# Bloodborne viruses

**blood-borne viruses**

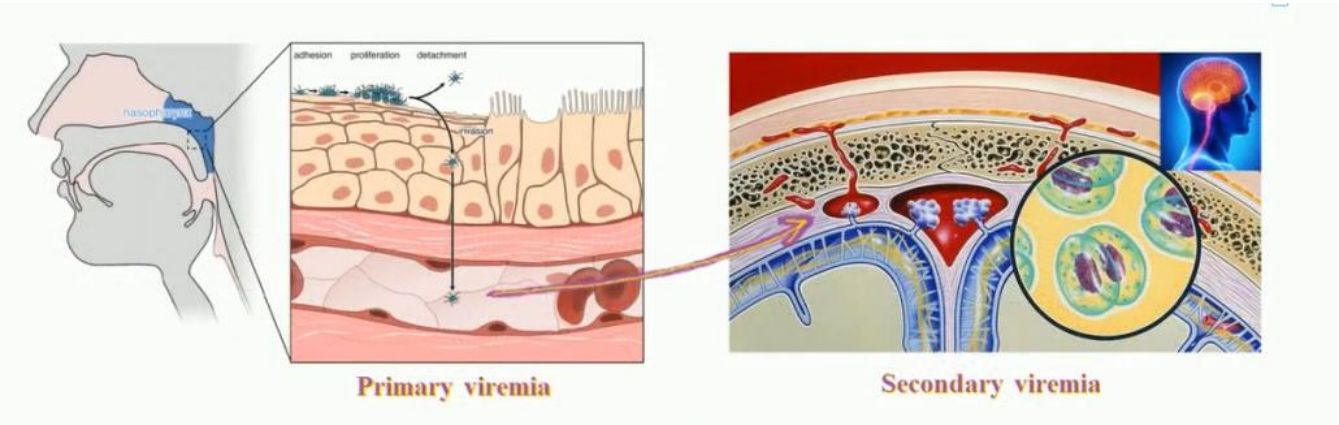
**sepsis of viral etiology**

**viral hemorrhagic fevers**

# VIREMIA

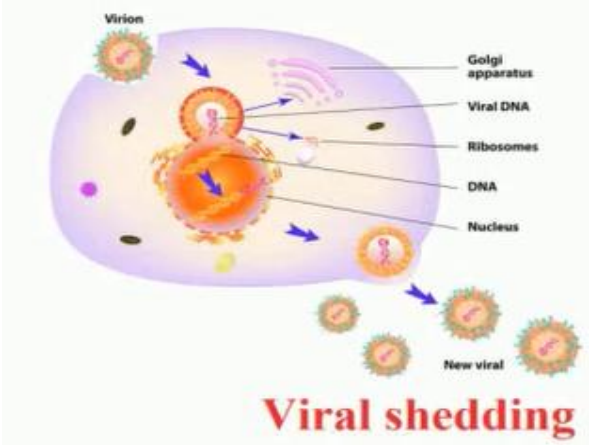
## Types of the presence of viruses in the blood:

PRIMARY
SECONDARY

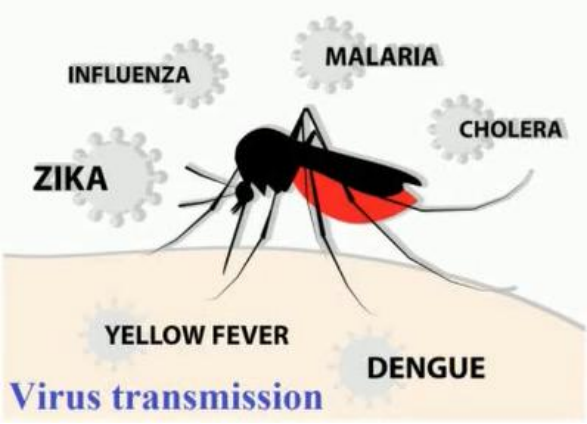



rabies virus

ACTIVE
PASSIVE




measles



# infectious material - risk of potential infection

- **high risk material** – blood, vaginal secretions
- **semen low risk material** – CSF and fluids: synovial, pleural, peritoneal, pericardial, amniotic very
- **low risk material** – feces, urine, saliva, sputum, nasal secretions, tears, sweat

CAUTION! the risk increases when blood is present in the above biological materials

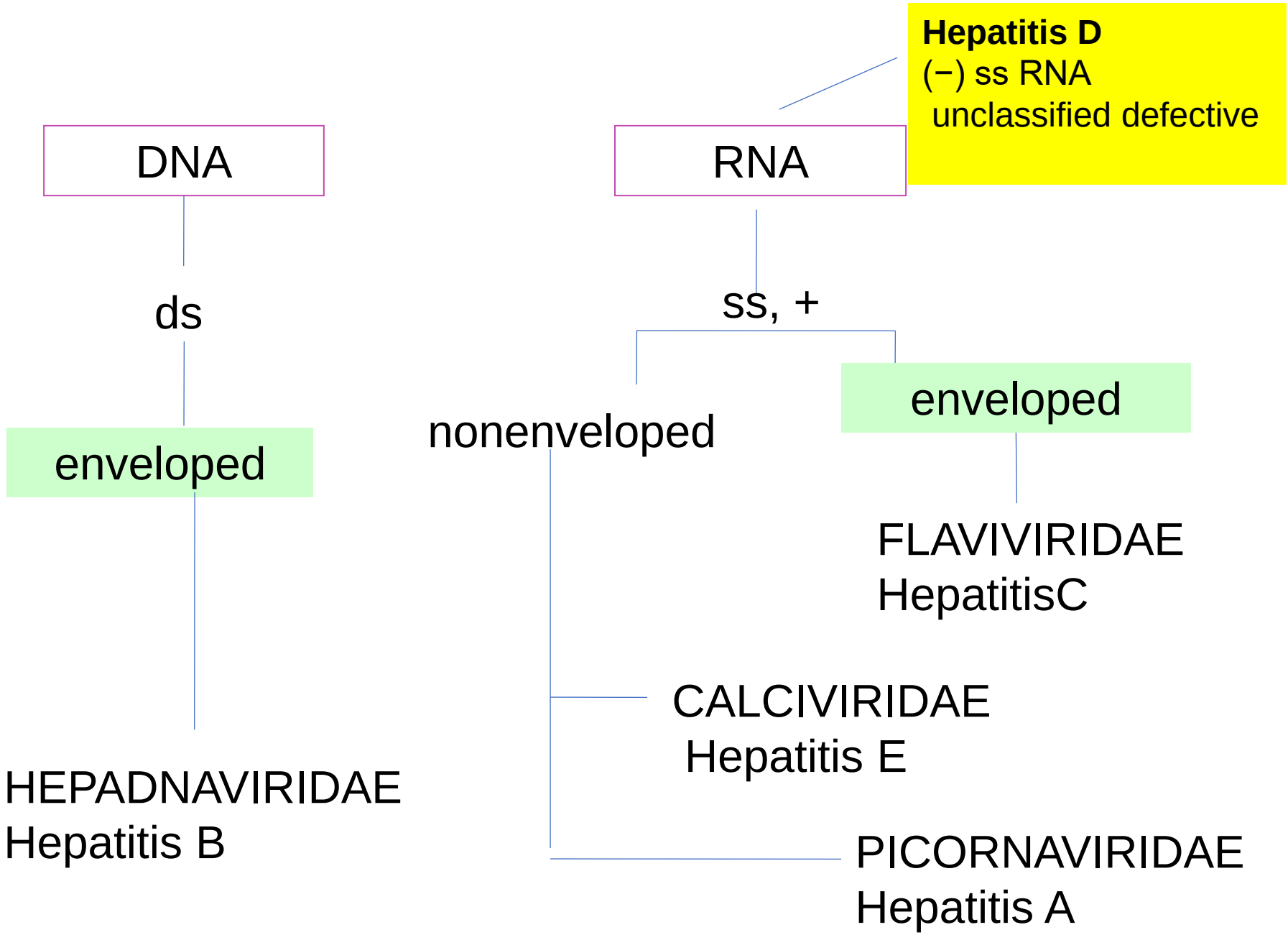
# Any contact with someone else's blood carries a potential risk of infection

Transmission of pathogenic microrganisms:

**direct** : with fresh blood

**indirect** : through dried blood on objects

# The most common blood-borne pathogens
# HBV, HCV, HDV, HIV and Ebola virus


Hepatitis D
(−) ss RNA
unclassified defective
DNA
RNA
ds
ss, +
enveloped
nonenveloped
enveloped
FLAVIVIRIDAE
HepatitisC
CALCIVIRIDAE
Hepatitis E
PICORNAVIRIDAE
Hepatitis A
HEPADNAVIRIDAE
Hepatitis B

# Survival of viruses outside the body according to the CDC

- HBV - can survive outside the body for at least 7 days. During this time, the virus can still cause infection if it enters the body of a person who is not infected
- HIV - does not survive long outside the human body (e.g. on surfaces) and cannot reproduce outside the human host (a matter of minutes or hours, depending on conditions)
- HCV - at room temperature, on environmental surfaces, up to 3 weeks. Its survival depends on the ambient temperature (in a liquid environment, HCV could be detected for up to 5 months at lower temperatures)

# General principles of conduct after contact with infectious material

- Percutaneous exposure

-Do not stop or squeeze out the blood

-Rinse the wound/puncture thoroughly under running water and wash with soap

-Do not use alcohol-based disinfectants

-Protect the injured area with a dressing

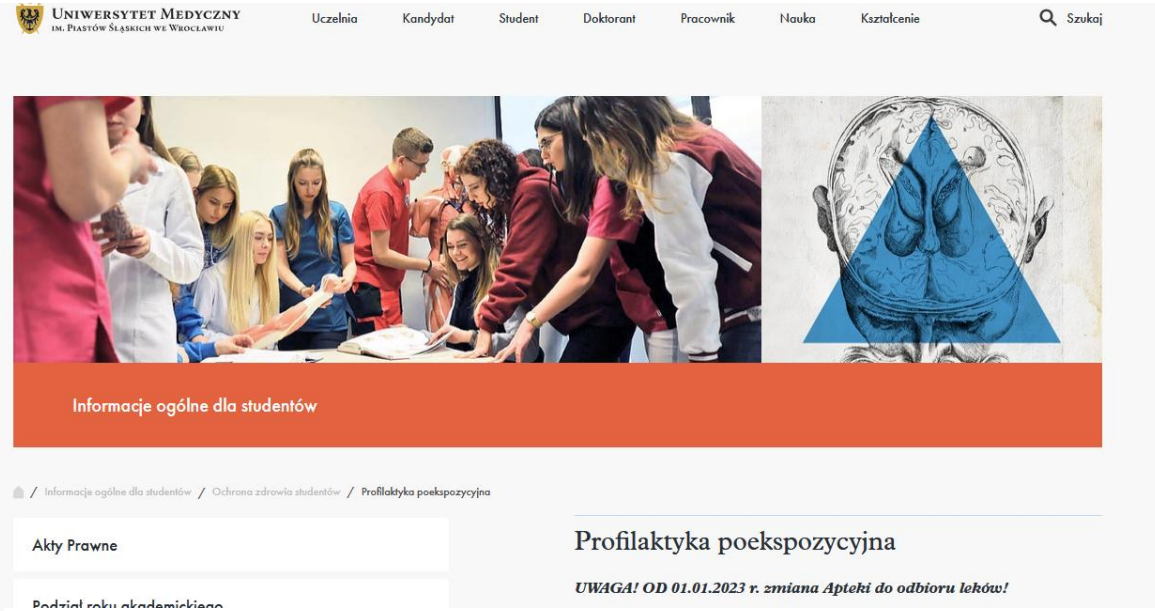
- Splashing of mucous membranes

- Wash thoroughly with a large amount of water or physiological saline solution

Follow the procedure for occupational exposure (who should be notified in the event of a possible exposure to infectious material)

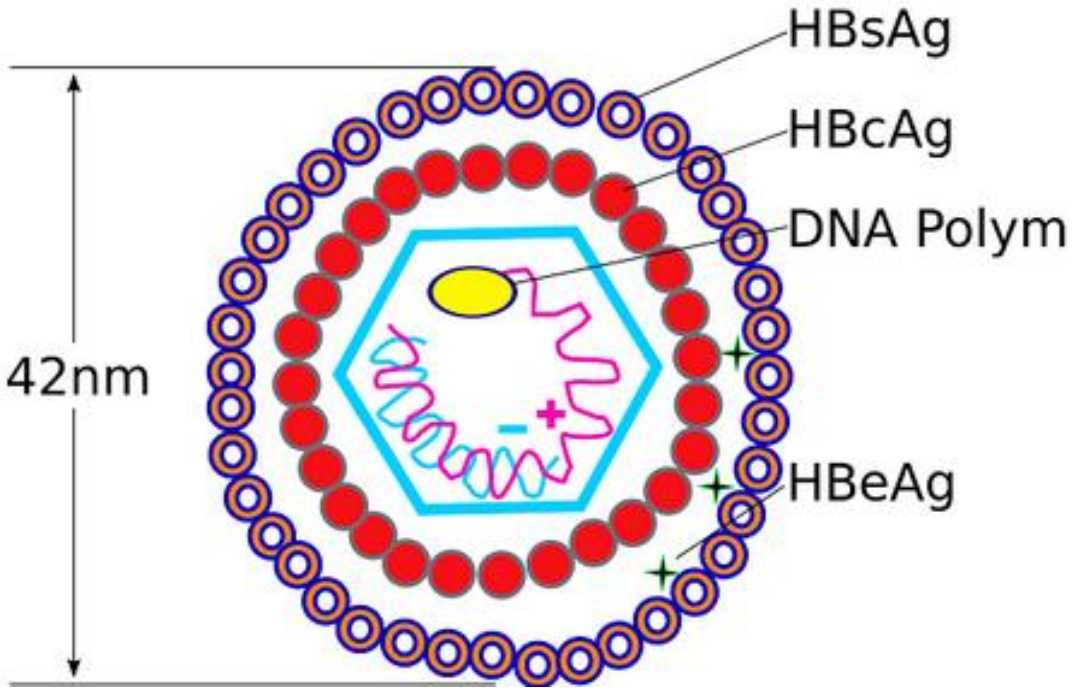
*Zarządzenie nr 233/XVI R/2021 Rektora Uniwersytetu Medycznego we Wrocławiu z dnia 1 października 2021 r. w sprawie wprowadzenia dla pracowników i studentów, doktorantów oraz uczestników wszystkich form kształcenia podyplomowego "Procedury postępowania po ekspozycji zawodowej na zakażenie wirusem HIV, HBV, HCV"*

załącznik nr 1 – Procedura postępowania po ekspozycji zawodowej na zakażenie wirusem HIV, HBV, HCV
załącznik nr 1 do Procedury – potwierdzenie zapoznania się z procedurą
załącznik nr 2 do Procedury – skierowanie do szpitala
załącznik nr 3 do Procedury – oświadczenie/zgoda od osoby źródłowej
załącznik nr 4 do Procedury – zlecenie na wykonanie badań (materiał osoby źródłowej)
załącznik nr 5 do Procedury – oświadczenie/zgoda osoby eksponowanej
załącznik nr 6 do Procedury – karta zgłoszenia ekspozycji zawodowej
załącznik nr 7 do Procedury – zgoda osoby eksponowanej na zastosowanie profilaktyki poekspozycyjnej
załącznik nr 8 do Procedury – zlecenie na wykonanie badań (materiał osoby eksponowanej)
załącznik nr 2 – Rejestr ekspozycji zawodowych




https://www.umw.edu.pl/pl/informacje-ogolne-dla-studentow/profilaktyka-poekspozycyjna

# Risk of infection transmission following occupational exposure

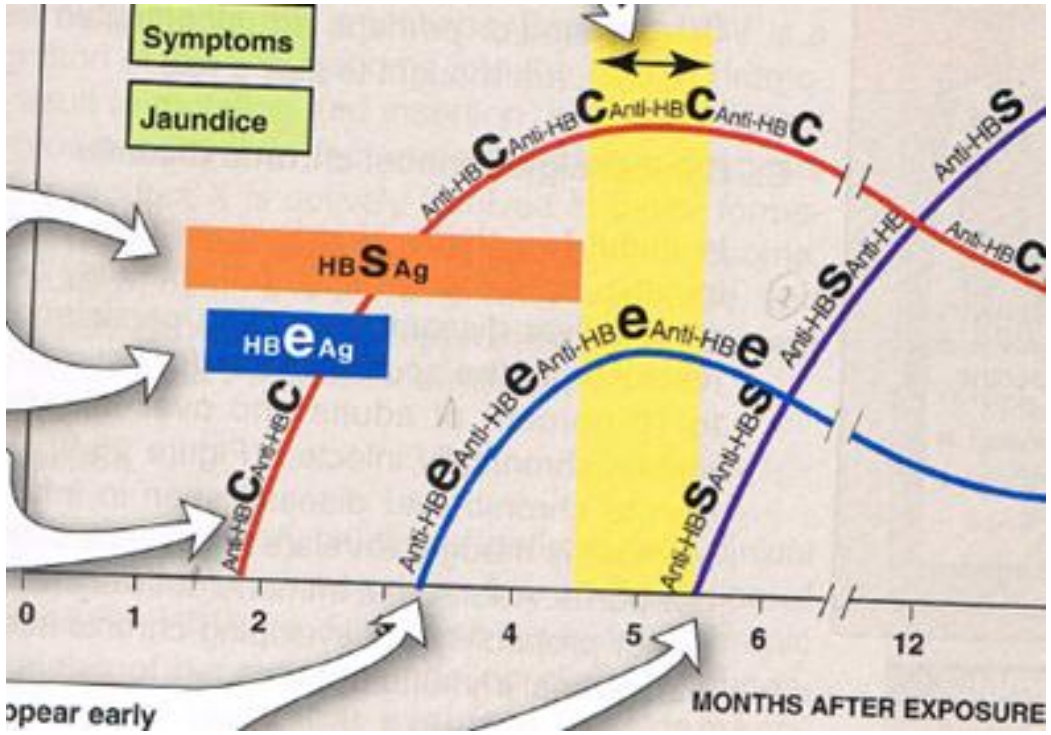



## HBV

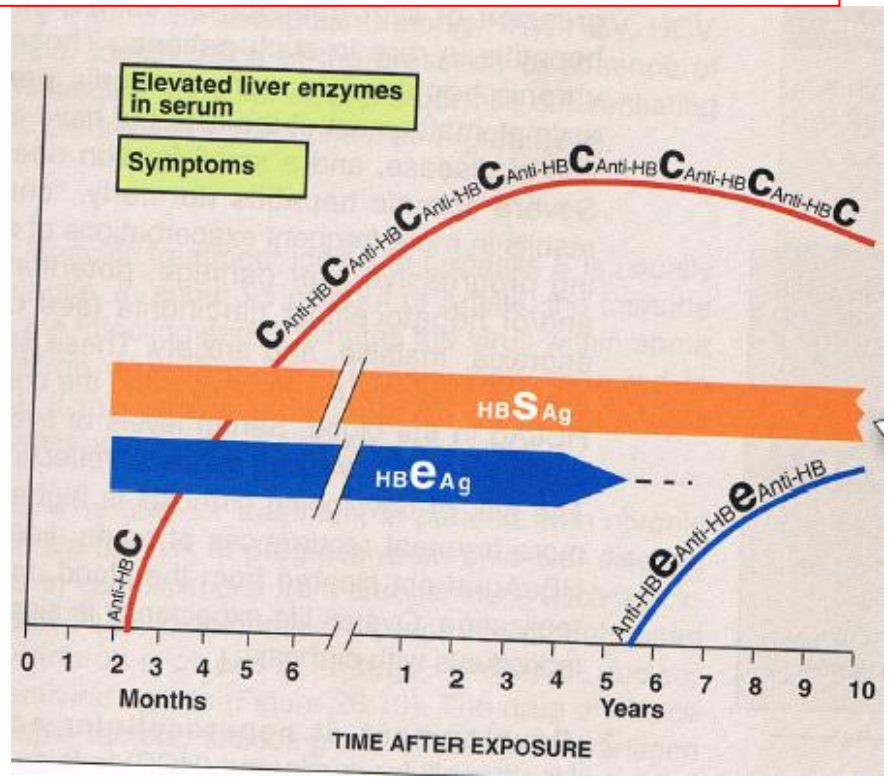
- Risk 6-30% depending on the status of the "e" antigen (HBeAg) and the level of HBV viremia in the source patient with confirmed infection

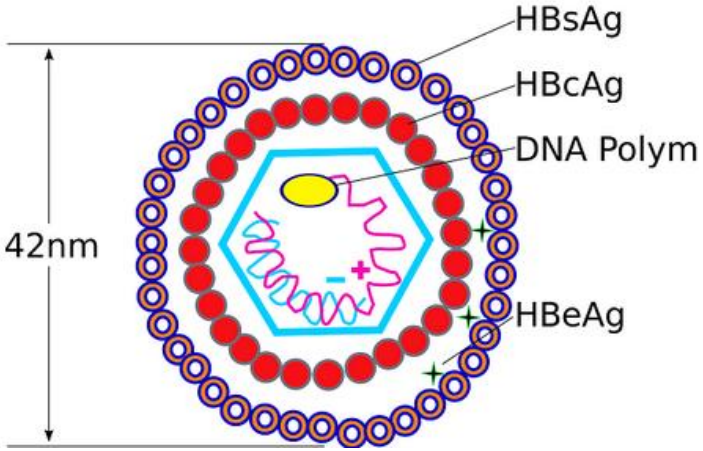
- vaccinated individuals who have developed immune antibodies - are not at risk of infection

# Acute infection




# Chronic infection



# Hepatitis B virus (HBV)

| source person | exposed person |
|---|---|
| If possible, HBsAg should be determined in the source patient | Both HBsAg and anti-HBc are tested |
| | In a vaccinated person, post-vaccination anti-HBs antibodies are additionally determined |
| | after 6 months, it is recommended to test HBsAg and anti-HBc in the exposed person |

In prophylaxis, the HBV vaccine and HBIG, i.e. anti-HBs antibodies (anti-HBs immunoglobulin) or both agents are used simultaneously. Prophylaxis should be started as soon as possible, preferably within 24 hours of exposure, no later than within 7 days.

# Hepatitis C virus (HCV)

- The risk of HCV infection after exposure to blood is relatively low, 2–4% after a needle prick and below this percentage after contact through mucous membranes.
- There is no anti-HCV serum or vaccine for HCV, so specific post-exposure prophylaxis is not possible
- The doctor orders tests for a possible, existing and unrecognized HCV infection in the exposed person. If the result is positive, it means that the person being tested requires further specialist tests
- In the case of a negative result, the possible presence of the virus in the blood should be assessed again after 5–6 weeks using a molecular test (RT PCR) or after 6 months, by determining the concentration of anti-HCV antibodies and ALT enzyme activity.

# Human immunodeficiency virus (HIV)

The risk of HIV infection is assessed by a specialist in infectious diseases.

The risk of HIV infection is assessed based on the type of exposure, infectious material and, if possible, the condition of the source patient.

People infected with HIV who regularly take anti-HIV drugs and whose viral load is undetectable in control tests are not infectious to others.

the doctor orders an HIV test for the exposed person and the source person (if their infection status is unknown and there is a possibility of taking a blood sample for testing)

risk :

0.3% through damaged skin

0.1% through mucous membranes

# HIV post-exposure prophylaxis

IF there are grounds for specific HIV prophylaxis, it is implemented as soon as possible. Ideally within 1–2 hours of exposure, but no later than 48 hours, and exceptionally after 72 hours. The treatment involves taking a combination of 3 drugs for 28 days.

A person offered such post-exposure prophylaxis is required to sign a consent form for treatment after receiving appropriate information on potential benefits and adverse effects.

During treatment, the patient undergoes medical and laboratory monitoring. The first is performed after 2 weeks. Control serological tests for HIV infection should be performed after 2 and 4 months of exposure. Control tests for the presence of HIV in the blood (HIV RNA) are not recommended.

Until HIV infection is ruled out, the exposed person should be considered potentially infectious. To reduce the risk of potential infection of other people, they should avoid risky behaviors

# sepsis of viral etiology

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection

Septic shock is a subset of sepsis in which particularly profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone

# sepsis of viral etiology

Up to 42% of sepsis cases are culture negative on standard media (non-bacterial cause?)

The incidence of viral sepsis is unknown and there is insufficient information to make an accurate estimate

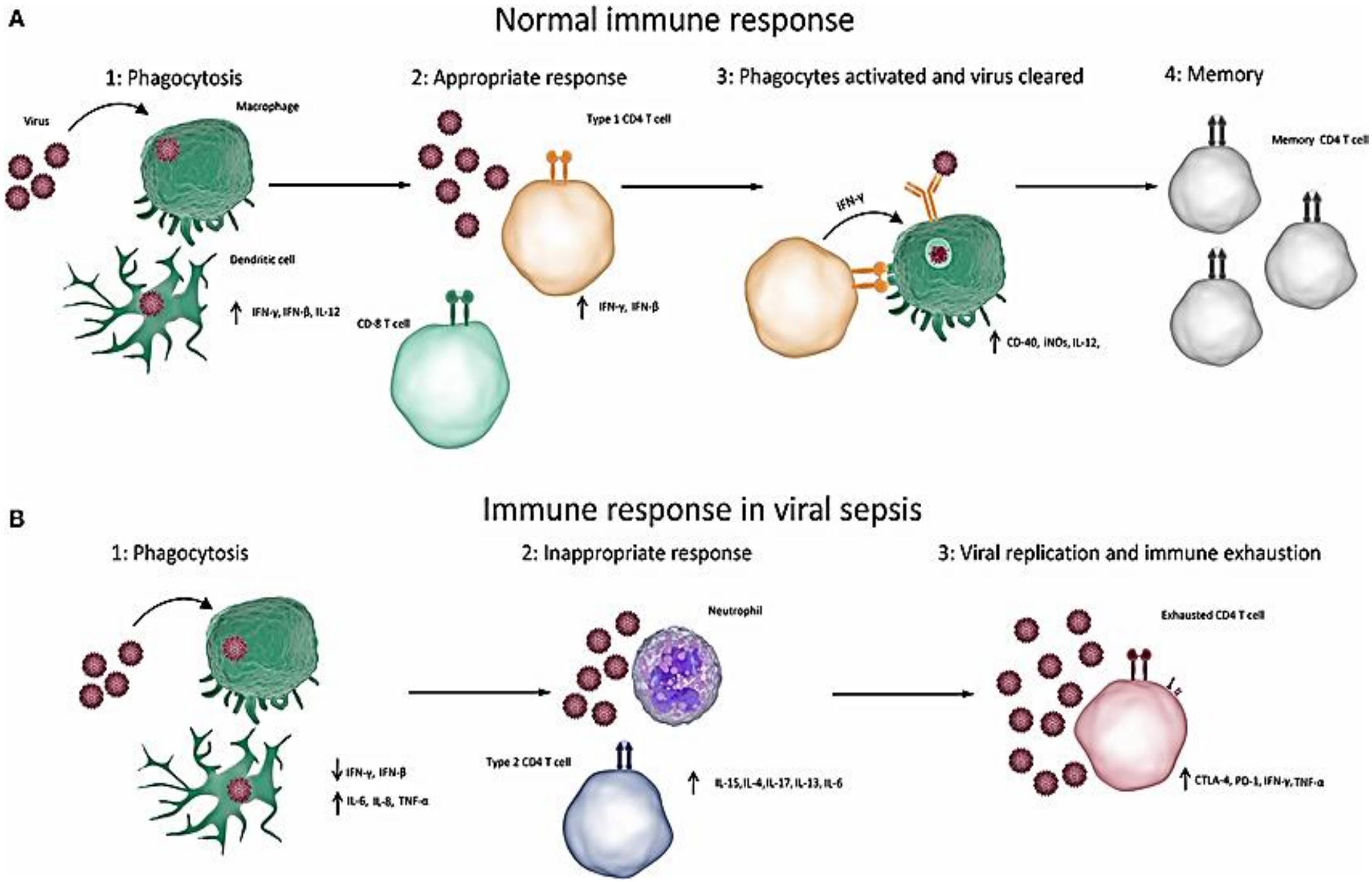
# Can viruses cause sepsis?

**Table 1 Examples of key PAMPs and DAMPs in sepsis pathophysiology.**

| | Origin | PRR |
|---|---|---|
| **PAMPs** | | |
| (Diacyl/triacyl) lipopetides | Gram-positive/Gram-negative bacteria | TLR1,TLR2,TLR6 |
| LTA | Gram-positive bacteria | TLR2 |
| Peptidoglycan | Gram-positive/Gram-negative bacteria | TLR2 |
| dsRNA | Double-stranded RNA virus | TLR3, RIG-1 |
| LPS | Gram-negative bacteria | TLR4 |
| Flagellin | Gram-positive/Gram-negative bacteria | TLR5 |
| ssRNA | Singe-stranded RNA virus | TLR7, TLR8 |
| CpG DNA | Bacteria | TLR9 |
| **DAMPs** | | |

PAMPs: pathogen-associated molecular patterns;
PRR: pattern-recognition receptor
DAMPs: damage-associated molecular patterns

Almost any virus can cause sepsis in vulnerable patients (e.g., neonates, infants, and other immunosuppressed groups)
Despite this, diagnosis of viral sepsis remains very rare


A
Normal immune response
1: Phagocytosis
2: Appropriate response
3: Phagocytes activated and virus cleared
4: Memory
Virus
Macrophage
Dendritic cell
↑ IFN-γ, IFN-β, IL-12
Type 1 CD4 T cell
CD-8 T cell
↑ IFN-γ, IFN-β
IFN-γ
↑ CD-40, iNOs, IL-12,
Memory CD4 T cell
B
Immune response in viral sepsis
1: Phagocytosis
2: Inappropriate response
3: Viral replication and immune exhaustion
↓ IFN-γ, IFN-β
↑ IL-6, IL-8, TNF-α
Neutrophil
Type 2 CD4 T cell
↑ IL-15,IL-4,IL-17, IL-13, IL-6
Exhausted CD4 T cell
↑ CTLA-4, PD-1, IFN-γ, TNF-α

# Which viruses are a leading cause of sepsis?

## DENGUE VIRUSES
**are a leading cause of sepsis in some tropical countries[2]**

Dengue virus is one of the most widespread viruses transmitted by mosquitos.[2]

*Symptoms Include:*[4]
- Fever
- Severe Headache
- Joint/Muscle Pain

## INFLUENZA VIRUSES
**are a major cause of severe infection[2]**

About 60% of mortality from seasonal influenza occurs in people older than 65 years of age.[2]

Influenza A and B viruses cause seasonal and non-seasonal outbreaks worldwide.[2]

*Symptoms Include:*[4]
- Fever
- Cough
- Runny Nose

## HERPES
**is the leading cause of NEONATAL SEPSIS[2]**

## Fast Fact:

**In newborns, Herpes simplex virus (HSV) can cause three types of disease: skin, eye and mouth disease, encephalitis, and disseminated disease. *Disseminated HSV disease is the most severe form of HSV infection, with a***

| | Clinical syndromes | Epidemiology | Risk factors for sepsis |
|---|---|---|---|
| HSV | Disseminated disease<br>Hepatitis | Neonatal disseminated disease<br>Incidence: 2–15 per 100,000 live births<br>Mortality: up to 29% | Newly-acquired maternal genital infection near term<br>HSV-2 infection (compared with HSV-1 infection) |
| Enterovirus | Sepsis-like illness<br>Myocarditis<br>Encephalomyelitis<br>Pulmonary oedema or haemorrhage | Incidence: 37% of young infants (<90 days of age) with sepsis[a] and without signs of localised infection<br>Mortality of neonatal enteroviral sepsis: up to 42% | Lack of maternal antibodies<br>Maternal infection just before or at delivery<br>Neonatal infection with echovirus 6, 9, 11, 19 or coxsackievirus B2–B5<br>Enterovirus A71 infection in young children |
| HPeV | Sepsis-like illness<br>Meningoencephalitis | Incidence: 15% of young infants (<90 days of age) with sepsis[a] and without signs of localised infection | HPeV3 infection (compared with infection with other types of HPeV) |
| Influenza virus | ARDS<br>Myocarditis<br>Encephalopathy | Incidence: 1 million cases of severe respiratory infections in children <5 years of age worldwide annually<br>Mortality: 290,000–650,000 respiratory deaths worldwide annually (all age groups) | People of extreme age (<5 or >65 years)<br>Immunosuppression<br>Pregnancy<br>Influenza A (H3N2) virus infection (compared with influenza A (H1N1) or B virus infections) |
| Dengue virus | Severe dengue[b]<br>Dengue shock[b] | Incidence: 58–96 million symptomatic dengue infections with 250,000–500,000 progressing to severe disease worldwide annually; 8% of sepsis cases[c] in Southeast Asian<br>Mortality: 9,000–24,000 deaths worldwide annually | Previous dengue infection (with a different [illegible]) |
| Adenovirus | Disseminated disease<br>Meningoencephalitis<br>Severe pneumonia | Disseminated disease in children<br>Incidence: 2.5% of adenovirus infection<br>Mortality: 55% | [illegible] immunosuppression (particularly allogeneic HSCT)<br>Young children<br>Infection with adenovirus serotypes 3 and 7 |

## Viral sepsis - etiology

Neonates – HSV and enteroviruses

Young children – enteroviruses (Coxsackie, ECHO, EV71) and parechoviruses (HPeVs)

All age groups – influenza viruses (young children, elderly, pregnant women, immunosuppressed

# *Coronaviridae*

SARS – CoV
Severe Acute Respiratory Syndrome
Chiny, 2002

MERS CoV
Middle East Respiratory Syndrome
Arabia Saudyjska, 2012

SARS-CoV-2
Severe Acute Respiratory Syndrome
Corona Virus-2
Wuhan, Chiny 2019

CFR -case fatality rate

10%

35%

2%

J Family Med Prim Care. 2022 Jan 31;11(1):10–17. doi: 10.4103/jfmpc.jfmpc_839_21

**SARS, MERS and CoVID-19: An overview and comparison of clinical, laboratory and radiological features**

Manas Pustake [1,✉], Isha Tambolkar [2], Purushottam Giri [3], Charmi Gandhi [1]

# VHFs –
# Viral Hemorrhagic Fevers

# Viral Hemorrhagic Fevers (VHFs)

- A group of diseases that are caused by several distinct families of viruses
- VHF – severe multisystem syndrome with microvascular instability, capillary leak, and impaired homeostasis, which may lead to shock

## VHFs common characteristics

- Enveloped ssRNA viruses
- Tropism to dendritic cells and macrophages
- Sporadic cases or outbreaks
- Both genders and all age groups affected
- Generally asymptomatic or flu-like symptoms
- Severe cases associated with high levels of virus in blood
- Geographically restricted by the presence of natural hosts – these viruses are zoonotic and maintained in nature in mammals

# VHF

## ARBOVIRUSES

| Flaviviruses | Bunyaviruses | Reovirus | |
|---|---|---|---|
| Mosquito-borne | Mosquito-borne | Tick-borne | Tick-borne |
| Yellow fever<br>Dengue | Rift Valley fever | Congo-Crimean VHF | Colorado Tick virus |

VECTORS

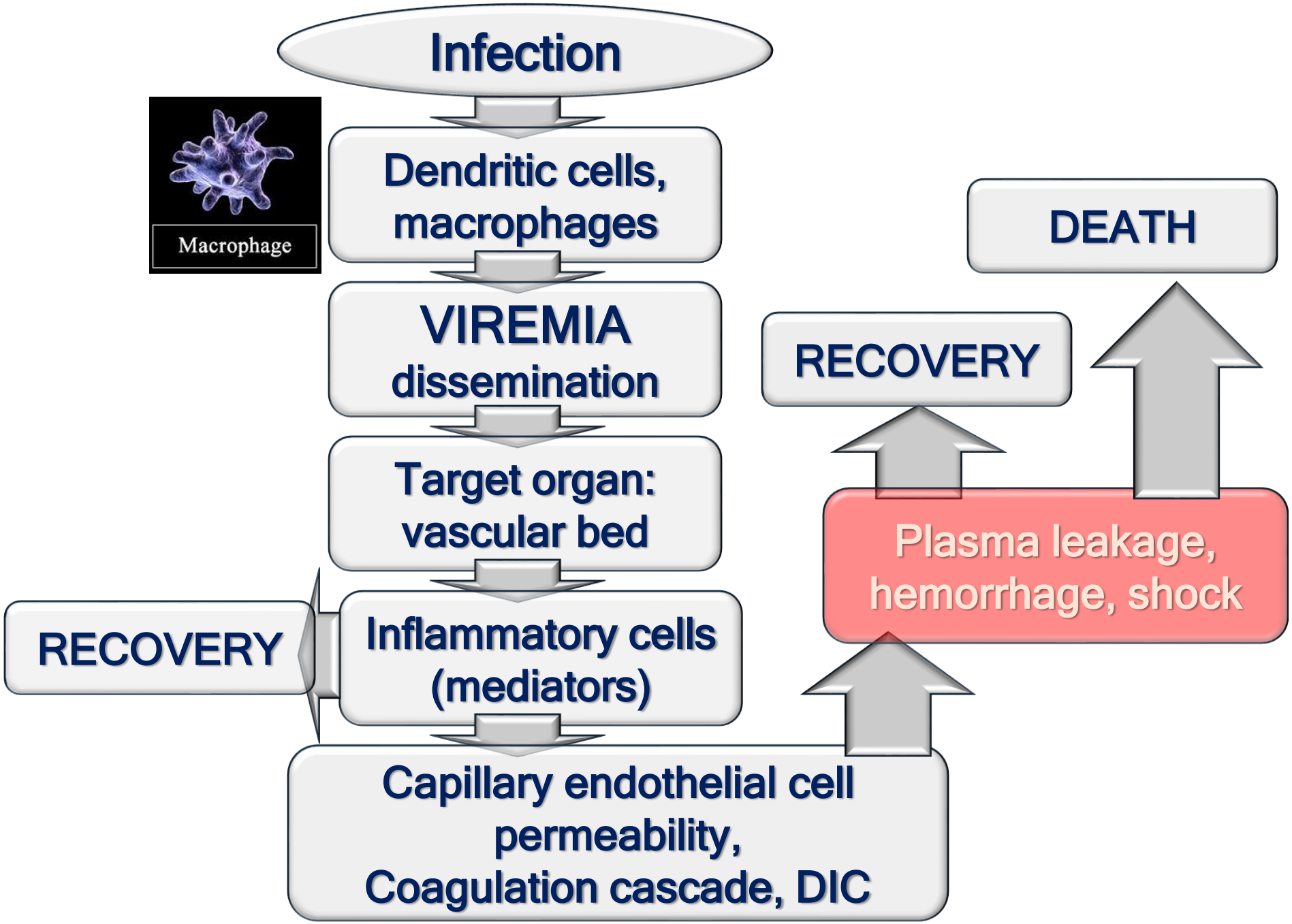
## NOT ARBOVIRUSES

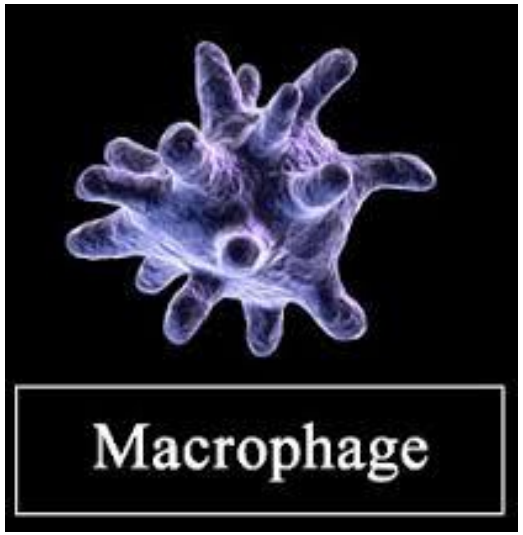
| Bat viruses | Rodent viruses | |
|---|---|---|
| Filoviruses | Bunyavirus | Arenaviruses |
| Ebola<br>Marburg | Hantavirus | Lassa fever<br>South American VHF |

RESERVOIRS

# VHFs clinical features

- Spectrum from mild or asymptomatic infection to severe vascular permeability with shock, MOSF, and death
- Clinical presentation may differ for each VHF as it progress
- Incubation period: days to weeks (2-21 days)
- Symptoms: fever, general malaise, anorexia, headache, myalgia, arthralgias, sore throat, chest pain
- GTI features: nausea, vomiting, abdominal pain (tenderness), diarrhea (may become bloody) or constipation
- Conjunctival hemorrhage
- Skin rash: maculopapular, petechial
- Severe hemorrhages (but in severe cases)
- Hepatic and renal involvement
- Neurological manifestations may occur (arenaviruses)


Infection
Macrophage
Dendritic cells, macrophages
VIREMIA dissemination
Target organ: vascular bed
Inflammatory cells (mediators)
Capillary endothelial cell permeability, Coagulation cascade, DIC
Plasma leakage, hemorrhage, shock
RECOVERY
DEATH
RECOVERY



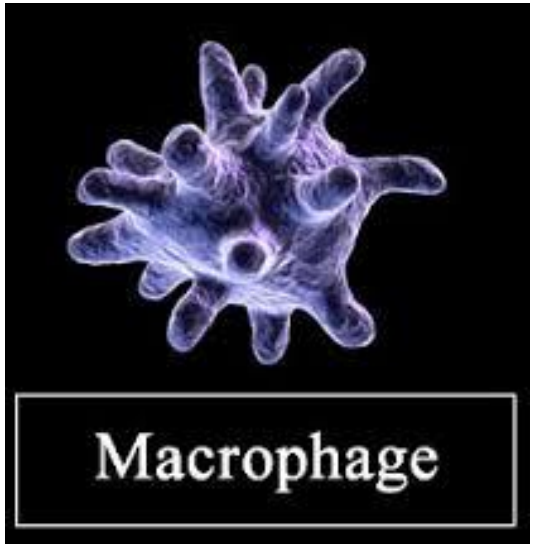

TNFα → -chemoattractant for neutrophils
-activation of the coagulation system

MCP-1 → **monocyte chemotactic protein 1:** recruits monocytes ,memory T cells dendritic cells to the sites of inflammation

NO → contribute to the hypotension, cardiodepression and vascular hyporeactivity

Impairs the synthesis of clotting factors

Dissemination to hepatocytes, adrenal cortical cells, fibroblasts = extensive tissue necrosis




Increase permeability of vascular endothelium = easier entry into endothelial cells (2nd target )

# Ebola virus

was discovered in 1976

nomenclature: EBOV (Ebola virus) & EVD (Ebola Virus Disease)

Ebolavirus genus consists of six species:

-Zaire

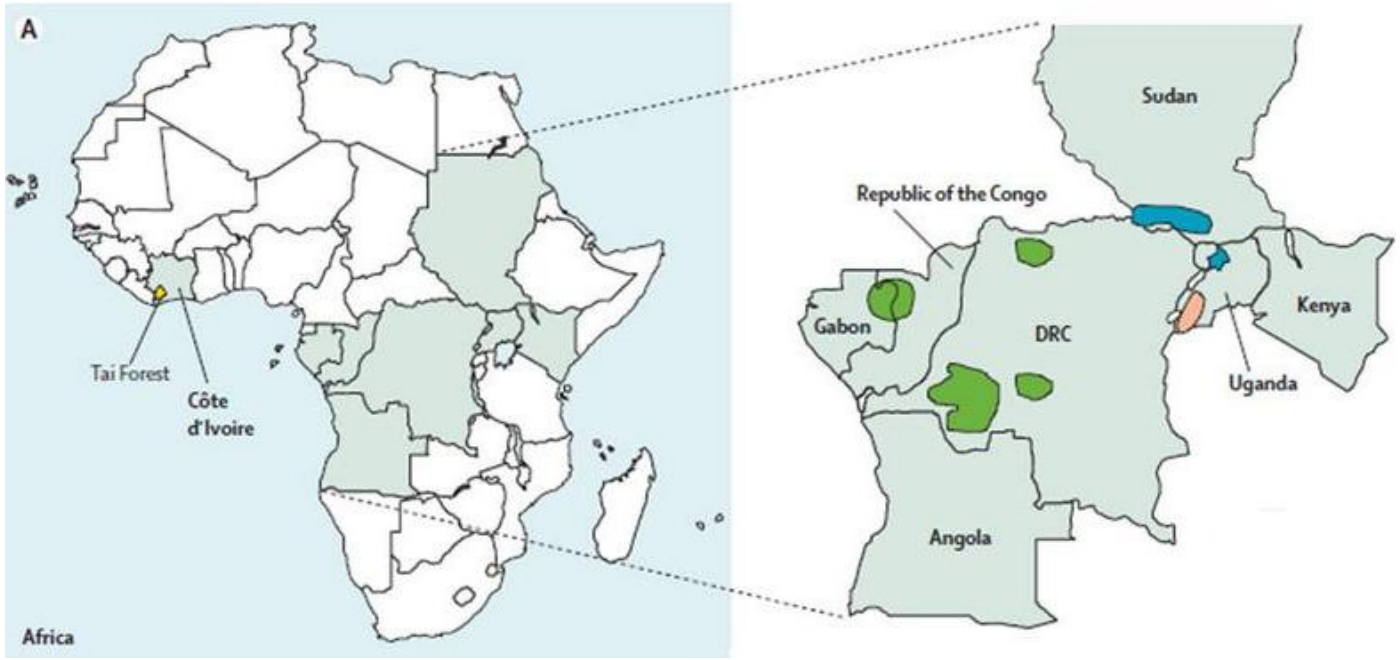
-Sudan

-Tai Forest

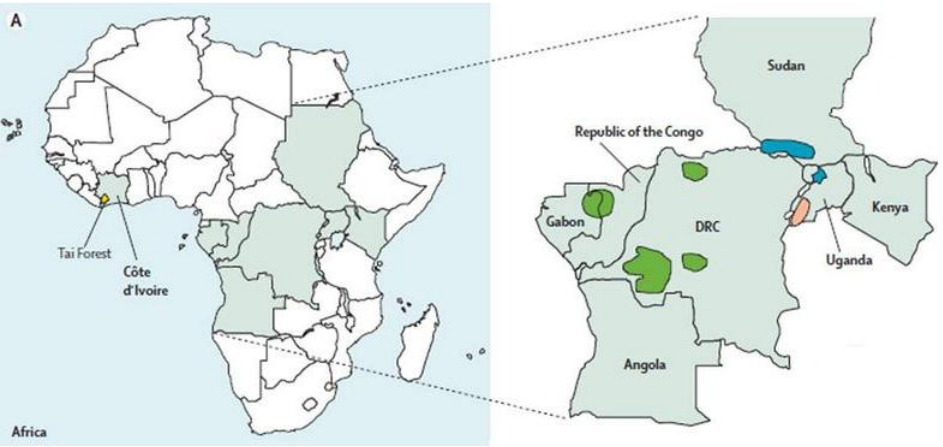
-Reston

-Bundibugyo

-Bombali



# Ebola virus




Ebola epidemics in recent years:
2014–2016 West Africa (Zaire virus)
2021 Guinea

| Genus | Species | Year | Outbreak location | Human cases (mortality) |
|---|---|---|---|---|
| *Marburgvirus* | *Lake Victoria marburgvirus* | 1967 | Germany, Yugoslavia | 31 (7) |
| | | 1975 | South Africa | 3 (1) [a] |
| | | 1980 | Kenya | 2 (1) |
| | | 1987 | Kenya | 1 (1) |
| | | 1998-2000 | Democratic Republic of Congo (DRC) | 154 (128) |
| | | 2004-2005 | Angola | 252 (227) |
| | | 2007 | Uganda | 2 (2) |
| | | 2008 | USA | 1 (0) [b] |
| | | 2008 | Netherlands | 1 (1) [c] |
| *Ebolavirus* | *Zaire ebolavirus* | 1976 | DRC | 318 (280) |
| | | 1977 | DRC | 1 (1) |
| | | 1994 | Gabon | 52 (31) |
| | | 1995 | DRC | 315 (250) |
| | | 1996 | Gabon | 37 (21) |
| | | 1996-1997 | Gabon | 60 (45) |
| | | 1996 | South Africa | 2 (1) [d] |
| | | 2001-2002 | Gabon, Republic of Congo (RC) | 122 (96) |
| | | 2002-2003 | RC | 178 (158) |
| | | 2005 | RC | 12 (9) |
| | | 2007 | DRC | 264 (187) |
| | | 2008-2009 | DRC | 32 (15) |
| | *Sudan ebolavirus* | 1976 | Sudan | 284 (151) |
| | | 1976 | UK | 1 (0) [c] |
| | | 1979 | Sudan | 34 (22) |
| | | 2000-2001 | Uganda | 425 (224) |
| | | 2004 | Sudan | 17 (7) |
| | *Cote d'Ivoire ebolavirus* | 1994 | Cote d'Ivoire | 1 (0) |
| | *Bundibugyo ebolavirus* | 2007-2008 | Uganda | 149 (37) |

The infection is transmitted mainly by contact - through direct contact of damaged skin or intact mucous membrane with blood, secretions or excretions of a person infected with or who died from hemorrhagic fever

# Environmental Survival of EBOV

- In West African climates (28°C, 90% relative humidity), Ebola virus can survive in dried blood for 7 to 10 days
- When dried in tissue culture medium on glass and stored at 4°C, Ebola virus survived for more than 50 days
- Ebola virus suspended in serum can persist in the environment for up to 46 days
- In average West African climates, Ebola virus strain can survive
on gloves (<1 hour), cotton and goggles (<24 hours) and other personal protective equipment such as respirators, coveralls and hoods (<72 hours)

# EBOV – virus inactivation

Disinfection :

Sensitive to 3% acetic acid, 1% glutaraldehyde, alcohol based products, chlorinated lime (Calcium hypochlorite; normally used for disinfection of drinking water, swimming pool water, surface disinfection)

WHO removal of blood or body fluids from surfaces suggests flooding the area with a 1:10 solution of 5.25% household bleach (i.e. 1 part household bleach diluted in 9 parts water or 0.525% sodium hypochlorite) for 10 minutes

Blood smears: can be inactivated with a 15 minute fixation step with 100% methanol

Heat inactivation

30 - 60 minutes, 60°C

boiling 5 minutes

1 hour with 0.5% Tween-20 at 56°C

Radiation:

gamma irradiation combined with 1% glutaraldehyde

virus moderately sensitive to UVC radiation

# Ebola

- infectious dose is 1–10 organisms via aerosol in nonhuman primates
- infectiousness begins at the onset of symptoms, and the risk of transmission is greatest when the viral load is highest
- person-to-person transmission is by direct physical contact with the body fluids of a living or deceased patient source of biological weapons

(CDC Category A) laboratory biosafety level BSL-4

# Ebola

- Broad cell tropism: monocytes, macrophages, dendritic cells, endothelial cells, fibroblasts, hepatocytes, adrenal cortex cells

- The duration of the disease depends on its severity, but recovery usually occurs after four weeks

# EBOLA COURSE OF INFECTION

Incubation period 2 to 21 days
disease begins with flu-like symptoms
5-7 days of illness a papular rash appears, located in the center, which after 24 hours transforms into large, well-defined, confluent maculopapular lesions, which may even be hemorrhagic

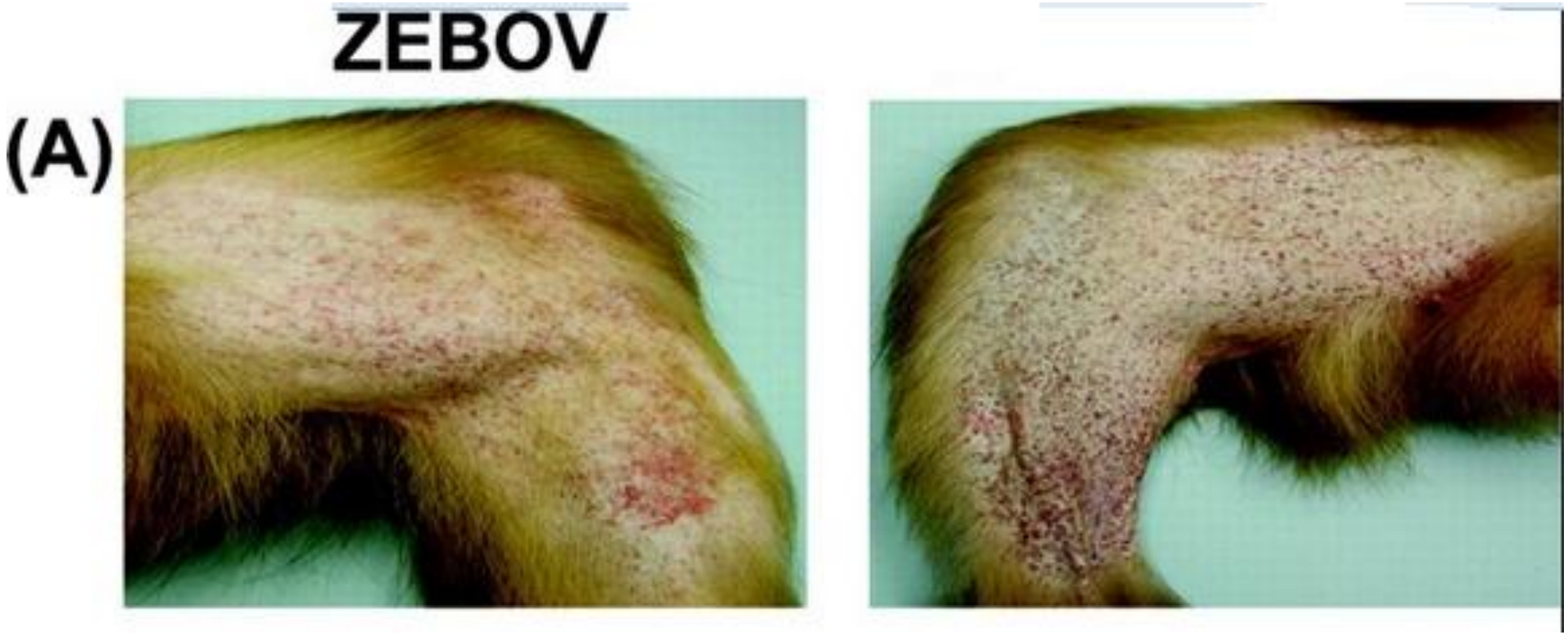
Respiratory system involvement occurs in the form of sore throat, cough and hiccups

Central nervous system involvement: headaches, excessive agitation, fatigue, confusion, coma

The result of impaired integrity of the blood vessel wall is bleeding from the nose, vagina, gums, bloody vomiting, tarry stools and hemoptysis

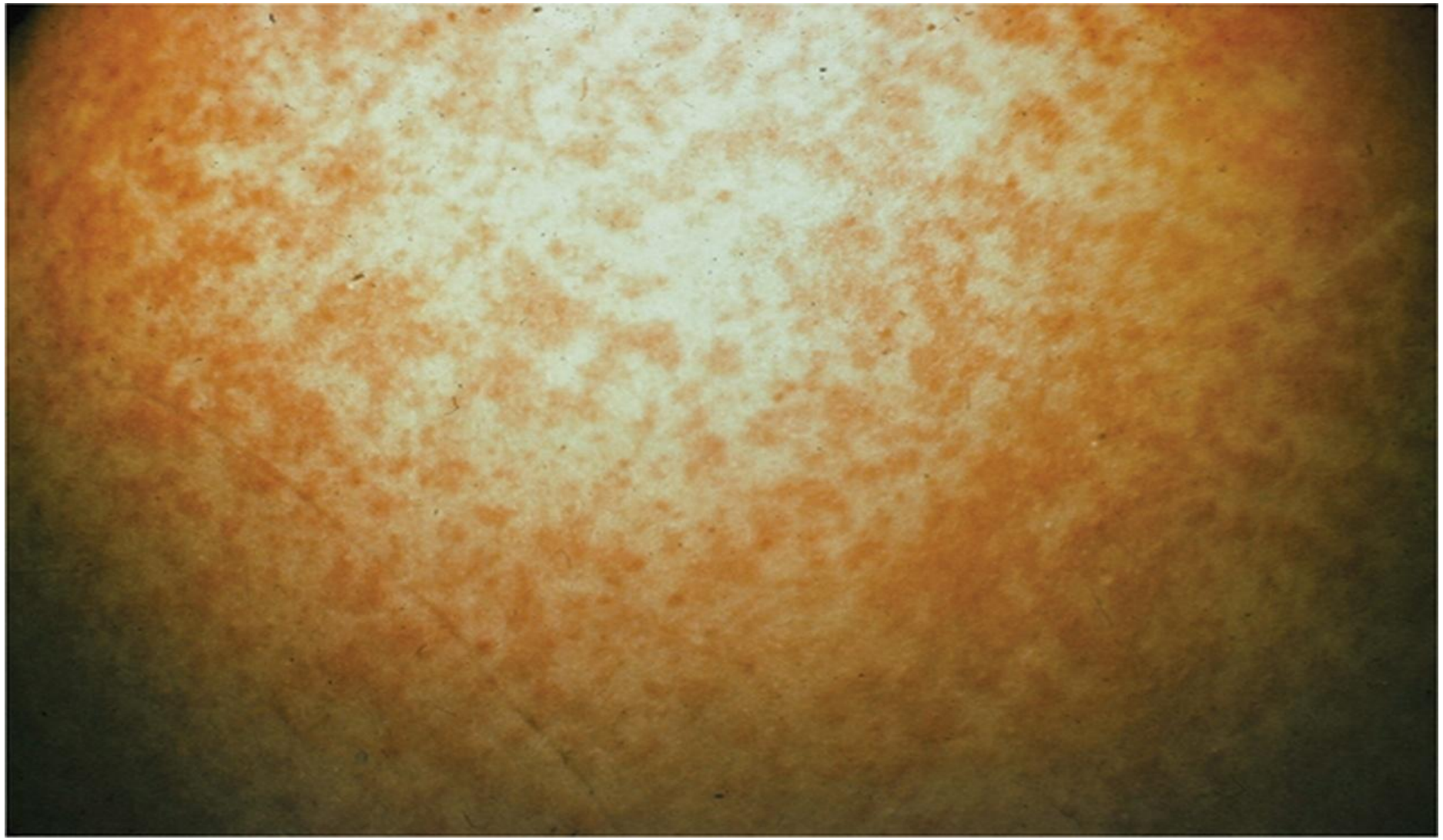
Other skin symptoms: petechiae and hematomas

Patients infected with Ebola virus die between the 7th and 16th day of illness. Death occurs as a result of multiple organ failure associated with increasing hypotension, DIC and focal tissue necrosis.



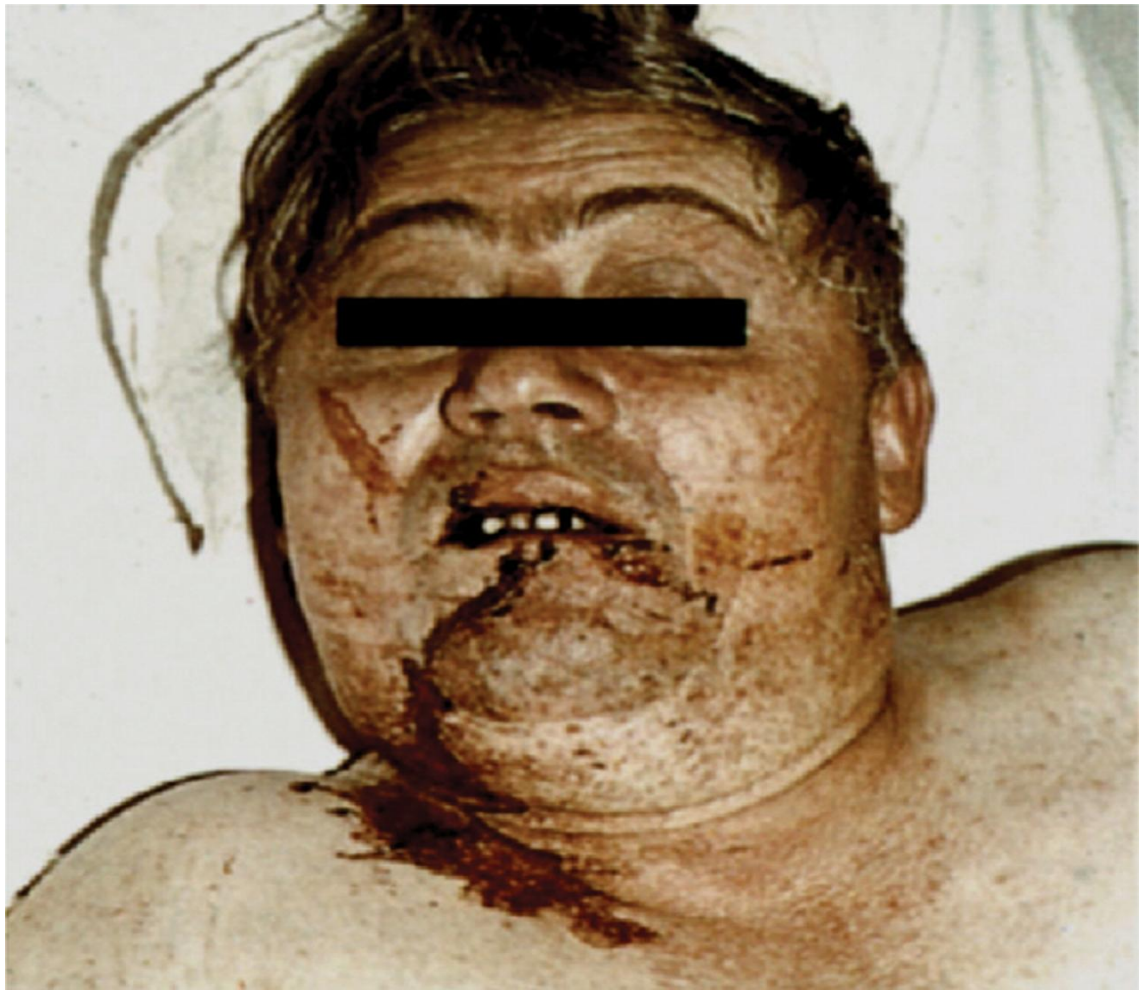

Skin sign in the ZEBOV monkey

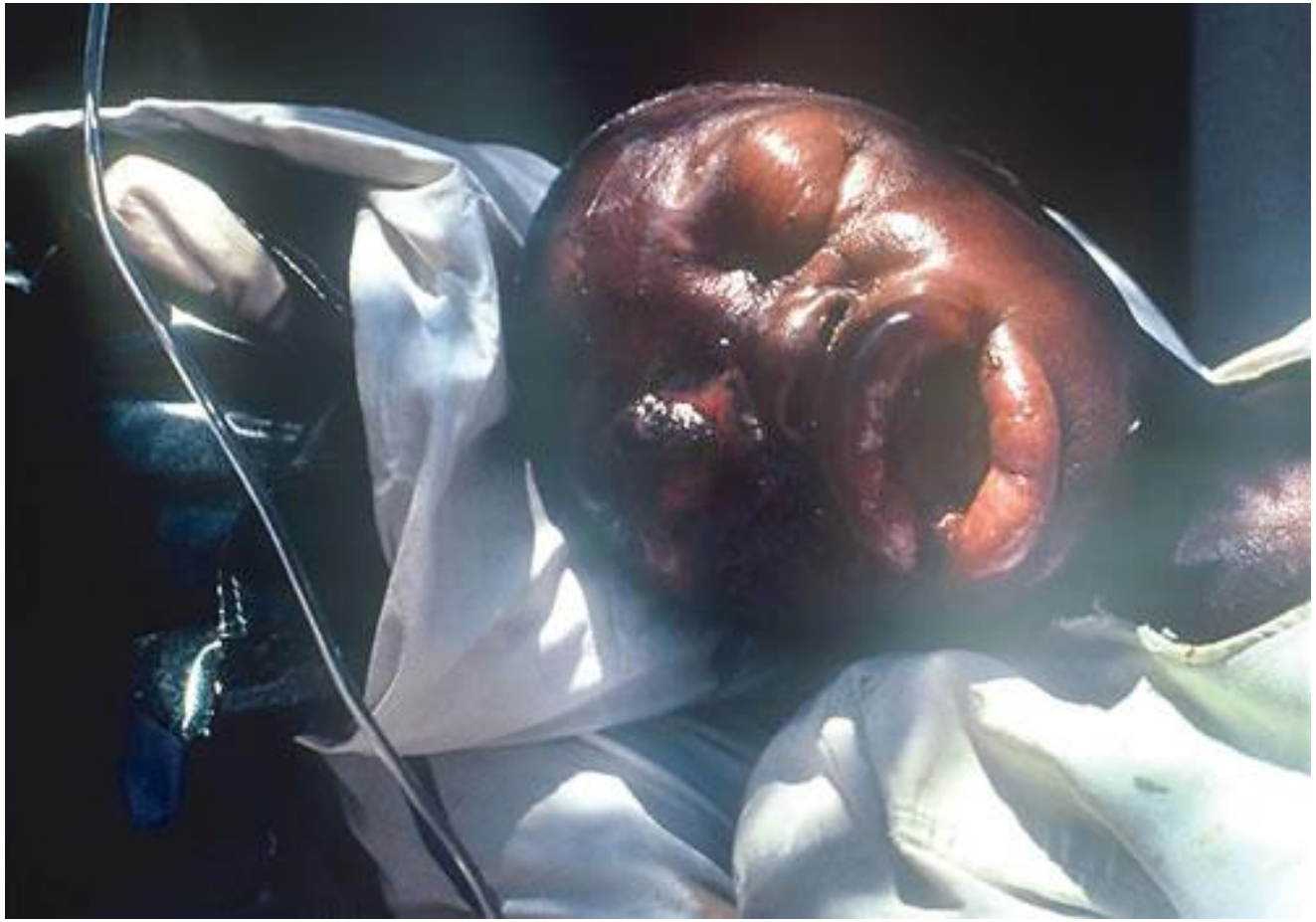
# Ebola virus rash acquired from a laboratory accident



J. ter Meulen; Oxford Textbook of Medicine: Filoviruses (Courtesy of Professor D I H Simpson.)

# Hemorrhage and swelling of the face and neck in Marburg hemorrhagic fever

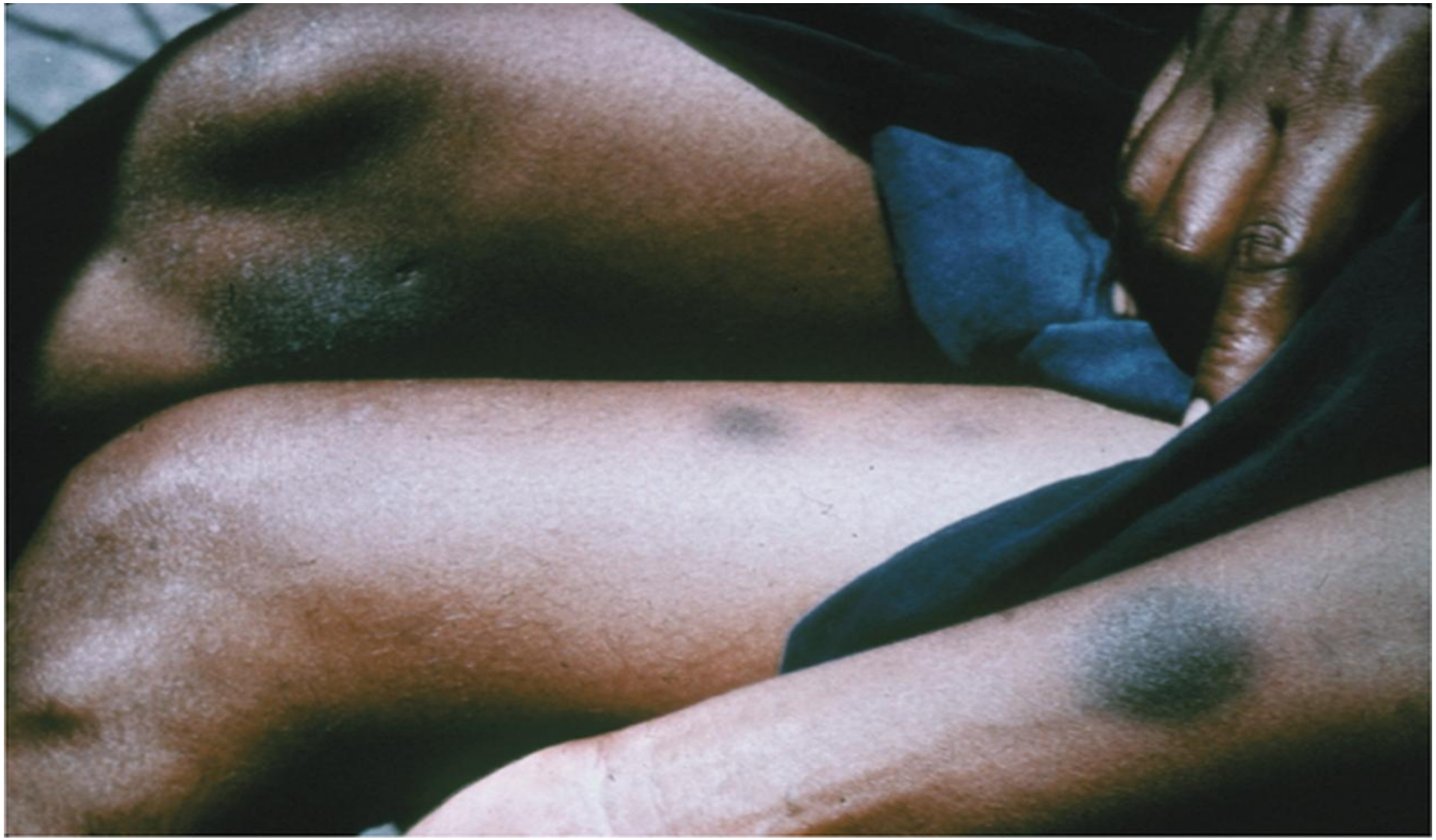




J. ter Meulen
Oxford Textbook of Medicine: Filoviruses

(Courtesy: Professor S Stille.)

Fig. 7.5.18.3 Ecchymoses in a patient with Ebola haemorrhagic fever.



J. ter Meulen
Oxford Textbook of Medicine: Filoviruses

(Courtesy of Professor D I H Simpson.)

# Criteria for the diagnosis of EVD

1.Clinical criteria

temperature>38°C

severe headache, abdominal pain, vomiting, bloody diarrhea (cough may also be a symptom of EVD)

bleeding and hemorrhages of unclear origin

multiple organ failure (rapid course)

2. Laboratory criteria

Detection of Ebola virus RNA in the patient's biological material

Virus isolation from biological material

3. Epidemiological criterion

Applies to a symptomatic person who stayed in an area of EVD incidence within 21 days before falling ill (A person who had direct contact with a patient, probable case or suspected case of EVD

# EVD differential diagnosis

- Tropical malaria
- Typhoid fever
- Ricketsioses
- Other hemorrhagic fevers

VIRUS REPLICATION

micropinocytosis

release of the viral genome into the cell cytoplasm

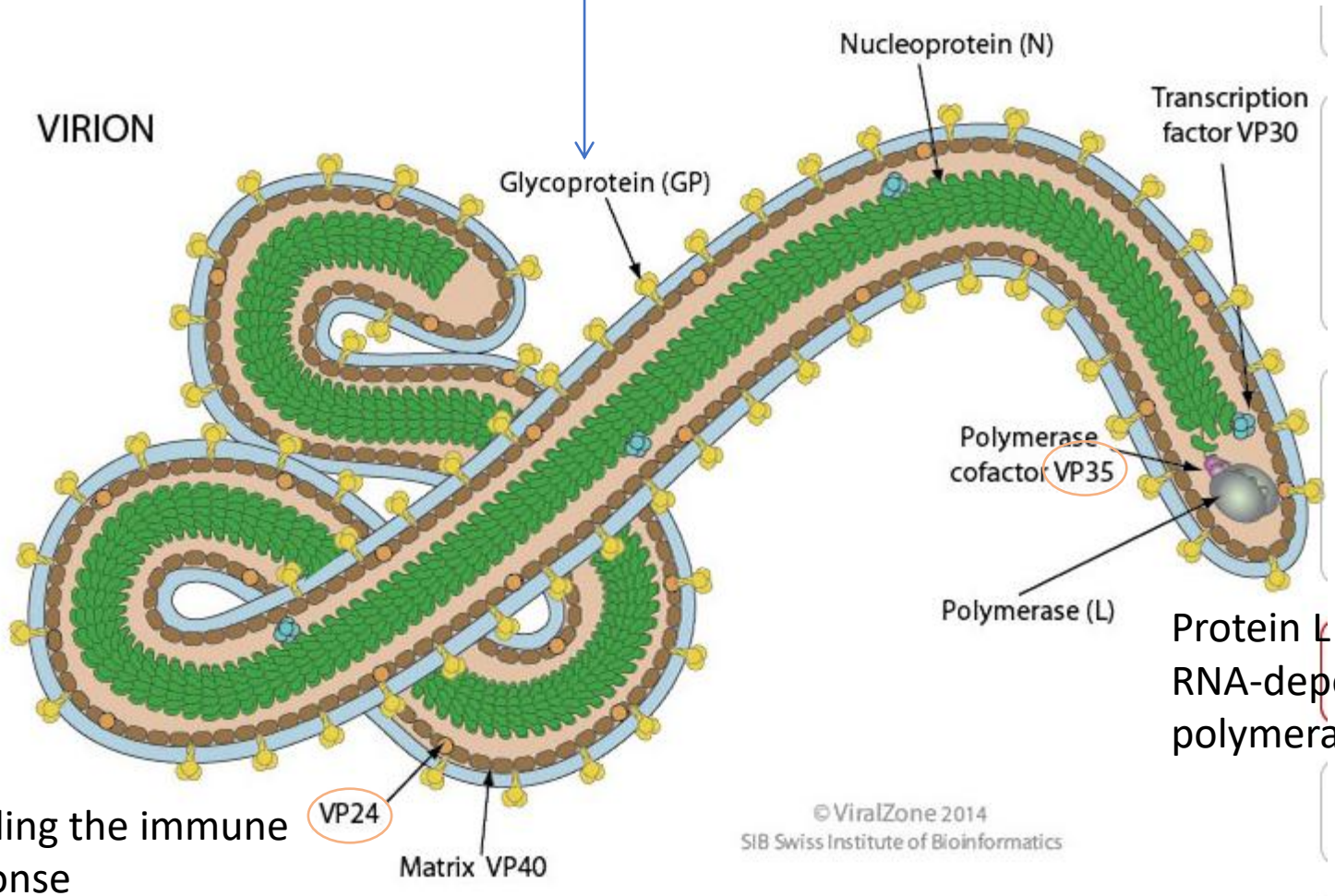
virus replication

assembly of virions to form nucleocapsid

gemmation

60-70 kDa sGP
glycoprotein produced in vivo
inhibits the neutralizing effect of serum

150-170 kDa GP
**ENVELOPE PROTEIN**
binding to host cell surface




Protein L contains an RNA-dependent RNA polymerase domain

avoiding the immune response

# Ebola

**Leukopenia** — lymphopenia, followed by elevated neutrophil counts, with an increased percentage of immature forms

**Thrombocytopenia** — platelet counts usually reach their nadir around day six to eight of illness

**Transaminases** — elevated serum levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT)

**Coagulation abnormalities** — prothrombin (PT) and partial thromboplastin (PTT) times are prolonged, and fibrin degradation products are elevated, consistent with disseminated intravascular coagulation (DIC)

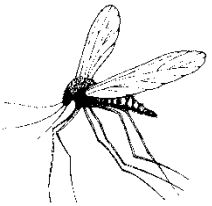
**Renal abnormalities** — proteinuria is a common finding, and renal failure occurs with disease progression

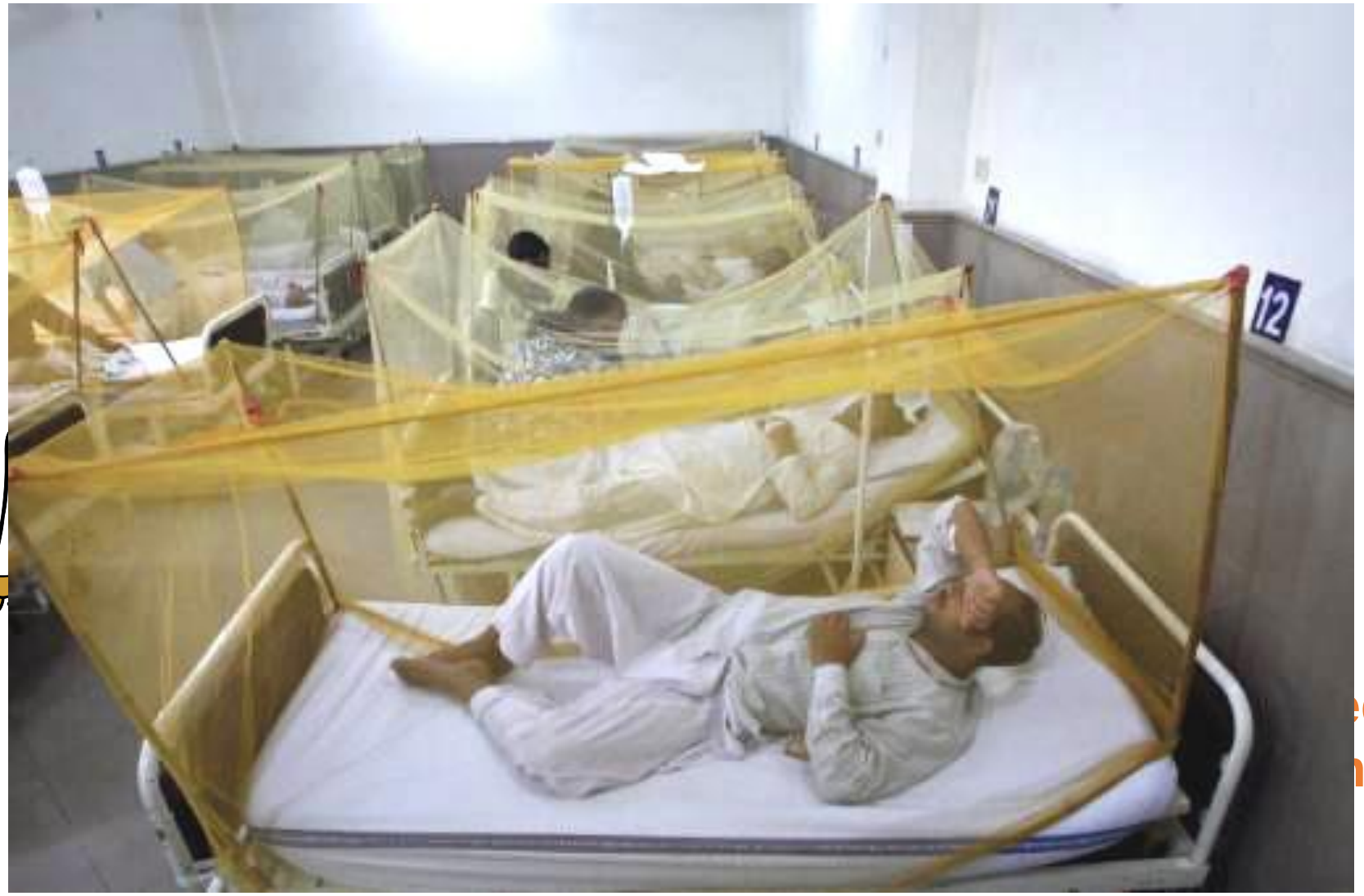
## Recommendations for travellers:

observe hand hygiene avoid all contact with sick people or the bodies of deceased people
avoid casual sexual contact
avoid all contact with wild animals (especially monkeys, forest antelope species, rodents, bats), including the bodies of dead animals
do not eat wild animal meat
wash and peel vegetables and fruit thoroughly before eating them
avoid visiting places where bats live
if you become ill during your stay, seek medical advice immediately see a doctor immediately, informing about your travel history if you experience at least one of the symptoms suggesting infection within 21 days of returning from a region where Ebola is reported

# Flaviviridae: Denga

**breakbone fever**

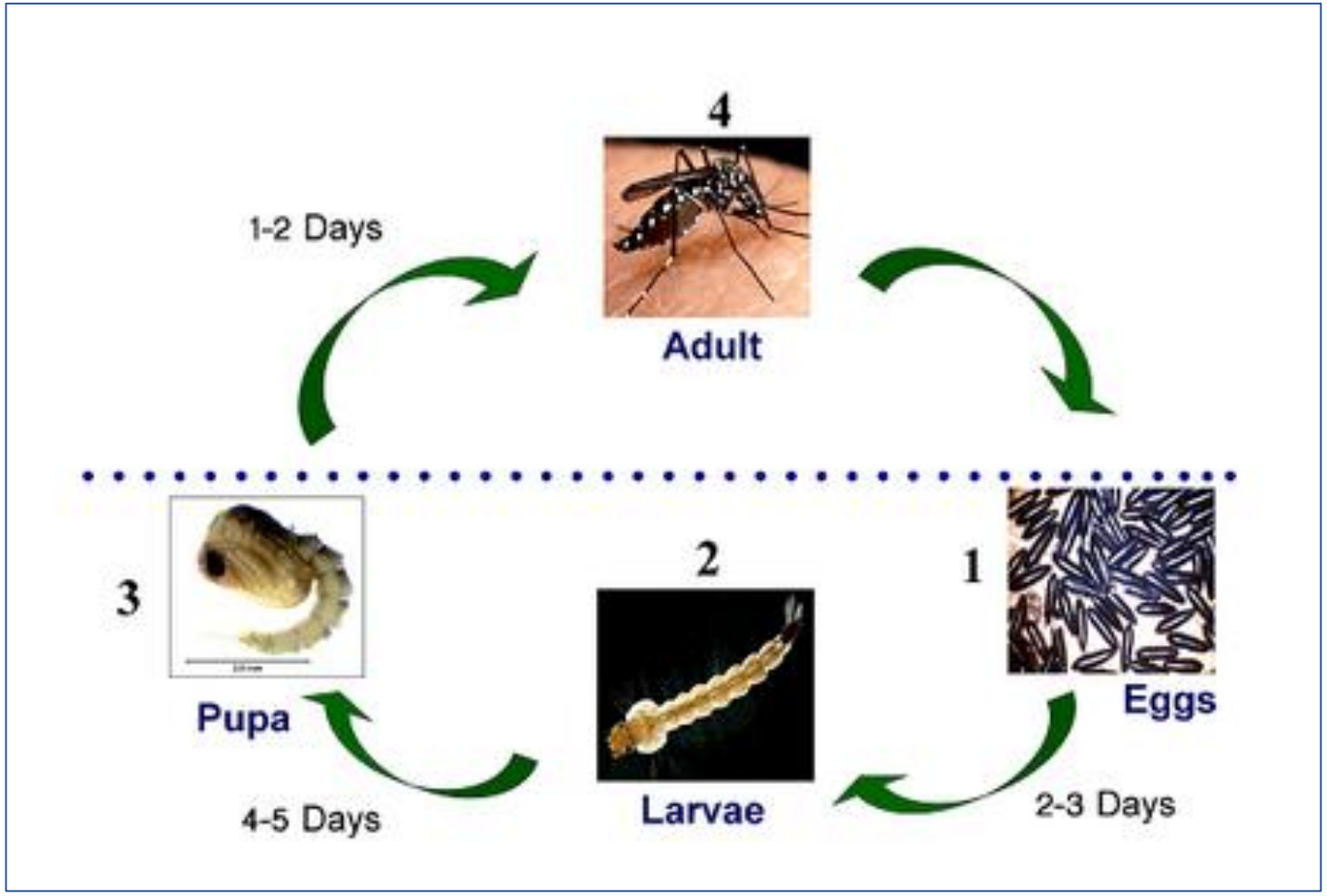




# Flaviviridae: Denga

**breakbone fever**

*Aedes aegypti,  Aedes albopictus*





Africa, America, Eastern Mediterranean, Southeast Asia and Western Pacific

Dengue virus
Main reservoir: monkeys

Most common hemorrhagic fever in the world
100 million cases, 128 countries, 30% of patients require hospitalization

Has four serotypes (DEN-1, 2, 3, 4) High immunological variability
Infection with any of these serotypes provides full protection against that serotype
 ADE-dependent antibody enhancement

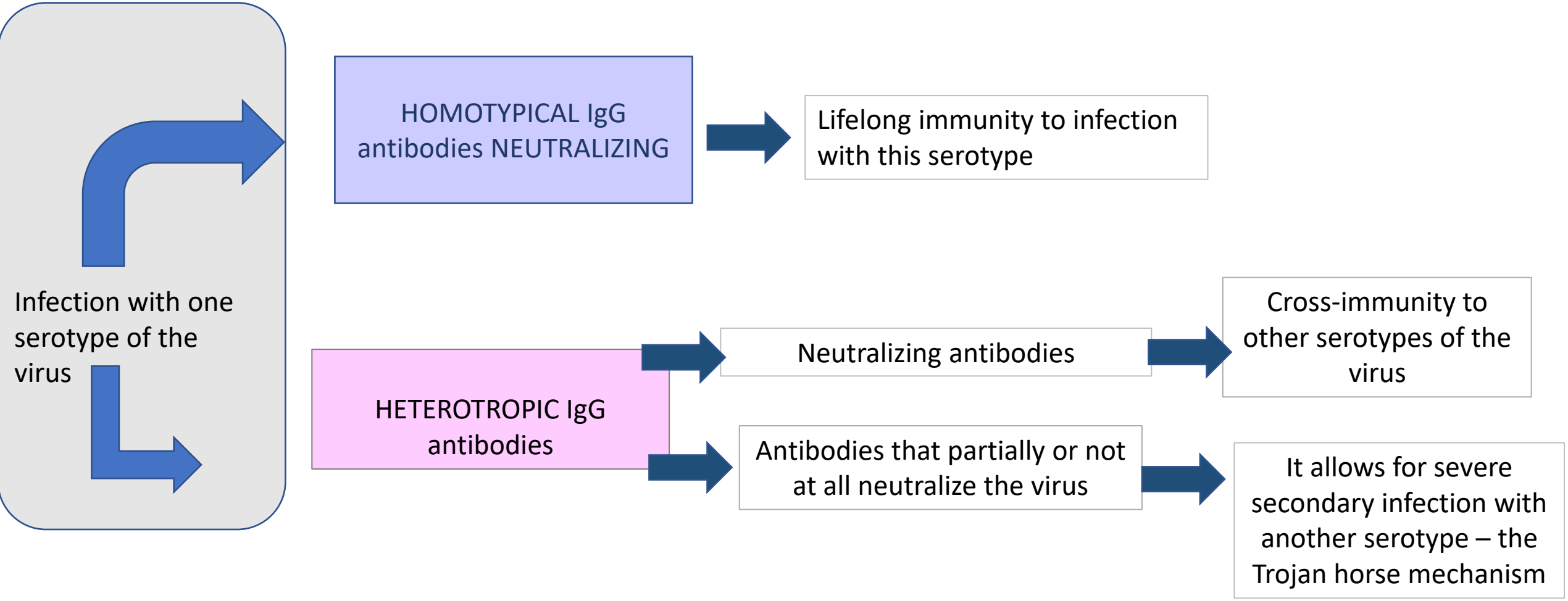
However, after infection with one serotype, infection with any other may result in exacerbation and more severe disease

**ADE mechanism**

Antibody-dependent enhancement (ADE) of infection

Weakly neutralizing antibodies produced during infection or vaccination cause an amplification of the course of the next infection.

The ADE reaction led to the withdrawal of Sanofi's dengue vaccine, which is widely used in Asia.


Infection with one serotype of the virus
HOMOTYPICAL IgG antibodies NEUTRALIZING
Lifelong immunity to infection with this serotype
HETEROTROPIC IgG antibodies
Neutralizing antibodies
Cross-immunity to other serotypes of the virus
Antibodies that partially or not at all neutralize the virus
It allows for severe secondary infection with another serotype – the Trojan horse mechanism

# Viral sepsis

| | Clinical syndromes | Epidemiology | Risk factors for sepsis |
|---|---|---|---|
| HSV | Disseminated disease<br>Hepatitis | Neonatal disseminated disease<br>Incidence: 2–15 per 100,000 live births<br>Mortality: up to 29% | Newly-acquired maternal genital infection near term<br>HSV-2 infection (compared with HSV-1 infection) |
| Enterovirus | Sepsis-like illness<br>Myocarditis<br>Encephalomyelitis<br>Pulmonary oedema or haemorrhage | Incidence: 37% of young infants (<90 days of age) with sepsis[a] and without signs of localised infection<br>Mortality of neonatal enteroviral sepsis: up to 42% | Lack of maternal antibodies<br>Maternal infection just before or at delivery<br>Neonatal infection with echovirus 6, 9, 11, 19 or coxsackievirus B2–B5<br>Enterovirus A71 infection in young children |
| HPeV | Sepsis-like illness<br>Meningoencephalitis | Incidence: 15% of young infants (<90 days of age) with sepsis[a] and without signs of localised infection | HPeV3 infection (compared with infection with other types of HPeV) |
| Influenza virus | ARDS<br>Myocarditis<br>Encephalopathy | Incidence: 1 million cases of severe respiratory infections in children <5 years of age worldwide annually<br>Mortality: 290,000–650,000 respiratory deaths worldwide annually (all age groups) | People of extreme age (<5 or >65 years)<br>Immunosuppression<br>Pregnancy<br>Influenza A (H3N2) virus infection (compared with influenza A (H1N1) or B virus infections) |
| Dengue virus | Severe dengue[b]<br>Dengue shock[b] | Incidence: 58–96 million symptomatic dengue infections with 250,000–500,000 progressing to severe disease worldwide annually; 8% of sepsis cases[c] in Southeast Asian<br>Mortality: 9,000–24,000 deaths worldwide annually | Previous dengue infection (with a different serotype) |
| Adenovirus | Disseminated disease<br>Meningoencephalitis<br>Severe pneumonia | Disseminated disease in children<br>Incidence: 2.5% of adenovirus infection<br>Mortality: 55% | Immunosuppression (particularly allogeneic HSCT)<br>Young children<br>Infection with adenovirus serotypes 3 and 7 |

Topics for course completion

1. Viral sepsis phenomenon (frequency of occurrence, most common etiological factors)

2. Explain the concept of Antibody-dependent enhancement (ADE) of infection
Give examples of the consequences this may have

3. What is the post-exposure procedure and follow-up laboratory testing like after a needlestick or other sharp injury  in the case of HBV, HCV and HIV?