APHL
8th National Conference on Laboratory Aspects of TB

Twenty years of molecular epidemiology of tuberculosis in San Francisco

Community Research in Tuberculosis : *Muscogee County Revisited*

Philip Hopewell
Curry International Tuberculosis Center
University of California, San Francisco

APHL web site

Francis J. Curry: Selected publications, 1962-1973

- Tuberculin skin testing in San Francisco schools
- Tuberculin skin testing in San Francisco schools as an instrument of tuberculosis case finding. A five year study
- Study of irregular discharge tb patients at San Francisco General Hospital
- District clinics for outpatient treatment of tuberculous problem patients
- Tuberculin skin testing in San Francisco schools, 1956-1966: an epidemiologic analysis
- Prophylactic effect of isoniazid in young tuberculin reactors.
- A new approach for improving attendance at tuberculosis clinics
- Neighborhood clinics for more effective outpatient treatment of tuberculosis
- Tuberculosis prophylaxis
- Tuberculin skin testing of children as an effective tool in tuberculosis casefinding.
- The effect of acceptable and adequate outpatient treatment on the length of hospitalization and on readmission for relapse or reactivation of pulmonary tuberculosis.

Comstock GW. Public Health Reports 79: 1964; 1045-56

Community Research in Tuberculosis
Muscogee County, Georgia

GEORGE W. COMSTOCK, M.D., Dr.P.H.

EIGHTEEN YEARS ago, in 1946, the Public Health Service, in cooperation with the Muscogee County Health Department and assisted by the Georgia Department of Public Health, undertook to establish in a community of about 100,000 people a cooperative facility with the principal purpose of combining effective tuberculosis control and a broad basic epidemiologic study of tuberculosis (bibliog. 1). This cooperative facility was the Muscogee County Tuberculosis Study, one of a series of communitywide studies conducted by tuberculosis investigators, who for a long time had a virtual monopoly on this type of population-based research.

Probably the first community study in this country was the Health Demonstration Pro-

including those in Cattaraugus County, N.Y.; St. Louis County, Minn.; Lee and Coffee Counties, Ala.; and Giles and Williamson Counties, Tenn. Although the contributions of these studies to our knowledge are not reviewed here, students of tuberculosis will recognize that the Muscogee County Tuberculosis Study was built to a considerable extent upon foundations suggested by its predecessors.

The Muscogee County study had three principal architects. The fundamental pattern was laid down by Dr. Jacob Yerushalmy before he left the Public Health Service for his present position as professor of biostatistics at the University of California. Arranging a suitable setting for a program of community research was the responsibility of a remarkably astute

Community Research in Tuberculosis

Principles From Muscogee County

- Combining effective tuberculosis control and a basic epidemiologic study
- Broad coverage, standardized procedures, quantitative independent measurements
- Based on entire population of county
- Integration of service and research
- One study to complement and reinforce findings from another

Differences between Muscogee and San Francisco Counties :

Genotyping as an epidemiologic tool:

JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 1988, p. 2240–2245 Vol. 26, No. 11
0095-1137/88/112240-06$02.00/0

Repetitive DNA Sequences as Probes for *Mycobacterium tuberculosis*

KATHLEEN D. EISENACH,[1,2]* JACK T. CRAWFORD,[1,3] AND JOSEPH H. BATES[1,3,4]

Medical Research Service, John L. McClellan Memorial Veterans Hospital,[1] and Departments of Pathology,[2] Microbiology and Immunology,[3] and Medicine,[4] University of Arkansas for Medical Sciences, Little Rock, Arkansas 72205

Received 25 April 1988/Accepted 2 August 1988

Three cloned segments of *Mycobacterium tuberculosis* DNA which are promising as clinical probes were identified. An *Mbo*I digest of DNA from a clinical isolate of *M. tuberculosis* was cloned into bacteriophage M13. To identify recombinants specific for the *M. tuberculosis* complex, plaque lifts were hybridized with *M. bovis* and *M. kansasii* DNA. Recombinants which selectively hybridized with *M. bovis* DNA were characterized by probing slot blots and restriction digests of DNA from various mycobacteria. Three recombinants that did not hybridize to a significant extent with DNA from nontuberculous mycobacteria were identified. These three probes are of special interest because they are each repeated multiple (10 to 16) times in the *M. tuberculosis* chromosome. These probes were also shown to be useful for fingerprinting strains for epidemiological studies.

IS6110: Conservation of sequence in the *Mycobacterium*

JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 1993, p. 406–409
0095-1137/93/020406-04$02.00/0

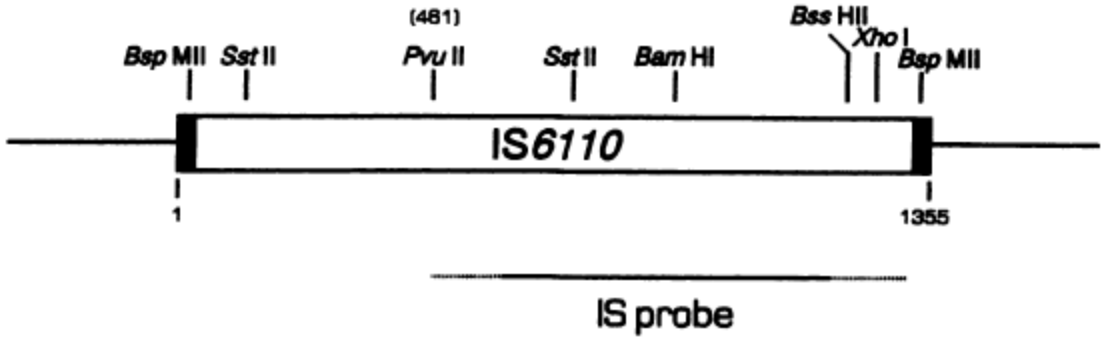
Vol. 31, No. 2

NOTES

Strain Identification of *Mycobacterium tuberculosis* by DNA Fingerprinting: Recommendations for a Standardized Methodology

JAN D. A. VAN EMBDEN,[1]* M. DONALD CAVE,[2] JACK T. CRAWFORD,[3] JEREMY W. DALE,[4] KATHLEEN D. EISENACH,[2] BRIGITTE GICQUEL,[5] PETER HERMANS,[6] CARLOS MARTIN,[7] RUTH McADAM,[8] THOMAS M. SHINNICK,[3] AND PETER M. SMALL[9]

Unit Molecular Microbiology, National Institute of Public Health and Environmental Protection, P.O. Box 1, 3720 BA Bilthoven, The Netherlands[1]; University of Arkansas for Medical Sciences. Little Rock. Arkansas 72205[2]: Division of Bac At



Department of Medicine, University of Texas Health Science Center, Tyler, Texas 75710,[1] and Departments of Anatomy,[2] Pathology,[3] Medicine,[4] and Microbiology,[5] University of Arkansas for Medical Sciences and J. L. McClellan Memorial Veterans Hospital, Little Rock, Arkansas 72204

Community-Based Molecular Epidemiology of TB in San Francisco:

- **SF DPH Division of Tuberculosis Control**

Gisela Schecter
Jennifer Grinsdale
Masae Kawamura
Tony Paz
Julie Higashi

- **CDHS/MDL**

Ed Desmond
Grace Lin

- **Molecular Epidemiology Laboratory at** Stanford

Peter Small
Kathy DeReimer
Gary Schoolnik
Sebastien Gagneux
Midori Kato-Maeda
Marcel Behr

- **Pulmonary/CCM at SFGH**

Phil Hopewell
Midori Kato-Maeda
Jillian Anderson
Chuck Daley
Laura Flores
Jordan Rose
Dan Chin
Elizabeth Fair
Joyce Barrozo
Bob Jasmer
George Yen
Leah Jarlsberg
Payam Nahid
Adithya Cattamanchi
John Metcalfe
Marcos Burgos
Dennis Osmond
Gompol Suwanpimolkul

Molecular Epidemiology of TB

- Uses a “stable” biomarker to track the organism through a population.
- Requires inclusion of a high proportion of cases and a reasonably “stable” population.
- Assumes that there is an epidemiological link between cases from whom the “same” organism (same pattern RFLP/DNA fingerprint) is isolated. (clustering)
- Assumes progression to disease within the time period between an index case and a “secondary” case.
- Cases without matching isolates (unique) assumed to result from activation of latent infection.
- Best interpreted in context of good epidemiological data

Molecular epidemiology of TB in San Francisco

- Outbreaks
- “Community epidemiology”
- Specific populations
  - Foreign-born (X2)
  - Homeless
  - Contacts
- Features of the disease
  - Smear negative cases
  - Extra-pulmonary disease
- Features of the organism
  - Drug resistance
  - Lineage/sub-lineage

Assessing an outbreak

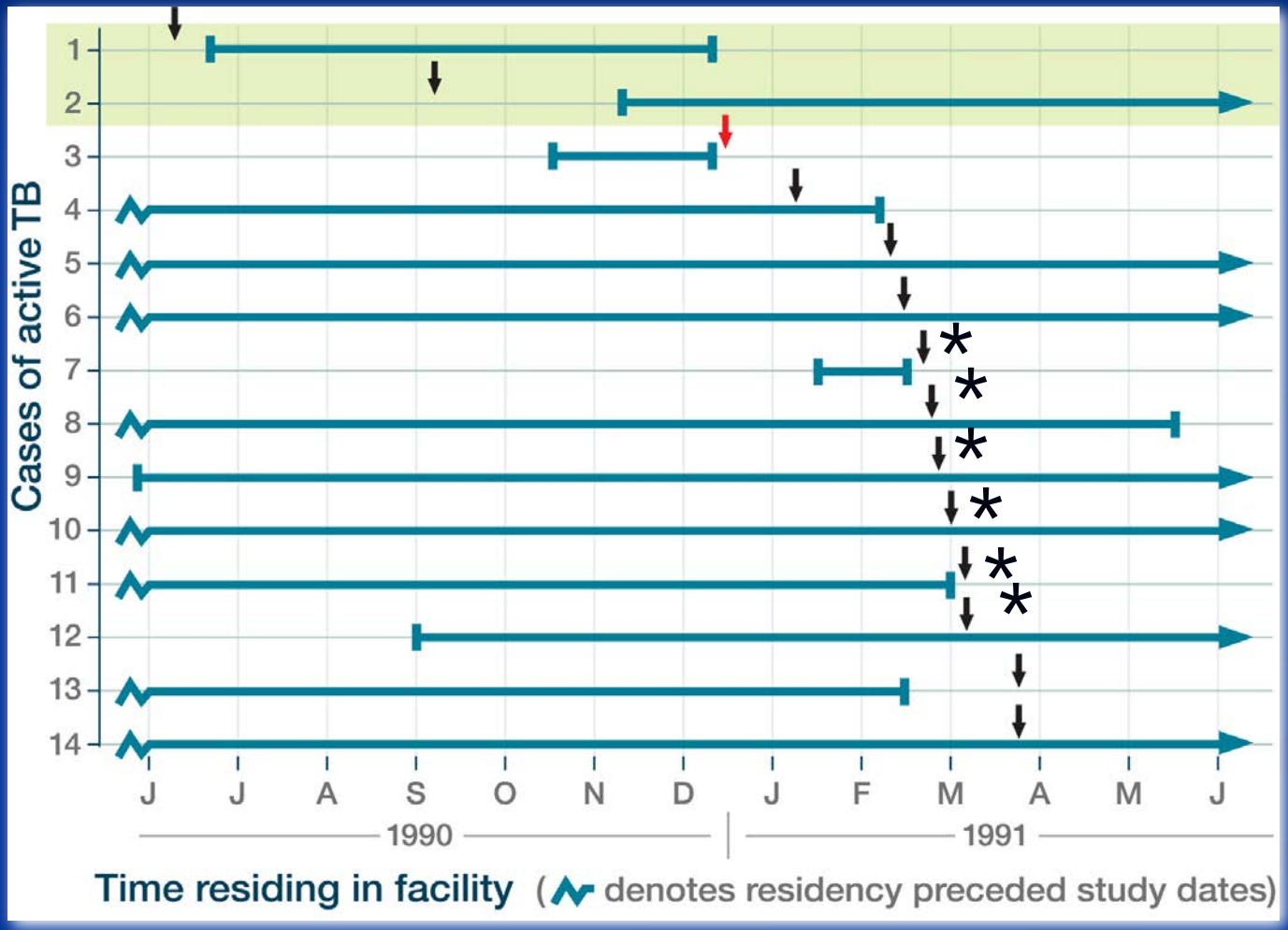
THE NEW ENGLAND JOURNAL OF MEDICINE Jan. 23, 1992

AN OUTBREAK OF TUBERCULOSIS WITH ACCELERATED PROGRESSION AMONG PERSONS INFECTED WITH THE HUMAN IMMUNODEFICIENCY VIRUS

An Analysis Using Restriction-Fragment–Length Polymorphisms

CHARLES L. DALEY, M.D., PETER M. SMALL, M.D., GISELA F. SCHECTER, M.D., M.P.H., GARY K. SCHOOLNIK, M.D., RUTH A. MCADAM, D.PHIL., WILLIAM R. JACOBS, JR., PH.D., AND PHILIP C. HOPEWELL, M.D.

An Outbreak of TB With Accelerated Progression Among Persons Infected With HIV



↓ = TB diagnosis

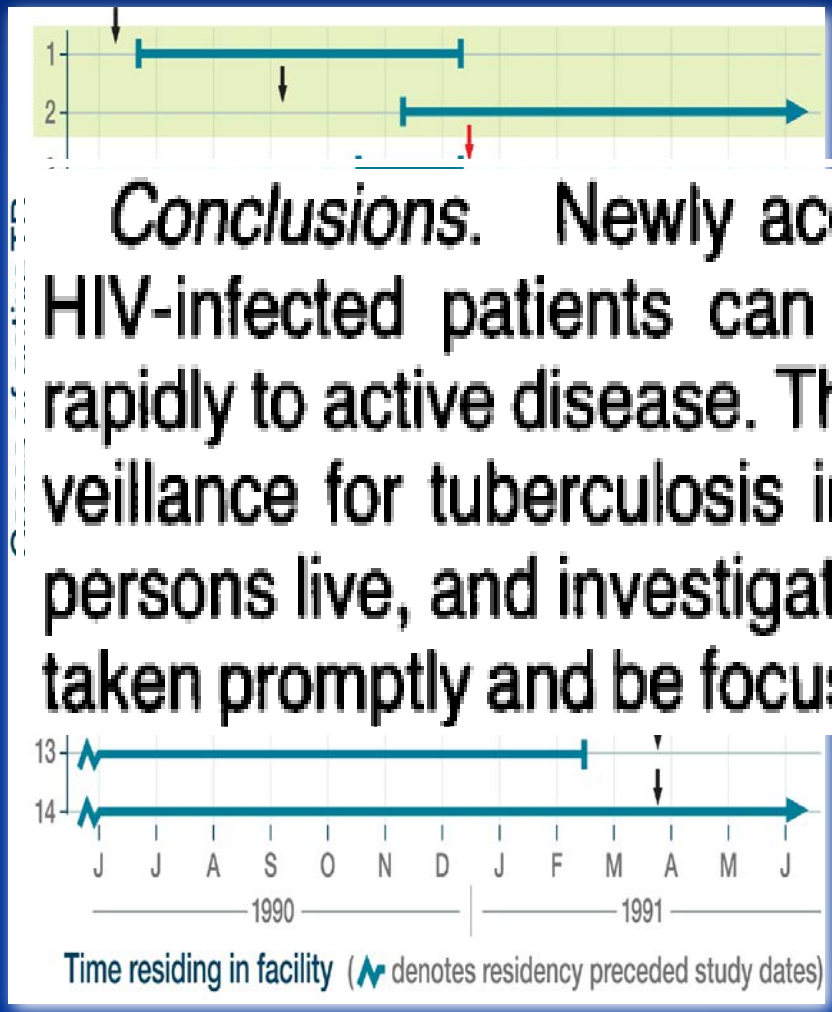
← Index case

secondary cases

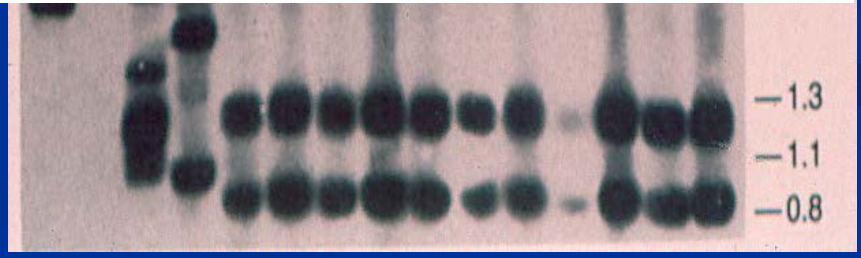
* found by contact investigation

Daley CL, et al. NEJM. 1992;326: 231

An Outbreak of TB With Accelerated Progression Among Persons Infected With HIV



Conclusions. Newly acquired tuberculous infection in HIV-infected patients can spread readily and progress rapidly to active disease. There should be heightened surveillance for tuberculosis in facilities where HIV-infected persons live, and investigation of contacts must be undertaken promptly and be focused more broadly than is usual.



Daley CL, et al. NEJM. 1992;326: 231

A broader look at the community epidemiology

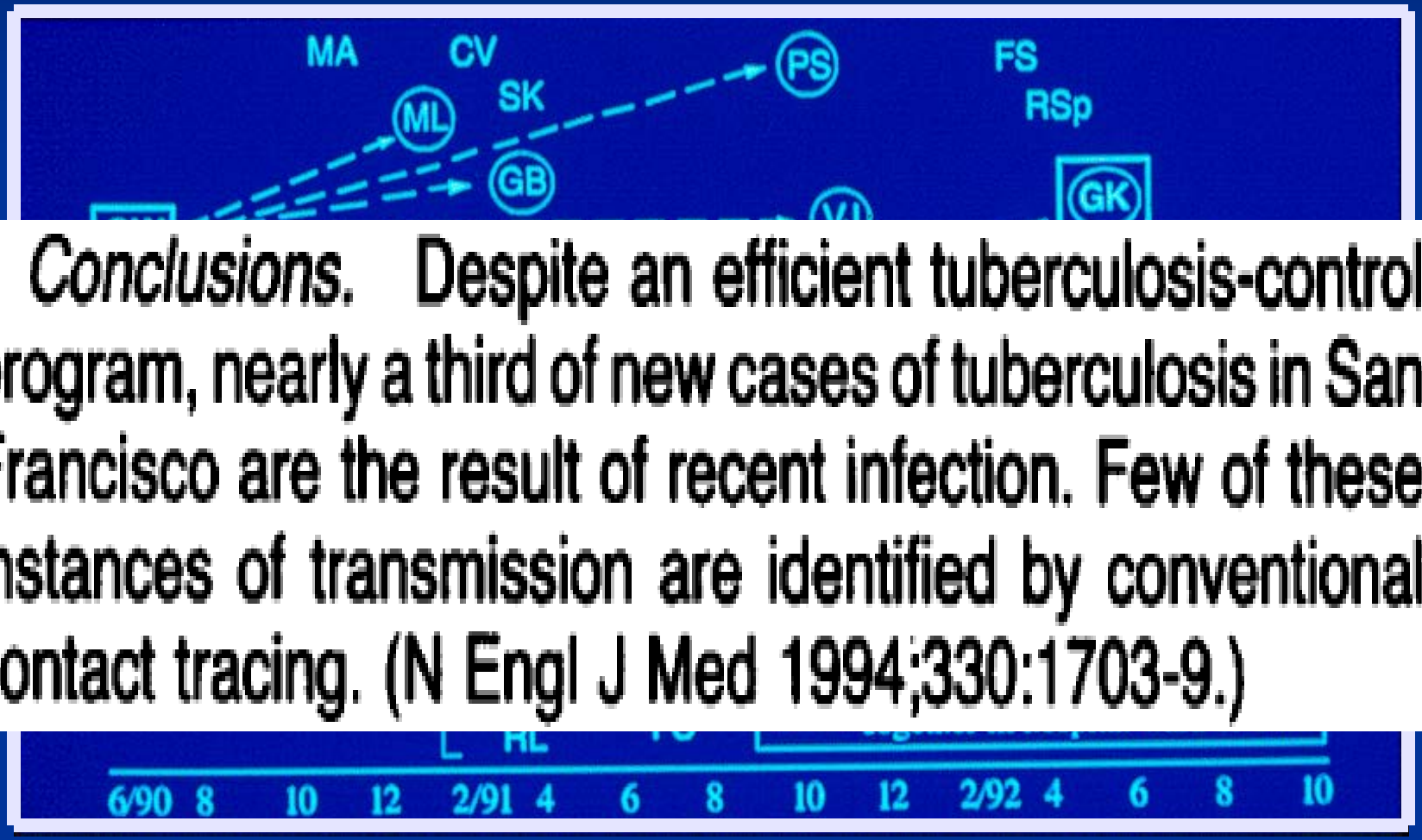
THE NEW ENGLAND JOURNAL OF MEDICINE June 16, 1994

THE EPIDEMIOLOGY OF TUBERCULOSIS IN SAN FRANCISCO

A Population-Based Study Using Conventional and Molecular Methods

PETER M. SMALL, M.D., PHILIP C. HOPEWELL, M.D., SAMIR P. SINGH, B.S., ANTONIO PAZ, M.D., JULIE PARSONNET, M.D., DELANEY C. RUSTON, B.S., GISELA F. SCHECTER, M.D., M.P.H., CHARLES L. DALEY, M.D., AND GARY K. SCHOOLNIK, M.D.

The Epidemiology of Tuberculosis in San Francisco: A Population-Based Study Using Conventional and Molecular Methods.



Conclusions. Despite an efficient tuberculosis-control program, nearly a third of new cases of tuberculosis in San Francisco are the result of recent infection. Few of these instances of transmission are identified by conventional contact tracing. (N Engl J Med 1994;330:1703-9.)

Small PM, et al NEJM.1994; 330: 1137

Specific populations: Foreign-born

AM J RESPIR CRIT CARE MED 1998;158:1797–1803.

Differences in Contributing Factors to Tuberculosis Incidence in U.S.-born and Foreign-born Persons

DANIEL P. CHIN, KATHRYN DERIEMER, PETER M. SMALL, ALFREDO PONCE de LEON, RACHEL STEINHART, GISELA F. SCHECTER, CHARLES L. DALEY, ANDREW R. MOSS, E. ANTONIO PAZ, ROBERT M. JASMER, CRISTINA B. AGASINO, and PHILIP C. HOPEWELL

Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital Medical Center, Department of Epidemiology and Biostatistics, San Francisco General Hospital, and the Department of Medicine, University of California, San Francisco; Tuberculosis Control Branch, California Department of Health Services; Division of Public Health Biology and Epidemiology, School of Public Health, University of California, Berkeley; Department of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California

Differences in Contributing Factors to TB Incidence in U.S.-born and Foreign-born Persons

Conclusions: None of the 252 foreign-born cases was recently infected (within 2 yr) in the city. Nineteen (17%) of 115 U.S.-born cases occurred after recent infection in the city; only two were infected by a foreign-born patient. Disease from recent infection in the city involved either a source or a secondary case with human immunodeficiency virus (HIV) infection, homelessness, or drug abuse. Failure to identify contacts accounted for the majority of secondary cases. In San Francisco, disease from recent transmission of *M. tuberculosis* has been virtually eliminated from the foreign-born but not from the U.S.-born population.

Chin DP, et al. AJRCCM. 1998; 158:1797

Specific populations: Homeless

Tuberculosis in the Homeless

A Prospective Study

Am J Respir Crit Care Med Vol 162. pp 460–464, 2000

ANDREW R. MOSS, JUDITH A. HAHN, JACQUELINE P. TULSKY, CHARLES L. DALEY, PETER M. SMALL, and PHILLIP C. HOPEWELL

Department of Epidemiology, Biostatistics, and Medicine, University of California San Francisco, San Francisco; Medical Service, San Francisco General Hospital, San Francisco; and Department of Medicine, Stanford University Medical Center, Stanford, California

60% of the cases had clustered patterns of restriction fragment length polymorphism, thought to represent recent transmission of infection with rapid progression to disease. Seventy-seven percent of African-American cases were clustered, and 88% of HIV-seropositive cases. The high rate of tuberculosis in the homeless was due to recent transmission in those HIV-positive and nonwhite. African Americans and other nonwhites may be at high risk for infection or rapid progression.

Specific populations: Contacts

Predictive Value of Contact Investigation for Identifying Recent Transmission of *Mycobacterium tuberculosis*

MARCEL A. BEHR, PHILIP C. HOPEWELL, E. ANTONIO PAZ, L. MASAE KAWAMURA, GISELA F. SCHECTER, and PETER M. SMALL

Cases of tuberculosis in San Francisco between 1991 and 1996 with positive cultures who had been previously identified as contacts ("contact cases") to active cases ("index cases") were studied. Of 11,211 contacts evaluated, there were 66 pairs of culture-positive index and contact cases. DNA fingerprints were available for both members of these pairs in 54 instances (82%). The index and contact cases were infected with the same strain of *Mycobacterium tuberculosis* in 38 instances (70%; 95% CI: 56 to 82%); 16 pairs (30%) were infected with unrelated strains. Unrelated infections were more common among foreign-born (risk ratio [RR] = 5.22, $p < 0.001$), particularly Asian (RR = 3.89, $p = 0.002$) contacts. Contact investigation is an imperfect method for detecting transmission

AM J RESPIR CRIT CARE MED 1998;158:465–469.

Disease features: smear-negative cases

ARTICLES

Transmission of *Mycobacterium tuberculosis* from patients smear-negative for acid-fast bacilli

M A Behr, S A Warren, H Salamon, P C Hopewell, A Ponce de Leon, C L Daley, P M Small

Findings 1574 patients with culture-positive tuberculosis were reported and DNA fingerprints were available for 1359 (86%) of these patients. Of the 71 clusters of patients infected with strains that had matching fingerprints, 28 (39% [95% CI 28–52]) had a smear-negative putative source. There were 183 secondary cases in these 71 clusters, of whom a minimum of 32 were attributed to infection by smear-negative patients (17% [12–24]). The relative transmission rate of smear-negative compared with smear-positive patients was calculated as 0·22 (95% CI 0·16–0·32). Sensitivity analyses and stratification for HIV-1 status had no impact on these estimates.

THE LANCET • Vol 353 • February 6, 1999

Disease features: extrapulmonary

A Molecular Epidemiological Assessment of Extrapulmonary Tuberculosis in San Francisco

Adrian Ong,[1,2] Jennifer Creasman,[1] Philip C. Hopewell,[1] Leah C. Gonzalez,[1] Maida Wong,[3] Robert M. Jasmer,[1] and Charles L. Daley[1]

[1]Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital Department of Medicine, University of California, San Francisco, and [2]Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University Medical Center, Stanford, California; and [3]Department of Medicine, University of Iowa, Iowa City

The epidemiology of extrapulmonary tuberculosis (TB) is not well understood. We studied all cases of extrapulmonary TB reported in San Francisco during 1991–2000 to determine risk factors for extrapulmonary TB and the proportion caused by recent infection. Isolates were analyzed by IS*6110*-based restriction fragment–length polymorphisms analysis. There were 480 cases of extrapulmonary TB, of which 363 (76%) were culture positive; isolates were genotyped for 301 cases (83%). Multivariate analysis identified young age, female sex, and HIV infection as independent risk factors for nonrespiratory TB (excluding pulmonary, pleural, and disseminated TB). Pleural TB was less common in HIV-seropositive persons and women than were nonrespiratory forms of extrapulmonary TB. Pleural TB is different from other forms of extrapulmonary TB and is associated with the highest clustering rate (35% of cases) of all forms of TB. This high rate of clustering occurs because pleural TB is often an early manifestation of recent infection.

Clinical Infectious Diseases 2004; 38:25–31

Secondary Case Rate Ratio

$$SCRR = \frac{n_{S\ L(X)} / N_{U+I\ L(X)}}{n_{S\ L(Y+Z)} / (N_{U+I\ (Y+Z)})}$$

Where:

$n_{S\ L(X)}$ = no. of secondary (clustered) cases for lineage X;

$n_{s\ L\ (Y+Z)}$ = no. of secondary (clustered) cases for lineages Y+Z;

$N_{U+I\ (X)}$ = total number of unique+index cases for lineage X;

$N_{U+I\ L\ Y+Z)}$ = total number of unique+index cases for lineages Y+Z

Features of the organism: Lineage

Variable host–pathogen compatibility in *Mycobacterium tuberculosis*

Sebastien Gagneux[a,b,c], Kathryn DeRiemer[b,d], Tran Van[b], Midori Kato-Maeda[b,e], Bouke C. de Jong[b,f], Sujatha Narayanan[g], Mark Nicol[h], Stefan Niemann[i], Kristin Kremer[j], M. Cristina Gutierrez[k], Markus Hilty[l], Philip C. Hopewell[e], and Peter M. Small[a,m]

Mycobacterium tuberculosis remains a major cause of morbidity and mortality worldwide. Studies have reported human pathogens to have geographically structured population genetics, some of which have been linked to ancient human migrations. However, no study has addressed the potential evolutionary consequences of such longstanding human–pathogen associations. Here, we demonstrate that the global population structure of *M. tuberculosis* is defined by six phylogeographical lineages, each associated with specific, sympatric human populations. In an urban cosmopolitan environment, mycobacterial lineages were much more likely to spread in sympatric than in allopatric patient populations. Tuberculosis cases that did occur in allopatric hosts disproportionately involved high-risk individuals with impaired host resistance. These observations suggest that mycobacterial lineages are adapted to particular human populations. If confirmed, our findings have important implications for tuberculosis control and vaccine development.

PNAS | February 21, 2006 | vol. 103 | no. 8 | 2869–2873

Secondary Case Rate Ratio by Lineage and Race/ethnicity

12

10.74

Table 2. Risk factors independently associated with one of three *M. tuberculosis* lineages in 490 U.S.-born patients from San Francisco

M. tuberculosis lineage	Risk factor	Adjusted odds ratio	(95% CI)	*P* value
East-Asian	Chinese ethnicity	19.8	(4.6–84.2)	<0.001
	Homelessness	3.0	(1.4–6.2)	0.004
Indo-Oceanic	Filipino ethnicity	43.2	(5.6–335)	<0.001
	Age ≥45 years	3.9	(1.5–10.1)	0.004
	HIV positive	3.4	(1.3–8.7)	0.01
Euro-American	Chinese ethnicity	0.18	(0.06–0.6)	0.004

Lineage-specific Prevalence and Transmission of *M.Tuberculosis*

A collaboration with

- CDC TBESC Task order 2
  - CDC PI: Mary Reichler
  - TBESC PI: Tim Sterling
- UCSF
  - PI: Phil Hopewell (Midori Kato-Maeda)
- Health departments: Arkansas, New York, Tennessee, Maryland, Georgia, New Jersey, San Francisco

Features of the organism: drug resistance

Effect of Drug Resistance on the Generation of Secondary Cases of Tuberculosis

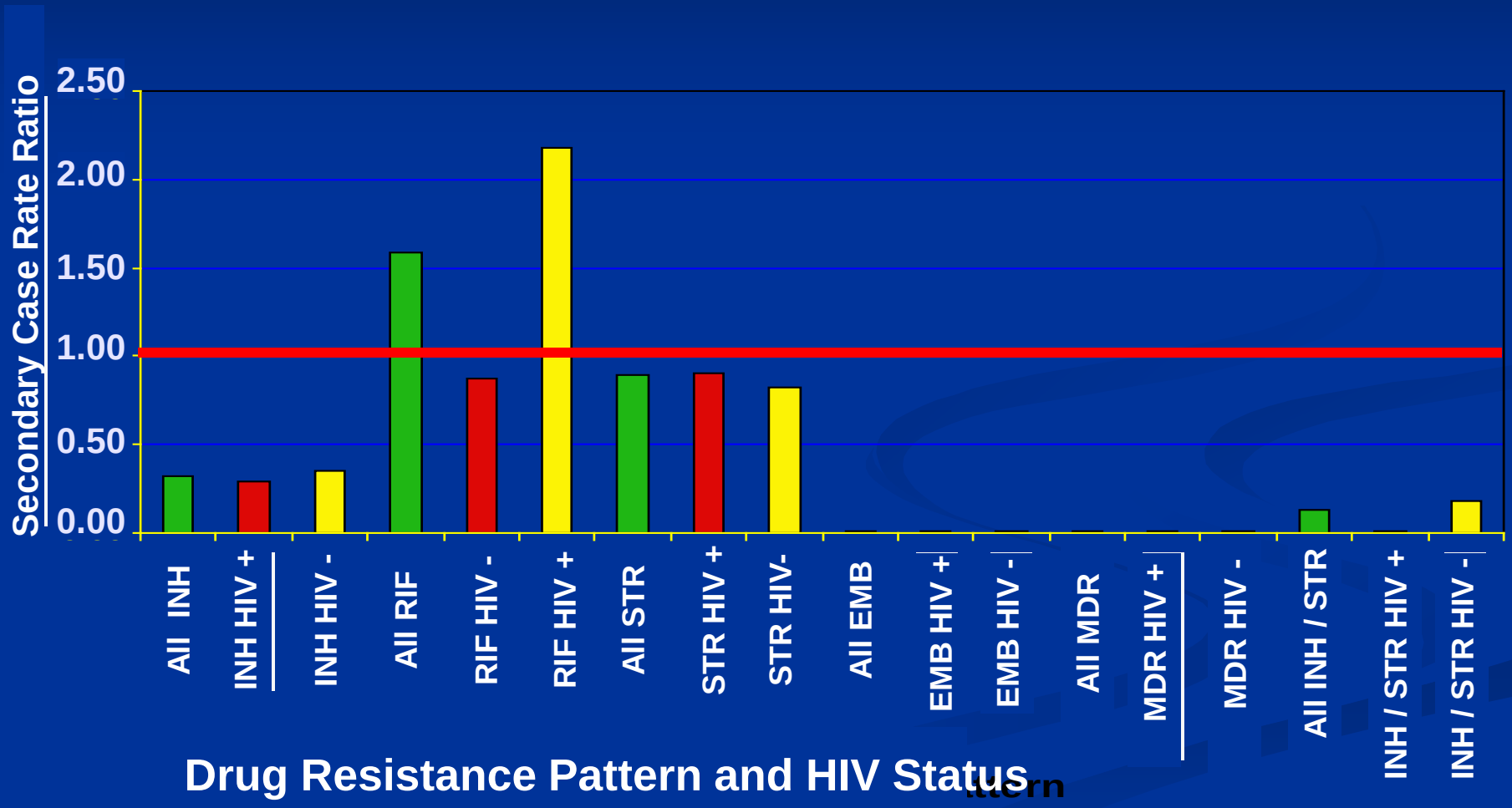
Marcos Burgos,[1,2,a] Kathryn DeRiemer,[1] Peter M. Small,[1] Philip C. Hopewell,[2] and Charles L. Daley[2]

[1]Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University Medical Center, Stanford, and [2]Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital and the University of California, San Francisco

Conclusion. In the context of an effective TB program in San Francisco, strains that were resistant to isoniazid either alone or in combination with other drugs were less likely to result in secondary cases than were drug-susceptible strains. In this setting, isoniazid-resistant and MDR TB cases were not likely to produce new, incident drug-resistant TB cases.

The Journal of Infectious Diseases 2003; 188:1878–84

Secondary Case Rate Ratio: Effect of Resistance Pattern and HIV



Burgos M, et al. JID. 2003; 188:1878-84

Effect of Drug Resistance on Transmissibility and Pathogenicity of *Mycobacterium tuberculosis*

- CDC-TBESC Task Order 8
  - CDC PI: Patrick Moonan
  - TBESC PIs: Jenny Flood, California DHS
    Ed Graviss, Methodist Hospital Research Institute, Houston, TX.
- CDC- Universal Genotyping program
  - California DHS TB Branch and Mycobacterial Diseases Laboratory: Jenny Flood, Ed Desmond

Lineage/Sub lineage determination/differences

INT J TUBERC LUNG DIS 15(1):131–133

SHORT COMMUNICATION

Strain classification of *Mycobacterium tuberculosis*: congruence between large sequence polymorphisms and spoligotypes

M. Kato-Maeda,* S. Gagneux,†‡§ L. L. Flores,* E. Y. Kim,* P. M. Small,¶ E. P. Desmond,# P. C. Hopewell*

*Francis J Curry National Tuberculosis Center, Division of Pulmonary and Critical Care Medicine, San Francisco General Hospital, Department of Medicine University of California San Francisco, San Francisco, California, USA; †Medical Research Council National Institute for Medical Research, London, UK; ‡Swiss Tropical and Public Health Institute, Basel, §University of Basel, Basel, Switzerland; ¶Bill and Melinda Gates Foundation, Seattle, Washington, #Microbial Diseases Laboratory, California Department of Public Health, Richmond, California, USA

CVI
Journals.ASM.org

Beijing Sublineages of *Mycobacterium tuberculosis* Differ in Pathogenicity in the Guinea Pig

Midori Kato-Maeda,[a] Crystal A. Shanley,[b] David Ackart,[b] Leah G. Jarlsberg,[a] Shaobin Shang,[b] Andres Obregon-Henao,[b] Marisabel Harton,[b] Randall J. Basaraba,[b] Marcela Henao-Tamayo,[b] Joyce C. Barrozo,[a] Jordan Rose,[a] L. Masae Kawamura,[c]* Mireia Coscolla,[d,e] Viacheslav Y. Fofanov,[f] Heather Koshinsky,[f] Sebastien Gagneux,[d,e] Philip C. Hopewell,[a] Diane J. Ordway,[b] and Ian M. Orme[b]

Curry International Tuberculosis Center, Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, San Francisco, California, USA[a]; Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, Colorado, USA[b]; San Francisco Tuberculosis Clinic, San Francisco Department of Public Health, San Francisco, California, USA[c]; Swiss Tropical & Public Health Institute, Basel, Switzerland[d]; University of Basel, Basel, Switzerland[e]; and Eureka Genomics, Hercules, California, USA[f]

Use of Whole Genome Sequencing to Determine the Microevolution of *Mycobacterium tuberculosis* during an Outbreak

Midori Kato-Maeda[1]*, Christine Ho[2,3], Ben Passarelli[4], Niaz Banaei[5], Jennifer Grinsdale[2], Laura Flores[1], Jillian Anderson[1], Megan Murray[6], Graham Rose[7], L. Masae Kawamura[2], Nader Pourmand[8], Muhammad A. Tariq[8], Sebastien Gagneux[9,10], Philip C. Hopewell[1]

1 Curry International Tuberculosis Center, Division of Pulmonary and Critical Care Medicine, University of California San Francisco, San Francisco, California, United States of America, **2** Tuberculosis Control Section, San Francisco Department of Public Health, San Francisco, California, United States of America, **3** Centers for Disease Control (CDC), Division of TB Elimination, Field Services and Evaluation Branch (CDC/DTBE/FSEB), Atlanta, Georgia, United States of America, **4** Department of Bioengineering, Stanford University, Palo Alto, California, United States of America, **5** Department of Pathology, Stanford University, Palo Alto, California, United States of America, **6** Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts, United States of America, **7** MRC National Institute for Medical Research, London, United Kingdom, **8** Department of Biomolecular Engineering, University of California Santa Cruz, Santa Cruz, California, United States of America, **9** Swiss Tropical and Public Health Institute, Basel, Switzerland, **10** University of Basel, Basel, Switzerland

Specific populations: foreign-born (are not all the same)

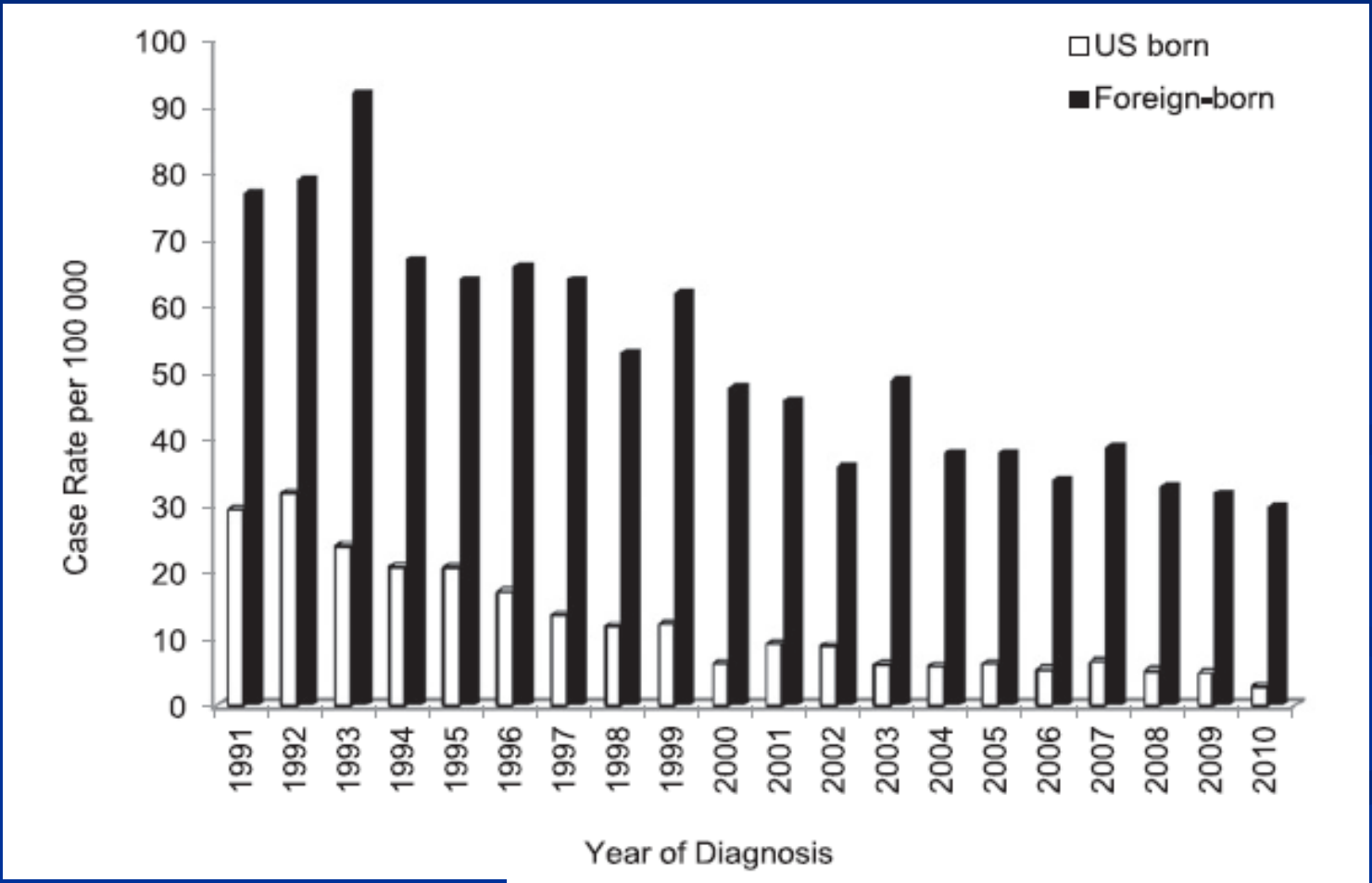
Molecular Epidemiology of Tuberculosis in Foreign-Born Persons Living in San Francisco

Gompol Suwanpimolkul[1,2], Leah G. Jarlsberg[1], Jennifer A. Grinsdale[3], Dennis Osmond[1], L. Masae Kawamura[3*], Philip C. Hopewell[1], and Midori Kato-Maeda[1]

Conclusions: There are differences in the characteristics and the risk factors for tuberculosis due to recent transmission among the major foreign-born and U.S.-born populations in San Francisco. These differences should be considered for the design of targeted tuberculosis control interventions.

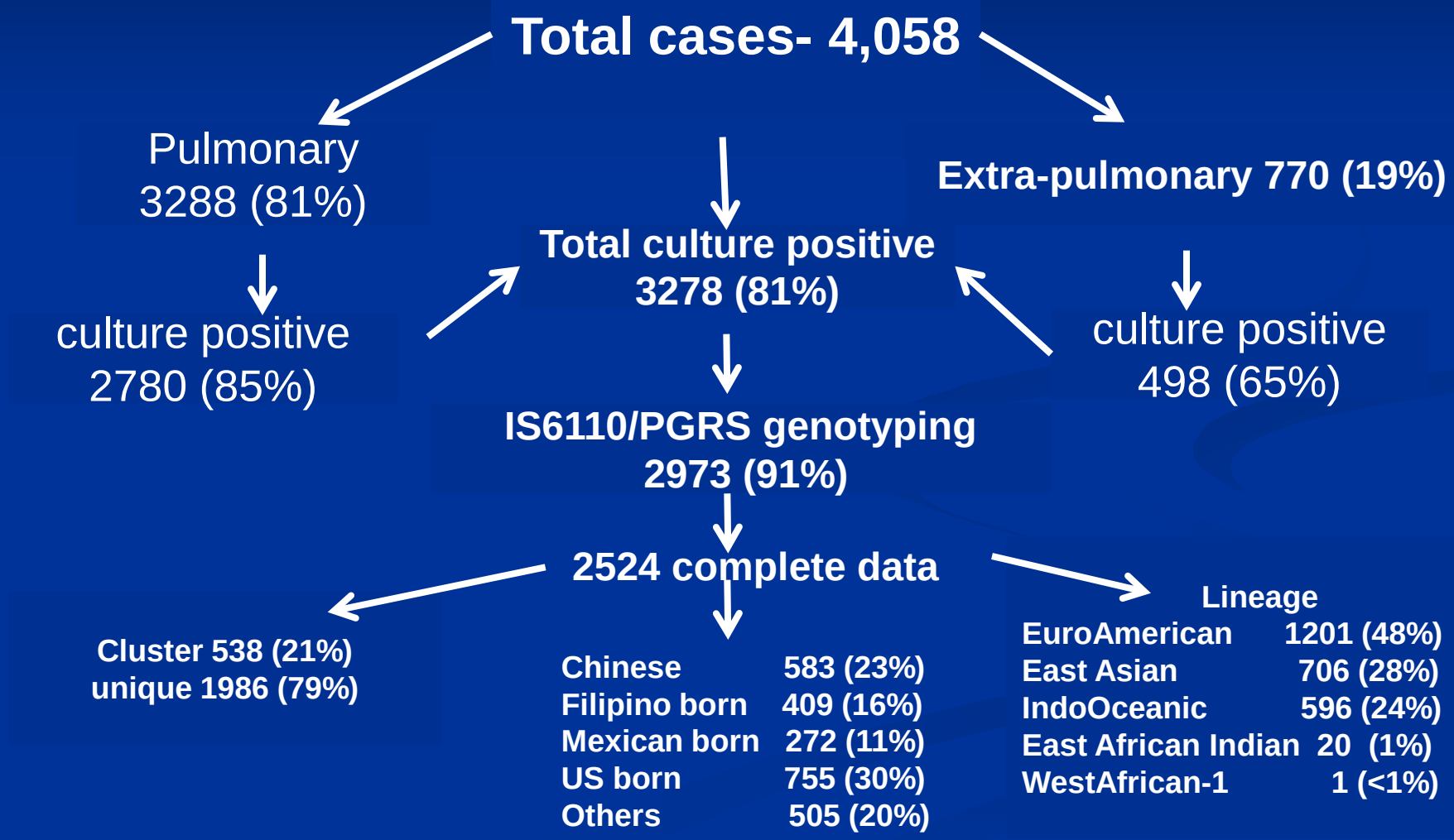
Am J Respir Crit Care Med Vol 187, Iss. 9, pp 998–1006, May 1, 2013

Case rates: US-born/foreign-born: San Francisco 1991-2010

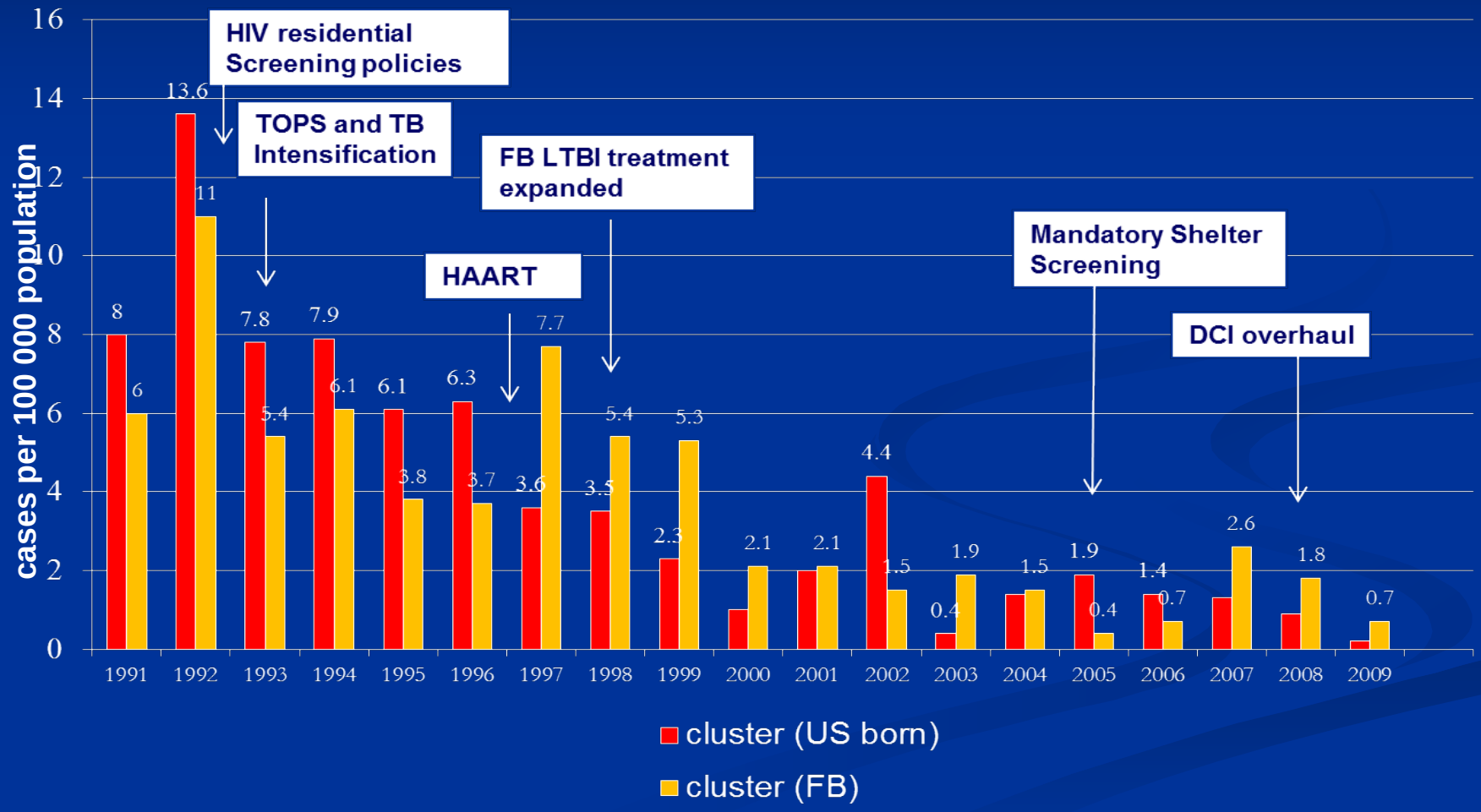


Am J Respir Crit Care Med Vol 187, Iss. 9, pp 998–1006, May 1, 2013

Community-Based Molecular Epidemiology of TB in San Francisco: 1991-2010



Twenty Years of Molecular Epidemiology of Tuberculosis in San Francisco



Conclusions of studies reviewed

- Targeted interventions have decreased incidence and disproportionately decreased clustering.
- There is little interaction between the epidemics in US-born and foreign-born populations.
- Transmission from smear-negative cases is less but still important compared with smear positive cases.
- An important % of contacts have disease as the result of infection from sources other than the index case.
- Pleural tuberculosis is likely a result of recent infection.
- There may be specific adaptation of pathogens to race/ethnic groups.
- Mutations that result in nonfunctional *kat* G cause a reduction in pathogenicity of *M. tb.*
- Foreign-born populations are not epidemiologically the same.

Thanks for your attention