Faculty of Medicine

Sohag University

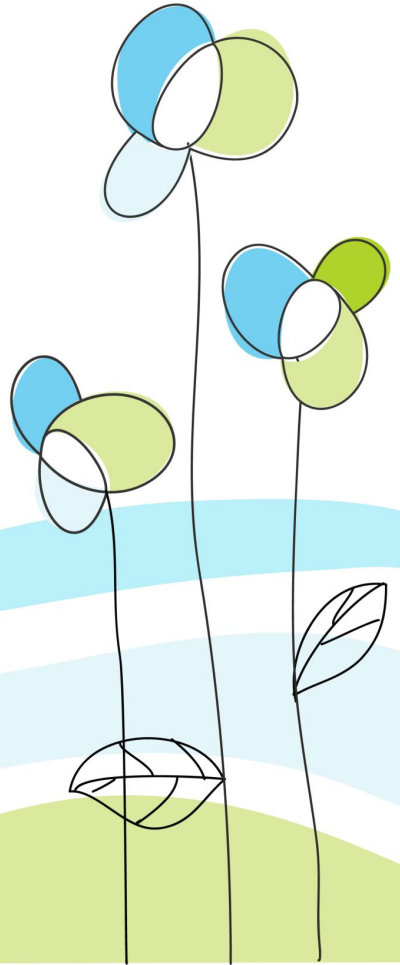
Clinical Pathology Department

Clinical Immunology

Immunological Diagnosis of

Infectious Diseases

Clinical Pathology Department – Immunology Unit



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis

Acute Hepatitis

Common Causes
- **Hepatitis Viruses (A,B, C, D, E)**
- Epstein-Barr virus
- Cytomegalovirus
- Herpes simplex virus
- Autoimmune hepatitis

Chronic Hepatitis

Common Causes
- **Post viral hepatitis B, C and D**
- Autoimmune hepatitis.
- α1 antitrypsin deficiency
- Wilson's disease.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis A Infection

1. **Chemistry** Marked ↑ serum ALT and AST (up to 100× the normal levels)
   ↑ serum alkaline phosphatase and serum bilirubin.

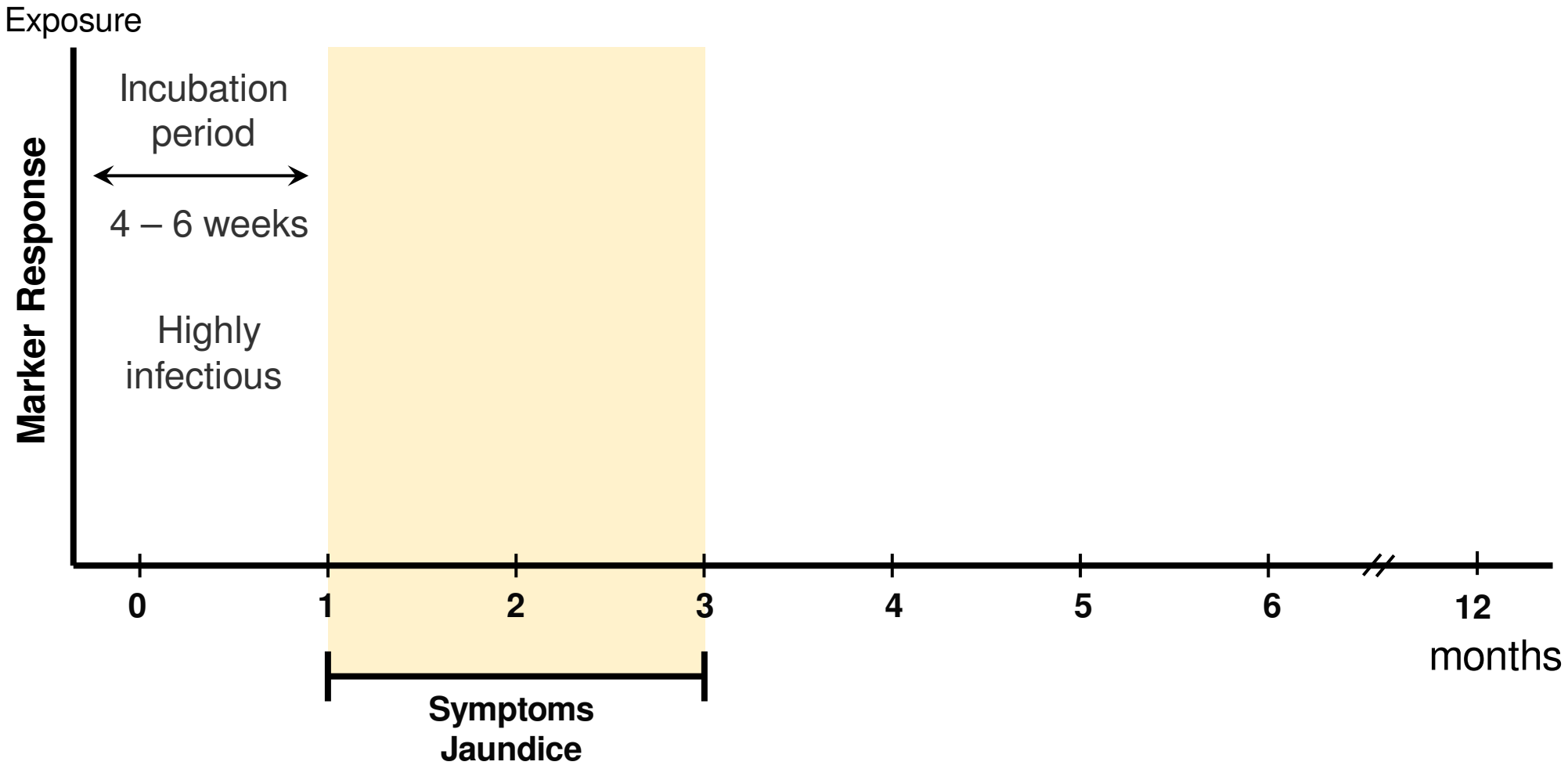
2. **Urine** Orange color, bilirubin is detected in urine.

3. **Stool** **HAV antigen:** Positive 1 – 2 weeks before the onset of disease.
   HAV PCR detection in stool (or blood by) (coincident with stool HAV Ag)

4. **Serology** Anti-HAV antibody test: the most common used
   — Positive **anti-HAV IgM** indicates recent infection.
   — Positive **anti-HAV IgG** indicates past infection and persists for life.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis A Infection



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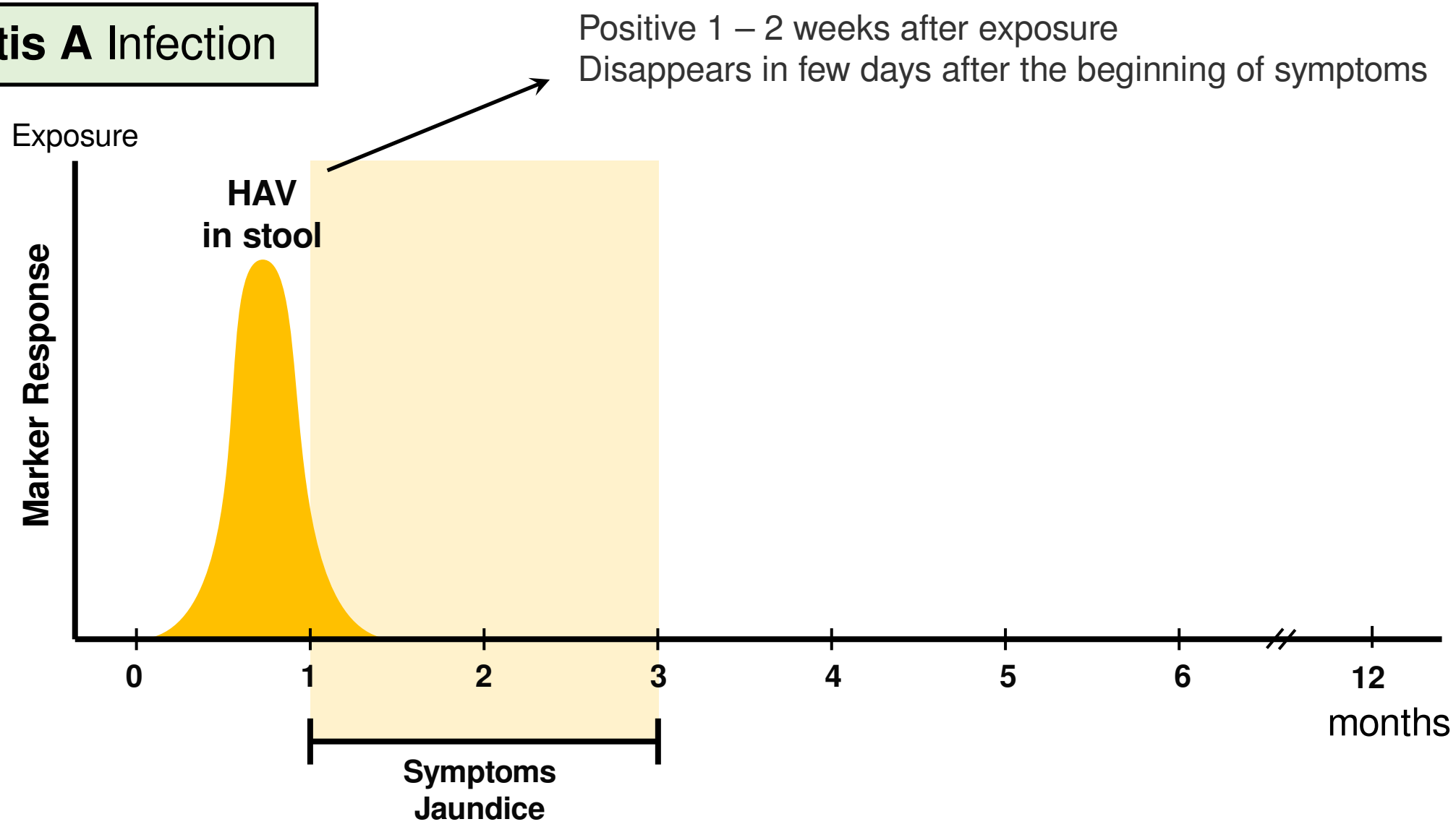
Hepatitis A Infection



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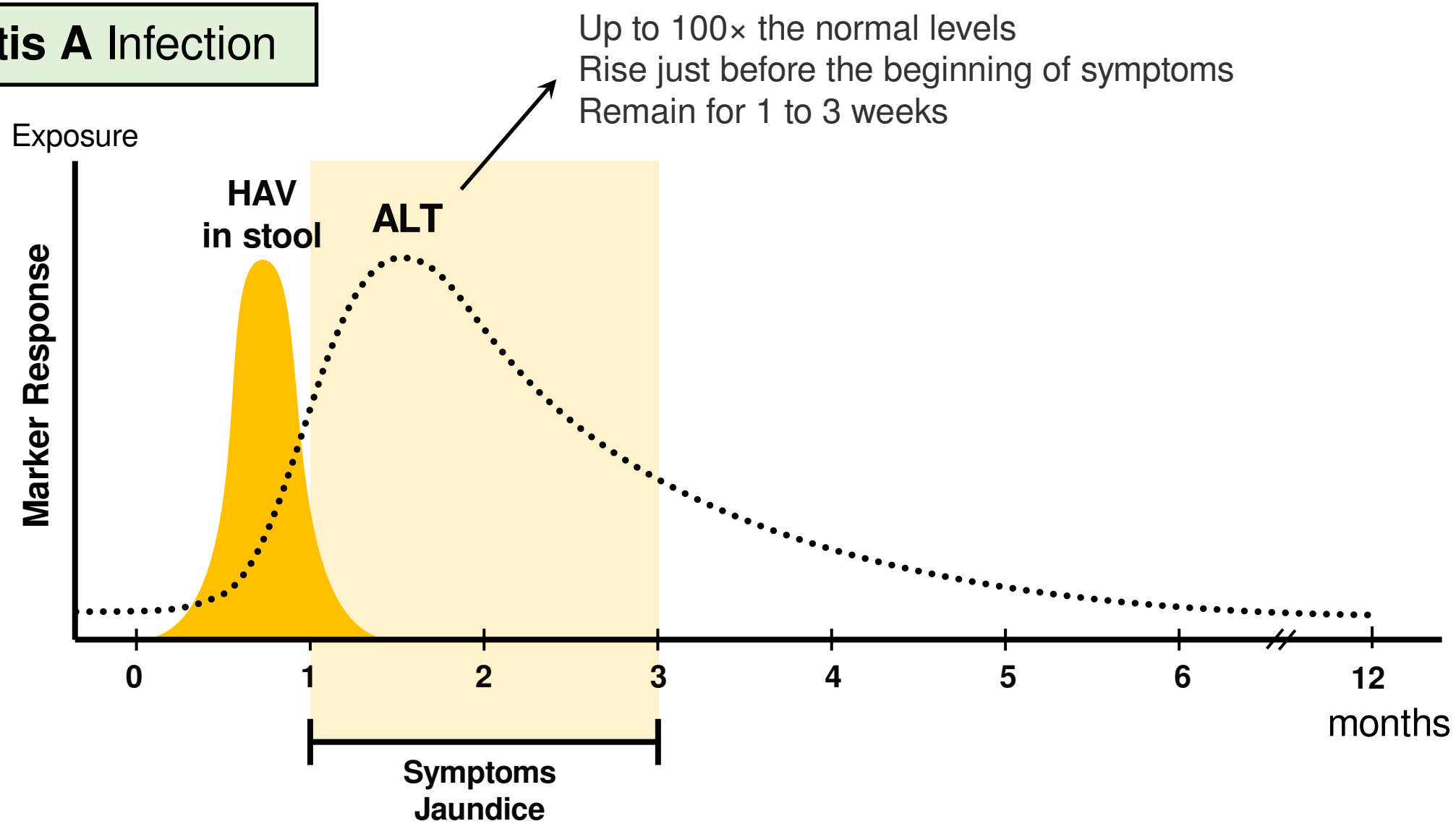
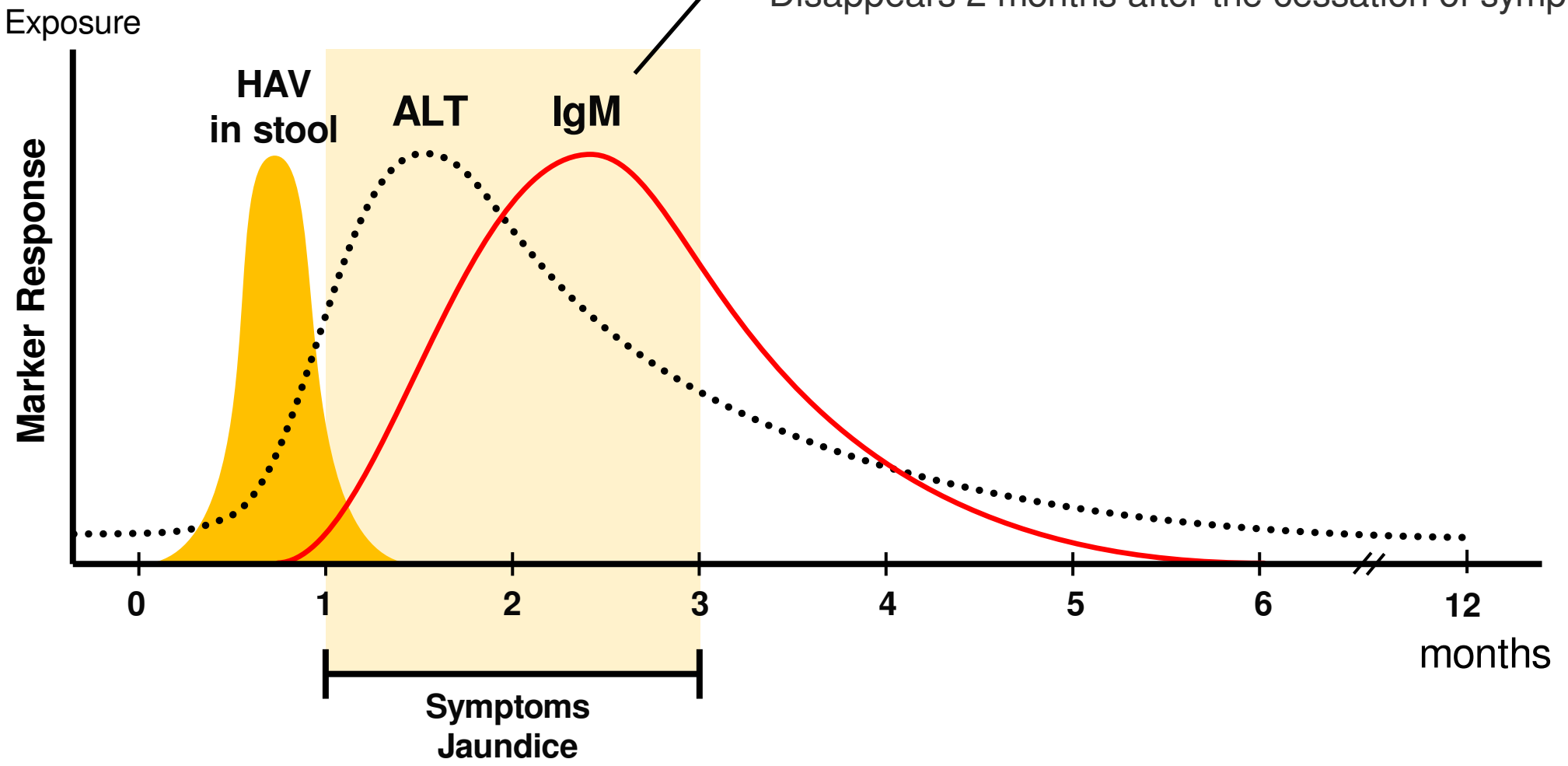
Hepatitis A Infection



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis A Infection

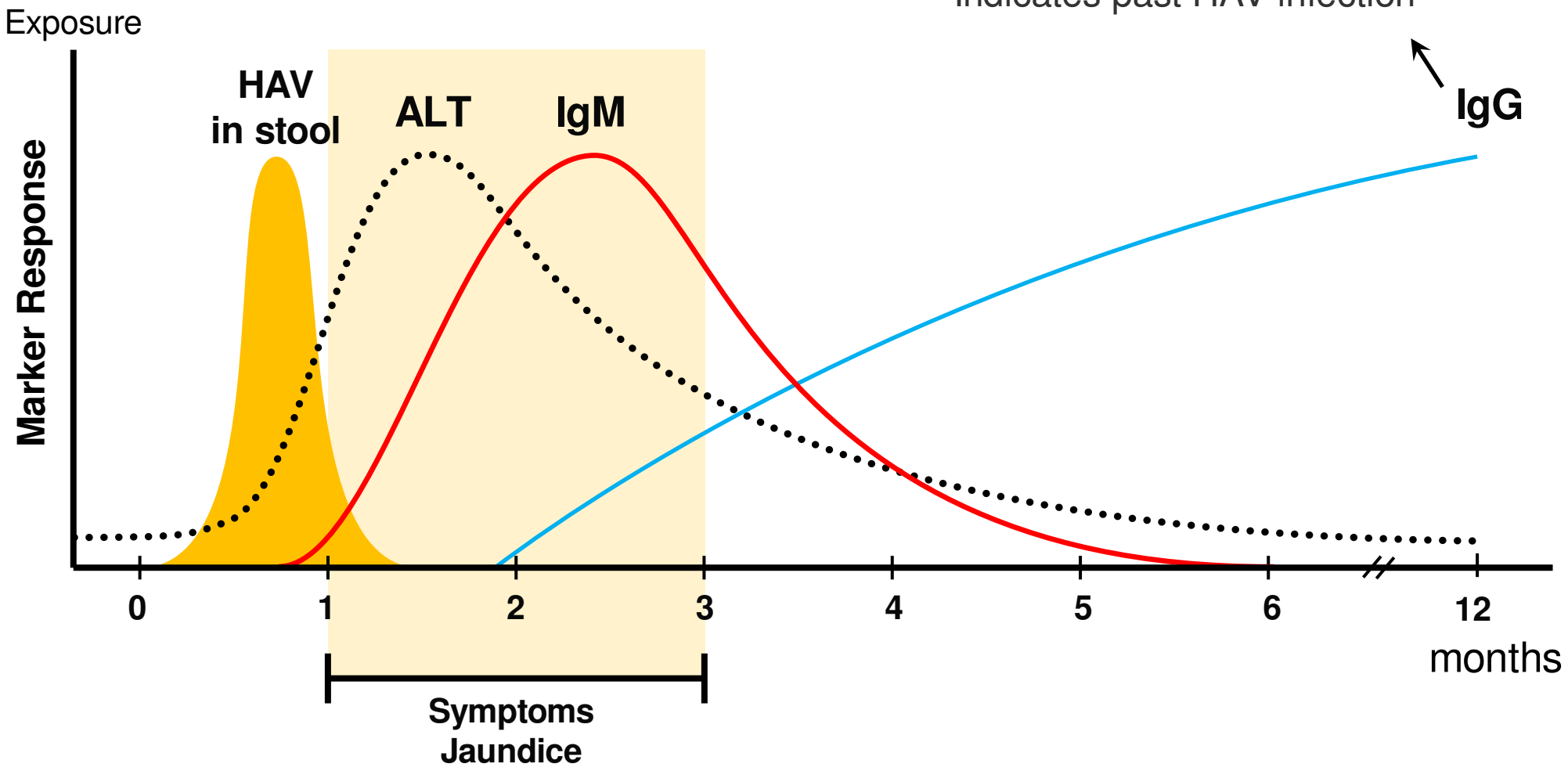
Appear 3 – 4 weeks after exposure
Appear with appearance of symptoms
Disappears 2 months after the cessation of symptoms



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis A Infection

Appear 1 – 2 weeks after appearance of IgM
Persistent throughout life
Indicates past HAV infection



Quiz

As regards diagnosis of HAV infection, which of the following is the first marker to appear?

a. Serum ALT
b. HAV antigen in stool
c. HAV IgG in serum
d. HAV IgM in serum

Quiz

As regards diagnosis of HAV infection, which of the following is the first marker to appear?

a. Serum ALT
b. HAV antigen in stool
c. HAV IgG in serum
d. HAV IgM in serum

Quiz

Which of the following is NOT TRUE as regards HAV IgG?

a. Indicates past HAV infection
b. Appear 1 – 2 weeks before appearance of IgM
c. Persistent throughout life
d. Indicates post HAV vaccination

Quiz

Which of the following is NOT TRUE as regards HAV IgG?

a. Indicates past HAV infection
b. Appear 1 – 2 weeks before appearance of IgM
c. Persistent throughout life
d. Indicates post HAV vaccination

REPORT INTERPRETATION

Test	Result		Reference Interval	
HAV Antigen in stool	Positive		Negative	
HAV IgM	10.7	Index	Non-reactive Gray zone Reactive	< 0.9 0.9 – < 1.1 ≥ 1.1
HAV Antibody (total)	7.3	COI	Non reactive Reactive	< 1.0 ≥ 1.0

REPORT INTERPRETATION

Acute HAV infection (Early)

Test	Result		Reference Interval	
HAV Antigen in stool	Positive		Negative	
HAV IgM	10.7	Index	Non-reactive Gray zone Reactive	< 0.9 0.9 – < 1.1 ≥ 1.1
HAV Antibody (total)	7.3	COI	Non reactive Reactive	< 1.0 ≥ 1.0
ALT	**280**	**IU/ml**	**0 – 40**	

REPORT INTERPRETATION

Test	Result	Reference Interval
HAV Antigen in stool	Negative	Negative
HAV IgM	22.7 Index	Non-reactive < 0.9 Gray zone 0.9 – < 1.1 Reactive ≥ 1.1
HAV Antibody (total)	13.8 COI	Non reactive < 1.0 Reactive ≥ 1.0

REPORT INTERPRETATION

Acute HAV infection

Test	Result		Reference Interval	
HAV Antigen in stool	Negative		Negative	
HAV IgM	22.7	Index	Non-reactive Gray zone Reactive	< 0.9 0.9 – < 1.1 ≥ 1.1
HAV Antibody (total)	13.8	COI	Non reactive Reactive	< 1.0 ≥ 1.0
ALT	**3250**	**IU/ml**	**0 – 40**	

REPORT INTERPRETATION

Test	Result		Reference Interval	
HAV Antigen in stool	Negative		Negative	
HAV IgM	0.2	Index	Non-reactive Gray zone Reactive	< 0.9 0.9 – < 1.1 ≥ 1.1
HAV Antibody (total)	13.8	COI	Non reactive Reactive	< 1.0 ≥ 1.0

REPORT INTERPRETATION

Past HAV infection or Post HAV vaccination

Test	Result		Reference Interval	
HAV Antigen in stool	Negative		Negative	
HAV IgM	0.2	Index	Non-reactive Gray zone Reactive	< 0.9 0.9 – < 1.1 ≥ 1.1
HAV Antibody (total)	13.8	COI	Non reactive Reactive	< 1.0 ≥ 1.0
ALT	**18**	**IU/ml**	**0 – 40**	

I. Laboratory Diagnosis of **Viral Hepatitis**

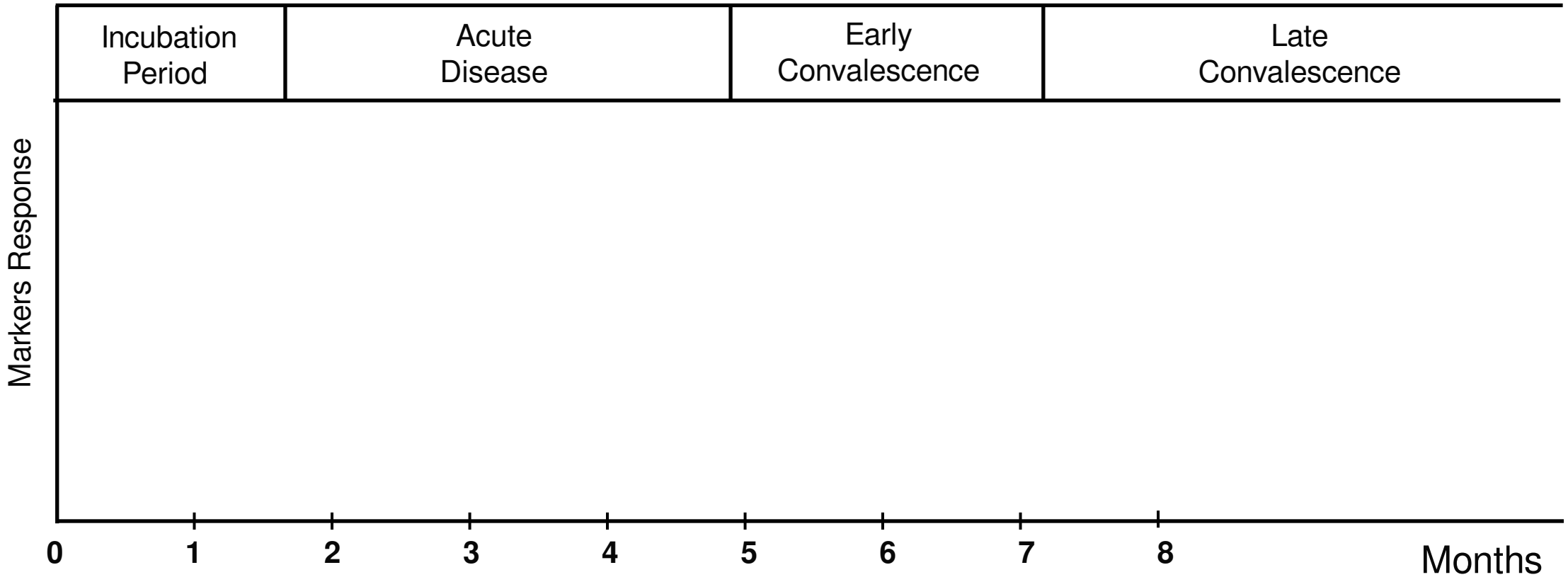
Hepatitis B Infection

1. **Blood Chemistry:**
   - Elevation of serum ALT, AST, ALP and bilirubin.
2. **Serological Tests:** (Hepatitis B Markers)
   - **Antigens:** HBsAg and HBeAg
   - **Antibodies:** anti-HBc IgM, anti-HBc IgG, anti-HBs, anti-HBe
3. **HBV DNA by PCR**
   - PCR assess HBV DNA viral load blood which is a measure of viral replication in the liver.
   - Indicator of chronic HBV infection 6 months after diagnosis.
   - Monitor response to therapy.
4. **HBV Genotype**
   - Identify mutations associated with anti-viral resistance.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers | **Acute** followed by **Recovery**



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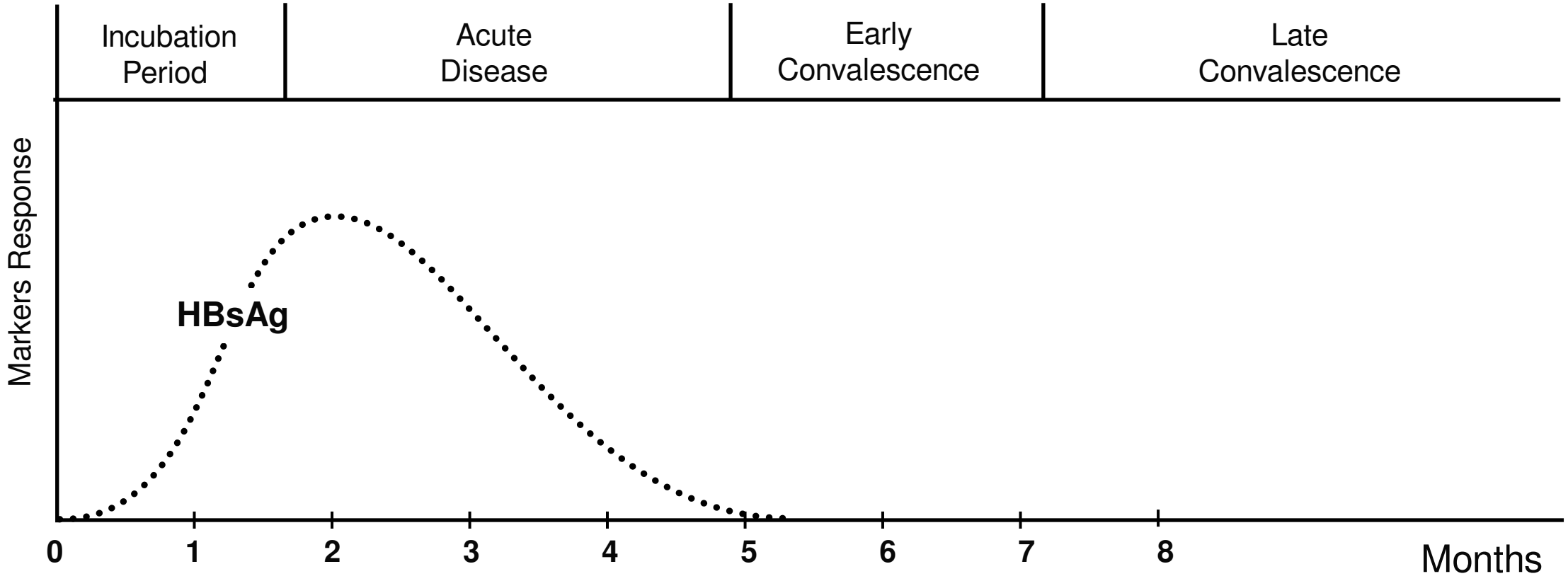
Hepatitis B Infection

Hepatitis B Markers | **Acute** followed by **Recovery**



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Hepatitis B Infection

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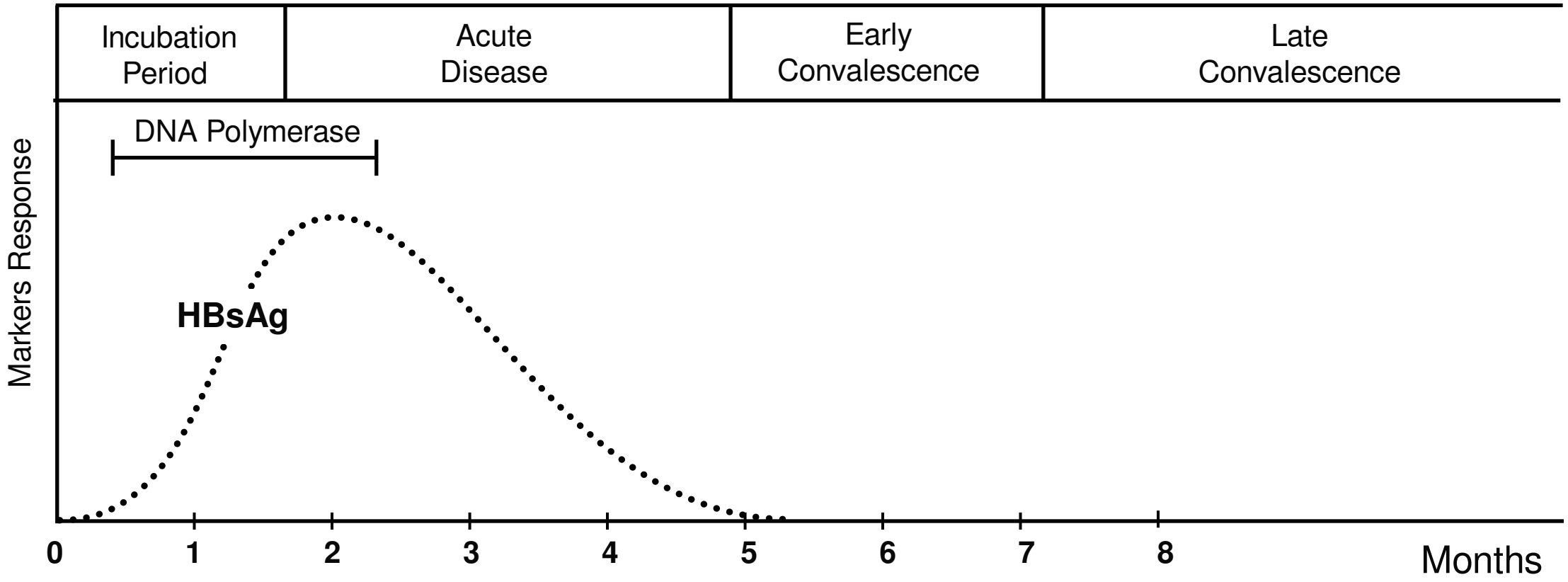

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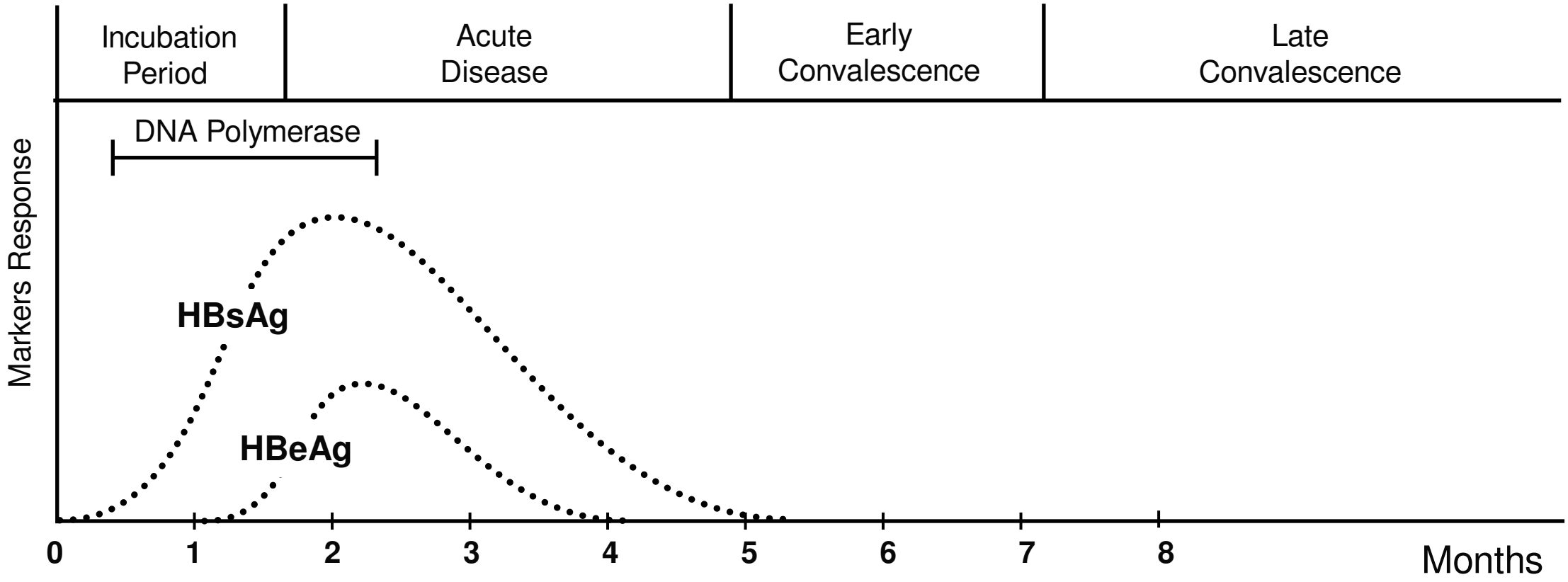

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Hepatitis B Infection

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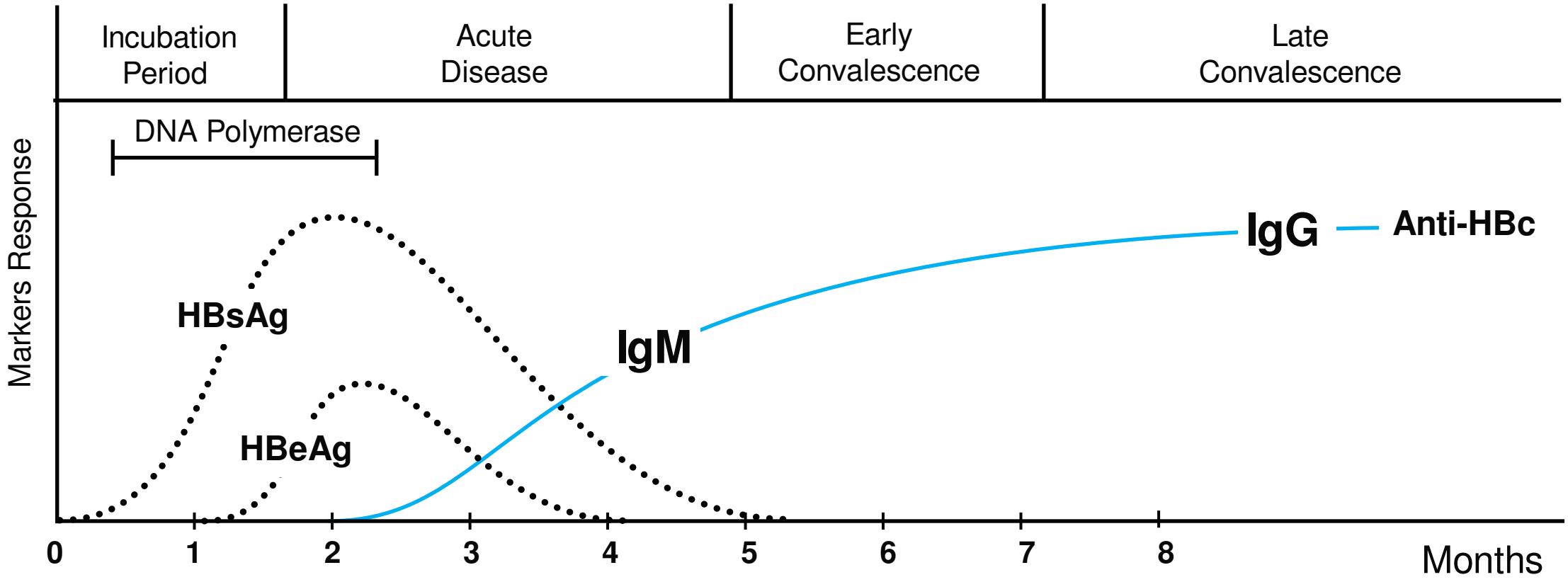

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Hepatitis B Infection

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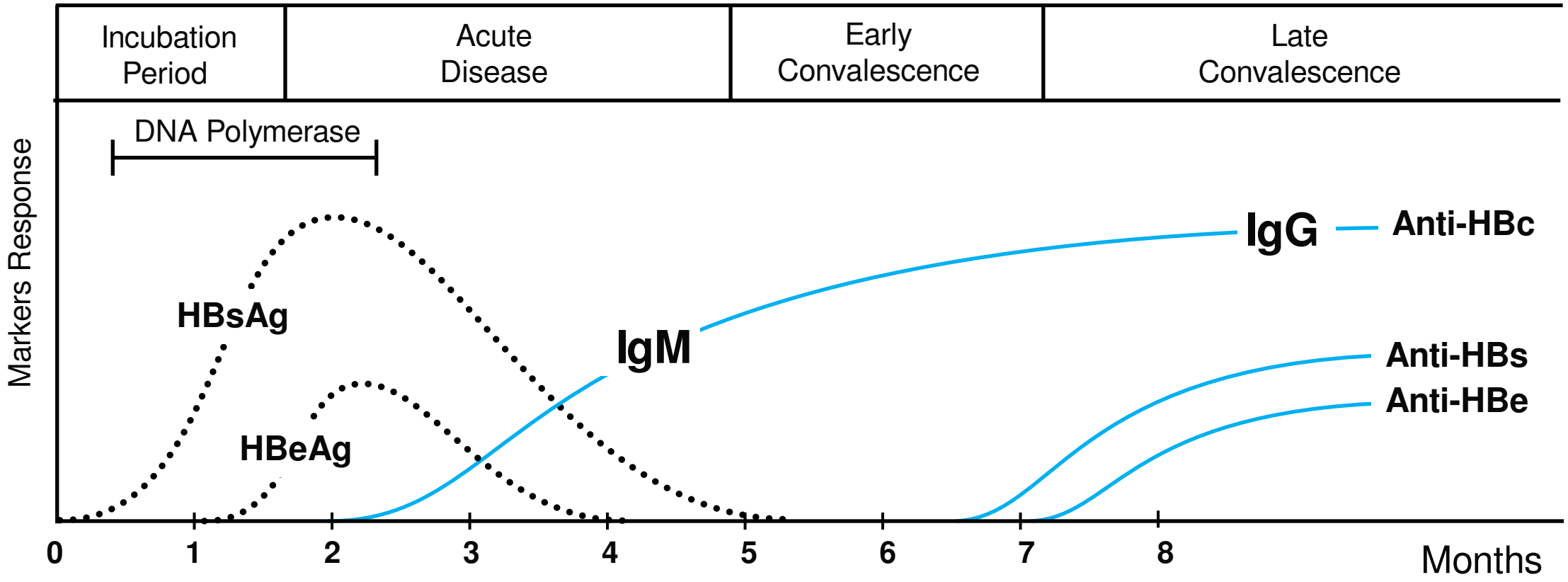

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Hepatitis B Infection

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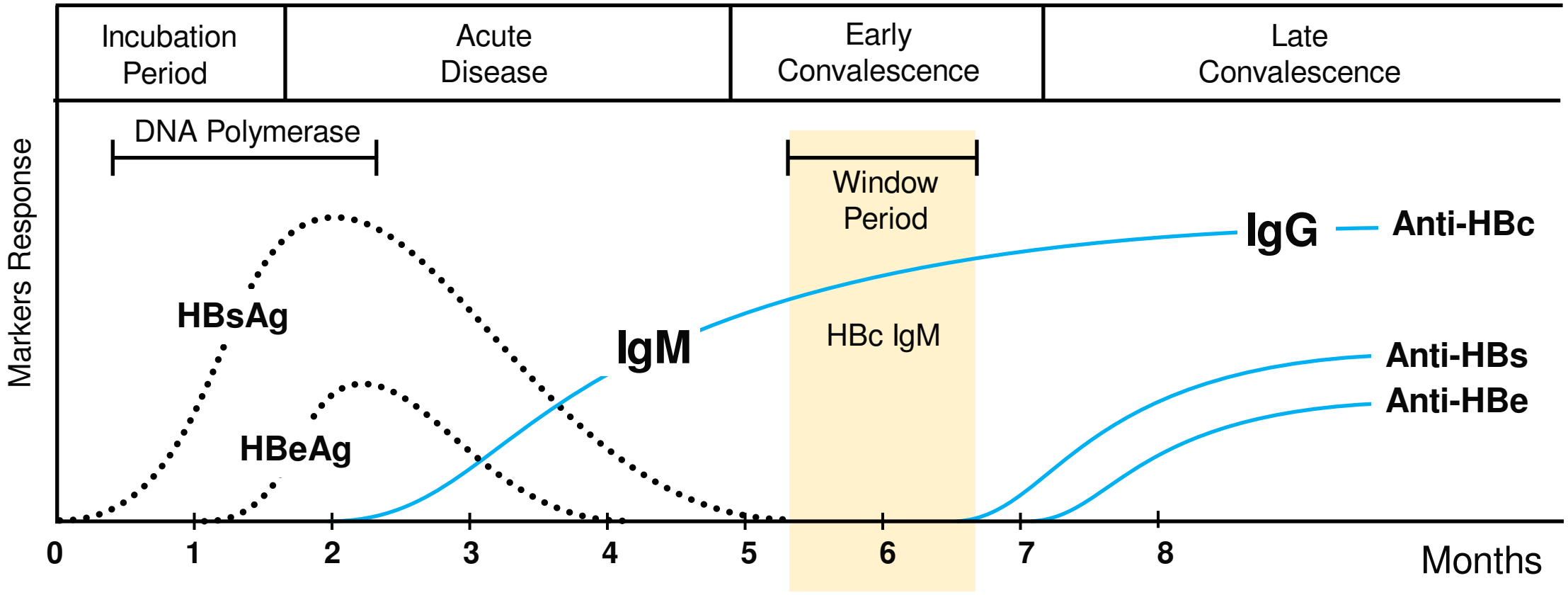
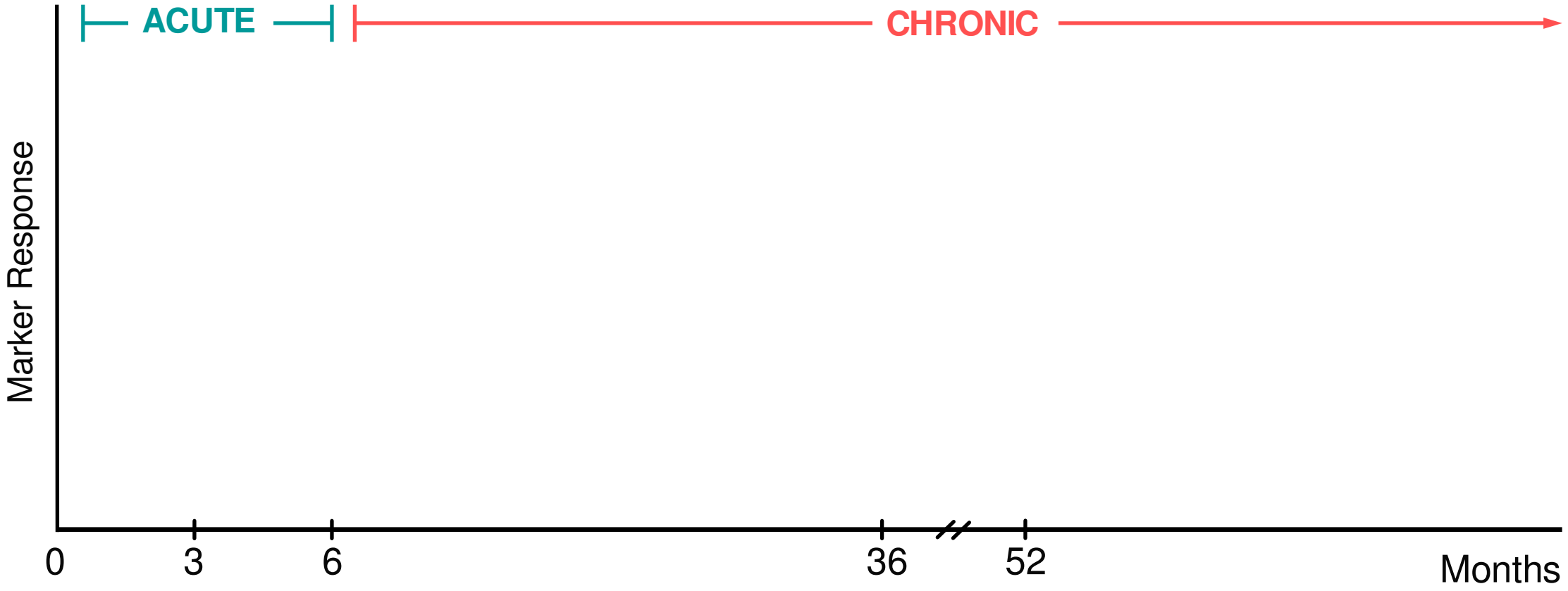


I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers | **Acute** followed by **Chronic**



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Hepatitis B Infection

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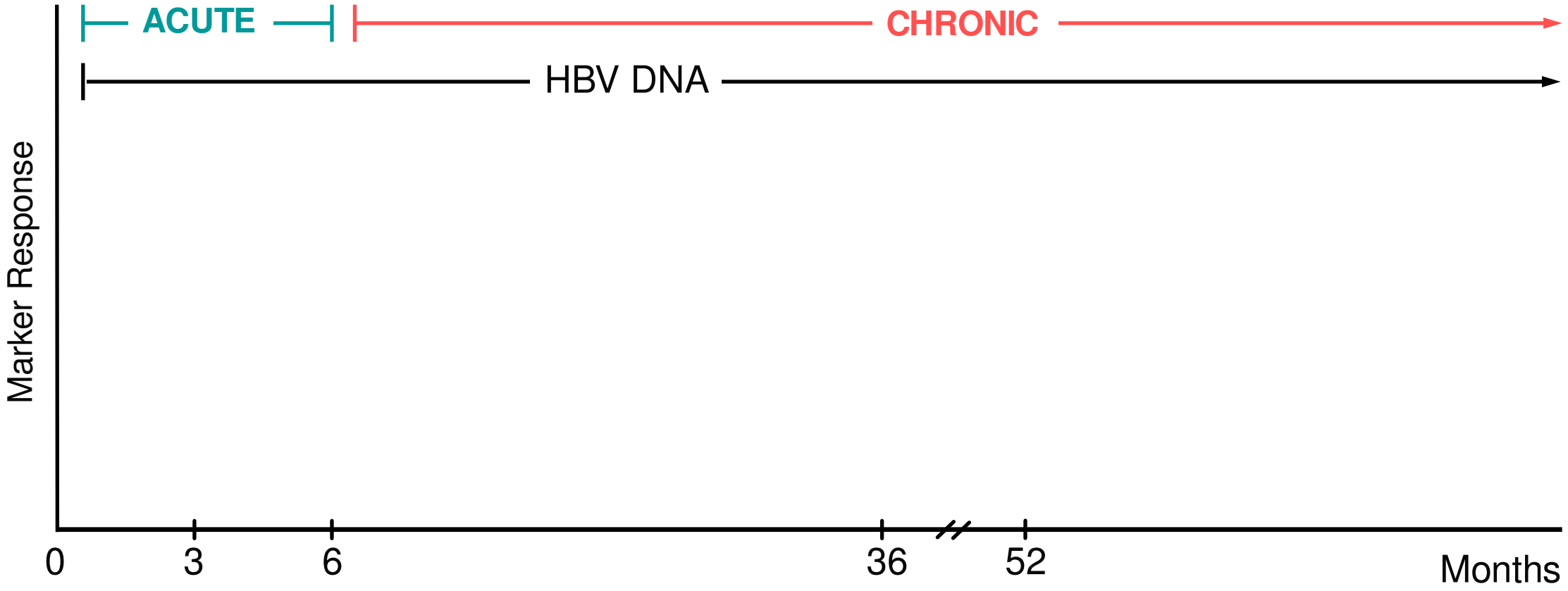

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Hepatitis B Infection

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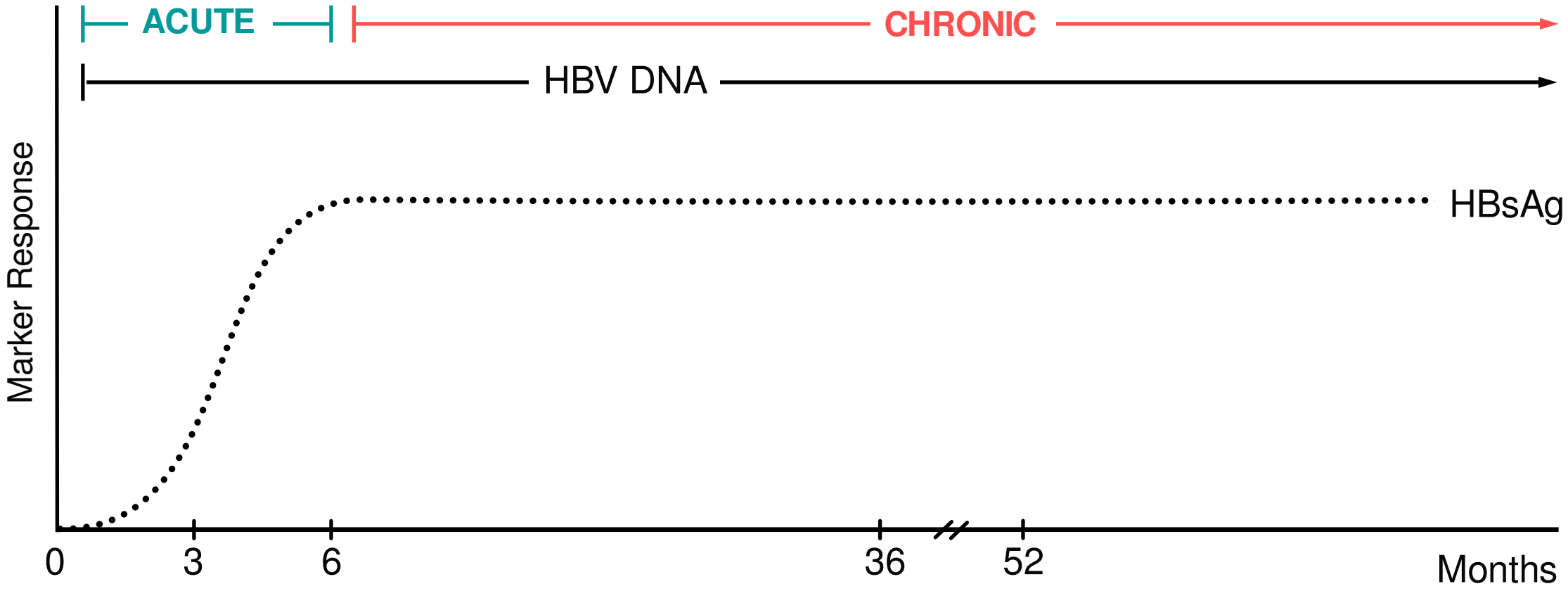

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Hepatitis B Infection

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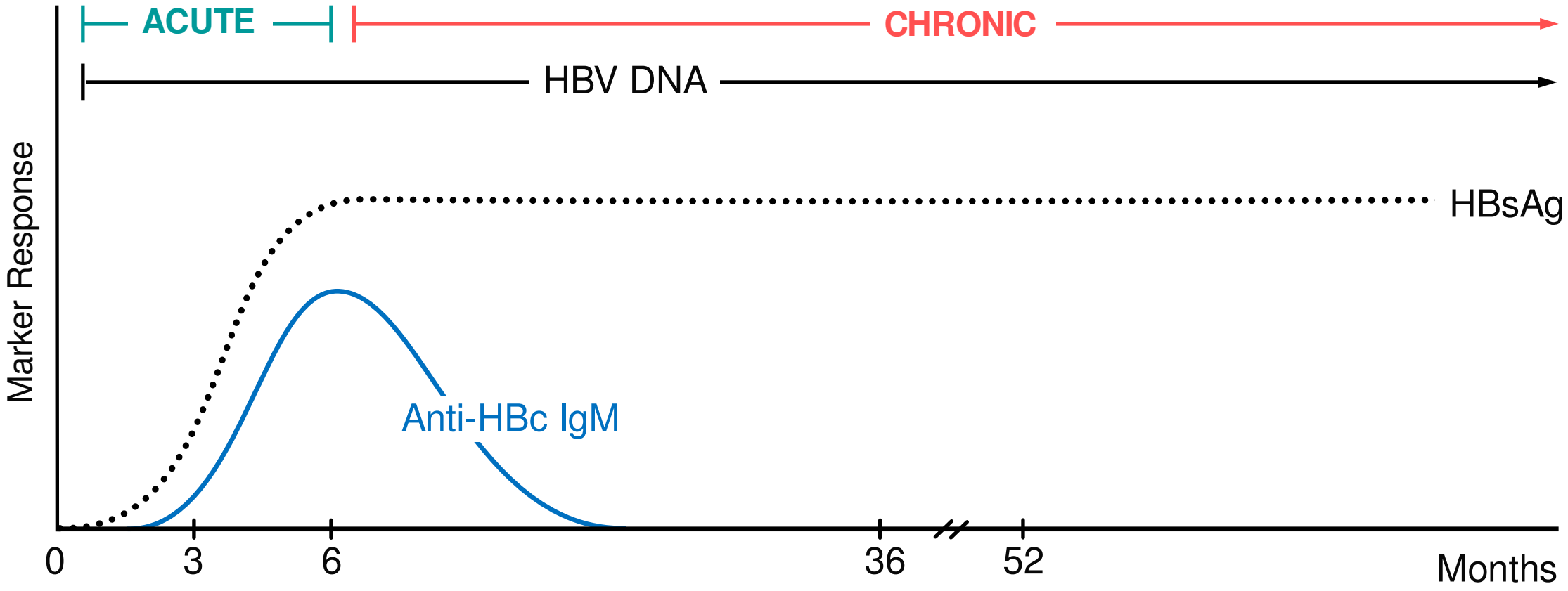

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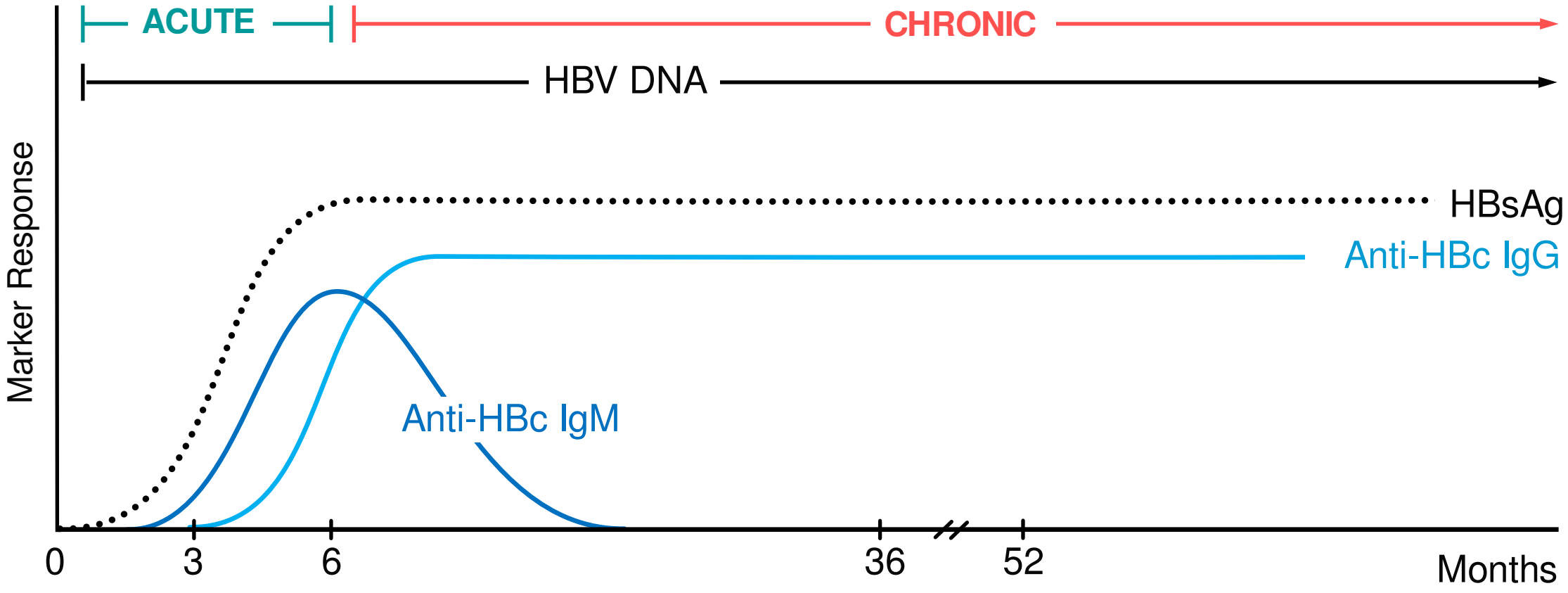
Hepatitis B Infection

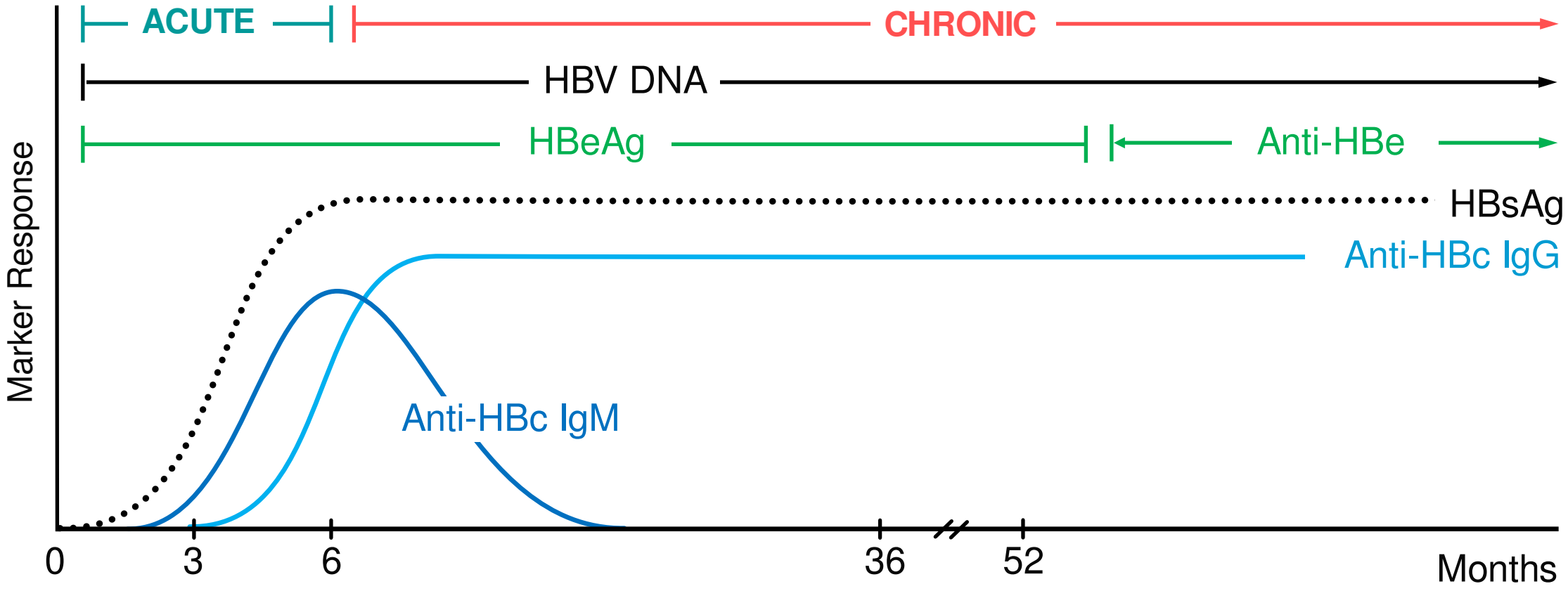
Hepatitis B Markers | **Acute** followed by **Chronic**



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers | **Acute** followed by **Chronic**



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers

HBsAg (HBs Antigen)

- First marker to appear in an acute HBV infection (detected 1 – 3 months after exposure).
- Persistence for > 6 months indicates chronicity.
- Disappearance indicates recovery from HBV infection.
- Individuals tested within 72 hours after vaccine administration may be HBsAg positive.

HBeAg (HBe Antigen)

- Appears immediately after the appearance of HBsAg
- Indicates active HBV **replication** and a marker of infectivity.
- Used to monitor therapy of patients with chronic HBV infection.

NOTE: The most sensitive test of viral replication is **viral DNA by PCR** and **DNA polymerase**.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers

Anti-HBc IgM

- Predominates the first 6 months of acute infection.
- Precedes the appearance of anti-HBs by weeks to months.
- Used in diagnosis during the “window period”.

Anti-HBc IgG

- Predominates beyond 6 months of acute HBV infection.
- Indicates past infection with HBV or HBV chronicity usually persists for life.

Anti-HBe

- Seroconversion from HBeAg to anti-HBe is a good prognostic sign.
- Failure of seroconversion indicates progression to chronicity.

Anti-HBs

- Indicates past HBV infection and natural immunity.
- Used to assess protective immunity after Hepatitis B vaccination.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

Hepatitis B Markers

	HBsAg	HBeAg	Anti-HBs	Anti-HBe	Anti-HBc	
					IgM	IgG
Susceptible	Negative	Negative	Negative	Negative	Negative	Negative
Recovery from Infection	Negative	Negative	**Positive**	**Positive**	Negative	**Positive**
Post-vaccination	Negative	Negative	**Positive**	Negative	Negative	Negative
Acute Hepatitis	**Positive**	**Positive**	Negative	Negative	**Positive**	Negative
Window period	Negative	Negative	Negative	Negative	**Positive**	Negative
Chronic Hepatitis	**Positive**	Neg/**Pos**	Negative	Neg/**Pos**	Negative	**Positive**

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis B Infection

HBV chronicity

+ HBsAg
– Anti-HBs
– Anti-HBc IgM
+ Anti-HBc IgG

Chronic HBV infection

Mild elevated ALT & AST
+ HBsAg
– Anti-HBs
– Anti-HBc IgM
+ Anti-HBc IgG
HBV DNA PCR moderate to high ↑
DNA polymerase moderate to high ↑

+ HBeAg
– Anti-HBe

– HBeAg
+ Anti-HBe

Inactive carrier state

Persistently normal ALT & AST
+ HBsAg
– Anti-HBs
– Anti-HBc IgM
+ Anti-HBc IgG
HBV DNA PCR undetectable to mild ↑
DNA polymerase undetectable to mild ↑

– HBeAg
+ Anti-HBe

Quiz

_____ is a serological marker used in the diagnosis of HBV infection during the window period.

a. HBsAg
b. Anti-HBc IgM
c. HBV DNA PCR
d. Anti-HBs

Quiz

_____ is a serological marker used in the diagnosis of HBV infection during the window period.

a. HBsAg
b. Anti-HBc IgM
c. HBV DNA PCR ←
d. HBcAg

Quiz

_____ is the first serological marker to appear in of HBV infection.

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBe

Quiz

_____ is the first serological marker to appear in of HBV infection.

a. HBeAg
b. HBsAg
c. HBcAg
d. Anti-HBe

Quiz

Which of the following is NOT a marker for HBV replication?

a. HBV DNA Polymerase
b. HBV DNA in blood
c. HBsAg
d. HBeAg

Quiz

Which of the following is NOT a marker for HBV replication?

a. HBV DNA Polymerase
b. HBV DNA in blood
c. HBsAg
d. HBeAg

Quiz

Which of the following is NOT TRUE as regards HBsAb?

a. Indicates past HBV infection
b. Absent in chronic HBV infection
c. Assess the body response of HBV vaccination
d. Monitor response to HBV therapy

Quiz

Which of the following is NOT TRUE as regards HBsAb?

a. Indicates past HBV infection
b. Absent in chronic HBV infection
c. Assess the body response of HBV vaccination
d. **Monitor response to HBV therapy**

REPORT INTERPRETATION

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	**Positive**	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

HBV infection – Window period

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	**Positive**	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	**Positive**	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

Post HBV vaccination

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	**Positive**	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	**Positive**	Negative
Anti-HBe	**Positive**	Negative

REPORT INTERPRETATION

Recovery from HBV infection

Test	Result	Reference
HBs Ag	Negative	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	**Positive**	Negative
Anti-HBe	**Positive**	Negative

REPORT INTERPRETATION

Test	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	**Positive**	Negative
Anti-HBc IgM	**Positive**	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

Acute HBV infection

Test	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	**Positive**	Negative
Anti-HBc IgM	**Positive**	Negative
Anti-HBc IgG	Negative	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

REPORT INTERPRETATION

	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	**Positive**	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

Serum ALT: 65 IU/L (Normal: up to 40)
HBV DNA PCR: Moderate viremia

REPORT INTERPRETATION

Chronic HBV infection

	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	**Positive**	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	Negative	Negative
Anti-HBe	Negative	Negative

Serum ALT: 65 IU/L (Normal: up to 40)
HBV DNA PCR: Moderate viremia

REPORT INTERPRETATION

	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	Negative	Negative
Anti-HBe	**Positive**	Negative

Serum ALT: 32 IU/L (Normal: up to 40)
HBV DNA PCR: Undetectable

REPORT INTERPRETATION

Inactive HBV carrier

	Result	Reference
HBs Ag	**Positive**	Negative
HBe Ag	Negative	Negative
Anti-HBc IgM	Negative	Negative
Anti-HBc IgG	**Positive**	Negative
Anti-HBs	Negative	Negative
Anti-HBe	**Positive**	Negative

Serum ALT: 32 IU/L (Normal: up to 40)
HBV DNA PCR: Undetectable

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection

1. Blood chemistry

— Usually, non-icteric with mild ↑ of the liver enzymes

— Sometimes, can take the picture of acute hepatitis with elevated liver enzymes and jaundice.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection

1. **Blood chemistry**
   - Usually, non-icteric with mild ↑ of the liver enzymes
   - Sometimes, can take the picture of acute hepatitis with elevated liver enzymes and jaundice.
2. **Serology:** HCV Screening using anti-HCV antibody tests
   - Anti-HCV is detected at 3 – 6 months post infection;
   - Only 50-70% of acute infections show detectable antibody.
   - Represent only evidence of HCV infection, does not imply immunity.
   - Methods: immunoassays such as ELISA and RIBA

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection

1. **Blood chemistry**
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   - — Represent only evidence of HCV infection, does not imply immunity.
   - — Methods: immunoassays such as ELISA and RIBA
3. **Molecular methods:** Confirmation using HCV RNA by PCR
   - — Positive anti-HCV serology require confirmation with HCV PCR testing.
   - — Useful in:
     a. Diagnosis Early infection when anti-HCV antibody is undetectable.
     b. Diagnosis of HCV in immunocompromised patients who may not seroconvert.
     c. Prognosis/follow up: identifies genotypes and monitors HCV viral load.

I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection

Sometimes negative in acute cases since the antibody appears late

HCV Screening
anti-HCV antibody tests

ELISA

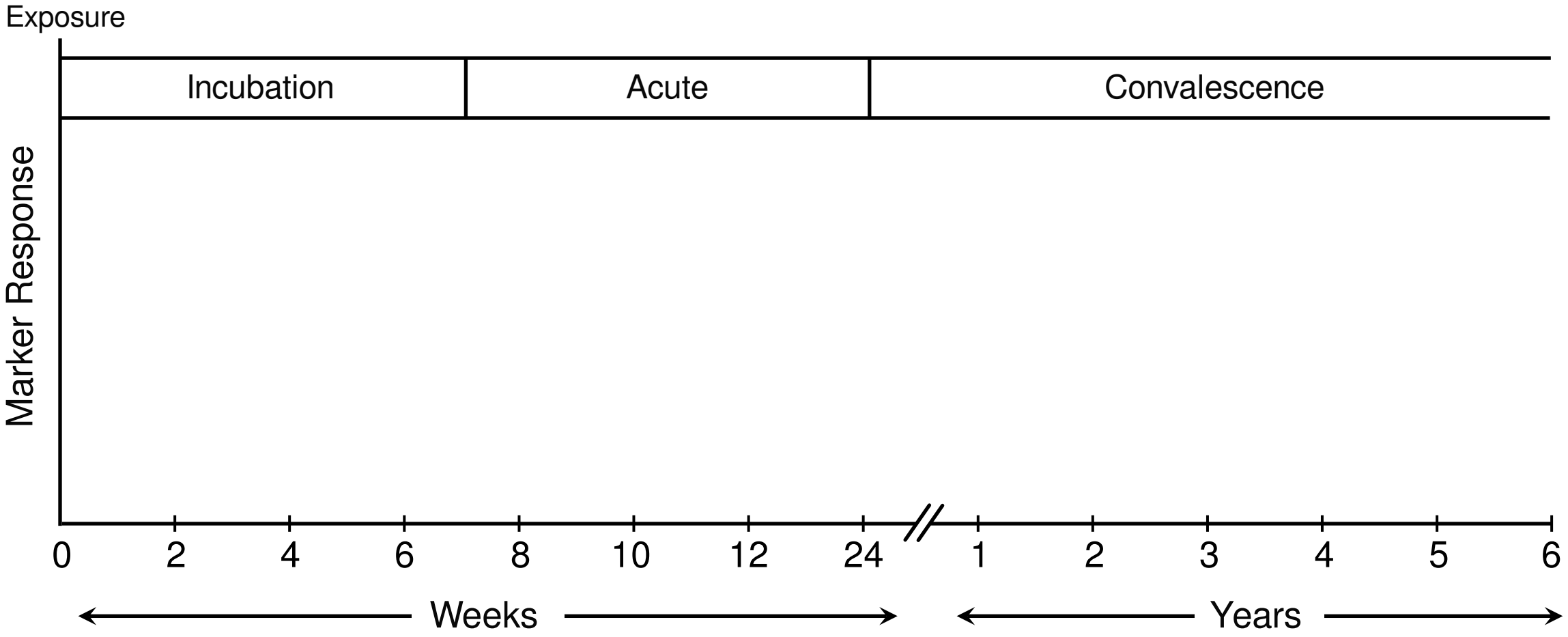
- Less specific than RIBA
- False positive results may be seen with hypergammaglobulinemia

RIBA

- More specific than ELISA
- Indeterminate results may be found in:
  - Early seroconversion,
  - Immunosuppressed patients.

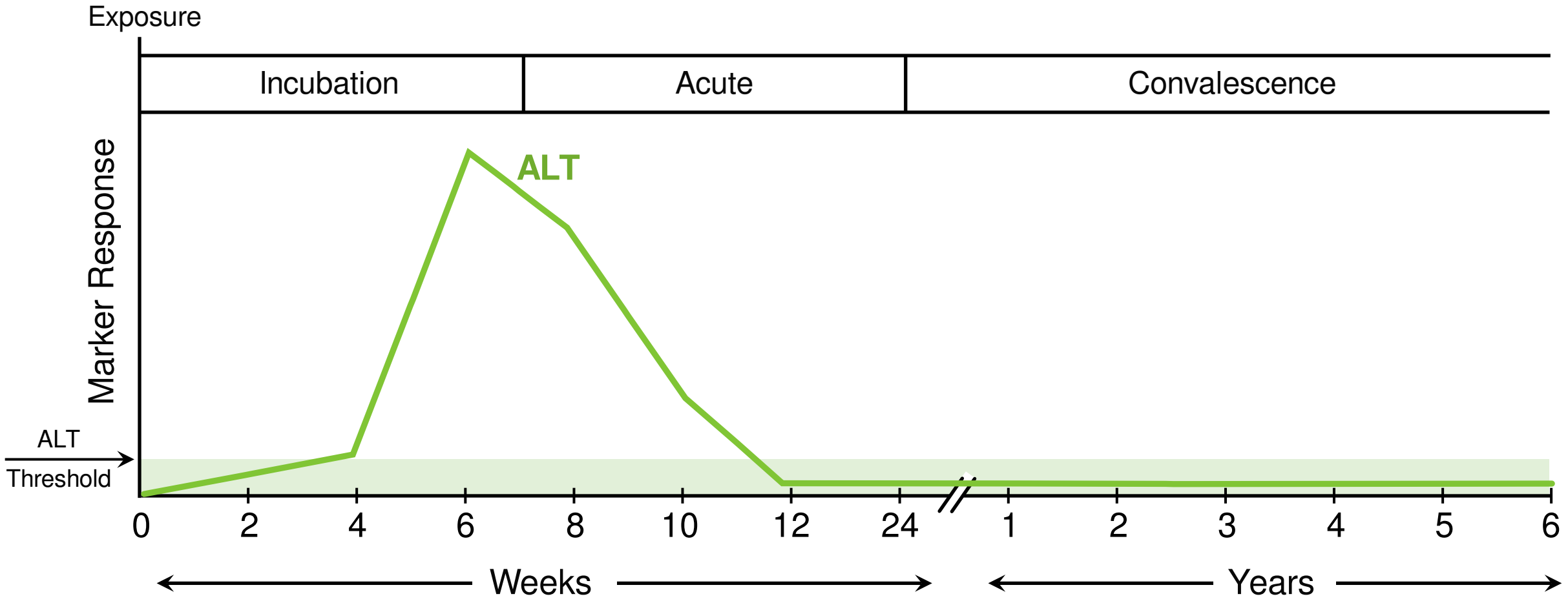
I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection



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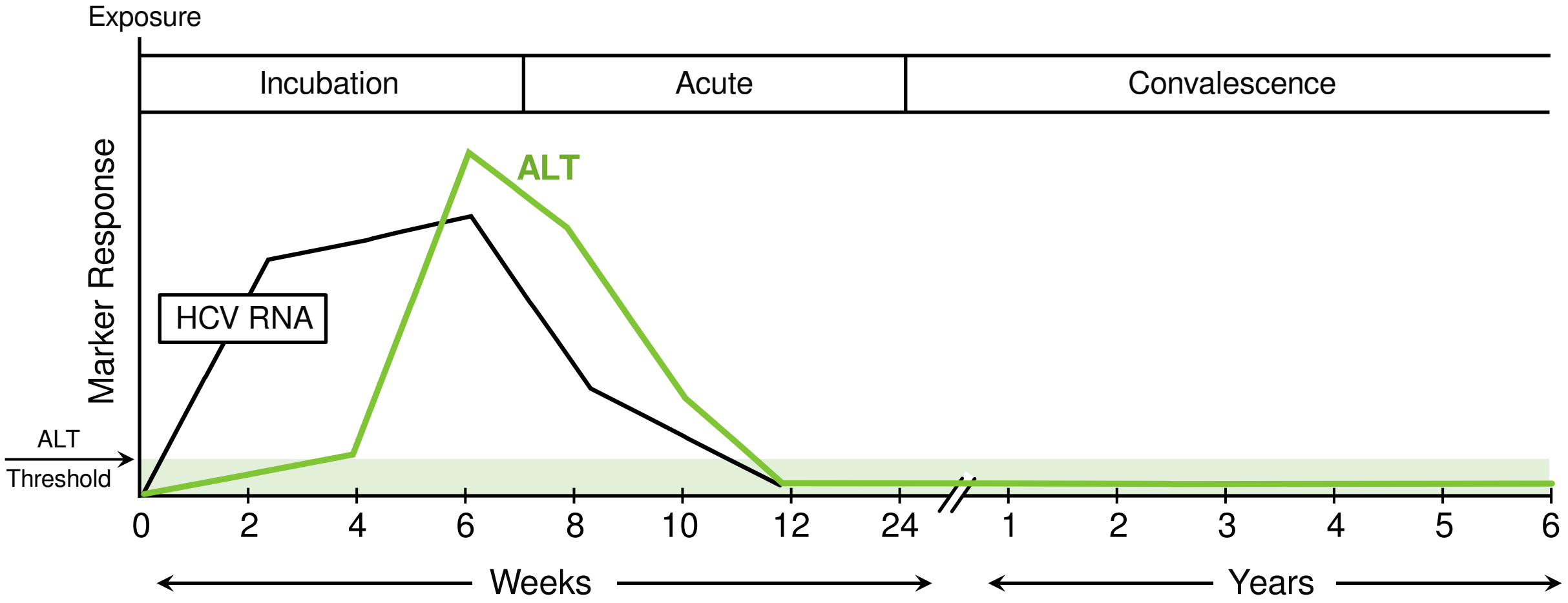
Hepatitis C Infection



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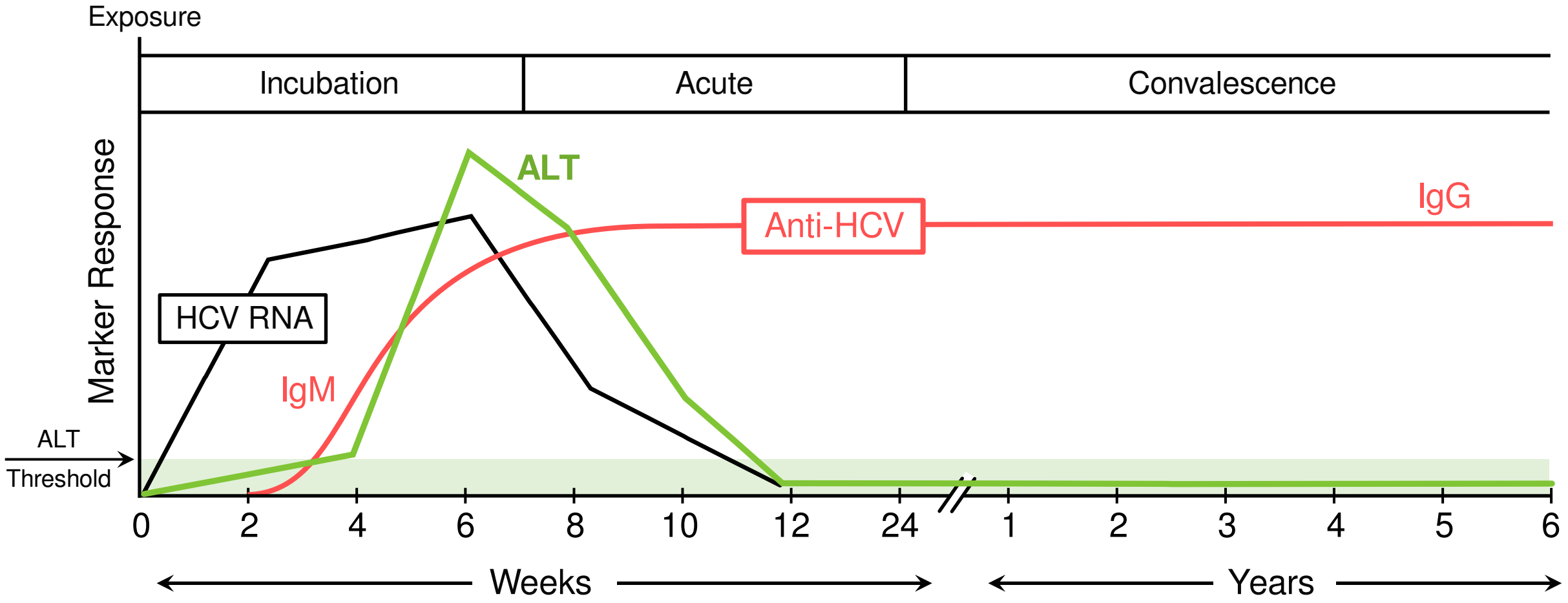
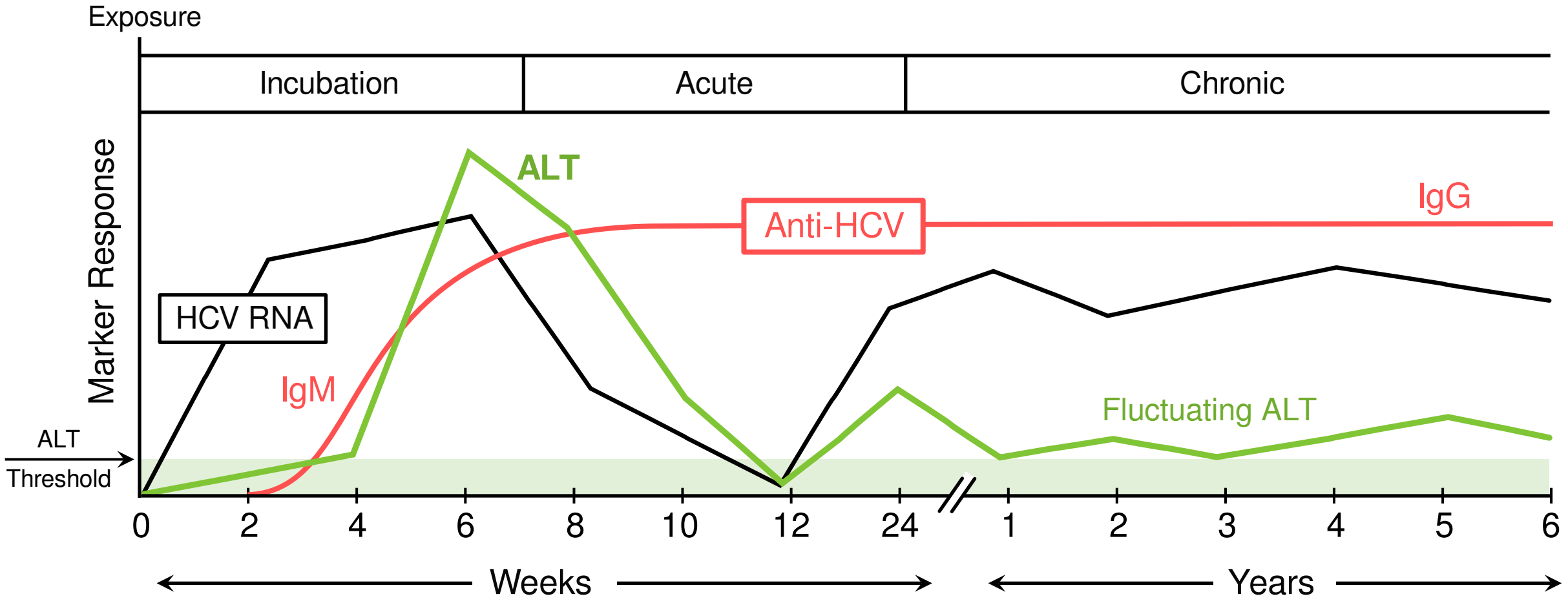
Hepatitis C Infection



I. Laboratory Diagnosis of **Viral Hepatitis**

Hepatitis C Infection



REPORT INTERPRETATION

Test	Result	Reference
Anti-HCV	22.82 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	4206 Copies/ml	Undetectable < 20

Serum ALT: 64 IU/L (Normal: up to 40)

REPORT INTERPRETATION

HCV Infection (acute or chronic)

Test	Result	Reference
Anti-HCV	22.82 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	4206 Copies/ml	Undetectable < 20

Serum ALT: 64 IU/L (Normal: up to 40)

REPORT INTERPRETATION

Test	Result	Reference
Anti-HCV	0.28 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	98 Copies/ml	Undetectable < 20

Serum ALT: 45 IU/L (Normal: up to 40)

REPORT INTERPRETATION

Early HCV Infection

Test	Result	Reference
Anti-HCV	0.28 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	98 Copies/ml	Undetectable < 20

Serum ALT: 45 IU/L (Normal: up to 40)

REPORT INTERPRETATION

Test	Result	Reference
Anti-HCV	31.22 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	< 20 Copies/ml	Undetectable < 20

Serum ALT: 28 IU/L (Normal: up to 40)

REPORT INTERPRETATION

Past HCV infection

Test	Result	Reference
Anti-HCV	31.22 Index	Non-reactive < 1.00 Reactive ≥ 1.00
HCV RNA PCR	< 20 Copies/ml	Undetectable < 20

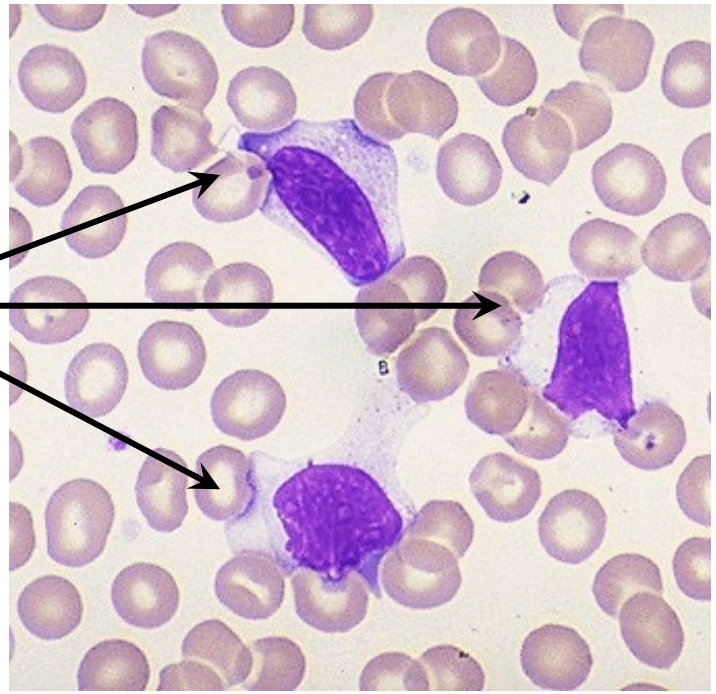
Serum ALT: 28 IU/L (Normal: up to 40)

II. Laboratory Diagnosis of **Infectious Mononucleosis (IMN)**

— **Caused by** Epstein-Barr virus (EBV).
— **Transmitted by** droplet infection.
— **Clinical picture:** sore throat, fever, lymphadenopathy and may be mild splenomegaly.
— **Complications:** AI thrombocytopenia, AIHA, encephalitis, hepatitis and myocarditis.

Pathogenesis

— The EBV replicates within **B cells** (which are invaded via their surface CD21 molecule).
— The host immune response involves **cytotoxic T cells** against infected B cells, resulting in **large, atypical lymphocytes**.



II. Laboratory Diagnosis of **Infectious Mononucleosis (IMN)**

Laboratory Findings

CBC

— Absolute lymphocytosis
— Atypical lymphocytes in blood film

Serological tests

Heterophile antibody tests

— Hemagglutination tests (use horse or sheep RBCs)
— Methods: Monospot and Paul-Bunnel test.
— Positive in 1st to 2nd week.
— High titers in 2nd and 3rd week
— Undetectable by the 2nd to 3rd months of EBV exposure
— False positive results: other viral infections and autoimmune diseases.
— False negative results: too early in disease course or in children < 4 years.

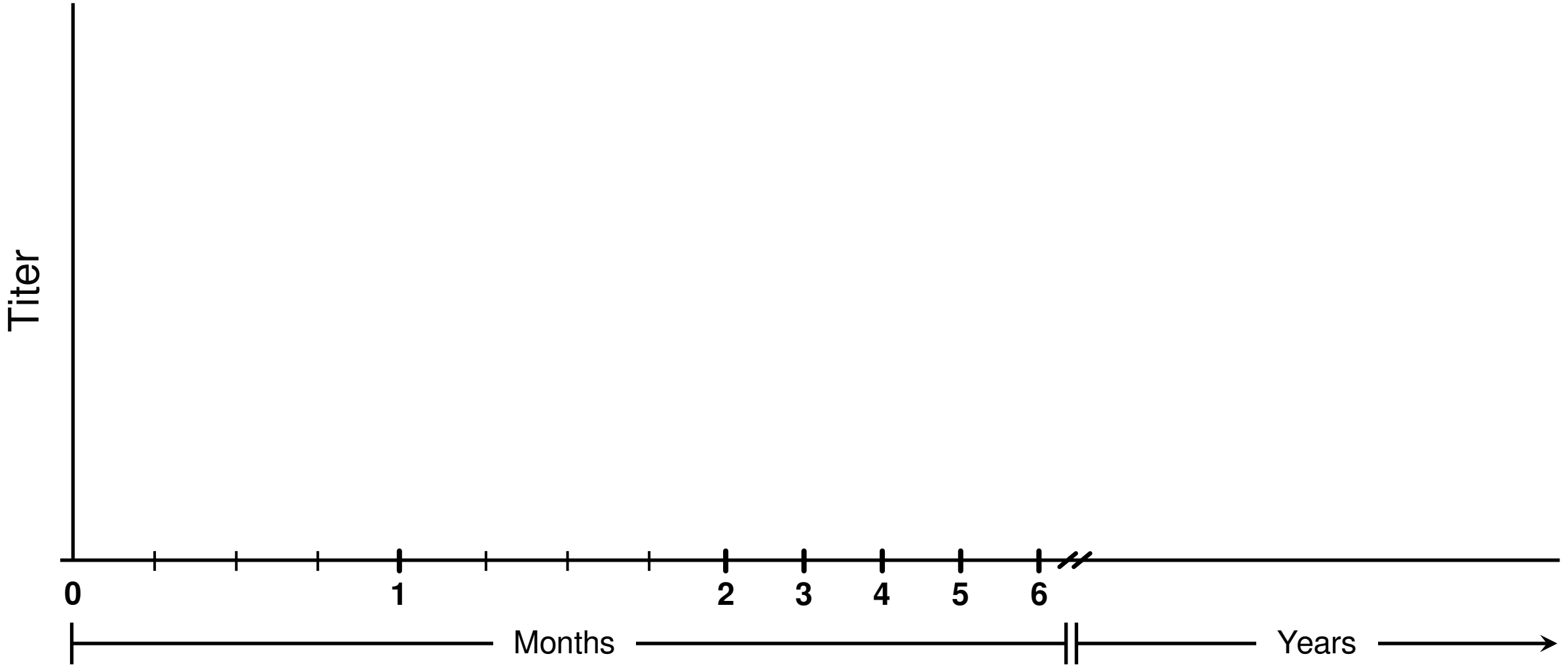
Specific EBV antibody tests

a. Early antigen (EA) IgG
b. Viral capsid antigen (VCA) IgM + IgG
c. EBV nuclear antigen (EBNA) IgG

Molecular testing

EBV DNA PCR

II. Laboratory Diagnosis of **Infectious Mononucleosis (IMN)**



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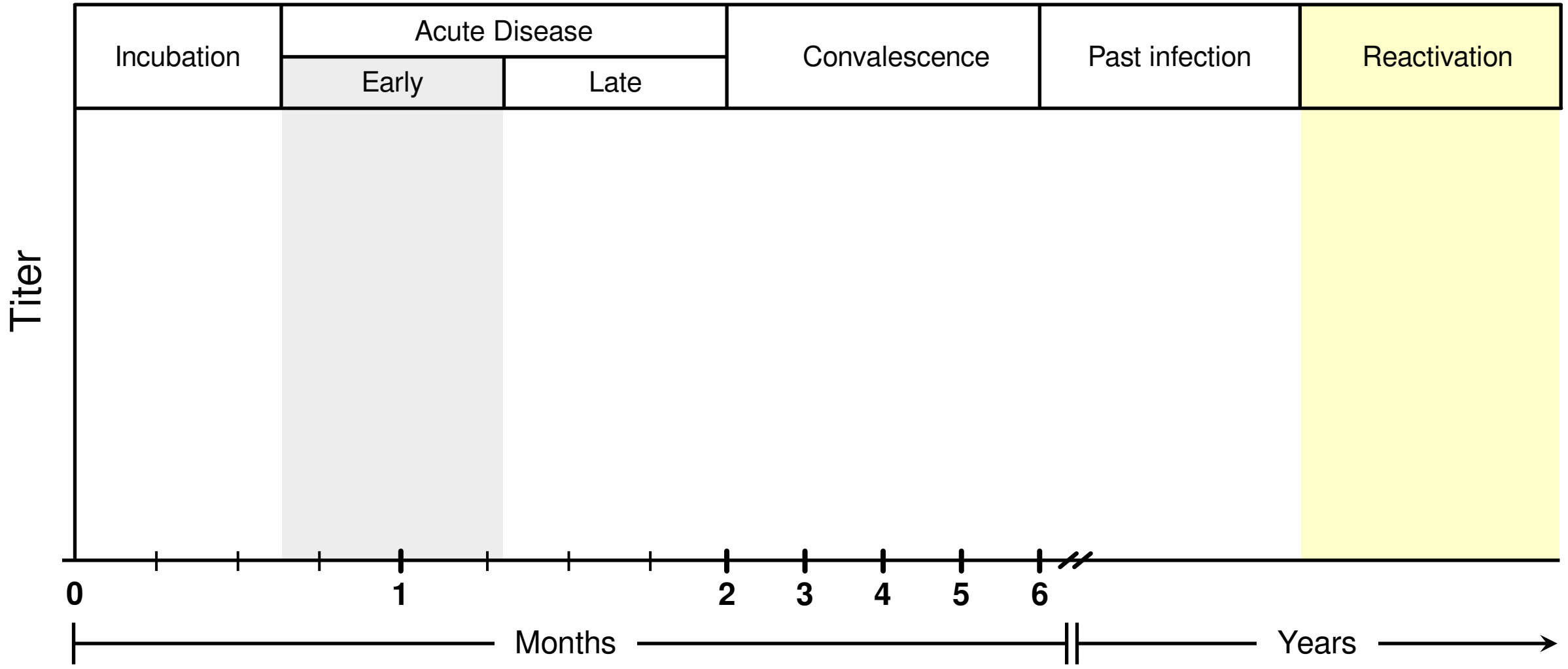

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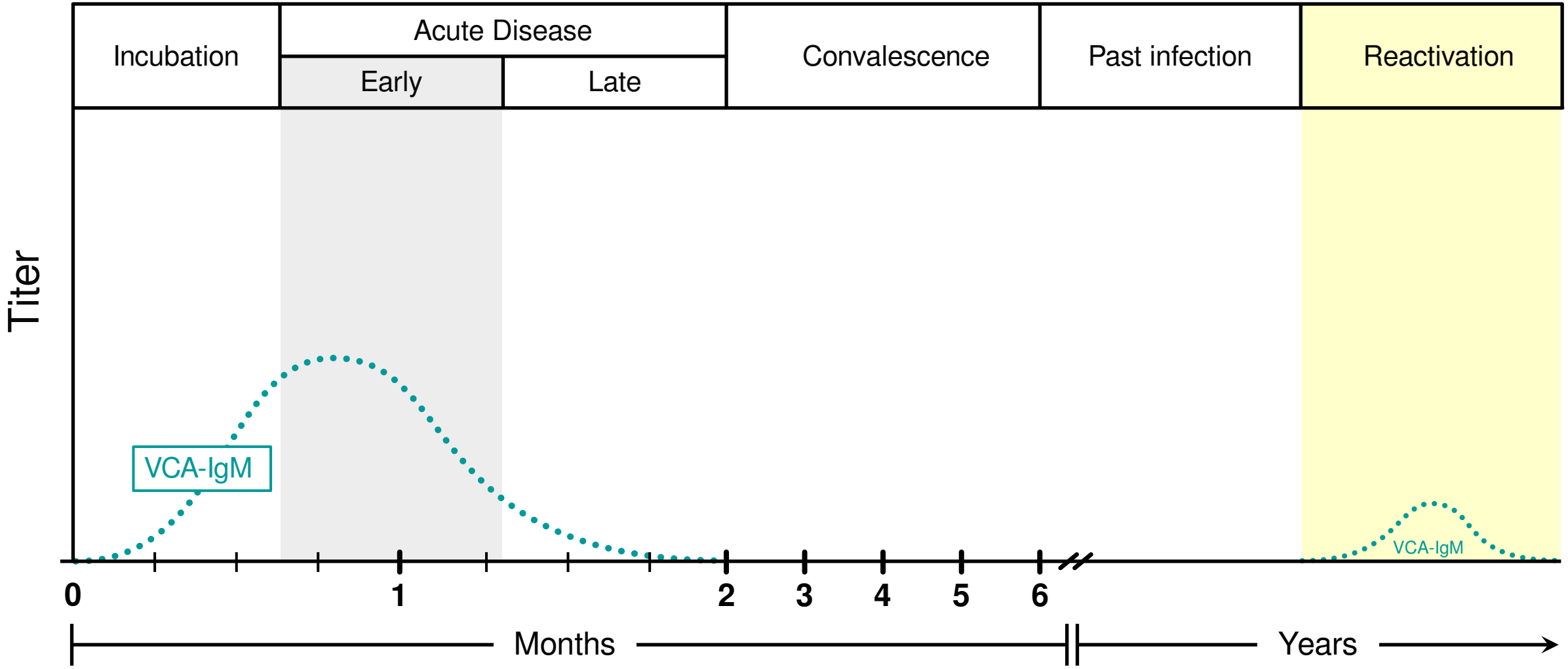

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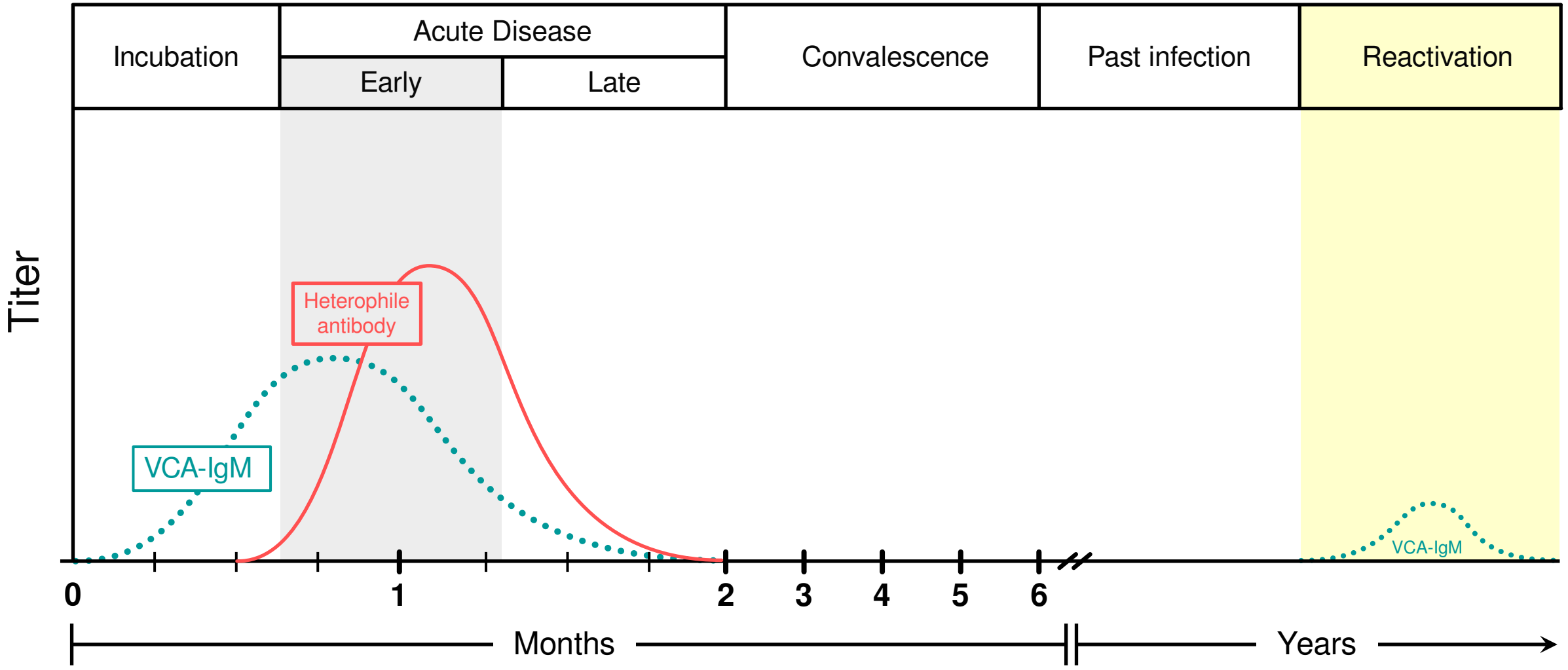

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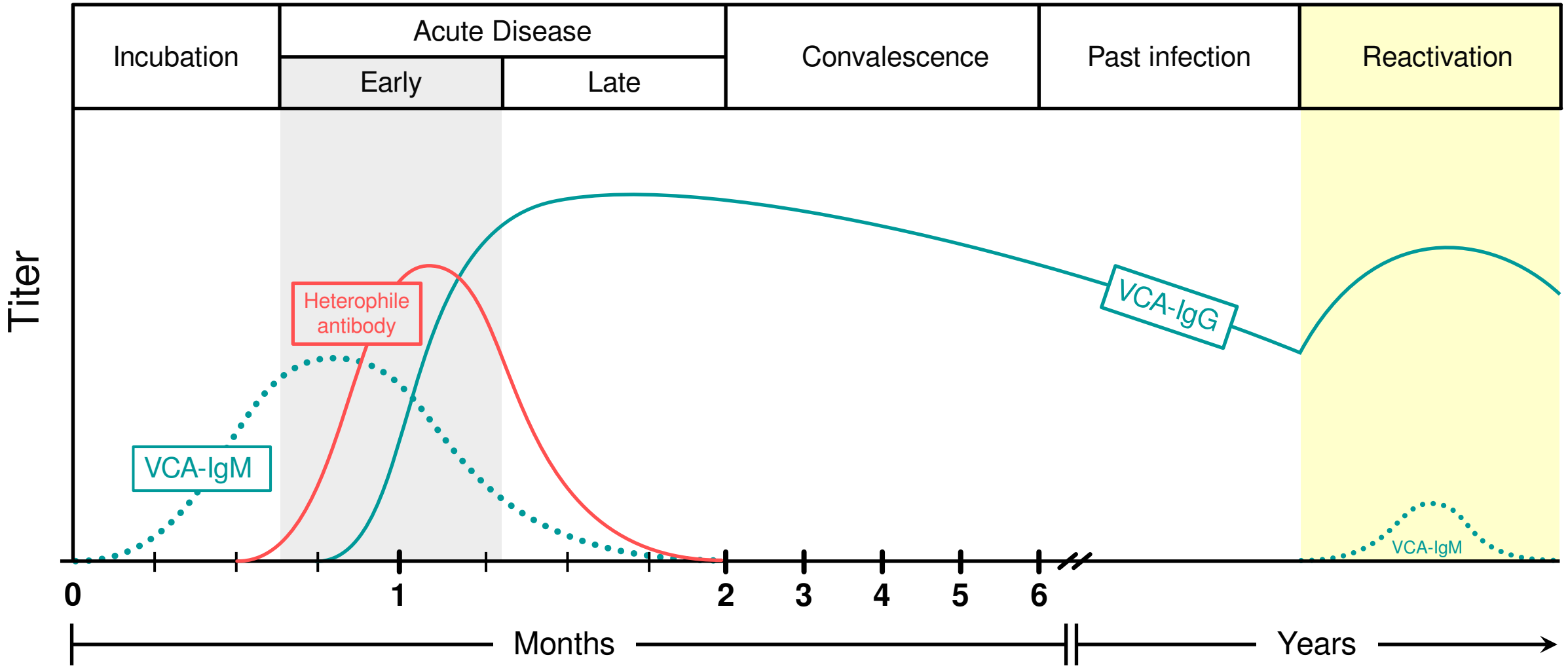

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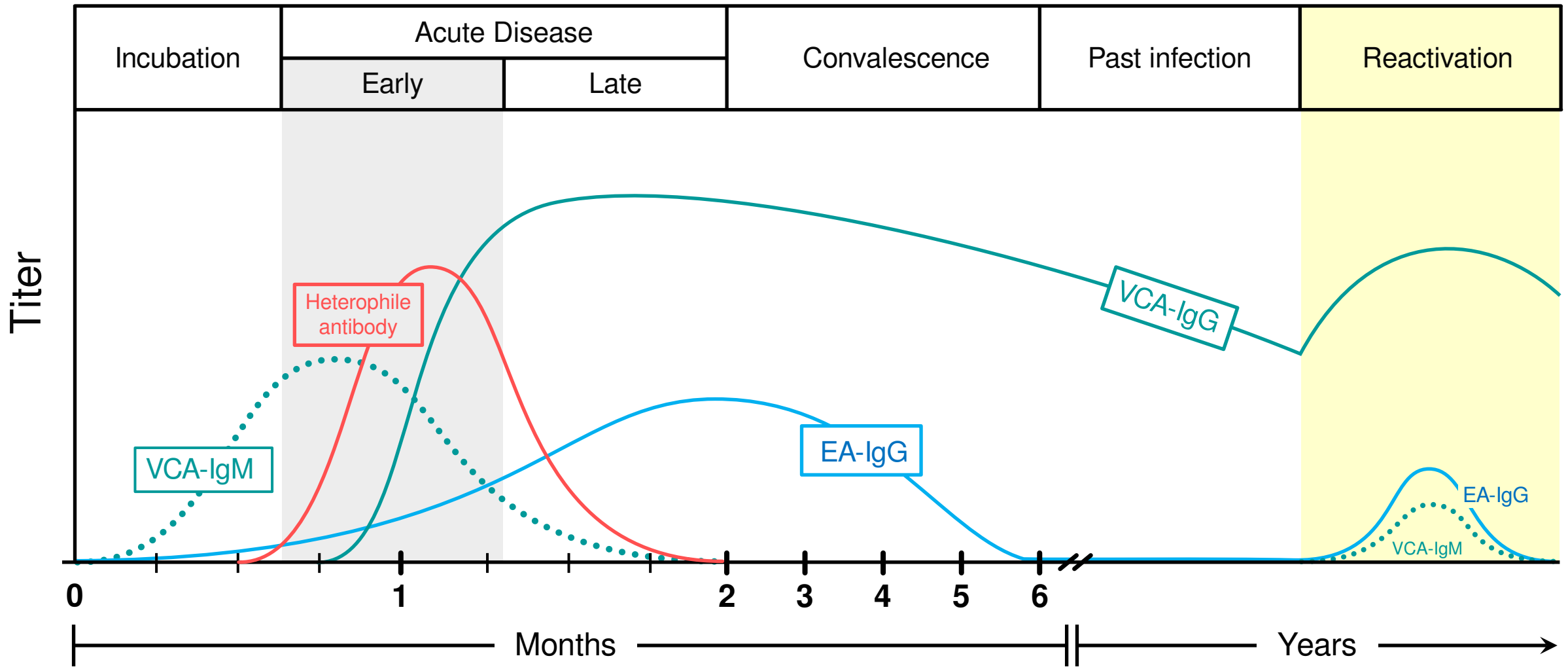

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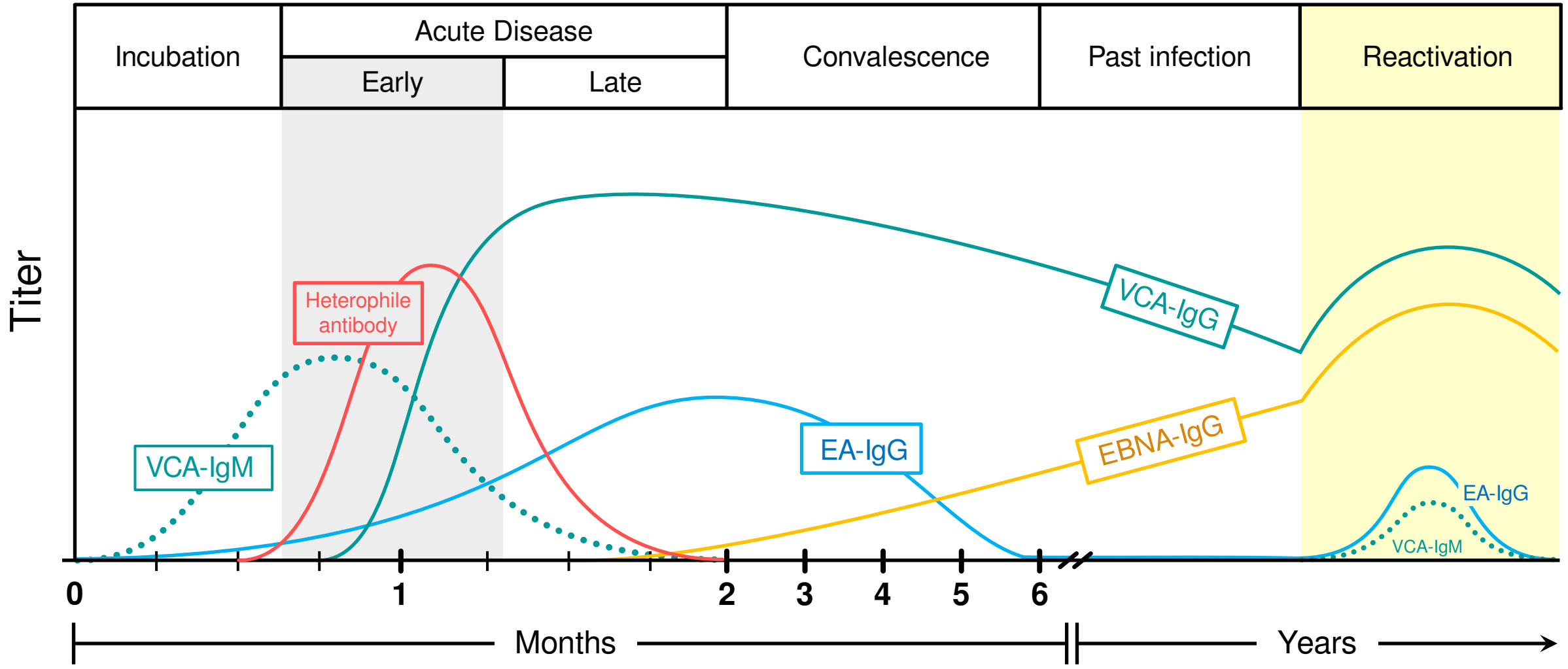
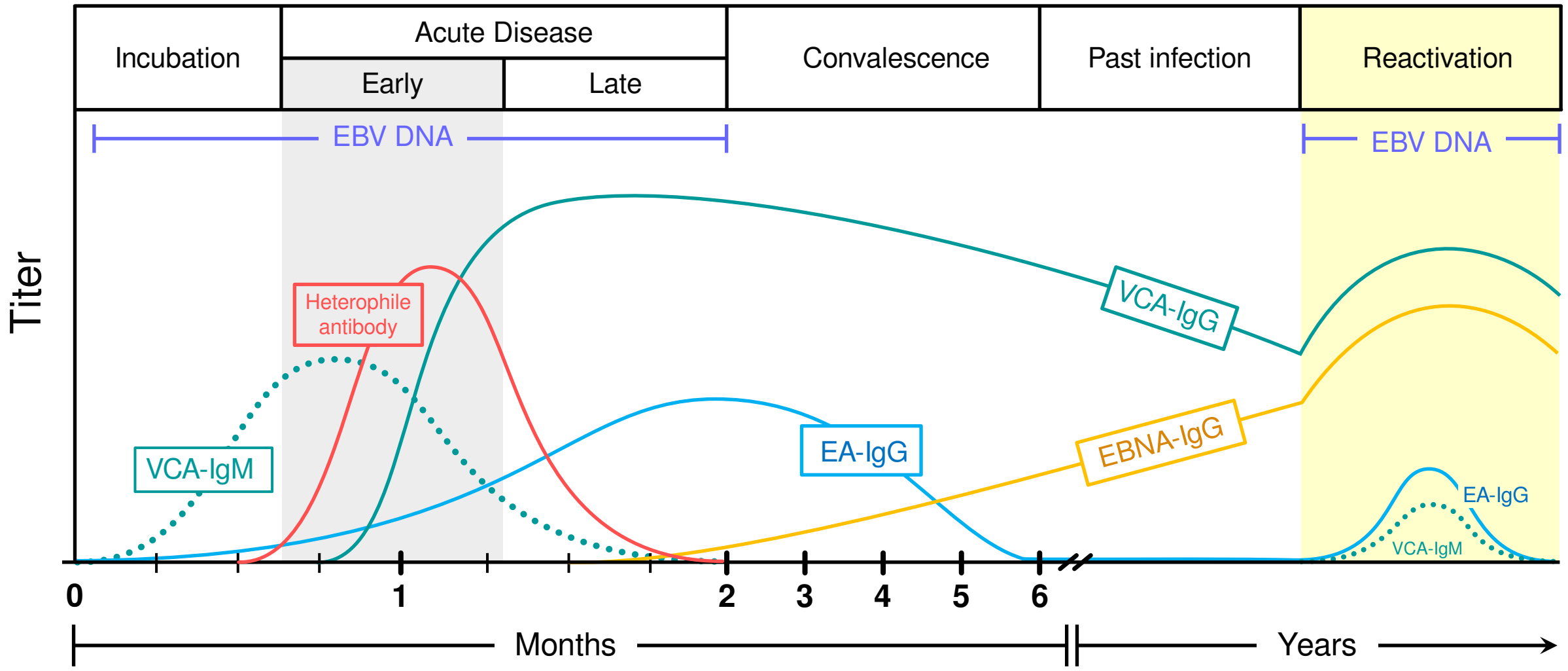


II. Laboratory Diagnosis of **Infectious Mononucleosis (IMN)**



II. Laboratory Diagnosis of **Infectious Mononucleosis (IMN)**

VCA IgM	VCA IgG	EBNA IgG	Condition
−	−	−	Susceptible
+	−	−	Acute infection (Early)
+	+	−	Acute infection
+	+	+	Acute infection (Late)
−	+	+	Past infection
+	+	+	Reactivation

Quiz

EBV invades:

a. CD4+ T lymphocytes
b. CD8+ T lymphocytes
c. B Lymphocytes
d. Macrophages

Quiz

EBV invades:

a. CD4+ T lymphocytes
b. CD8+ T lymphocytes
c. **B Lymphocytes**
d. Macrophages

Quiz

EBV invades B cells via their:

a. surface CD19 molecule
b. surface CD20 molecule
c. surface CD21 molecule
d. surface CD22 molecule

Quiz

EBV invades B cells via their:

a. surface CD19 molecule
b. surface CD20 molecule
c. **surface CD21 molecule**
d. surface CD22 molecule

Quiz

Atypical lymphocytes that seen in blood film in cases of infectious mononucleosis are:

a. Activated B lymphocytes
b. Activated Helper T lymphocytes
c. Activated Cytotoxic T lymphocytes
d. Activated Macrophages

Quiz

Atypical lymphocytes that seen in blood film in cases of infectious mononucleosis are:

a. Activated B lymphocytes
b. Activated Helper T lymphocytes
c. Activated Cytotoxic T lymphocytes
d. Activated Macrophages

REPORT INTERPRETATION

Test	Result	Reference
Monospot test	**Positive**	Negative
VCA IgM	**Positive**	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	Negative	Negative
EBV DNA PCR	**Detectable**	Undetectable

REPORT INTERPRETATION

Test	Result	Reference
Monospot test	**Positive**	Negative
VCA IgM	**Positive**	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	Negative	Negative
EBV DNA PCR	**Detectable**	Undetectable

Acute EBV Infection

REPORT INTERPRETATION

3 years old child,
Complaining of fever, fatigue, sore throat and lymphadenopathy (posterior cervical LNs)
Examination: tonsilitis, palatal petechia, mild hepatomegaly and mild splenomegaly

Test	Result	Reference
Monospot test	Negative	Negative
VCA IgM	**Positive**	Negative
VCA IgG	Negative	Negative
EBNA IgG	Negative	Negative
EBV DNA PCR	**Detectable**	Undetectable

REPORT INTERPRETATION

3 years old child,
Complaining of fever, fatigue, sore throat and lymphadenopathy (posterior cervical LNs)
Examination: tonsilitis, palatal petechia, mild hepatomegaly and mild splenomegaly

Test	Result	Reference
Monospot test	Negative	Negative
VCA IgM	**Positive**	Negative
VCA IgG	Negative	Negative
EBNA IgG	Negative	Negative
EBV DNA PCR	**Detectable**	Undetectable

Early acute EBV Infection

REPORT INTERPRETATION

Test	Result	Reference
VCA IgM	**Positive**	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	**Positive**	Negative
EBV DNA PCR	**Detectable**	Undetectable

REPORT INTERPRETATION

Test	Result	Reference
VCA IgM	**Positive**	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	**Positive**	Negative
EBV DNA PCR	**Detectable**	Undetectable

Late acute EBV Infection or EBV reactivation

REPORT INTERPRETATION

Test	Result	Reference
Monospot test	Negative	Negative
VCA IgM	Negative	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	**Positive**	Negative
EBV DNA PCR	Undetectable	Undetectable

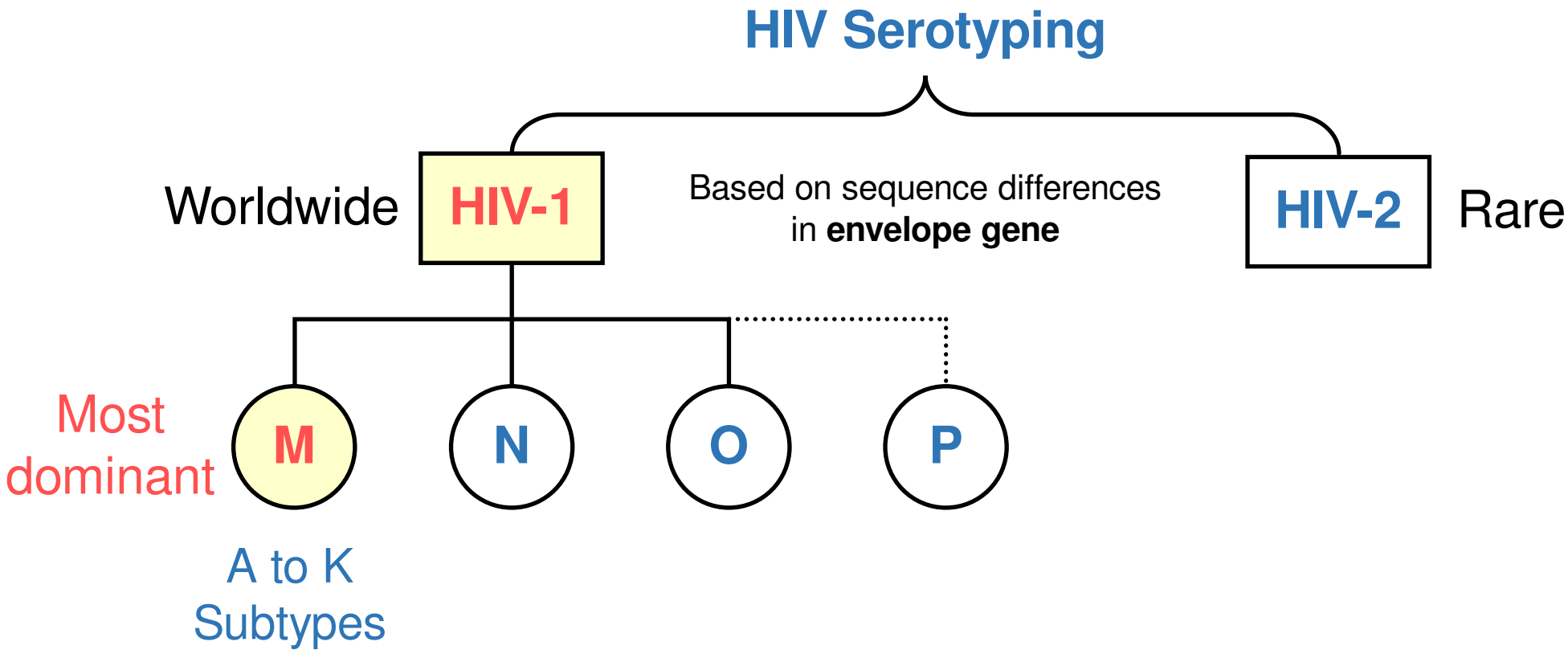
REPORT INTERPRETATION

Test	Result	Reference
Monospot test	Negative	Negative
VCA IgM	Negative	Negative
VCA IgG	**Positive**	Negative
EBNA IgG	**Positive**	Negative
EBV DNA PCR	Undetectable	Undetectable

Past EBV Infection

II. Laboratory Diagnosis of **HIV Infection**

- HIV is the cause of Acquired Immunodeficiency Syndrome (AIDS)
- Both HIV-1 and HIV-2 cause AIDS, but HIV-1 is found worldwide.

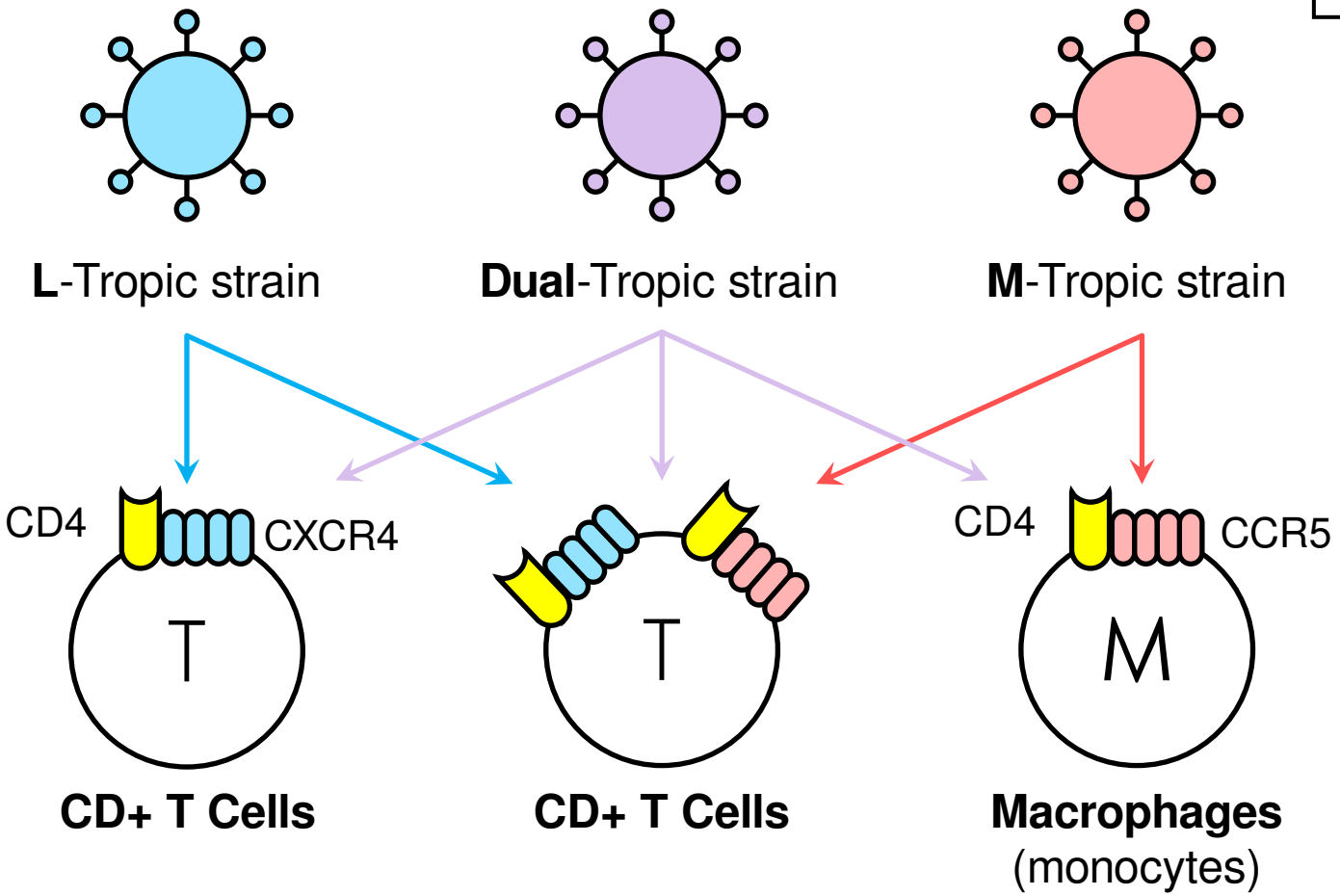


II. Laboratory Diagnosis of **HIV Infection**

Pathogenesis

HIV preferentially infects and destroys **CD4+ cells**

- CD4+ T Lymphocytes
- Monocyte/Macrophage
- Dendritic cells



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- CD4+ T Lymphocytes
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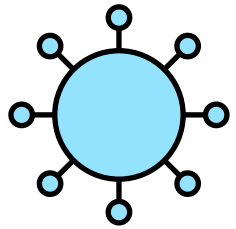
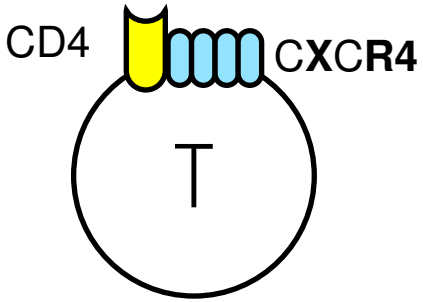
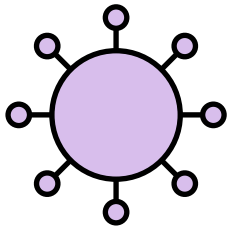


L-Tropic strain

HIV XR4 strain

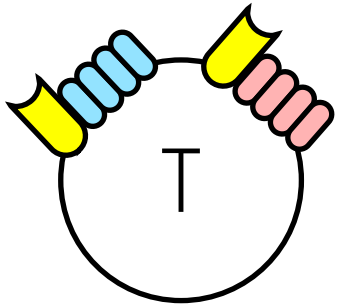


CD+ T Cells

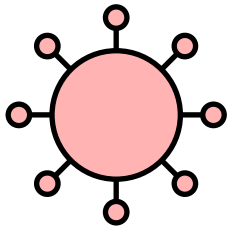


Dual-Tropic strain

HIV R5XR4 strain

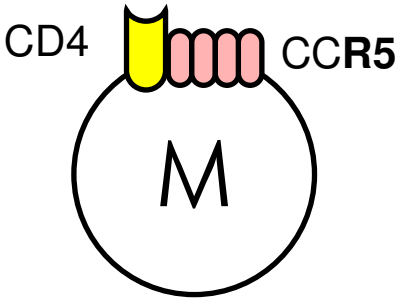


CD+ T Cells



M-Tropic strain

HIV R5 strain



Macrophages
(monocytes)

II. Laboratory Diagnosis of **HIV Infection**

Pathogenesis

According to Blood CD4+ T cell count HIV infection could be classified into in **3 stages** :

1	**Acute infection**	The virus uses CD4+ T cells to replicate and destroys them, so the CD4+ T cell count fall rapidly
2	**Clinical Latency**	A steady decline in the CD4+ T cells count in blood and lymphoid tissues
3	**AIDS**	Blood CD4+ T cell count drops < 200 cells/mm^3

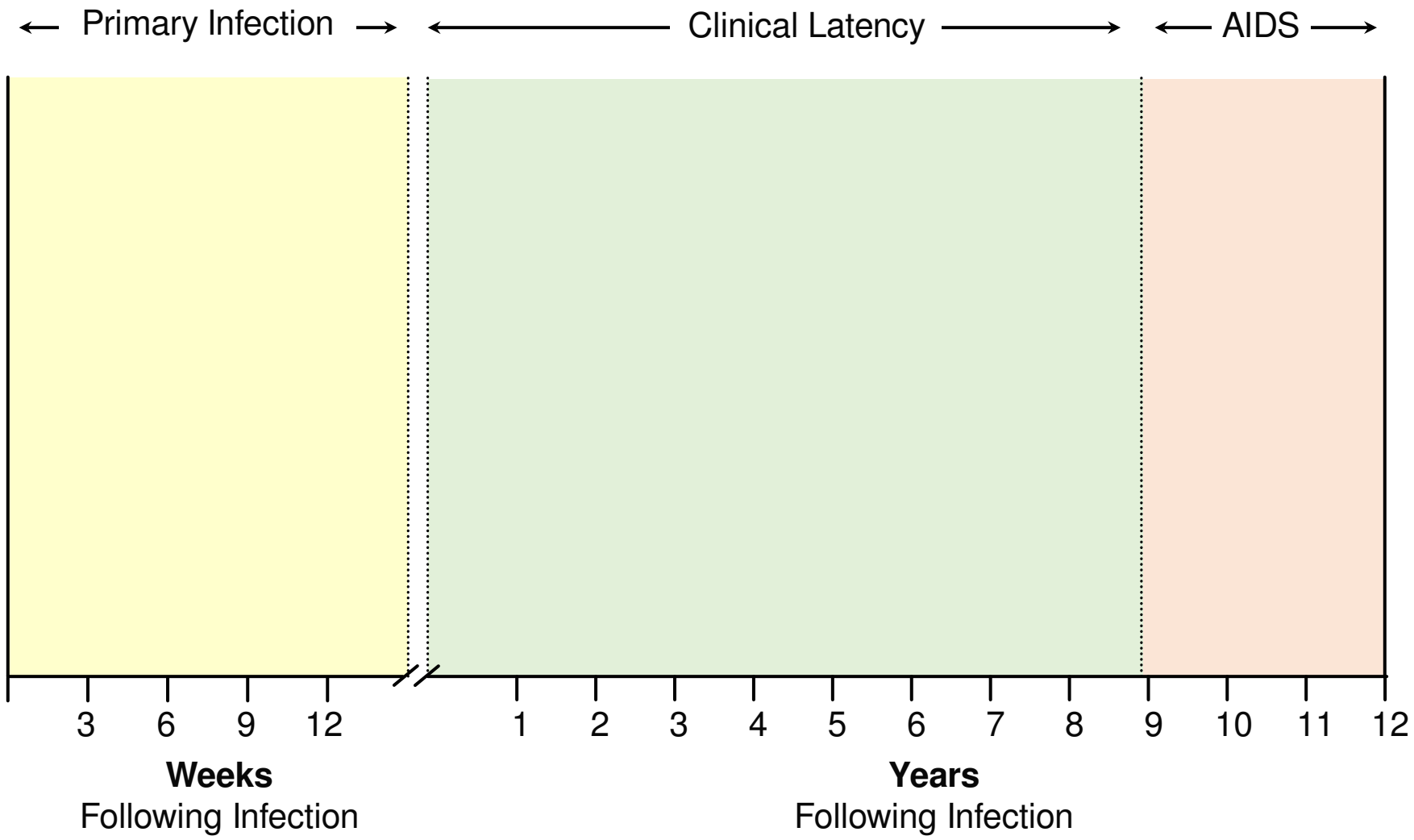
II. Laboratory Diagnosis of **HIV Infection**

Pathogenesis

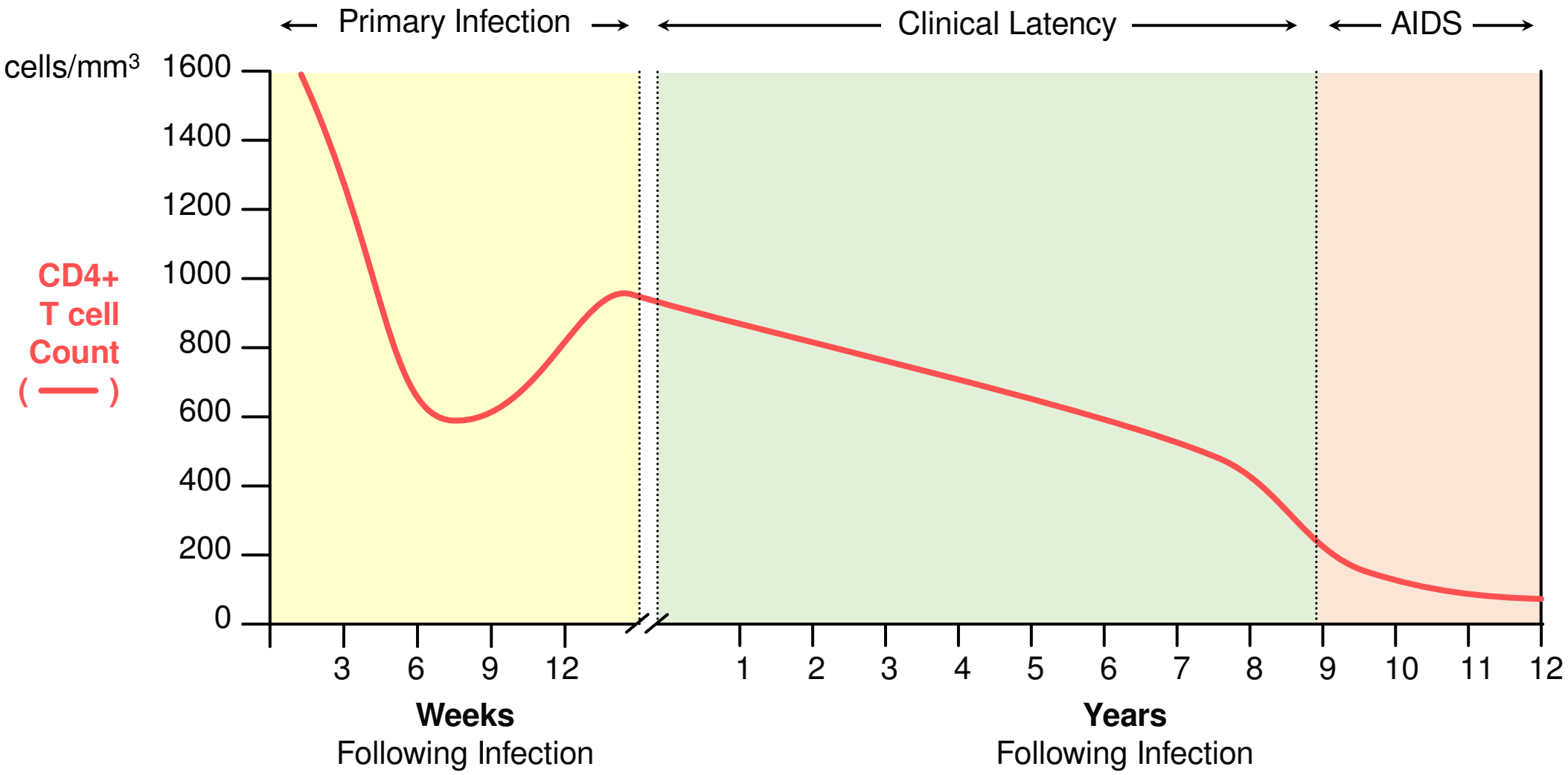
According to Blood CD4+ T cell count HIV infection
could be classified into in **3 stages** :

1	**Acute infection**	Flu-like Symptoms (fever, fatigue, headache, muscle pain, sore throat, cough, sneezing)
2	**Clinical Latency**	Lymphadenopathy Hairy Leukoplakia (white tongue patch causes by EBV) Oral Candidiasis
3	**AIDS**	Persistent fever | Fatigue | Weight loss | Diarrhea Recurrent bacteria pneumonia | Candidiasis (esophagus) Kaposi sarcoma (skin lesion) | Primary Lymphoma (lymphadenopathy)

II. Laboratory Diagnosis of **HIV Infection**



II. Laboratory Diagnosis of **HIV Infection**



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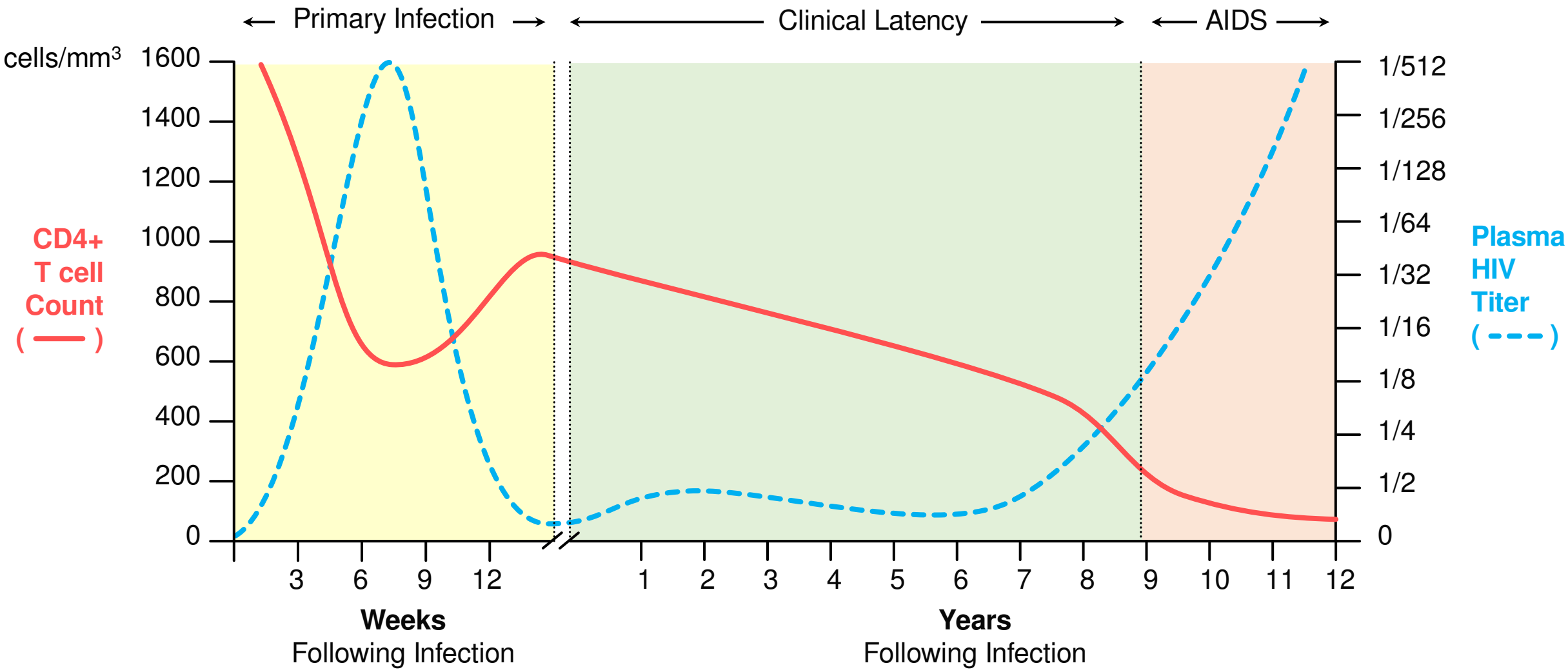


II. Laboratory Diagnosis of **HIV Infection**

Immunological Diagnosis

Screening Tests
Detection of serum HIV_{1+2} antibodies

- HIV antibodies **Rapid** Tests
  - ↑ false +ve results
- HIV antibodies **ELISA** (3^{rd} generation)
  - More Sensitive

HIV Combo Test
(4^{th} generation immunoassay)
detect both HIV_{1+2} Abs + p24 Ag
Best Screening Test

Confirmatory Tests
- **Western blot (WB)** technique
- **NAT** Testing
  - Measure Plasma viral load
  - Monitor Progression
  - Monitor therapy
  - **RT-PCR**
  - **Branched DNA**

(More sensitive and specific than screening test)

Window Period Tests
- **p24 antigen** (ELISA)

Follow Up Tests
- **CD4+ T cell** count
  - Monitor Progression
  - Monitor therapy

II. Laboratory Diagnosis of **HIV Infection**

Immunological Diagnosis

HIV Window Period (HIV Seroconversion):

— The time from HIV exposure to first anti-HIV antibody screening reactivity.

— Duration: 3 to 6 weeks from exposure to HIV.

— During this period the infected individual is **highly infectious** but anti-HIV antibody screening tests is seronegative.

— HIV infection during window period could be detected directly by **p24 antigen** or **NAT**.

II. Laboratory Diagnosis of **HIV Infection**

Immunological Diagnosis

p24 antigen is a useful HIV diagnostic tool: (positive 1 – 3 weeks after HIV exposure)

a. during the HIV window period,
b. during very late symptomatic stages of infection
c. Help to diagnose HIV infection the newborns born to HIV-infected mothers.

HIV_{1+2} Ag/Ab Combo Test (4^{th} generation screen immunoassay)

— A recent screening test using **a combination of 2 tests:**
  a. p24 antigen test: cover the window period.
  b. HIV1+2 antibody test
— Better diagnostic sensitivity compared to 3^{rd} HIV antibody screen immunoassay.

II. Laboratory Diagnosis of **HIV Infection**

Immunological Diagnosis

Neonatal Diagnosis of HIV Infection

— **A difficult sero-diagnostic problem**

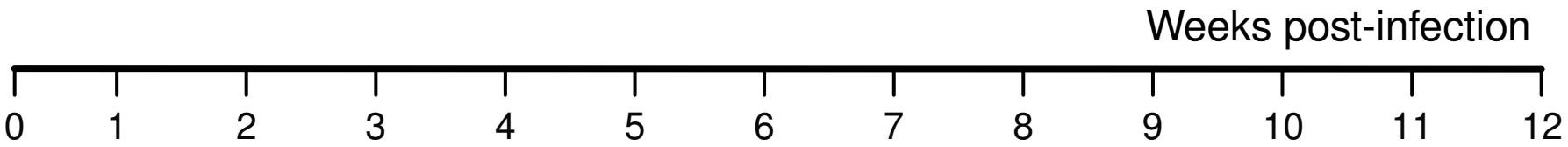
— Maternal **IgG** antibody **crosses the placenta**.

— Thus, infants passively acquire HIV antibody, which may persist for up to 15 months which could be detected by screening serological tests.

— The level of antibody in uninfected infants declines **too slowly** to be of clinical value for making treatment decisions.

— **Serum p24 antigen** and **NAT testing** for the neonates is the cornerstone for confirmation or exclusion of neonatal HIV infection.

II. Laboratory Diagnosis of **HIV Infection**



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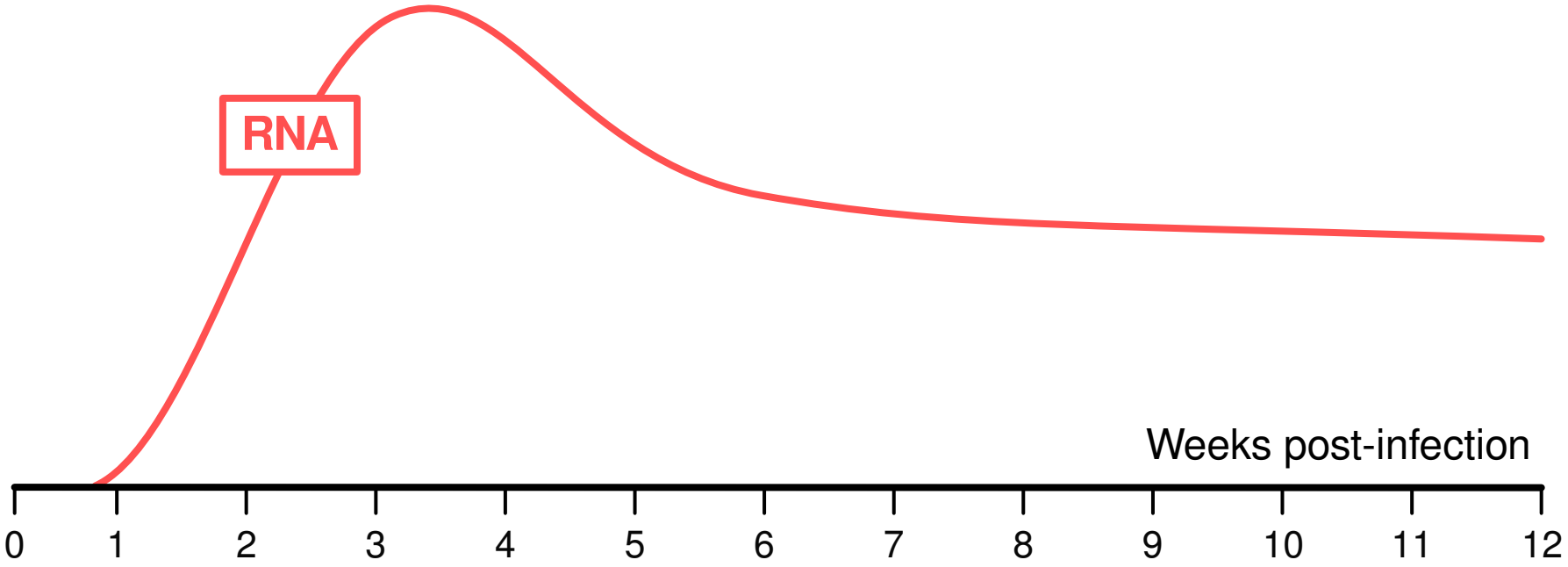

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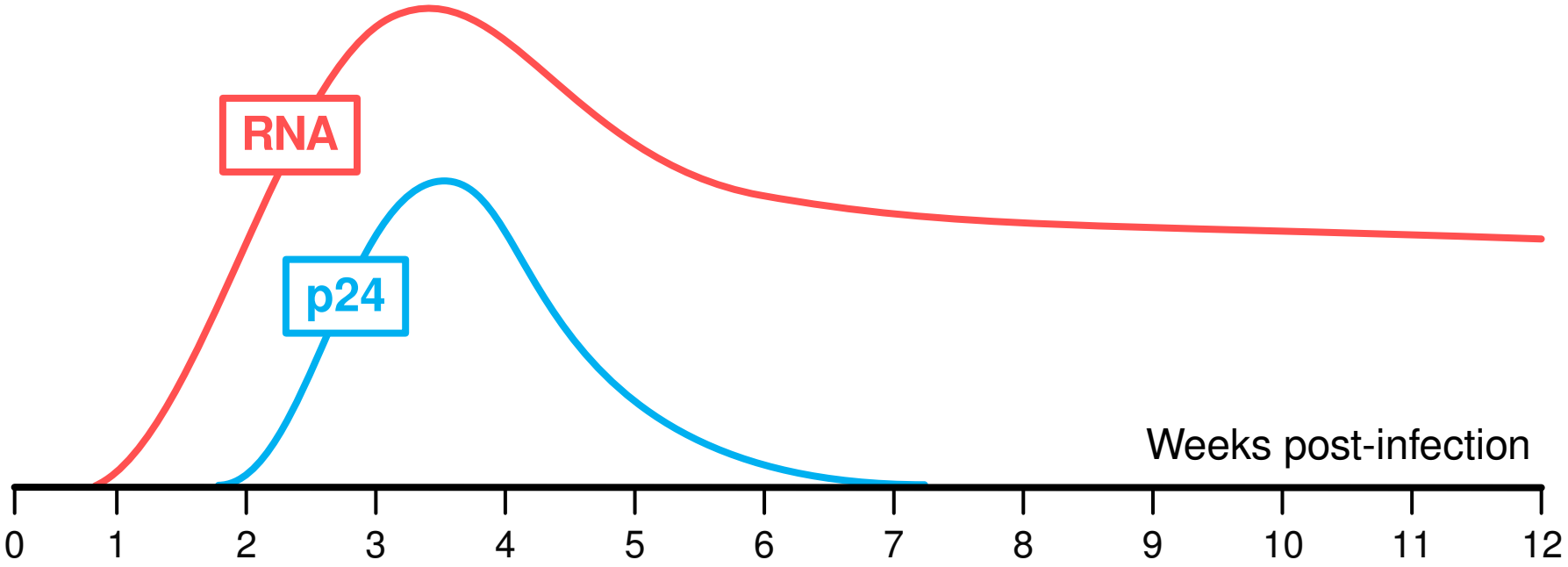

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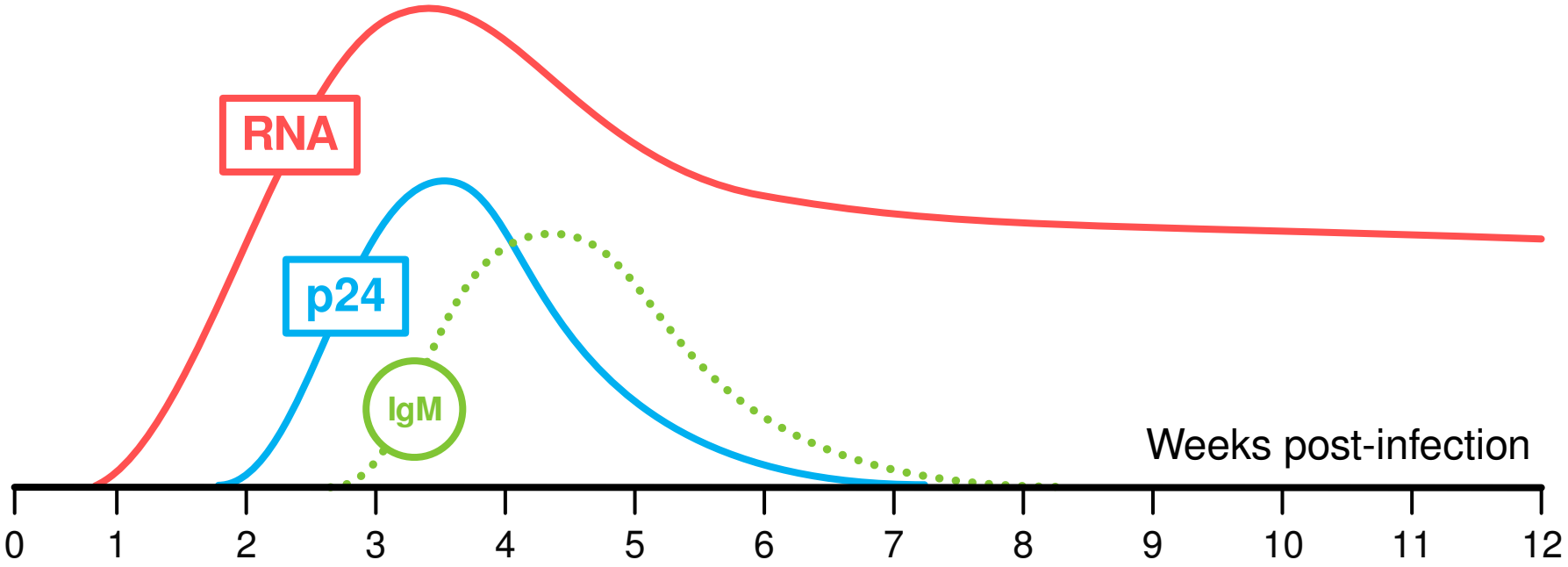

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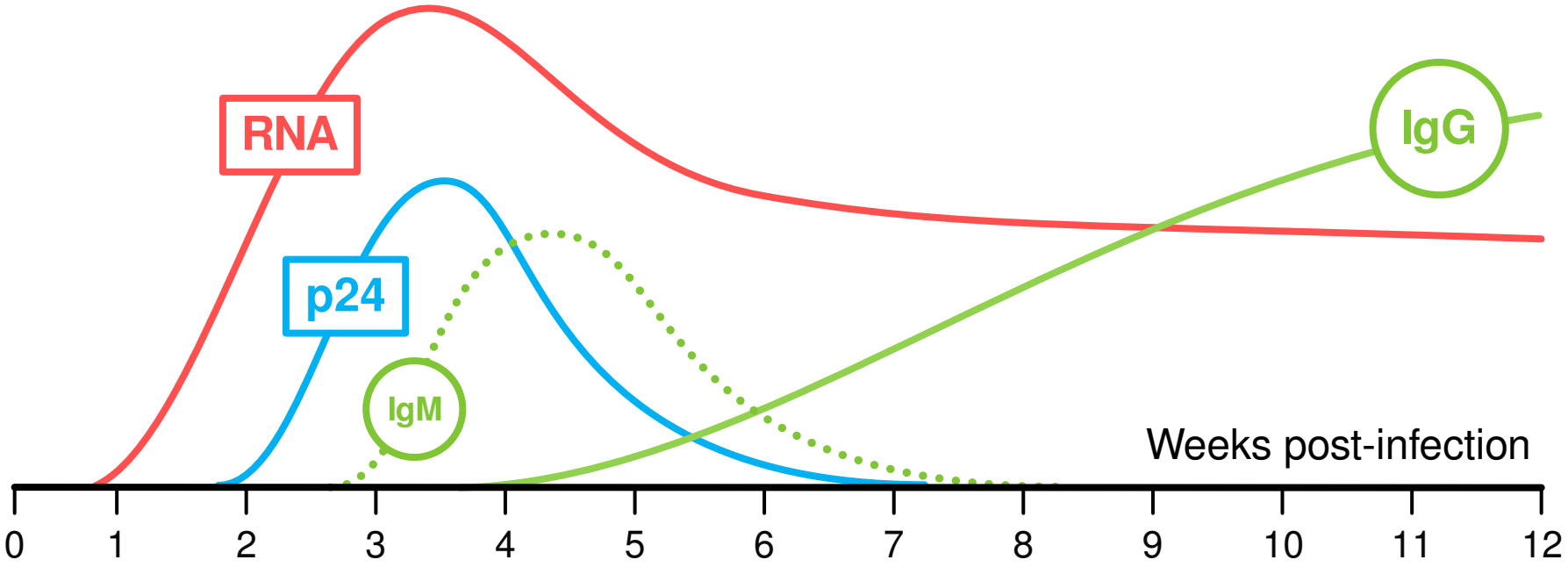

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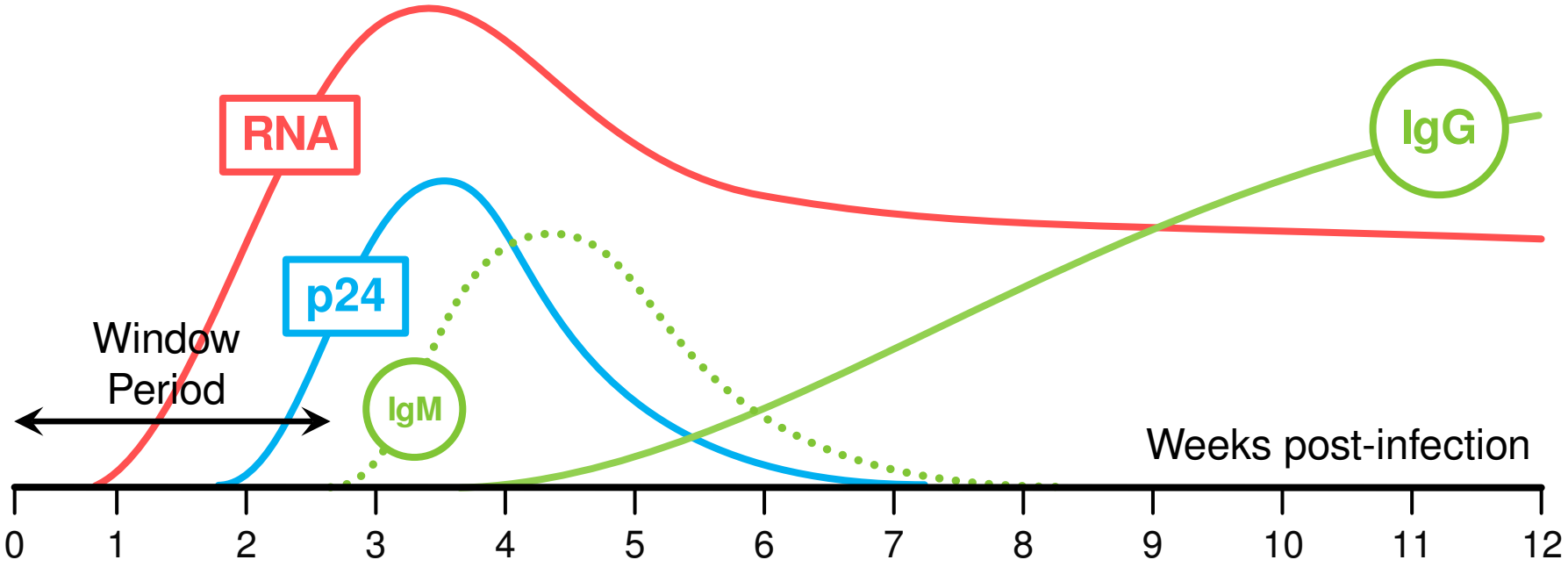

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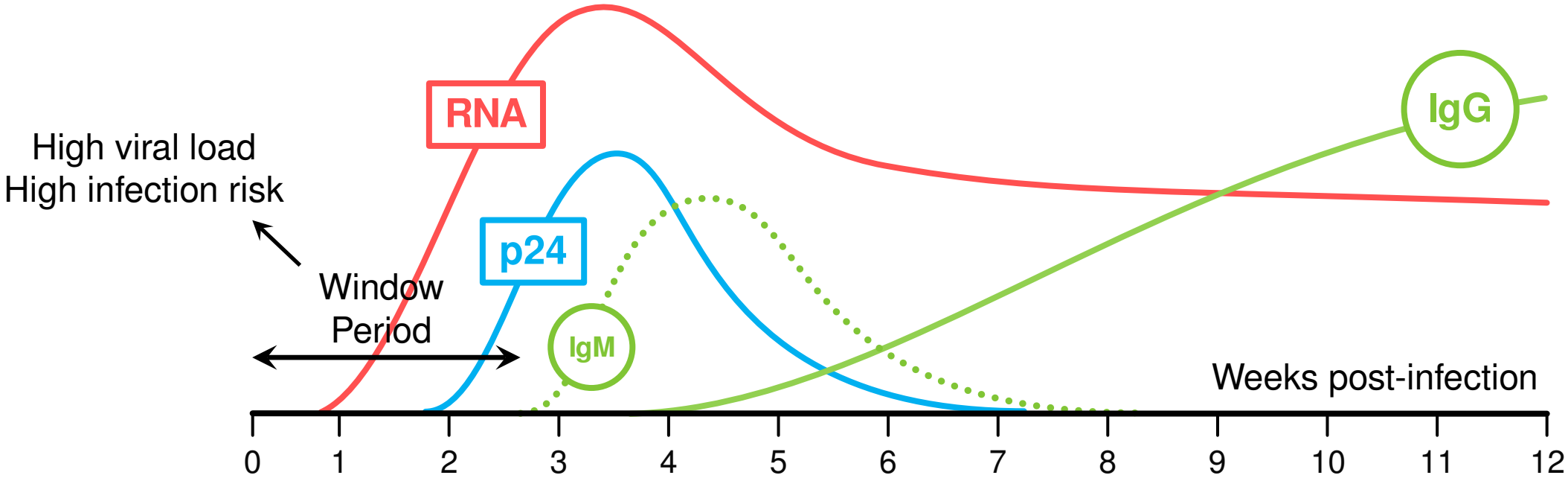

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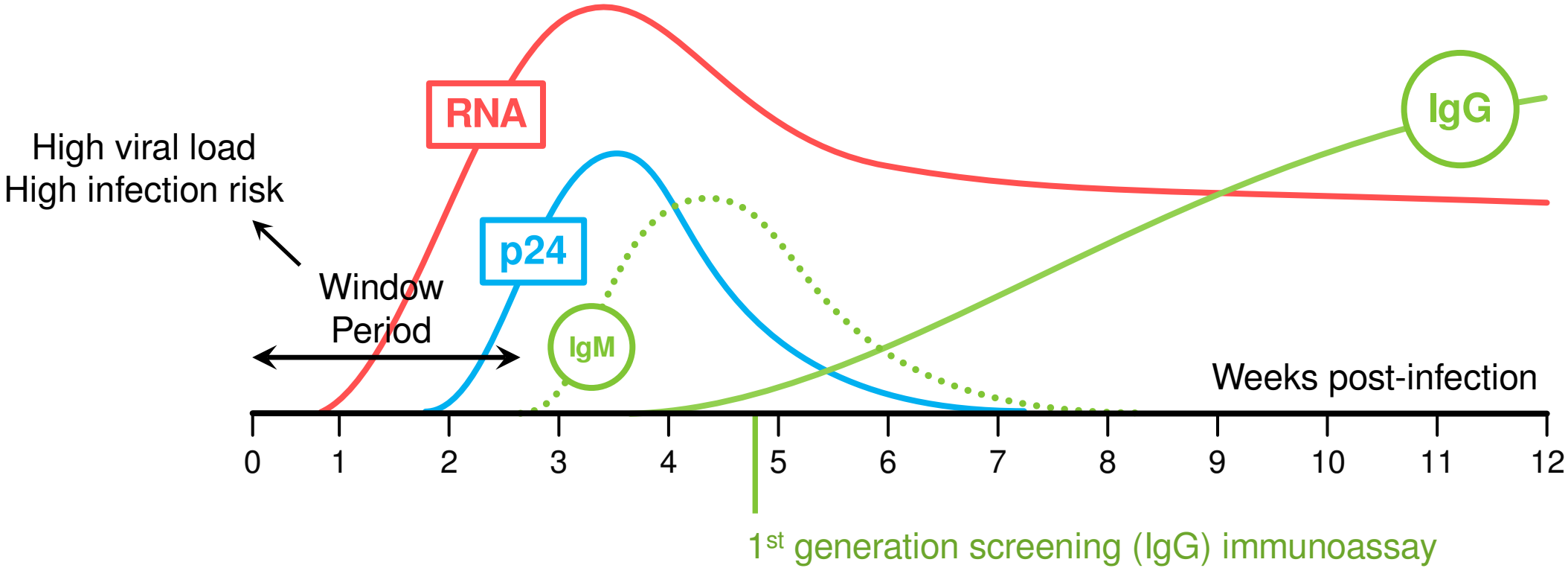

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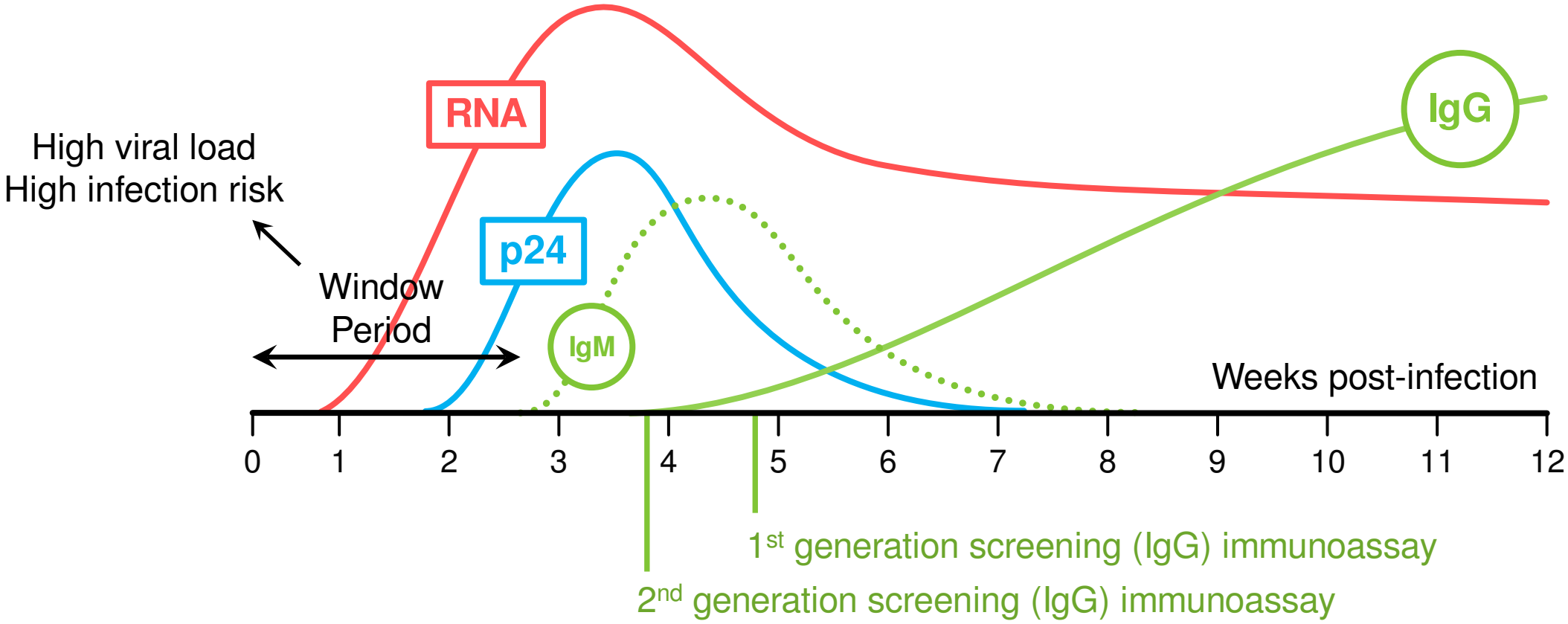

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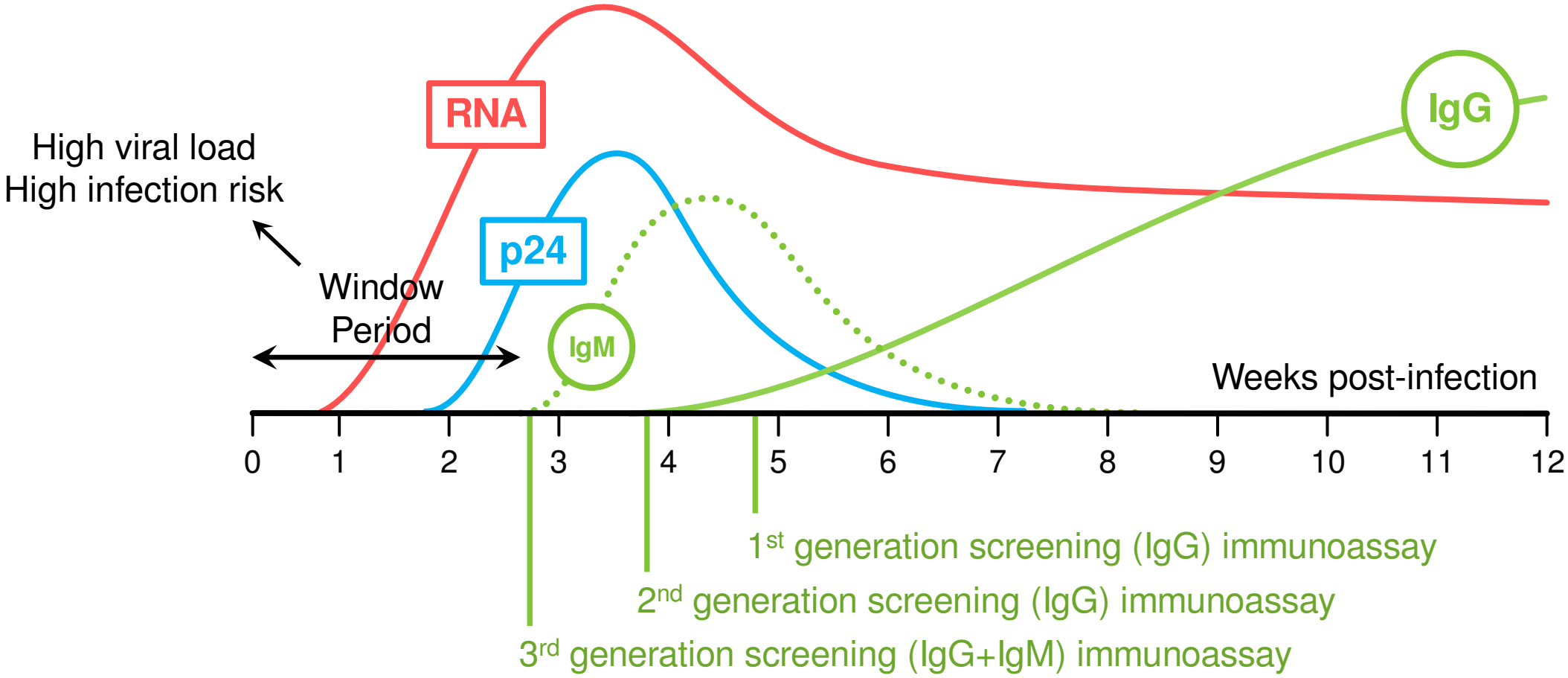

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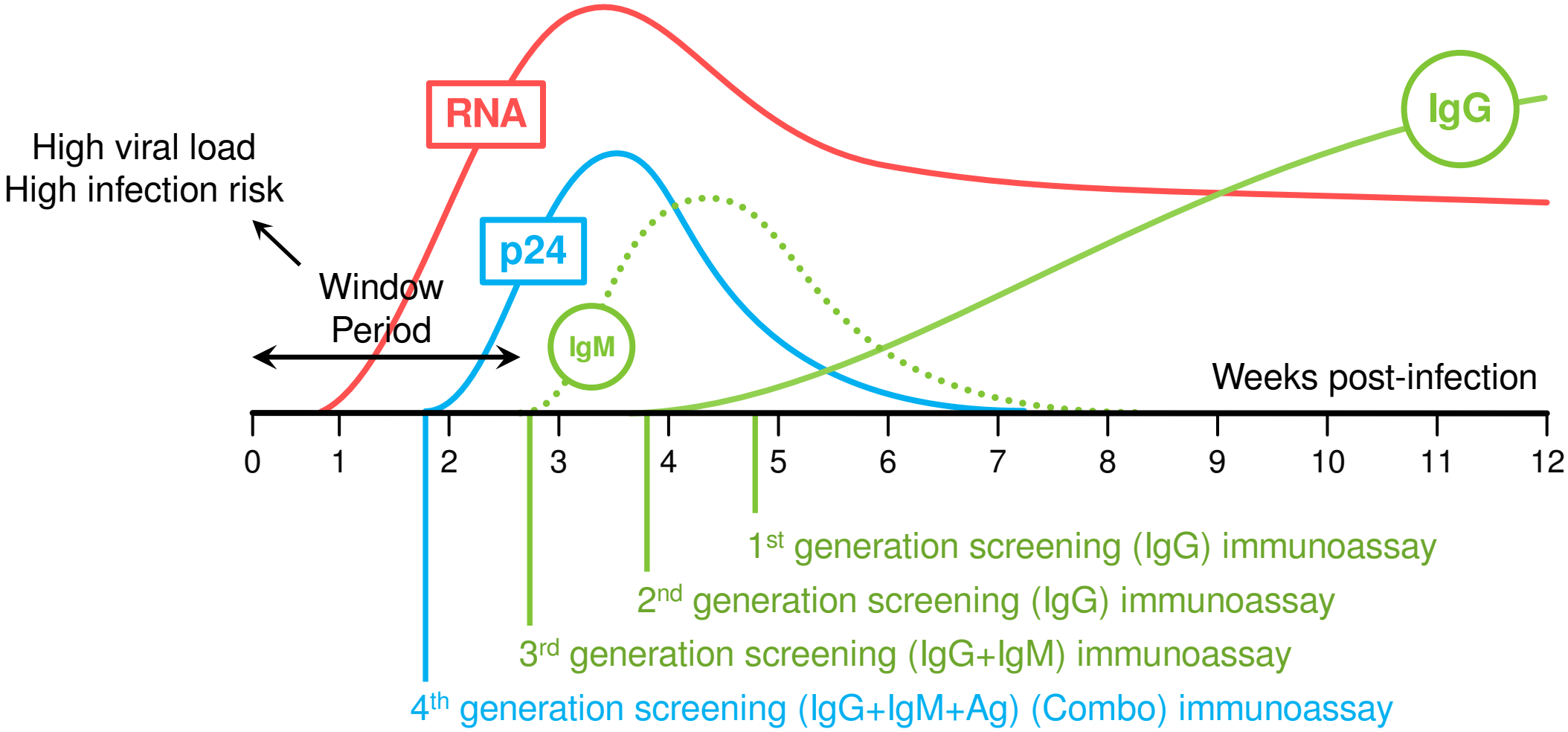

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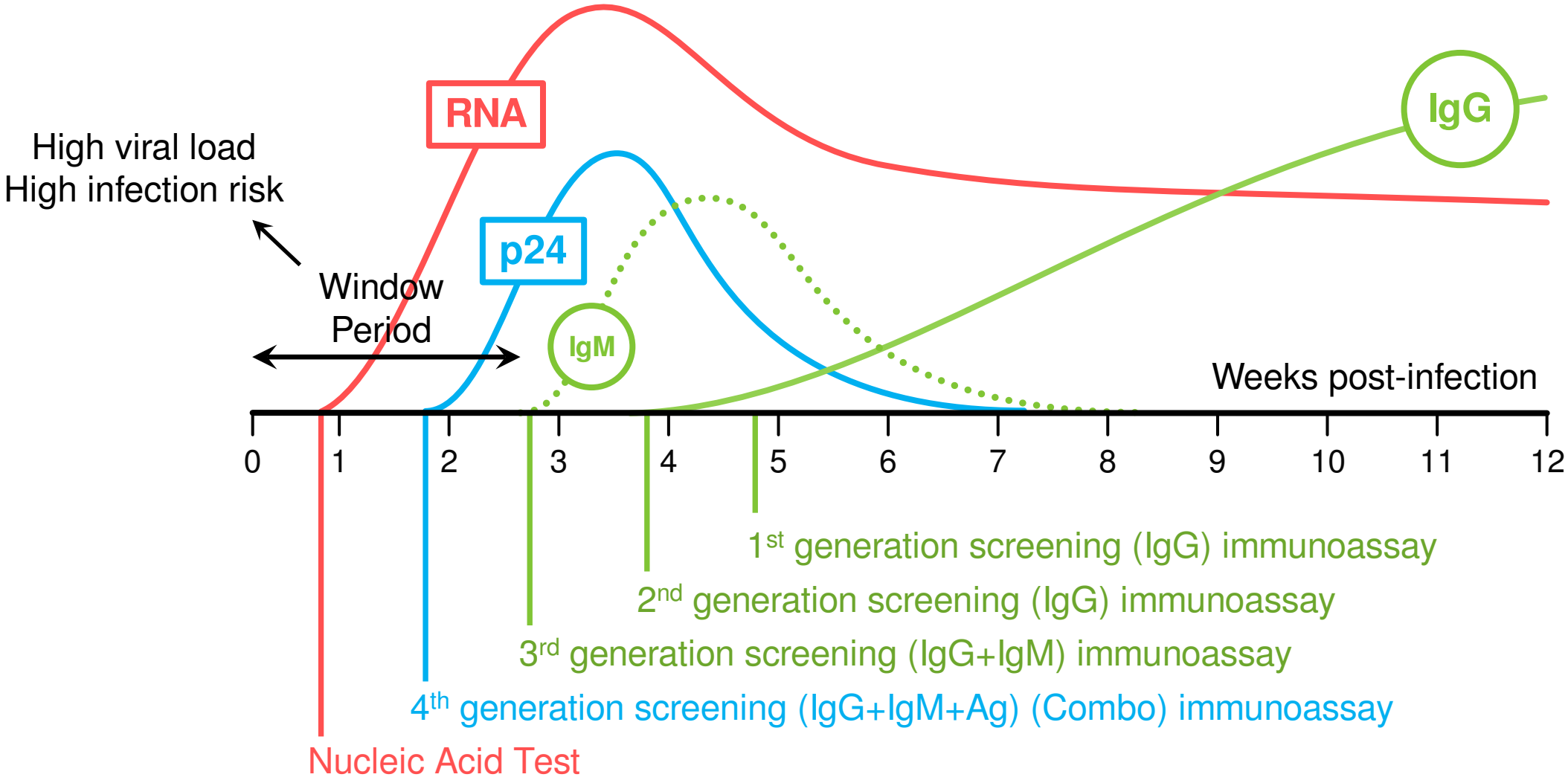

Quiz

HIV_{1+2} Combo Test is a combination of:

a. HIV PCR and p24 Antigen tests
b. HIV antibodies and p24 Antigen tests
c. HIV antibodies and CD4+ T cell count
d. HIV IgG and IgM antibodies tests

Quiz

HIV_{1+2} Combo Test is a combination of:

a. HIV PCR and p24 Antigen tests
b. HIV antibodies and p24 Antigen tests
c. HIV antibodies and CD4+ T cell count
d. HIV IgG and IgM antibodies tests

Quiz

p24 antigen is a useful HIV diagnostic tool in all of the following, except:

a. In the newborns born to HIV-infected mothers.
b. Detection of HIV seroconversion.
c. Monitoring retroviral therapy
d. During very late symptomatic stages of infection

Quiz

p24 antigen is a useful HIV diagnostic tool in all of the following, except:

a. In the newborns born to HIV-infected mothers.
b. Detection of HIV seroconversion.
c. **Monitoring retroviral therapy**
d. During very late symptomatic stages of infection

Quiz

In The AIDS stage of HIV infection, the circulating CD4+ T cell count drops to:

a. Less than 500 cells/mm^3
b. Less than 300 cells/mm^3
c. Less than 200 cells/mm^3
d. Less than 100 cells/mm^3

Quiz

In The AIDS stage of HIV infection, the circulating CD4+ T cell count drops to:

a. Less than 500 cells/mm^3
b. Less than 300 cells/mm^3
c. **Less than 200 cells/mm^3**
d. Less than 100 cells/mm^3

Quiz

All of the following is used to detect HIV in the window period, except:

a. HIV NAT
b. HIV ELISA 3rd Generation Test
c. HIV Combo Test
d. HIV p24 Antigen Test

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Quiz

A steady decline in the circulating CD4+ T cells count between 200 and 500 cells/mm^3 is characteristic for:

a. Acute Infection Stage
b. Clinical Latency Stage
c. Window Period
d. AIDS Stage

Quiz

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Quiz

L-tropic HIV enters inside lymphocytes by binding to:

a. CD4 receptor and CCR5 co-receptor
b. CD4 receptor and CXCR4 co-receptor
c. CD8 receptor and CCR5 co-receptor
d. CD8 receptor and CXCR4 co-receptor

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Quiz

What is NOT true as regards HIV NAT:

a. Measure plasma HIV viral load
b. A very sensitive HIV screening test
c. Monitor HIV disease progression
d. Monitor HIV therapy

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Quiz

Which one of the following tests is used to monitor HIV disease progression:

a. HIV 3rd Generation ELISA
b. HIV Combo Test
c. HIV p24 Antigen Test
d. Blood CD4+ T cells count

Quiz

Which one of the following tests is used to monitor HIV disease progression:

a. HIV 3rd Generation ELISA
b. HIV Combo Test
c. HIV p24 Antigen Test
d. Blood CD4+ T cells count

REPORT INTERPRETATION

Test	Result	Reference Interval
HIV1+2 antibody	Positive	Negative

Recommend Further Lab Investigations

REPORT INTERPRETATION

Test	Result	Unit	Reference Interval
HIV Ag/Ab Combo test	2.53	COI	Non reactive < 0.90 Gray zone 0.90 – 1.00 Reactive > 1.00
HIV RT-PCR (Quantitative)	23480	copies/ml	Undetectable < 20
CD3+ CD4+ cell count	110	/mm^3	500 – 1500

REPORT INTERPRETATION

HIV infection (AIDS Stage)

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thank
you