

36th REMINGTON WINTER COURSE IN
INFECTIOUS DISEASES

VAIL, CO

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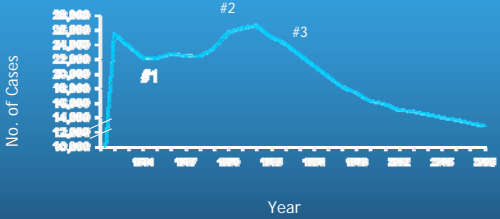
TB: "WHAT'S UP DOC"?

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What's Up, Doc?



"TB: WHAT'S UP DOC"?



No. of Cases

Year

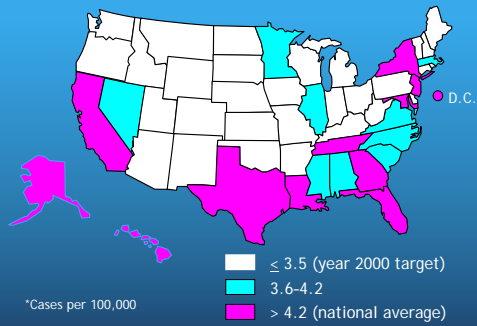
*Updated as of May 20, 2009.

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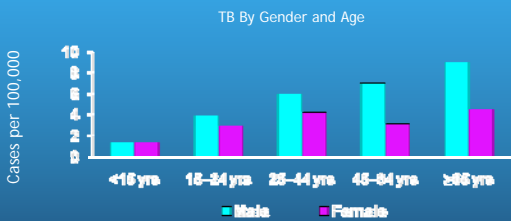
Year	No.	Rate*
2003	14,836	5.1
2004	14,500	4.9
2005	14,067	4.7
2006	13,727	4.6
2007	13,288	4.4
2008	12,904	4.2

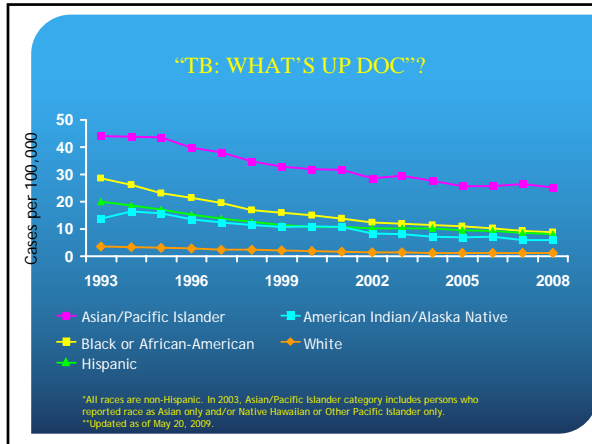
*Cases per 100,000, updated as of May 20, 2009.

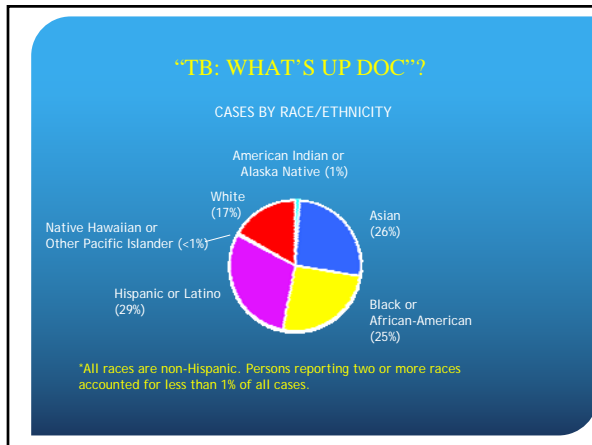
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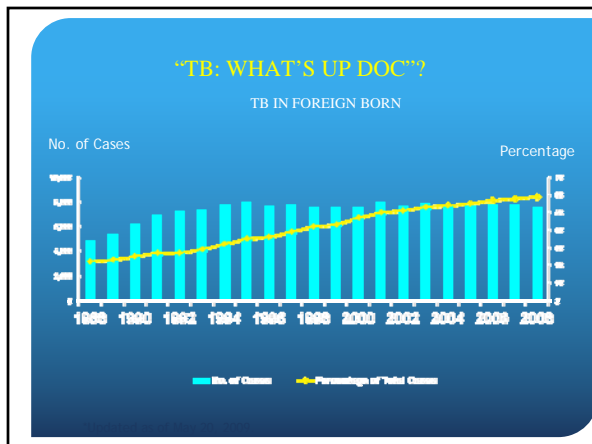


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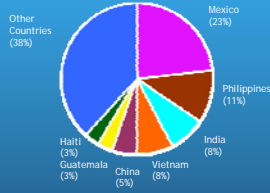






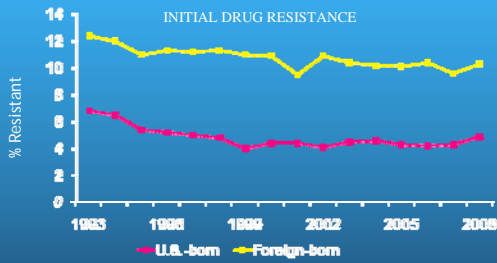
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TB BY COUNTRY OF ORIGIN



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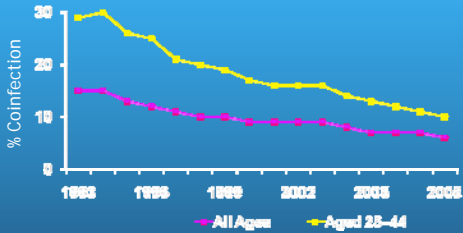
INITIAL DRUG RESISTANCE



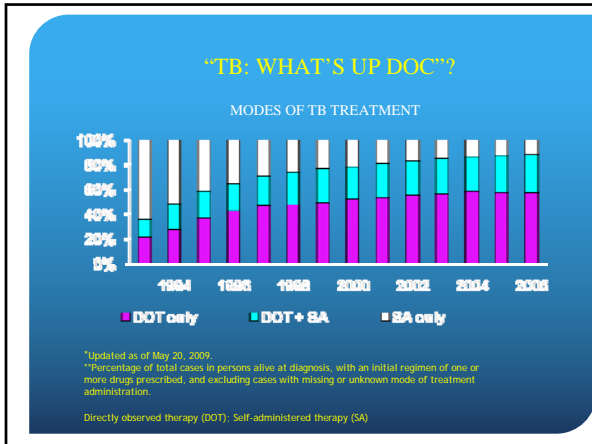
*Updated as of May 20, 2009.
 Note: Based on initial isolates from persons with no prior history of TB

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RATES OF HIV INFECTION AMONG THOSE WITH TB



*Updated as of May 20, 2009.
 Note: Minimum estimates based on reported HIV-positive status among all TB cases in the age group.



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Treatment of Latent TB Infection (LTBI)

***ATS/CDC Guidelines (2000): options –**

- a. INH 9 mos
- b. INH 6 mos
- c. RIF/PIA 2 to 3 mos
- d. RIF 4 mos

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LTBI: Rationale for RIF use –

1. Superior sterilizing capacity:
 - *INH based regimens – 18 mos to cure
 - *RIF based regimens – 6 to 9 mos to cure
2. Lesser risk for serious/lethal hepatitis
3. Fewer CNS side-effects
4. Averts INH-resistance
5. Substantially better completion rates

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TLTI: Should RIF-4 be our 1st choice?

*Not as a member of the ATS, CDC Advisory Committee, NJH faculty or University of Colorado faculty, but –

*Based on clinical study of Menzies' group,⁽¹⁾ Reichman's decision Analysis,⁽²⁾ Stout's cost effectiveness analysis,⁽³⁾ and my personal experience,

Yes!

¹AJRCM, 170:445-449 (2004)

²Chest 130:1712-1717 (2006)

³AJRCM 179:1055-1060 (2009)

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Drawbacks to RIF:

1. Risk of acquired (R) to RIF [not for use in HIV (+)]
2. Drug interactions
3. Thrombocytopenia
4. Inertia (initial costs)

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"HIV IN THOSE WITH MDR-TB/XDR-TB RESULTS IN HIGH EARLY MORTALITY"

- Population: 272 MDR and 382 XDR cases, Tugela-Ferry, 2005-7
- High rates of HIV: MDR = 245 of 272 (90%) HIV (+)
XDR = 374 of 382 (98%) HIV (+)
- Mortality:

	<u>MDR</u>	<u>XDR</u>
1 month	40%	51%
1 year	71%	83%

Gandhi et al, AJRCM, 181:80-86, 2010

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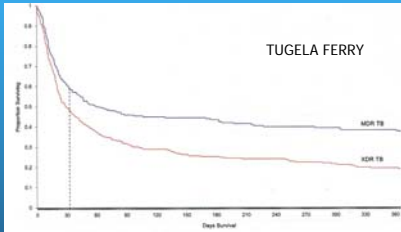


Figure 1. Kaplan-Meier survival plot among multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) patients, 2005 to 2007 (log-rank, $P < 0.0001$).

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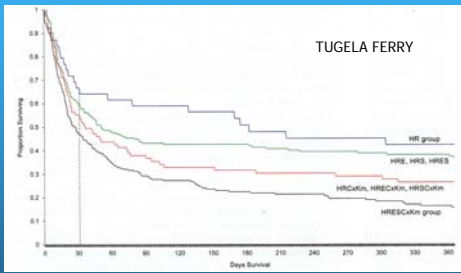


Figure 2. Kaplan-Meier survival plot by drug resistance pattern among patients with multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB), 2005 to 2007 (log-rank, $P < 0.0001$). Letters indicate drugs to which isolate was resistant: H, Isoniazid; R, Rifampin; E, Ethambutol; S, Streptomycin; Cx, Ciprofloxacin; Km, Kanamycin. Median survival was 182 days (95% CI, 31-395 d) for patients with MDR-TB and resistance to only HR; 50 days (95% CI, 35-106 d) for patients with MDR-TB and resistance to HRE, HRS, or HRES; 36 days (95% CI, 23-74 d) for patients with XDR-TB and resistance to HRCaKm, HRECaKm, or HRSCaKm; and 27 days (95% CI, 20-38 d) for patients with XDR-TB and resistance to HRESCaKm.

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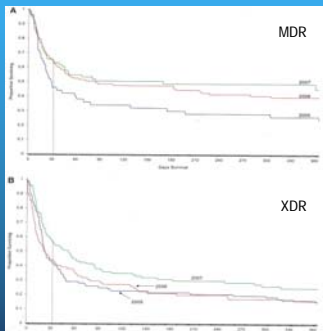


Figure 3. (A) Kaplan-Meier plot among patients with multidrug-resistant (MDR) tuberculosis (TB) by calendar year of sputum collection, 2005 to 2007 (log rank, $P = 0.02$). (B) Kaplan-Meier survival plot among patients with extensively drug-resistant (XDR) TB by calendar year of sputum collection, 2005 to 2007 (log rank, $P = 0.01$).

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A MYSTERIOUS SUB-GROUP OF TB ORGANISMS:

A Sentinel Insight or Voodoo?

"Is there a population of tubercle bacilli in sputum which is not detected on routine culture, which can be stimulated to growth by RESUSCITATION-PROMOTING FACTORS" (Rpf) produced by the mycobacteria?"

Mukamolova, et al, AJRCCM; 181:174-180, 2010

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Findings regarding **Rpfs** in pre-treatment samples:

- 80% to 99% of cells ultimately identified on cultivation "could be detected only with RPF stimulation"
- During chemotherapy, "THE PROPORTION OF RPF-DEPENDENT CELLS WAS FOUND TO INCREASE RELATIVE O THE SURVIVING COLONY-FORMING POPULATION."
- Rpf dependent bacillary populations varied widely between patients; Rpf = proteins produced by bacilli
- Query role in slow sterilization and relapses of TB

Mukamolova, et al, AJRCCM; 181:174-180, 2010

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"THAT WASCAL WABBIT WILL NOW TWY TO ANSWER YOUR INQUIWIES"
