Late diagnosis of HIV-infection

B. Salzberger

Topics

- Definition
- Epidemiology
- Management
  - acute complications
  - initiation of antiretroviral therapy
  - immune reconstitution inflammatory syndrome (IRIS)
- Prevention

Late diagnosis of HIV-infection

- diagnosis of HIV-infection
  - concomitant or close in time with opportunistic complication or
  - with a low CD4-cell count
- how close in time to clinical event?
- CD4-cells how low?

Late diagnosis of HIV-infection

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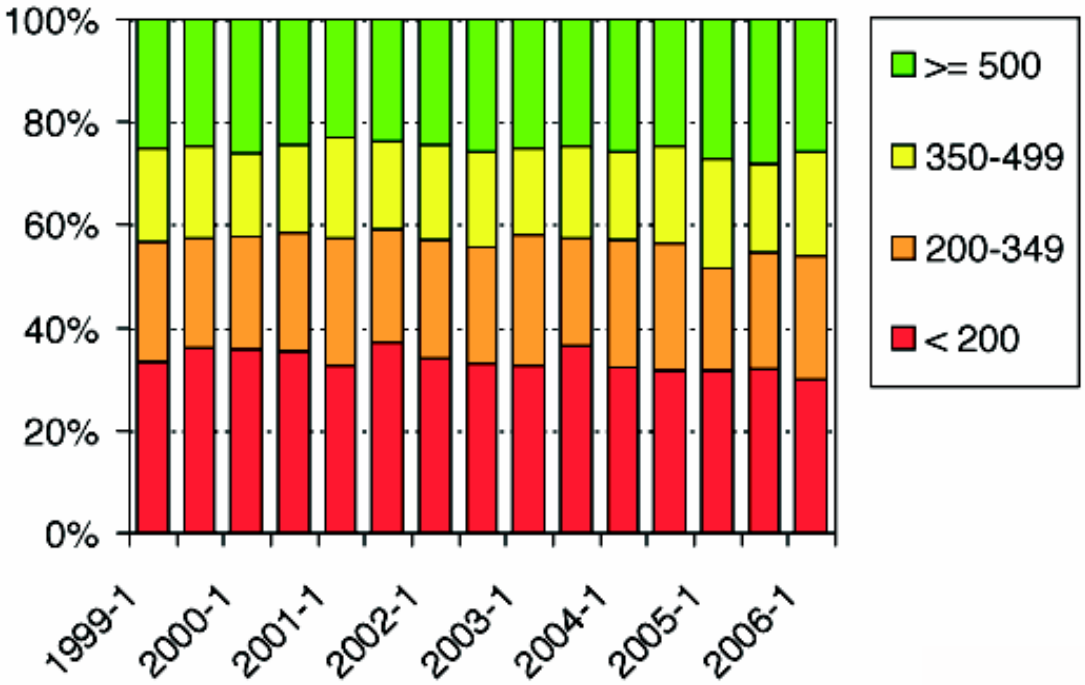
- how close in time to clinical event? 3, 6, 12months?
- CD4-cells how low? below 200

How frequent is late diagnosis of HIV?

- different cohorts from Italy, France, UK, Germany
- rate of late HIV-diagnosis relatively uniform 25-40%
  - risk factors
    - migrants
    - women
    - age < 30 or age >50
    - unknown or not reported risk of transmission
    - heterosexual men, living in long-term relationships

Late diagnosis in Germany

- 682 AIDS cases 2003-4
  - >50% no ART before AIDS diagnosis
- CD4 cell count at diagnosis of HIV 1999-2006



ClinSurv-Cohort, RKI 2006; Epid. Bull, April 2005

Late diagnosis in UK

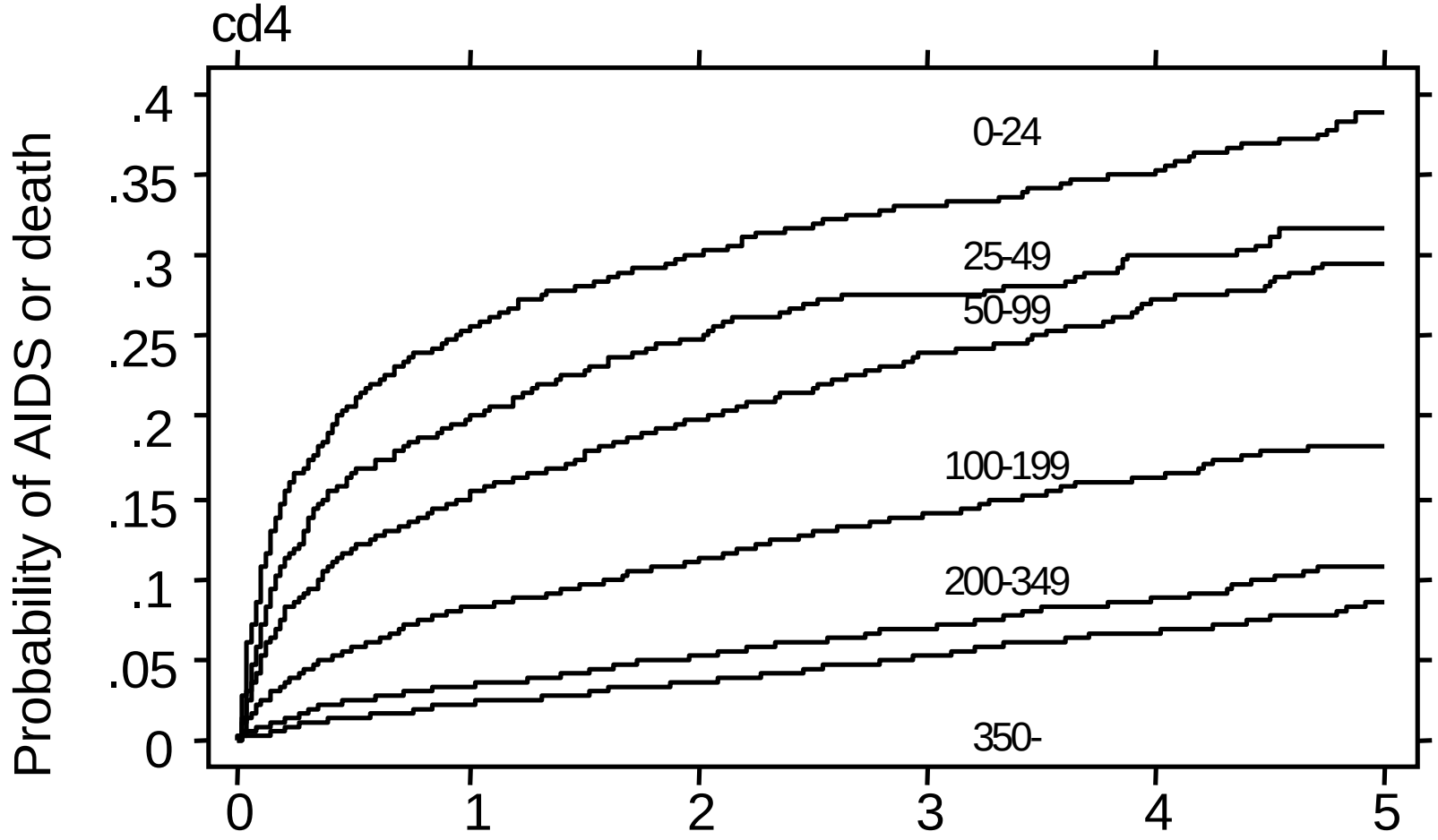
- In GB 14000 cases of newly diagnosed HIV-infection between 1993 and 2002 analyzed
  - 31% below 200 CD4/mcl, positive trend to 25% 2002
  - late diagnoses mainly outside London, higher age, non caucasian origin
  - one year mortality with late diagnosie 14 vs. 1%, down to 9,9 vs. 0,5% 2001

Chadborn AIDS 2005

Are there consequences of late HIV-diagnosis?

- lower rate of viral suppression if ART is started late
- higher rate of opportunistic infections until immune reconstitution is sufficient
- higher rate of adverse effects of ART, especially when initiated with concurrent OI-therapy
- higher rate of immune reconstitution syndrome
- higher mortality

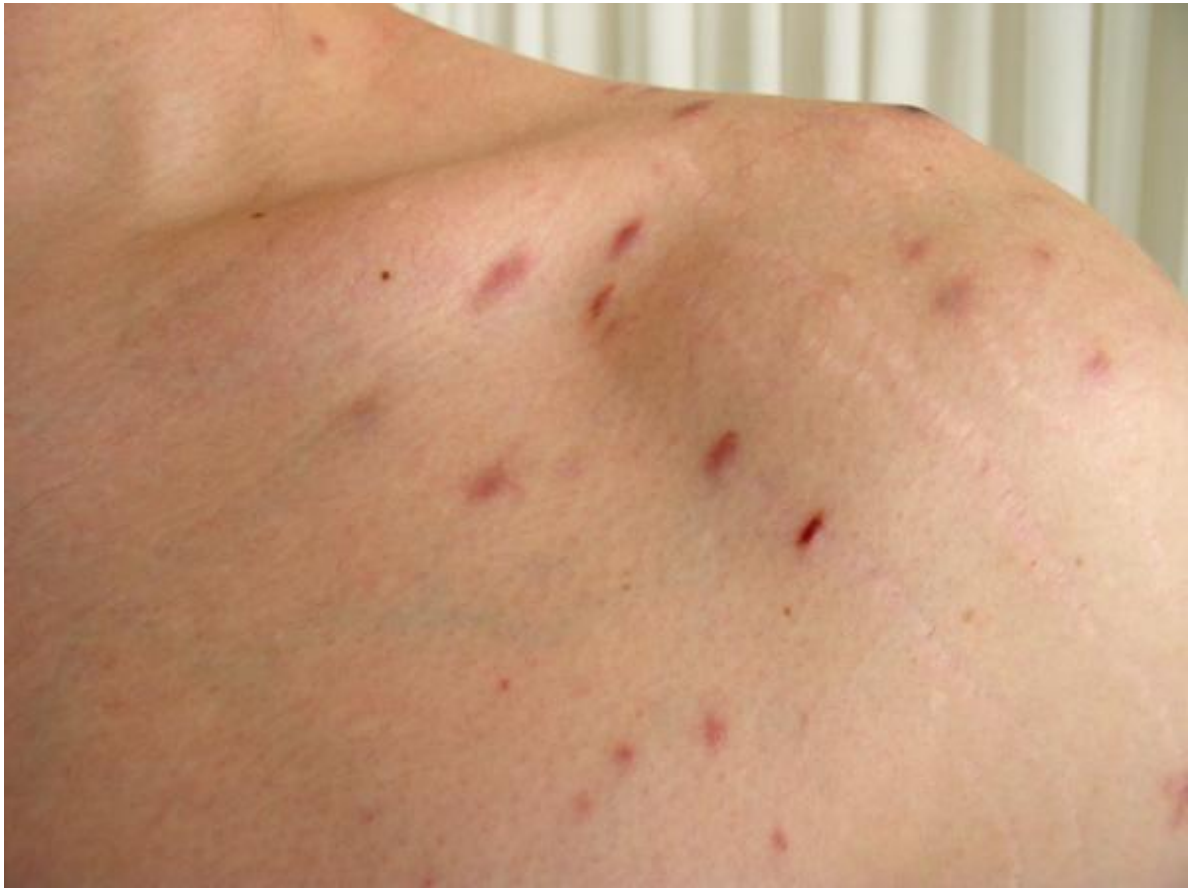
Clinical events after starting HAART by initial CD4-cell count



Eggers, Lancet 2005

Case 1

- 28yo male



Case 1

- Patient with multiple cutaneous nodules, biopsy reveals Kaposi´s-sarcoma, HIV-test positive
- CD4-cell count 230/mcl, Viral load 260.000 copies/ml
- history of repeated deep vein thrombosis and pulmonary embolism - on long-term cumarin-therapy
- Late diagnosis?
- How to treat?

Case 1

- Chance of remission with antiretroviral therapy, so no initial anti-Kaposi therapy
- started on LPV/r +ZDV+3TC, because of case reports of remission of KS in patients treated with PI-based HAART
- Viral load suppressed, lesions blanching
- effective anticoagulation not possible, even with 4 tbls Cumarin/d
- what to do?

Case 1

- Switched to EFV+ZDV+3TC
- good response in CD4-cell-count, good progress with remission of KS
- now for 3 years below limit of detection, complete remission of KS

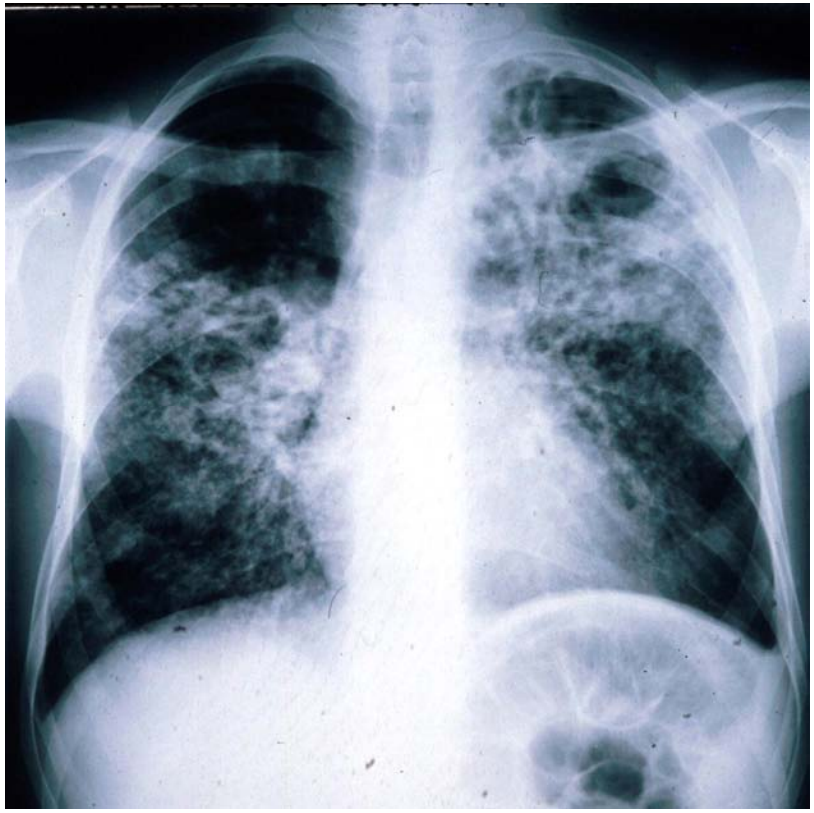
Case 2

- 43yo male, interstitial pneumonia not responding to empiric therapy with fluorquinolones
- in bronchoscopy Pneumocystis jirovecii, HIV-positive
- rapidly deteriorating respiratory function
- initiate ART concomitant to OI-therapy?

Case 2

- No data if concurrent ART is helpful in acute OIs
- potential for adverse drug reactions, complication clinical management
- therefore rather withhold ART in acute OI?

Case 3



- 28yo female, recently immigrated from Ukraine
- fever, generalized lymphadenopathy and pulmonary infiltrates
- smear positive for AFB
- culture growing *M. tuberculosi*

Case 3

- HIV+, HCV+
- Viral load 120.000 copies/ml, CD4-cell count 80/mcl
- How to treat?

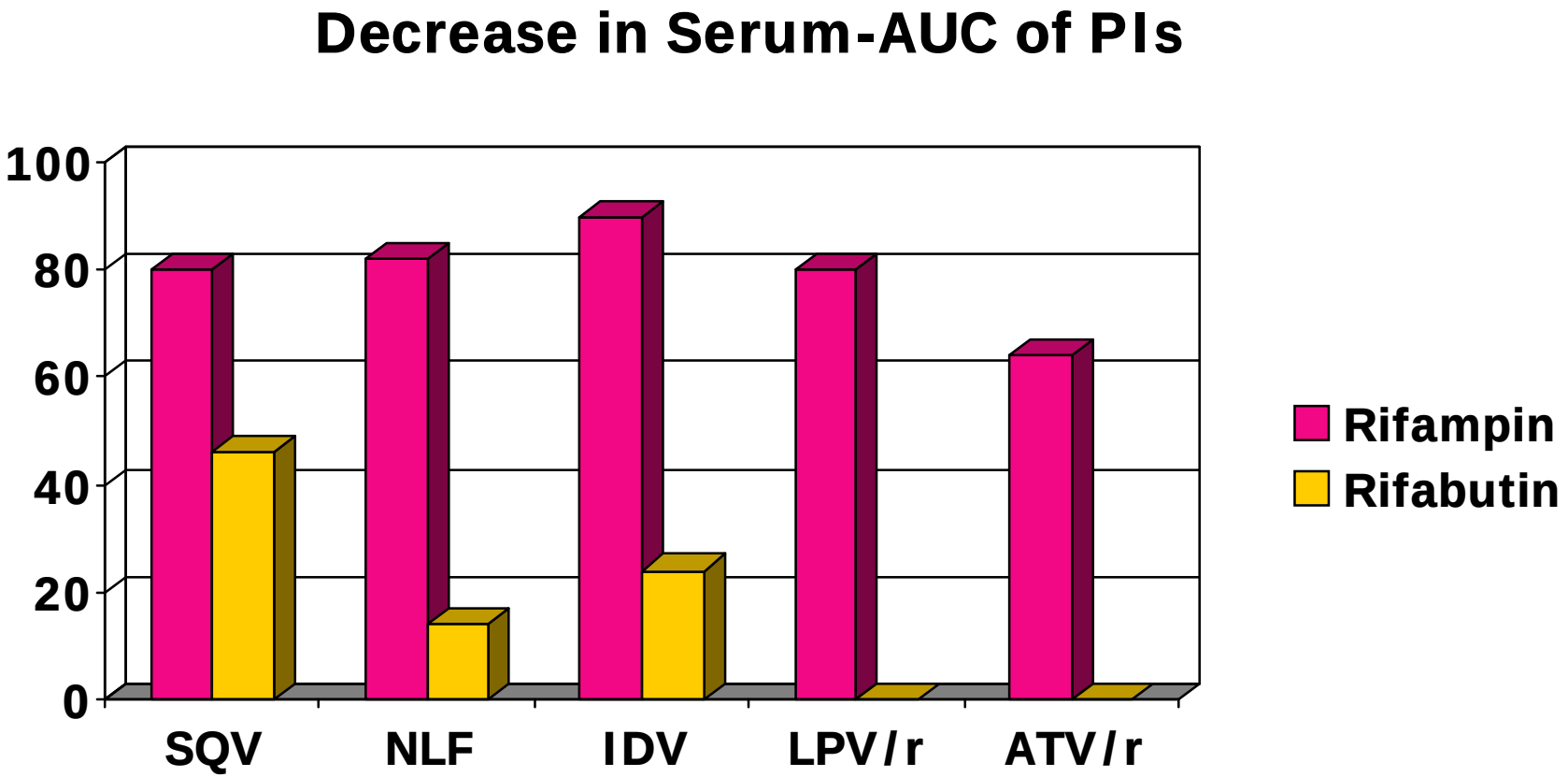
Key questions in HIV- TBC

- how to treat TBC?
- when to start highly active antiretroviral therapy (HAART)?
- which HAART?
  - adverse effects
  - interactions with TB treatment

Which TBC treatment?

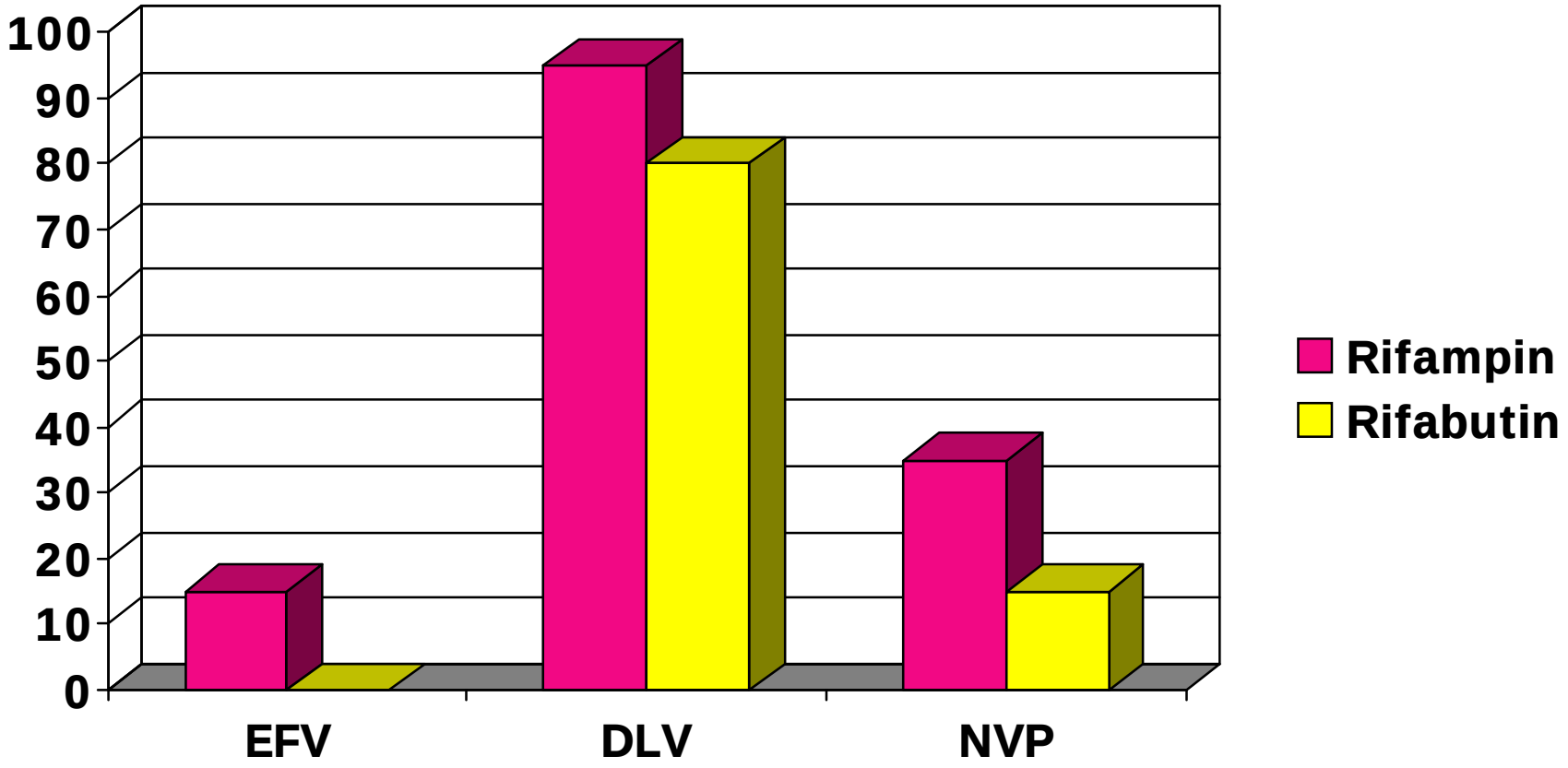
- standard regimen
  - 2 months: INH, RIF, EMB, PZA
  - 4 months: INH, RIF
  - directly observed therapy (DOT)
- rifamycins crucial for success of short- term TBC treatment (6 months)
- which rifamycin?
  - rifampicin
  - rifabutin

Rifampin, Rifabutin and PIs



CID 1999, 28, 419ff

Rifampin, Rifabutin and NNRTIS



CID 1999, 28, 419ff

What is the best time to start HAART in a patient with HIV/ TBC?

Use of antiretroviral therapy during Tb-infection

- CD4-cell count at diagnosis of Tb
  - <200 start during Tb-therapy
  - 200-350 monitor, start if CD4 declines rapidly
  - >350 monitor,

W. Burmann, 12th CROI, Boston 2005

TB/HIV Co-Infection: Treatment Considerations

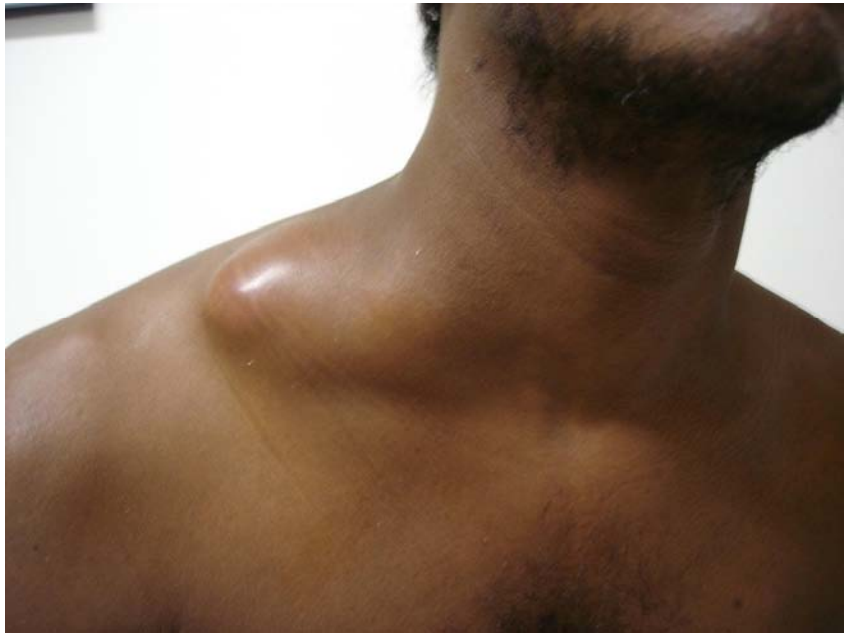
- In patients on ARV therapy, evaluate ARV regimen for interactions with TB drugs
- In ARV-naive patients, avoid simultaneous initiation of treatment for TB and HIV
  - consider delay of ARVs for 4-8 weeks after initiation of TB treatment to avoid overlapping of adverse reactions and paradoxical reactions

DHHS Guidelines July 2005; http://www.aids-etc.org

Case 4

- 44yo male, husband of case 4
- Pleural tuberculosis 2 months after diagnosis of tb in spouse
- HIV+, CD4+cell count 440/mcl, VL 80.000 copies/ml
- How to treat?

Case 5



- 37yo male patient with fever and enlarging lymph nodes after 2 months of HAART and TBC treatment
- Is this clinical deterioration
- what are the likely causes?
- how to manage?

Case 4

- Likely causes for deterioration
  - resistance (HIV/Tb)
  - non- adherence (HIV/Tb)
  - superinfection
  - **immune reconstitution syndrome (IRS)**
- How to manage IRS in TB/HIV-coinfection?
  - continuation of TBC treatment
  - consider stop of ART
  - consider cortisone

IRIS

- worsening of preexisting clinical condition after starting ART
- pathogenesis?
- broad spectrum of conditions with IRIS
  - mykobacterial infections
  - PCP, PML
  - infections with Herpesviruses (CMV, VZV, genitale HSV, Kaposi Sarkome)
  - hepatitis B flare
  - cryptococcososis, Histoplasmosis
  - Parvo B19, Graves´disease, lung cancer..

IRIS

- with anti-tuberculosis therapy reported
  - paradoxical reaction with initial or delayed worsening after starting therapy
  - absceding and growing lymphadenopathy
  - enhanced inflammation with tuberculos meningitis, CNS-tuberculomas with focal neurologic deficits

    treated successfully with steroids
- reversion of specific immunosuppression with initial imbalance?

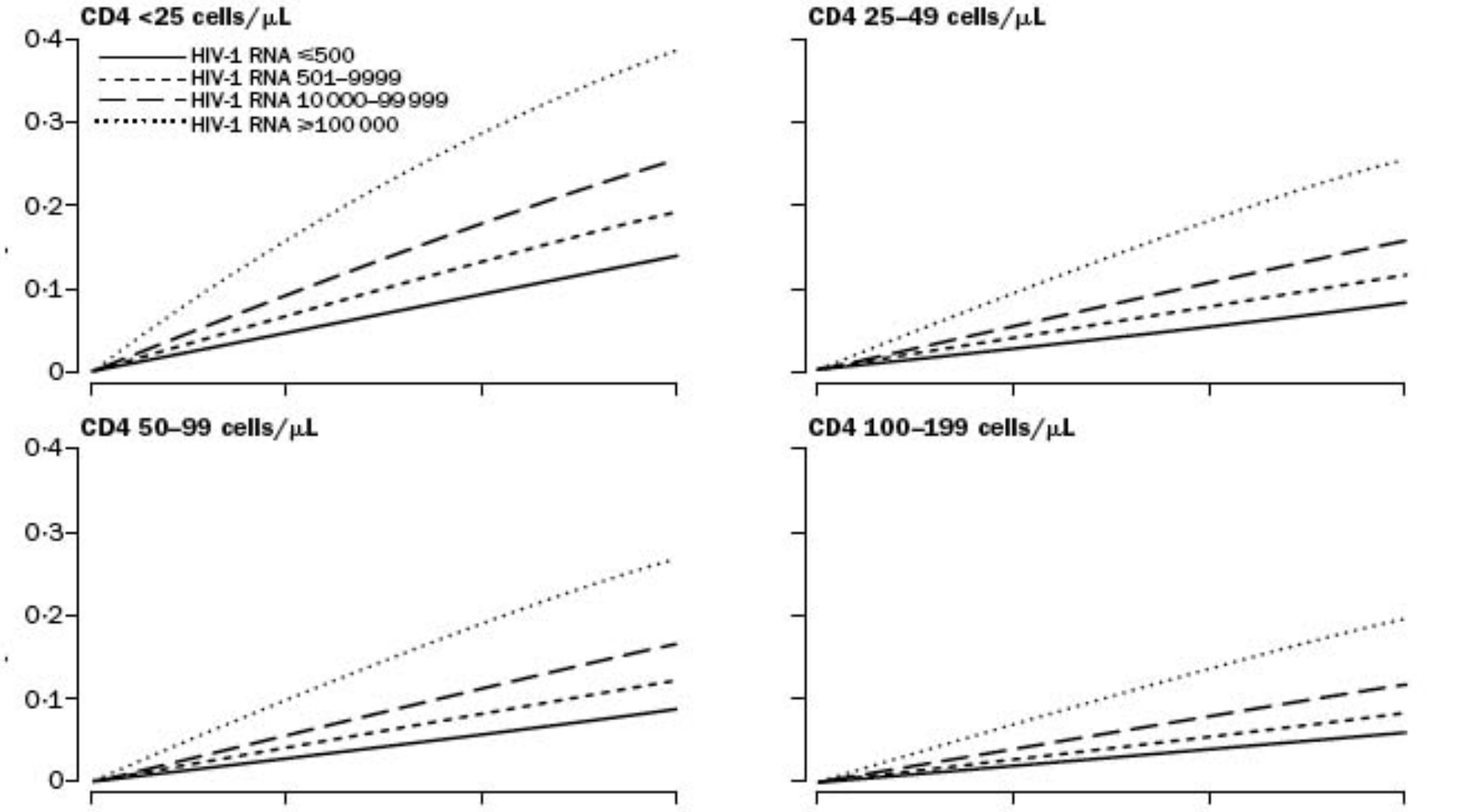
IRIS-Epidemiology

- Frequency
  - 10-25%
  - in a small London cohort 23%
  - depending on
    - prevalence of infections
    - CD4-cell-nadir?
- risk factors
  - younger age
  - low CD4-cell count

Pathogenesis IRIS

- pathogenesis largely unknown
- antigen-specific immune responses enhanced or diminished ?

the good news.... all is forgotten after 6 months of therapy



ART-CC, Lancet 2003

the bad news - prevention

- population at risk is difficult to target
  - not a group with „one denominator “: e.g. gay men, drug users
  - risk of infection not acknowledged

Conclusion

- late diagnosis of HIV is common, risk factors are known
- patient populations difficult to target for prevention
- clinical problems in late HIV-diagnosis
  - time to immune reconstitution crucial
  - concurrent management of acute opportunistic infections and ART
  - immune reconstitution syndrome