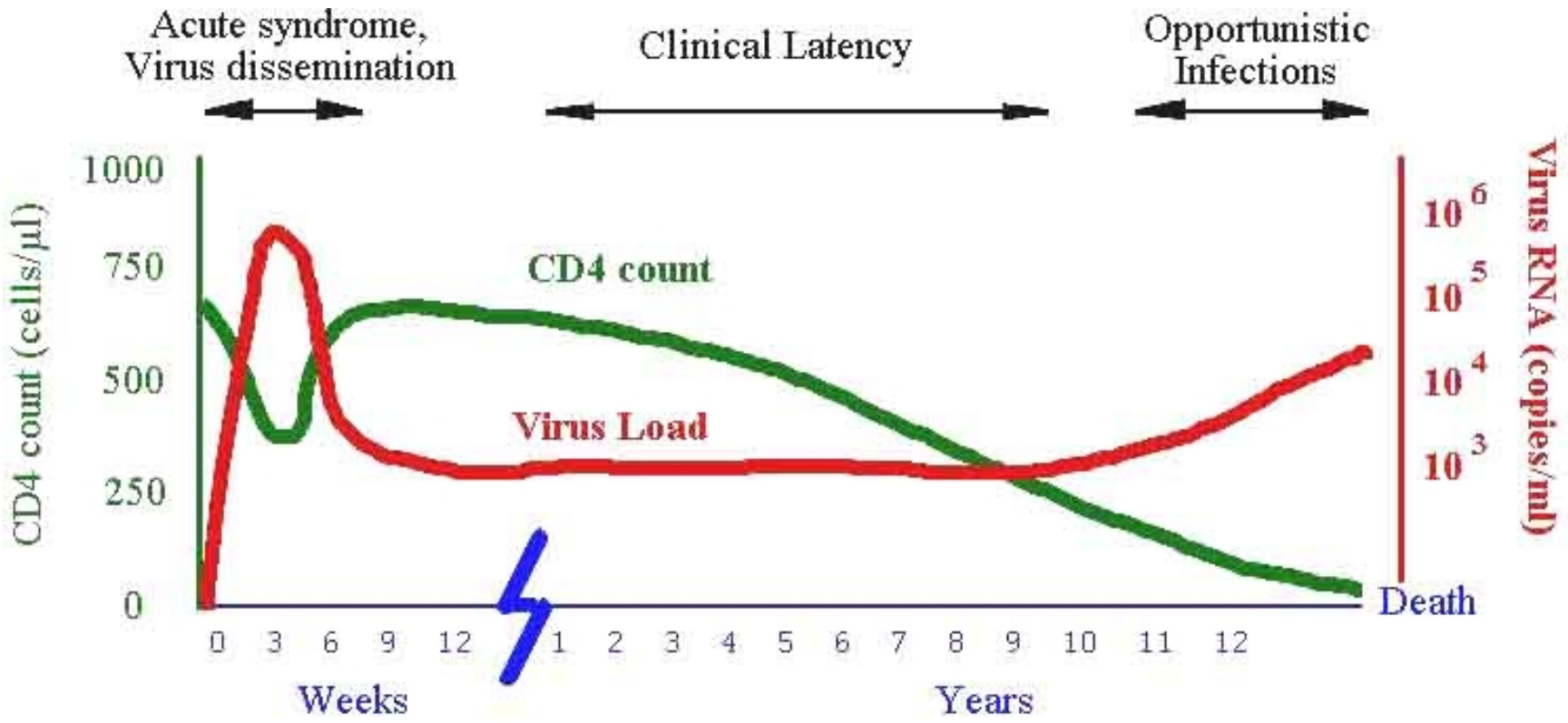
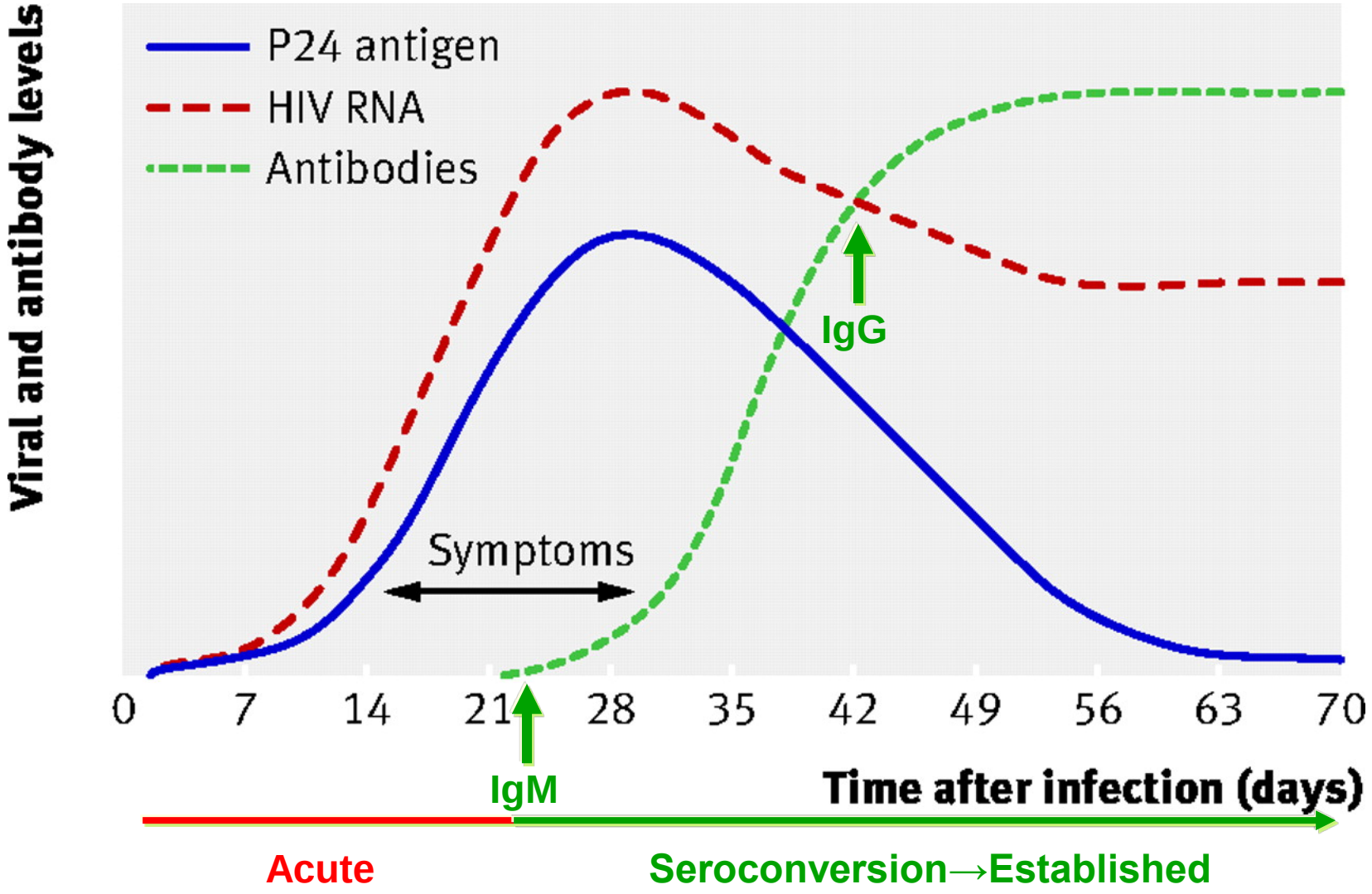
Overcoming the Challenges and Barriers to Implementing the HIV Diagnostic Testing Algorithm in your Laboratory

2016 HIV Diagnostics Conference

HIV Progression and Immune Response

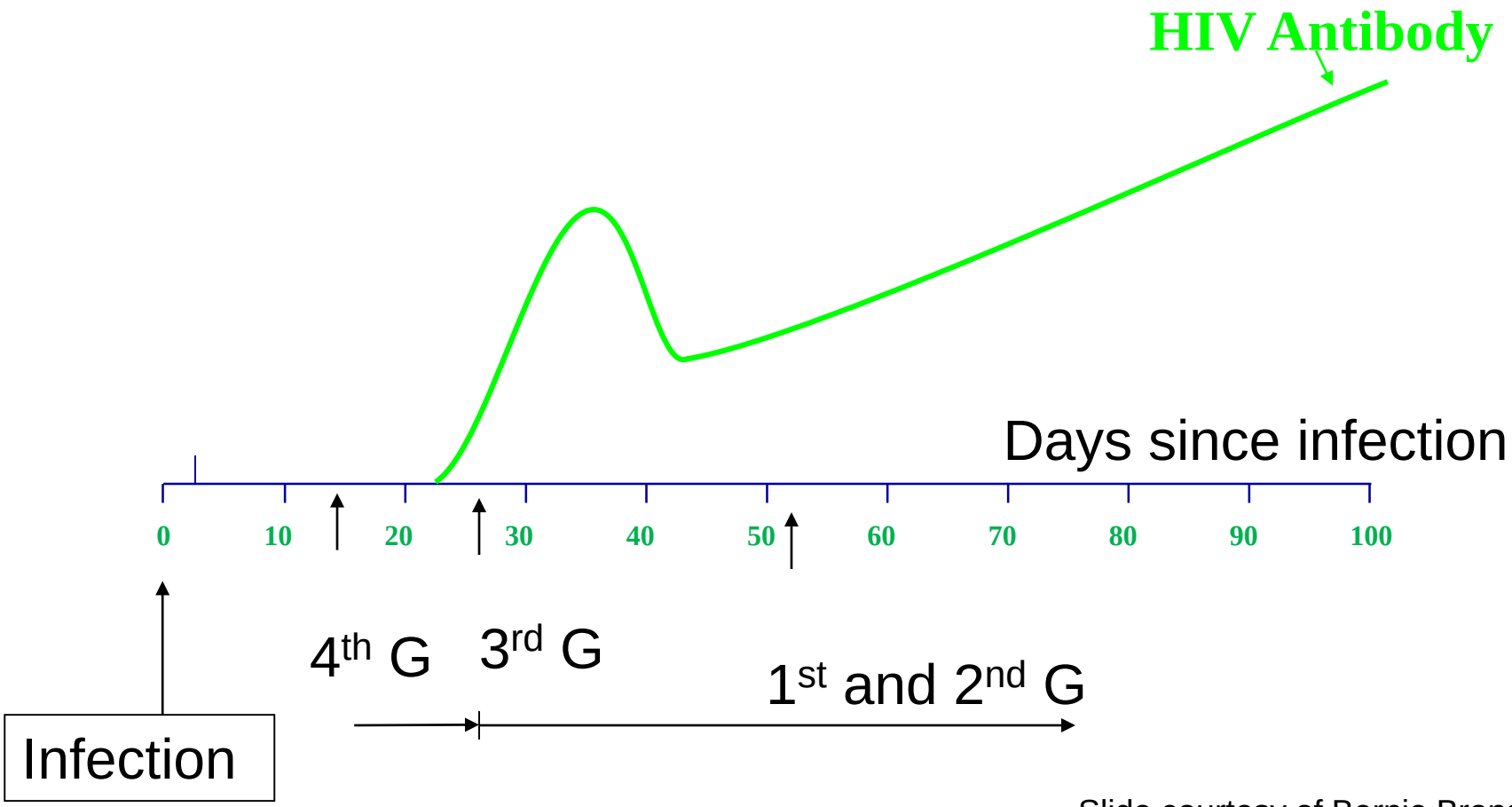


Progression of HIV Viral Markers



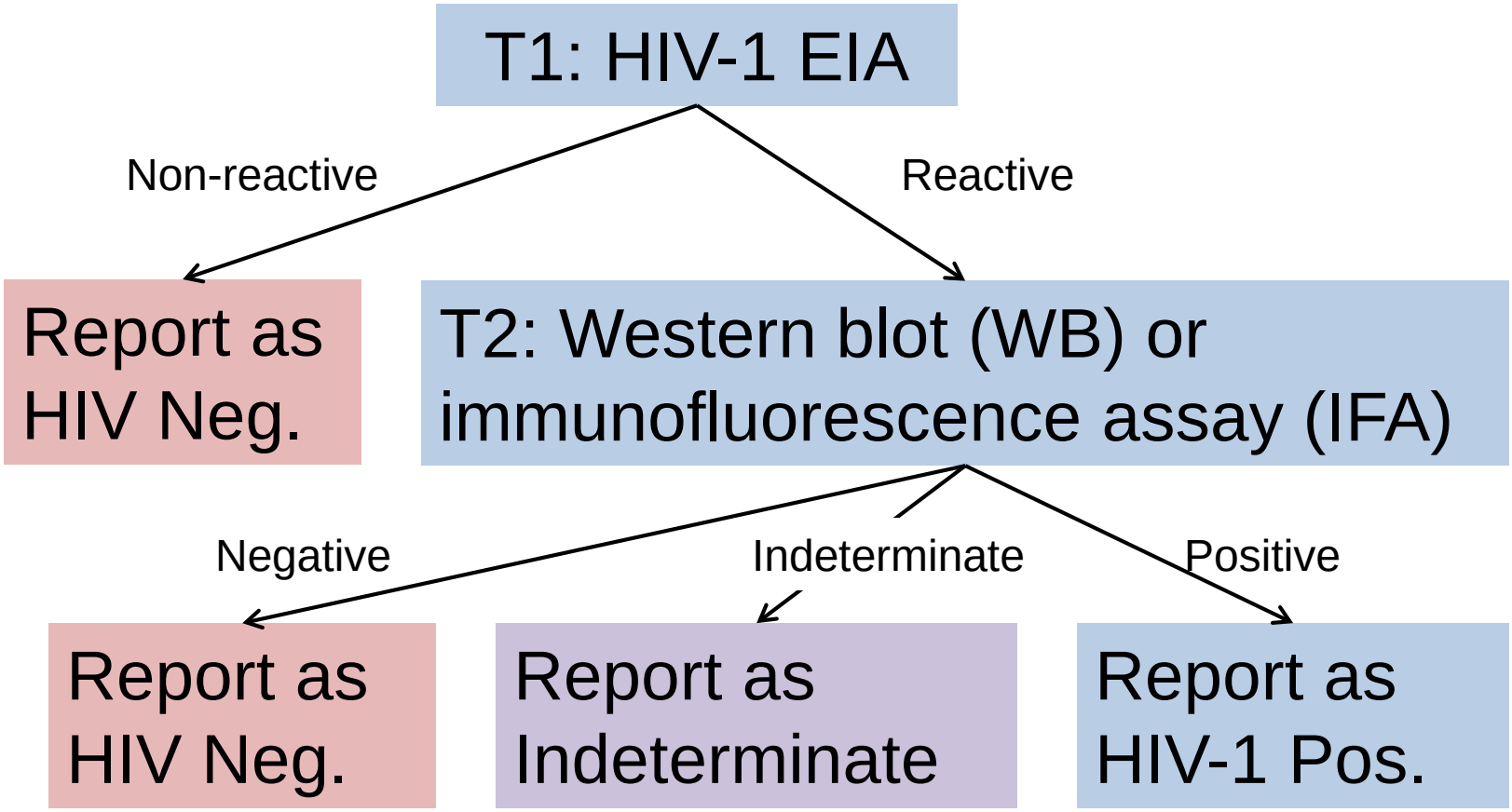
Das G et al. BMJ 2010;341:bmj.c4583

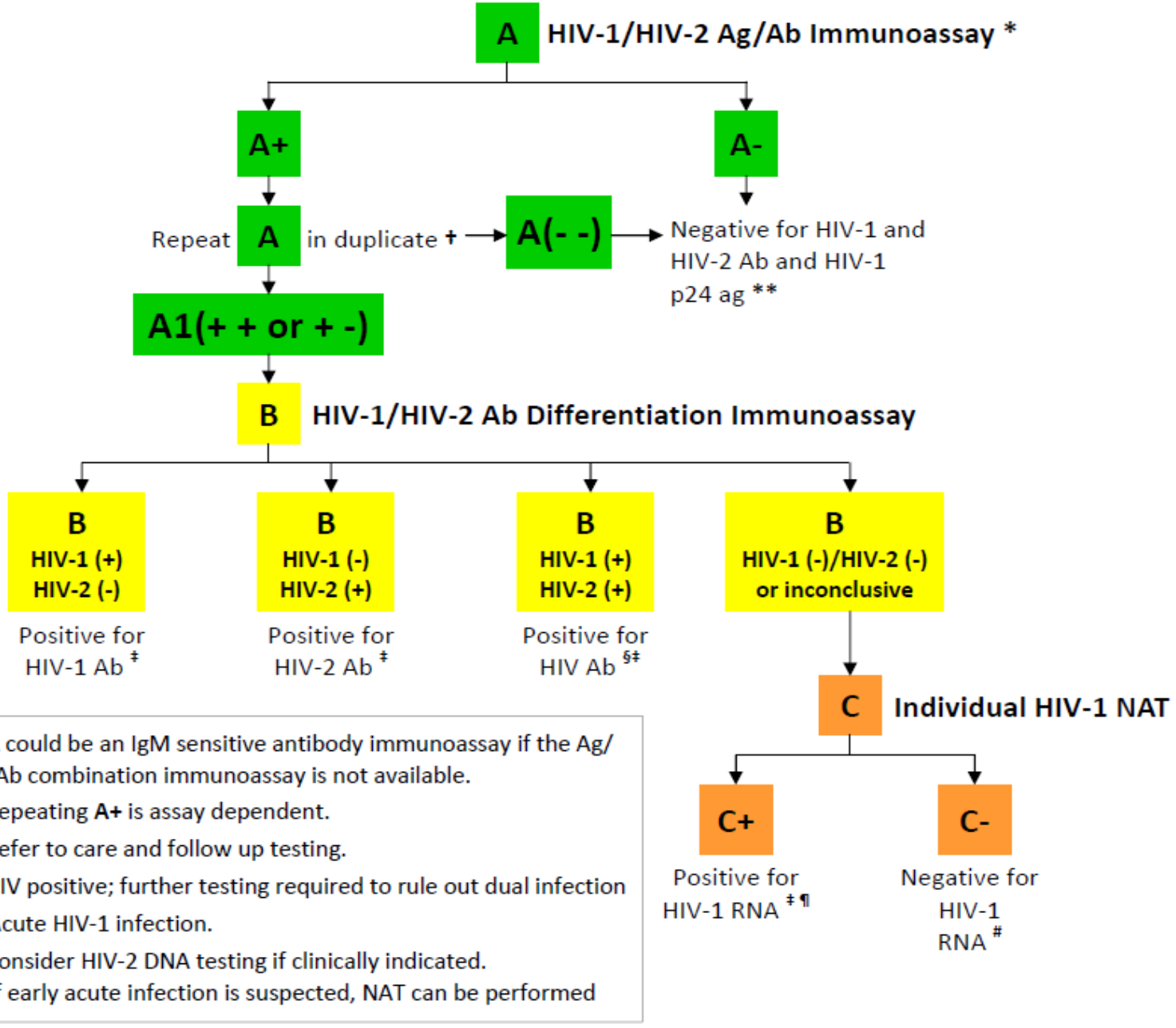
HIV Progression and Detectable Response



Slide courtesy of Bernie Branson

1989: CDC recommended two-test algorithm for HIV diagnosis




A HIV-1/HIV-2 Ag/Ab Immunoassay *
A+
A-
Repeat A in duplicate †
A(- -)
Negative for HIV-1 and HIV-2 Ab and HIV-1 p24 ag **
A1(+ + or + -)
B HIV-1/HIV-2 Ab Differentiation Immunoassay
B HIV-1 (+) HIV-2 (-)
Positive for HIV-1 Ab ‡
B HIV-1 (-) HIV-2 (+)
Positive for HIV-2 Ab ‡
B HIV-1 (+) HIV-2 (+)
Positive for HIV Ab §‡
B HIV-1 (-)/HIV-2 (-) or inconclusive
C Individual HIV-1 NAT
C+
Positive for HIV-1 RNA ‡ ¶
C-
Negative for HIV-1 RNA #
* A could be an IgM sensitive antibody immunoassay if the Ag/Ab combination immunoassay is not available.
† Repeating A+ is assay dependent.
‡ Refer to care and follow up testing.
§ HIV positive; further testing required to rule out dual infection
¶ Acute HIV-1 infection.
# Consider HIV-2 DNA testing if clinically indicated.
** If early acute infection is suspected, NAT can be performed

4th Generation Ag/Ab Test

- ARCHITECT HIV Ag/Ab Combo (Abbott) Detects HIV-1 p24 Ag, HIV-1 and HIV-2 antibodies
- GS HIV Ag/Ab Combo EIA (Bio-Rad) Detects HIV-1 p24 Ag, HIV-1 and HIV-2 antibodies
- BioPlex 2200 HIV Ag-Ab (BioRad) detects and differentiates HIV-1 Ag, HIV-1 Ab and HIV-2 Ab

- Reactive result:
  - Preliminary positive
  - Supplemental testing required according to current algorithm

Why did we need new HIV testing strategies/algorithms?

- Laboratory algorithm established by CDC and APHL (ASTPHLD) in the late 1980's
  - Over 20 years later remains largely unchanged
- More is known about

  the disease
  - HIV-1 and HIV-2
  - Window Period
- Evolving technology
  - Tests recently approved by FDA are not included
  - Availability of rapid tests
  - Increased sensitivity of screening assays
    - Western blot and IFA now less sensitive than some screening assays which they are intended to "confirm"

Continued: Why do we need new HIV testing strategies/algorithms?

- Evolving technology
  - Tests recently approved by FDA are not included
  - Availability of rapid tests
  - Increased sensitivity of screening assays
    - Western blot and IFA now less sensitive than some screening assays which they are intended to "confirm"

Relative Sensitivity of Tests

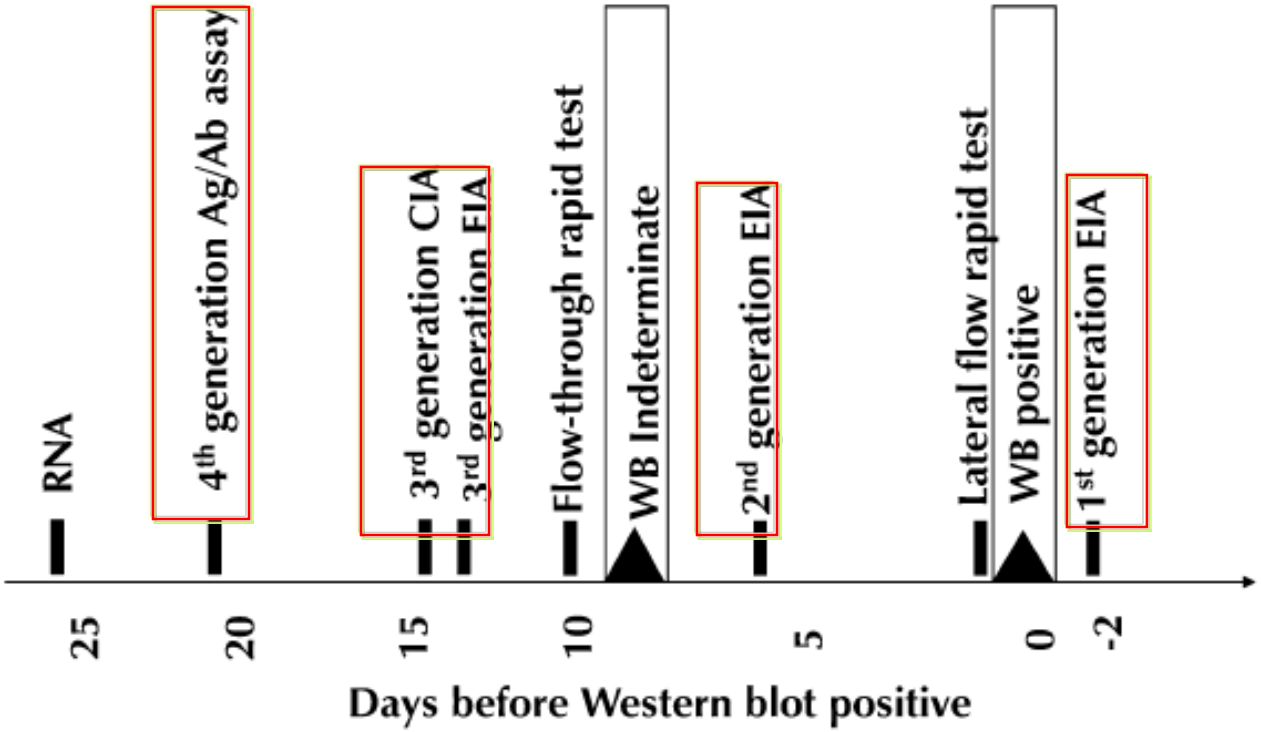


FIGURE 2. Reactivity of FDA-approved assays for HIV-1 compared with Western blot.

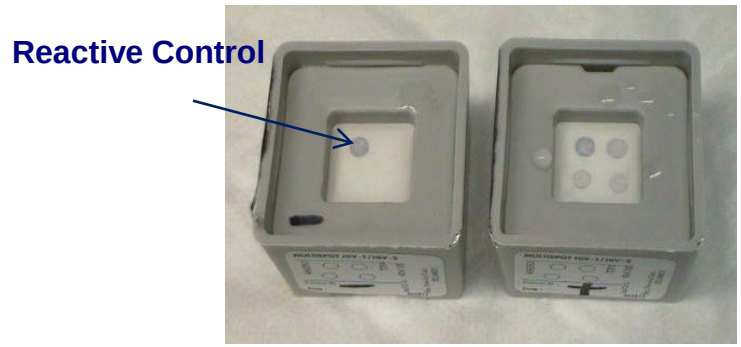
From: Branson, JAIDS, 2010, 55 (S2): S102-S105

What were we looking for from these new testing strategies?

- Resolution of indeterminates
- Ability to confirm HIV-2 infections
- Increased detection of acute infection
- Use of assays as screening or confirmatory/ supplemental tests and as part of multi-test algorithms

Multispot HIV Ab Test

- Supplemental test
  - used after a reactive 4th Gen EIA
- Replaces WB
  - More sensitive and specific than WB
  - Faster and less expensive than WB
- Will differentiate HIV-1 and HIV-2



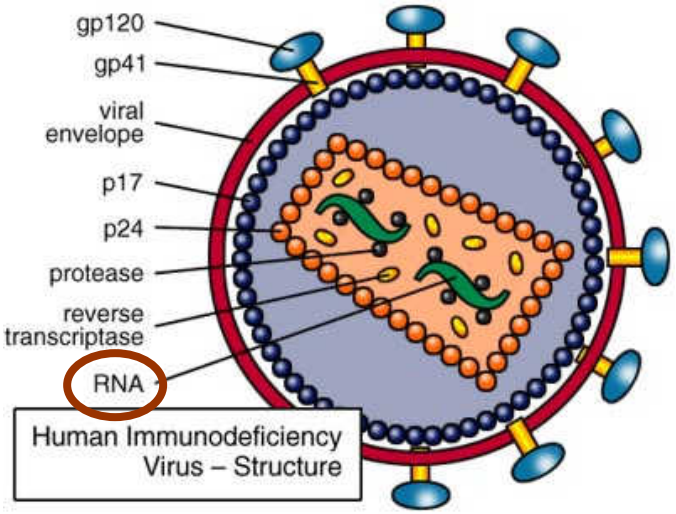
BioRad has discontinued this test as of July 2016

BioRad Geenius replaces MultiSpot

- HIV-1/HIV-2 supplemental assay
- Designed to align with the algorithm

Nucleic Acid Amplification Test for HIV-1 RNA

- Supplemental test
  - Used after a reactive EIA and a non-reactive Multispot
- Highly sensitive test which can detect the presence of viral RNA
- HIV-1 RNA/NAAT testing can detect acute HIV-1 infection



PHL Performing WB

Year of APHL Survey	Labs Reporting Performing WB
2009	78.6% (48/61)
2012	66.2% (43/65)
2015	13.5% (10/74)

CAP VMA 2016

Anti-HIV-1 Western Blot Results by Manufacturer

VM1-01

Manufacturer	Reactive/Positive No.	Reactive/Positive %	Indeterminate No.	Indeterminate %	Non-Reactive/Negative No.	Non-Reactive/Negative %
Bio-Rad GS	1	2.3	-	-	43	97.7
MP Diagnostics	-	-	-	-	15	100.0

VM1-02

Manufacturer	Reactive/Positive No.	Reactive/Positive %	Indeterminate No.	Indeterminate %	Non-Reactive/Negative No.	Non-Reactive/Negative %
Bio-Rad GS	85	98.8	1	1.2	-	-
Calypte/Cambridge Biotech	6	100.0	-	-	-	-
Innogenetics	7	100.0	-	-	-	-
MP Diagnostics	22	100.0	-	-	-	-

VM1-03

Manufacturer	Reactive/Positive No.	Reactive/Positive %	Indeterminate No.	Indeterminate %	Non-Reactive/Negative No.	Non-Reactive/Negative %
Bio-Rad GS	-	-	-	-	43	100.0
MP Diagnostics	-	-	-	-	15	100.0

VM1-04

Manufacturer	Reactive/Positive No.	Reactive/Positive %	Indeterminate No.	Indeterminate %	Non-Reactive/Negative No.	Non-Reactive/Negative %
Bio-Rad GS	-	-	2	4.7	41	95.3
MP Diagnostics	-	-	1	6.7	14	93.3

VM1-05

Manufacturer	Reactive/Positive No.	Reactive/Positive %	Indeterminate No.	Indeterminate %	Non-Reactive/Negative No.	Non-Reactive/Negative %
Bio-Rad GS	85	97.7	1	1.1	1	1.1
Calypte/Cambridge Biotech	6	100.0	-	-	-	-
Innogenetics	7	100.0	-	-	-	-
MP Diagnostics	22	100.0	-	-	-	-

Questions?

1. What are barriers to adopting the algorithm?
2. If your lab has adopted the new algorithm, what challenges did you face?
3. What reasons can you provide to help labs abandon the western blot?
4. How has your lab overcome obstacles to the new algorithm?

Questions?

5. What recommendations would you make to labs that have not yet adopted the algorithm?

6. From data with MultiSpot, this algorithm is thought to produce fewer indeterminate results, will this hold true with Geenius? In general, does the introduction of Geenius incentivize the adoption of the algorithm or is an additional barrier?

Questions?

7. Does new instrumentation (BioPlex2200) that is able to differentiate with the screening test change your perspective of the algorithm when you consider turnaround time, cost, approved tests, and the need for verification of results?