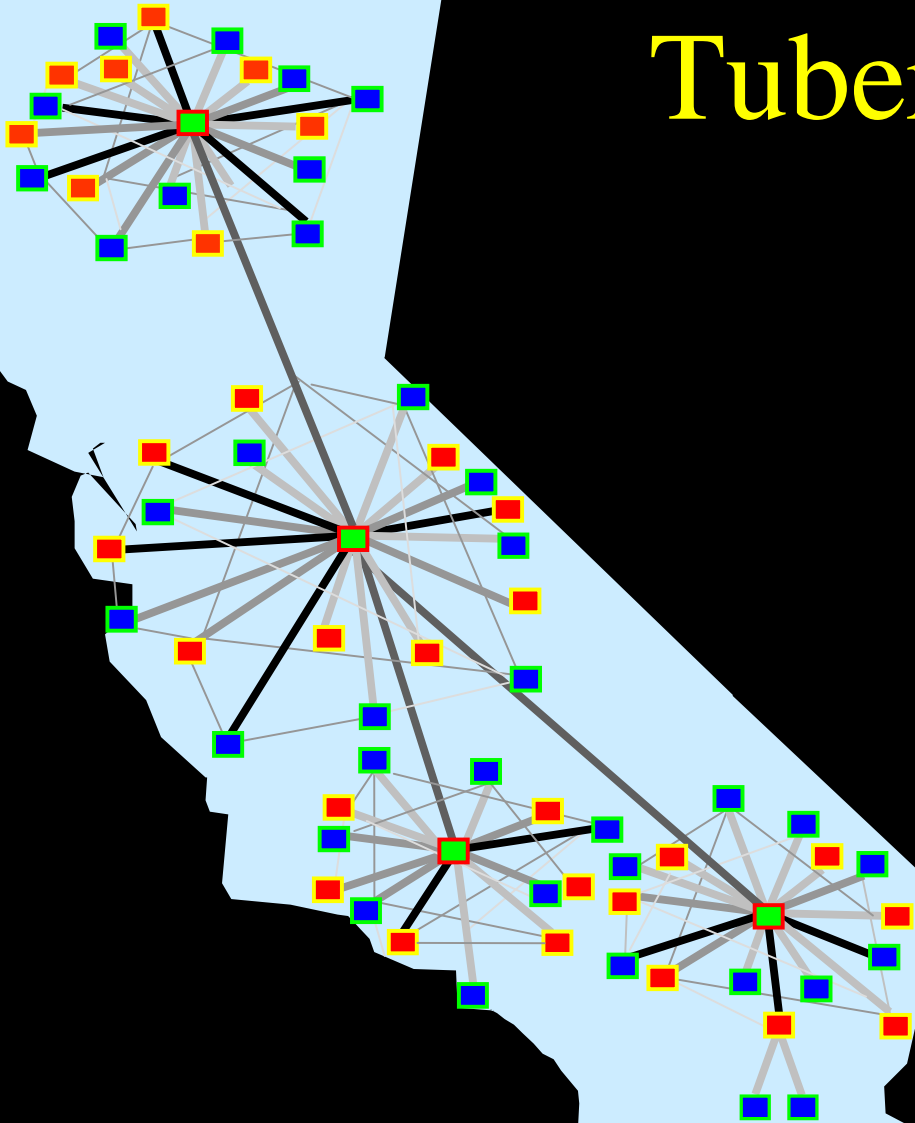


Tuberculosis Control in California

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Feb 27, 2006



Outline

- **Why TB?**
- **Transmission/pathogenesis**
- **Diagnosis and treatment**
- **Control strategies**
- **Tuberculosis trends**
- **Who is affected?**
- **TB outcomes and public health impact**
- **Current challenges in controlling TB**



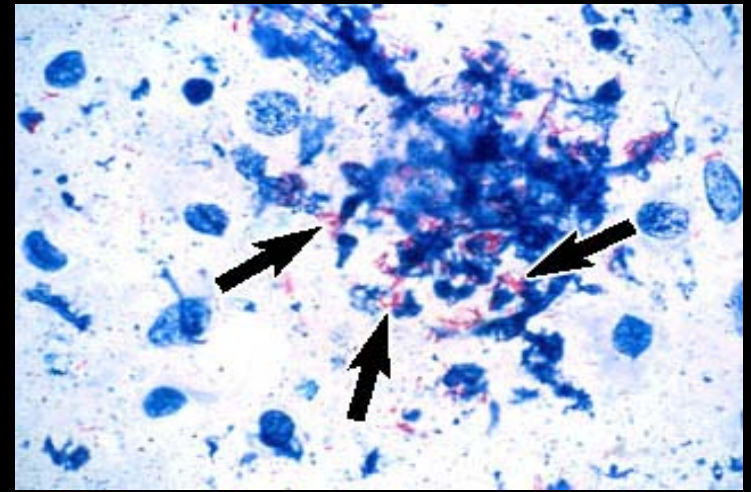
Why TB?

Global Burden of Disease

- 10 million develop TB each year
- 2 million die from disease; a leading cause of death worldwide
- 3 billion persons with latent TB infection = global reservoir
- Translates to 1 in 3 infected worldwide



Transmission and Pathogenesis



- *Mycobacterium tuberculosis*, the causative agent, is spread by droplet aerosol from TB patients to exposed contacts
- Unusual modes: transplantation, bronchoscopy, raw milk ingestion from infected cattle

Pathogenesis

- After exposure, 1/3 become infected
- within 2-8 weeks (Positive TST)
- Progression to disease in 5-10%(lifetime risk)
- 1-5% infected contacts promptly develop active TB
- Infection latent in 90%



What Can We Do to Stop TB Transmission?

- Early case finding
- Effective treatment
- Successful contact investigation
- Infection Control measures
- Detect and treat latent infection

Diagnostic tool set

- **Clinical suspicion**
- **Tuberculin skin test**
- **QuantiFERON (gamma interferon assays)**
- **Chest xray**
- **AFB Smear**
- **Culture**
- **PCR**
- **Susceptibility results**

Case-finding Challenges: Delays in Diagnosis

Study population: Pulmonary TB cases reported
8/2000 - 3/2002 from Santa Clara County (n=138)

Definition: Delay in diagnosis:
> 60 days from symptom onset to treatment start

Preliminary Findings:

- 51 (37%) had diagnosis delay; mean delay:
90 days (2-1190)
- Delays in 40% sputum smear positive cases
- Delays in 43% cases with cavitary disease
- 74% “patient”; 18% “provider”, 8% both

Case-finding in Foreign-born: B-notification

- 3,489 B-notifications to California in 2004;
(> 1/3 of US total)
- 3.0 - 7% have active TB on US evaluation
- Among foreign-born cases diagnosed within a year of arrival, B-notification cases found earlier (3 months vs 5 months without B-notification)
- Increased proportion of TB cases with B-notification that have MDR TB: (1.5% in 2000 to 4.7% in 2004)
- Evaluation and treatment can avert 40 cases and 6 deaths in next 20 years

TB Treatment:

Treatment and its completion is the single most important factor in controlling TB in a population

- Halts transmission
- Decreases morbidity and mortality
- Prevents acquired drug resistance

Making an early diagnosis and knowing when to start treatment in a suspect is key!

Treatment of Tuberculosis

Unscientific and Probably Ineffective

- Wolf's liver boiled in wine
- Flesh of a she-ass with broth
- Smoke of dried cow dung
- Elephant's blood
- Woman's milk
- Mice boiled in salt and oil

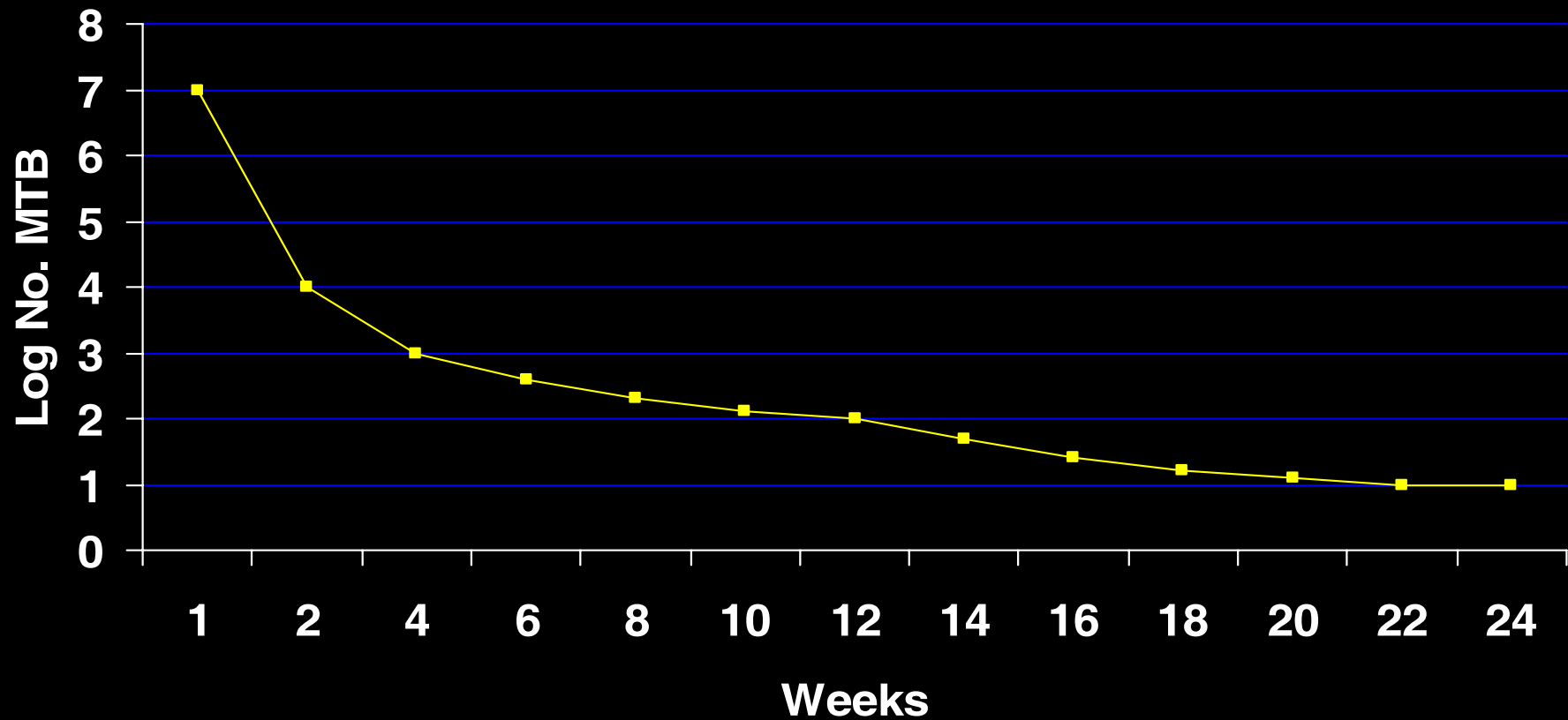
Effective Treatment



Goals of Antituberculosis Chemotherapy

- Kill tubercle bacilli rapidly
- Prevent the emergence of drug resistance
- Eliminate persistent bacilli to prevent relapse

Effects of Therapy on *M. tuberculosis*



Directly Observed Therapy

- Observe ingestion of each dose of medicine
- Opportunity for patient-centered management
- Provide support, education and monitoring throughout therapy

Contact Investigation: What is it?

Purpose = Interrupt transmission

Evaluate exposed individuals to:

1. Find and treat new cases of active TB to render cases noninfectious

and

2. Identify and treat persons with latent TB infection to prevent future cases



Why Perform Contact Investigations?

- Contact investigation provides high yield of secondary case finding; if treated and isolated can interrupt further transmission
- Recently exposed and infected persons (contacts) have a high likelihood of developing active disease in first two years post-exposure
- INH is effective treatment to prevent disease development

Approach: Contact Investigation

- Case of active infectious TB confirmed or strongly suspected
- Case interviewed to give names of contacts who shared airspace during infectious period

CA Code of Regulations :2500, 2502.
Reports by Local Health Officer to State
Department of Health Services

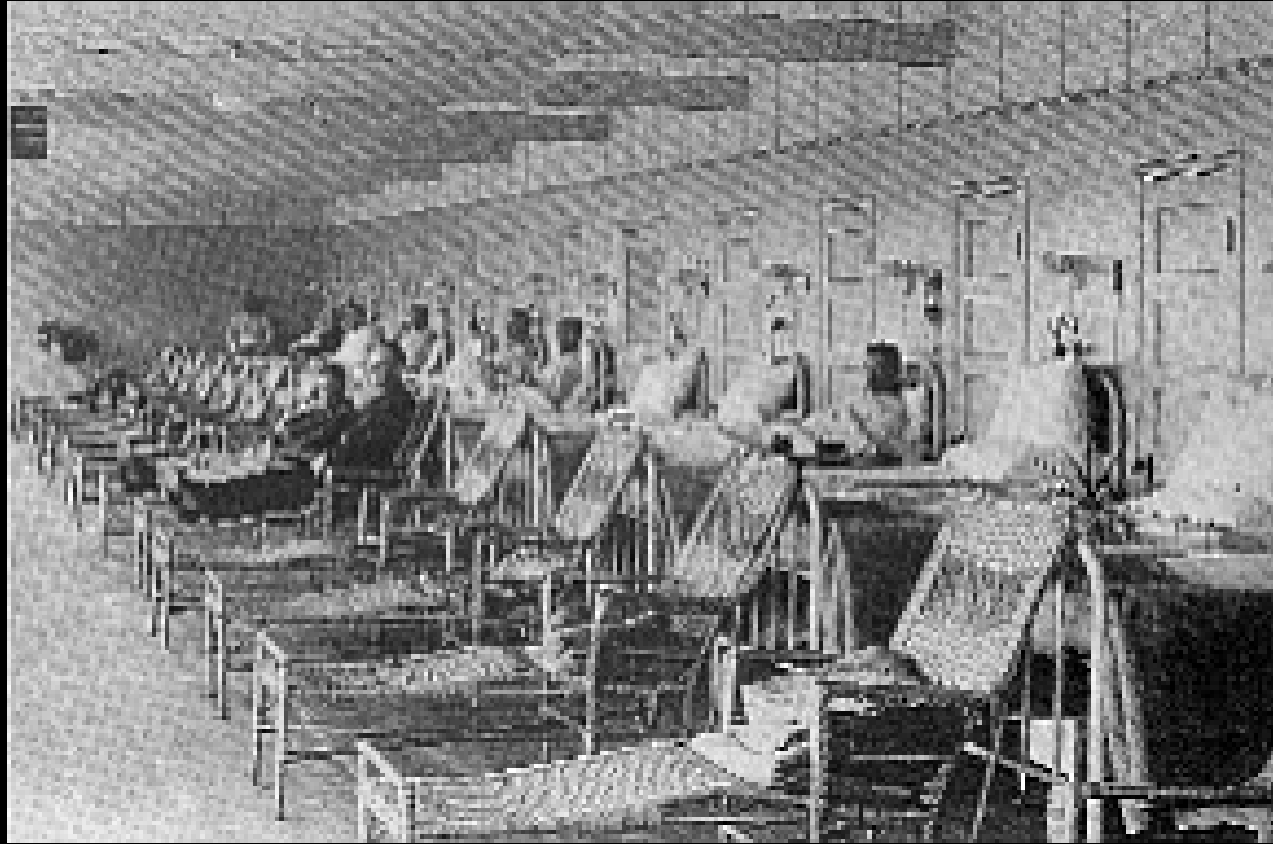
*2502. Each local health officer shall report weekly to the director the number of cases of those diseases, conditions or unusual diseases or **outbreaks** of disease reported pursuant to Section 2500.*

OUTBREAKS of ANY DISEASE *be reported immediately by telephone.*

Summary: TB Control Strategies

- Surveillance
- Case finding
- Case treatment with direct observation
- Contact investigation
- Targeted testing and treatment of latent TB infection
- Isolation and detention
- Legal orders
- Provider and public education
- Global TB control

Tuberculosis Epidemiology



Questions:

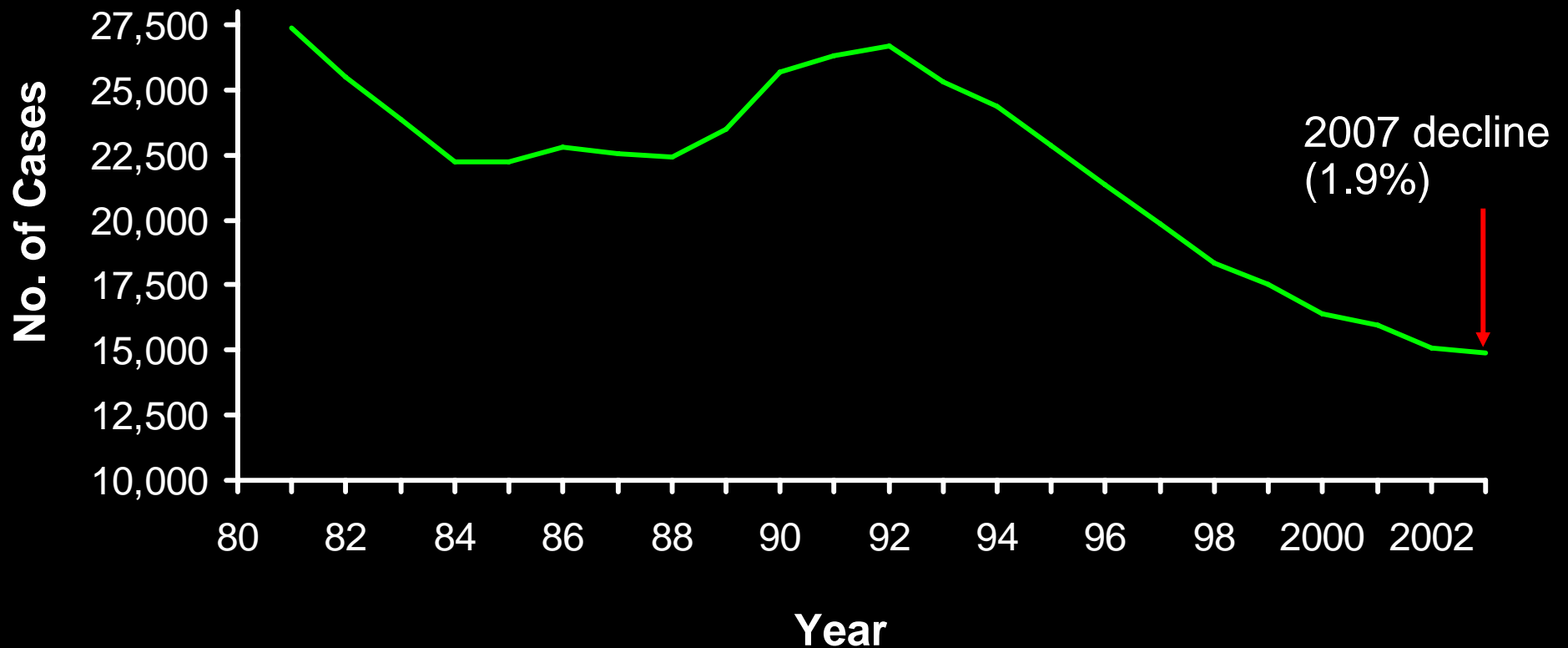
- Are we making progress in California?
- How much TB transmission is occurring?
- How does transmission influence our epidemic?
- What can we do about it?

Trends in the U.S. and California

- Since 1993, cases have steadily declined in US to ~ 15,000 /year
- CA contributes the most cases of all states and case increases occurred recently in 2001 and 2003
- Outbreaks, pediatric cases, and deaths due to TB continue to occur regularly

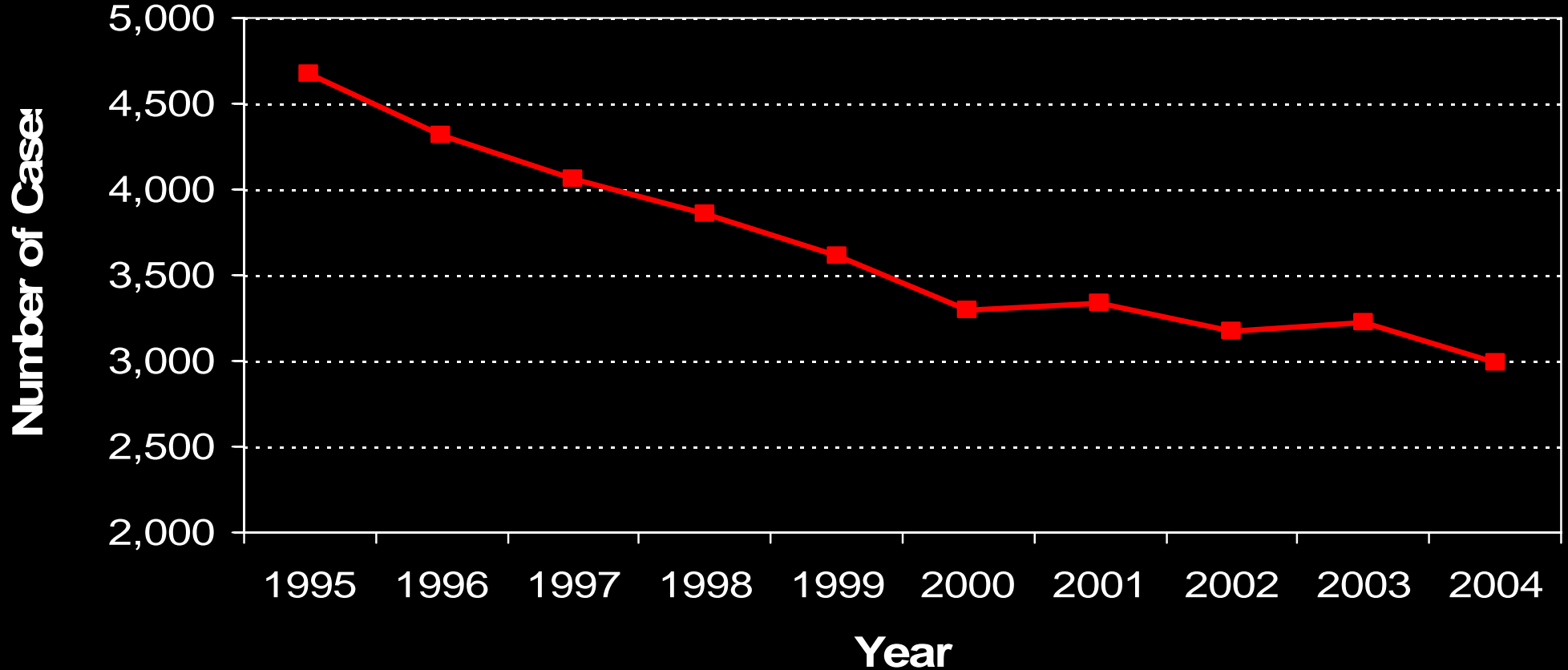
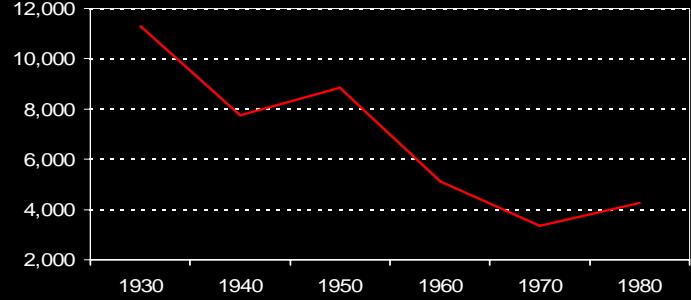


Reported TB Cases United States, 1981-2007

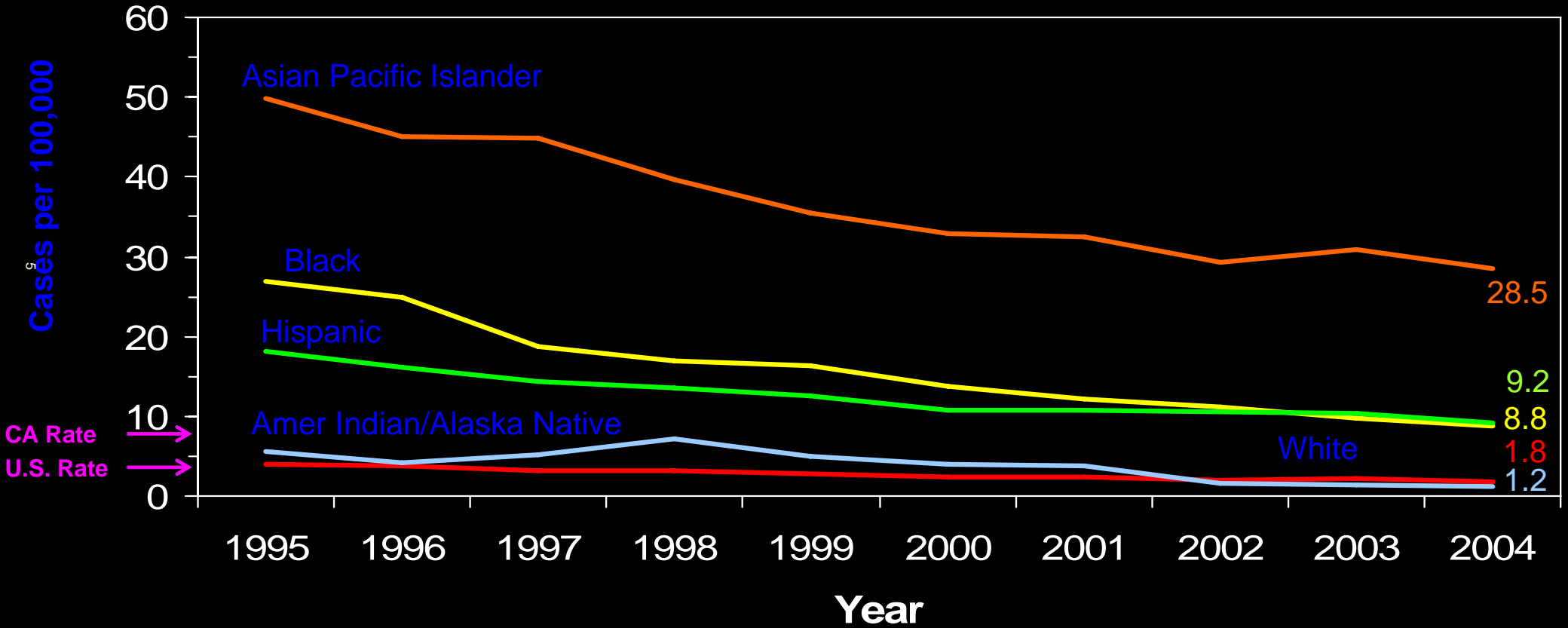


Tuberculosis Cases In California, 1995-2004

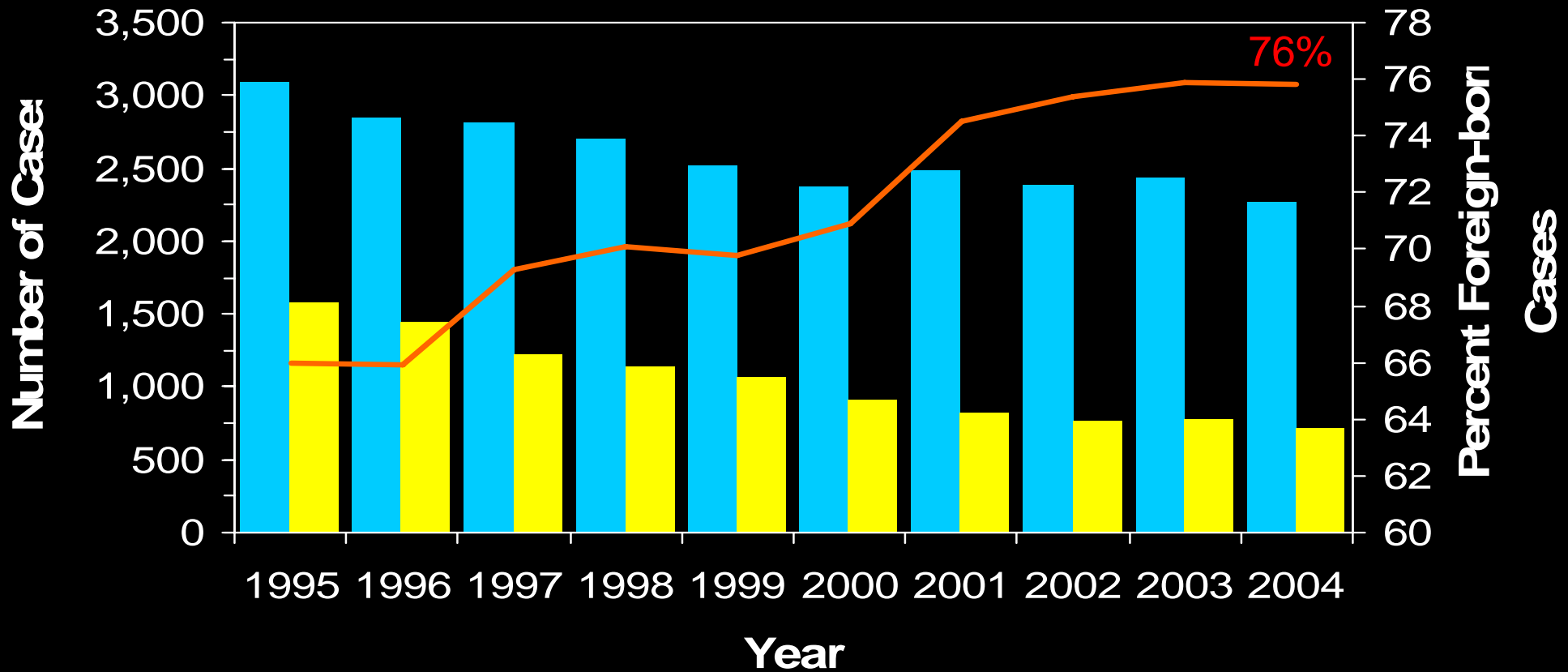
Tuberculosis Cases In California. 1930-1980



Tuberculosis Case Rates by Race/Ethnicity: California, 1995-2004



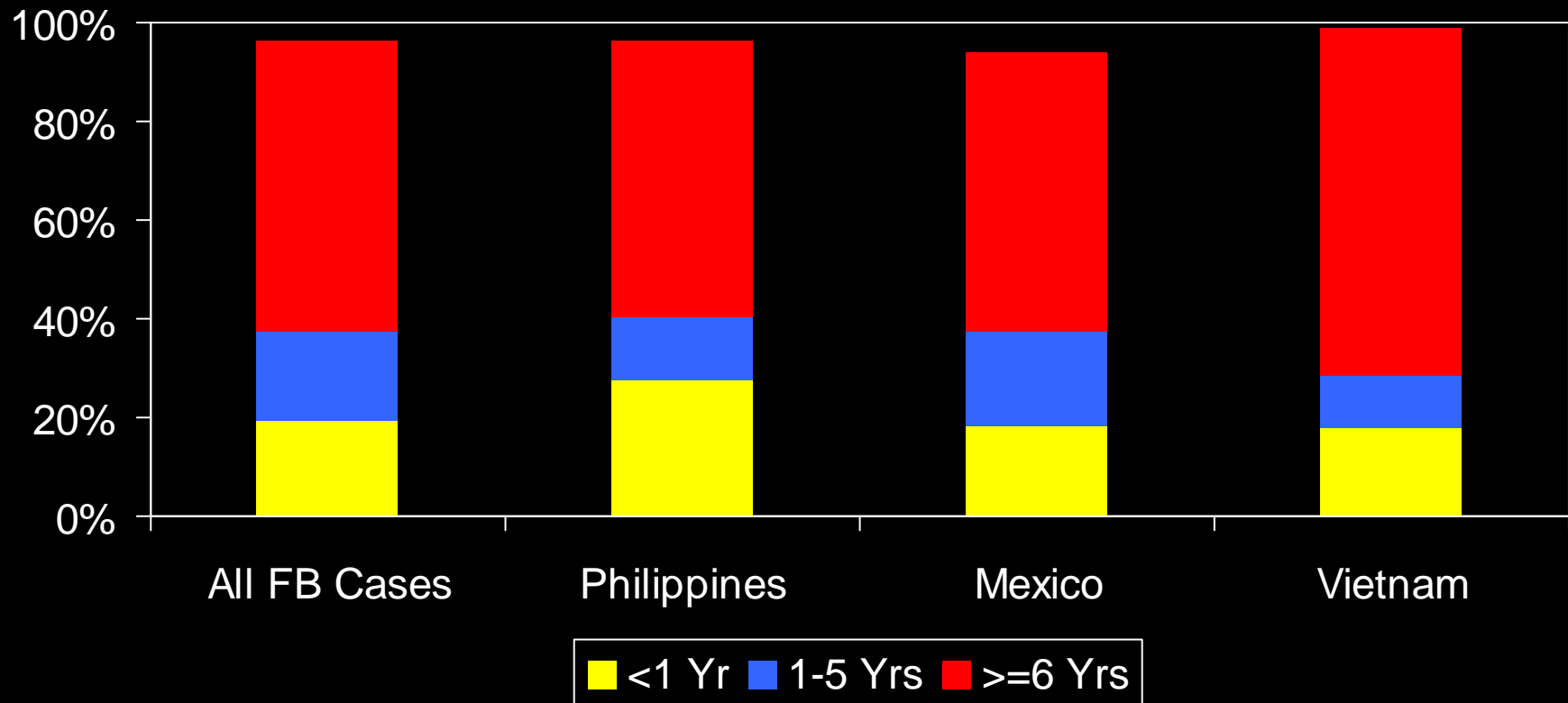
Tuberculosis Cases among the Foreign-born and US-born , California, 1995-2004



Tuberculosis Cases by Country of Origin: California, 2004

Country	No.	%
Mexico	822	33.8
Philippines	474	19.5
Vietnam	285	11.7
China	148	6.1
India	113	4.6
Korea, South	77	3.2
Guatemala	50	2.0
El Salvador	42	1.7
Cambodia	40	1.6
Laos	35	1.4

Length of U.S. Residence Prior to TB Diagnosis, California, 2003



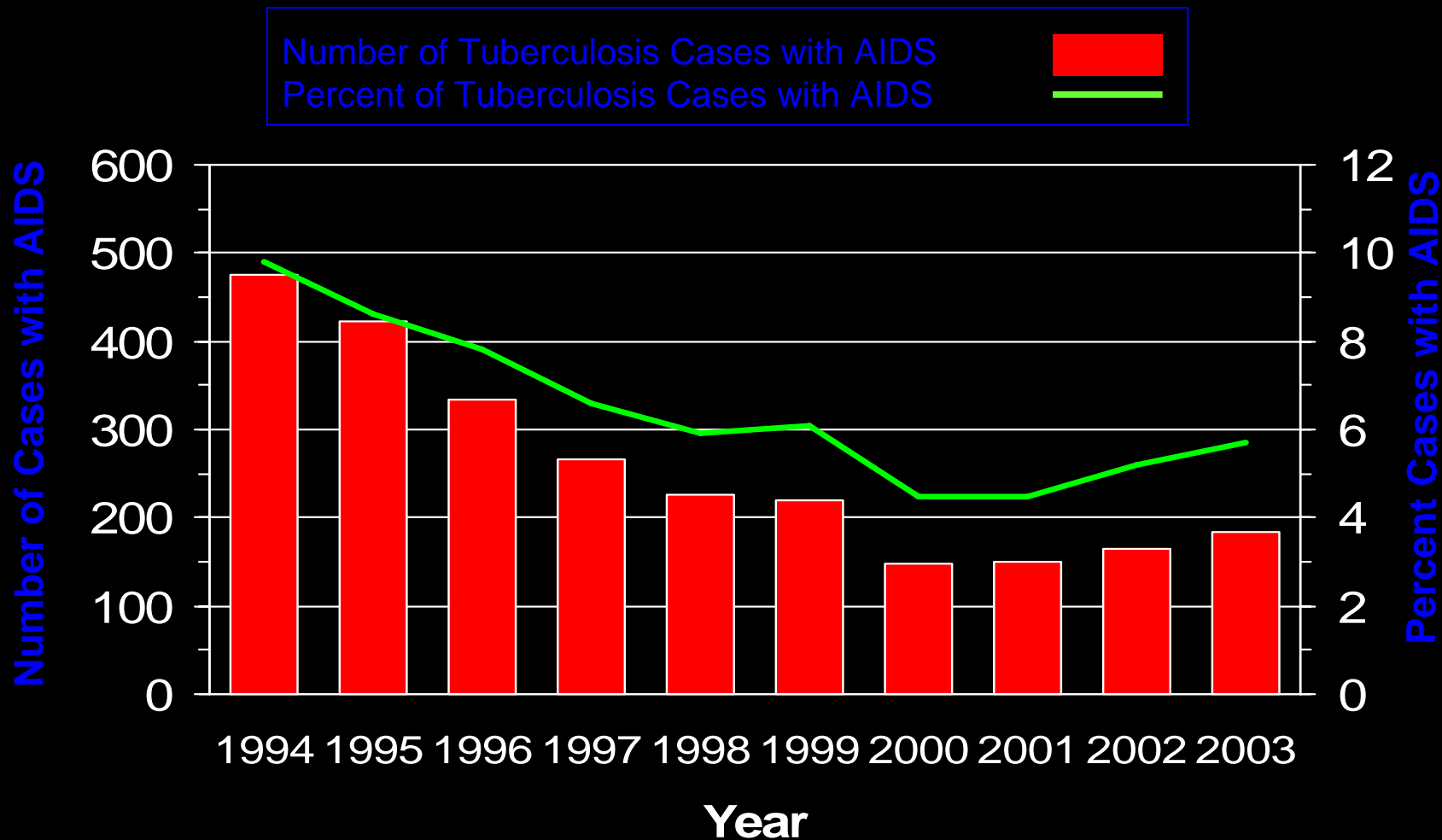
TB Among Persons of High Risk, California, 2003

Category	No.	%*
Excess alcohol	344	11.0
Homeless	224	7.0
Non-injecting drug use	196	6.3
Correctional facilities	91	2.8
Injecting drug user	73	2.3
Long-term care facility	69	2.1

* Based on number of respondents to category



Tuberculosis Cases by AIDS Diagnosis*: California, 1994-2003



* Match found in AIDS Case Registry, California Office of AIDS

"A chilling account." —*The New York Times*

Timebomb

The Global Epidemic of
Multi-Drug-Resistant
Tuberculosis

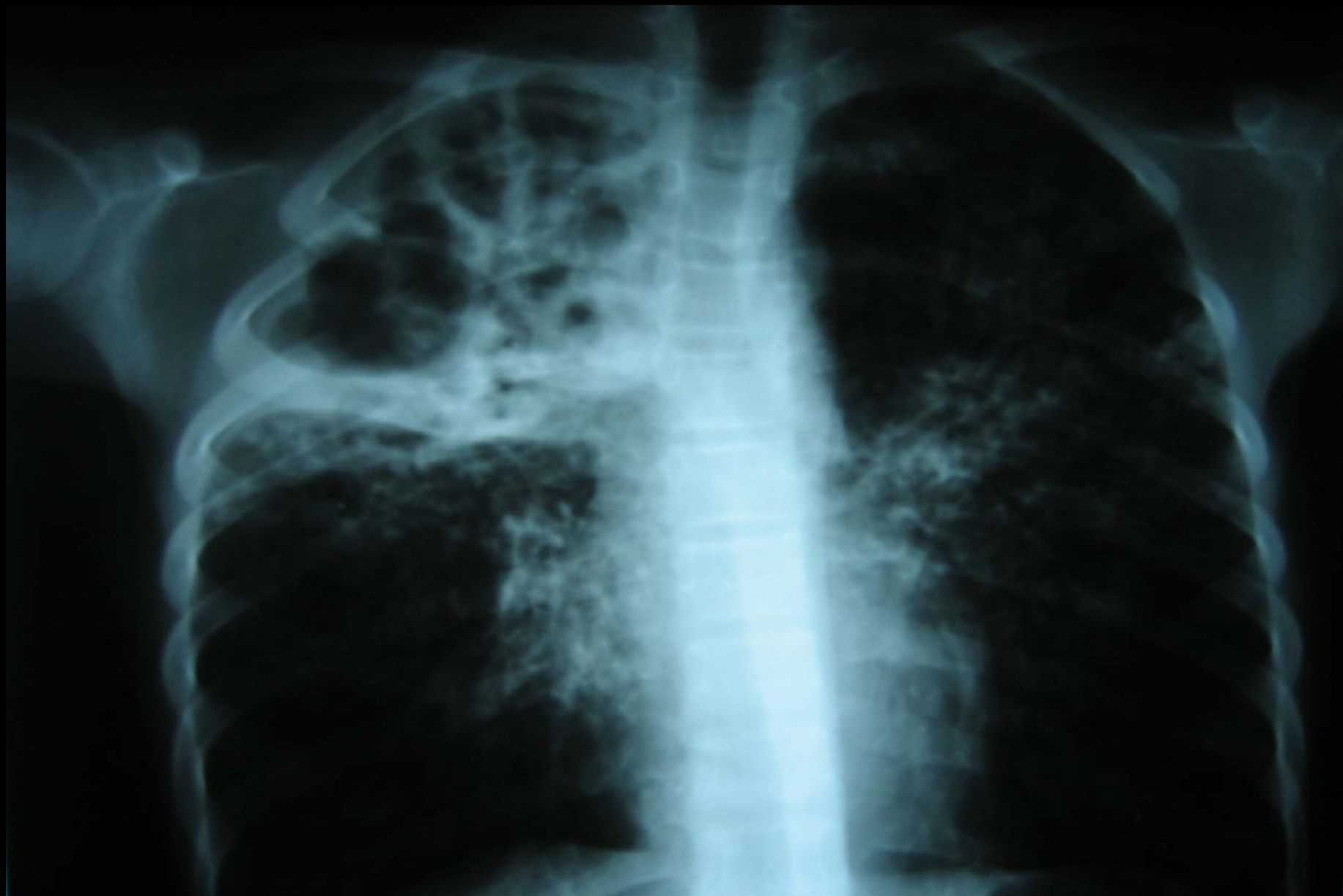
Lee B. Reichman, M.D., M.P.H.
with Janice Hopkins Tanne

MDR TB Cases in CA, 1994-2003

- 407 MDR TB cases reported from 38 (62%) of CA's LHJs
- MDR TB increased from 7% to 21% in LHJs < 30 cases
- 83% were foreign-born; 35% in US < 1 year
- 90% with pulmonary disease; twice as likely to be cavitary
- Significantly less likely to complete treatment (67%)
- Deaths and moves much more common
- 83% had resistance in addition to I and R

Case Example

- 32 yo female recently arrived from Mexico with long history of multiple TB treatment episodes
- 4+ smear positive, CXR: extensive cavitary disease
- Isolate: resistant to all drugs but PAS, linezolid
- 2 children with skin test conversion



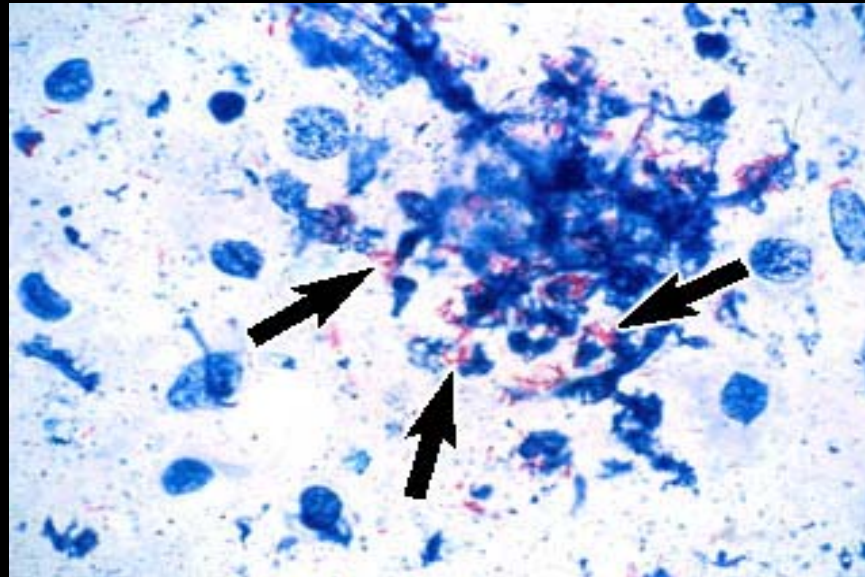
What is the Magnitude of TB Transmission in California?

Estimates of transmission:

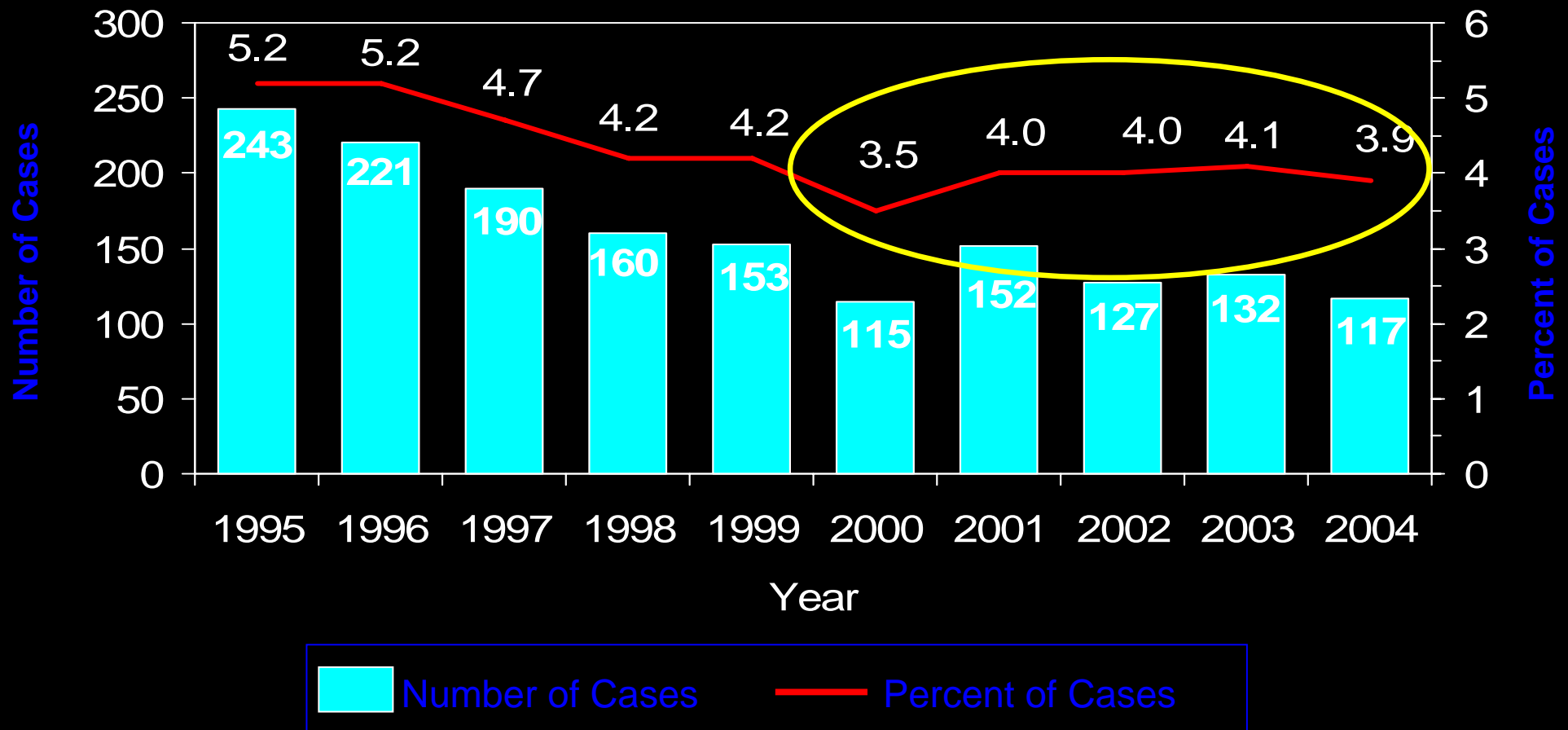
- Pediatric cases < 5
- Outbreaks
- Cases in genotype clusters

Infectious Status of TB Cases in California, 2004

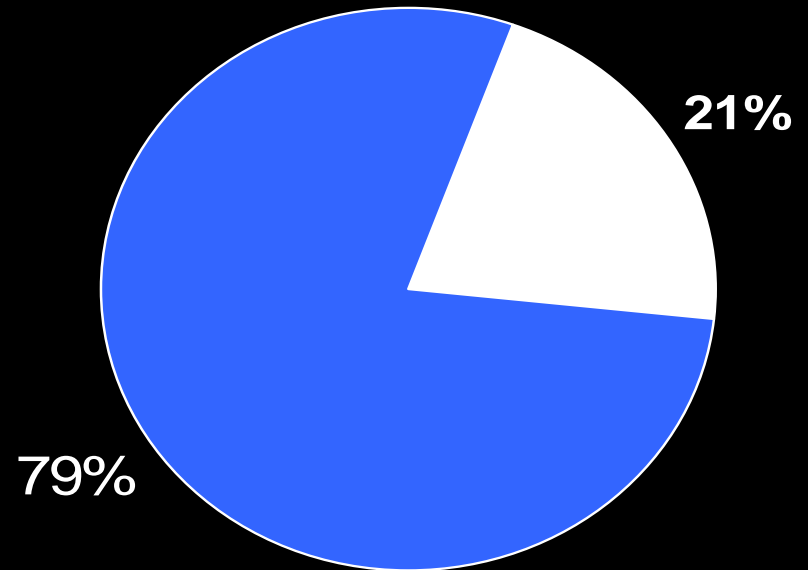
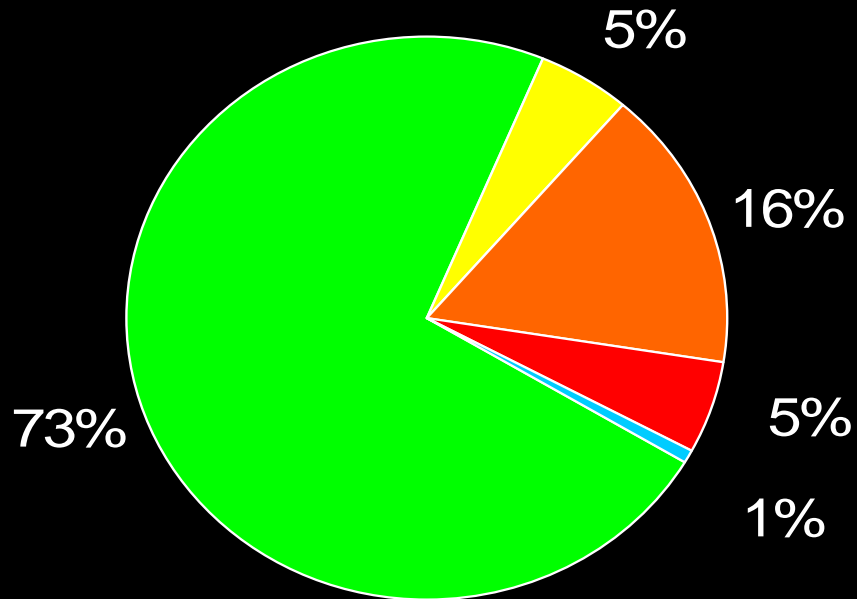
- 2,379 (80%) with culture positive pulmonary TB
- 1,081 (45.5%) with positive AFB sputum smear
- 529 (22.9%) with cavitory disease



Pediatric Cases in California, 1995-2004



Characteristics of Pediatric Cases, California, 2004

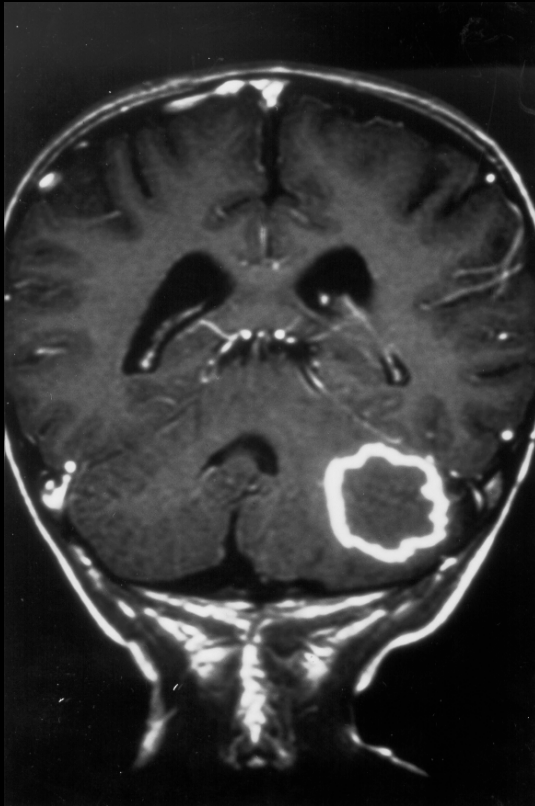


- Hispanic
- Black
- Asian/Pacific Islander
- White
- Amer Ind/Alaska Native

- U.S.-born
- Foreign-born

Pediatric Tuberculosis

- 2 year old male
- Fever, weight loss, seizures
- Meningitis with cerebellar and pulmonary lesions



Reasons for Pediatric Cases: Findings from the TBESC Pediatric Study

Study population:

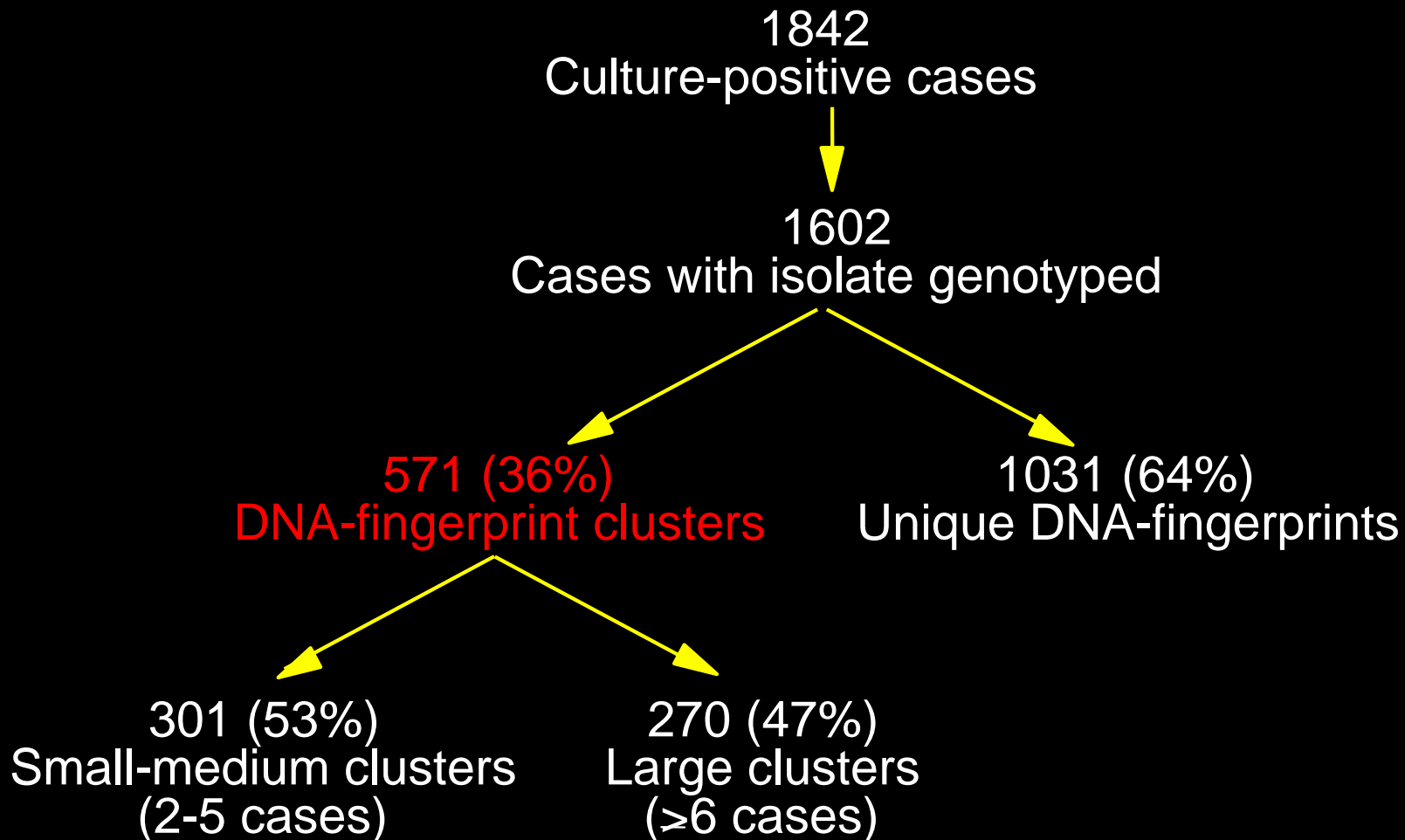
Pediatric cases < 5 years of age in San Diego and Alameda counties

Time period: 2002-2004

- Total n=61
 - 56 (91.8%) U.S.-born
 - 5 (8.2%) Foreign-born
- 44 (72%) Foreign-born parents
- 19 (31%) Source case identified
- Delays in diagnosis of source case common

Population-based Molecular Evidence of Transmission

San Francisco Bay Area, (pop. 5 million)
1996-1998



Selected Outbreak Investigations California, 1998-2004

Year	No. Case	No. Contacts	Characteristics
1998			
Humboldt	6	>200	Rural, Native Amer., INH-resistant
Tuolumne	5	>100	Prison
1999			
Monterey	2	>100	Renal dialysis center, INH-resistant
San Joaquin	3	> 75	Renal dialysis center
2000			
Sacramento	14	>600	Homeless, multi-institution
Yuba	3	>100	Pediatric, school, MDR
2001			
Fresno	7	~100	Hispanic women/children
2002			
Kern	3	>200	High school, MDR
Alameda	5	> 60	4 pediatric cases
San Francisco	32	>500	Homeless, IVDU, HIV+



Selected Outbreak Investigations California, 1998-2004 (Cont'd)

Year	No. Case	No. Contacts	Characteristics
2003			
Los Angeles	3	> 30	MDR in extended family; college
Shasta	3	>170	Jail
2004			
Orange	7	> 50	Pediatric; extended family
Sacramento	4	40	Workplace exposure
Santa Barbara	3	>300	Homeless shelter
Solano	3	>400	Prison inmates
Yuba	4	>400	MDR; high school; workplace; Hmong; U.S.-born military recruit

TB Outbreak Among Newly Arrived Among Refugees in California, 2004- 2005

- Between 6/04 – 3/05, ~3,400 Hmong refugees arrived in CA (19 counties)
- As of 5/6/05, 27 TB cases have been reported
- Case rate ~800/100,000
- Age < 15 years ; n=12 (44%)
- 4/8 (50%) culture positive cases = MDR TB



Why did this outbreak
occur?



Infectious MDR TB Cases Among Newly Arrived Among Refugees

Age	Date Overseas Exam	Date U.S. Arrival	H/O TB-RX	TB B-notif	Days U.S. Arrival To Exam	CXR	Smear
41	4/04	6/18/04 (1.6 mos)	+	-	1 day	cavitary	+
62	6/04	9/16/04 (3 mos)	+	B2	32 days	Nodular infiltrate	+
17	11/04	12/16/04 (1 mos)	+	B1	17 days	cavitary	+
66	5/04	1/22/05 (2.5 mos)	+	B2	12 days	LUL Infiltrate/fibrosis	+

TB History of Outbreak Case

OVERSEAS: 3/04-11/04

- 17 yo male with class B1, overseas exam in 11/04 TB treatment in Thailand
- 3/04 smear positive, cavitory disease
- Treated with IREP X 2 mos; then IRE X 4 mos.
- CXR at 2 mos , no change in LUL , increased R lung markings
- Monthly smears neg until 8/04 (3/3 smear positive)
- Culture results: resistance to INH , strep
- 11/04 completed rx, smear neg X 3; CXR –no change

US EXAM: 1/05

- 1/05: Smear numerous AFB; + MDR; CXR LUL, RUL cavitory disease

Impact of an Outbreak

- Cases \$
- Contacts \$
- Future cases \$
- Hampered ability to maintain ongoing TB control work
 - Human impact: death and disability
 - Community: disruption and loss

How Does Transmission Influence Our Epidemic?

Generation of Tuberculosis Cases in California, 2003

TB3
Entry active case
(prevalent) from
outside U.S.

TB2

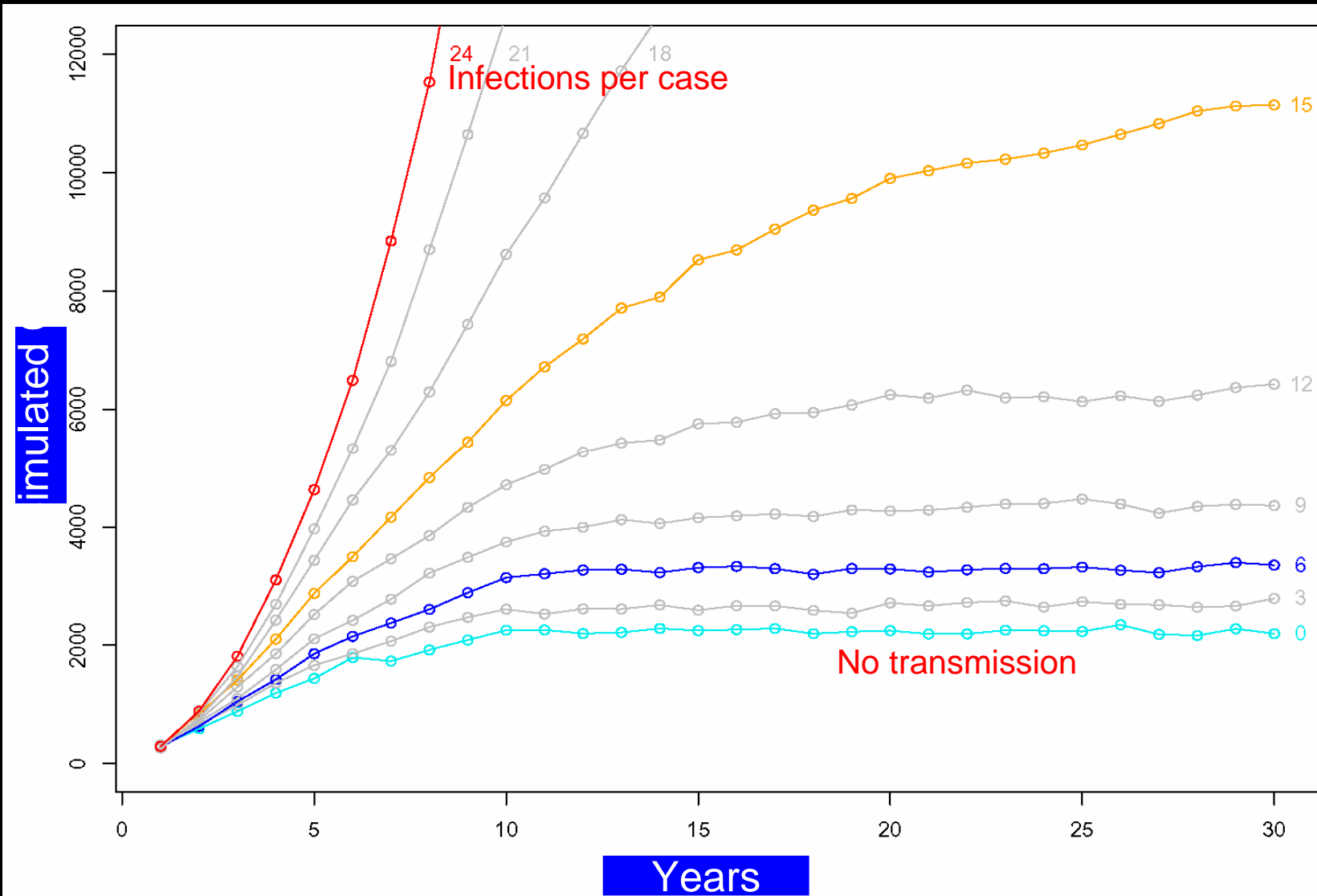
- Recently infected progress to active disease
- Remote infection progress to active disease
- Reinfection with progression to active disease

TB4

TB3
3,230

- Relapse of disease in previous treated TB3 (TB4)
- Remote infection with inactive disease (TB4) progresses to active disease
- Reinfection of person with inactive disease (TB4) and progression to active disease

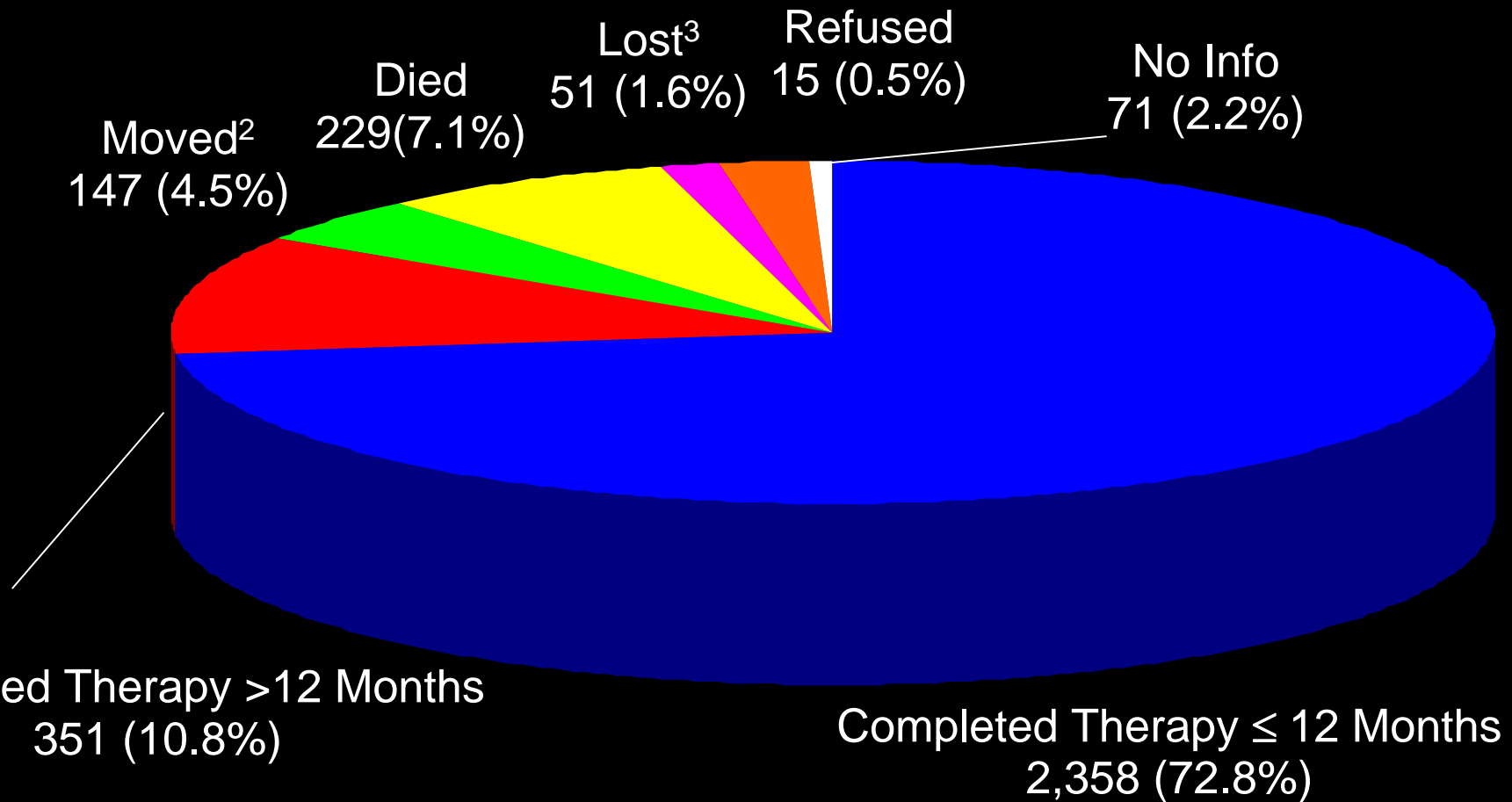
Simulation of Case Count Resulting From Increasing Transmission



Public Health Impact

- Outcomes of TB treatment
- Deaths
- Cost
- Individual Health
- Stigma
- Factors influencing TB outcomes

Tuberculosis Cases¹ by Reason Therapy Stopped: California, 2003



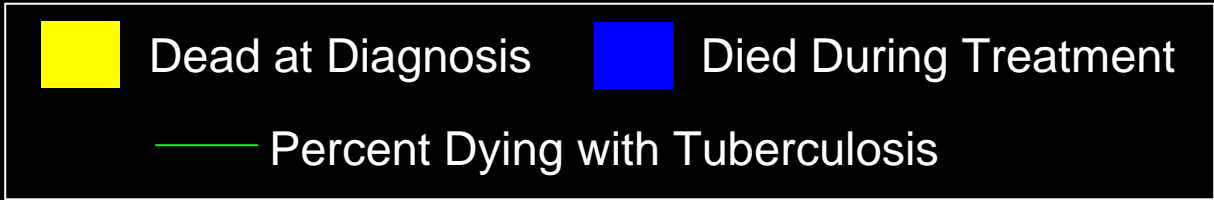
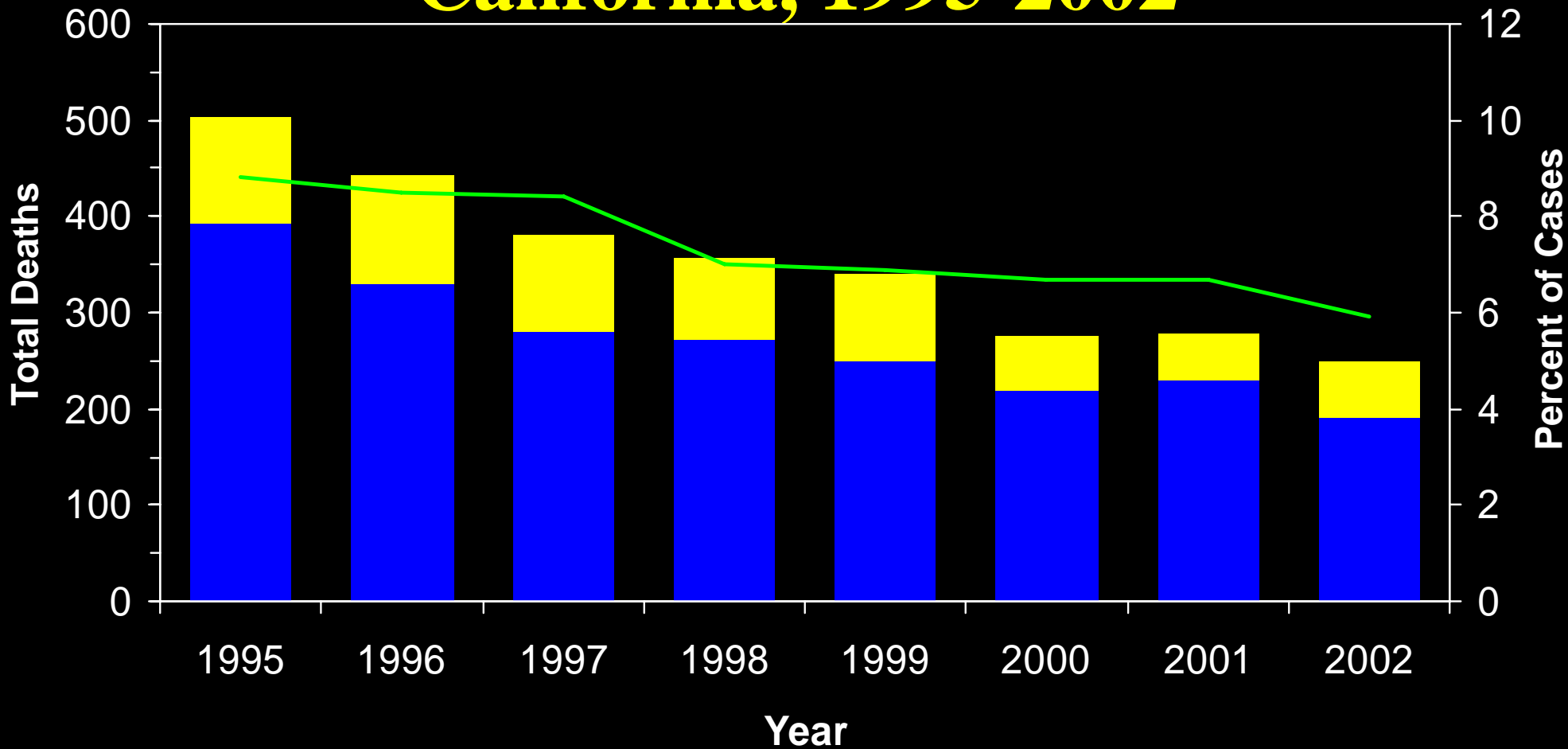
¹Patient alive at diagnosis and started on an initial drug regimen of 1 or more drugs.

²Patient moved to another jurisdiction with a known forwarding address before treatment was completed.

³Patient could not be located prior to the completion of treatment.



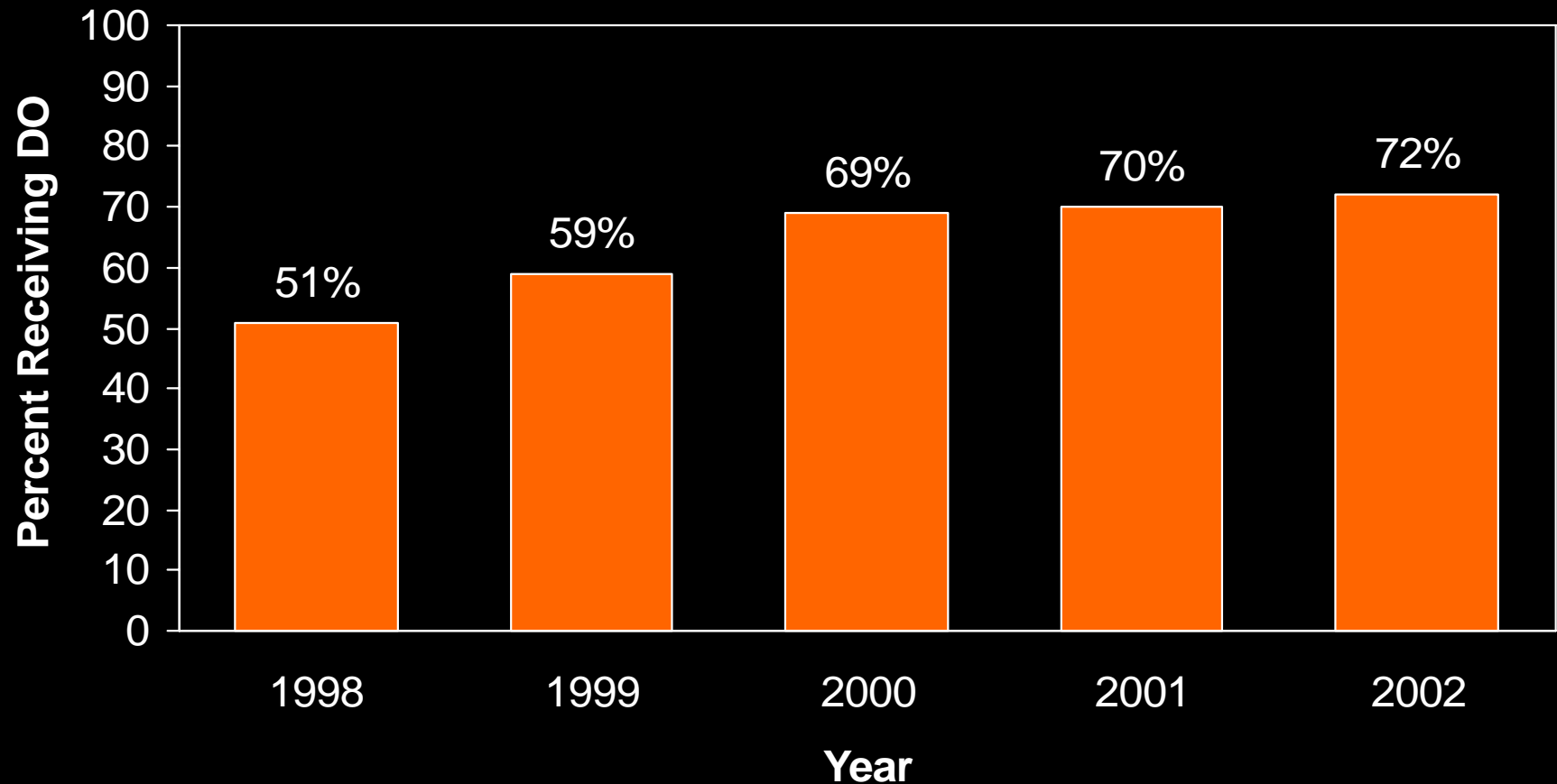
Deaths in Persons with Tuberculosis: California, 1995-2002



Cost

- \$ 20,000-\$25,000 spent for each TB case
- MDR TB is 10 times cost of non-MDR
- Productivity lost
- Disability incurred
- Incurable cases- lifetime isolation

Proportion of TB Cases Recommended for DOT Who Receive DOT Throughout Course of Treatment



Summary: TB Control Progress

- CA disproportionately impacted by TB
- Rate of case decline has slowed
- Case rate disparities persist
- 2/3 CA cases are foreign-born
- Receive 1/3 of U.S. B-notifications
- AIDS/TB increased
- MDR TB complicating epidemic

Summary: How Much TB Transmission is Occurring and How Important Is It?

Estimates of transmission:

- A new pediatric case <5 occurs every other day
- Genotype clustering suggests 1/3 cases involved in chain of recent transmission
- Outbreaks continue to occur in diverse settings /populations
- Transmission can propel an epidemic and amplify case counts rapidly

Summary: How Can We Intervene?

- Preventing /interrupting transmission must occur for continued case decline
- Identifying and preventing disease in newcomers is critical
- Shorten delays in diagnosis
- Strengthen B-notification and Contact investigation
- Global partnership more critical than ever

Challenges

- Institutional memory of TB fading
- TB control = resource intensive
- TB elimination dependent upon global TB efforts
- New strategies for case finding among foreign-born needed
- Efficient and effective approaches to identify and treat large pool of contacts and persons with LTBI also critical

Challenges

- Few rapid TB diagnostics
- Absence of truly short course treatment
- No effective vaccine
- HIV epidemic propelling TB increases
- Well trained public health workforce needed
- Lack of political will, diminished interest

TB and complacency

- National and global policy associated with tuberculosis has routinely suffered from “Aren’t we done with that disease yet?” syndrome.

Reason for Optimism

Private funding sources: Gates and others

New drugs in pipeline

Diagnostics = priority research activity

TB vaccine?



Revision of technical instructions

- Culture with drug susceptibility testing in addition to smear all with CXR abnormality
- Treat and clear if culture negative at end of treatment and smear negative 3 weeks prior to travel
- CXR on children in addition to adults
- Test children for latent TB infection

Goals of overseas screening

CURRENT

- Exclude most infectious TB
- Identify those at risk for progression and culture positive TB to have follow-up in US

PROPOSED

- Exclude all with active TB until cured

Benefits

- Increase case detection overseas in high risk group
- Decrease entry into US of active infectious TB
- Increase TB laboratory and treatment capacity overseas
- ?? Bring more resources to bear on overseas screening/ treatment
- ?? Create local capacity in countries of origin

Risks

- Resources required to do this right are huge
- Adequate investment in quality assurance needed
- OR will create more MDR TB by poor treatment and inadequate lab capacity
- Cost and delays will climb for immigrants applying for permanent visas

Scenario 4

You are notified by local health department about 6 TB cases identified over an 11 month period in a single renal dialysis unit in a Northern California county

Is this an outbreak?

- Is this a public health emergency?
- What steps would you take to confirm or refute an outbreak?
- What is the time frame for your response?