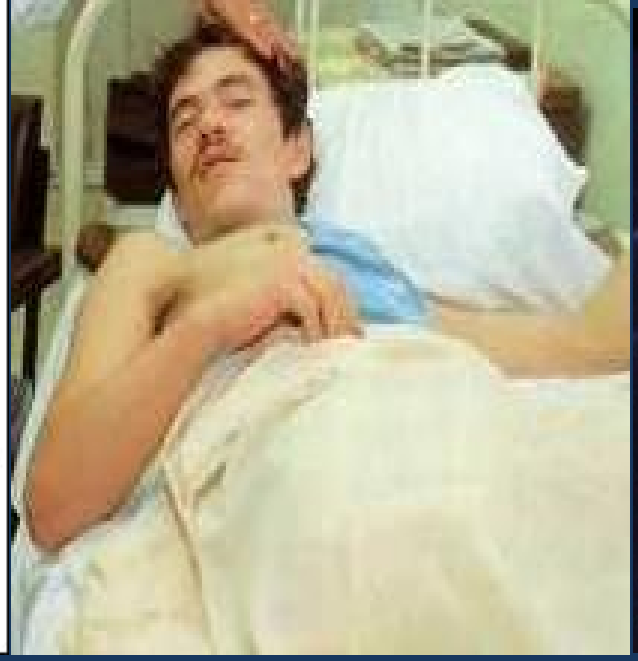
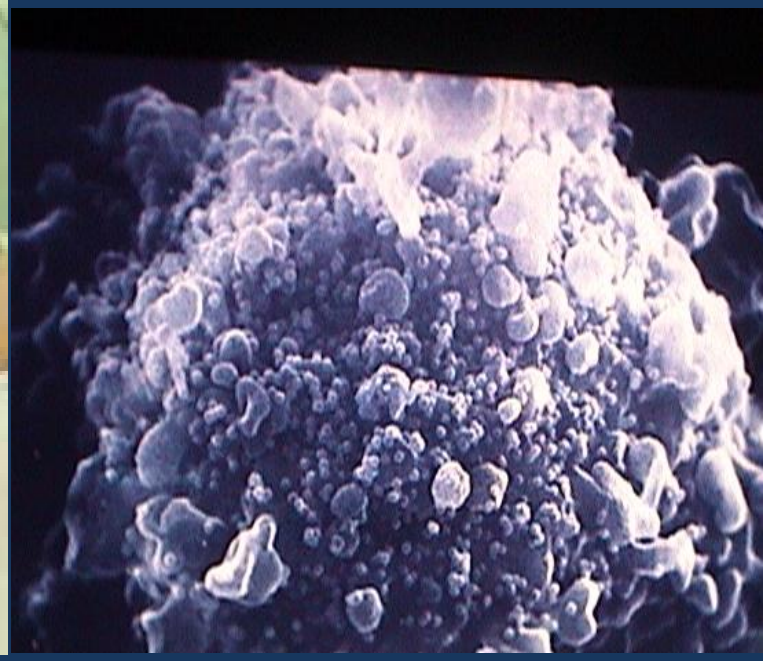

Infection à VIH et SIDA

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Objectifs Pédagogiques

1. **Connaitre les modes de transmission, Informer et conseiller en matière de prévention de la transmission sanguine et sexuelle**
2. **Savoir reconnaître les principales manifestations**
3. **Savoir reconnaître les principales infections opportunistes et pathologies malignes associées à l'infection à VIH.**
4. **Savoir Diagnostiquer une infection à VIH (dépistage – confirmation)**
5. **Savoir Annoncer les Résultats et Organiser la PEC (CDR)**

- **Maladie infectieuse émergente pandémique**
- **Rétrovirus : Virus de l' Immunodéficience Humaine (VIH)**
- **Tropisme cellulaire systémique**

Transmission interhumaine: VIH = IST (implique au moins 2 partenaires)

- **Rapports sexuels +++**
- **Sang et dérivés**
- **Liquides biologiques**
- **Mère-enfant**

- **Maladie Chronique +++ : 3 phases (PI, chronique asymptomatique, SIDA)**
- **Problème mondial de santé publique**
- **Trois priorités OMS : TBC, Palu, VIH (les grandes tueuses)**
- **Grands progrès : DG, TTT, Prophylaxie : on peut vivre avec le VIH**
- **Projet OMS : Elimination d'ici 2030**

Eléments d'histoire

The NEW ENGLAND JOURNAL of MEDICINE

Volume 305:1425-1431 **December 10, 1981** **Number 24**

Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men:
evidence of a new acquired cellular immunodeficiency

MS Gottlieb, R Schroff, HM Schanker, JD Weisman, PT Fan, RA Wolf, and A Saxon

- Abstract
- Four previously healthy homosexual men contracted Pneumocystis carinii pneumonia, extensive mucosal candidiasis, and multiple viral infections.
- In three of the patients these infections followed prolonged fevers of unknown origin.
- In all four cytomegalovirus was recovered from secretions. Kaposi's sarcoma developed in one patient eight months after he presented with esophageal candidiasis.
- All patients were anergic and lymphopenic; they had no lymphocyte proliferative responses to soluble antigens, and their responses to phytohemagglutinin were markedly reduced. Monoclonal-antibody analysis of peripheral-blood T-cell subpopulations revealed virtual elimination of the Leu-3 / helper/inducer subset, an increased percentage of the Leu-2 + suppressor/cytoxic subset, and an increased percentage of cells bearing the thymocyte-associated antigen T10. The inversion of the T/ helper to suppressor/cytotoxic ratio suggested that cytomegalovirus infection was an important factor in the pathogenesis of the immunodeficient state. A high level of exposure of male homosexuals to cytomegalovirus-infected secretions may account for the occurrence of this immune deficiency.

La maladie des H

Homosexuels : Gay Related Immune Deficiency

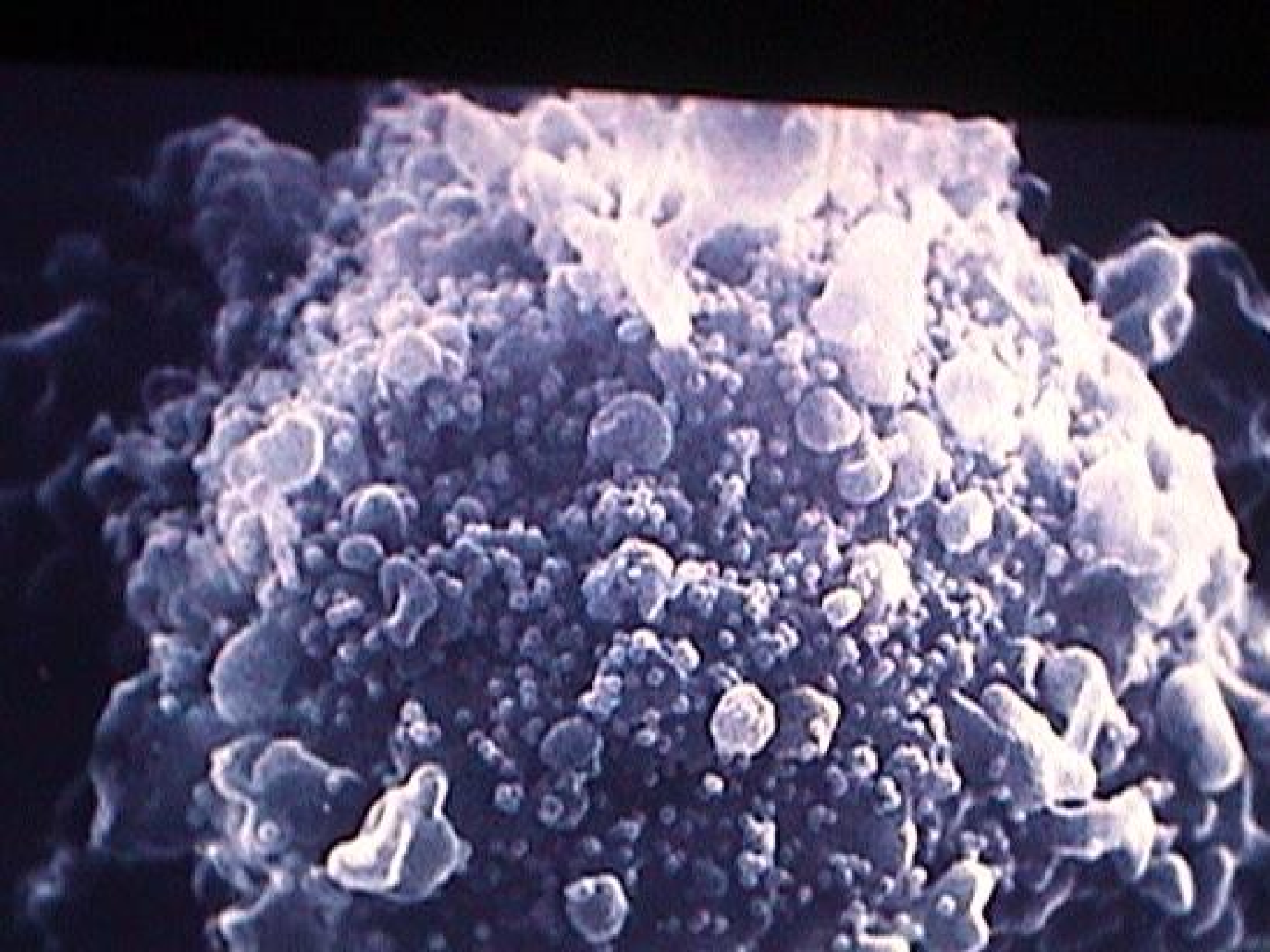
Gay sarcomes

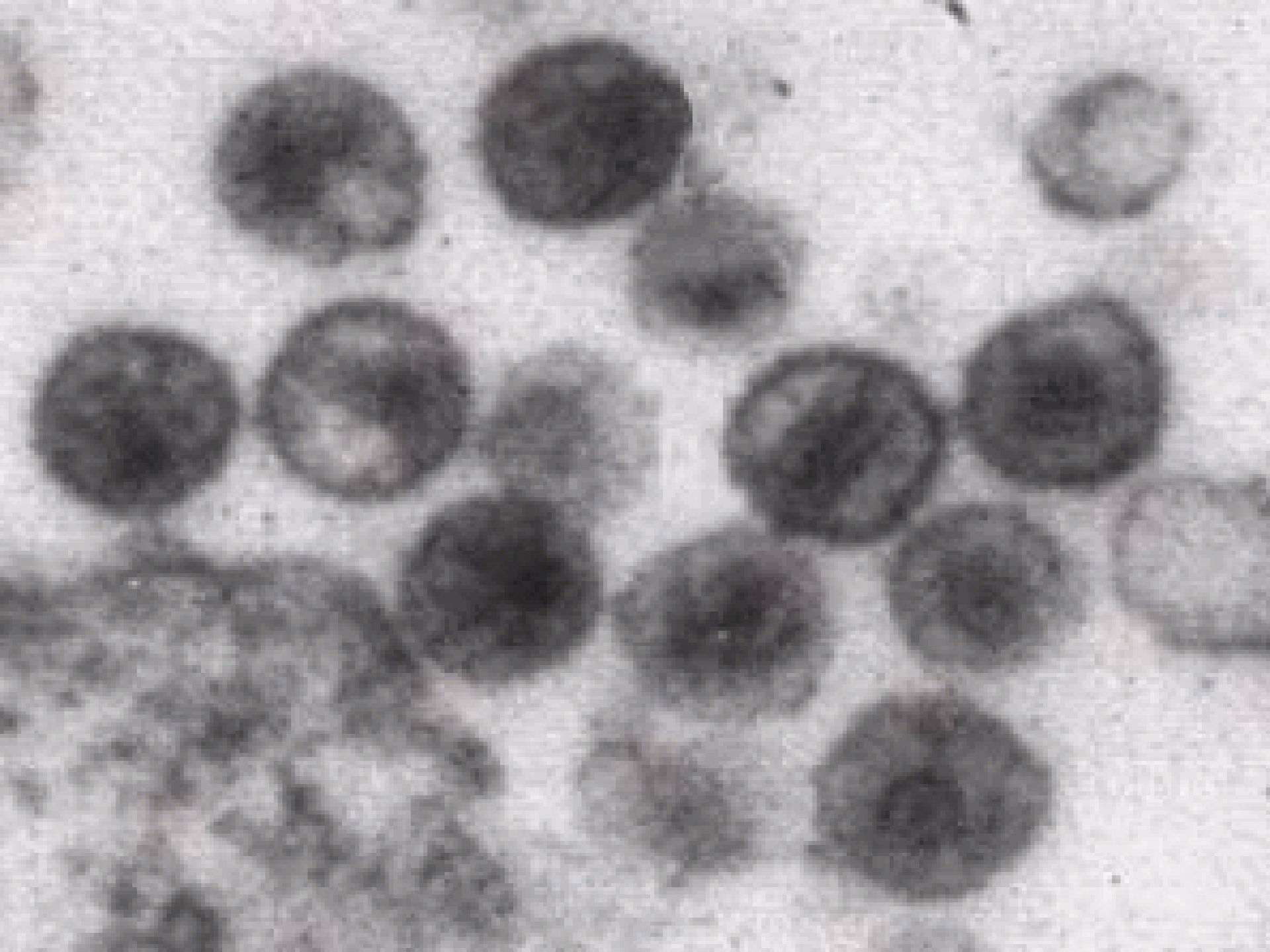
Héroïnomanes

Haïtiens

Hémophiles

Hétérosexuels





Rétrovirus

LENTIVIRUS

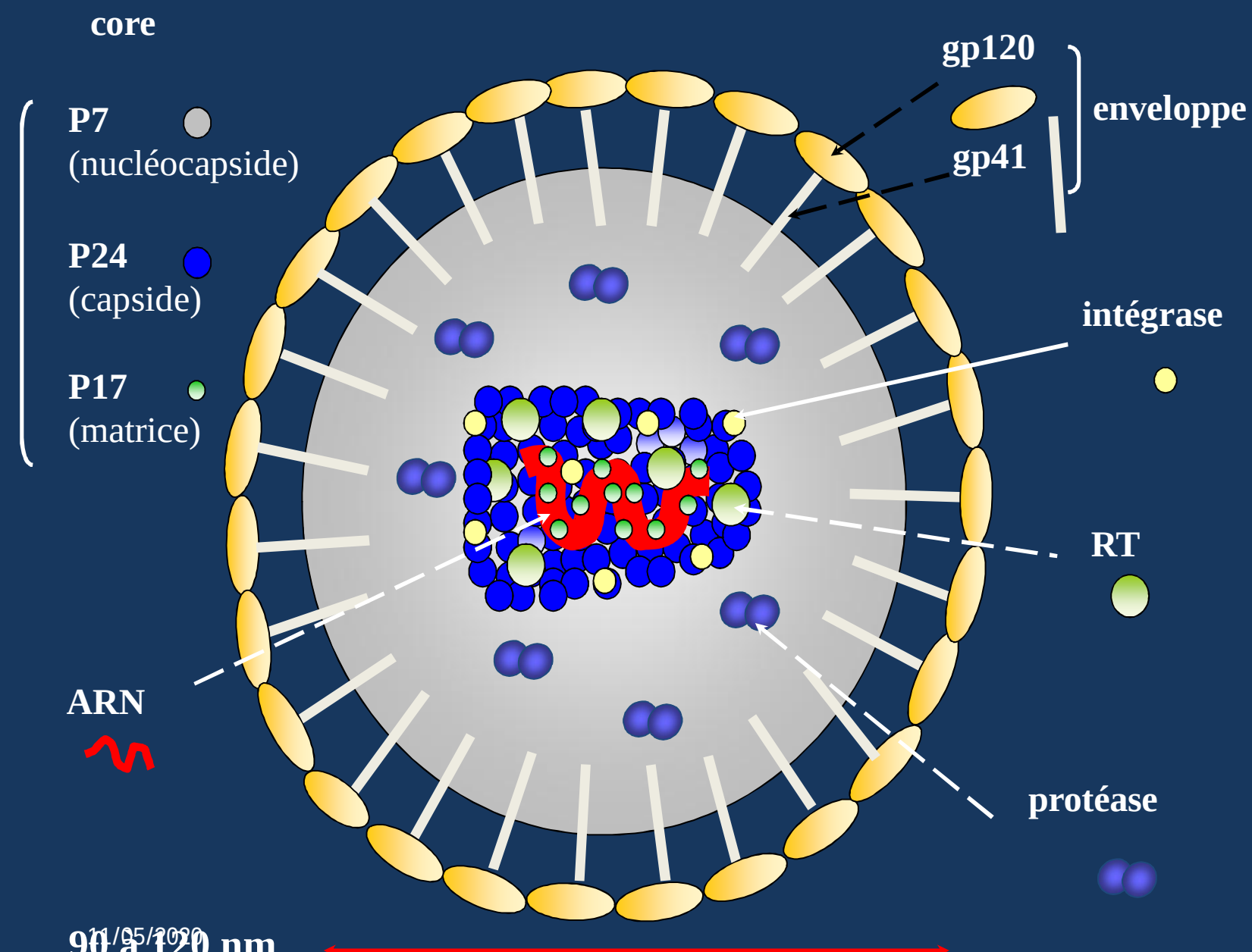
Mouton : VISNA
Chèvre : CAEV
Chat : FN,FIV
Singe : SIV

HIV ou VIH
1ere fois chez Homme :

ONCOVIRUS

Homme HTLV1, HTLV 2
Souris : MLV, MMTV
Poulet RSV
Singe : MPMV

STRUCTURE DU VIH



VIH: Diversité et origine

Afrique de l'Ouest

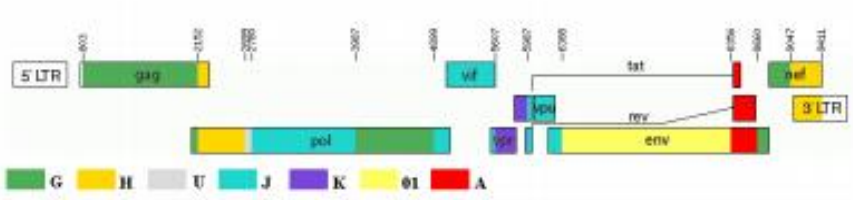
VIH-1 — types — VIH-2

M : majeur | N | O : outlier | P — groupes — A B C D E F G H

A B **C** D F G H J K

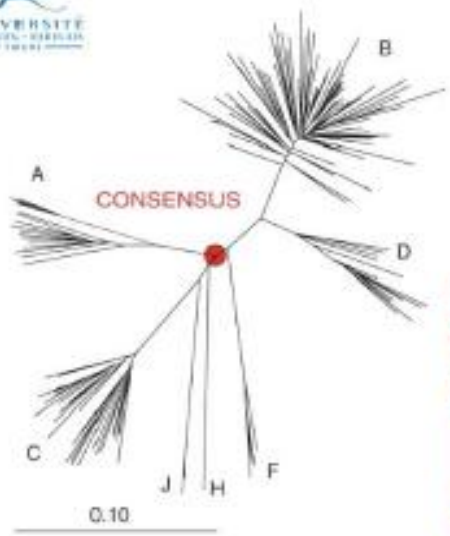
56 recombinants (CRF 01 à 56)

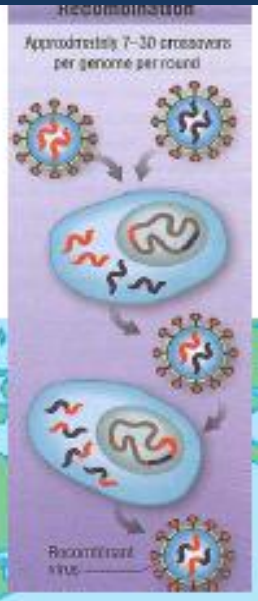
Sous-types



CRF: Circulating Recombinant Form

Distribution géographique





1. Origine du virus

Origine simienne : actuellement admise

Tracing the Origin of the AIDS Pandemic

Beatrice H. Hahn, MD
Professor of Medicine and Microbiology
University of Alabama at Birmingham
Birmingham, Alabama

Summary by Tim Horn
Edited by Lucia Torian, PhD

Reprinted from *The AAN Notebook*® | 14 September 2005 | Dr. James F. Braun, Editor-in-Chief | Tim Horn, Executive Editor.
Published in New York City by the Physicians' Research Network, Inc.® | John Graham Brown, Executive Director
For further information and other articles available online, visit http://www.prn.org

For those lucky enough to be in attendance, the keynote lecture delivered at the 6th Conference on Retroviruses and Opportunistic Infections (CROI) at the end of January 1999 was nothing short of a jaw-dropping experience. Dr. Beatrice Hahn of the University of Alabama at Birmingham presented the first concrete evidence of the primate origin of HIV-1, the much more prevalent of the HIV types responsible for the AIDS pandemic. The official report of her team's findings, published in a February 1999 issue of Science, was a no less captivating example of seminal scientific research (Gao, 1999).

Since 1999, Dr. Hahn's group has been working tirelessly in the laboratory and in the chimpanzee communities of sub-Saharan Africa to illuminate the pathways leading to the emergence of HIV-1, the adaptive changes that followed, and the mechanisms underlying its pathogenicity in humans. The genetic similarities between chimpanzees and humans—they share more than 98% sequence identity across their genomes (Watanabe, 2004)—and the newly demonstrated relationship between HIV and SIV may be useful to researchers searching for key differences in virus-host interactions that may explain why and how HIV causes immune deficiency in humans, while SIV is nonpathogenic to its natural host. It is this research that continues to guide current studies evaluating the susceptibility of humans to zoonoses such as AIDS and may guide the development of new treatments and vaccines.

The Origin of HIV and SIV

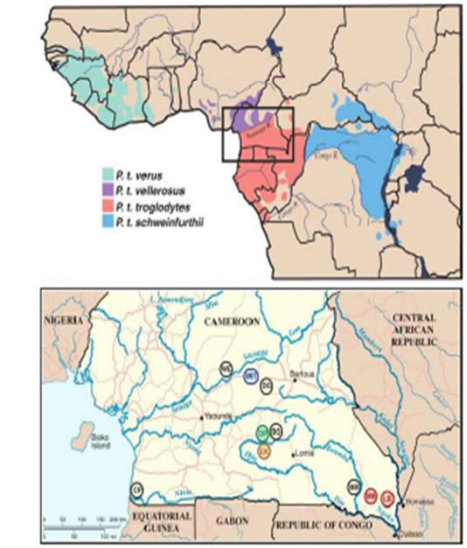
There are two known genetically distinct AIDS viruses: human immunodeficiency virus-1 (HIV-1) and human immunodeficiency virus-2 (HIV-2). HIV-1 is divided into three major clades, groups M, N and O; group M is the clade most widely distributed and associated with the majority of disease globally. Both HIV-1 and HIV-2 are of primate origin. The origin of HIV-2 has been established to be the sooty mangabey (*Cercocebus atys*), an Old World monkey of Guinea Bissau, Gabon, and Cameroon (Hirsch, 1989; Gao, 1992). The origin of HIV-1 is the central common subspecies of chimpanzee (see Figure 1).

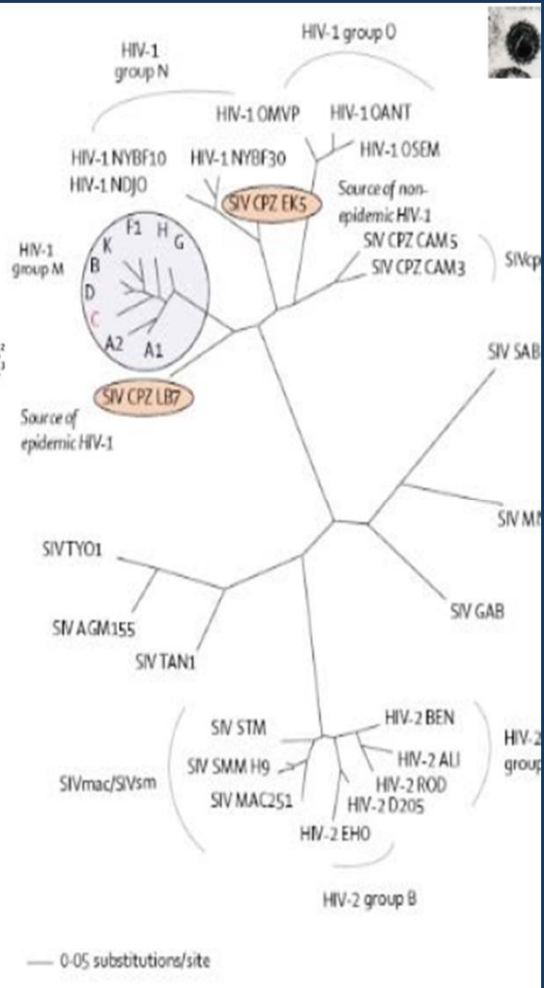
FIGURE 1. ***Pan troglodytes:*** **The Primate Source of HIV-1**
Both HIV-1 and HIV-2 are of primate origin. The origin of HIV-2 has been established to be the sooty mangabey, an Old World monkey of Guinea Bissau, Gabon, and Cameroon. The origin of HIV-1 is the central subspecies of chimpanzee, pictured here.

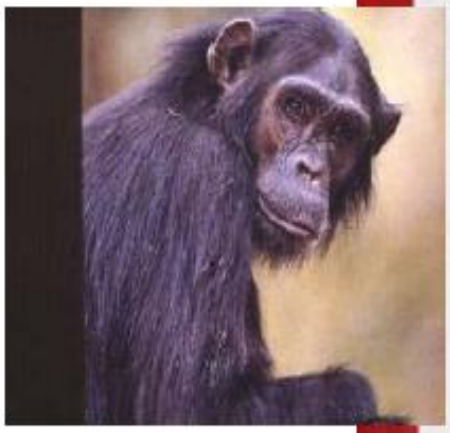
Origine du VIH-1

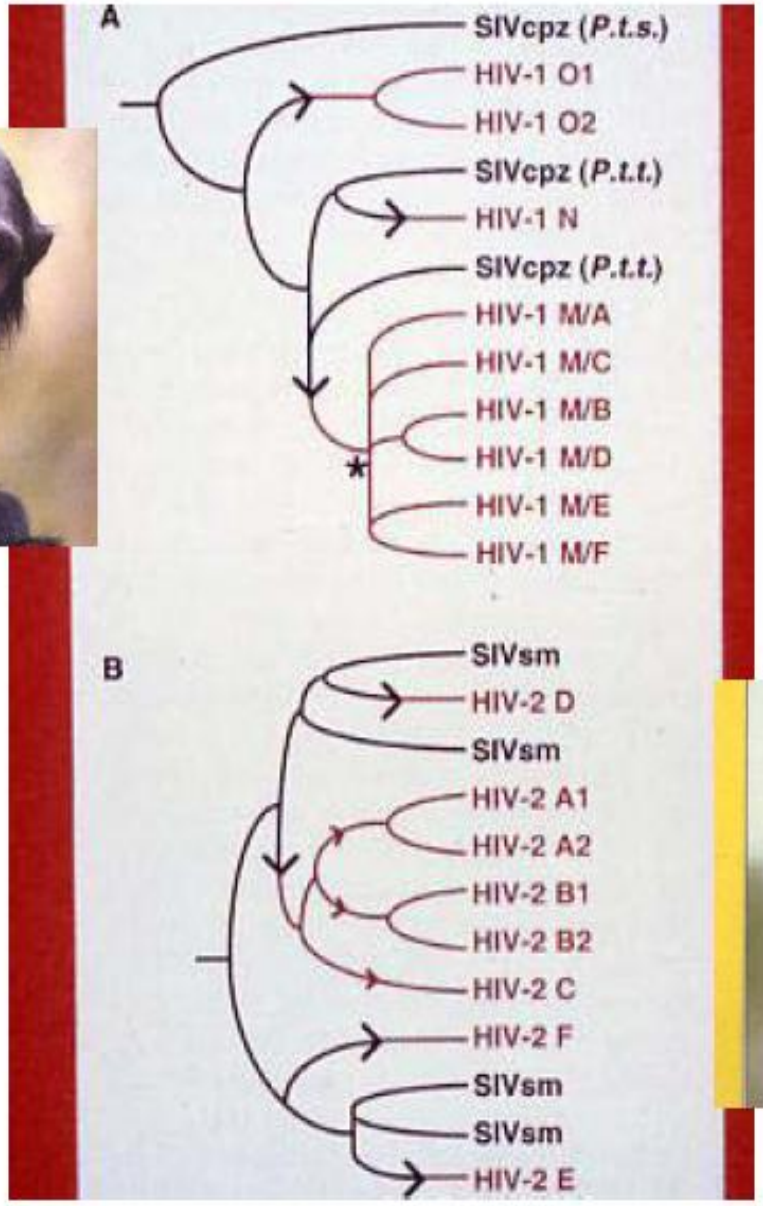
Chimpanzee Reservoirs of Pandemic and Nonpandemic HIV-1

Brandon F. Keele,[1] Fran Van Heuverswyn,[2] Yingying Li,[2] Elizabeth Bailes,[3] Jun Takehisa,[1] Mario L. Santiago,[1,4] Frederic Bibollet-Ruche,[3] Yalu Chen,[1] Louise V. Wain,[3] Florian Liegeois,[2] Severin Loul,[5] Eitel Mpoudi Ngole,[6] Yanga Bienvenue,[6] Eric Delaporte,[2] John F. Y. Brookfield,[3] Paul M. Sharp,[3] George M. Shaw,[1,5] Martine Peeters,[2] Beatrice H. Hahn[1]†








A
SIVcpz (P.t.s.)
HIV-1 O1
HIV-1 O2
SIVcpz (P.t.t.)
HIV-1 N
SIVcpz (P.t.t.)
HIV-1 M/A
HIV-1 M/C
HIV-1 M/B
HIV-1 M/D
HIV-1 M/E
HIV-1 M/F
B
SIVsm
HIV-2 D
SIVsm
HIV-2 A1
HIV-2 A2
HIV-2 B1
HIV-2 B2
HIV-2 C
HIV-2 F
SIVsm
SIVsm
HIV-2 E

Hypothèses de franchissement de la barrière inter-espèces Comment ?

Deux théories :

la théorie du chasseur

la théorie du vaccin

Autres :

pratique de sorcellerie
zoophilie

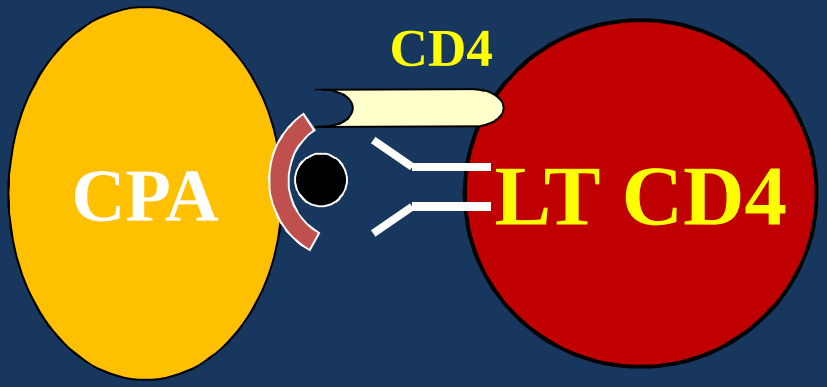
Hypothèses de franchissement de la barrière inter-espèces Quand ?

- Cas répondant à la définition clinique du SIDA
- (1960, 1953)
- Etude phylogénique : 1920-1930
- Lieu : Congo
- Pourquoi maintenant ?
  - Decolonisation, exodes, bidonvilles
  - Progrès en chir, transfusion+++
  - Libéralisation sexualité

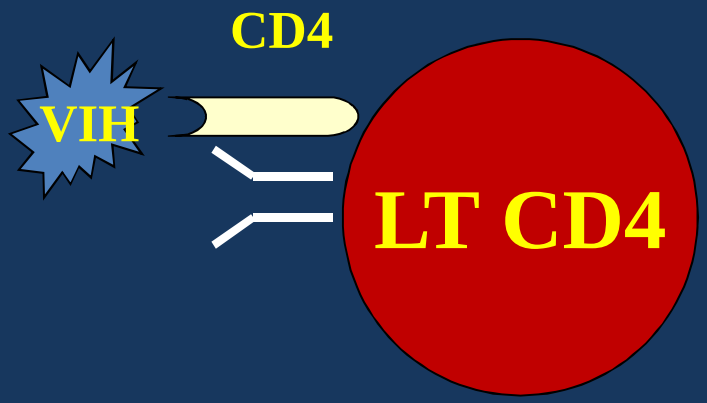
Pathogénie

LA MOLECULE CD4 : le récepteur principal

Tropisme cellulaire et non d'organe



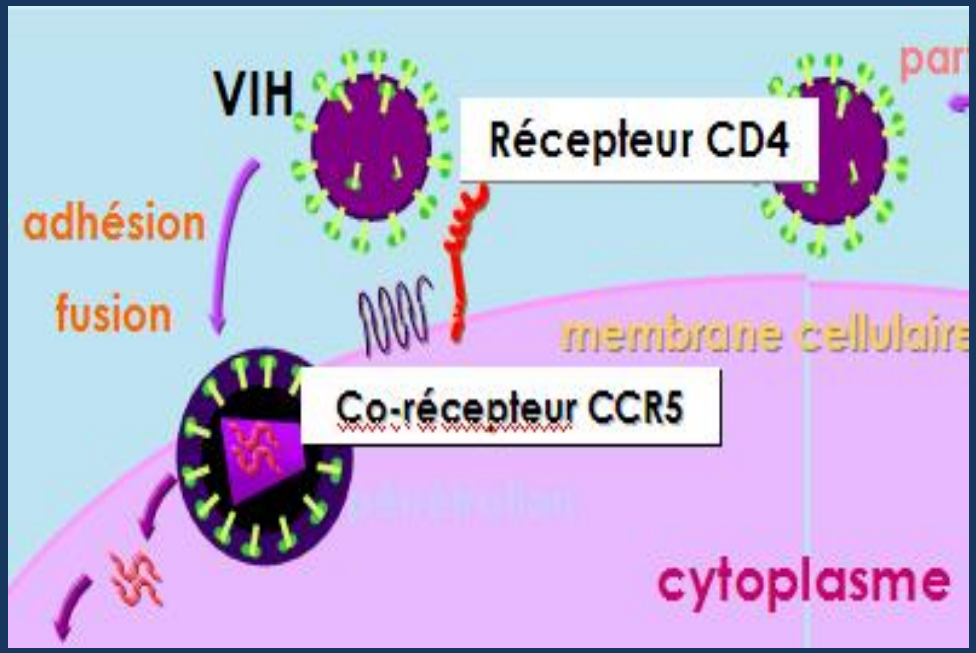
Ligand naturel



Récepteur de haute affinité de la gp120

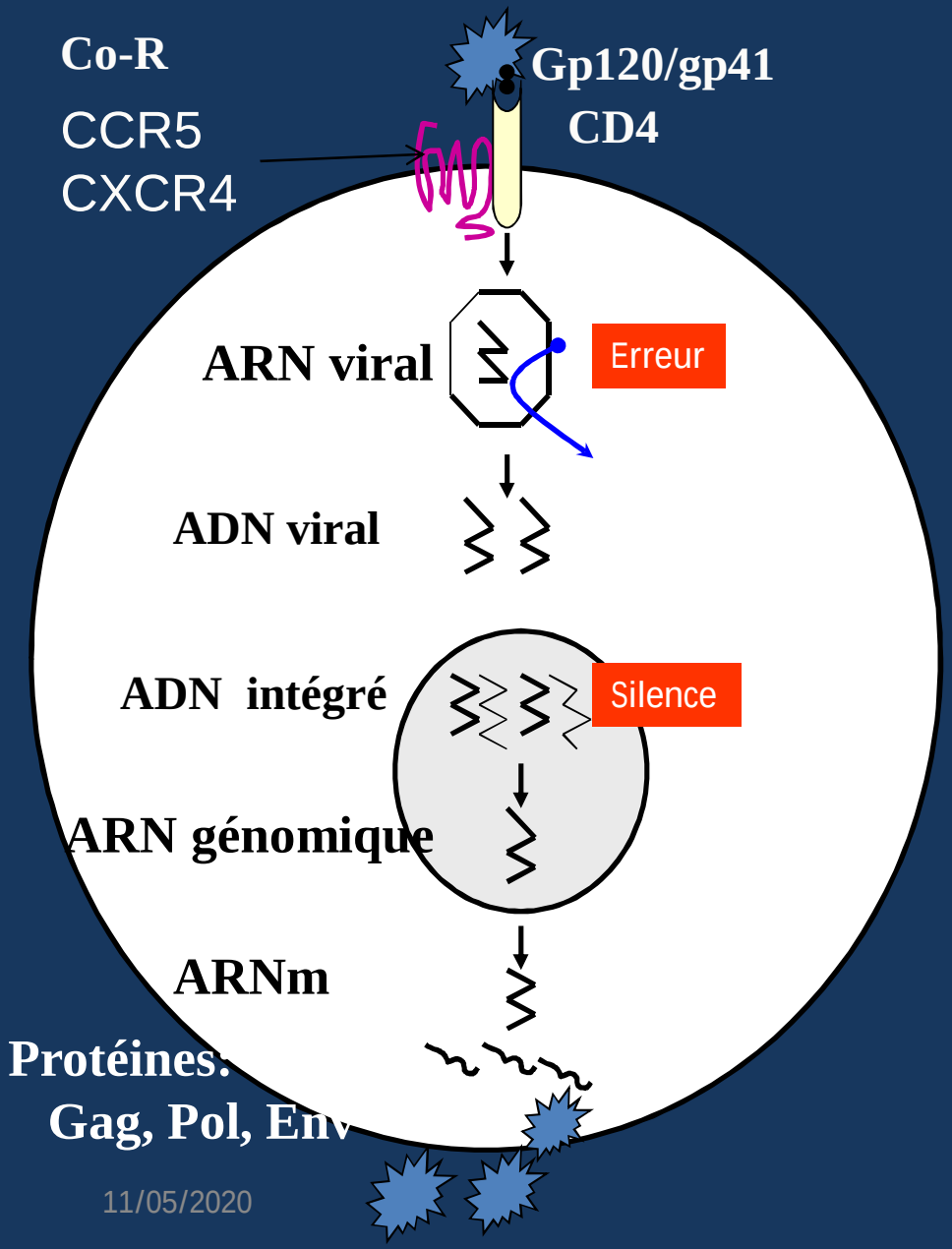
Lymphocytes CD4, monocytes/macrophages
cellules dendritiques , de Langherhans, microglie cérébrale
RESERVOIRS : ganglions, intestins, sperme

Timothy Ray Brown, dit « le patient de Berlin »,



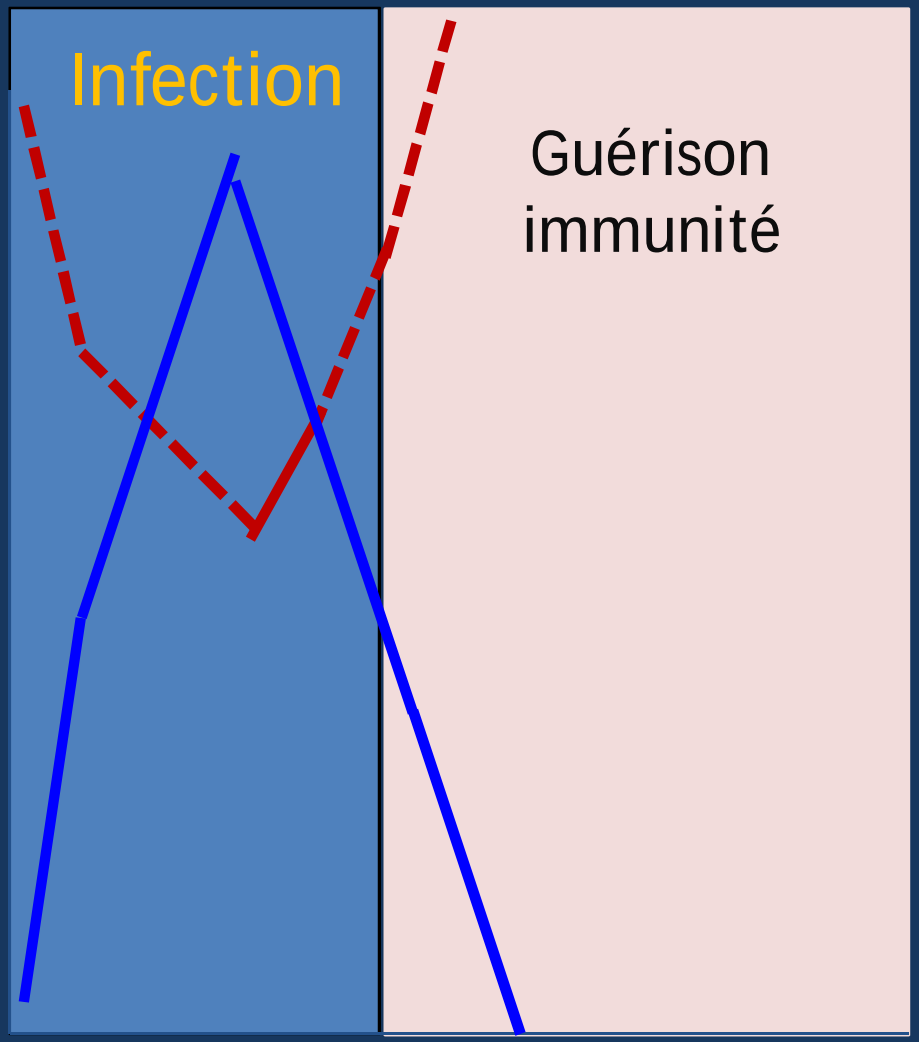
- **Patient de 40 ans suivi pour infection VIH depuis 1995**
- **2002 : leucémie.**
- **2007: greffe de moelle osseuse : donneur compatible + mutation du corécepteur CCR5 (Delta 32)**
- **Arrêt ARV en février 2007**
- **2012 : aucune trace de virus n'est détectable**

CYCLE REPLICATIF DU VIH



- Liaison, pénétration
- Rétro transcription: RT
- Transport
- Intégration: intégrase
- Transcription: ARN pol
- épissage et transport
- traduction
- découpage, assemblage protéase

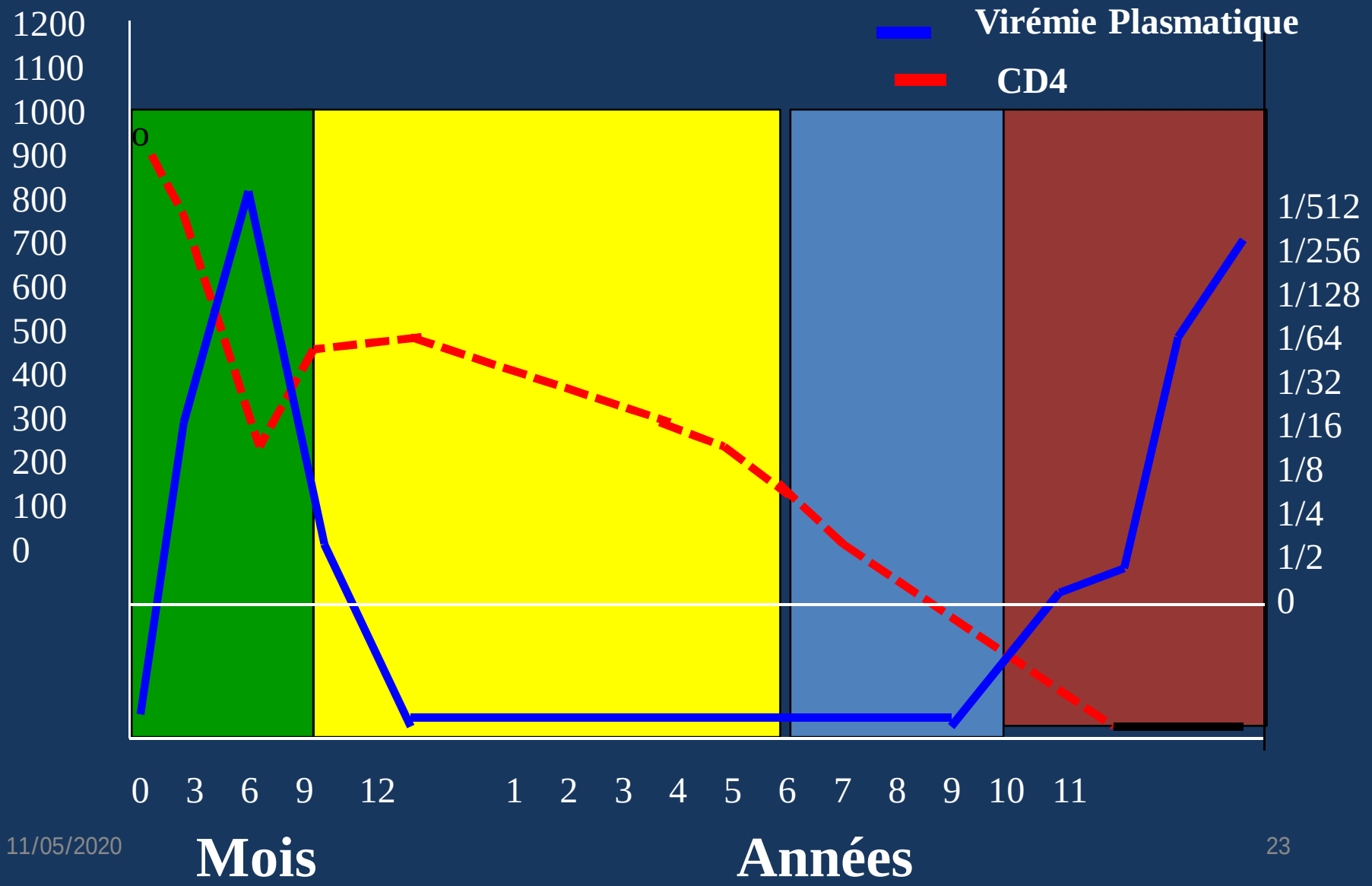
Évolution d'une infection virale aigue contrôlée



Virus

Réponse immune :
Ex: lymphocytes

Évolution des CD4 et de la virémie plasmatique



LA VARIABILITE GENETIQUE
et ses conséquences

réplication

1/1.000 à 10.000 nucléotides copiés
1 mutation/cycle réplicatif

Erreurs de copie

Production virale journalière :
- 10^{11} virions produits
- 10^{9} nouvelles cellules infectées

variations virales

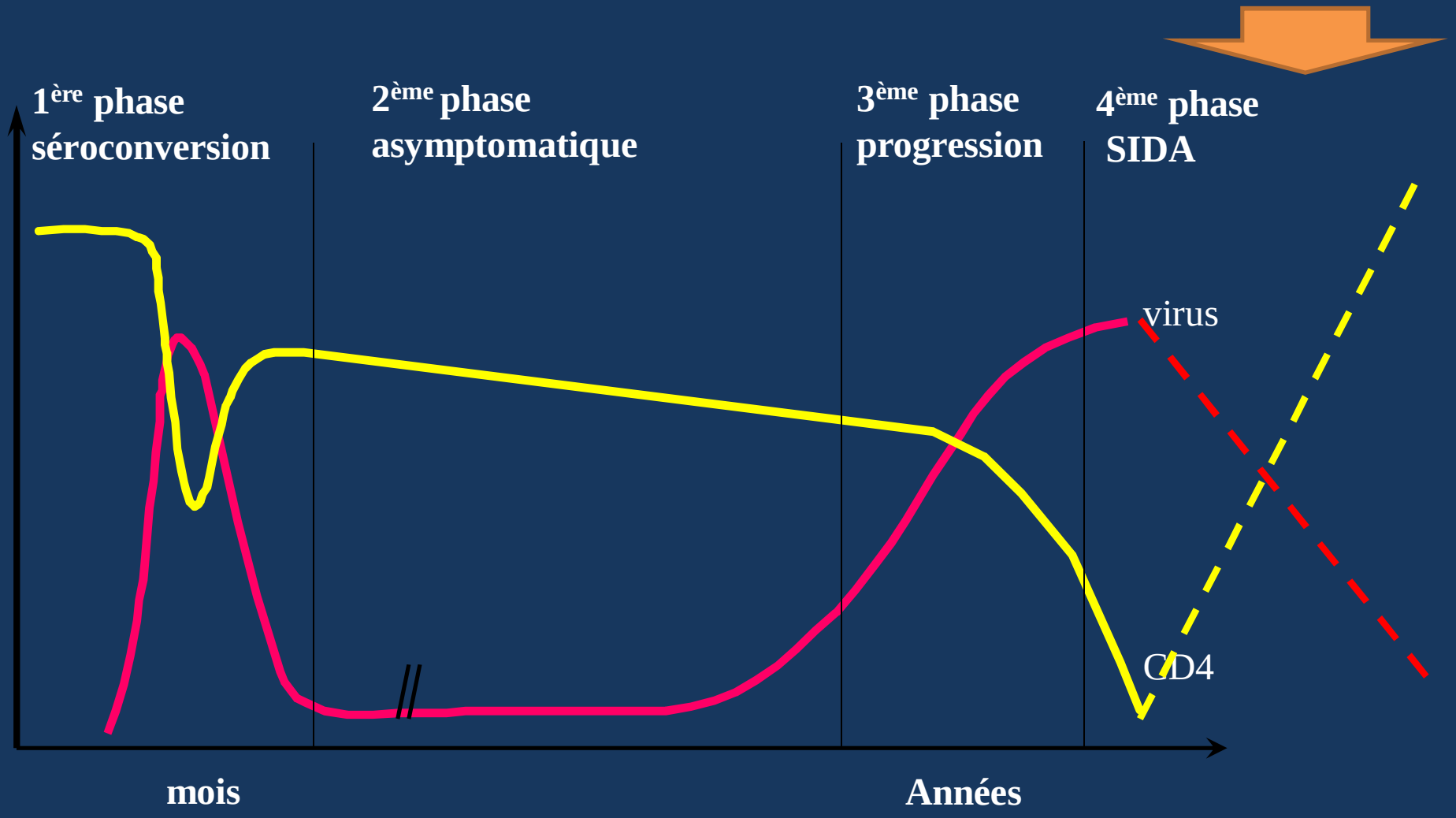
VIH = virus hyper-mutant

évolution par sélection naturelle = mutation

Progression de l'infection la lymphopénie CD4

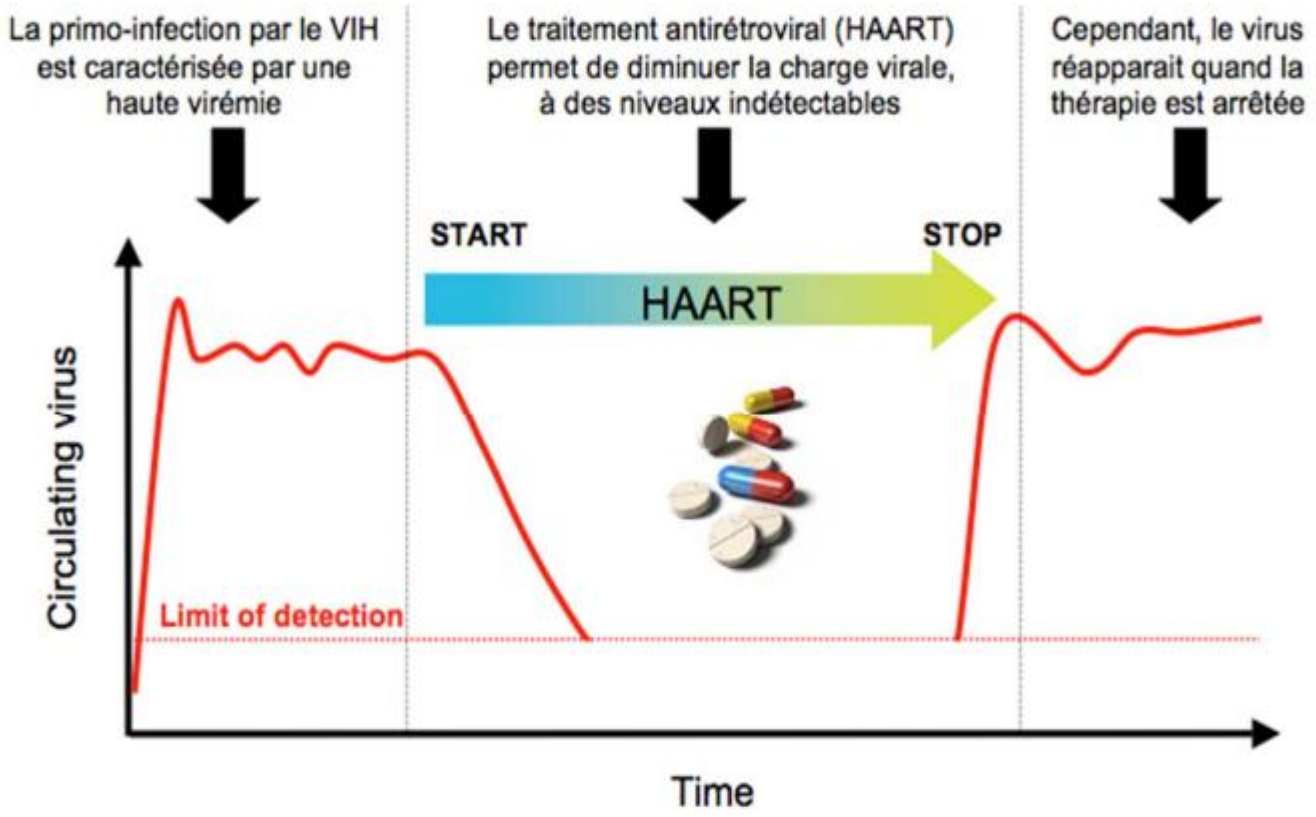
HAART
Trait. antiviral hautement actif

Primo-infection



Evidence d'un réservoir du VIH

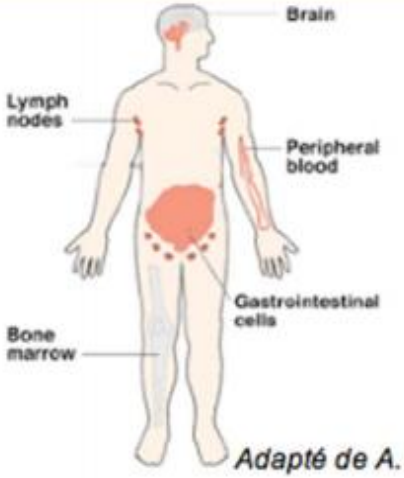
91



Où le VIH persiste t'il?

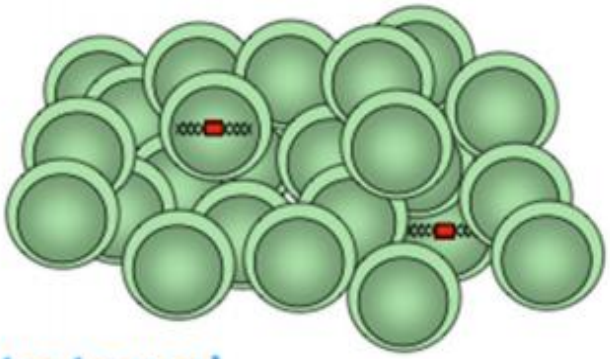
92

- *Au niveau anatomique: "cachettes" potentielles du VIH*
  - SNC
  - ganglions
  - sang
  - intestin
  - moelle osseuse



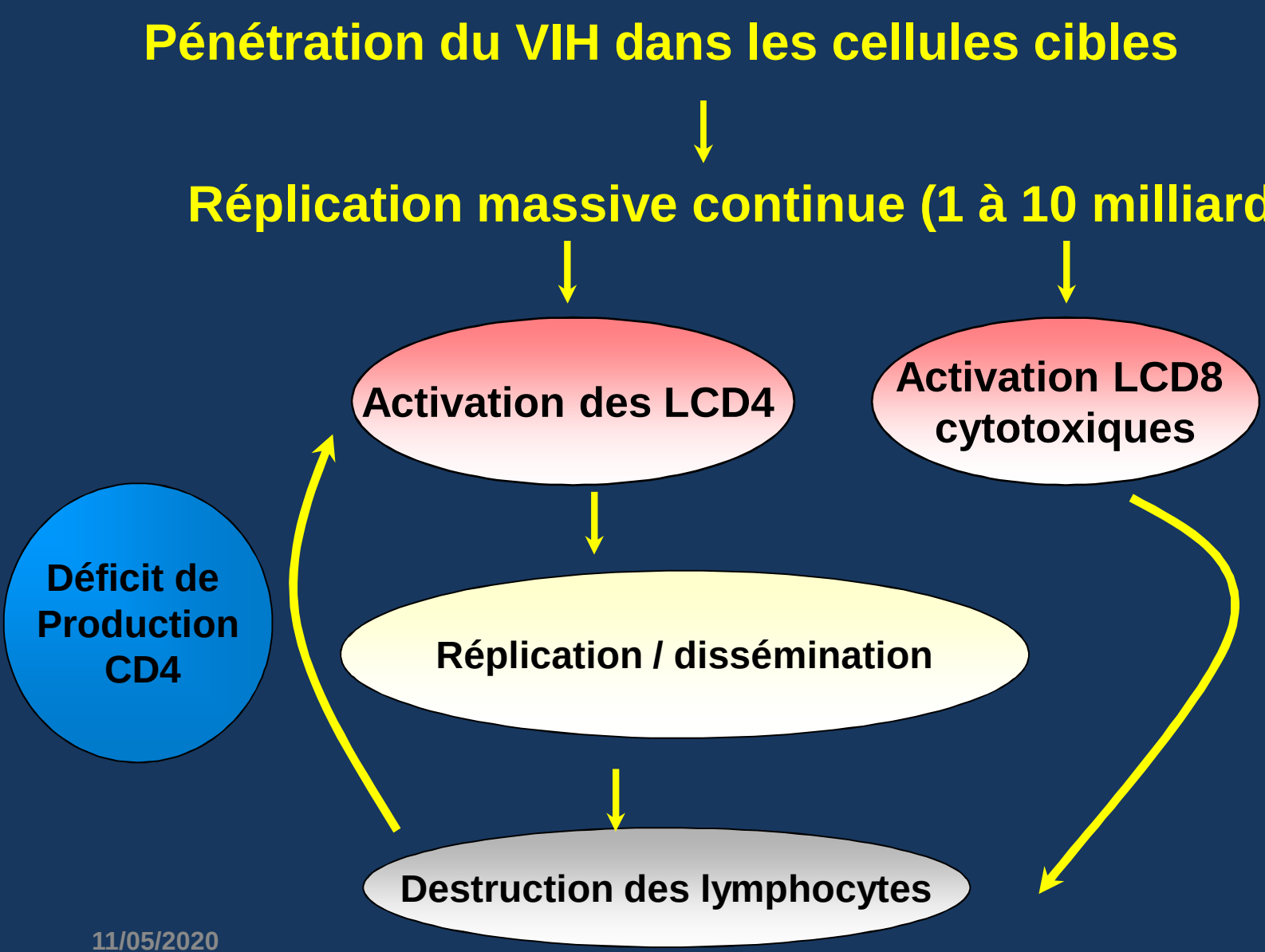
Adapté de A. Fauci

- *Au niveau cellulaire:* Un petit nombre de cellules qui portent l'ADN du VIH intégré dans leur génome. La fréquence des ces cellules est très faible (moins de 1 sur 1 million).



Le VIH peut persister dans cet état latent aussi longtemps que la cellule qui le porte

PHYSIOPATHOLOGIE DE L'INFECTION VIH



MECANISMES DE LA LYMPHOPENIE CD4

Perte moyenne 50 CD4/mm3/j ➔ 10^9 /j
1/2 vie CD4 infecté = 2 jours

Mécanismes

- réplication virale
- effet cytopathogène?
- destruction par les CD8
- activation chronique/anergie/mort
- déficience de régénération

CONSEQUENCES CLINIQUES

Lymph. CD4 :

- **cibles principales du virus**
- **diminution du taux par déficit progressif,**
- **diminution de la fonction**

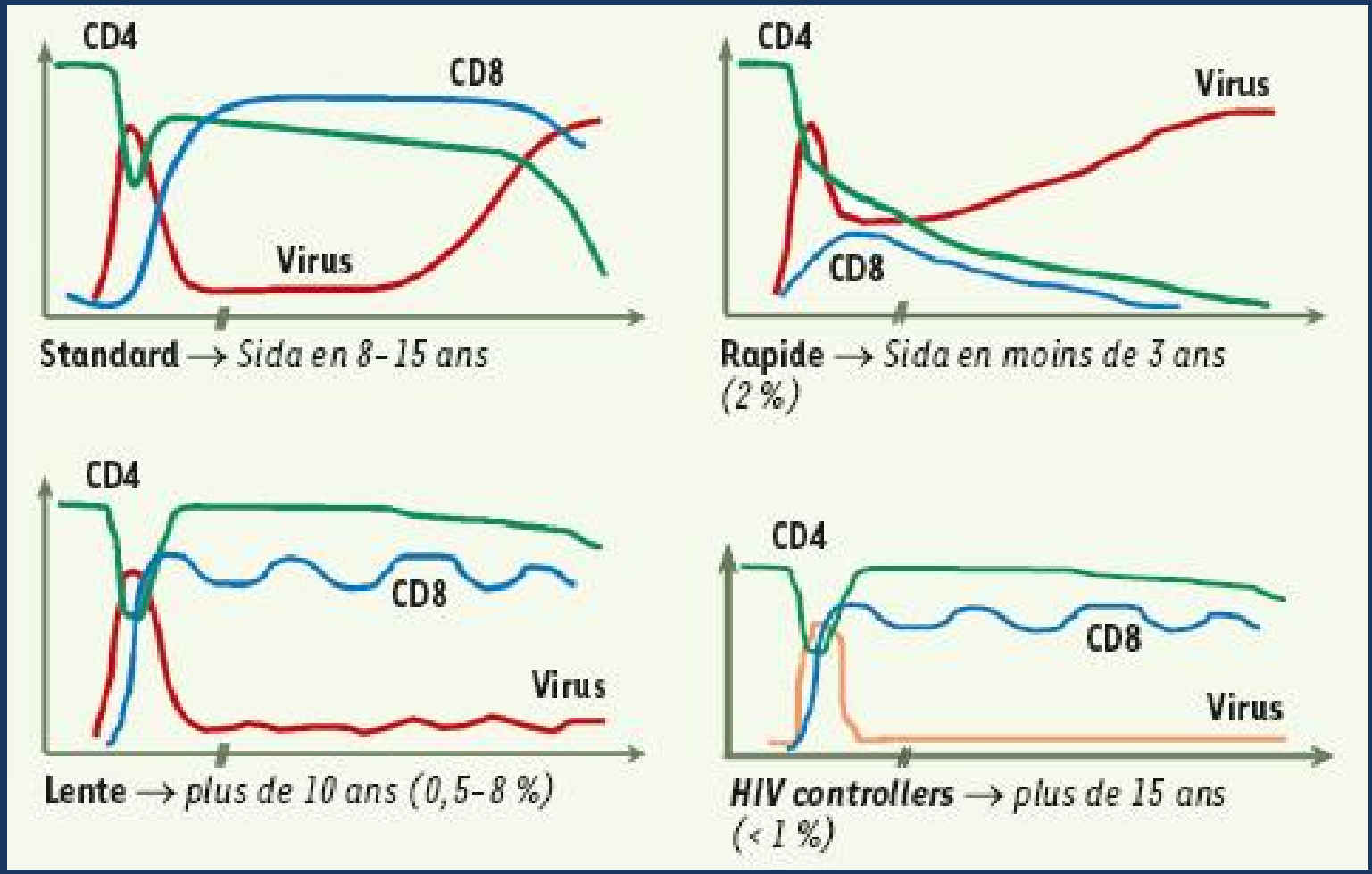
➔ Etat d ’immunodépression

➔ favorisant les Infections opportunistes et les processus tumoraux = ➔ SIDA

Réponse CD8 : Hyperstimulation / Hyperactivation

➔ Phénomènes d ’immunopathologie

Modes de progression de l'infection VIH



Taux de CD4 et infections opportunistes