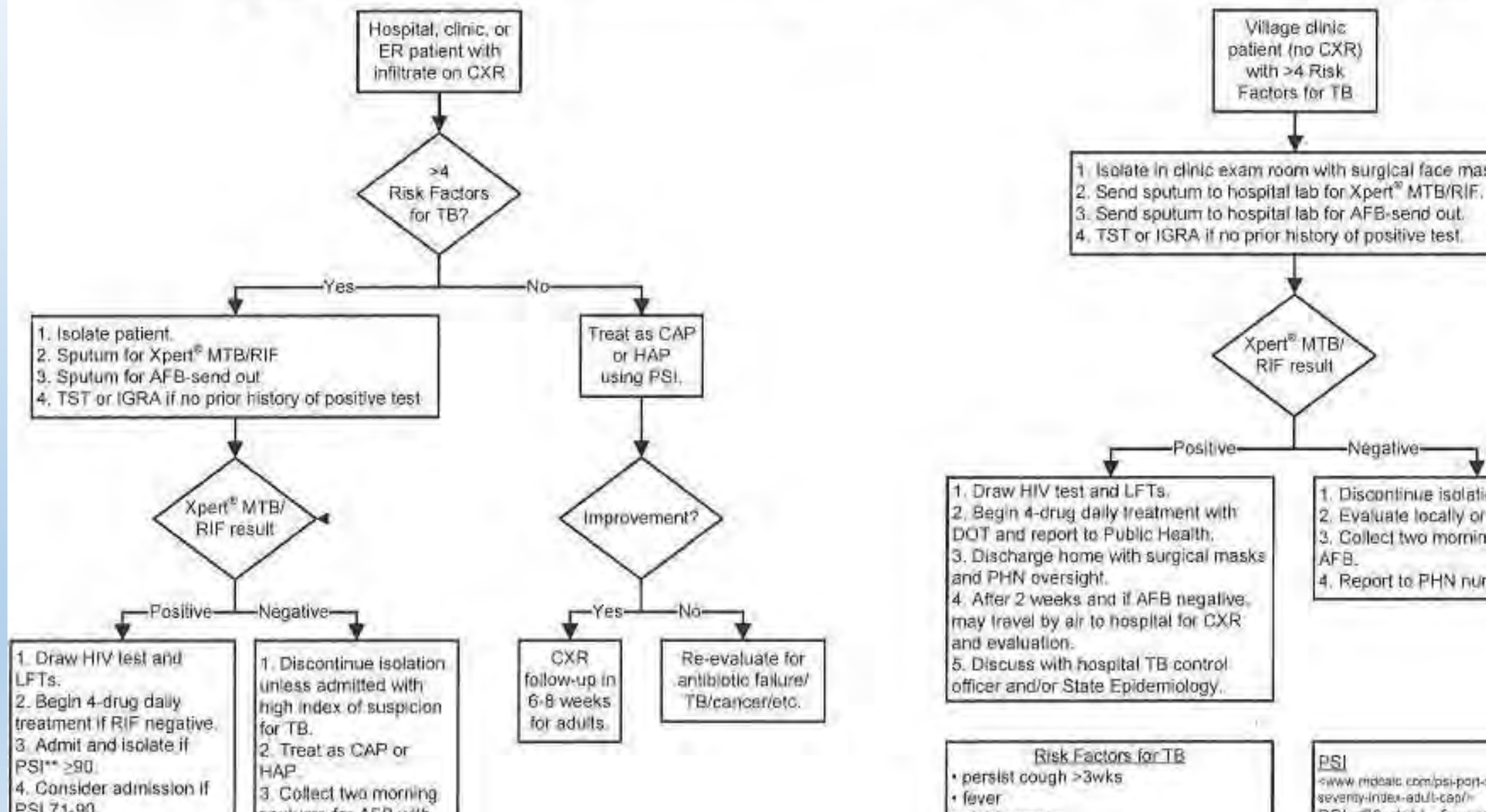


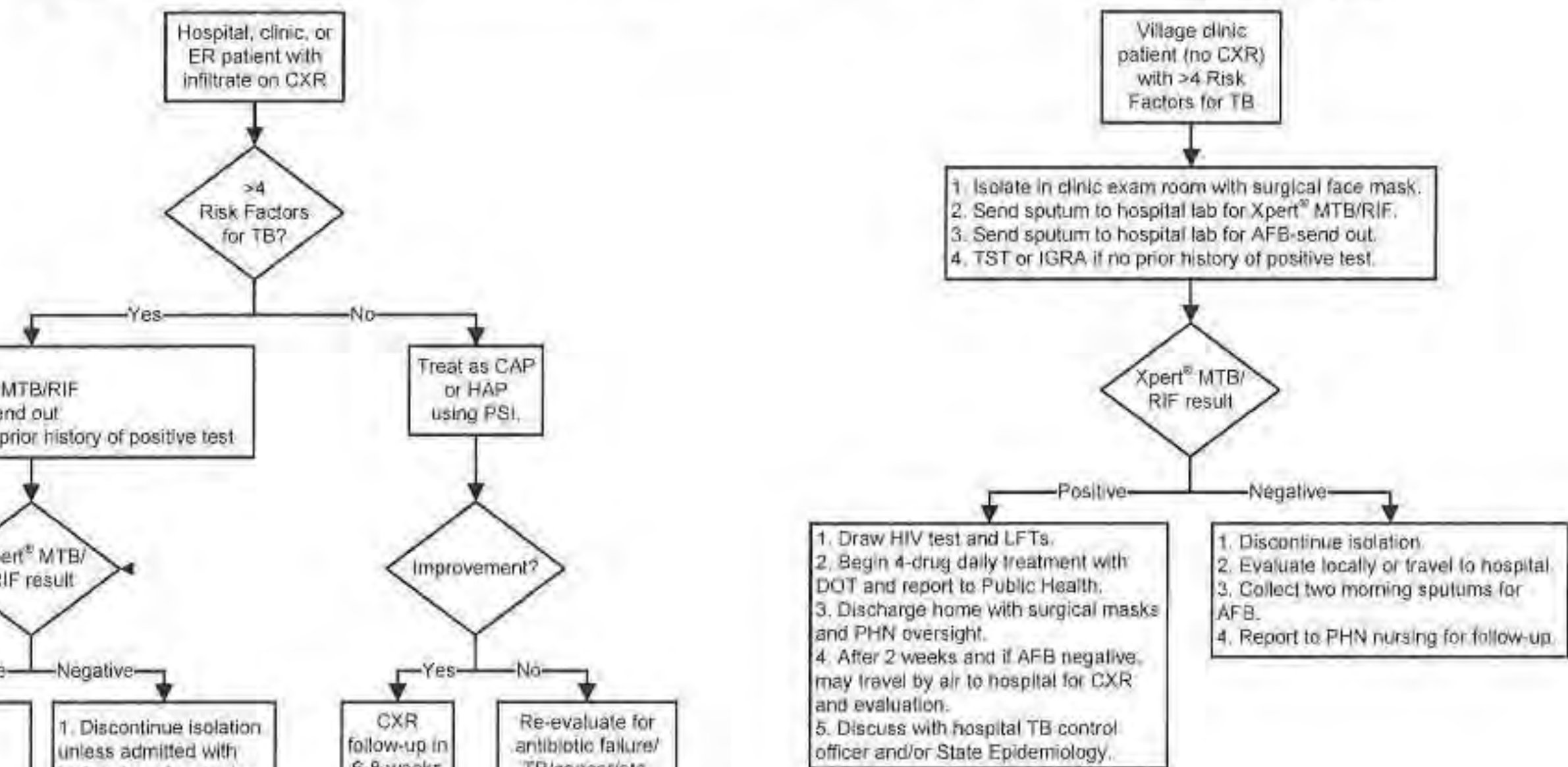
Tuberculosis

MSEC reviewed and approved 08/22/11



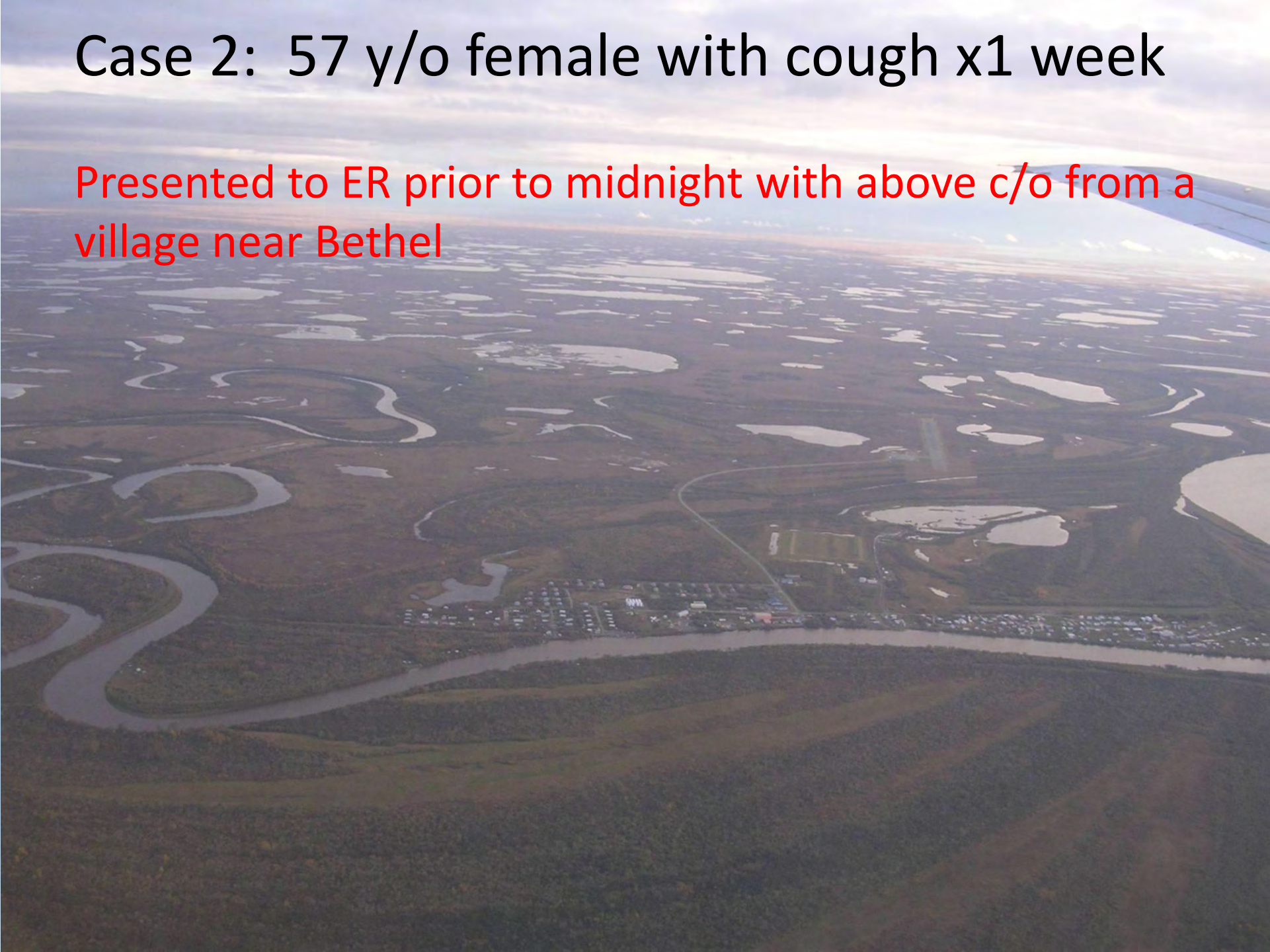






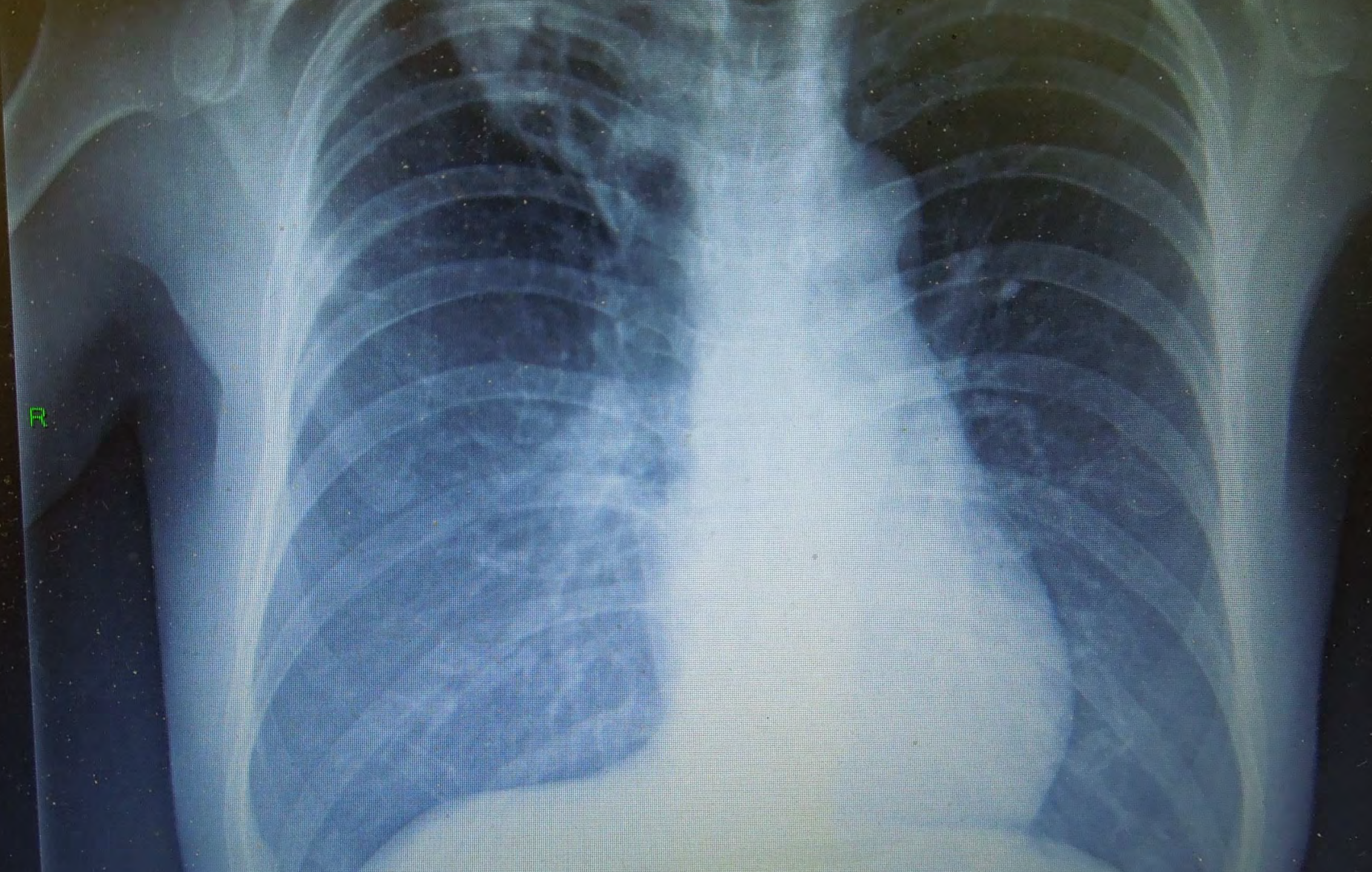
Case 2: 57 y/o female with cough x1 week

Presented to ER prior to midnight with above c/o from a village near Bethel



Case 2: continued

- Other Sx-fever, weight loss, but only slight sputum in AM
- Denies-night sweats, dyspnea
- Vitals: 100.5F, P 107, BP 121/78, RR 27
- PMHx-previously healthy but not feeling well-fatigued last 2 months
- Prior TST a year ago = 0mm
- CXR

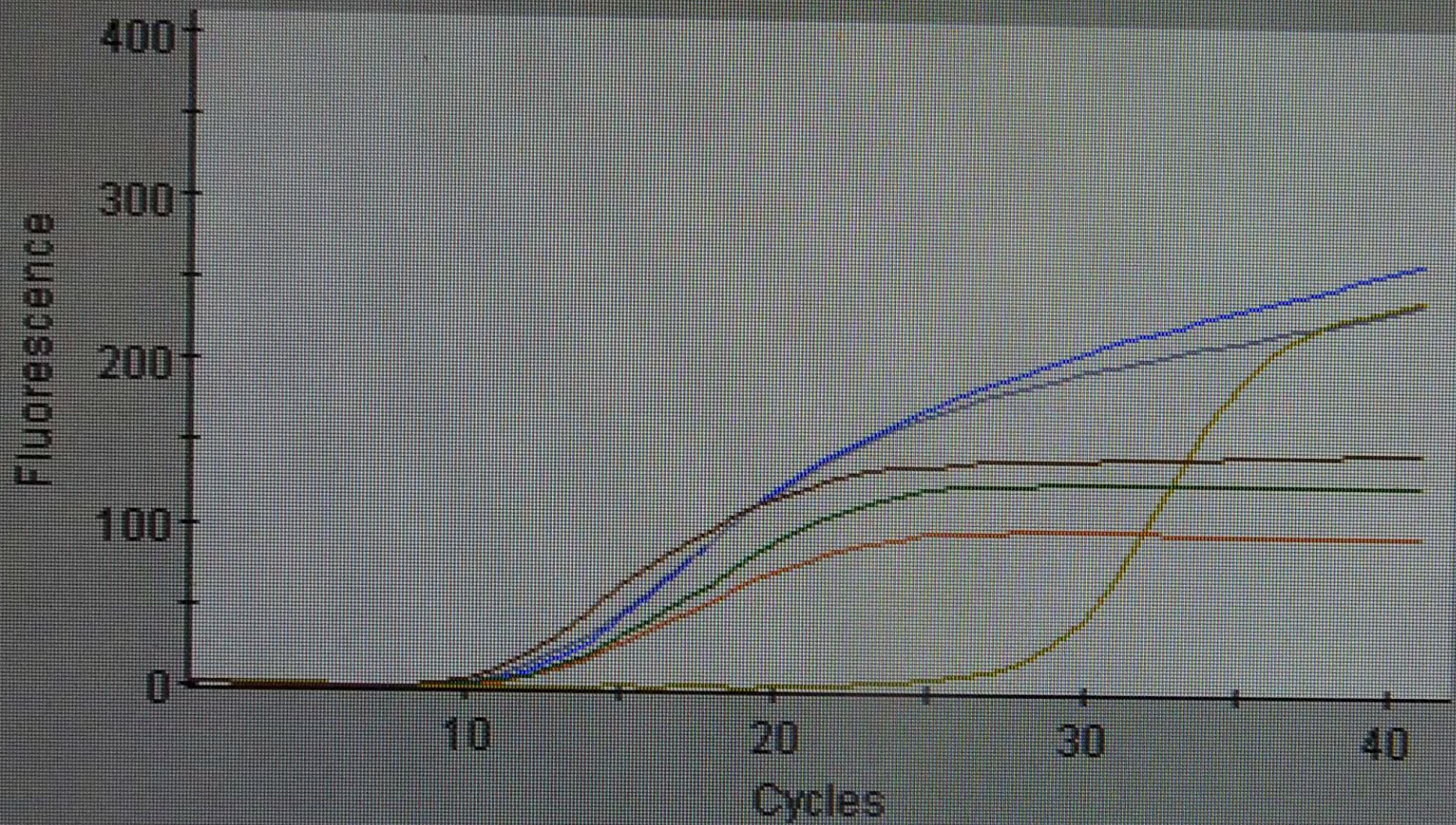


This patient is isolated in the ER to Negative Air Pressure (Airborne)

Sputum samples for Xpert MTB/RIF and AFB are collected

A TST is also placed

Within 2 hours (even though it is 2AM) the Lab calls with this result:



Legend		
<input checked="" type="checkbox"/>		Probe D
<input checked="" type="checkbox"/>		Probe C
<input checked="" type="checkbox"/>		Probe E
<input checked="" type="checkbox"/>		Probe B
<input checked="" type="checkbox"/>		SPC; Pr
<input checked="" type="checkbox"/>		Probe A
<input checked="" type="checkbox"/>		QC-1; Pr
<input checked="" type="checkbox"/>		QC-2; Pr

View Test

What's next?

- A. Discharge home on oral Augmentin, CXR f/u 6 wks
- B. Read TST with f/u in clinic 48-72hrs
- C. Start RIPE TB meds then admit to inpatient for more AFB sputum collection w/Airborne precautions with a PHN referral in the AM
- D. Start RIPE TB meds, discharge directly home (by open-air mode) with surgical face mask, and refer to PHN for outpatient management to include collection of 2 more AFB sputums

What's next?

- A. Discharge home on oral Augmentin, CXR f/u 6 wks
- B. Read TST with f/u in clinic 48-72hrs
- C. Start RIPE TB meds then admit to inpatient for more AFB sputum collection w/Airborne precautions with a PHN referral in the AM
- D. Start RIPE TB meds, discharge directly home (by open-air mode) with surgical face mask, and refer to PHN for outpatient management to include collection of 2 more AFB sputums

(could also be C)

Answer is “D”

- Since vital signs are stable, this TB patient could go home by private vehicle with the conditions listed
- AFB sputum collection initially is still necessary for culture and sensitivity as well as assessing when no longer contagious once on therapy
- If the patient is unable to get home except by plane or is not reliable, admission may still be the best option.

help is near

YKHC Hospital TB Control Officers

Elizabeth Roll, MD

Mien Chyi, MD

Ron Bowerman, MD, MPH

YKHC Hospital Infection Control Nurse

vacant

Bethel Public Health

Mary Berliner, RN

and all other public health nurses

more help

State of Alaska (TB Control Officer)

Michael Cooper, MD

Curry (National TB) Center UCSF Warmline

1-877-390-6682 toll free

1-415-502-4700

TB conferences

Curry National TB Center

2-day “TB Intensive”-SEA/SFO

National Jewish Hospital

4-day TB Conference-Denver



moving forward





YKHC Admin/Eye/Dental Clinics

YKDR Hospital



Post-lecture Quiz

How many Nobel laureates were mentioned in this lecture?

- A) 1
- B) 2
- C) 3
- D) 4
- E) none

- Koch
- Watson
- Crick
- Mullis

Thank you



“The past 10 years have seen the most rapid growth in new diagnostics for Mtb in over a century.”

Nyendak MR, Lewinsohn DA, Lewinsohn DM 2009. New diagnostic methods for tuberculosis. *Current Opinion in Infectious Diseases* 22 (2): 174-182.

Why a new Rapid TB diagnostic test?

Why a new Rapid TB diagnostic test?

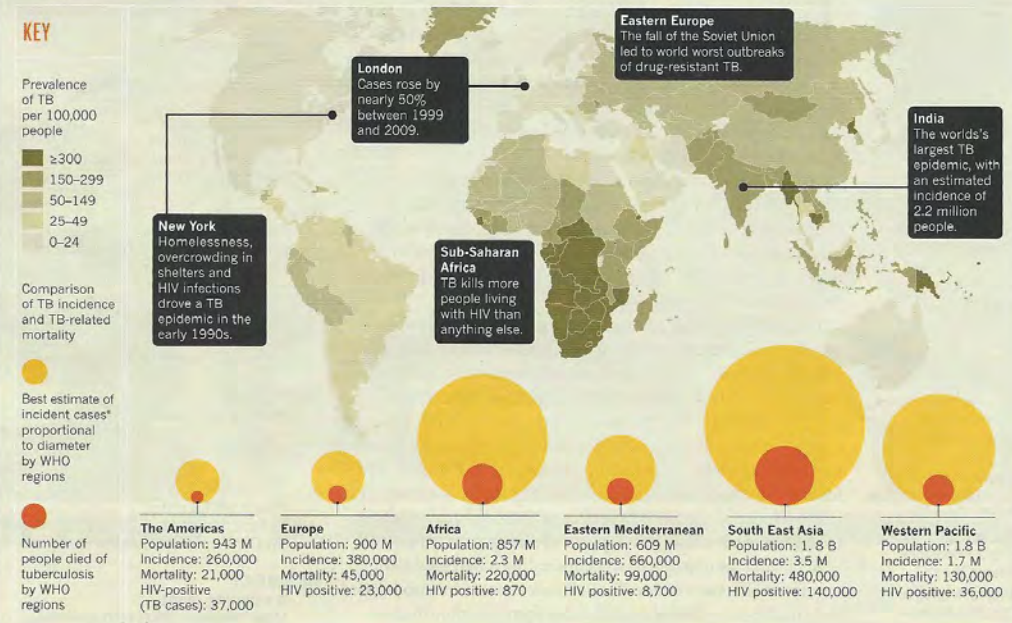
- The worldwide battle against TB is going poorly

A MORTAL FOE

Tuberculosis is one of the world's most lethal, infectious diseases. Further progress in consigning it to the past is a massive challenge. By Tom Paulson.

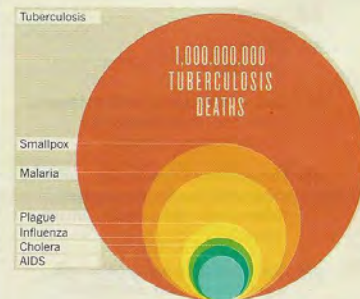
GLOBAL BURDEN OF TUBERCULOSIS

In 2011, nearly 9 million people fell ill from TB and 1.4 million died, mostly in poor countries, with 60% of cases in Asia and 24% in Africa.



THE BIGGEST KILLER

Tuberculosis has killed more than any other infectious disease in history. Over a billion lives in the past two hundred years.



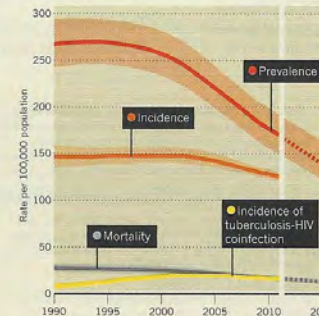
THE 100 YEARS BATTLE

Rising living standards in industrialized nations, interrupted by two World wars, and new antibiotics had tuberculosis in decline.



SLOW PROGRESS

Over the past fifteen years, an invigorated anti-TB effort has begun to reduce the global burden of disease worsened by HIV.



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- The worldwide battle against TB going poorly
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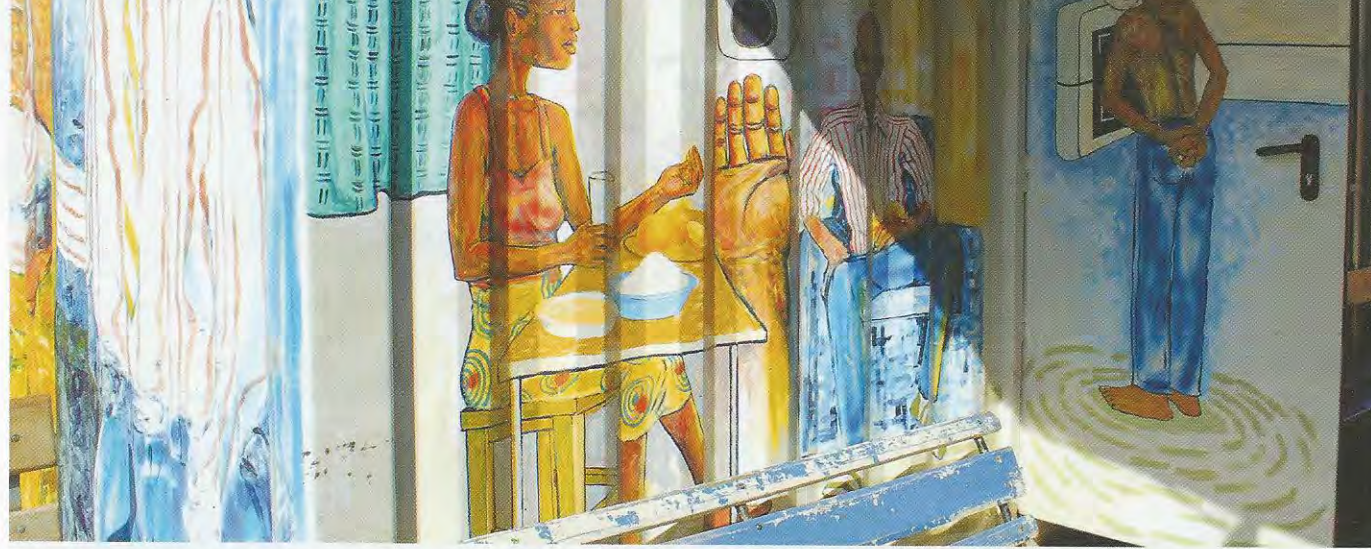
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The health clinic in Kanyama, a slum district of Lusaka, Zambia, is trying out a new device to test for tuberculosis.

DIAGNOSIS

Waiting for results

There are several new tests for tuberculosis in the pipeline, but they must be shown to be effective in areas with limited resources and a heavy burden of HIV.

BY CATHERINE DE LANGE

Tobias Hamooya says he is feeling a bit better these days, but even to the casual observer it is clear that he is still not doing well. Sitting on the porch outside the Macha Mission Hospital in rural Zambia, his slow, staggered speech is punctuated by a violent cough, and just talking seems to leave him drained.

A few weeks ago Hamooya's cough got so bad he left his wife to look after their newborn baby and six other children and travelled the 150 kilometres to get here. Did he have any idea what was wrong with him? His answer needs no translation: "TB". Since arriving at the clinic they also tested him for HIV, and the results came back positive for that too. Once his tuberculosis (TB) medication kicks in, he will begin

it. You may go all your life and never have a problem. Now with HIV, which destroys the immune system, it becomes a big issue."

The highest proportion of new TB cases is in sub-Saharan Africa: more than 260 people per 100,000 in 2011. By comparison, in the same year France saw 4 cases per 100,000. And the region is in the grips of an HIV epidemic; TB kills more people living with HIV than anything else, and detection and treatment of TB is vastly complicated by HIV co-infection. Where once treatment programmes operated independently, many countries like Zambia now try to test and treat the two together. In 2004, just 3% of TB patients in the World Health Organization (WHO)'s African Region were tested for HIV; in 2011, it was 69%. Hamooya was one of the lucky ones: detecting TB is extremely difficult in patients who also have an HIV infection,

public-health goal, and these efforts are beginning to bear fruit. Over the next few months, a new test called Xpert MTB/RIF that detects TB DNA will enter clinics in several high-burden countries in southern Africa; other tests are close behind. The question is, in the uncompromising settings that are home to the greatest burden of disease, will these new tests fulfil their potential?

NEED FOR SPEED

A fast TB diagnosis is important. The sooner a patient is diagnosed, the sooner they can start treatment to mitigate the debilitating symptoms of TB and limit the potential for transmission. But there is an added imperative for HIV-positive patients. "Starting someone on ARVs who has [untreated] TB means that, as their immune system

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- The Xpert MTB/RIF test is highly effective, simple, FAST, and addresses drug resistance

Video: new TB device

History of Xpert MTB/RIF Assay

- GeneXpert diagnostic system developed by Cepheid (Sunnyvale, CA)
- First deployed by USPS for rapid detection of ANTHRAX in mail sorting offices

Ulrich MP, Christenson DR, Coyne SR, et al. J. Appl Microbiol 2006; 100: 1011-16

Description: Xpert MTB/RIF Assay

“It is a self-contained, fully integrated, automatic platform that can be used with minimal technical skills. The cartridge-based system incorporates microfluidics technology and fully automated nucleic acid analysis to purify, concentrate, detect, and identify targeted nucleic acid sequences from unprocessed clinical samples.”

Lawn SD, Nicol MP. Future Microbiol 2011; 6: 167-82

Video: gas

Video: cartridge

GeneXpert Cartridge.Ink

Xpert MTB/RIF Test Endorsed

- WHO-endorsed 12/2010 as equivalent to AFB smear test for diagnosis of active TB
(currently in use in >87 countries)
- FDA-approved 2013
- CLIA-endorsed 2013 for general lab use

Xpert MTB/RIF test locations in PNG

