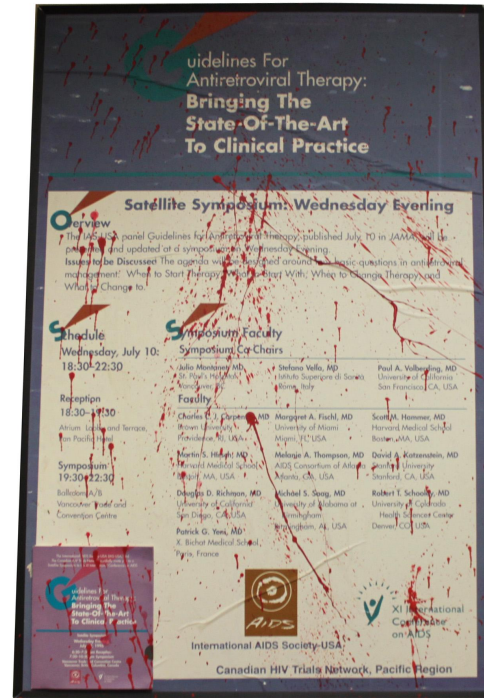


HIV for Primary Care Providers



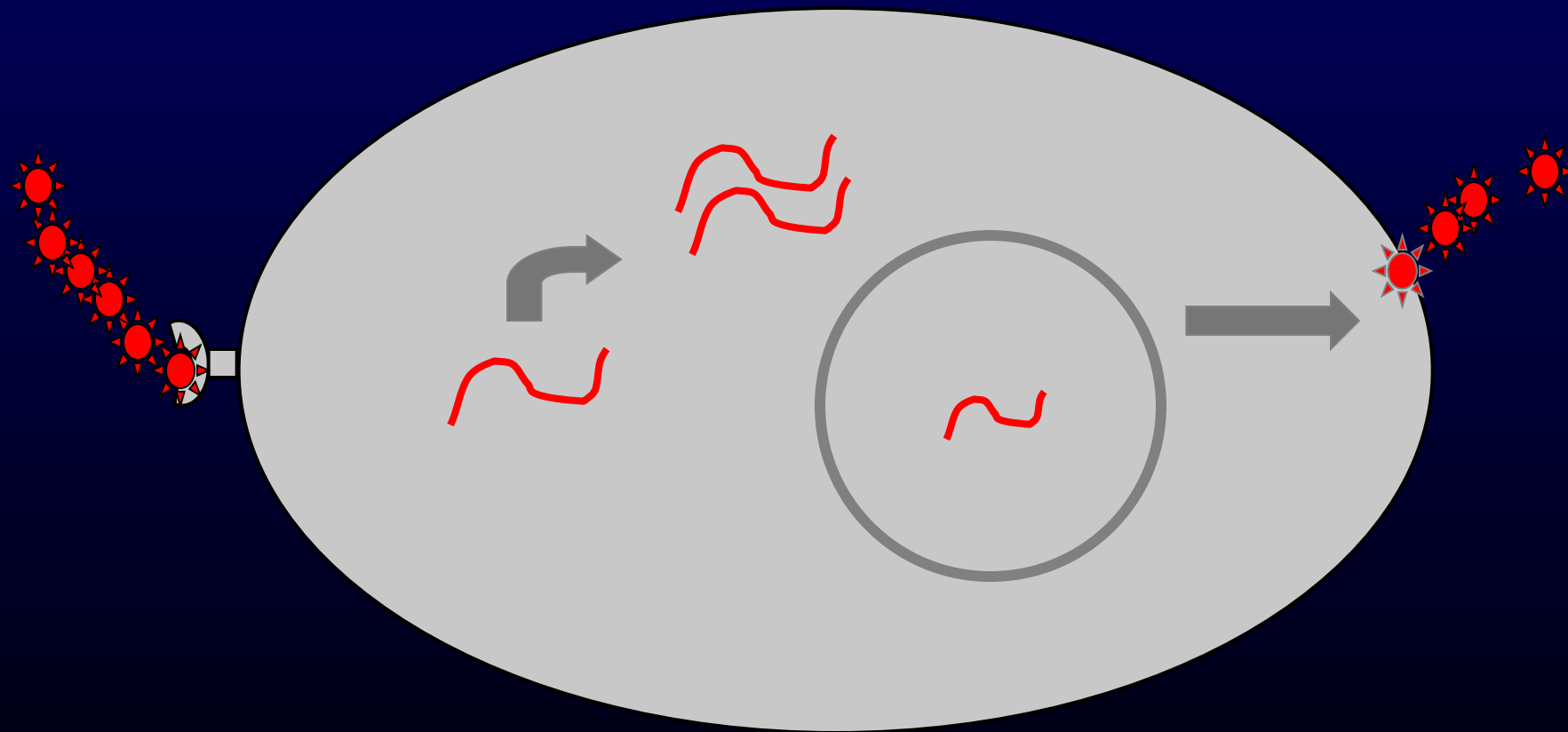
Michael S. Saag, MD
Professor of Medicine
Director, UAB Center for AIDS Research

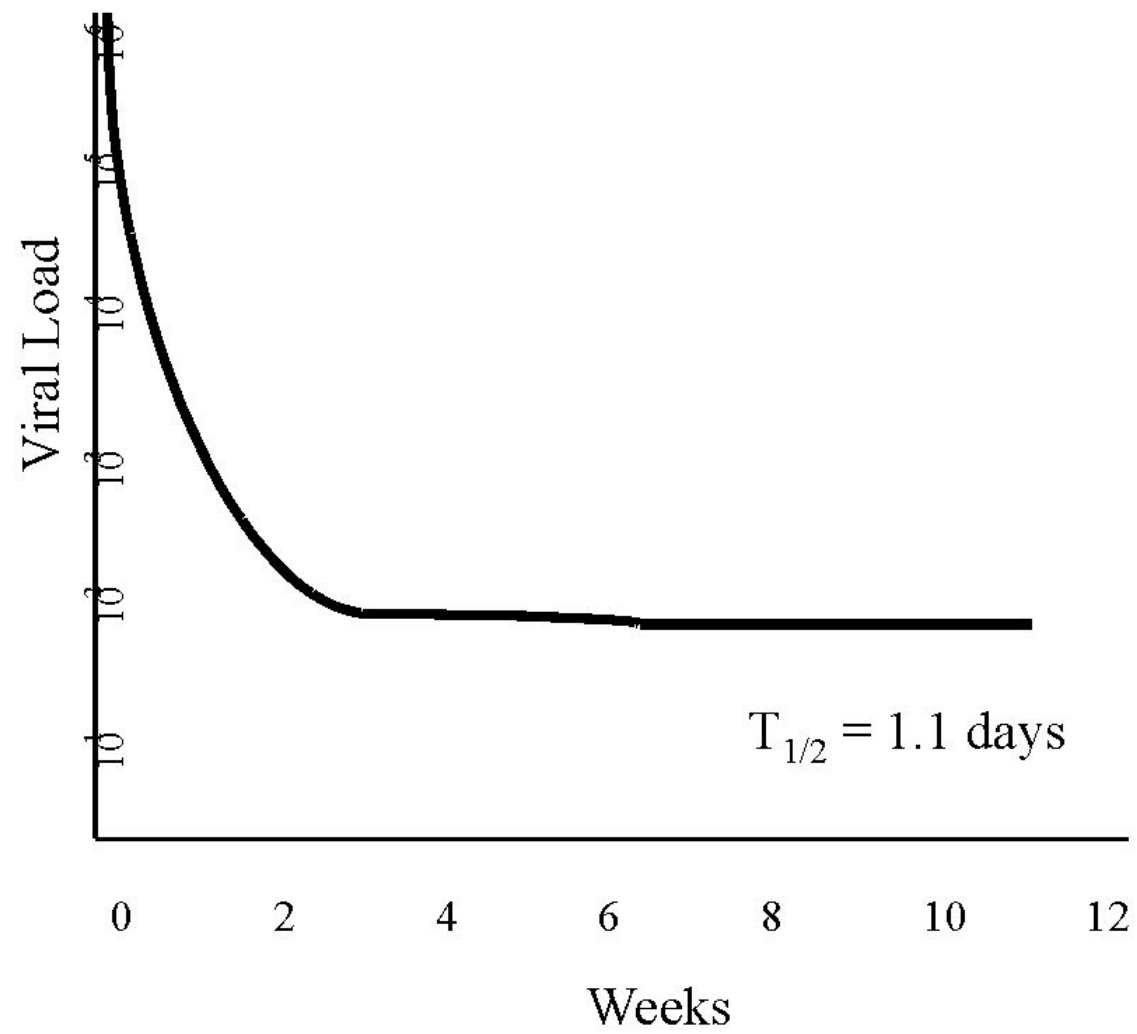
Financial Relationships With Commercial Entities

- Dr Saag has received research grants and support awarded to his institution from Gilead Sciences, Inc and ViiV Healthcare. (Updated 10/28/19)



BACK TO BASICS





How many HIV virions are produced a day in an infected person?

1. 1
2. ~ 1000
3. 570,342
4. ~ 1 million
5. > 1 billion

Viral dynamics in human immunodeficiency virus type 1 infection

Xiping Wei^{*}, Sajal K. Ghosh^{*}, Maria E. Taylor^{*}, Victoria A. Johnson[†],
Emilio A. Emini[‡], Paul Deutsch[§], Jeffrey D. Lifson^{||}, Sebastian Bonhoeffer[¶],
Martin A. Nowak[¶], Beatrice H. Hahn^{*}, Michael S. Saag[†]
& George M. Shaw^{*#}

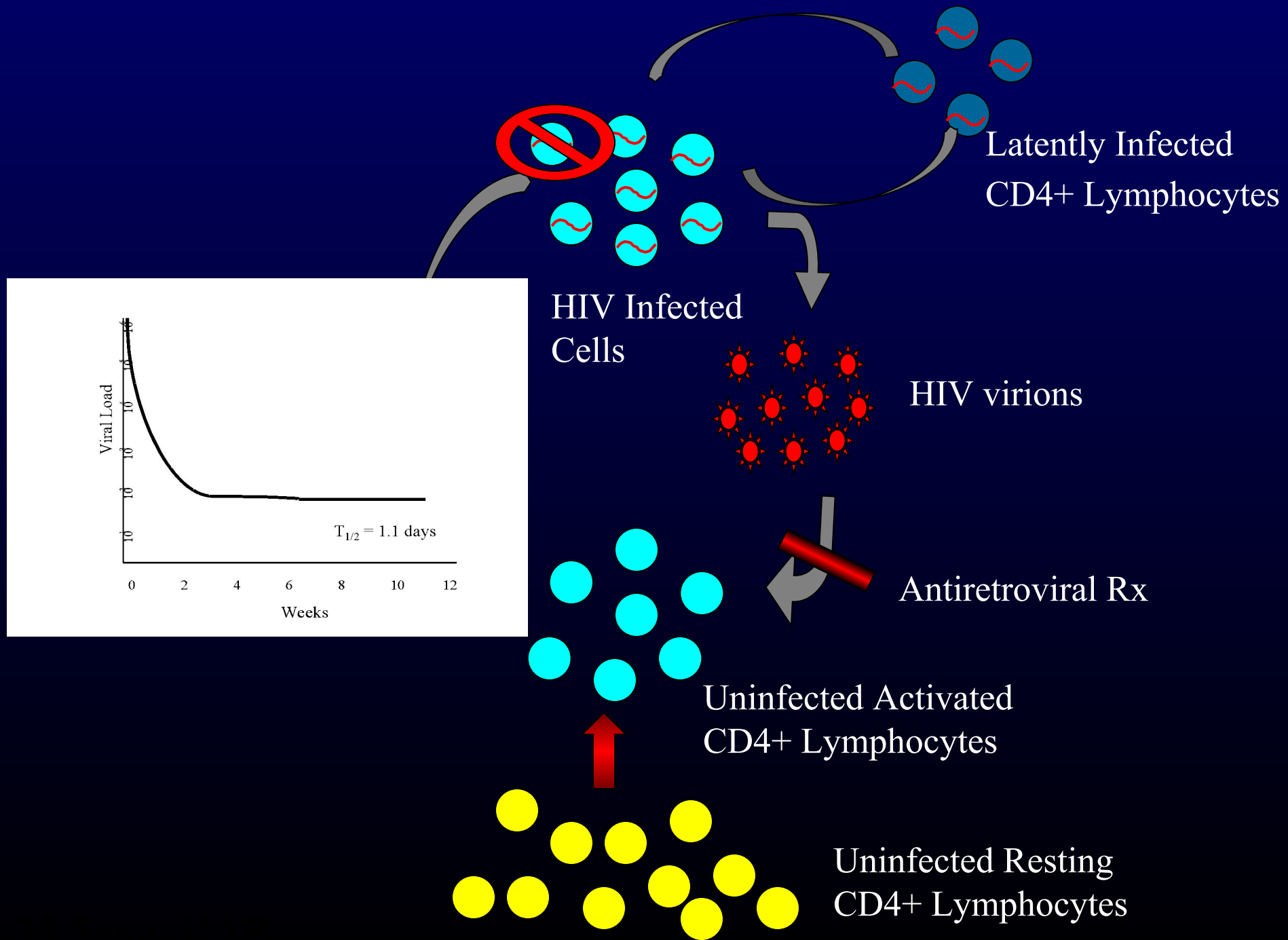
Divisions of ^{*} Hematology/Oncology and [†] Infectious Diseases, University of Alabama at Birmingham, 613 Lyons-Harrison Research Building, 701 South 19th Street, Birmingham, Alabama 35294, USA

Departments of [‡] Antiviral Research and [§] Clinical Pharmacology, Merck Research Laboratories, West Point, Pennsylvania 19486, USA

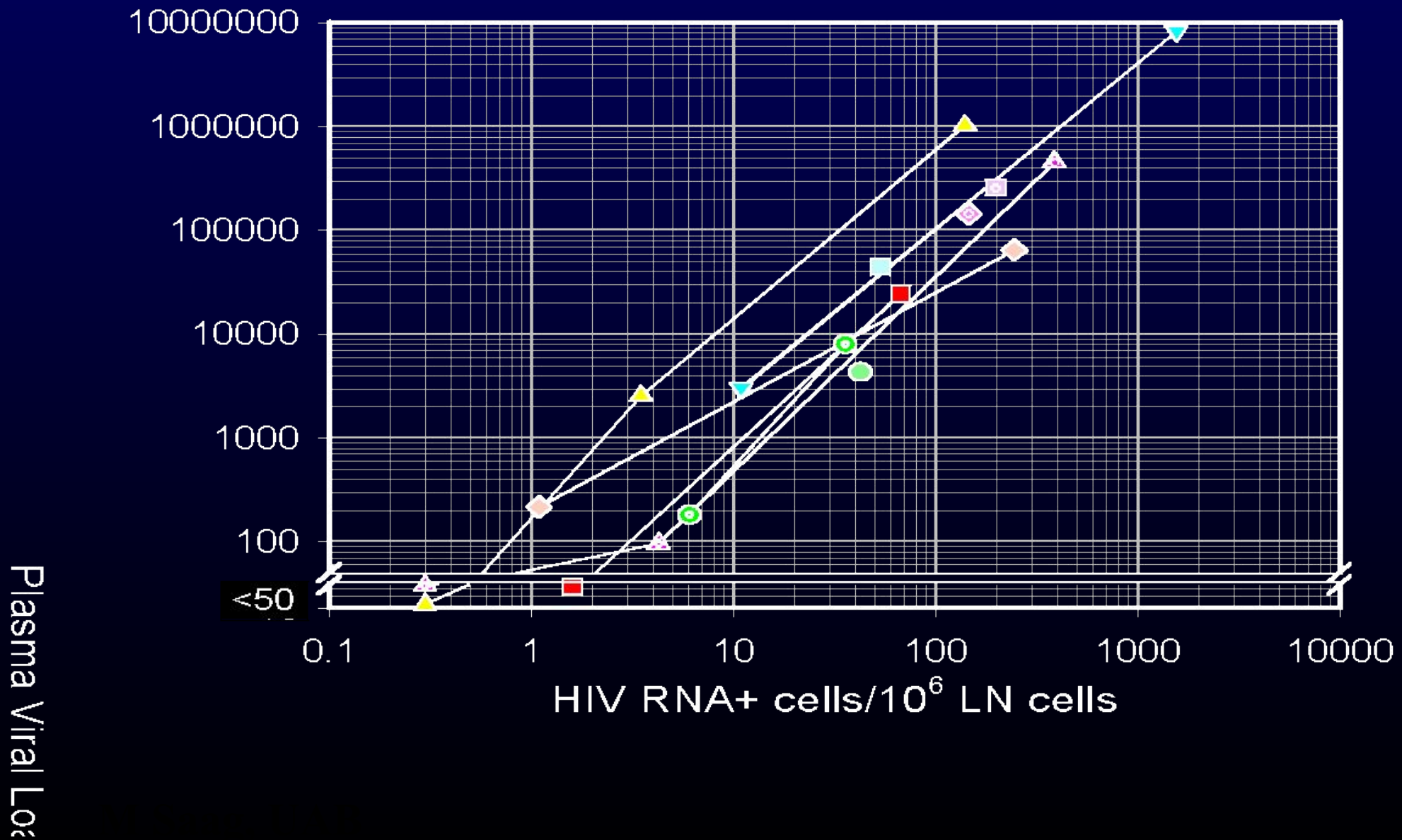
^{||} Division of HIV and Exploratory Research, Genelabs Technologies Inc., Redwood City, California 94063, USA

[¶] Department of Zoology, University of Oxford, Oxford OX1 3PS, UK

The dynamics of HIV-1 replication *in vivo* are largely unknown yet they are critical to our understanding of disease pathogenesis. Experimental drugs that are potent inhibitors of viral replication can be used to show that the composite lifespan of plasma virus and virus-producing cells is remarkably short (half-life ~2 days). Almost complete replacement of wild-type virus in plasma by drug-resistant variants occurs after fourteen days, indicating that HIV-1 viraemia is sustained primarily by a dynamic process involving continuous rounds of *de novo* virus infection and replication and rapid cell turnover.

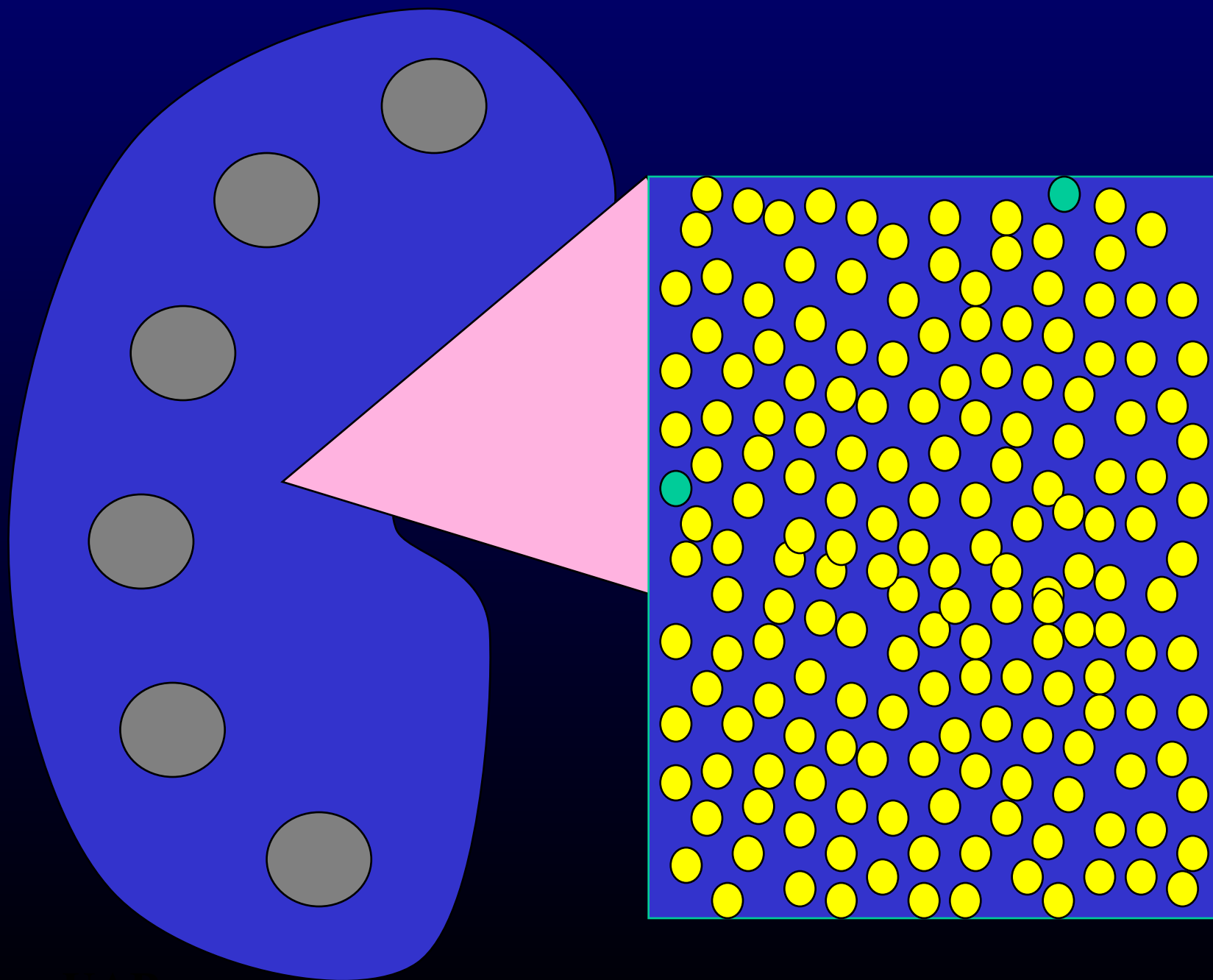


RNA+ cells in Lymph node vs RNA in Plasma

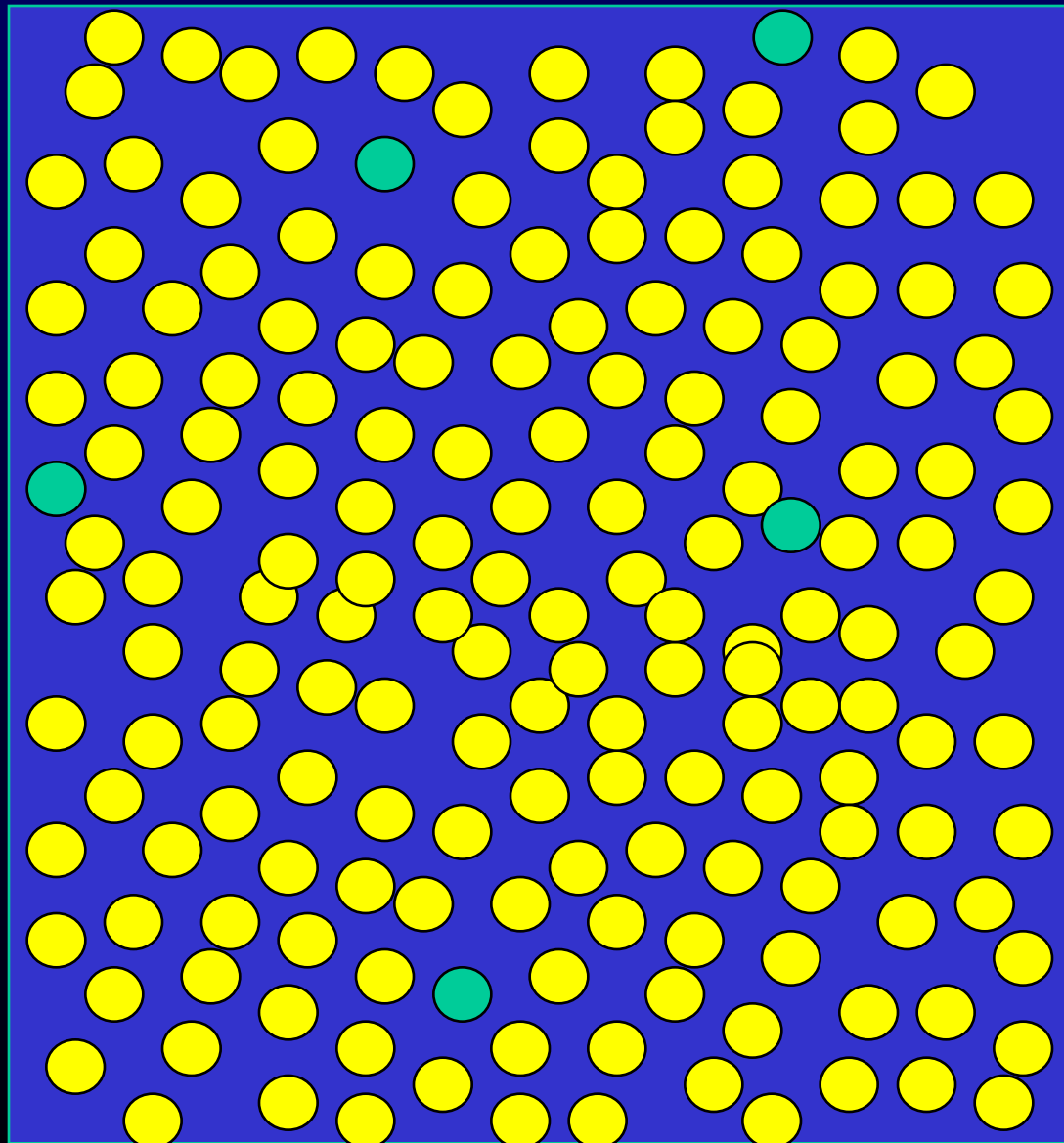


At steady state, when an actively producing cell dies, it is replaced by how many newly infected cells?

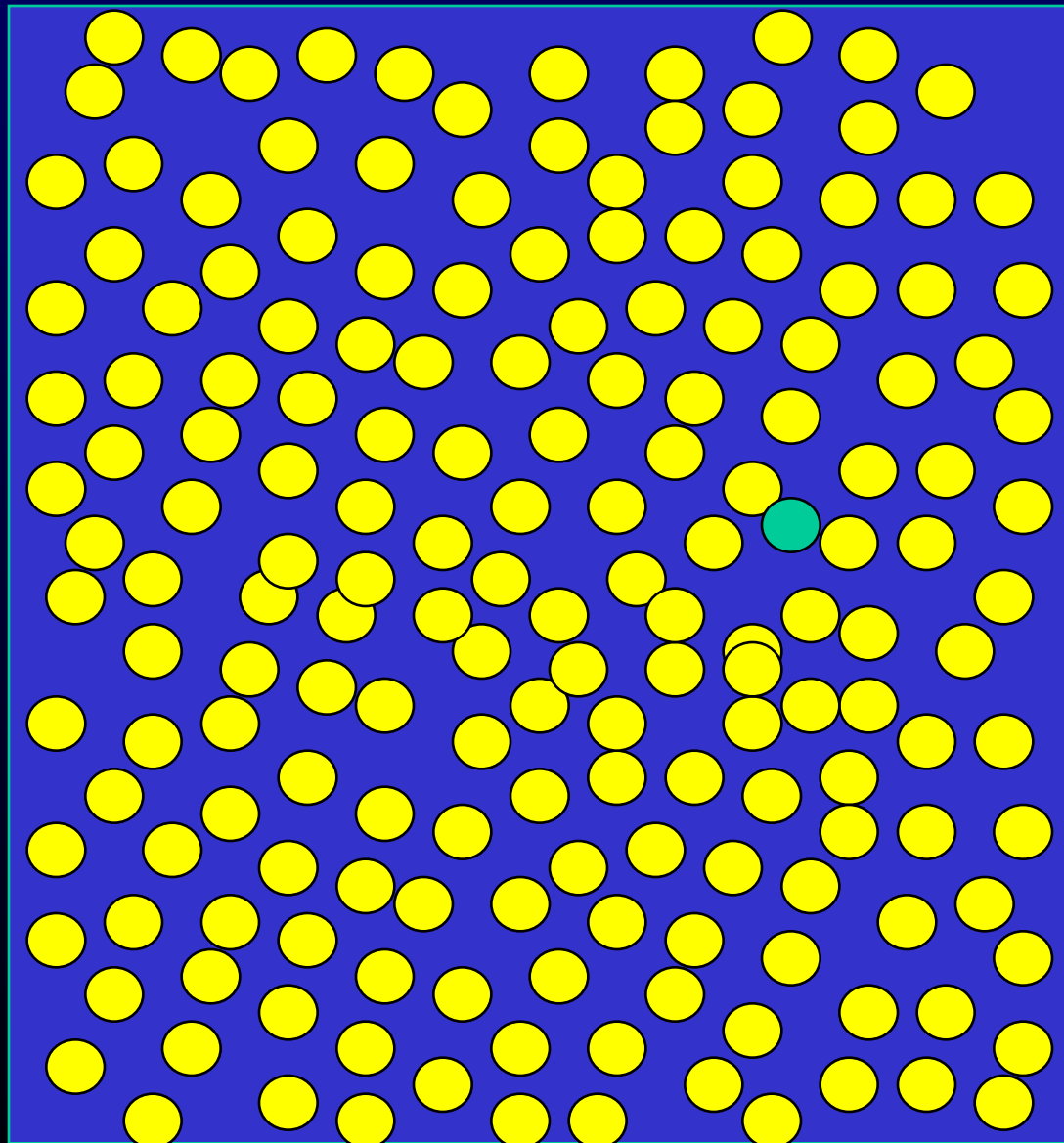
1. One
2. Twenty – Five
3. One Hundred
4. One Thousand
5. It depends on the viral load

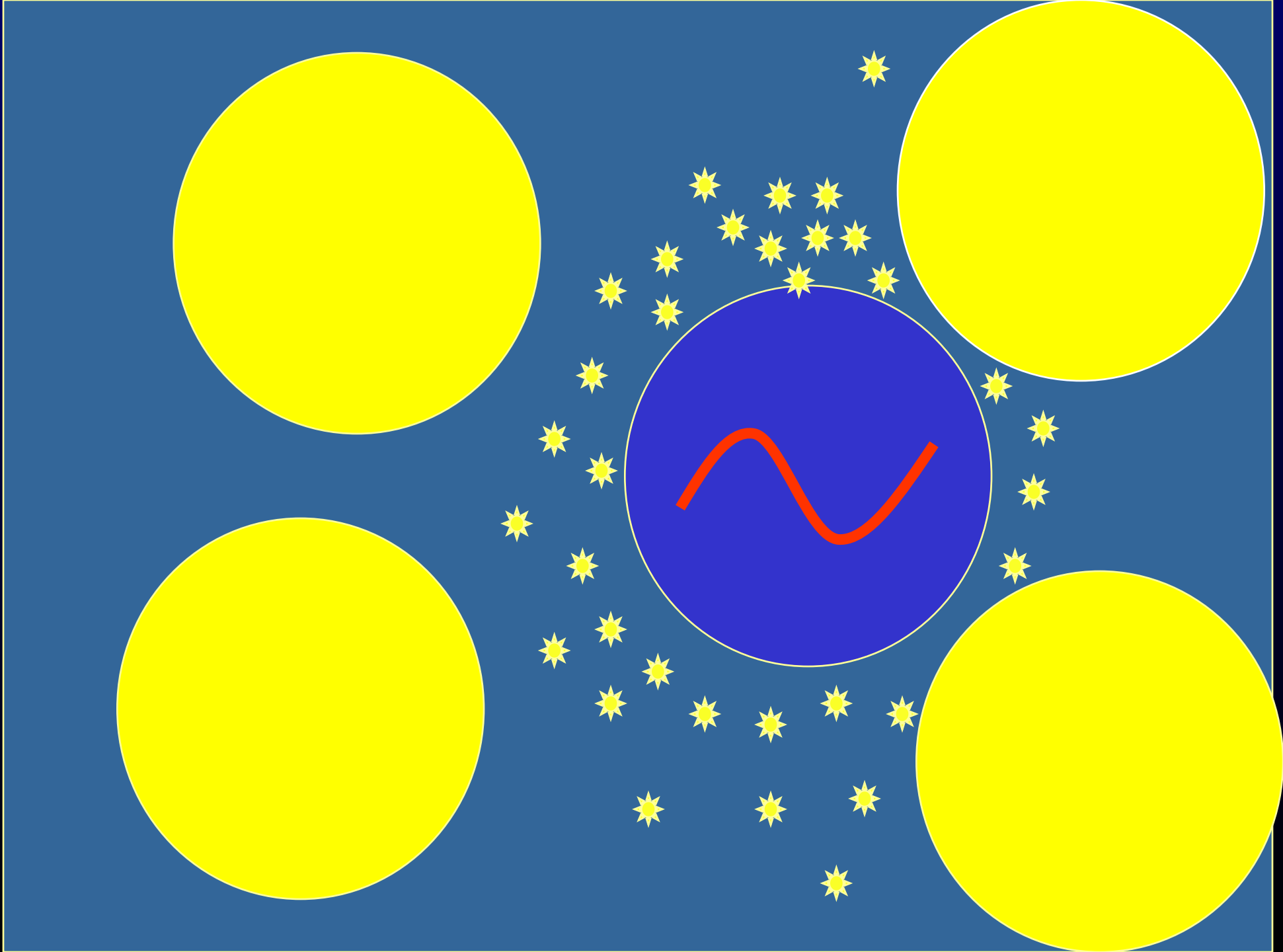


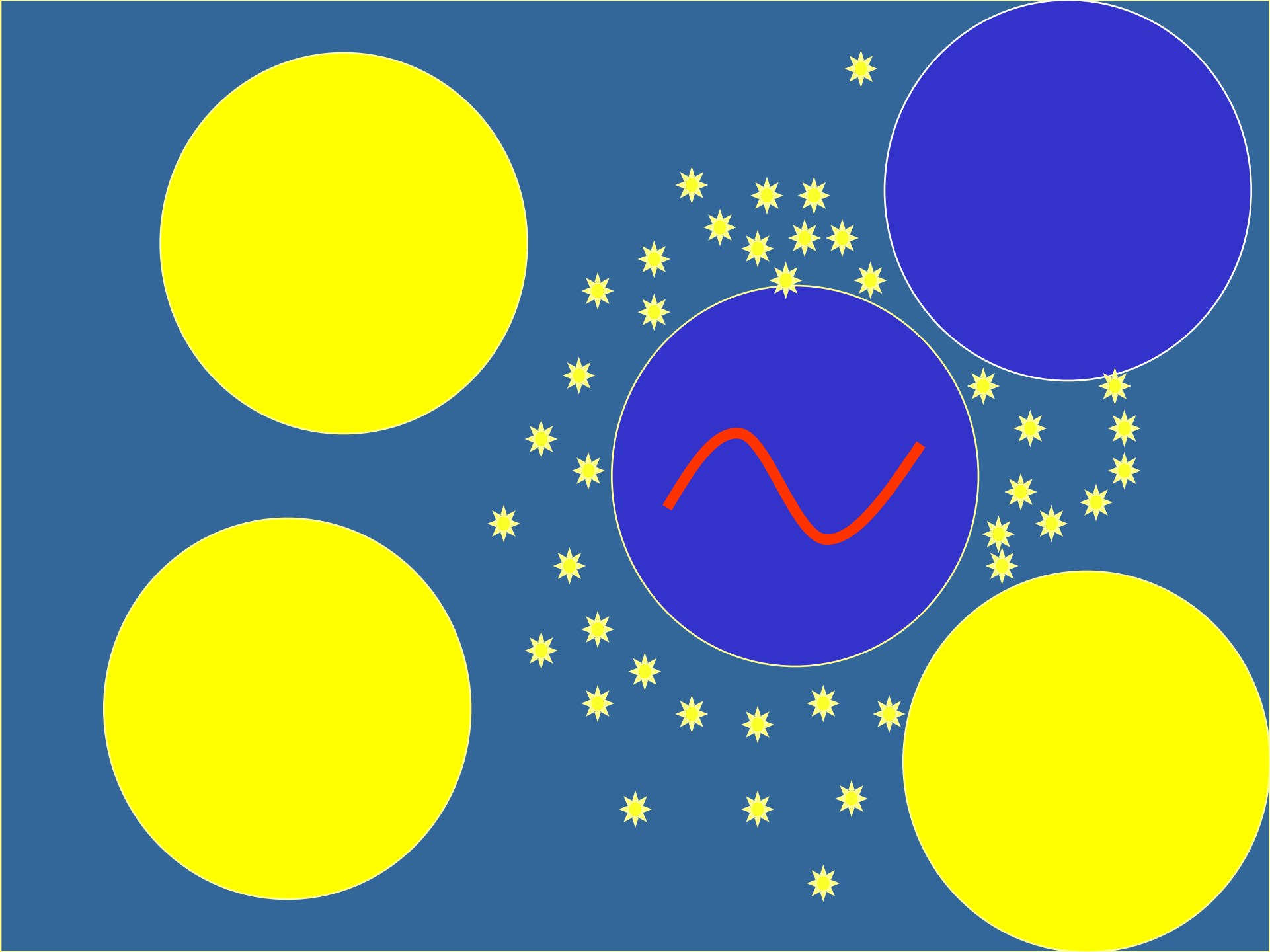
VL =
100,000

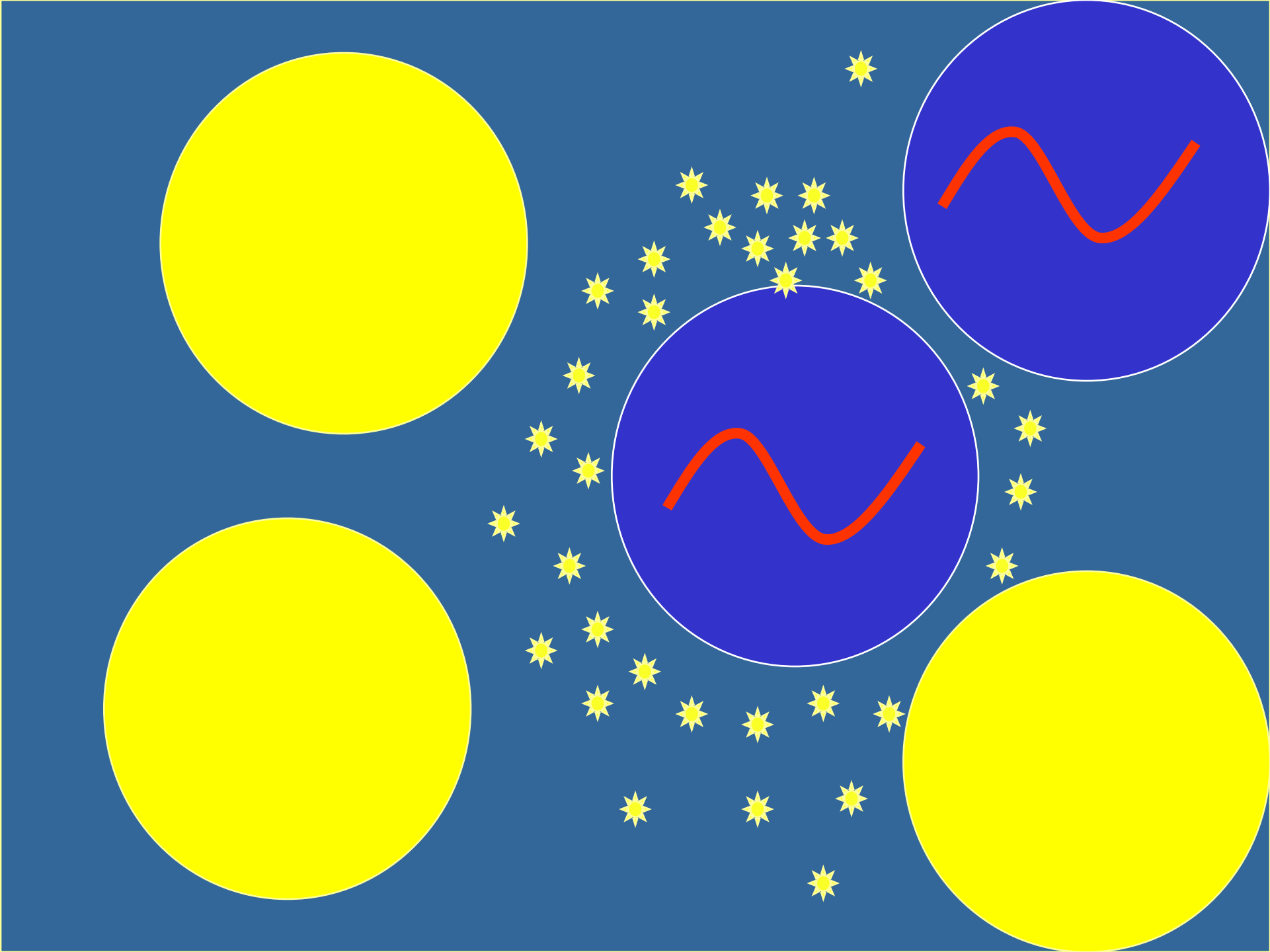


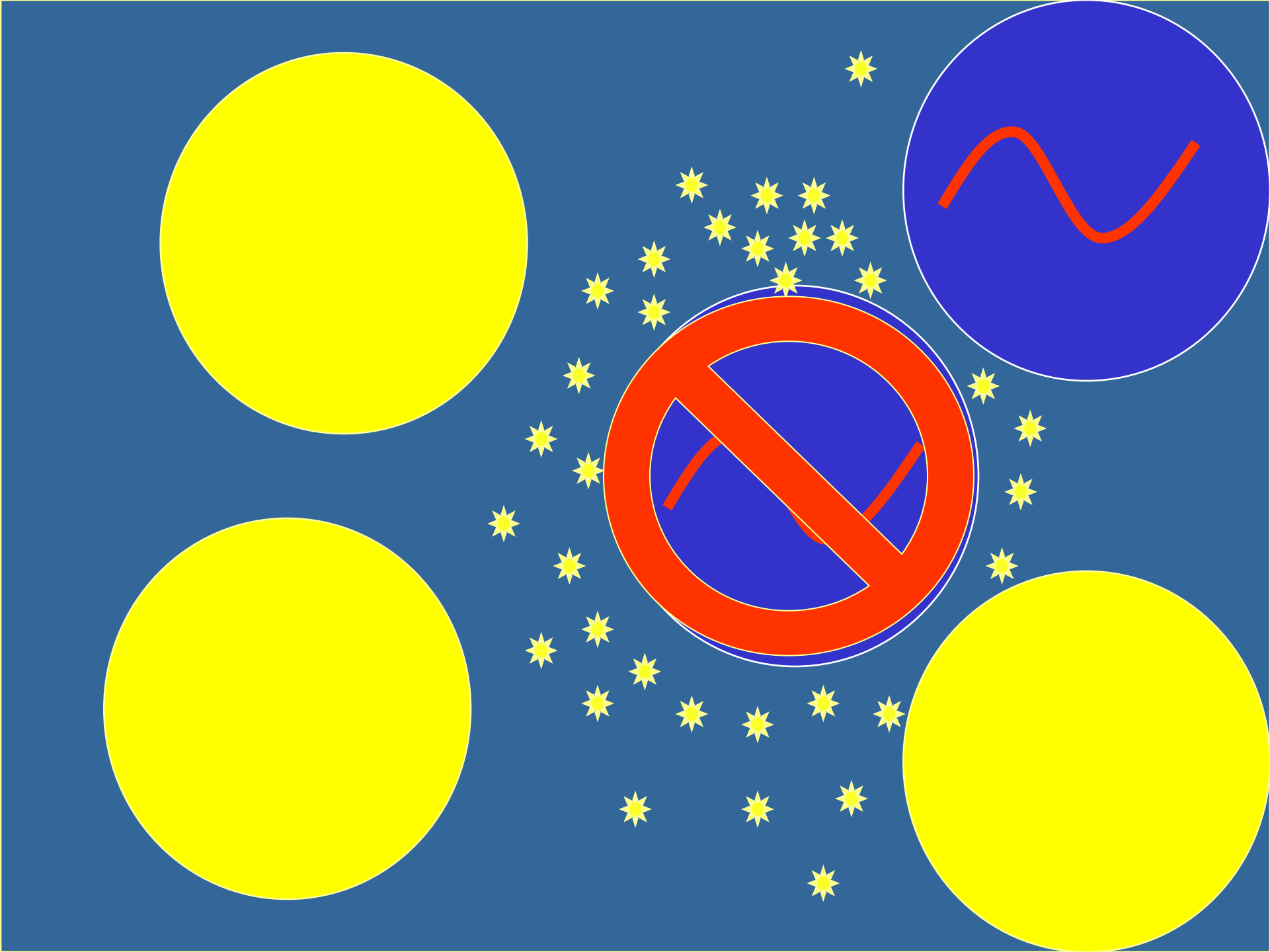
$VL < 50$

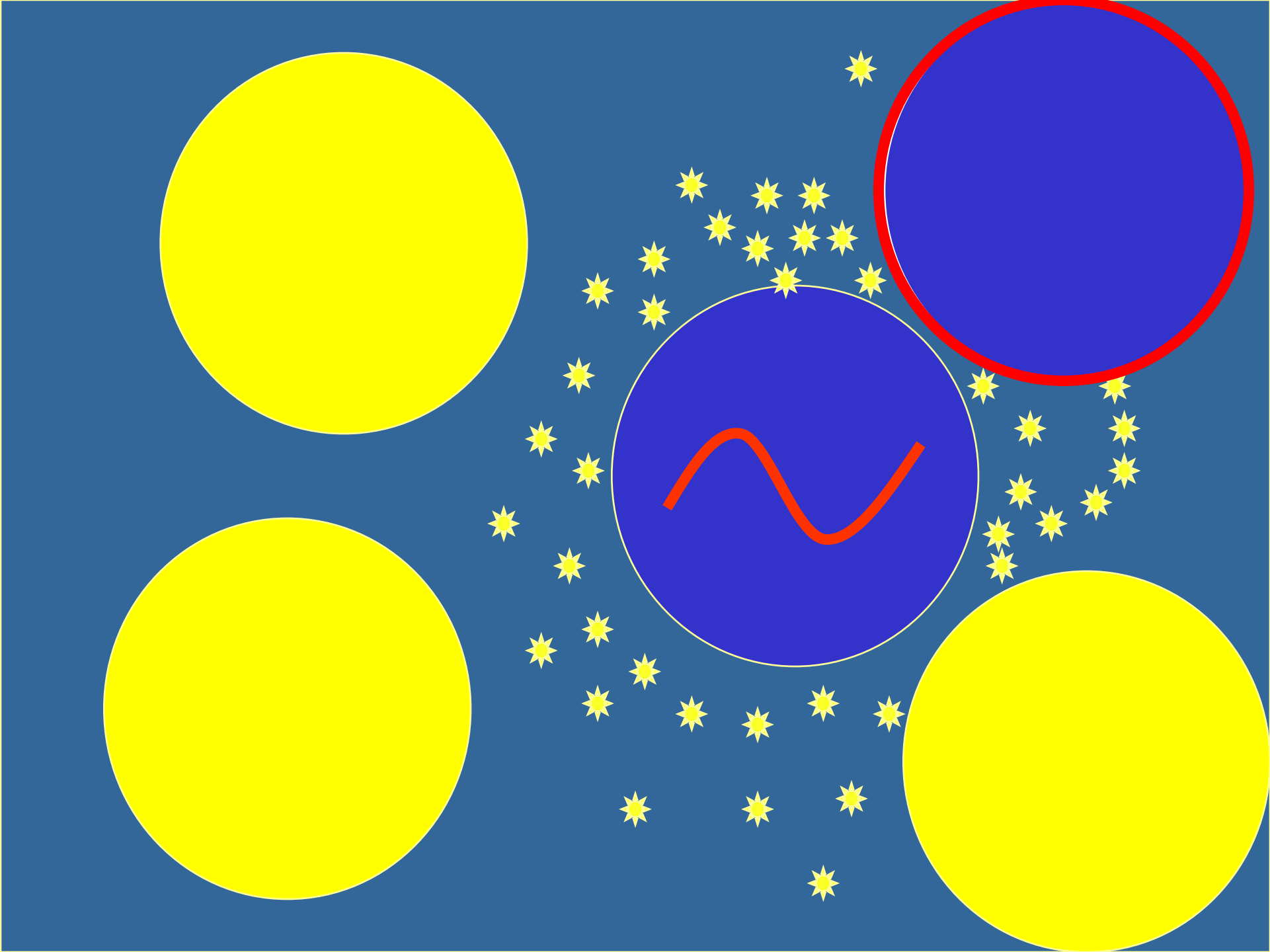


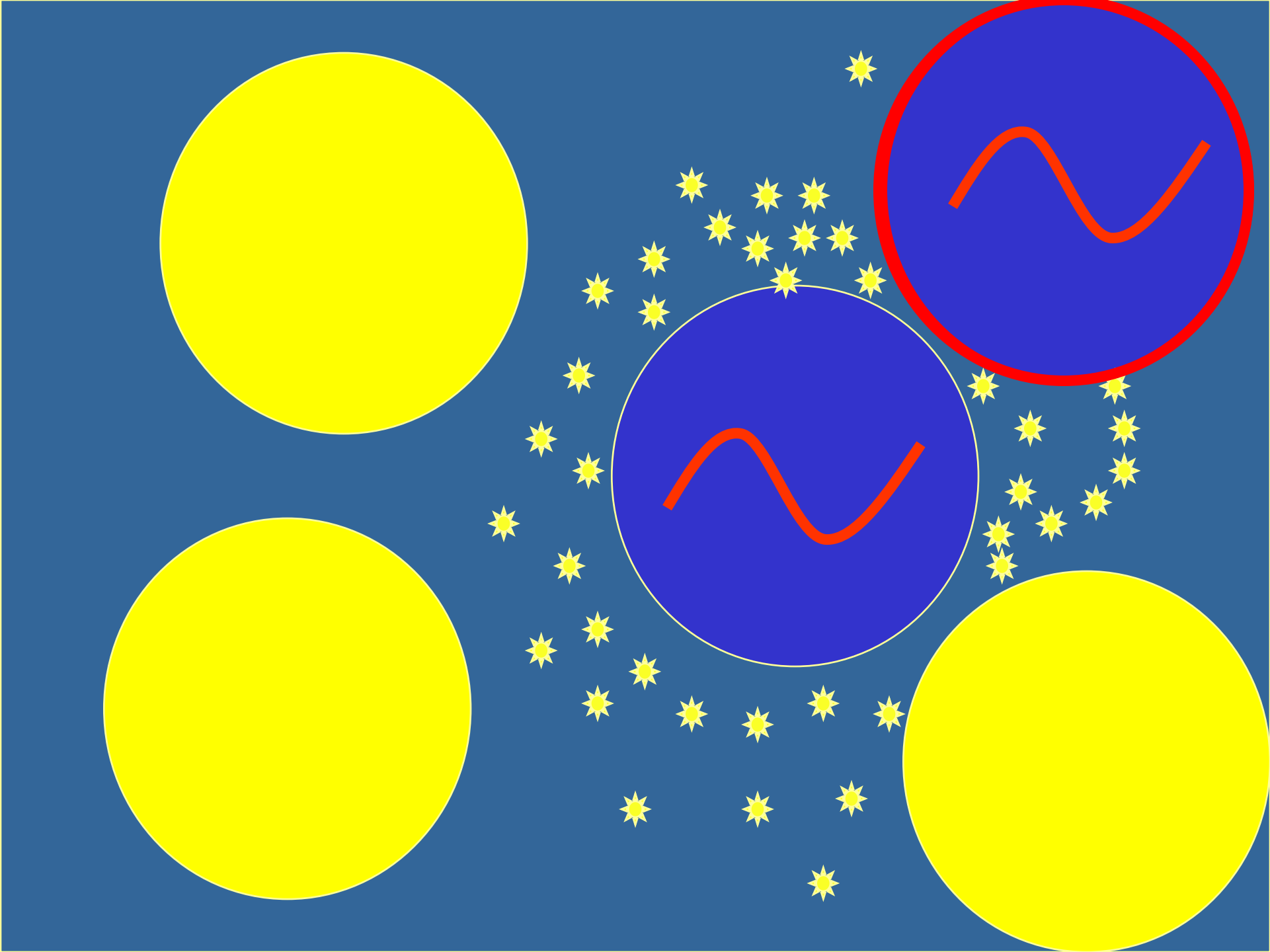


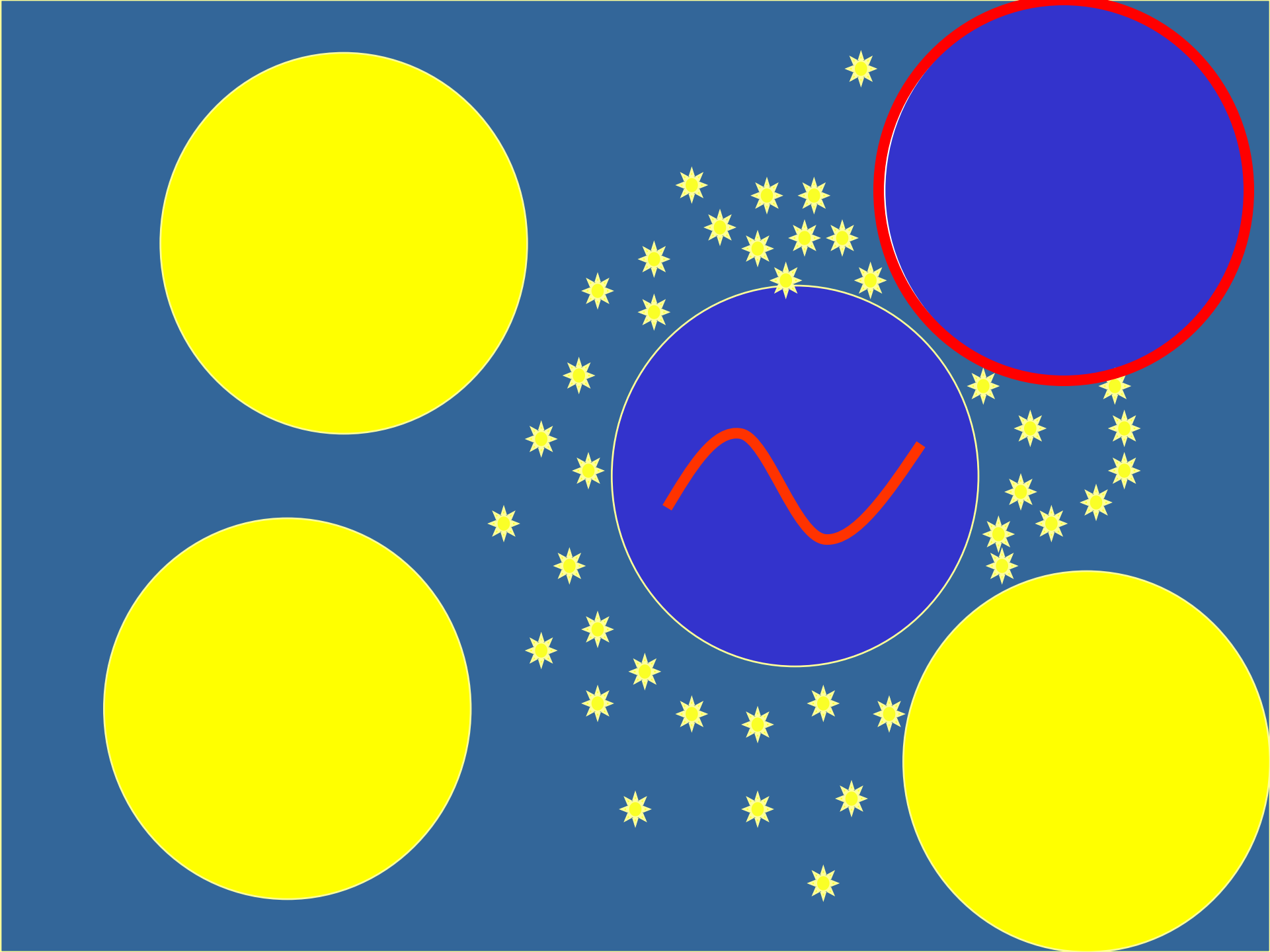


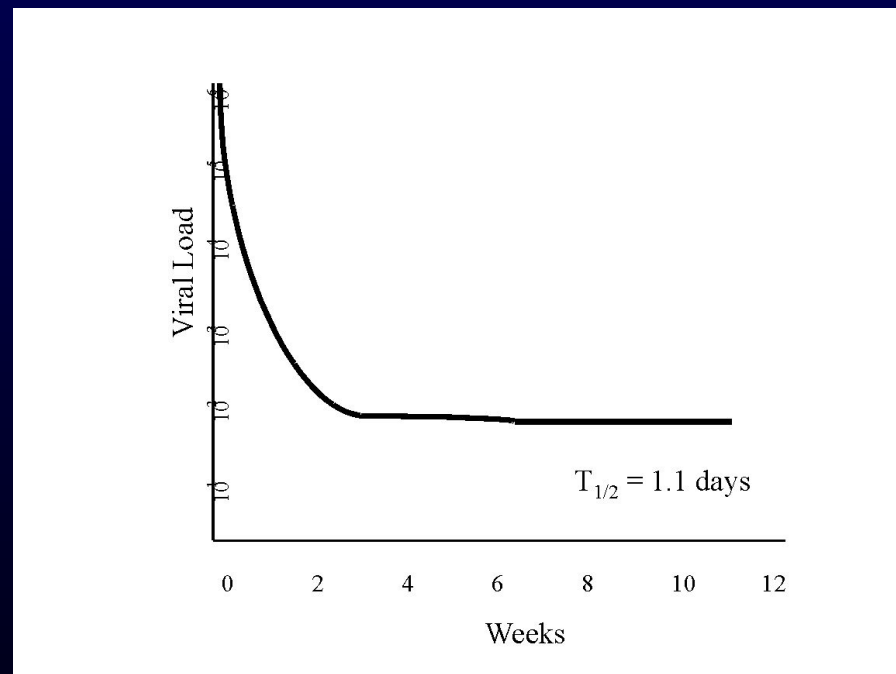






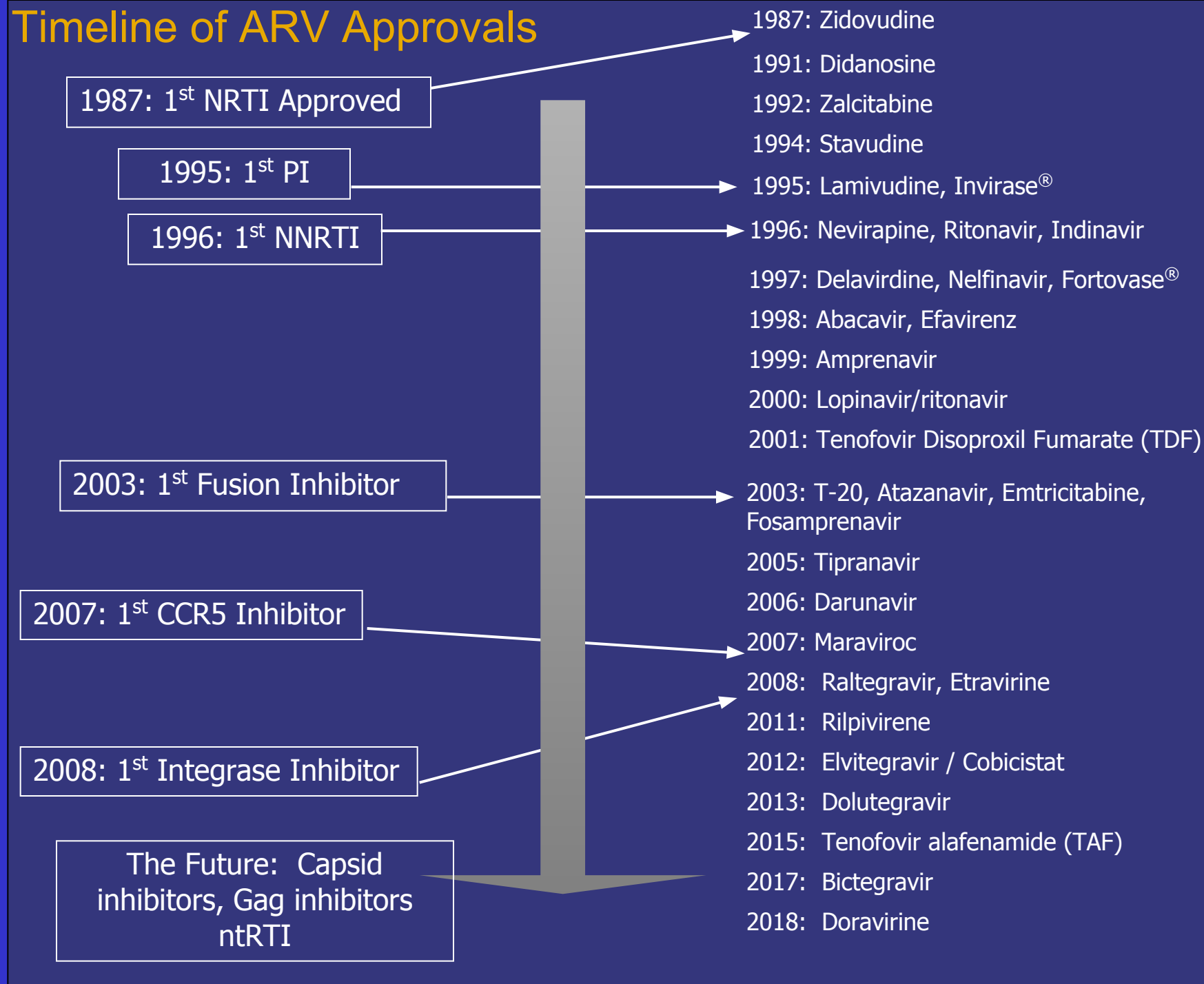






Timeline of ARV Approvals

Slide #22



When should antiretroviral therapy be started?

At a CD4 count of:

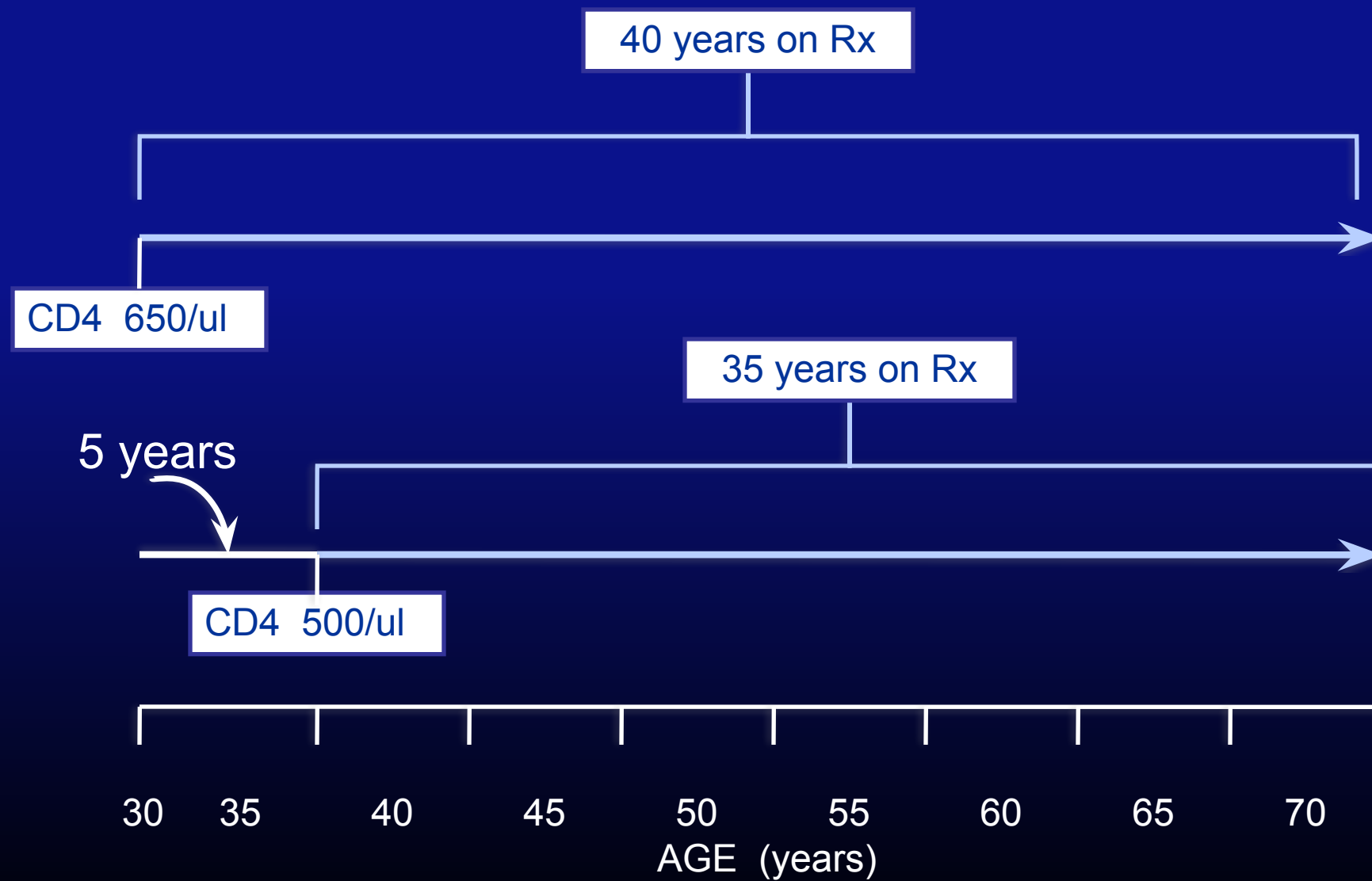
- A. 200 cells/ul or less
- B. 200 – 350 cells /ul
- C. 350 – 500 cells /ul
- D. 500 – 750 cells/ul
- E. Any CD4 count

Inverse Probability Weighted Cox Regression Multivariate Analysis

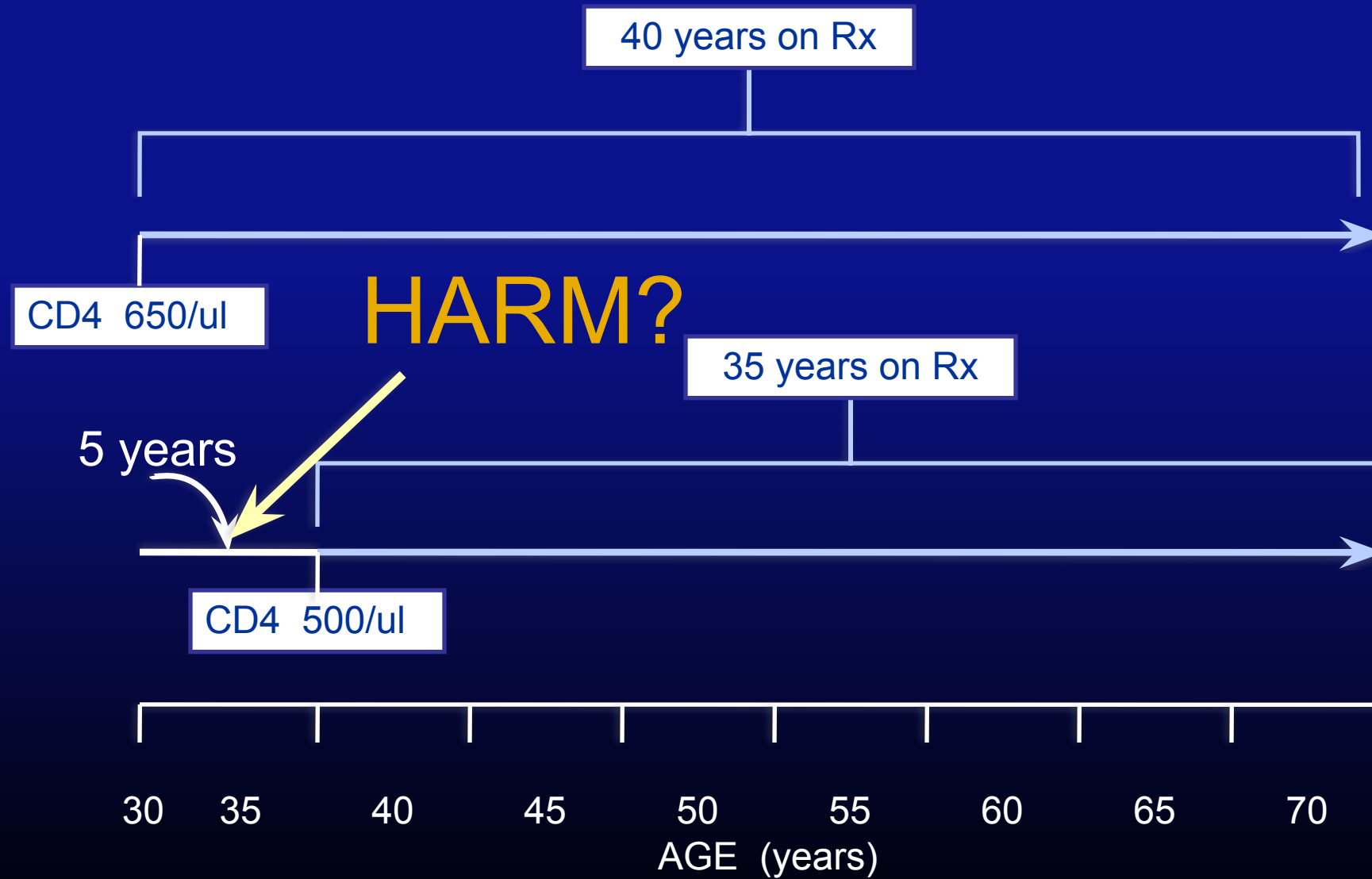
	Relative Hazard (RH)*	95% Confidence Interval	P-value
*Stratified by Cohort and Year			
Deferral of HAART at 351-500	1.7	1.4, 2.1	<0.001
Female Sex	1.1	0.9, 1.5	0.290
Older Age (per 10 years)	1.6	1.5, 1.8	<0.001
Baseline CD4 count (per 100 cells/mm ³)	0.9	0.7, 1.0	0.083

- Results were similar when restricting the analysis to the 77% of participants with baseline HIV RNA data
- Adjusted RH for deferral vs. immediate treatment was also 1.7
95% C.I. 1.4, 2.2; p <0.0001
- HIV RNA was not an independent predictor of mortality

Relative Time on Treatment...



Relative Time on Treatment...



Question

Seems like we are now starting ARV therapy for about everyone, what about starting therapy immediately at time of diagnosis?

Question

What regimen should I use
as initial therapy?

JAMA | Special Communication


Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults


2018 Recommendations of the International Antiviral Society-USA Panel

Michael S. Saag, MD; Constance A. Benson, MD; Rajesh T. Gandhi, MD; Jennifer F. Hoy, MBBS; Raphael J. Landovitz, MD; Michael J. Mugavero, MD, MHSc; Paul E. Sax, MD; Davey M. Smith, MD; Melanie A. Thompson, MD; Susan P. Buchbinder, MD; Carlos del Rio, MD; Joseph J. Eron Jr, MD; Gerd Fätkenheuer, MD; Huldrych F. Günthard, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Paul A. Volberding, MD

IMPORTANCE Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection.

 Editorial page 1

 Author Audio Interview

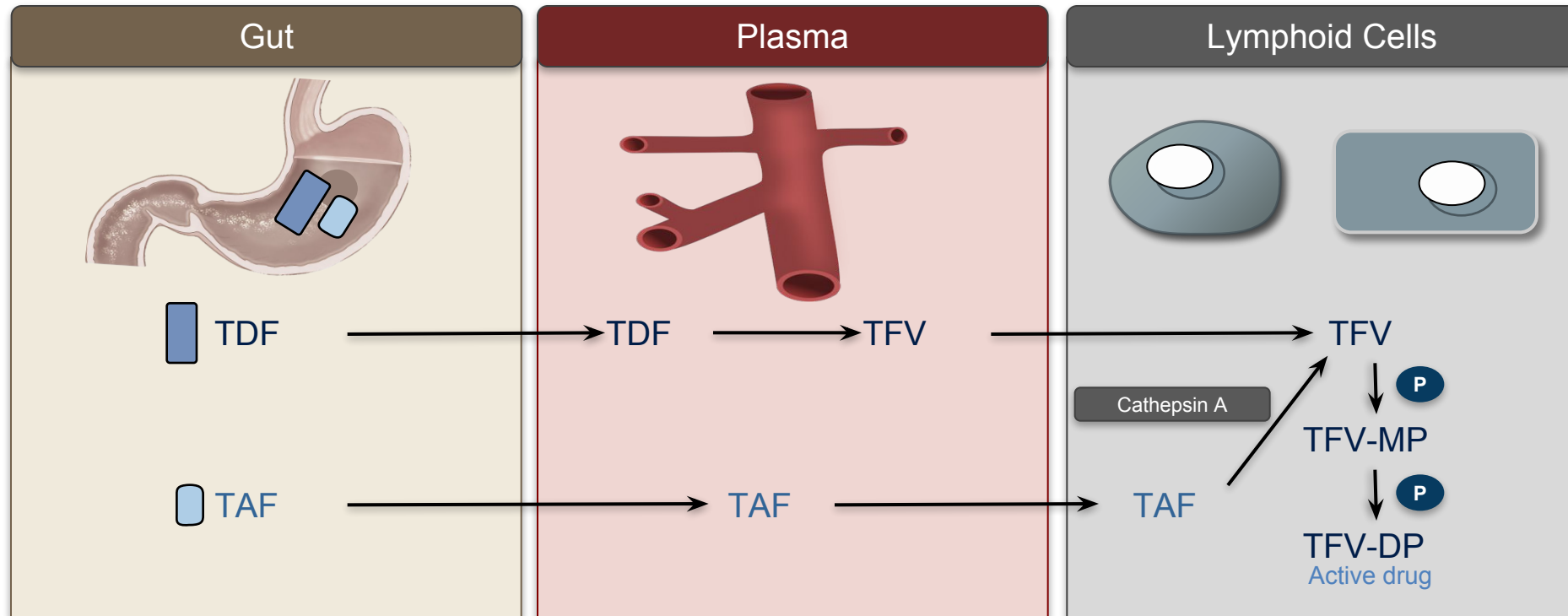
 Related article page 1

Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2018;320(4):1-18.

Recommended Initial Regimens: InSTI Plus 2 nRTIs

- Bictegravir/TAF/emtricitabine
- Dolutegravir/abacavir/lamivudine
- Dolutegravir plus TAF/emtricitabine

Tenofovir DF (TDF) Versus Tenofovir Alafenamide (TAF)



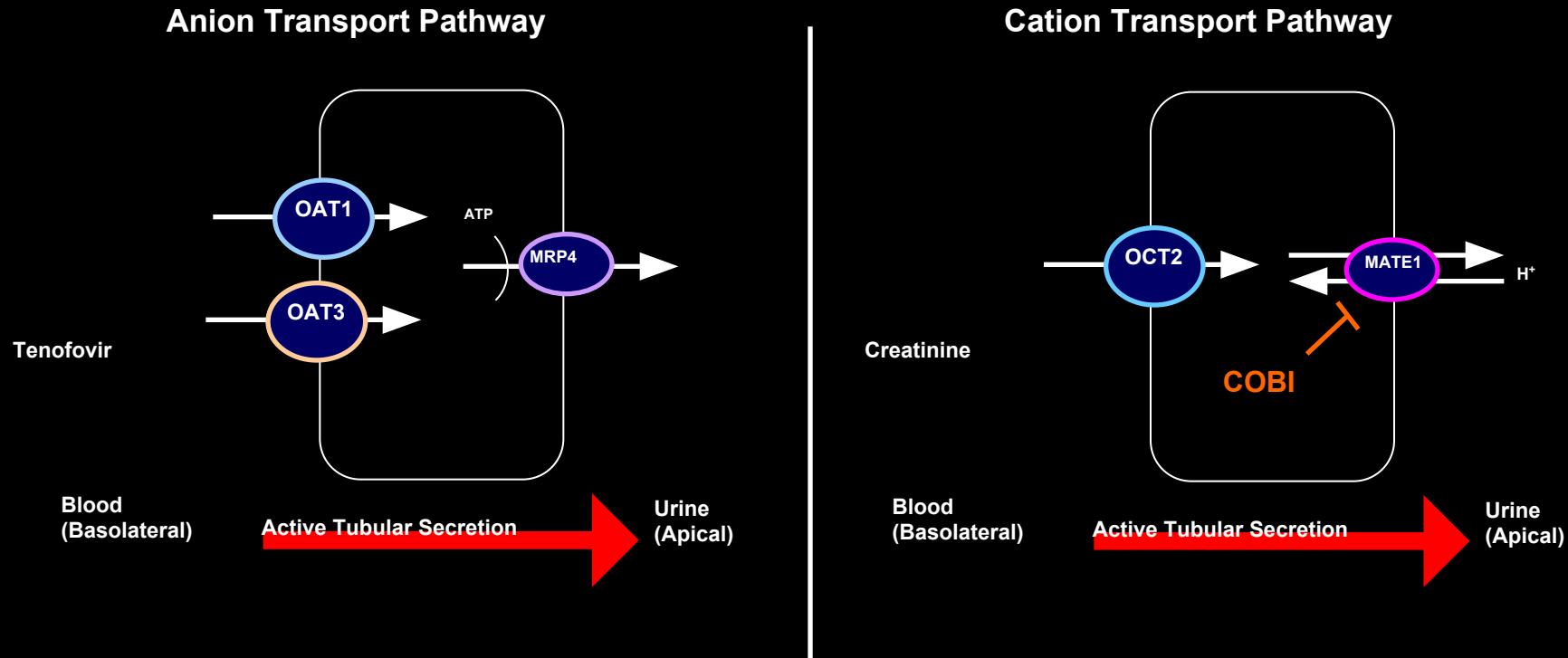
TDF = tenofovir disoproxil fumarate; TFV = tenofovir; MP = monophosphate; DP = diphosphate

ARS Question 3:

Which ARV drug is most likely to cause a 0.1 mg/dl jump in serum creatinine 1 week after starting Rx?

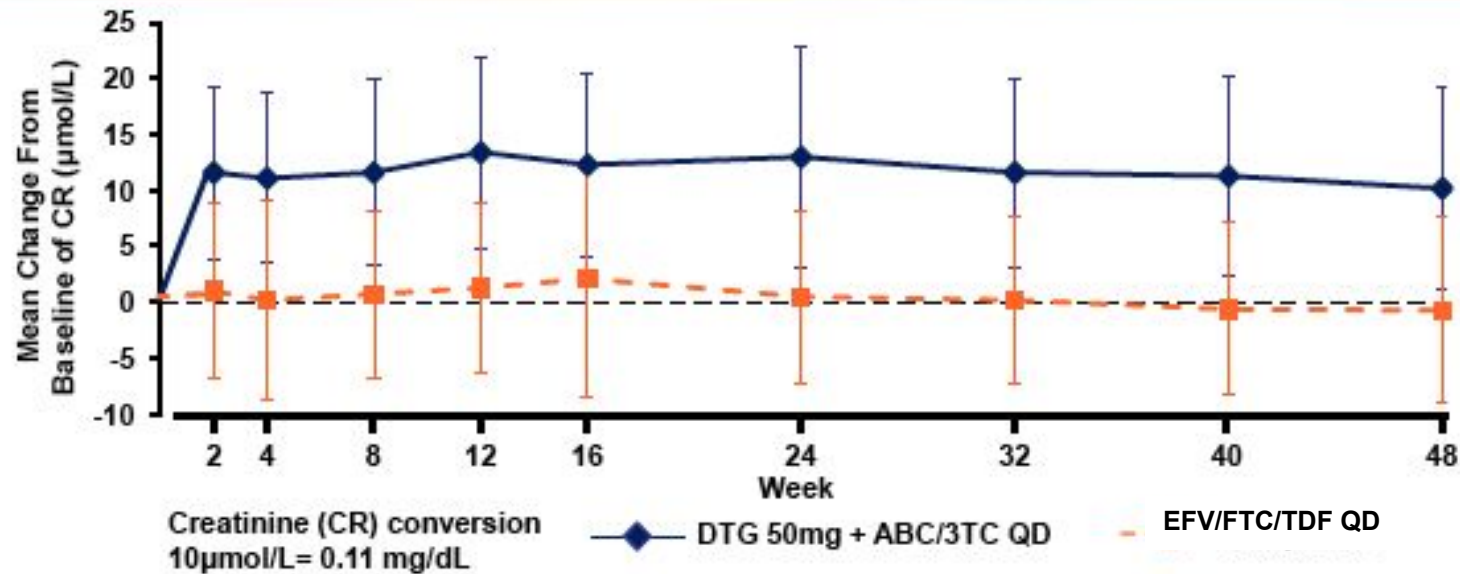
1. Bictegravir
2. Tenofovir DF
3. Tenofovir AF
4. Atazanavir
5. Emtricitabine

Tenofovir and COBI Interact with Distinct Renal Transport Pathways



- The active tubular secretion of tenofovir and the effect of COBI on creatinine are mediated by distinct transport pathways in renal proximal tubules

Renal Safety



DTG 50 mg+ABC/3TC QD

EFV/FTC/TDF QD

Ampia QD

Urine albumin/creatinine

Median change (IQR) from baseline (mg/mmol CR) to Week 48

0.00 (-0.30, 0.30)

+0.05 (-0.20, 0.30)

- Small increase in creatinine due to blockade of Cr secretion¹
- DTG does not affect actual glomerular filtration rate (GFR)¹

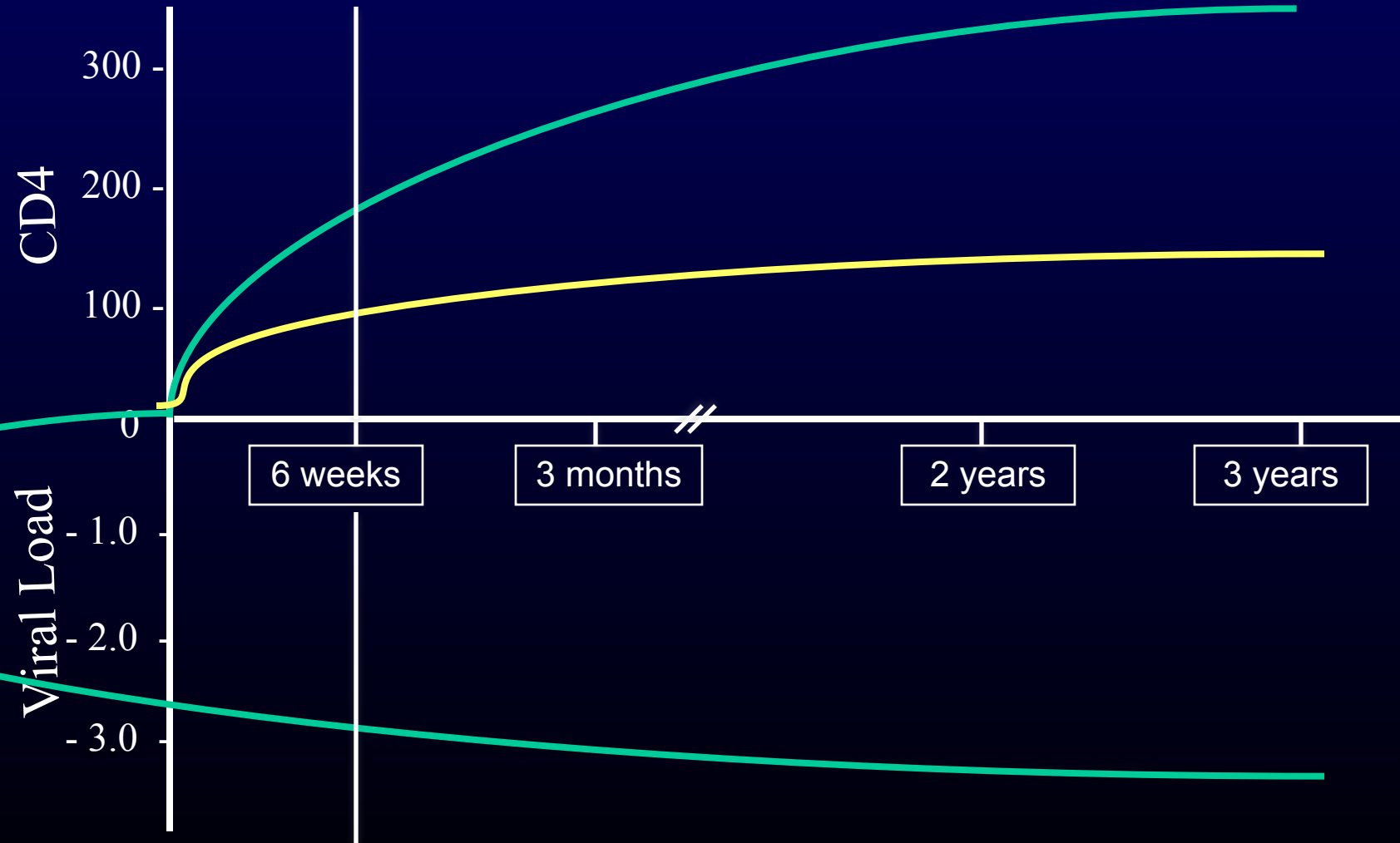
1. Koteff, J. et al. Br J Clin Pharmacol. In press; 2012 Aug.

Walmsley S, et al. 52nd ICAAC. 9-12 Sept 2012. Abstract H-556b.

Question

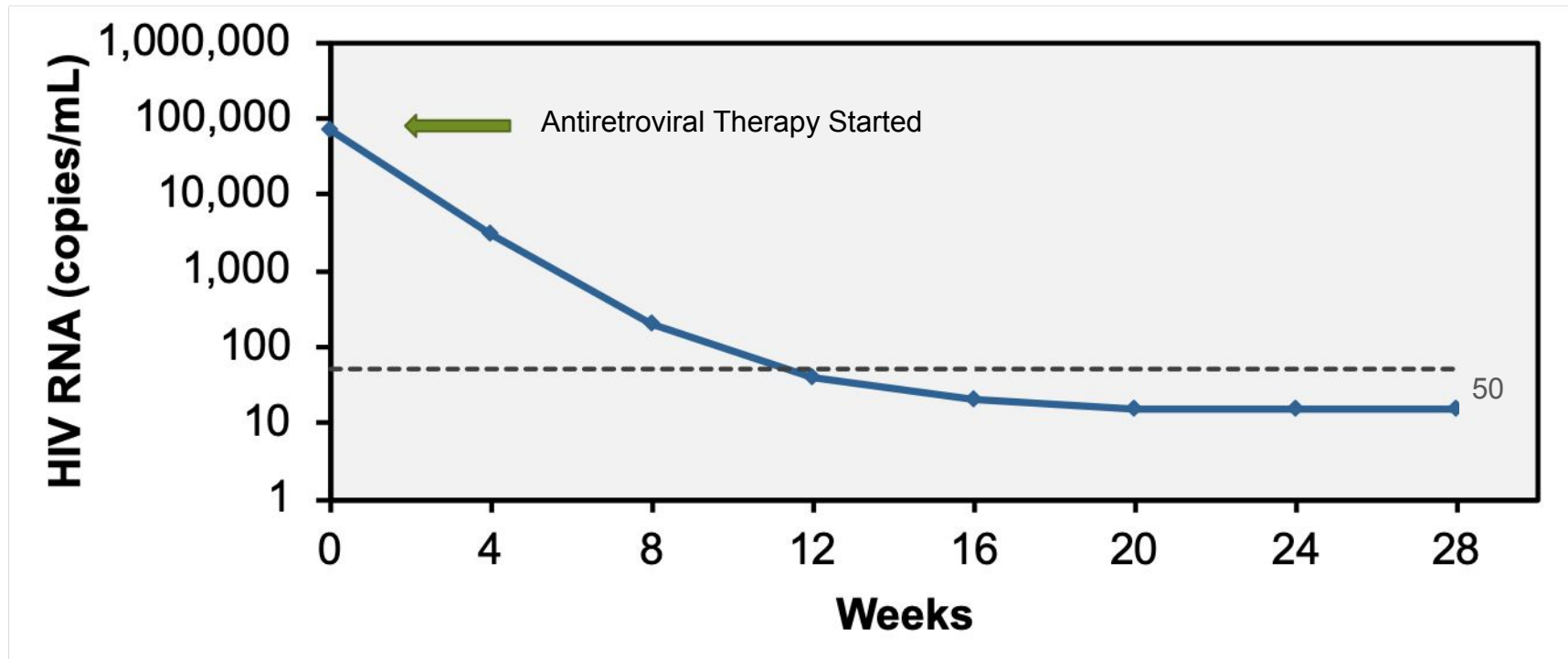
Do I change ARV regimen in a patient with a discordant CD4 count response?

What is Immunologic Failure ?



Virologic Responses on Antiretroviral Therapy

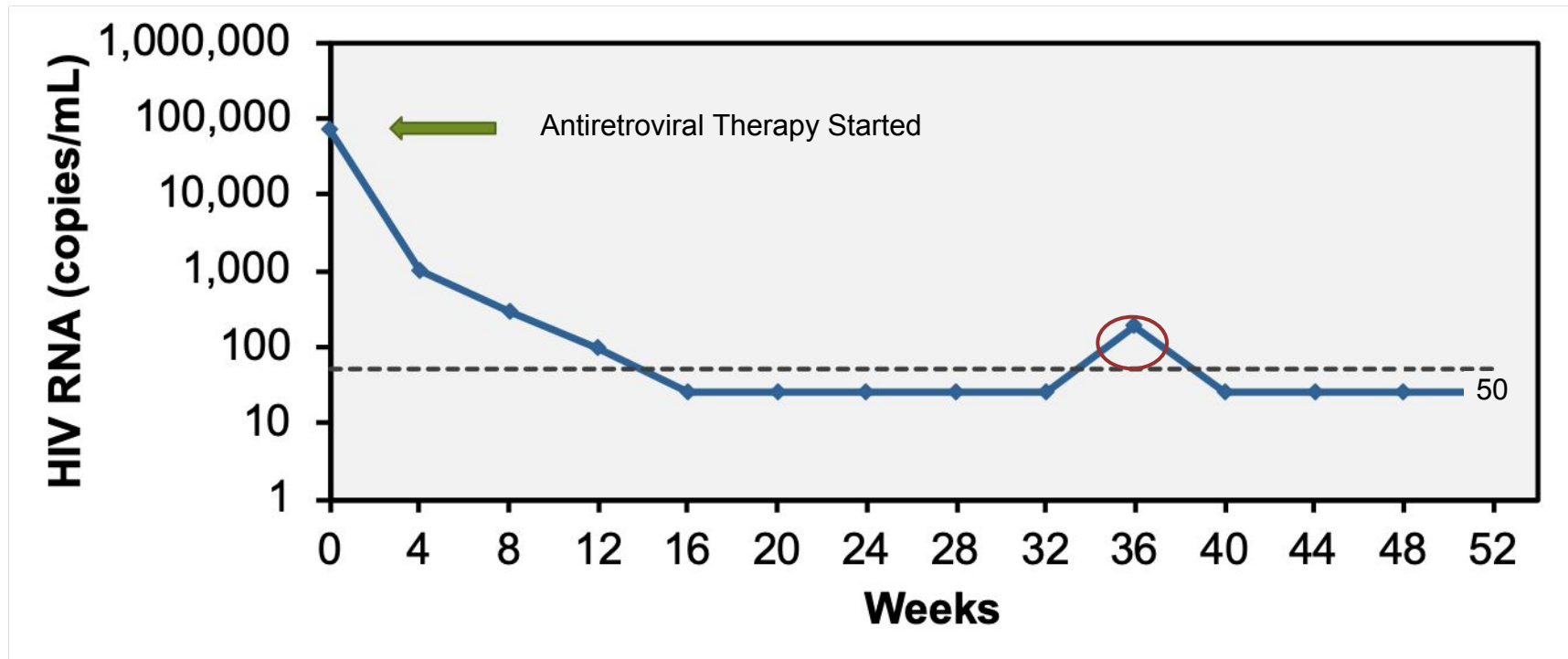
Virologic Suppression



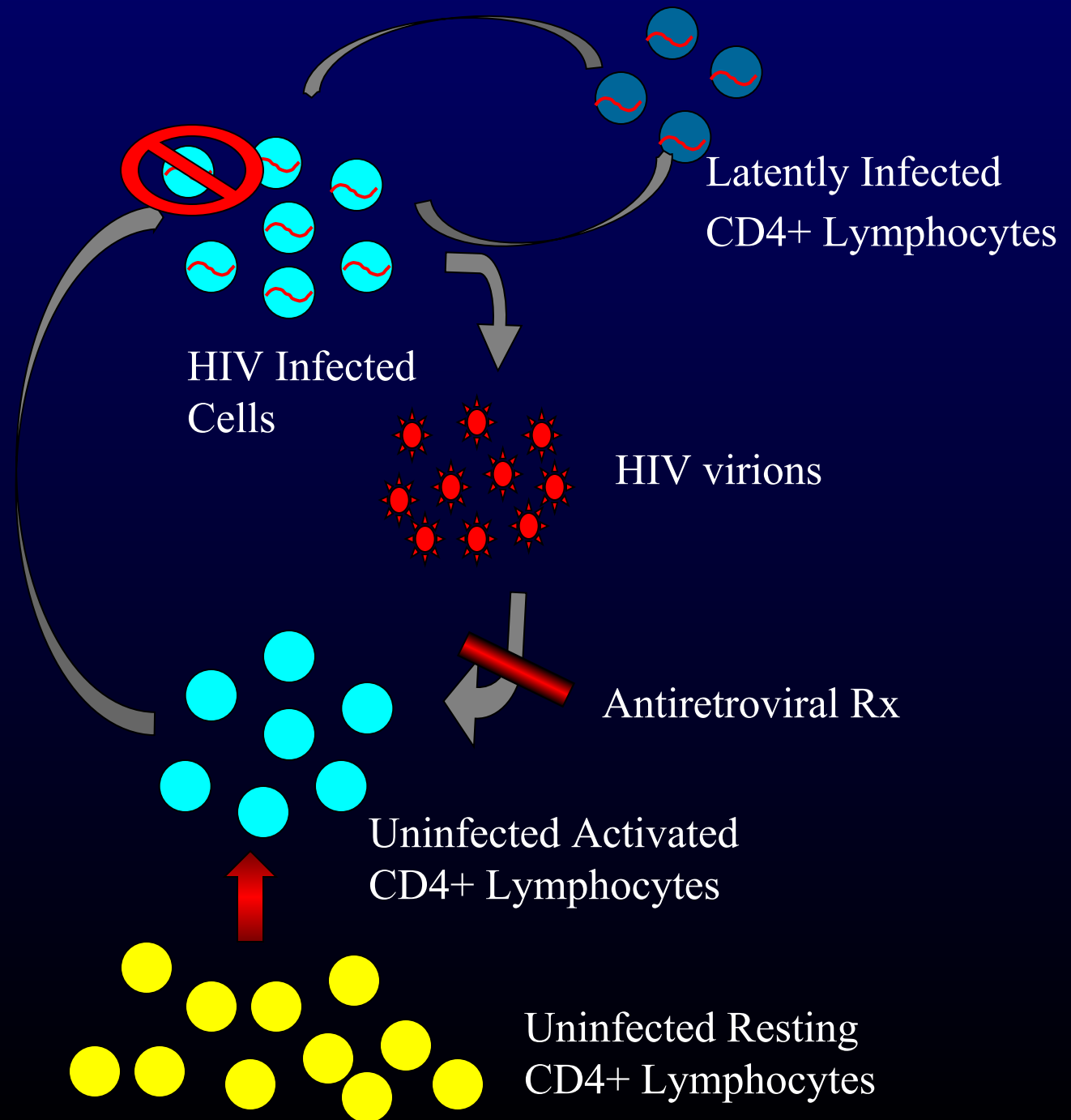
A confirmed HIV RNA level below the limit of assay detection (e.g., <48 copies/mL).

Virologic Responses on Antiretroviral Therapy

Virologic Blip



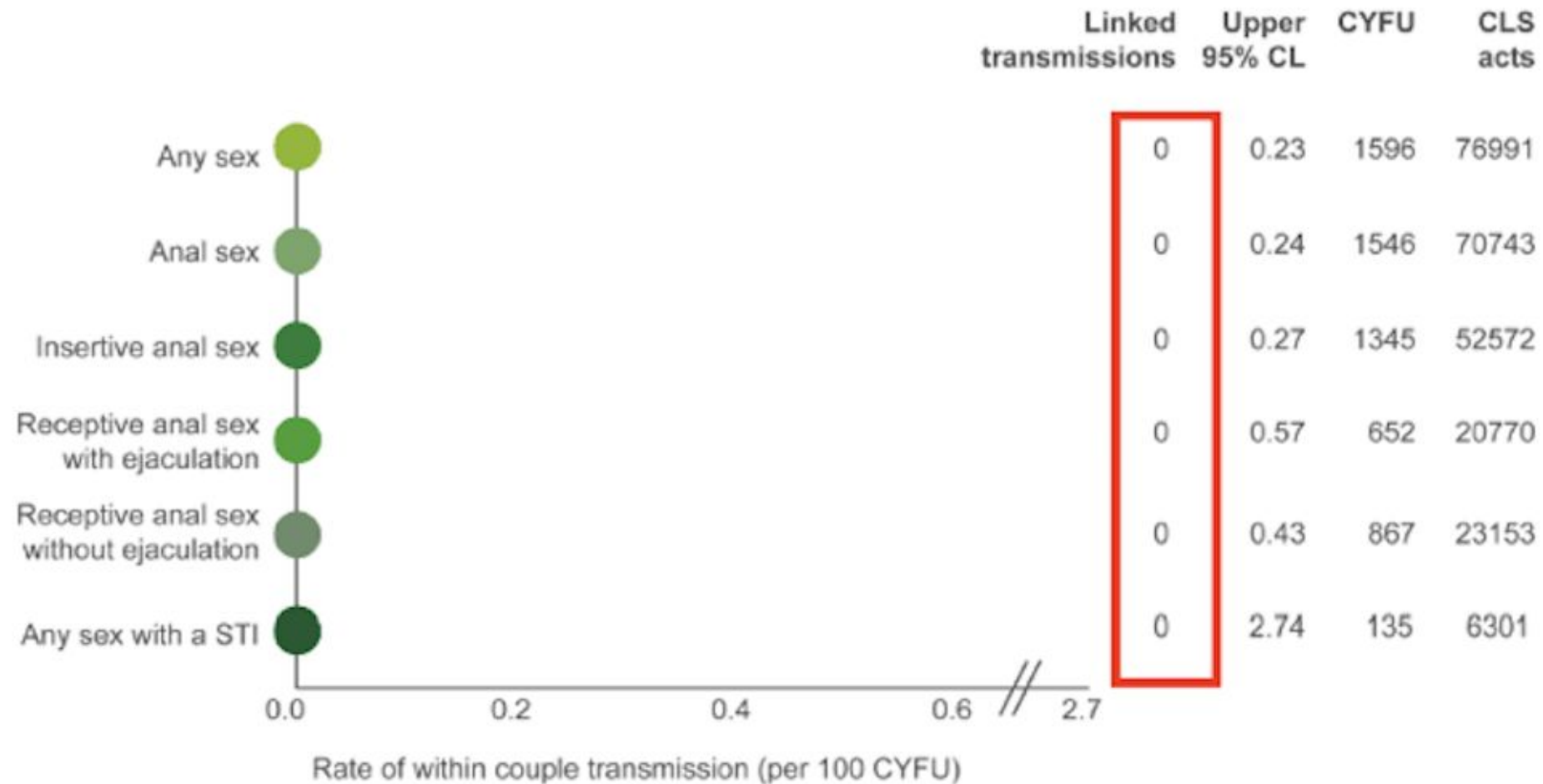
After virologic suppression, an isolated detectable HIV RNA level followed by return to virologic suppression.



Question

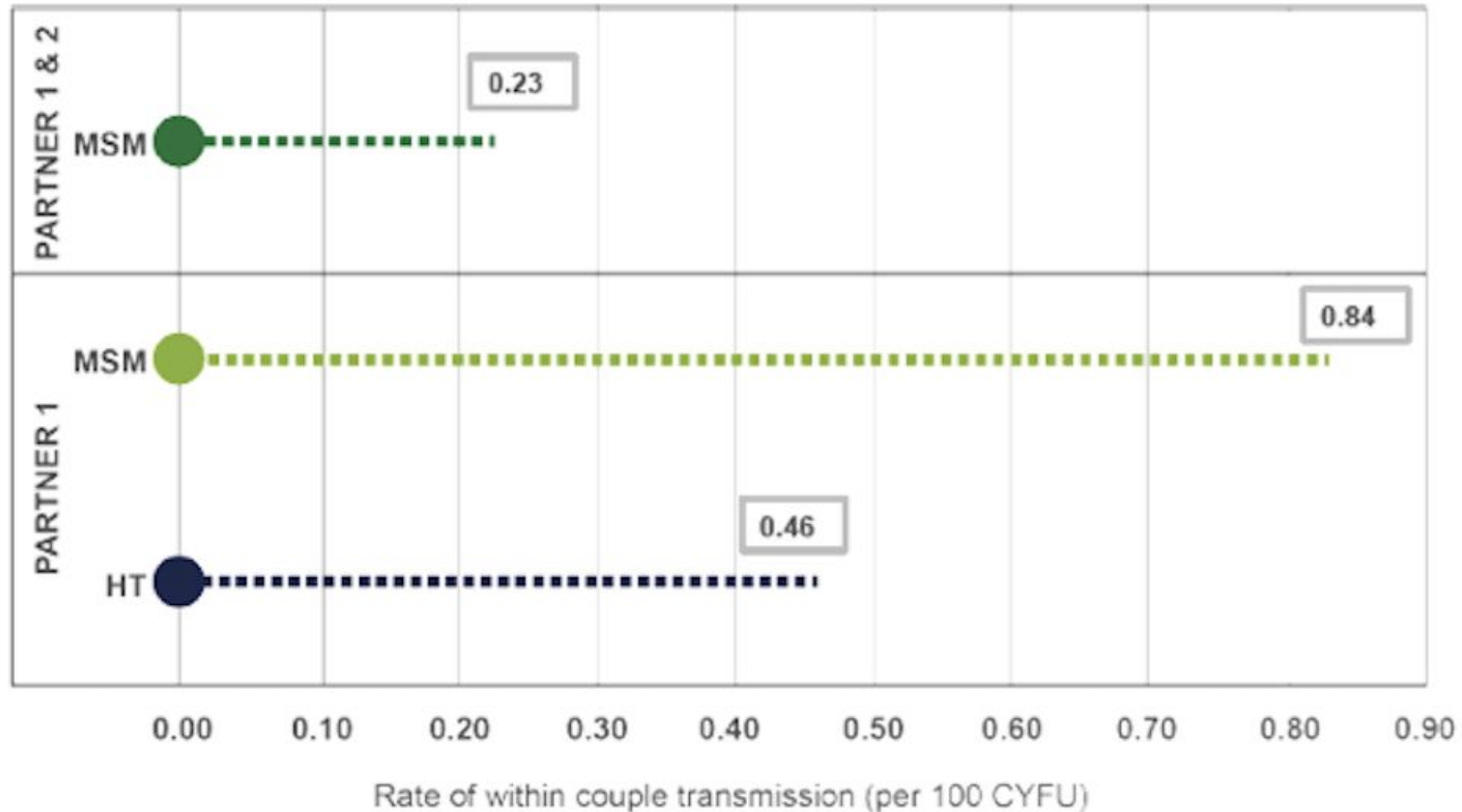
How should I counsel a patient with undetectable HIV RNA about sexual transmission risk?

Rate of HIV transmission according to sexual behaviour reported by the negative partner



Upper 95% CI around estimated rate of zero HIV transmissions: PARTNER 1 compared to PARTNER 1&2

22nd IAS, Amsterdam, Netherlands, July 23-27, 2018



U=U: Undetectable=Untransmittable



HIV & AIDS – sharing knowledge, changing lives

"The scientific evidence is clear. Someone whose HIV is undetectable does not pose an infection risk to their sexual partners."

For information on HIV you can rely on: www.aidsmap.com

#UequalsU

U=U Undetectable
Equals Untransmittable

New York State Becomes the First State in the U.S. to join U=U
September 28, 2017



Department
of Health



Dear Colleague

INFORMATION FROM CDC'S DIVISION OF HIV/AIDS PREVENTION

Dear Colleague: September 27, 2017

The International AIDS Society is proud to endorse the U=U consensus statement of the Prevention Access Campaign.

There has never been a more hopeful time in the history of AIDS. Revolutionary advances in HIV prevention and treatment can now bring the epidemics of HIV stigma and HIV to a halt.

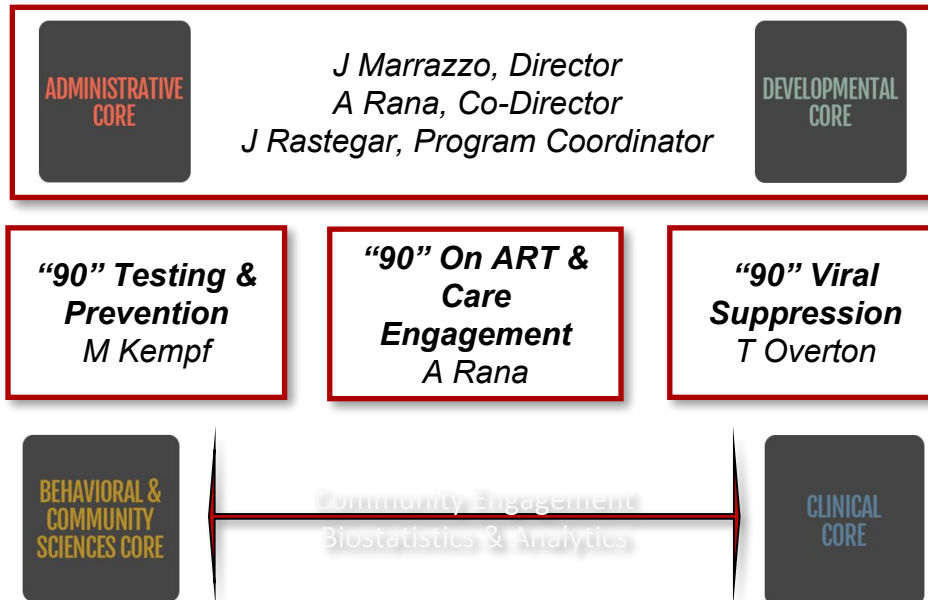


U=U

A PERSON LIVING WITH HIV
WHO HAS AN UNDETECTABLE
VIRAL LOAD DOES NOT
TRANSMIT THE VIRUS TO THEIR
PARTNERS.



'Ending HIV in Alabama' Scientific Working Group



Goal: Answer fundamental questions about HIV care in AL

- What aspects of our approach to HIV prevention and care are effective?
- What populations are not being served sufficiently or at all?
- How can we comprehensively yet cost-effectively improve access to and engagement with HIV care?
- How can we improve outreach to increase knowledge of services available?
- What broad community assets, resources, or programs are necessary to achieve these goals?

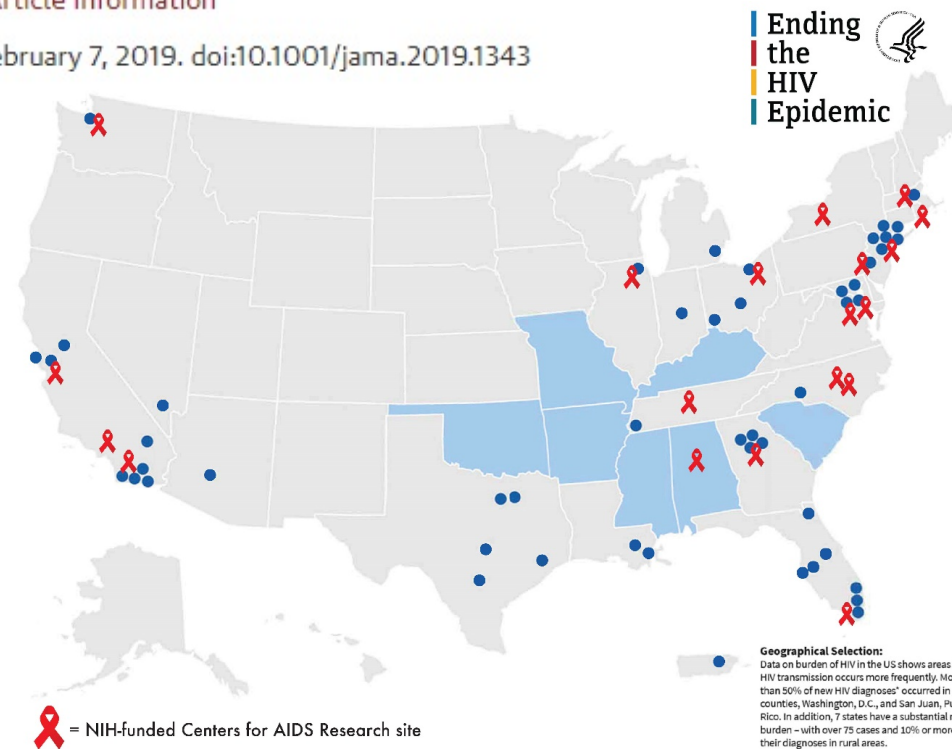
February 7, 2019

Ending the HIV Epidemic A Plan for the United States

Anthony S. Fauci, MD¹; Robert R. Redfield, MD²; George Sigounas, MS, PhD³; et al

» [Author Affiliations](#) | [Article Information](#)

JAMA. Published online February 7, 2019. doi:10.1001/jama.2019.1343



NIH to Fund HIV Care and Prevention Research in Vulnerable Southern U.S. Communities

New Program Leverages Partnerships to Discover Sustainable, Scalable Interventions
December 11, 2018



A variety of antiretroviral drugs used to treat HIV infection.

Credit: NIAID

Status Neutral Continuum of HIV Care: Prevention and Treatment

