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ART and Adherence

CPD NM3118 2010

Learning outcomes

- To consider the impact of highly active anti-retroviral therapy (HAART) in the management of HIV infection
- To understand HAART is only available for a lucky minority
- To discuss the care management issues for people living with HIV infection

Living with HIV: a chronic illness

- Diagnosis of HIV does not present the infected person with an established or predictable prognosis.
- It introduces the individual to the prospect of increasing ill health in the context of a changed lifestyle, and the very real threat of death after some unknown period.
- Uncertainty of HIV - May have a fluctuating course involving periods of good health followed by periods of illness

HIV infection

- Asymptomatic
  - May be asymptomatic for 1-10+years
  - How long will you remain asymptomatic? Patients tend to be diagnosed at a relatively late stage in the UK over 30% present with a CD4 count of less than 200.
- Symptomatic
  - Symptoms may be caused/ exacerbated by HIV infection or by antiretroviral therapy
  - There may be a need to weigh the benefit of starting treatment early against the risk of deferring therapy.
  - May have periods of ill health / hospitalization that could have effects on relationships/family/work.

Early stage HIV infection

Early infection:

- patient presents with severe flu-like illness while seroconversion takes place

- HIV diagnosis made by
  - PCR test (detects HIV RNA)
  - ELISA / Western Blot (detects antibody)

- Post-exposure prophylaxis (PEP)
  - following early infection, early HAART can suppress the virus to levels where it cannot take-hold in the lymph nodes

Mid stage HIV infection

Middle infection (1-5) years

- CD4 cell levels remain >500 cells / ml
- initiation of ART will be determined by CD4 and viral load levels and physician experience
- some transient infections may occur
- the ability of the patient to suppress viral blood levels is a prognostic factor for time without AIDS

End stage HIV infection

Late infection (AIDS):

Viral load high >50,000 copies/ml
CD 4 cells <100 cells/ml

A CD4 count below 200/ml will give a person with HIV an AIDS diagnosis, irrespective of the presence of major opportunistic infections. Of course, with such a reduction in CD4 count, the patient is vulnerable to opportunistic infection.

HAART – HIV's Treatment Revolution

Highly active anti-retroviral therapy

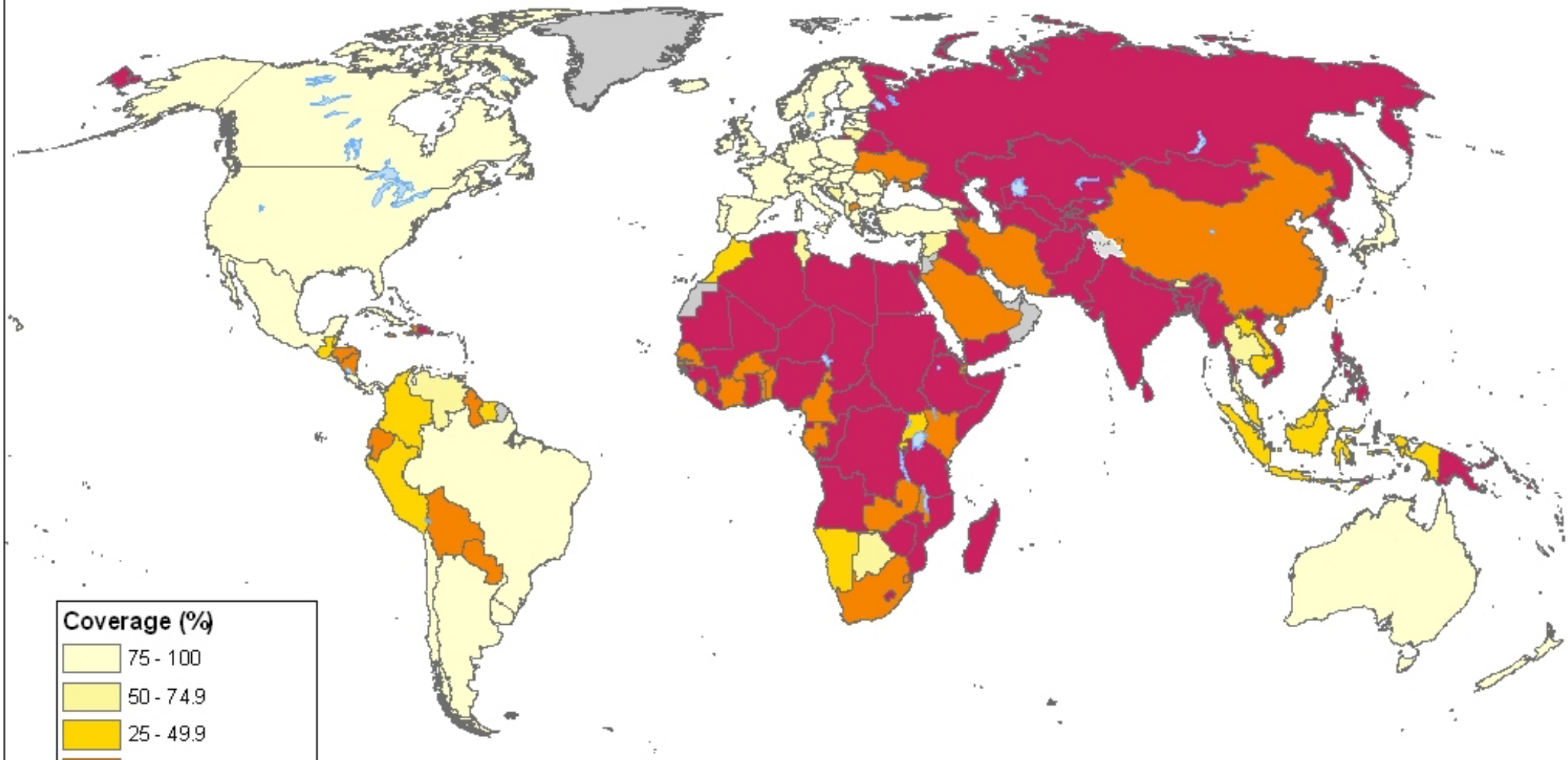
- Offers new hope
- Delays onset of symptoms
- Delays diagnosis of AIDS
- Extends and improves quality of life

Effective therapy for HIV

- **HIV is now a treatable disease**

- In 1995 there was the advent of HAART, with three anti-viral agents used in combination
- Mortality has progressively declined as anti-viral therapy has become progressively more aggressive, moving from mono to dual to triple therapy.

Estimated percentage of people on antiretroviral therapy among those in need, situation as of June 2005



Data Source: WHO/UNAI
Map Production:
Public Health Mapping an
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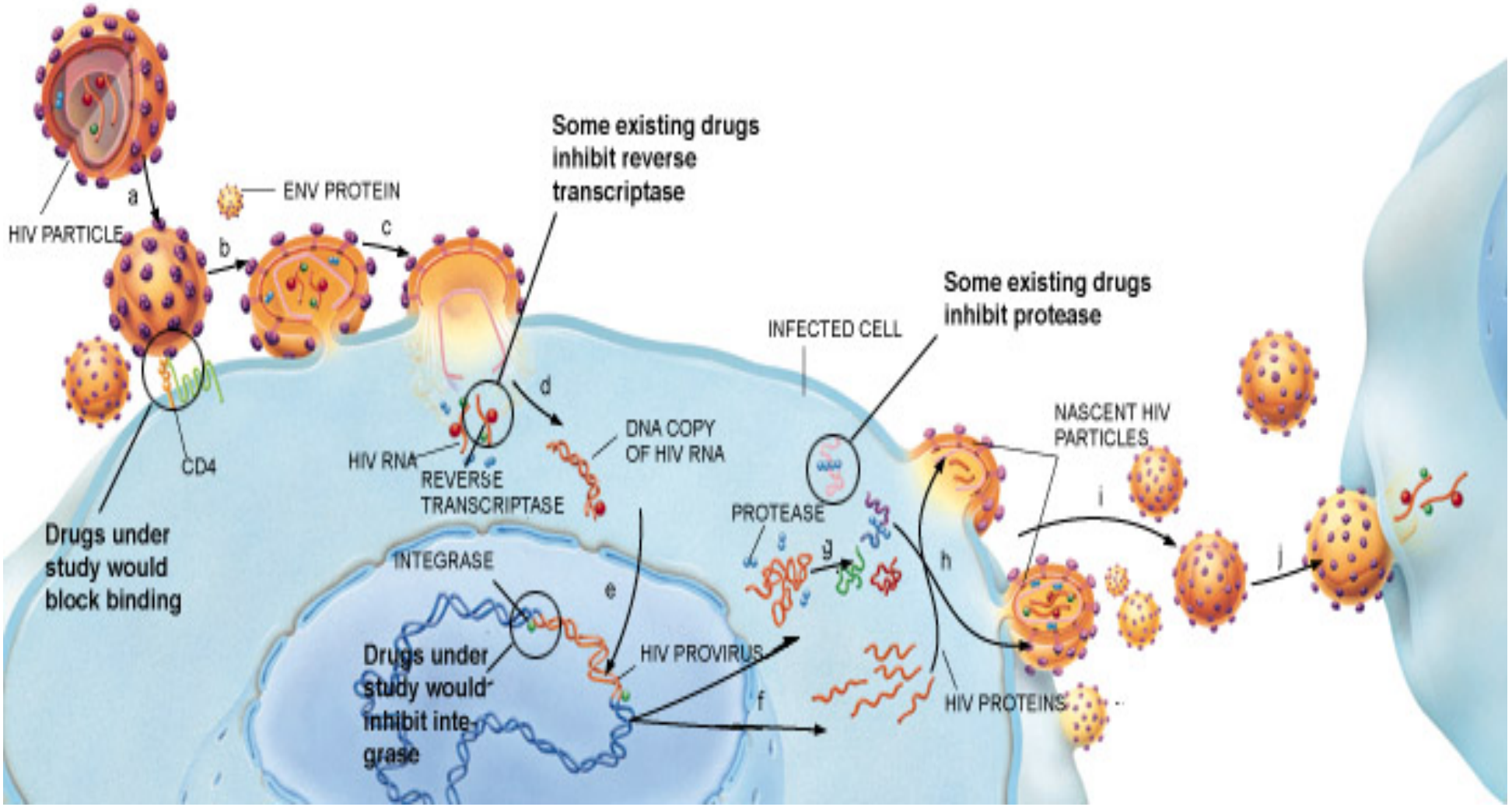
World Health Organization

Therapy

- ART (Anti-Retroviral Therapy)
- HAART (Highly Active Anti-Retroviral Therapy)
- Combo/combination therapy (a drugs are always given in combination, at least three drugs)

Key factors to consider when selecting first-line therapy

- Adherence
- Potency
- Durability
- Side effects
- Sanctuary site penetration
- Resistance profile
- Metabolic/intracellular interactions


HIV PARTICLE
a
ENV PROTEIN
b
c
Some existing drugs
inhibit reverse
transcriptase
CD4
HIV RNA
REVERSE
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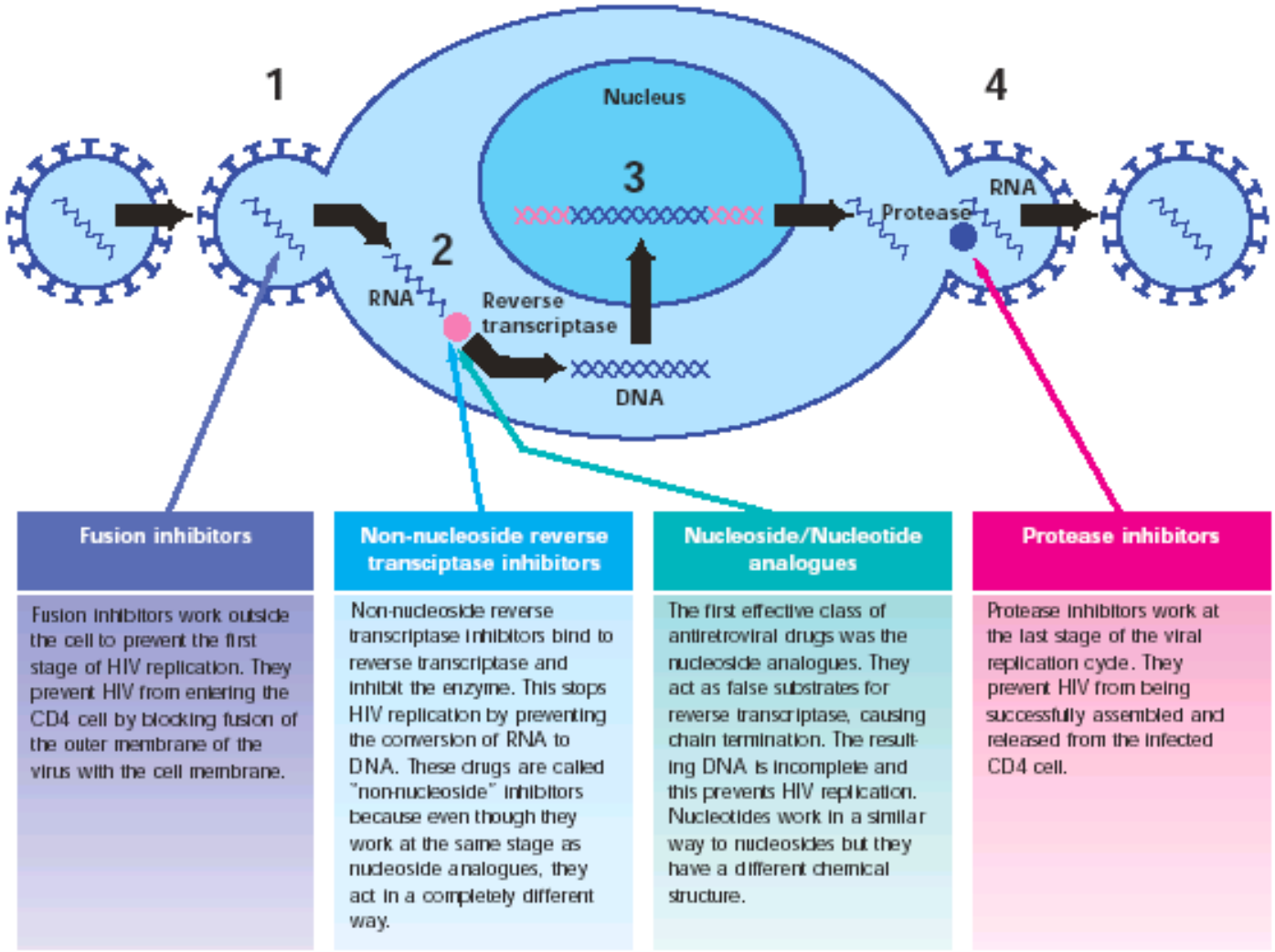
HOW HAART Works



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Groups of drugs

- ***NRTIs****: nucleoside reverse transcriptase inhibitors*
- ***NNRTIs****: non-nucleoside reverse transcriptase inhibitors*
- *(**NtRTIs**: nucleotide reverse transcriptase inhibitors)*
- ***PIs****: protease inhibitors*
- ***Integrase inhibitors***
- ***Fusion inhibitors***

Current BHIVA guidelines on Treatment of HIV

When do you start treatment?

- When patient agrees the time is right
- When benefits > risks
- If there is a major opportunistic infection
- CD4 drops < 350 cells/ml
- Consider if CD4 350 -500
  viral load >30, 000 copies/ml

Is 500 the new 350?

- Previously treatment at higher CD4 counts were avoided because of the problems associated with treatment failure due to poor compliance, thus resulting in the emergence of resistant virus.
- However, recent evidence from the US suggests a 70% improvement in survival for patients who initiate treatment with a CD4 count between 351 and 500

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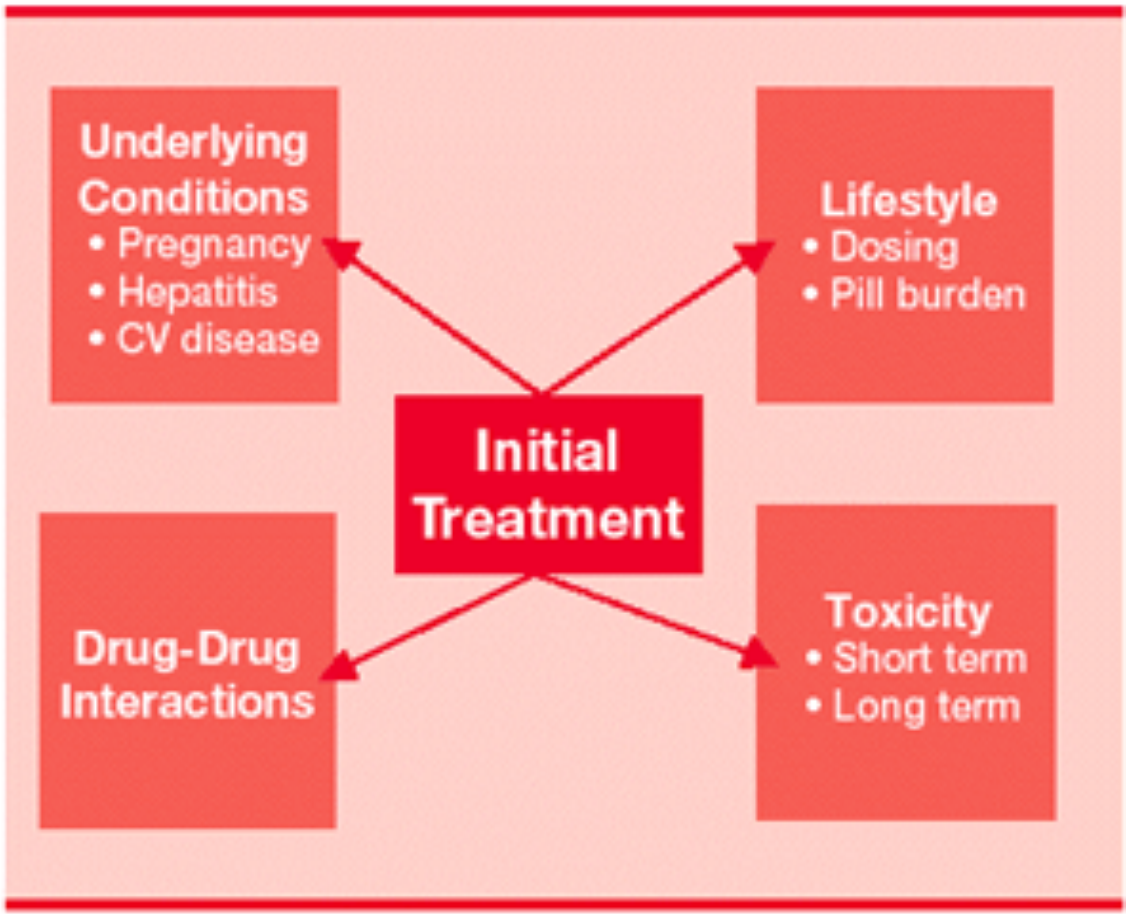
Figure 1. Considerations for choice of initial regimen.



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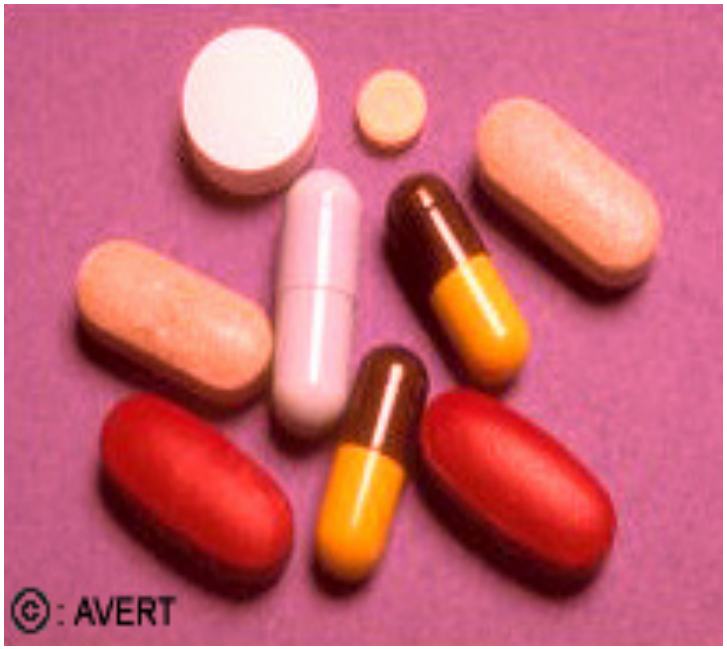
Aims of therapy

- Suppression of the virus
- Elevation of CD4 count
- Improved quality and length of life
- Slowing disease progression
- Preventing opportunistic infections (OIs)

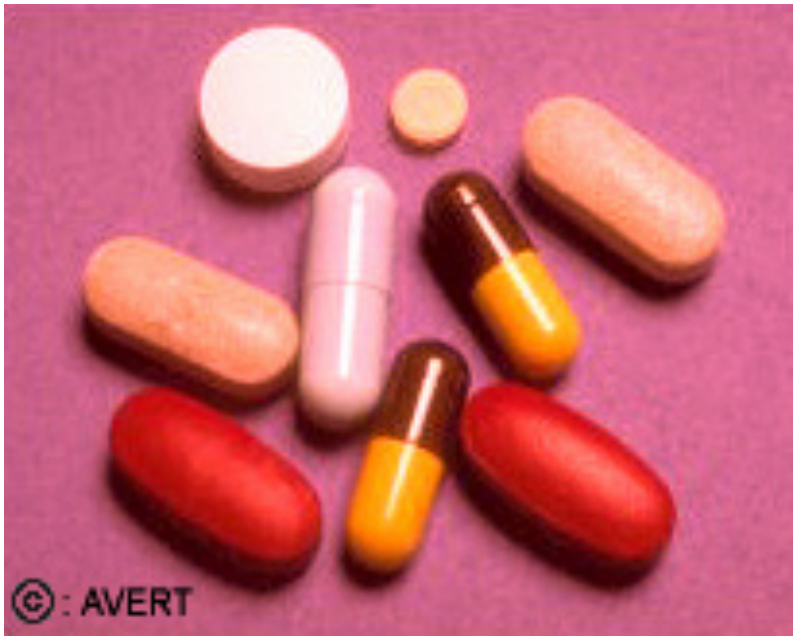
Challenges of HAART - 1



- Pill burden
- Punctuality
- Side-effects
- Dietary restrictions
- Confidentiality
- Other medication

Challenges of HAART - 2

- Social life
- Ongoing therapy
- Drug interactions (legal and illegal ones)
- Risk of resistance



Factors encouraging adherence to therapy

- Easily incorporated into patient lifestyle
- Convenient and simple dosing
- Dosing not affected by food
- Good tolerability
- Manageable side-effect profile
- Maintained quality of life
- Compact, easy-to-swallow tablets

Side effects – short term

- Nausea, vomiting, diarrhoea
- Allergic reactions
- Cognitive changes (insomnia, depression)
- Hepatitis or pancreatitis
- Fatigue
- Etc.

None of them has to occur, and most of them will stop after a while

Side effects – long term

- Peripheral neuropathy (painful arms and legs)
- Liver damage
- Lipodystrophy (abnormal fat distribution – losing in some areas, gaining at others)
- ? Diabetes (raised blood glucose levels)
- ? Cardiac disease (raised cholesterol)
- Etc.

Resistance is often a problem

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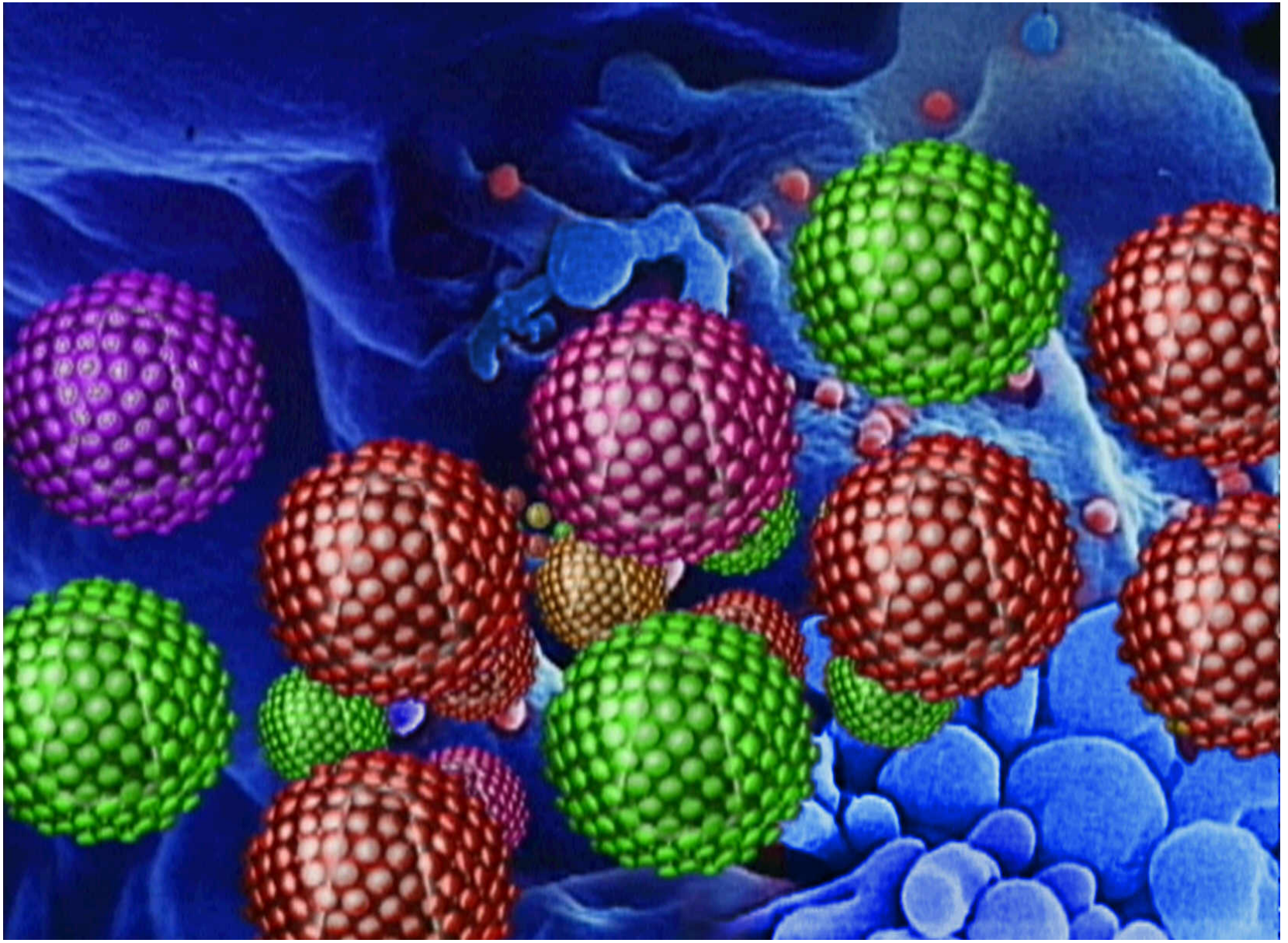
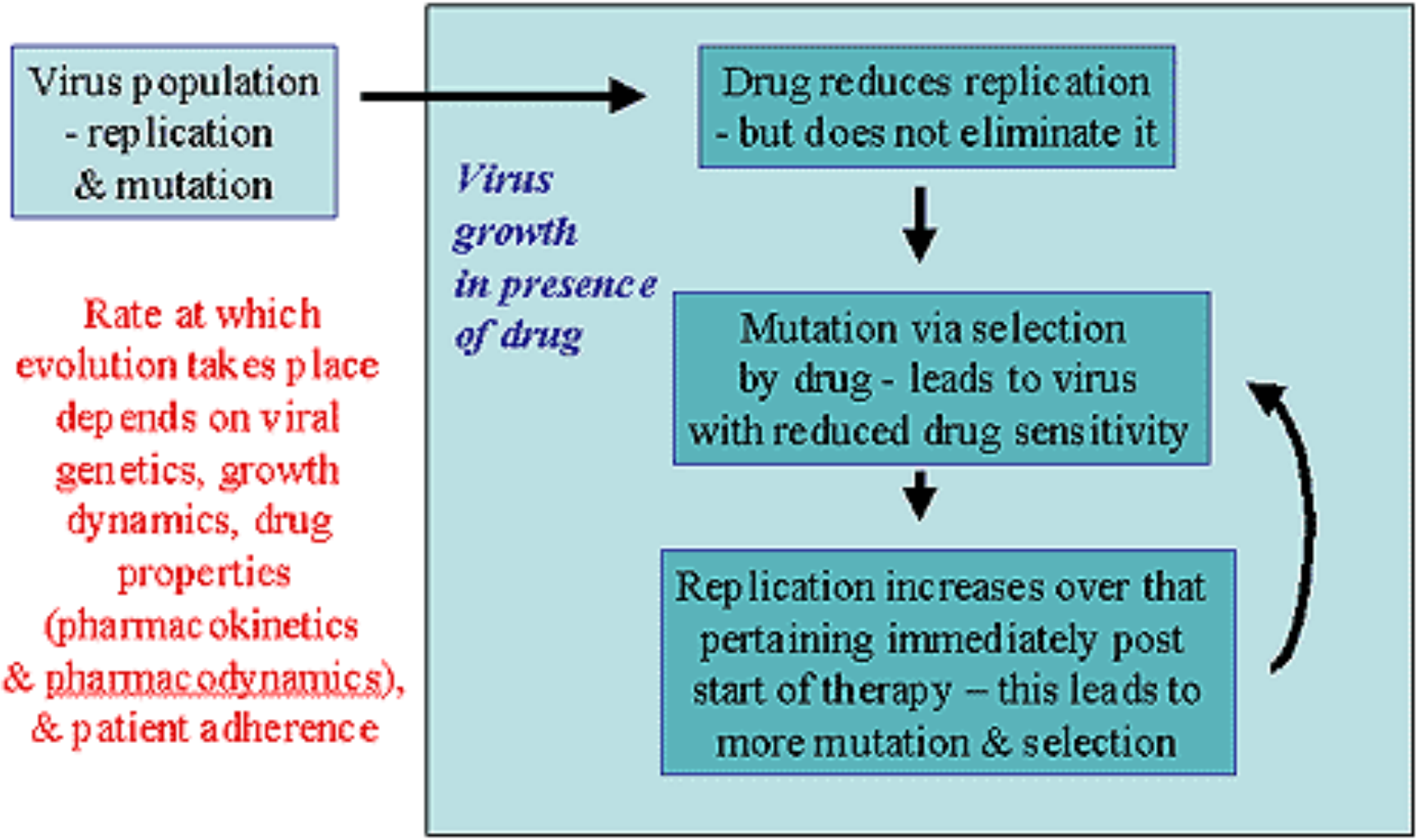


HIV replication and mutation

- Rapid replication> as many as 10 billion copies of the virus a day are formed in HIV infection
- HIV's reverse transcriptase moderated replication is "sloppy". There is no "proof-reading" function.
- Therefore, an average of one mutation to three HIV genomes copied

Medscape® www.medscape.com



Treatment Strategies

- Monotherapy
- Dual therapy
- Triple therapy (Current Standard of Care)
- Quad therapy etc
- Induction/maintenance
- Intensification
- Pulse therapy/ drug holidays
- Cycling
- Sequencing
- Salvage

Optimum HAART regimes

- The aim of HAART is to achieve a viral load of <50/ml within 4-6 months of starting therapy
- Efavirenz (an NNRTI) should be considered first line Rx for all patients commencing therapy
- Boosted PIs (PIs with the addition of low-dose Ritonavir) are useful for those patients who have built up to resistance to reverse transcriptase inhibitors

Current BHIVA guidelines on switching treatment

When to switch?

- increase in viral load > 50 copies/ml at 24 weeks (2 tests, at least 2 weeks apart)
- unacceptable toxicity
- poor adherence
- resistance testing recommended
- if toxicity arises, single agent switch with a similarly potent drug, but with better toxicity profile

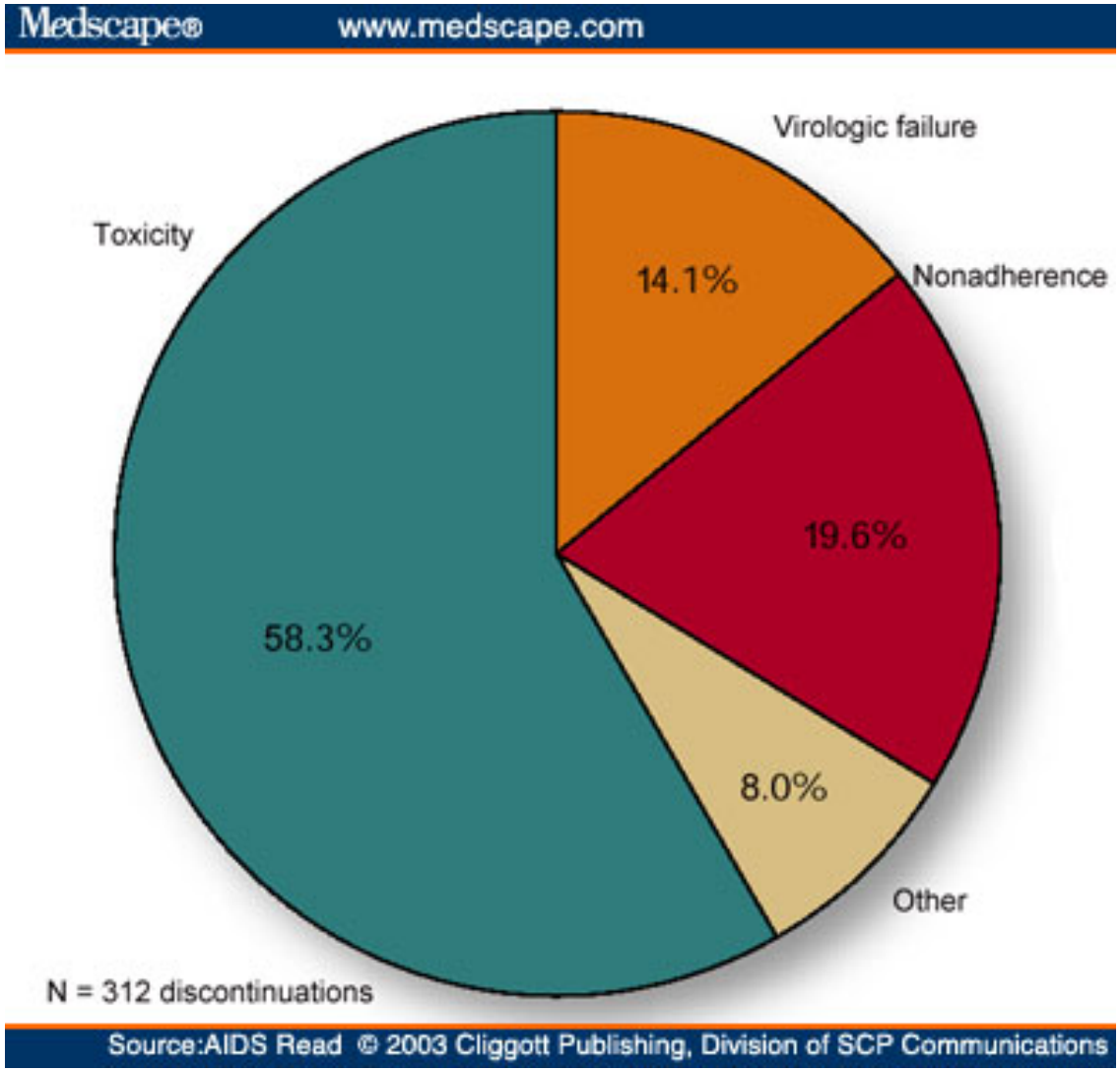
Resistance

- Poor adherence
- Poor absorption
- Pre-therapeutic resistance (10%)
- Doses are inadequate (miscalculation or patient shares medication)
- Mutation
- Cross-resistance

Adherence Issues

- **Adherence is a process not a single event**
- Any HAART regime should be individualized in order to achieve the best potency, adherence & tolerability; to minimize potential toxicity; & to avoid any likely drug - drug interactions.
- A measurement of a regimen's success is achieving a viral load of less than 50 HIV 1 copies/ml within 6 - 9 months.
- Interventions to support adherence should be multifaceted, responsive to the needs of the individual & an integral part of ongoing care (Haynes et al, 1996)

Main reasons for discontinuing HAART



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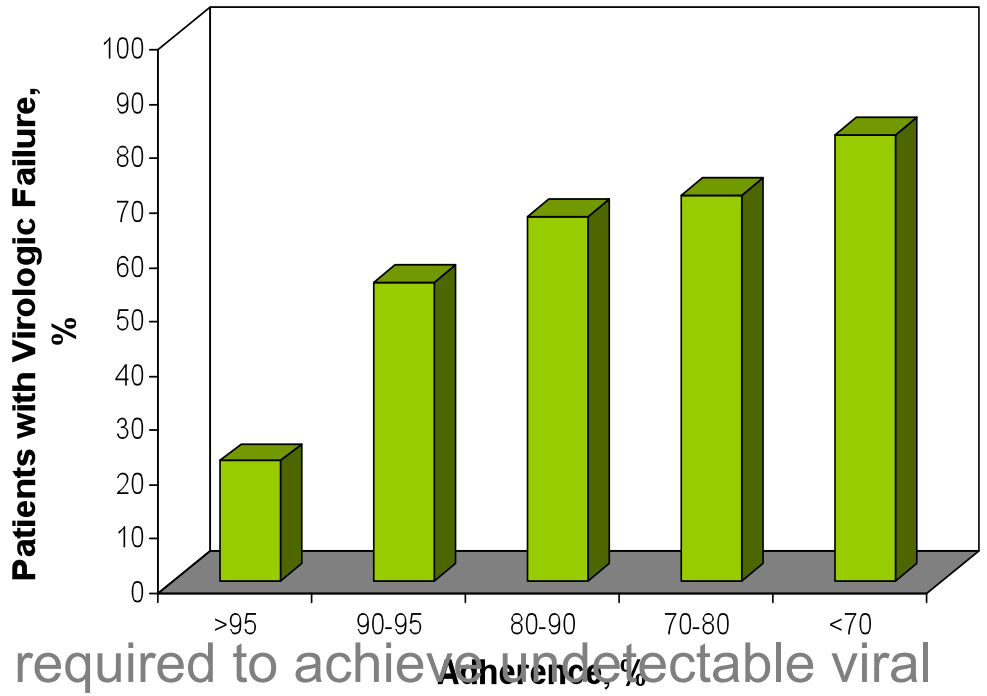
Correlation Between Adherence and Virological Failure



95% adherence is required to achieve undetectable viral loads in 80% of patients

Adherence in chronic illnesses

- Adherence levels are low in chronic disease such as diabetes, asthma and hypertension only 50% patients remain adherent over time
- Frequency of dosing is critical
- Once a day and twice a day regimens are associated with significantly better adherence (73% and 70% respectively) than three times daily (52%) and four times daily (42%) regimens
- Adherence changes over time

Promoting Adherence

- **Help ensure through advice and information, that the patient commits to therapy and wants to adhere.**
- **Help patients fit medication regimes into daily life, instead of structuring life around medication.**
- Providing memory aids to establish & maintain a pill taking routine.
- Treat any underlying mental health problems.
- Management of side effects.
- Understanding the potential risks & benefits of therapy in the short & long term.
- Make it easy to access advice and information, e.g. Helpline numbers.

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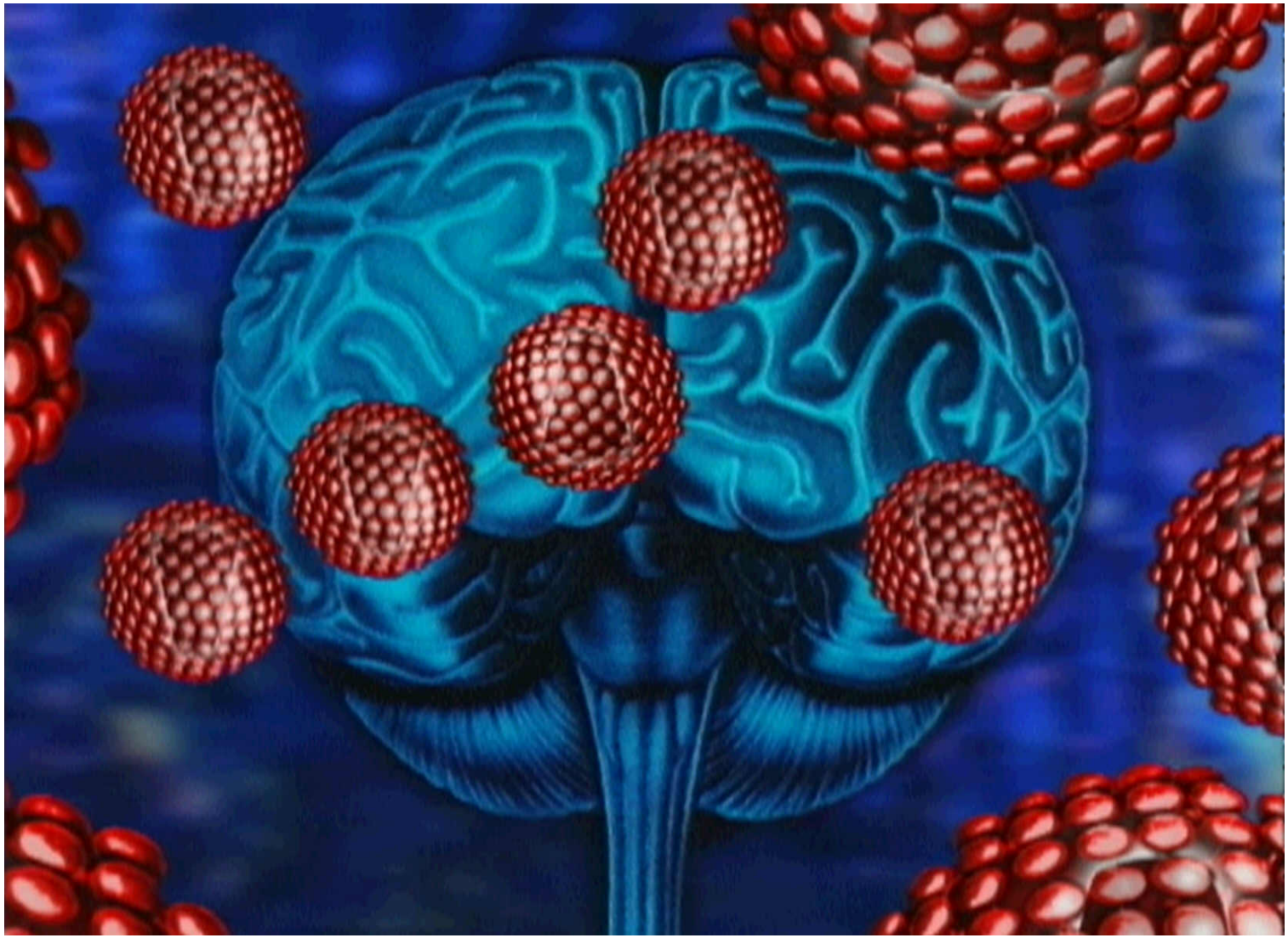

Role of the HIV Nurse

- **Principle Aims of HIV Nurse**
  - To provide seamless holistic care
  - Adherence education and support through treatment changes and adverse events
  - Information provision and advice around care decisions
  - Structured ongoing follow up
  - To act as facilitators for access to other services

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Typical support offered by HIV specialist Nurse

- Seeing the patient prior to starting therapy
- Two weeks into therapy (which will coincide with Nevirapine dose escalation) where they will take baseline bloods
- Four weeks into therapy where they will take a repeat viral load and monitor bloods
- Eight weeks into therapy to monitor post-short term transient side effects
- An offer of ongoing support at six monthly intervals

Summary

- Treatment success with antiretroviral therapy is directly related to adherence with prescribed medication
- Decreasing the complexity of regimens encourages adherence and may help sustain long term efficacy
- Patients need regular help and support to maintain good adherence
- Medication should be tailored to fit into patients lifestyle to help with adherence

Time Out Exercise

- In small groups, please discuss what factors are important for the nurse to consider with regard to adherence, when counselling a patient considering commencing HAART.

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