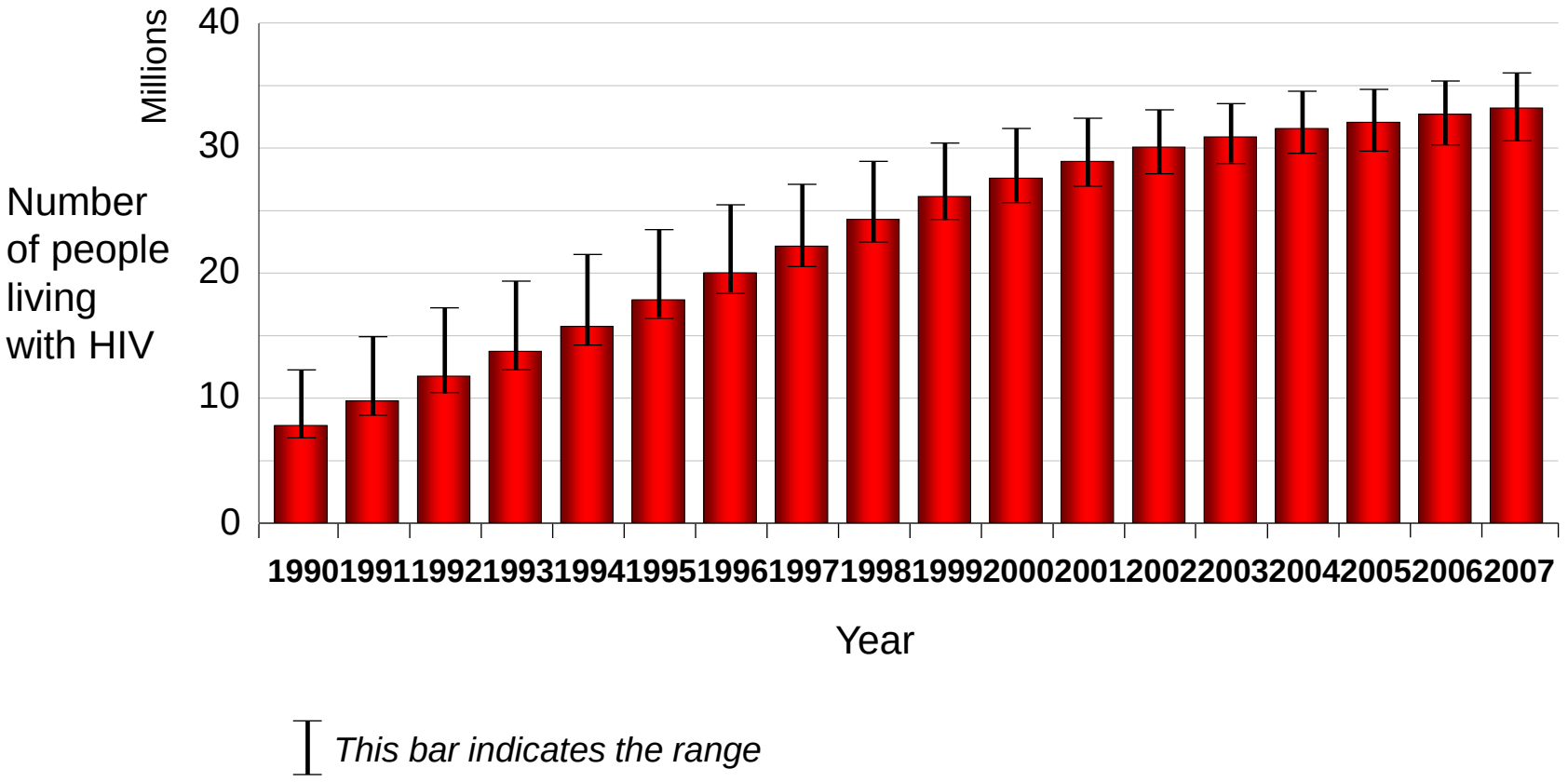
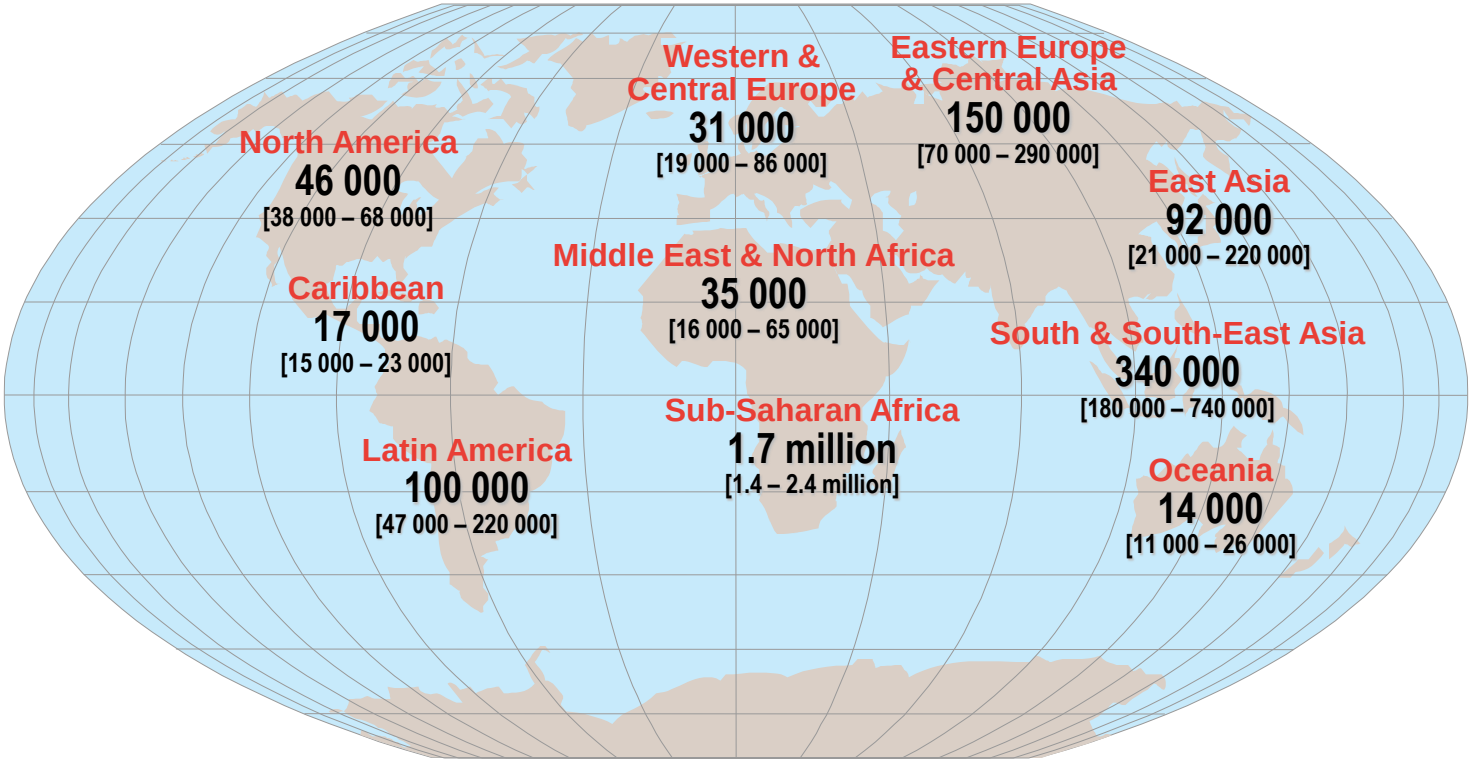
The patient with HIV/AIDS in intensive care

Brendan McCarron

Estimated number of people living with HIV globally, 1990–2007

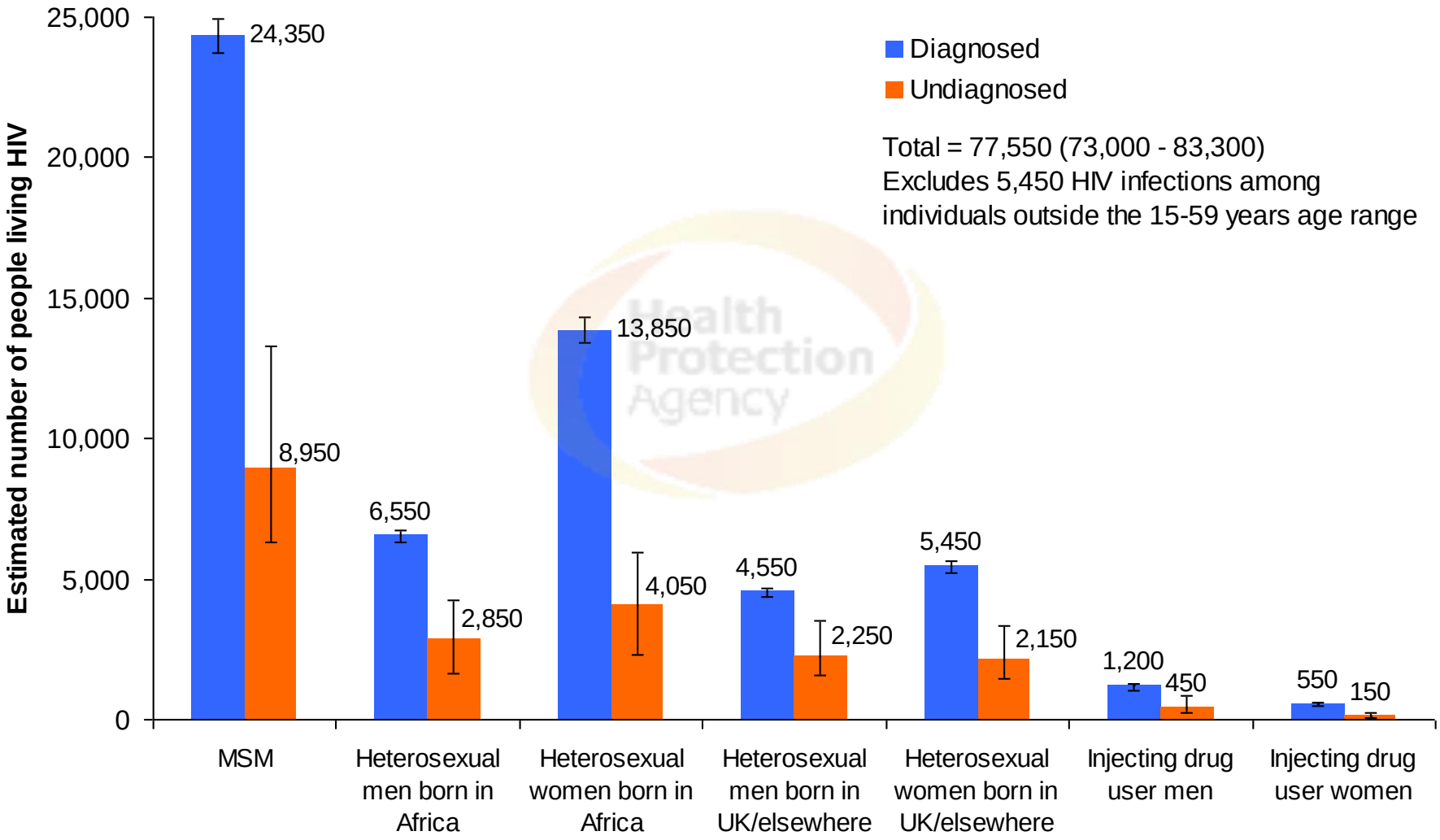


Estimated number of adults and children newly infected with HIV, 2007

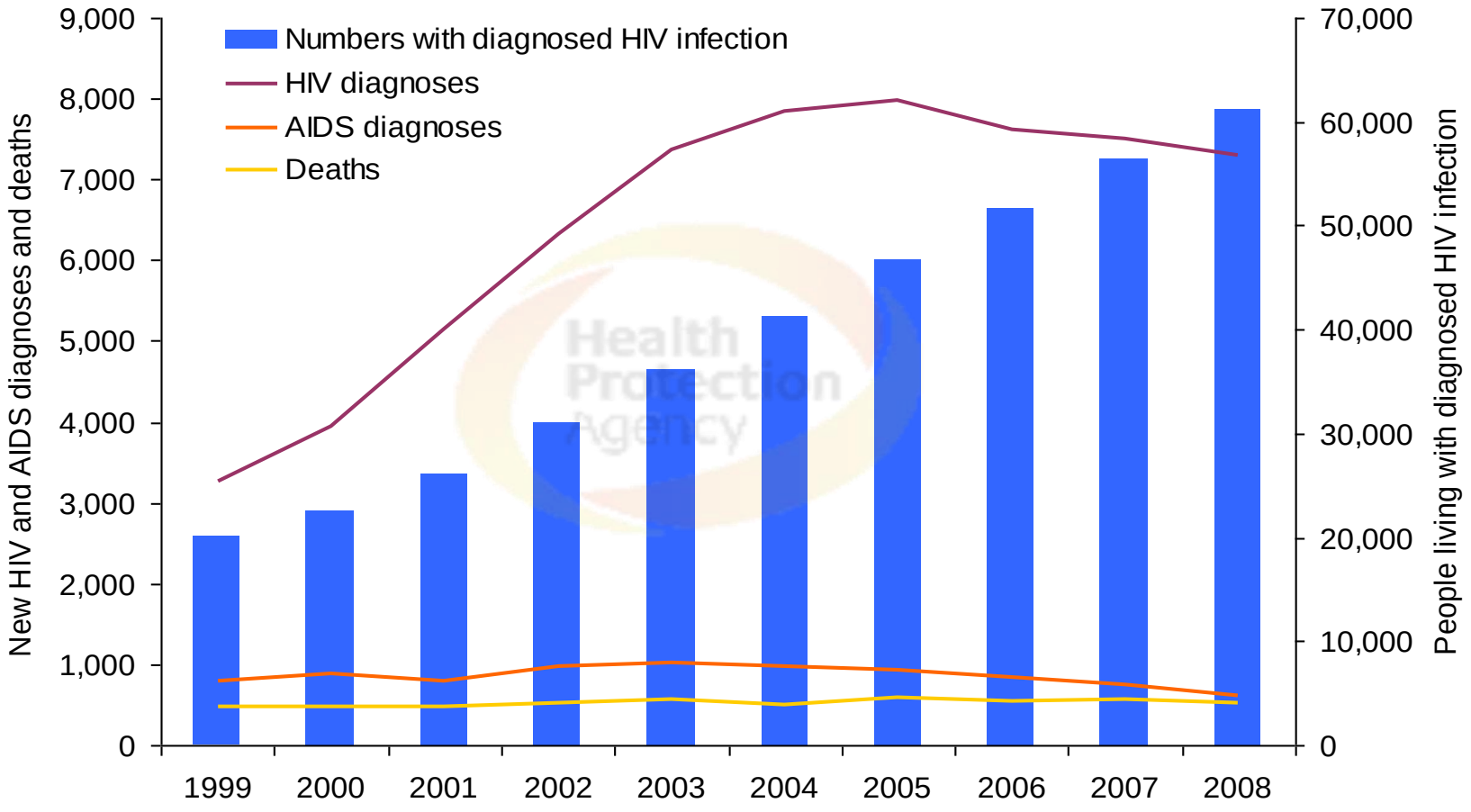


Total: 2.5 (1.8 – 4.1) million

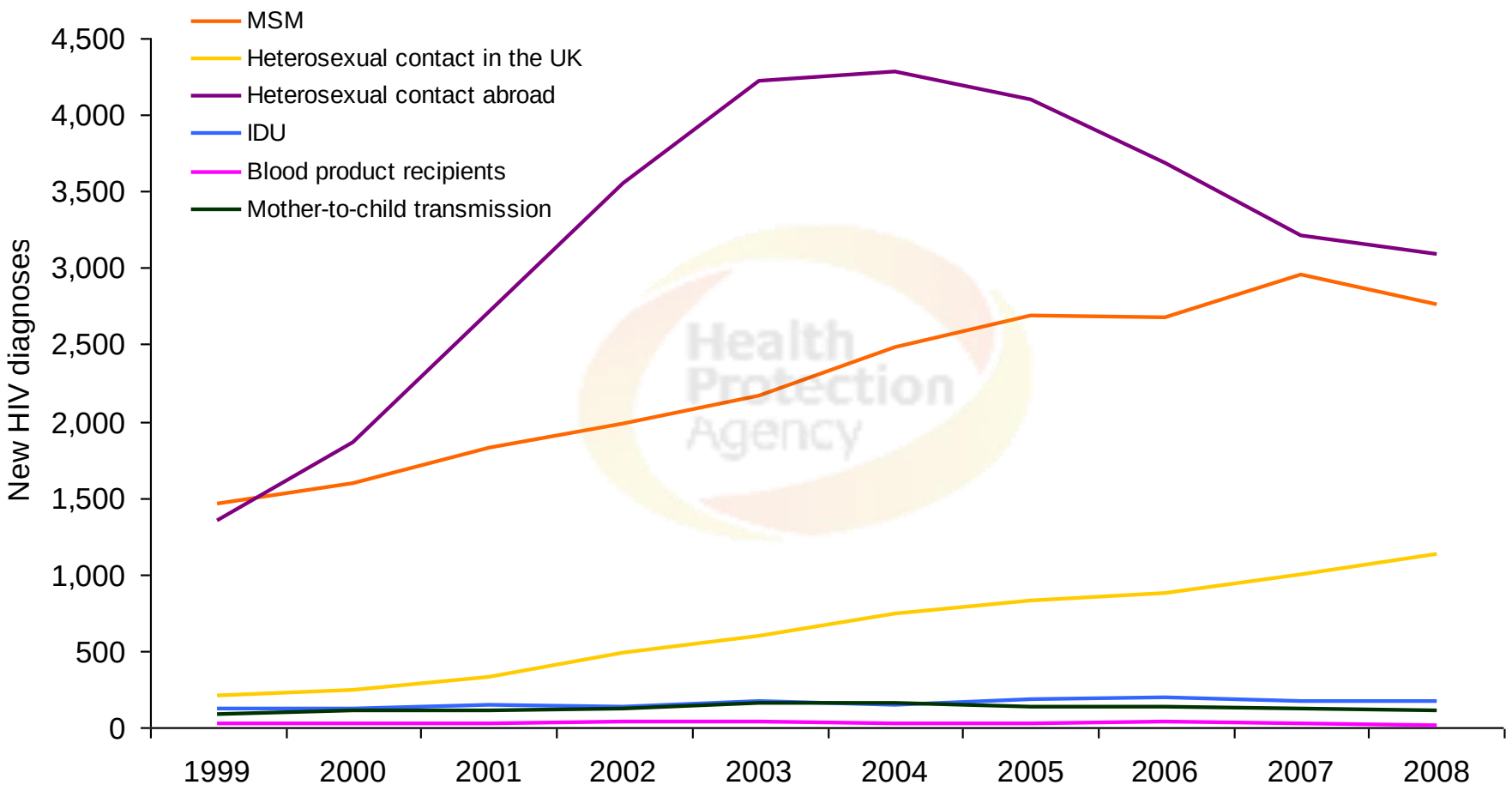
Estimated number of adults (15-59 years) living with HIV (both diagnosed and undiagnosed) in the UK: 2008



New HIV and AIDS diagnoses, people living with diagnosed HIV, and deaths, among HIV-infected people, UK: 1999-2008

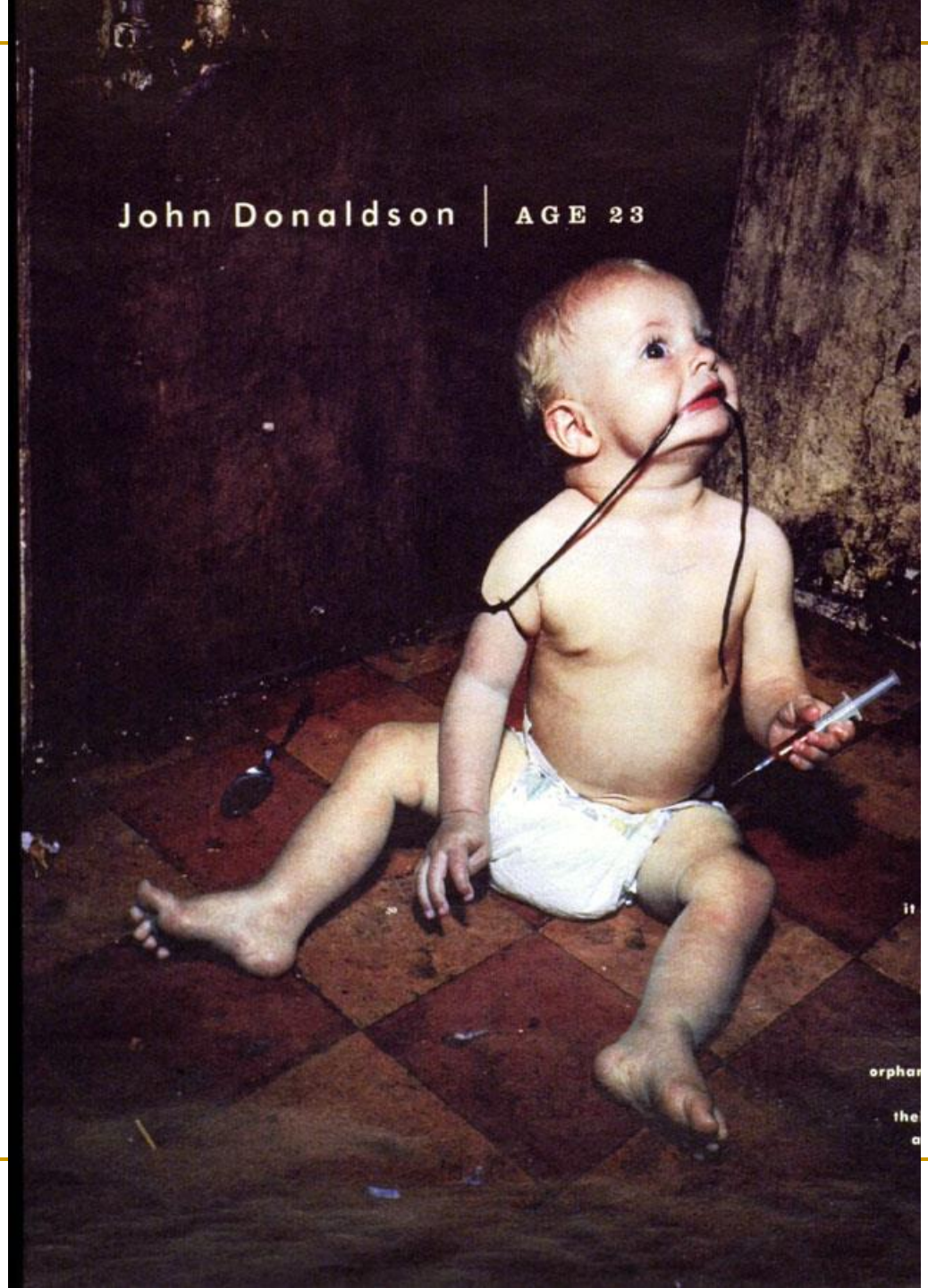


Number of new HIV diagnoses[1] by prevention group[2], UK: 1999-2008

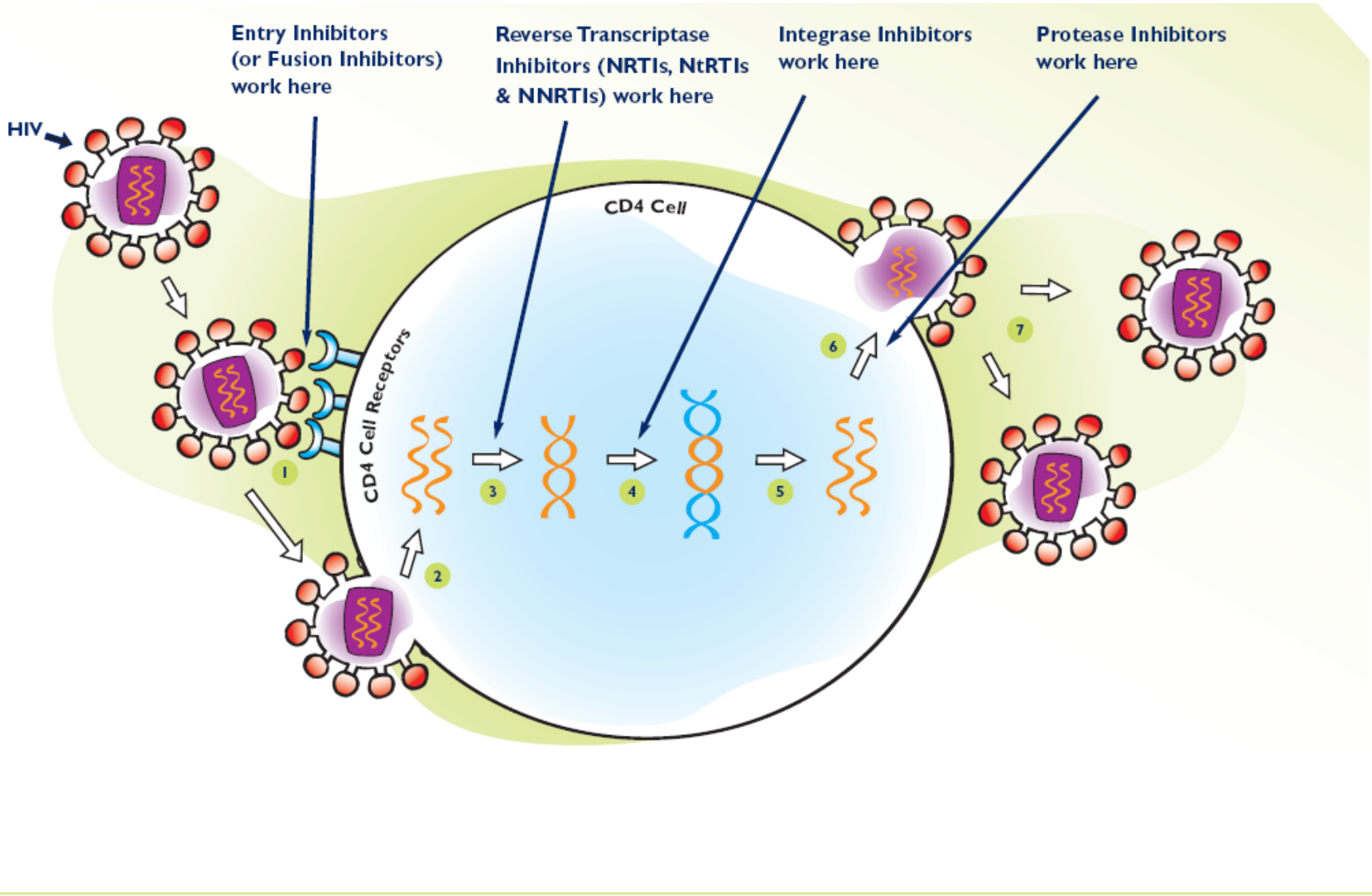


[1] Numbers will rise as further reports are received, particularly for recent years

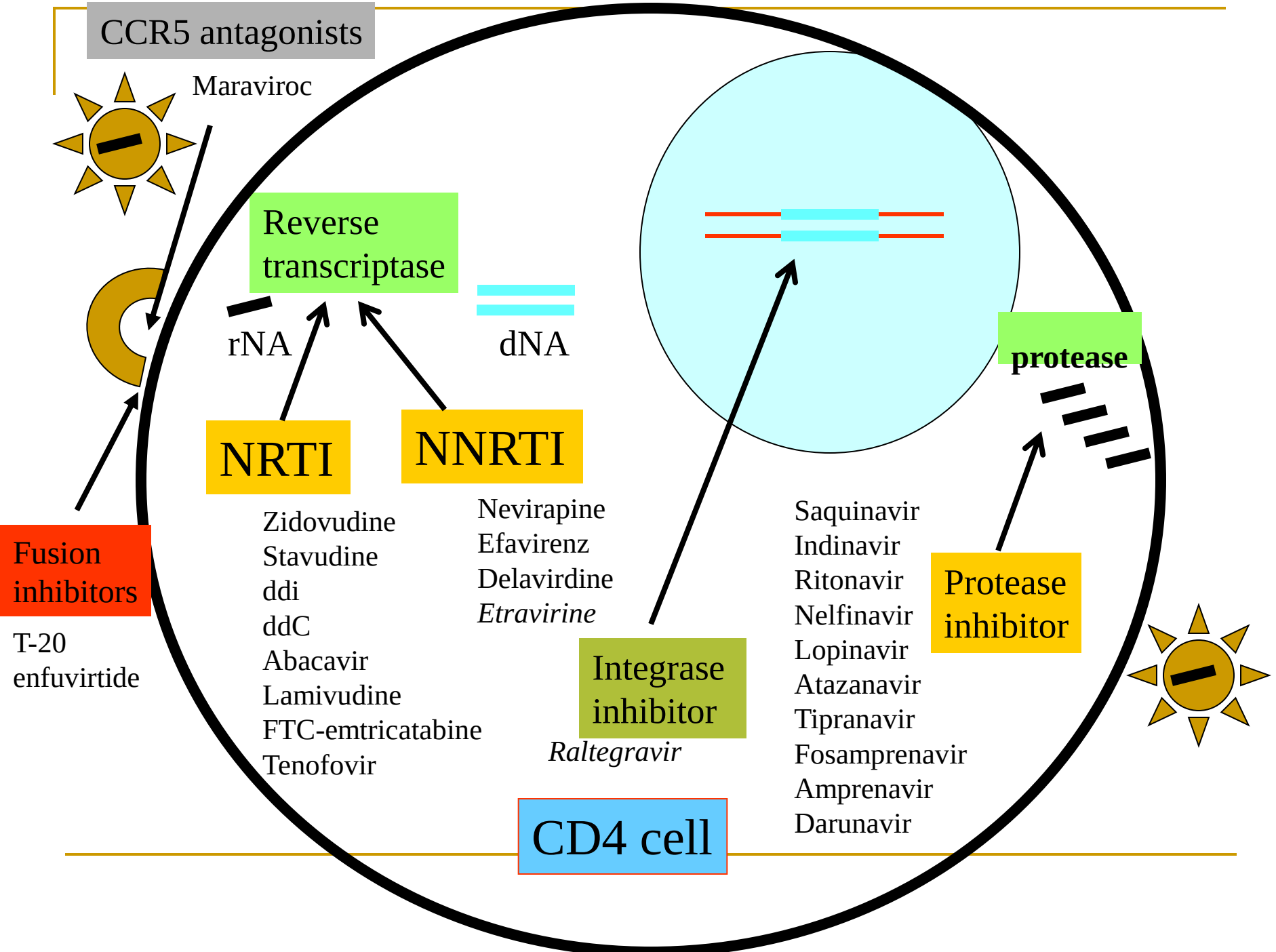
[2] Adjustments made for missing information relating to patient exposure


John Donaldson | AGE 23

Increased mobility



1. HIV binds to receptors on the CD4 cell
2. HIV enters the cell and inserts its genes (RNA)
3. HIV converts its genes into a form compatible with the CD4 cell's genes (DNA)
4. HIV inserts its genes into the CD4 cell's genes
5. The CD4 cell reads the infected genes and produces HIV components
6. HIV components are assembled to form new HIV
7. The new HIV destroys the CD4 cell as it exits, leaving to infect another CD4 cell


CCR5 antagonists
Maraviroc
Reverse transcriptase
rNA
dNA
protease
NRTI
NNRTI
Fusion inhibitors
T-20
enfuvirtide
Zidovudine
Stavudine
ddi
ddC
Abacavir
Lamivudine
FTC-emtricatabine
Tenofovir
Nevirapine
Efavirenz
Delavirdine
Etravirine
Integrase inhibitor
Raltegravir
Saquinavir
Indinavir
Ritonavir
Nelfinavir
Lopinavir
Atazanavir
Tipranavir
Fosamprenavir
Amprenavir
Darunavir
Protease inhibitor
CD4 cell

Approval of Antiretrovirals: 1987-2006

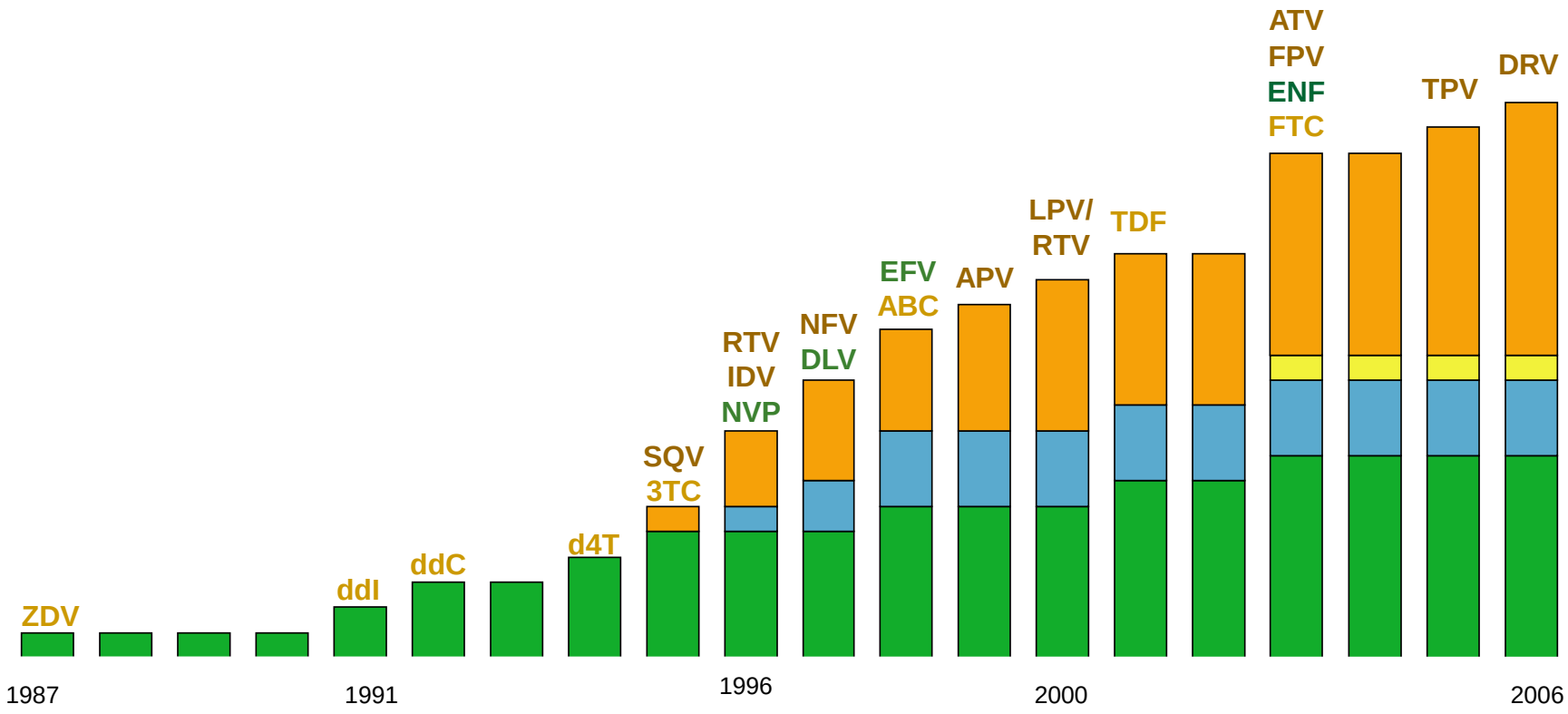
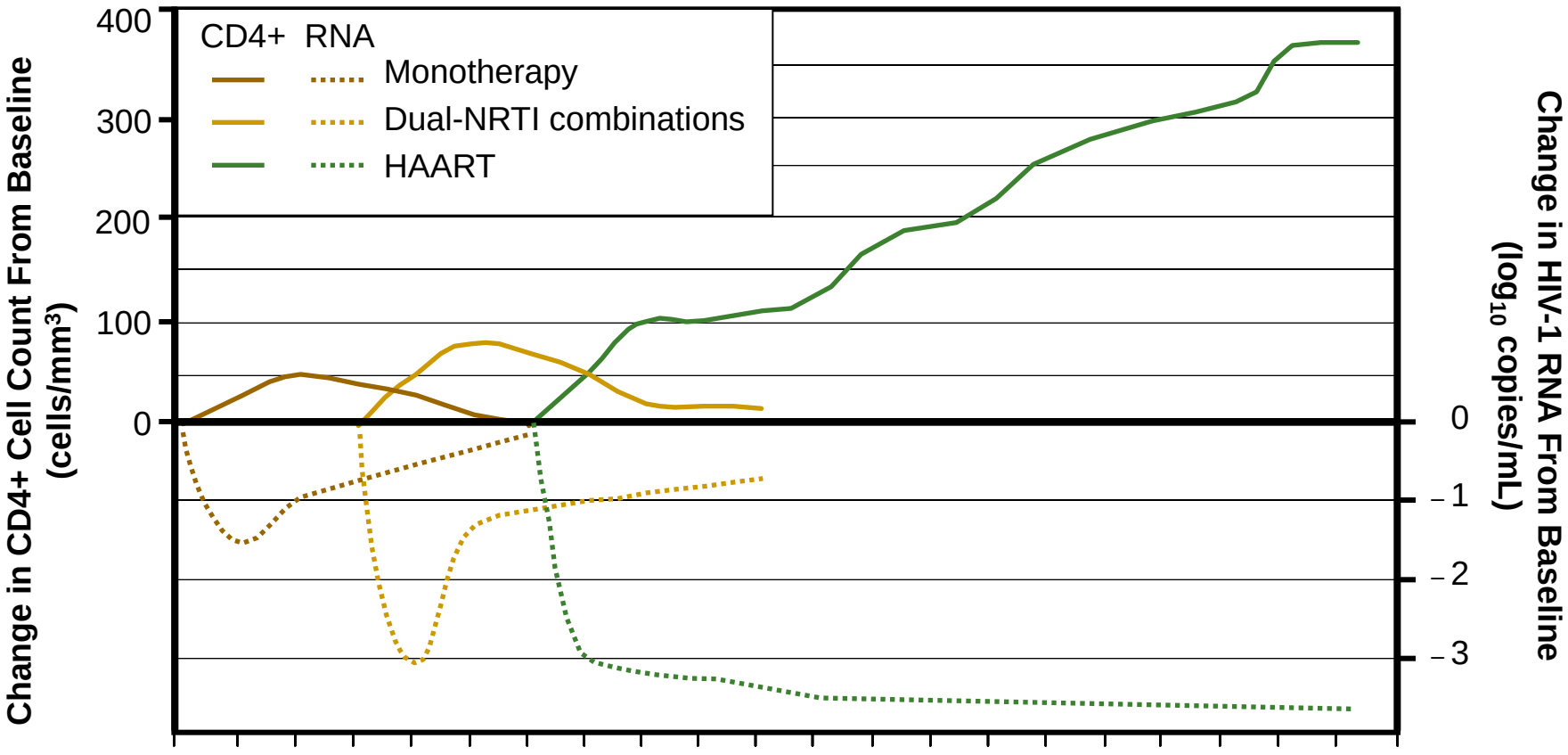


Figure does not include fixed-dose combinations

Improving Outcomes With Evolving Antiretroviral Regimens



Past

- High pill burden
- Food restrictions
- Multiple daily doses
- Poor tolerability

Present

HIV & Intensive Care

- Drug delivery
  - Some drugs available as suspensions, only AZT is used i.v.
- Renal impairment
  - All NRTI (except ABC) need dose adjustment
- Hepatic impairment
  - Some protease inhibitors need dose adjustment
  - Avoid nevirapine

Nucleoside Reverse Transcriptase Inhibitors (NRTI)

Zidovudine *Anaemia, myopathy, lipoatrophy*
Stavudine *Peripheral neuropathy, lipoatrophy*
Didanosine *Pancreatitis*
Zalcitabine *Peripheral neuropathy*
Lamivudine/emtricabine
Abacavir *Hypersensitivity, CVD*
Tenofovir *Renal toxicity, nausea, osteoporosis/osteopenia*

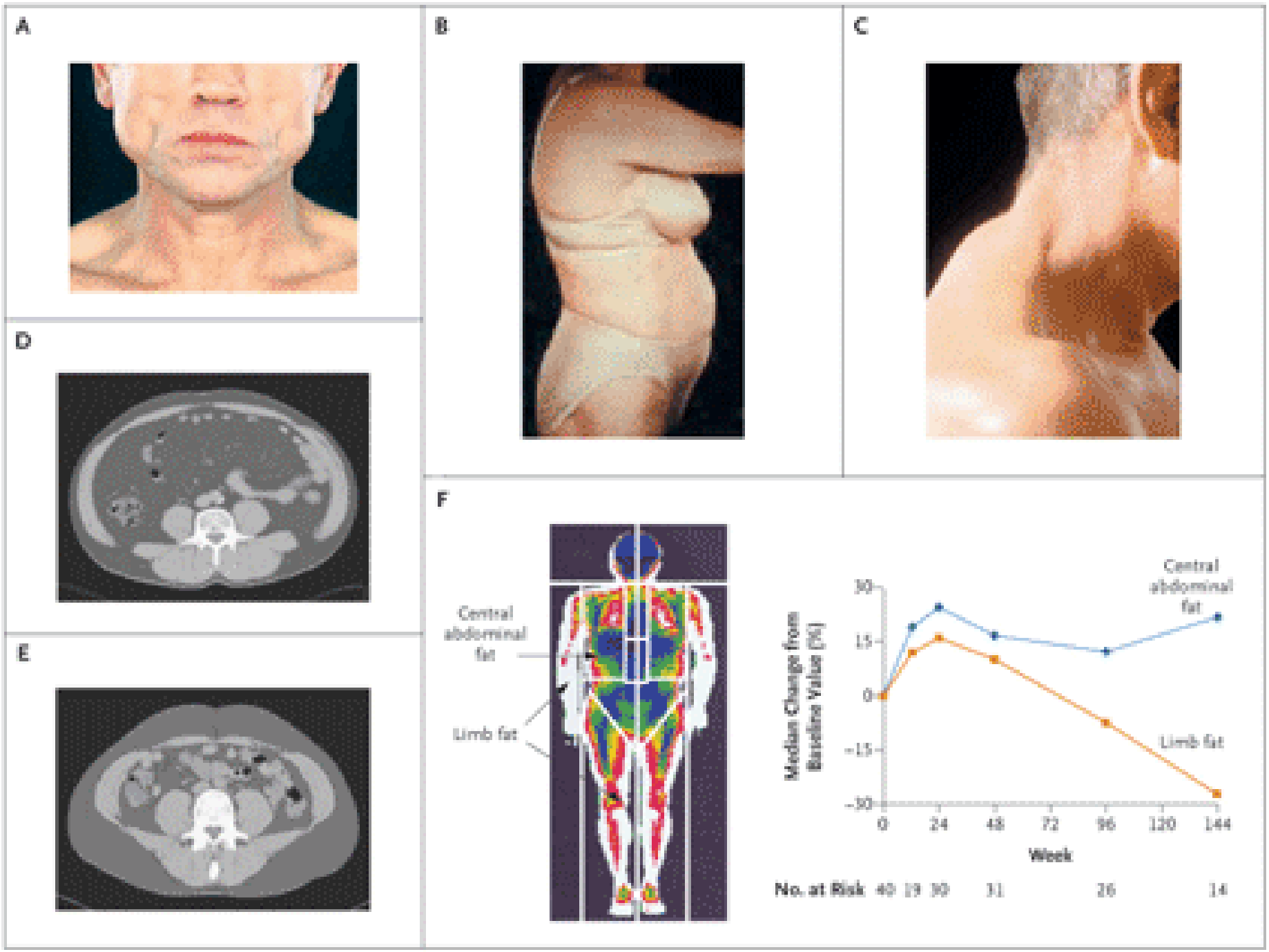
ALL CAUSE LACTIC ACIDOSIS
Mutations in mtDNA

Non-NRTI (NNRTI)

Delavirdine	*Rash*
Nevirapine	*Rash, abnormal LFTs*
Efavirenz	*CNS excitation, insomnia*

Protease inhibitor

Saquinavir	*Nausea, vomiting, diarrhoea*
Ritonavir	*Insulin resistance*
Indinavir	*Lipodystrophy*
Nelfinavir	*Hyperlipaemia*
Amprenavir	*Diabetes*
Atazanavir	*Increase in bilirubin*
Lopinavir	*Drug interactions +++*
Darunavir	

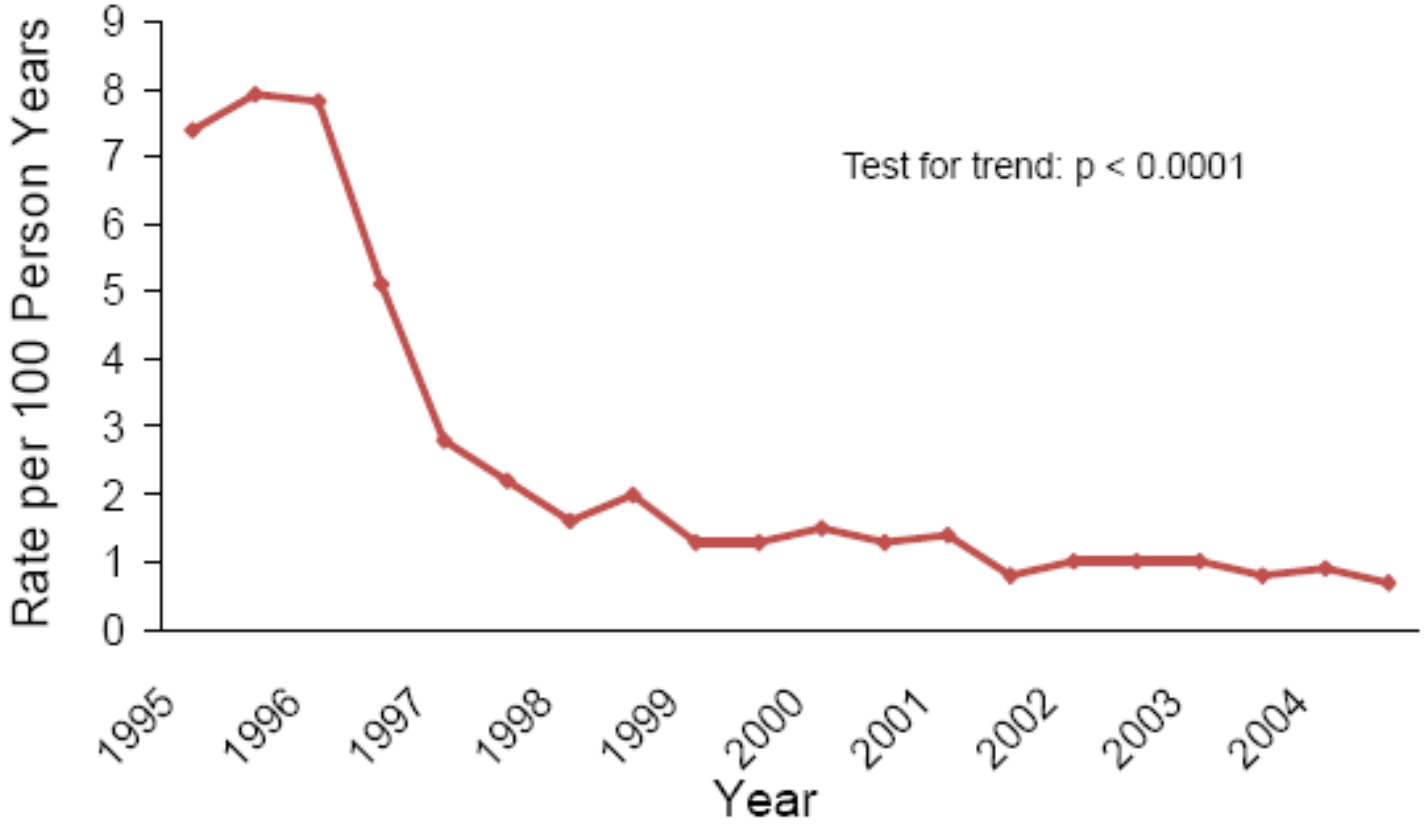

A
B
C
D
E
F
Central abdominal fat
Limb fat
Median Change from Baseline Value (%)
30
15
0
−15
−30
0
24
48
72
96
120
144
Week
Central abdominal fat
Limb fat
No. at Risk 40 19 30 31 26 14

D:A:D Study

- 23,000 prospective cohort study of HAART and CHD
  - 76,000 patient years median HAART exposure 4.5 years
  - MI incidence/1000 patient years
    - 2.53 if <1 year of HAART
    - 6.07 if >6 years of HAART
    - 1.39 in Rx naïve patients
      - HAART risk M=F; younger=older
    - Abacavir-90% increased risk of MI?
  - Rx at CD4 350
- Renal disease
- Bone disease
- Neurocognitive deficit

Incidence of non-AIDS death 1994-2004

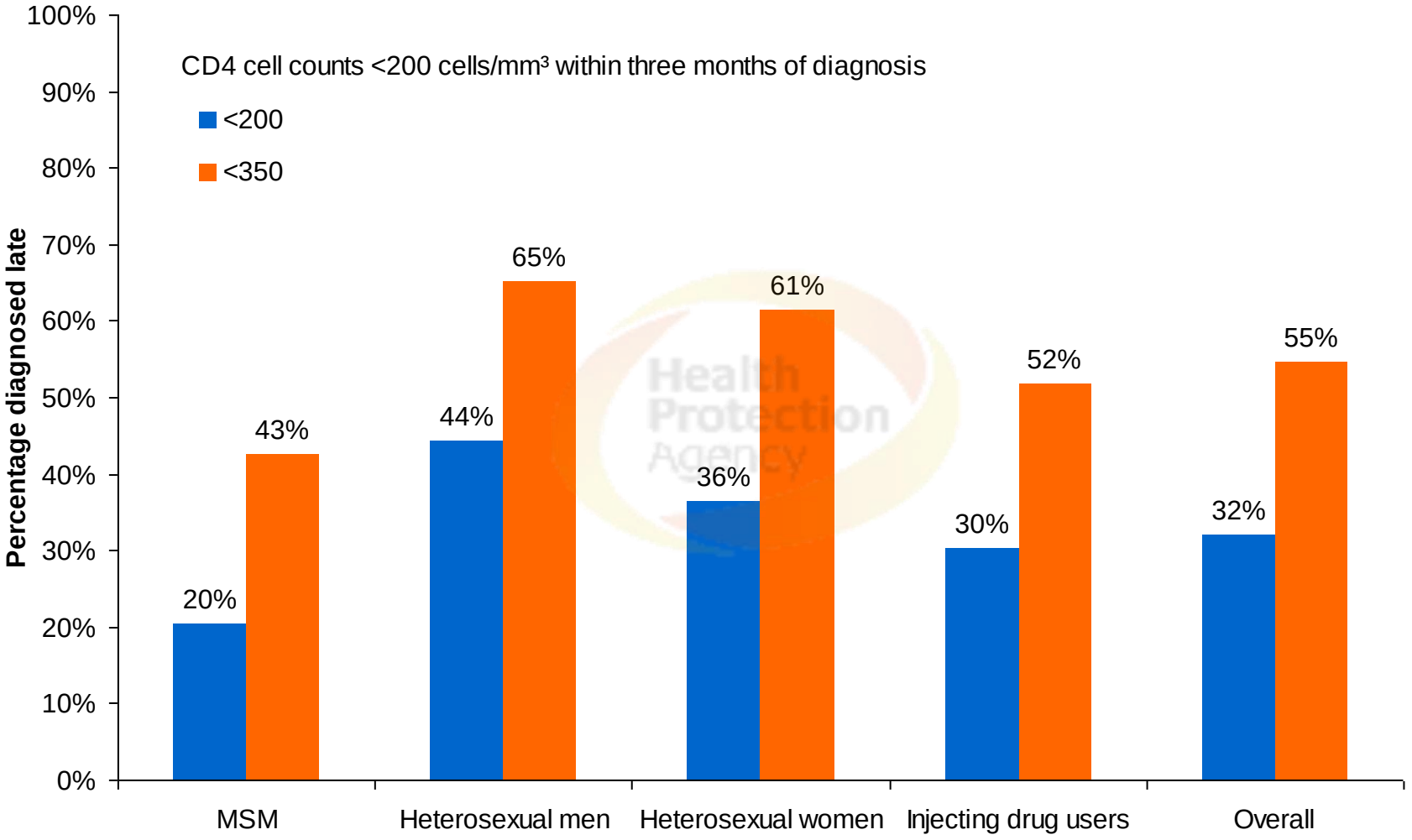
Excluding death from unknown causes



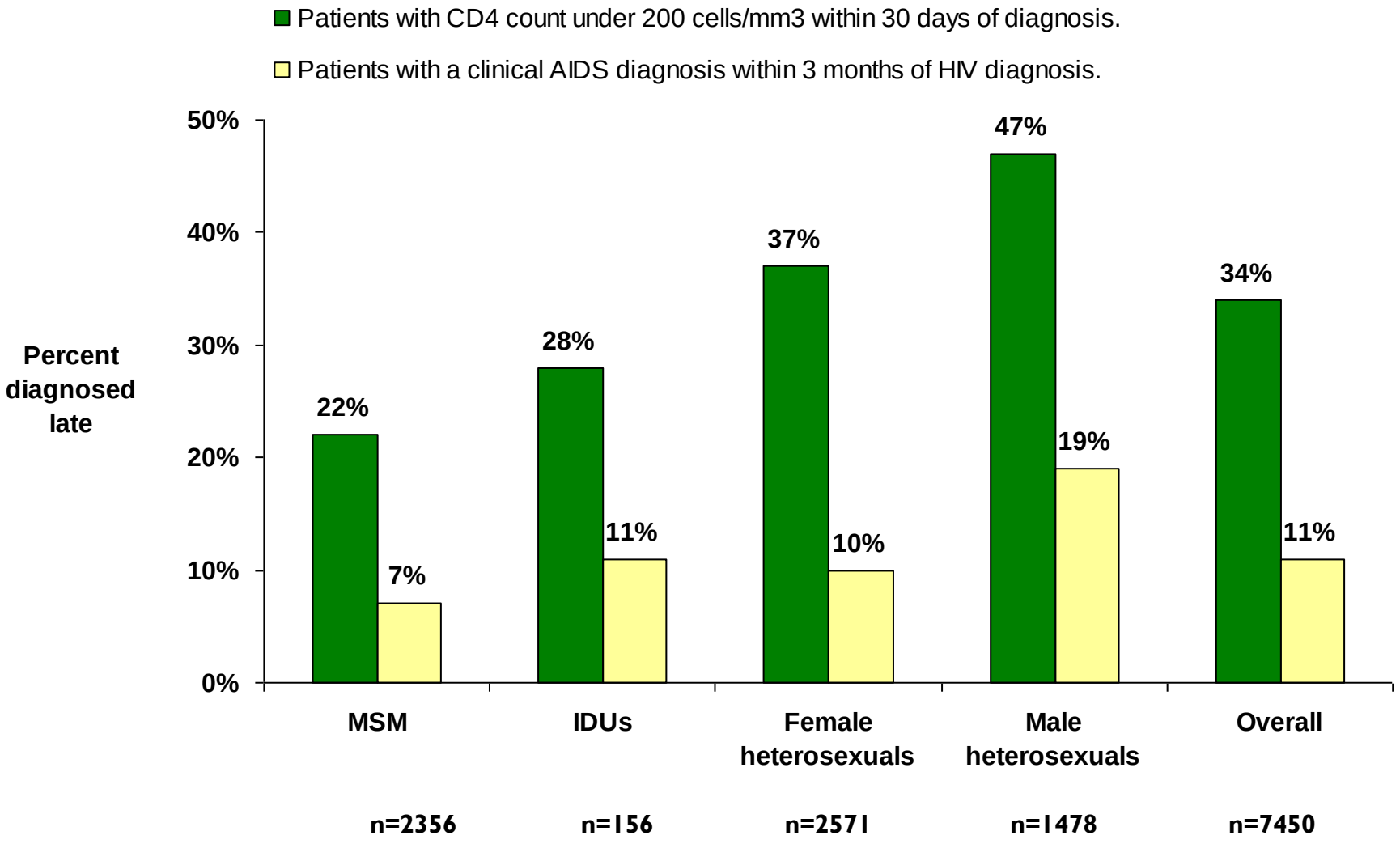
Phillips A CROI 2008

EuroSIDA; Mocroft, Lundgren et al, personal communication

Estimated late diagnosis of HIV infection by prevention group among adults aged ≥ 15 years, UK: 2008

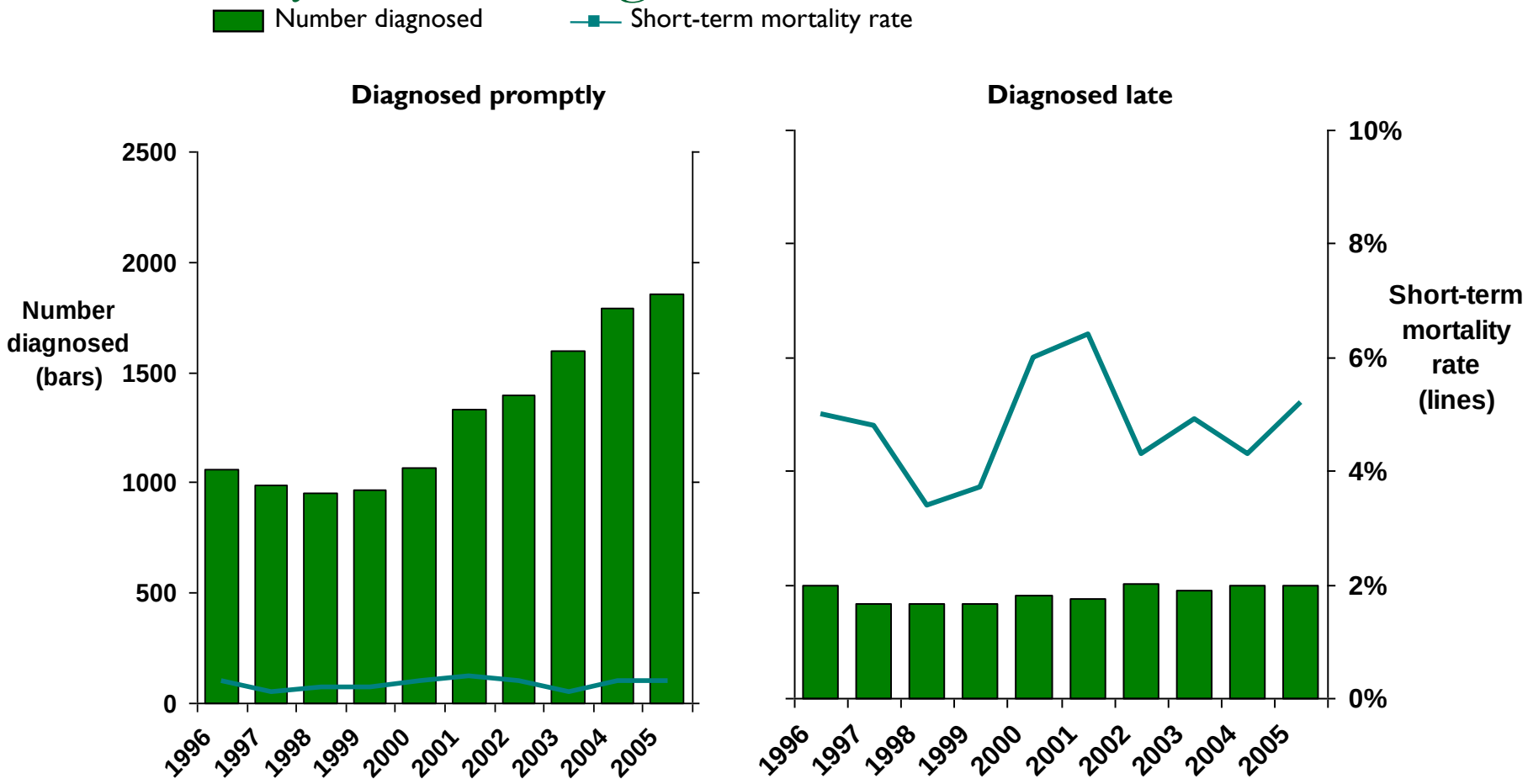


Late diagnosis of HIV infection



Reports of HIV/AIDS diagnosis and CD4 Surveillance

Pattern of diagnosis and associated short-term mortality rate among MSM



Late diagnosis CD4 count <200 cells/mm^3; prompt diagnosis ≥200 cells/mm^3.
Short-term mortality rate: percent of patients known to have died within a year of diagnosis.

Who to test?

Opt-out Testing

- GUM attendees
- Antenatal clinics
- TOP
- History of IDU
- Diagnosis of TB, HBV, HCV, Lymphoma
- “Indicator Diseases”
- Patients from high prevalence areas
- MSM
- Sexual partners of patients from high prevalence areas
- Acute admissions & new patients registering at GP surgeries if local undiagnosed prevalence > 1:1000

Indicator Diseases

- AIDS Defining:
  - TB, PCP, Cerebral toxoplasmosis, PML, NHL, Cervical cancer, CMV retinitis
- Other conditions:
  - Bacterial pneumonia, lung cancer, AIN, VIN, unexplained blood dyscrasias, oral candidiasis, retinopathies, PUO,shingles, salmonellae infections any STI

102 HIV-Patients admitted to UCLH ICU on 113 occasions

Diagnosis	N(%)
LRTI	**54 (48)**
▪ **PCP**	**26**
▪ **Bacterial pneumonia**	**17**
▪ **Tuberculosis**	**7**
▪ **Other**	**4**
Neurological problems	**16 (14)**
▪ **Meningitis**	**5**
▪ **Cerebral Toxoplasmosis**	**3**
▪ **HIV Encephalitis**	**3**
▪ **Other**	**5**
Sepsis	**10 (9)**
Post-cardiac arrest	**7 (6)**
Postoperative	**7 (6)**
Variceal haemorrhage	**5 (4)**
HAART-related	**3 (3)**
Miscellaneous	**11 (10)**

HIV and Intensive Care

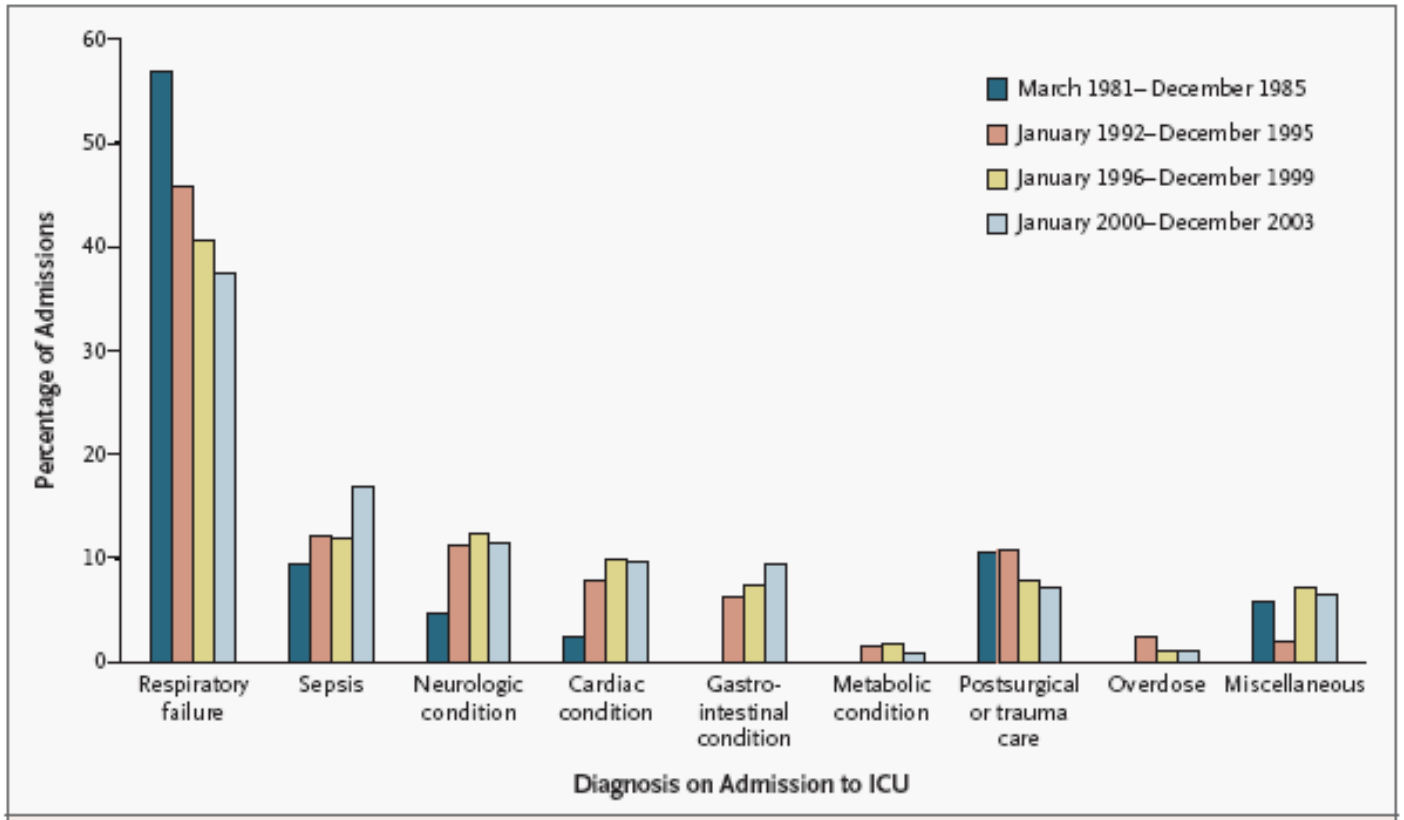
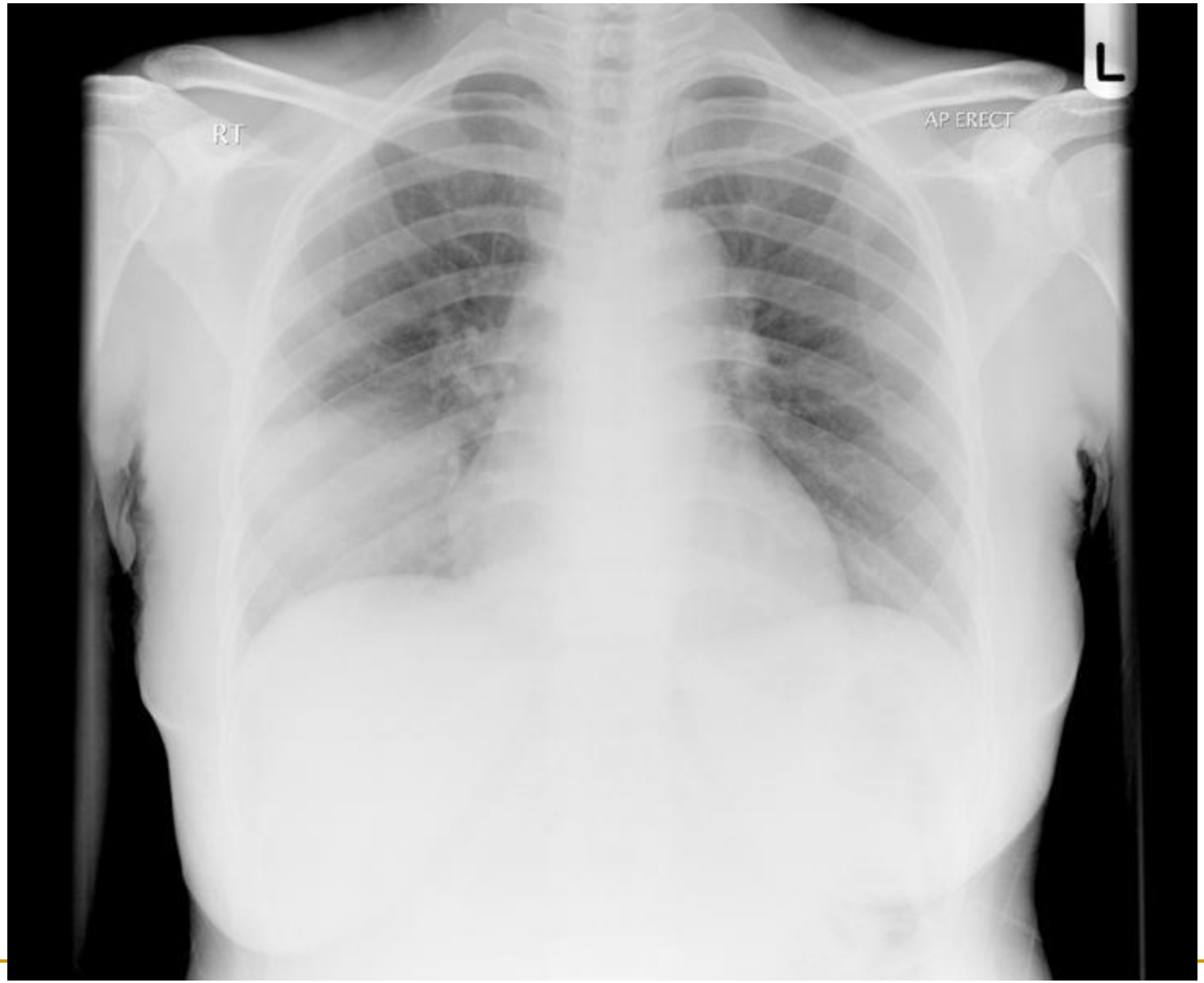
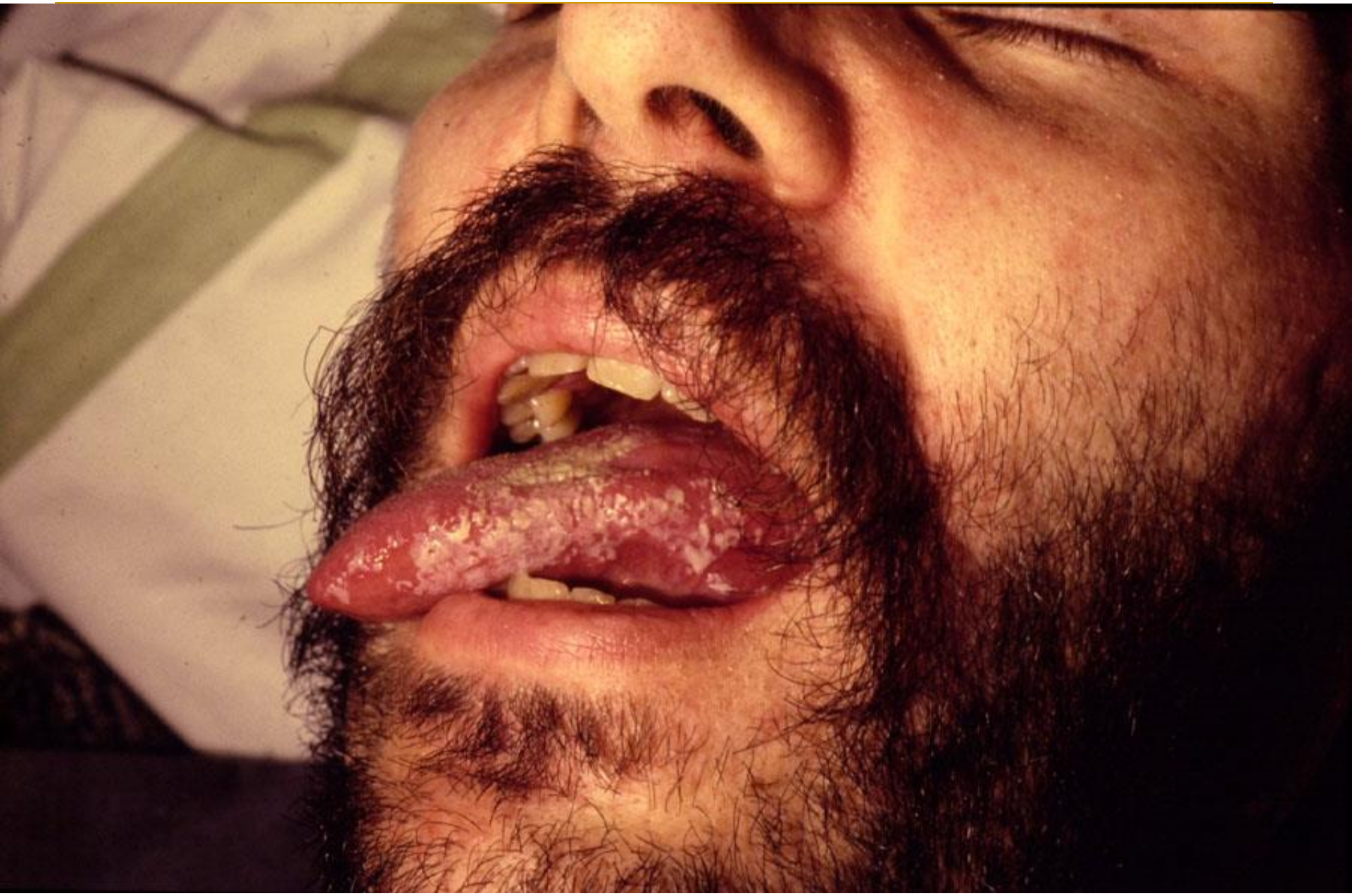
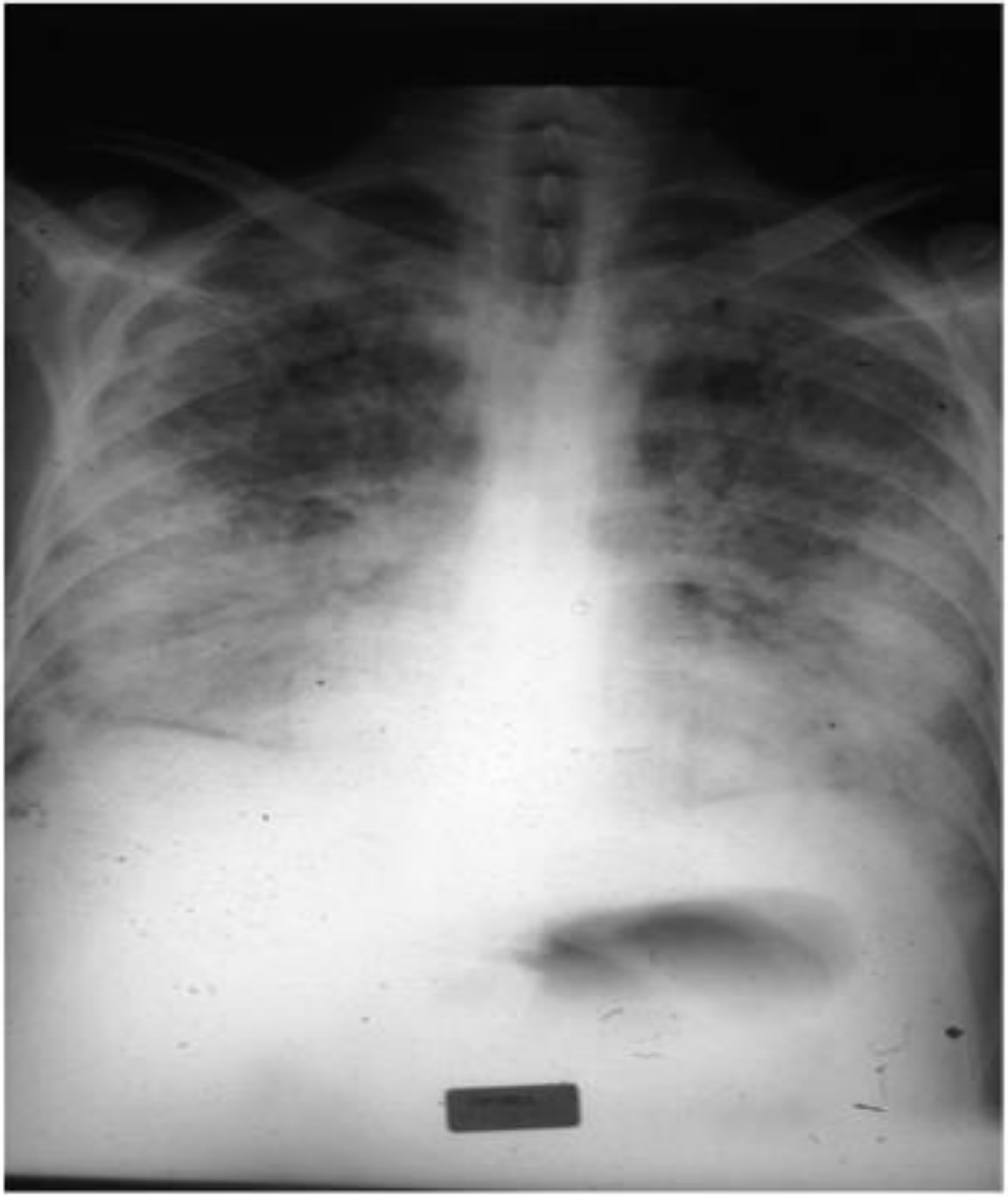


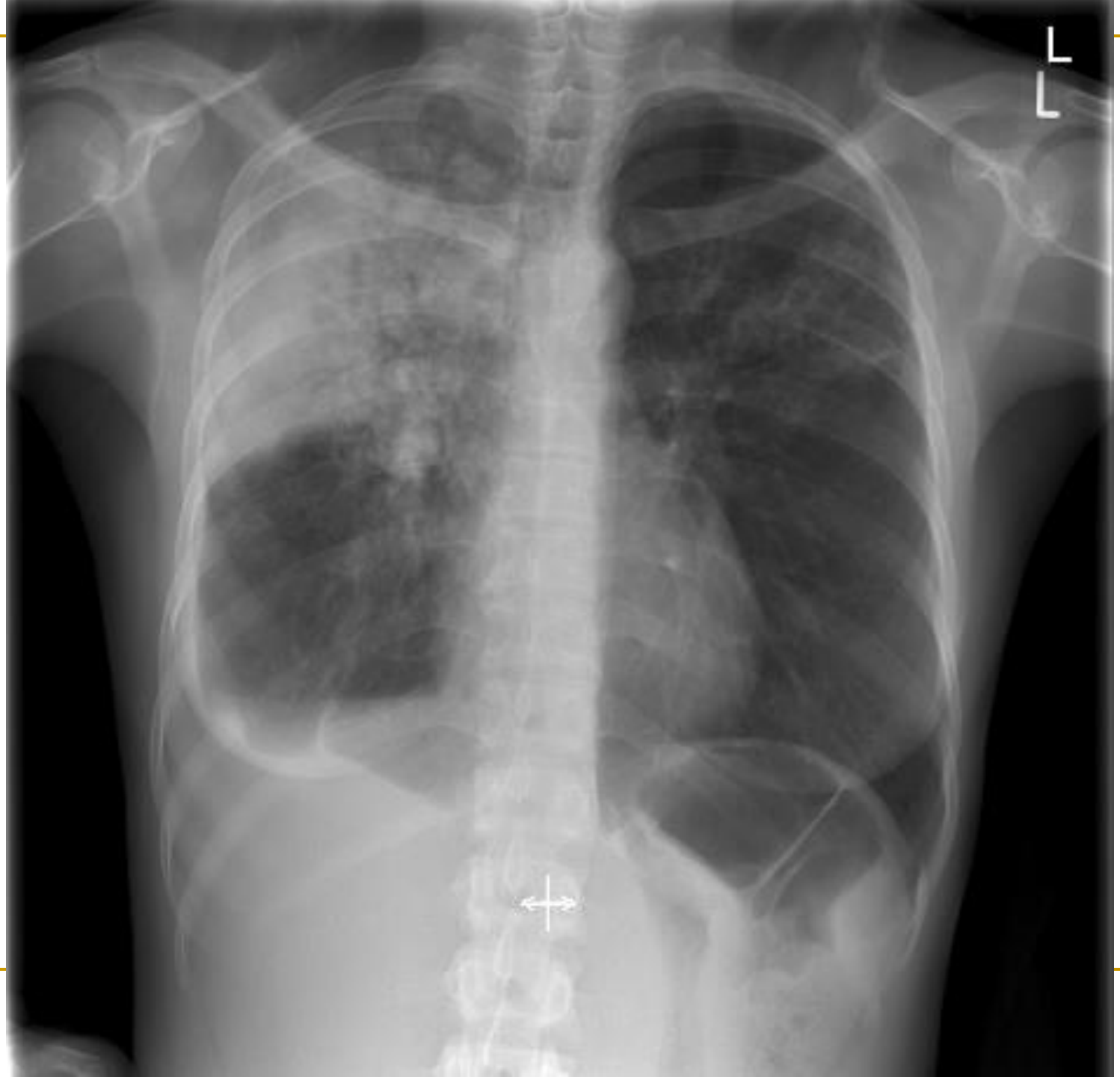
Figure 1. Principal Diagnosis Received by Patients with HIV on Admission to the Medical or Surgical ICU at San Francisco General Hospital between 1981 and 2003.

The principal diagnosis on admission to the ICU is reported for 86 patients from March 1981 to December 1985,[5] followed by a gap of six years; then for 443 patients (an average of 111 patients per year) from January 1992 to December 1995,[6] for 354 patients (an average of 88 patients per year) from January 1996 to December 1999,[1] and for 328 patients (an average of 82 patients per year) from January 2000 to December 2003.


RT
AP ERECT
L



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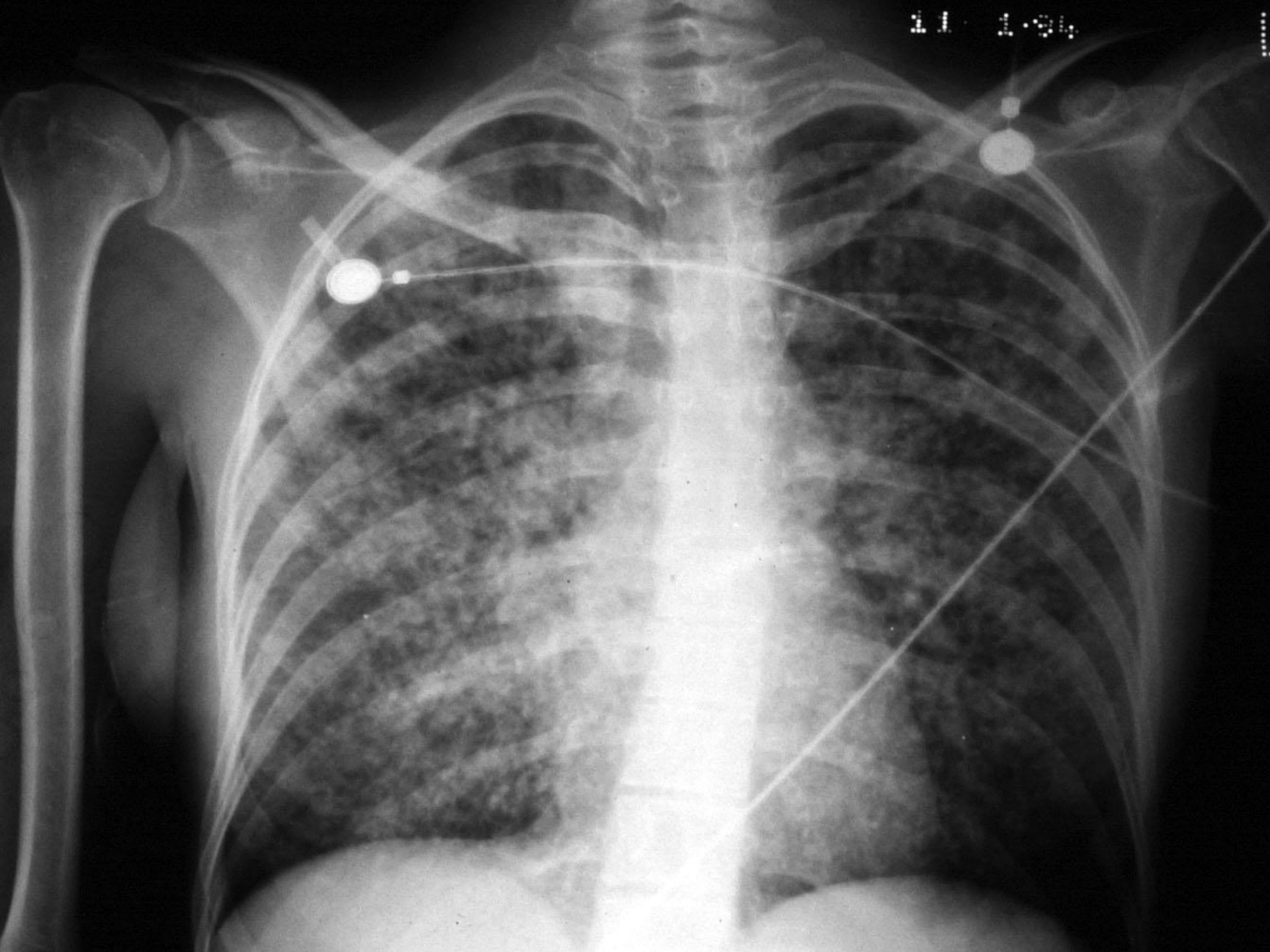
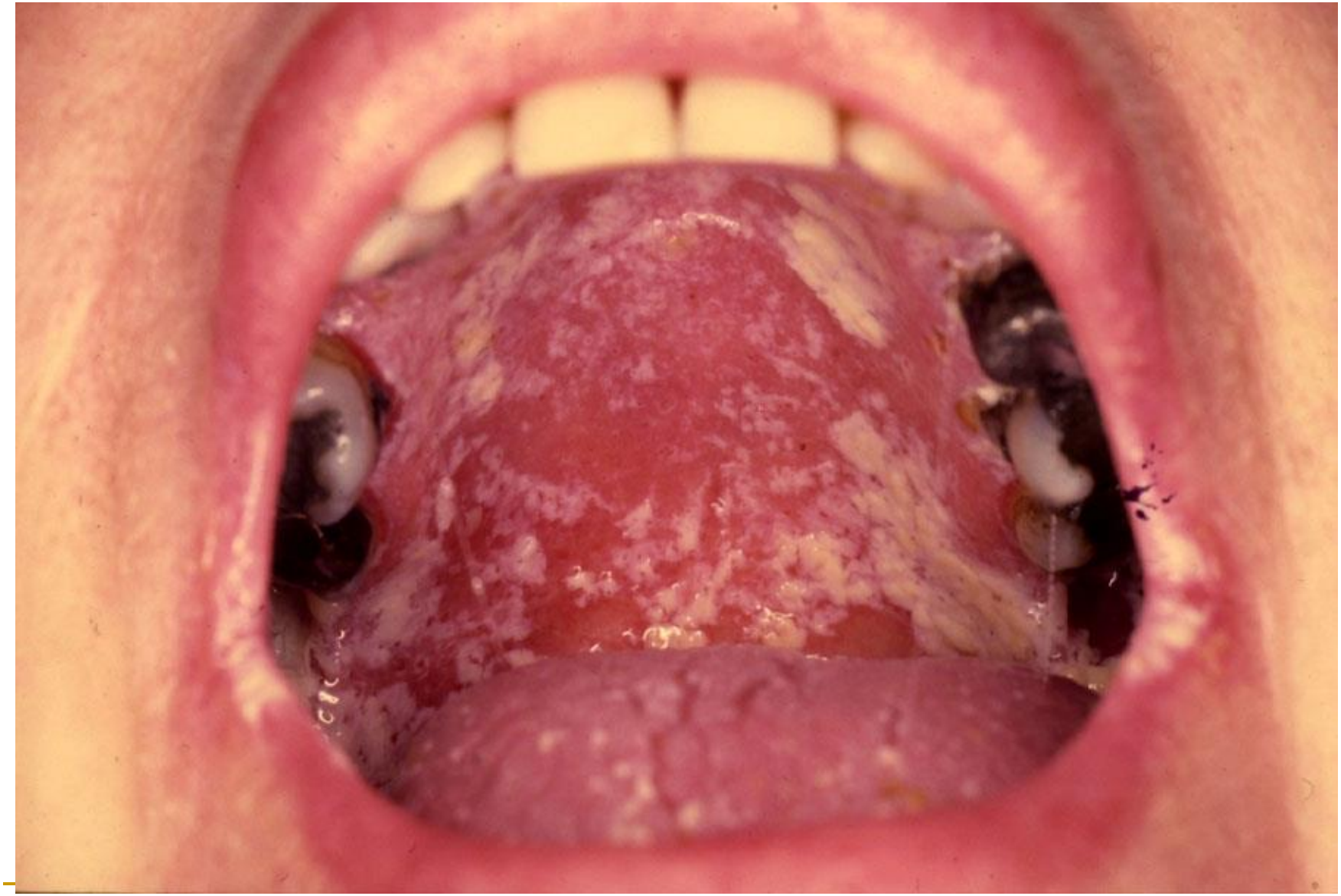
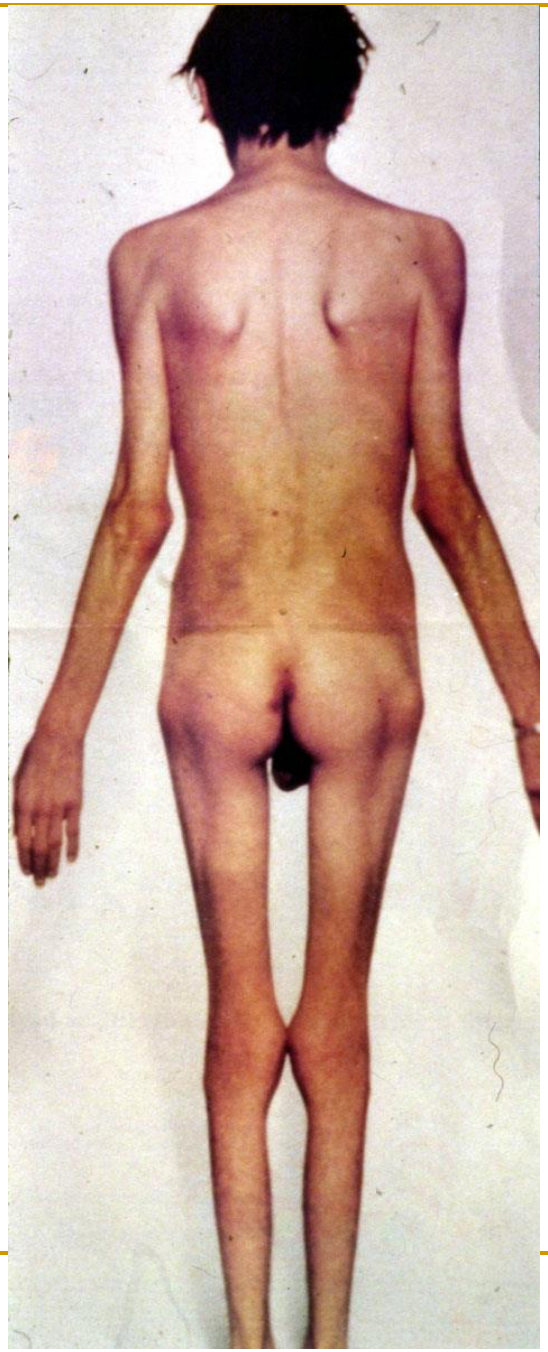
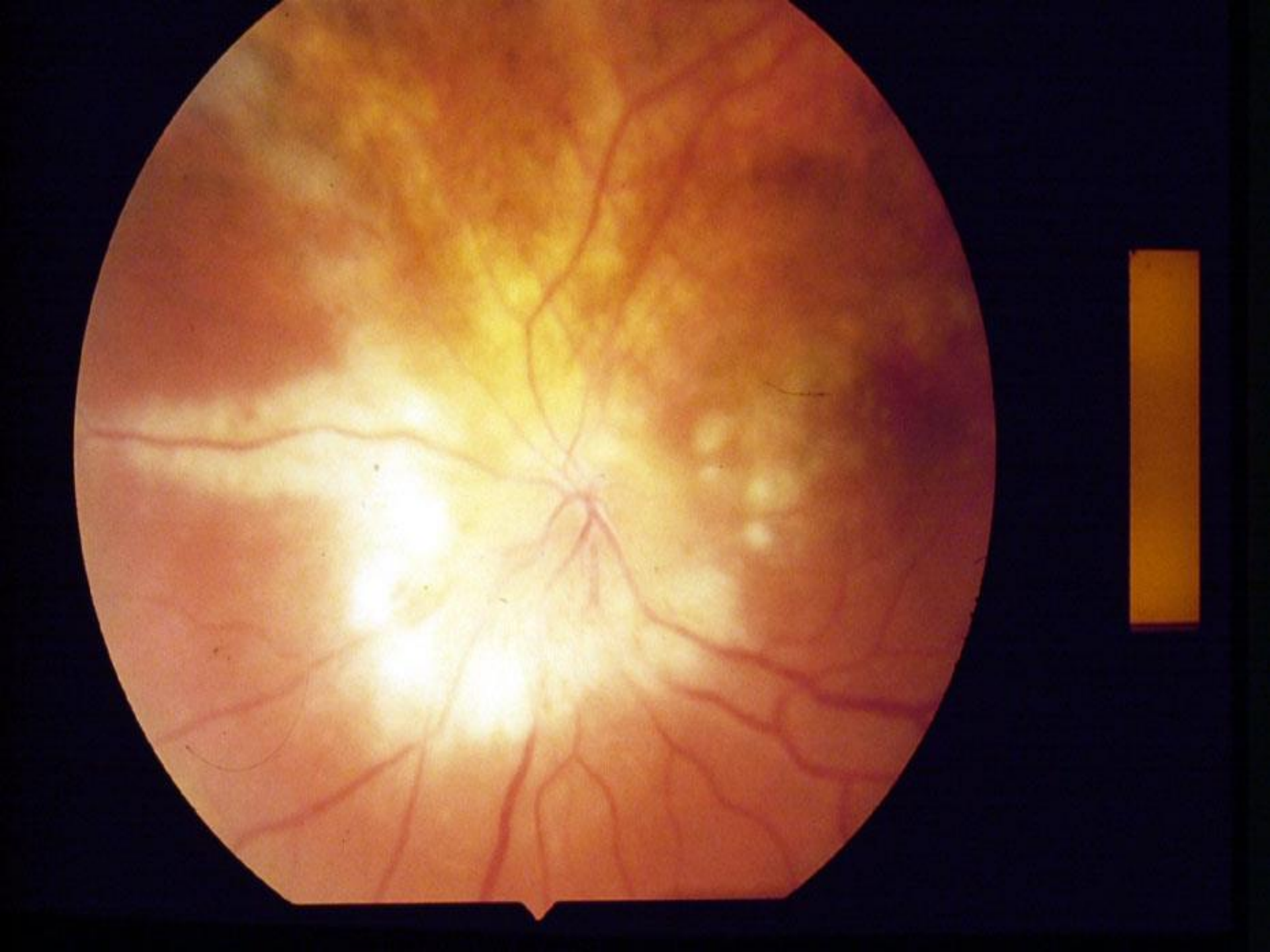
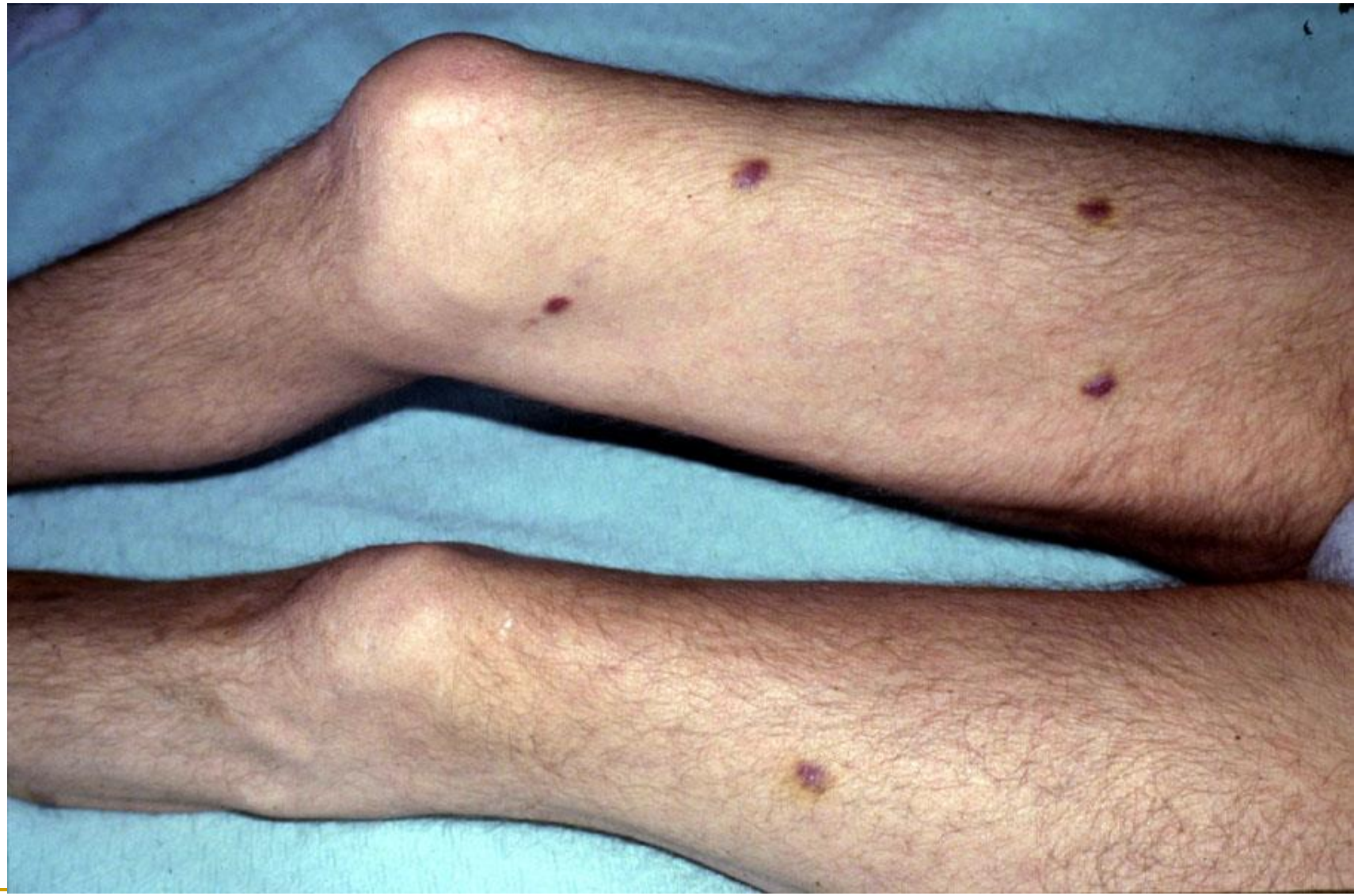
L

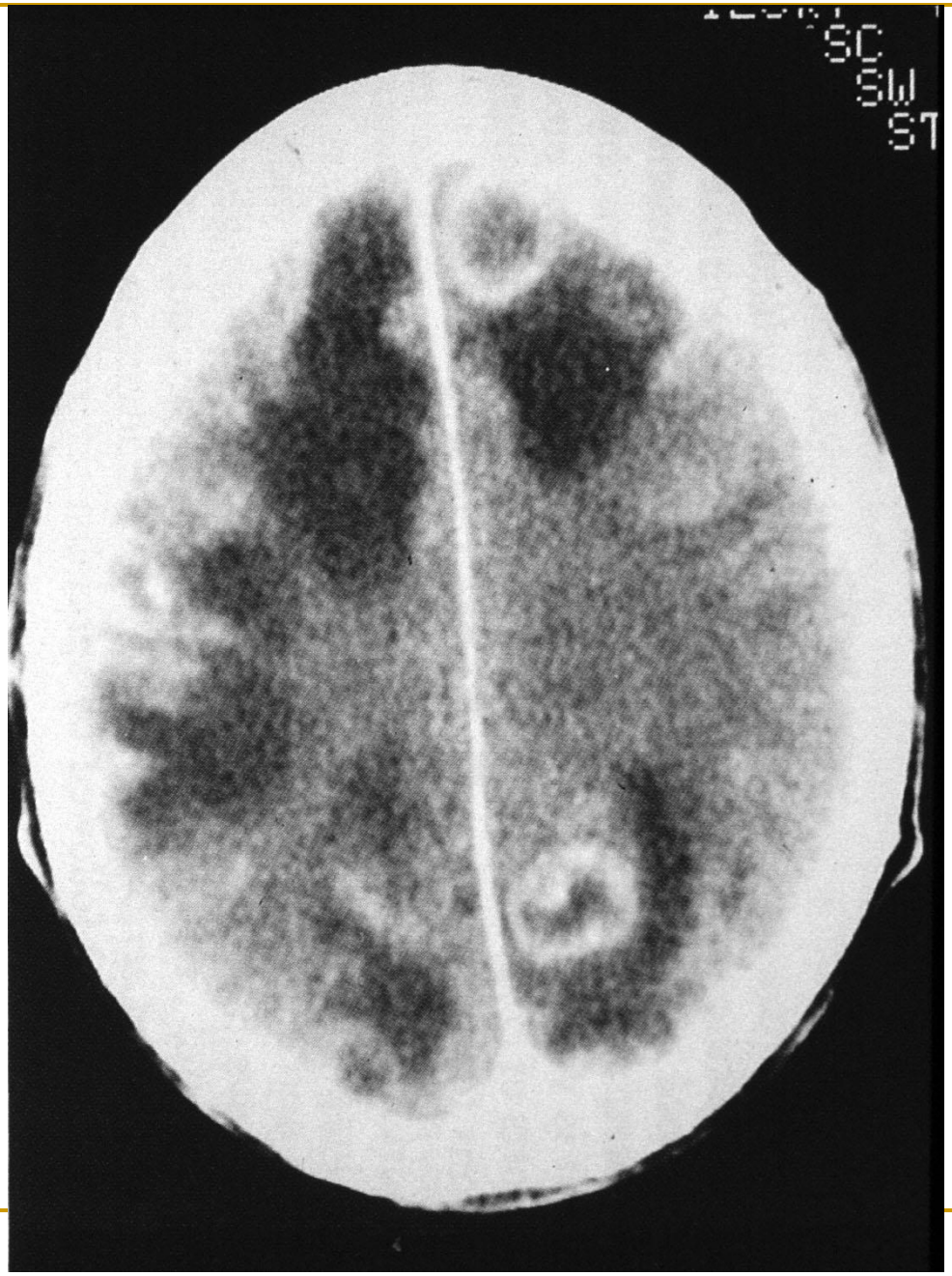

11 1-94







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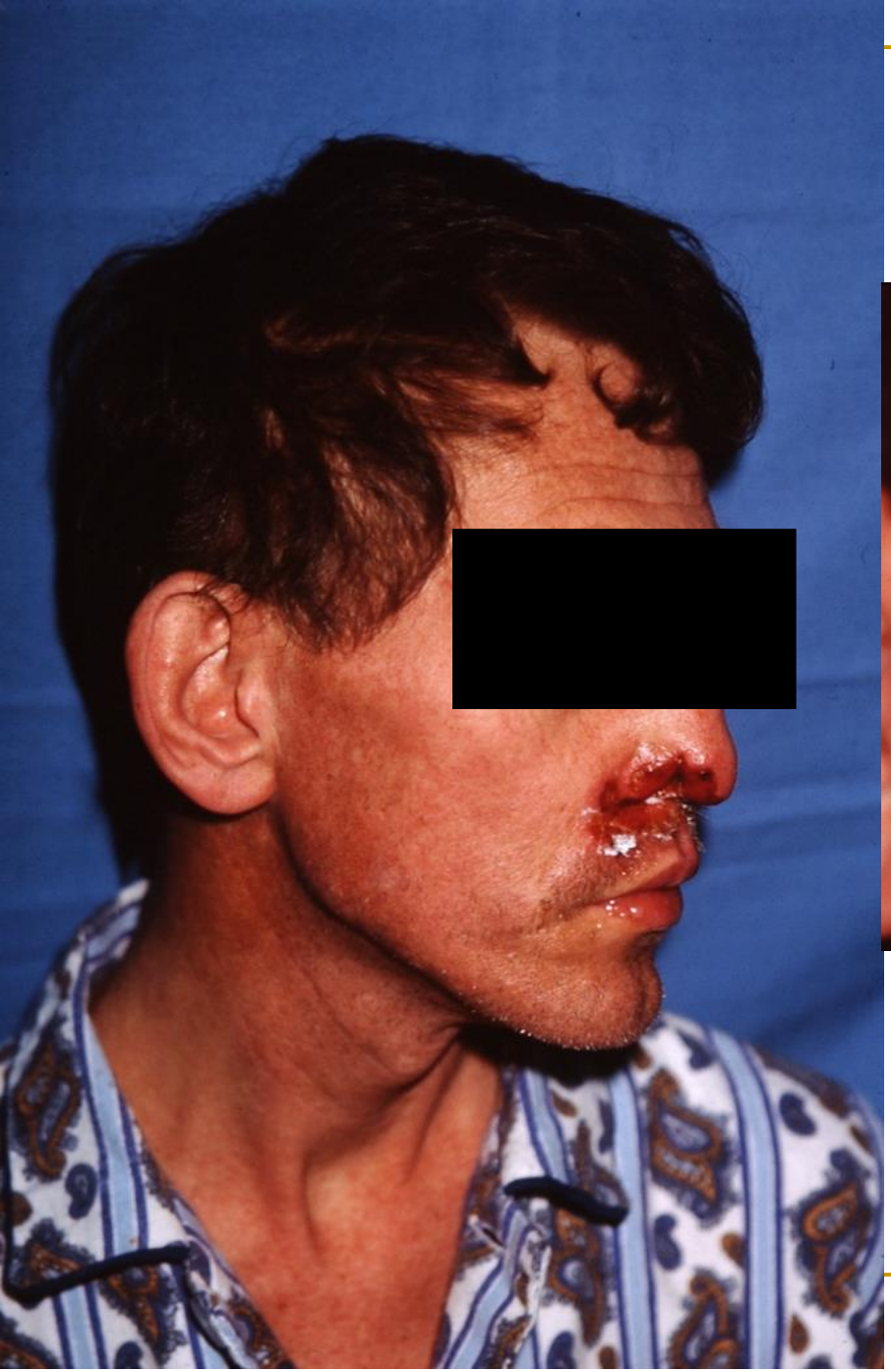
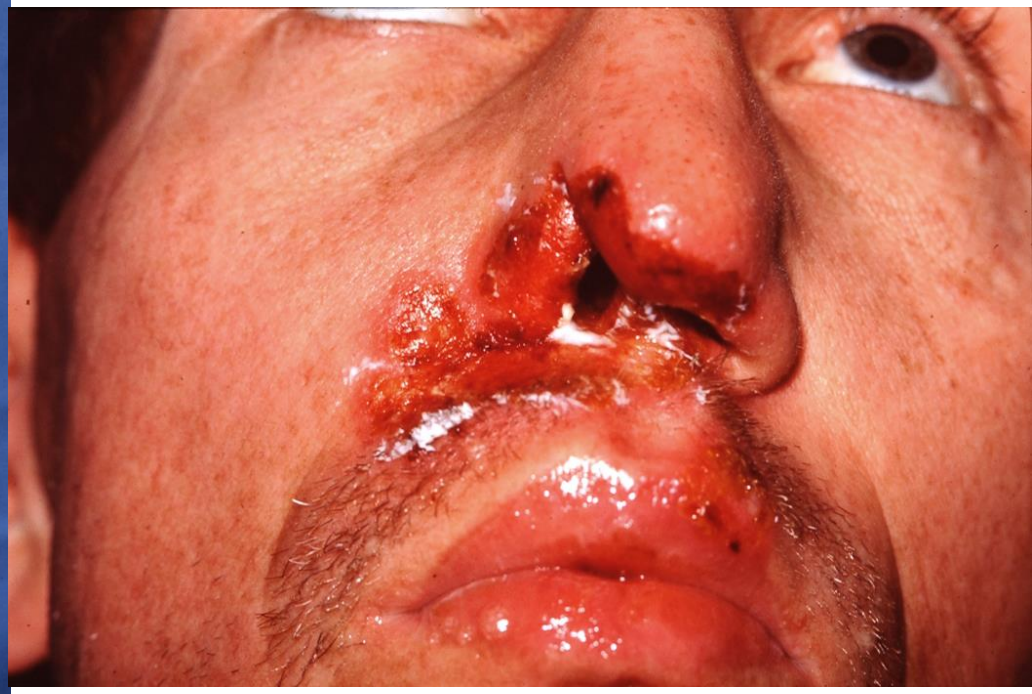
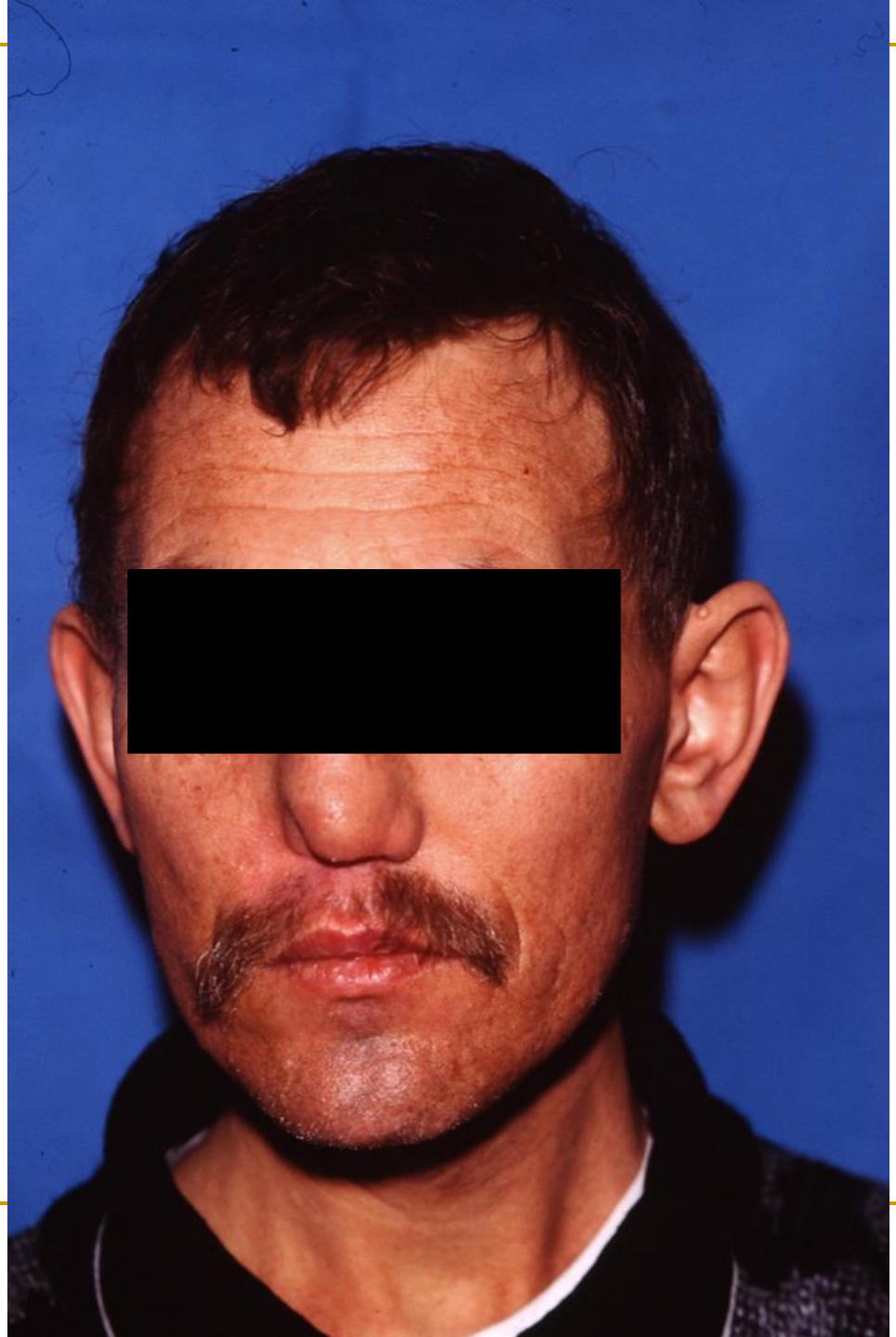


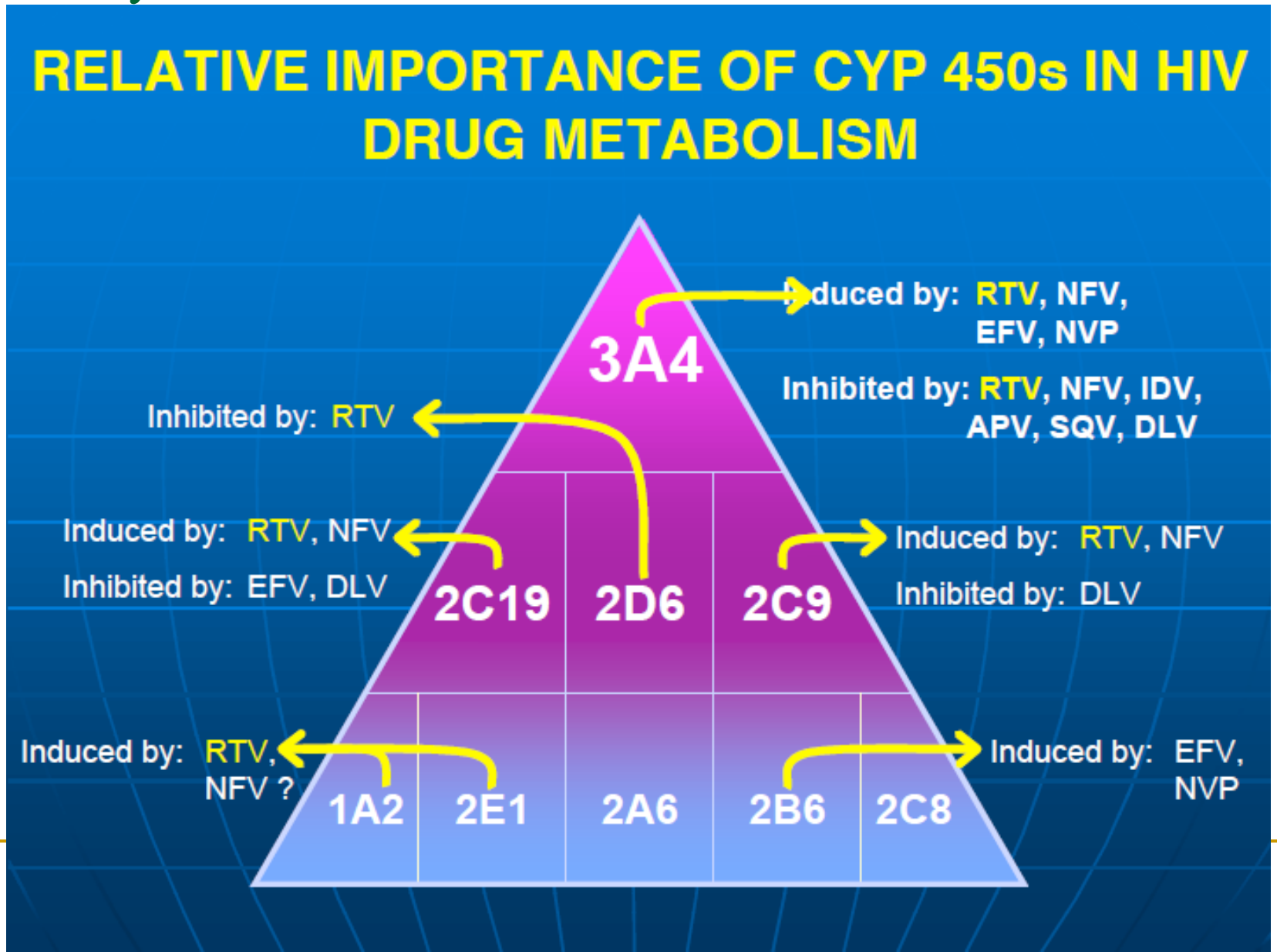




Common ICU drugs contraindicated with HAART

ICU Drug	HAART
Midazolam	Indinavir, Ritonavir, Tipranavir, EFV
Amiodarone	Indinavir, Ritonavir, Tipranavir
Proton Pump Inhibitors	Atazanavir
H2-blockers	Atazanavir
Propanfenone	Lopinavir, Ritonavir, Tipranavir
Quinidine	Ritonavir, Tipranavir
Rifampicin	PIs, nevirapine

Enzyme Induction & Inhibition



welcome to the www.hiv-druginteractions.org website

UNIVERSITY OF LIVERPOOL

This informative and educational HIV pharmacology resource is valuable for healthcare professionals, scientific researchers or anyone with an interest in HIV therapy. You can find reports on recent news and hot topics in HIV, discover comprehensive information and advice on drug interactions, read about advances in therapeutic drug monitoring (TDM), and much more!

LATEST NEWS

Hot Topics

Drug Interactions - Reviews on darunavir and tipranavir.

Drug Interactions - Interactions with Etravirine

Meeting Report - Drug Interactions at the 4th IAS Conference, Sydney.

Recent Publications

Drug Interactions - Acid Reducing Agents.

Drug Interactions - Fosamprenavir/ritonavir and ketoconazole.

Drug Interactions - Darunavir/ritonavir and efavirenz.

Click here for previous news items

SITE NEWS

Updates to Interaction Charts

Added: Thursday 6th September 2007

The following drugs have been added as rows to the interaction charts:
Etravirine – new NNRTI
Maraviroc – new entry inhibitor
Elvitegravir – new integrase inhibitor
Raltegravir – new integrase inhibitor

A summary and description have been provided for those interactions where studies have been performed.

more...

DRUG INTERACTION CHARTS

Access a wealth of information on HIV drug interactions by visiting our drug interactions page. The dynamically driven process allows you to build your own customised drug interaction chart, giving detailed information on predicted interactions of specified multiple drug combinations.

HIV-CHARTS2GO

HIV-Charts2Go, drug interaction charts for PDAs, are now available in a new and improved version.

Registration is required to access and download HIV-Charts2Go. Registration is free and you do not need to re-register if you used the old version of HIV-Charts2Go.

Click here to login and download the new version.

ASSOCIATED SITES

A new comprehensive resource for healthcare professionals and scientists who are interested in the expanding field of HIV pharmacogenomics.

ATIC is an initiative of Realta, an Irish NGO, dedicated to improving the treatment, as well as reducing the spread of HIV in Africa.

EMAIL UPDATES

Click here to register for the latest site updates via email.

Keep up-to-date with all the latest developments in HIV clinical pharmacology by registering for our regular email update service.

Last reviewed: 7 June 2007

Drug Interaction Charts

Printable charts | View all | View all Protease Inhibitors | View all NNRTIs | Back to start

Step 1	Searching by: **Atazanavir, Lopinavir, Ritonavir**	Amend selection
Step 2	Searching by: **Anxiolytics/Hypnotics/ Sedatives**	Amend selection
Step 3	Searching by: **Lorazepam, Midazolam, Temazepam**	Amend selection
Step 4	View results	

Key to symbols:

Protease Inhibitors **NNRTIs**

Clicking on the symbol within a table will give further information on the interaction where available (Denoted by a darkened table cell).

●	These drugs should not be coadministered
■	Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration
◆	No clinically significant interaction expected
○	There are no clear data, actual or theoretical, to indicate whether an interaction will occur
n/a	Data not available

Anxiolytics/Hypnotics/ Sedatives	Atazanavir	Lopinavir	Ritonavir
Lorazepam	◆	◆	◆
Midazolam	●	●	●
Temazepam	◆	◆	◆

Needlestick Injuries

- Report ASAP <1hour
- The risks:
  - HBV 1:3
  - HCV 1:30
  - HIV 1:300
- Serum for storage
- Hepatitis B status
- Risk assessed for PEP

Testing the Unconscious Patient

- Always best practice is to obtain informed consent
- Can consider testing the patient if it is in THEIR interests
  - **"Unconscious patients**
    You may test unconscious patients for serious communicable diseases, without their prior consent, where testing would be in their immediate clinical interests - for example, to help in making a diagnosis. You should not test unconscious patients for other purposes."
    - GMC "Serious Communicable Diseases" October, 1997
- The issue of testing unconscious patients following a needlestick injury is much more complex
  - Human Tissue Act 2004
  - Mental Capacity Act 2005

Confidentiality and Death

- Who needs to know basis
  - Many don't
    - Sexual contact-few others
- Death certificates are in the public arena
  - Immunocompromise-more information available later box useful

HIV Outcome

- Now an eminently treatable condition
- Near normal lifespan
- If treated electively rather than after presentation with an opportunistic infection, significantly less morbidity
- Many complications now due to long term exposure to drugs
- Can improve care by offering more patients testing with sentinel conditions

HIV Summary

- HIV is becoming much more common, with the greatest increase in the heterosexual population.
- Always offer patients with TB, HBV, HCV an HIV test.
- Consider offering patients a test when presenting with sepsis or recurrent infections.
- Consider testing in unexplained lymphadenopathy, lymphopaenia and hypergammaglobulinaemia.