Infectious diseases transmitted by transfusion, epidemiology, screening, prevention

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https://youtu.be/ptqI8MFBHPM

The significance of the topic

- Worldwide most death and disability related to blood transfusion is still caused by the transmission of infectious agents
- Infectious agents: viruses, bacteria, protozoa, prions
- Donor selection, blood screening: increase the safety of blood products, but even the most sensitive tests can not detect all infectious donors

Risk factors for transfusion-transmitted infection

- Donor is asymptomatic infected when he/she gives blood and the agent is in the bloodstream
- Pathogen can be transmitted parenterally
- Pathogen retain its infectivity during blood storage
- Screening test is unavailable or is not affordable
- Suboptimal sensitivity
- Window phase phenomenon

What does the danger of the pathogens and severity of the infection depend on?

- The danger of pathogens is influenced by several factors: infectivity, frequency of mutations, screening and inactivation methods, treatability of established infection
- Severity of the infection: amount of pathogens, strength of infectivity, patient conditions (transplanted patients and patients who receiving chemotherapy are at particular risk)

Reduction of transmission

- voluntary, non-remunerated blood donors from low-risk populations
- screening tests:
  - mandatory for all individual donations of all donors (transfusion in case of a negative result)
  - varie by country
  - do not provide 100% security because of unknown pathogens, unexpected/imported pathogens, screening unavailable or not affordable, sensitivity suboptimal, window phase
  - instead of serological methods (detection of antigen or antibody) viral RNA or DNA is detected by nucleic acid amplification test (NAT)

Screening tests used in Hungary

Pathogen	Illness	Screening tests in Hungary
HBV	acute /chronic hepatitis, cirrhosis, hepatocellular carcinoma	anti-HBc Ab (first donation) HBsAg; NAT
HCV	acute/chronic hepatitis, cirrhosis, hepatocellular carcinoma	anti-HCV Ab NAT
HAV	transient viraemia, rarely post-transfusion hepatitis, no carrier state	NAT
HIV	primary HIV infection chronic HIV disease leads to AIDS: opportunistic infections, malignant tumors	anti-HIV-1 Ab anti-HIV-2 Ab NAT
Treponema pallidum	pathogen of syphilis	anti-Treponema pallidum Ab
Human parvovirus B19	in child: febrile, rash in adults: fever, rash, polyarthritis, myalgia blood cell aplasia intrauterin infection: hydrops fetalis, heart disorder, spontaneous abortation	NAT

Screening methods

- Questionnaire for donors
- Physical examination
- Primary screening test
- Confirmatory test

Questionnaire

- History
  - Known chronic diseases, taking medication
  - Transfusions, transplants
  - Travel
  - Contacts
  - Vaccines, tattoos, animal/insect bites, operations, dental procedures, endoscopy, high risk sexual behaviour, iv. drugs
- Present symptoms (eg. fever, diarrhea, nausea, vomiting)

Lab screening

- Antibodies (immunoassays)
- Antigens
- Nucleic acid tests (NAT)
  - amplify a short specific sequence of viral DNA or RNA
  - allow earlier pathogen detection than with immunoassays
  - more costly and complex
  - plasma pool and single-donation testing

Transfusion transmitted hepatitis

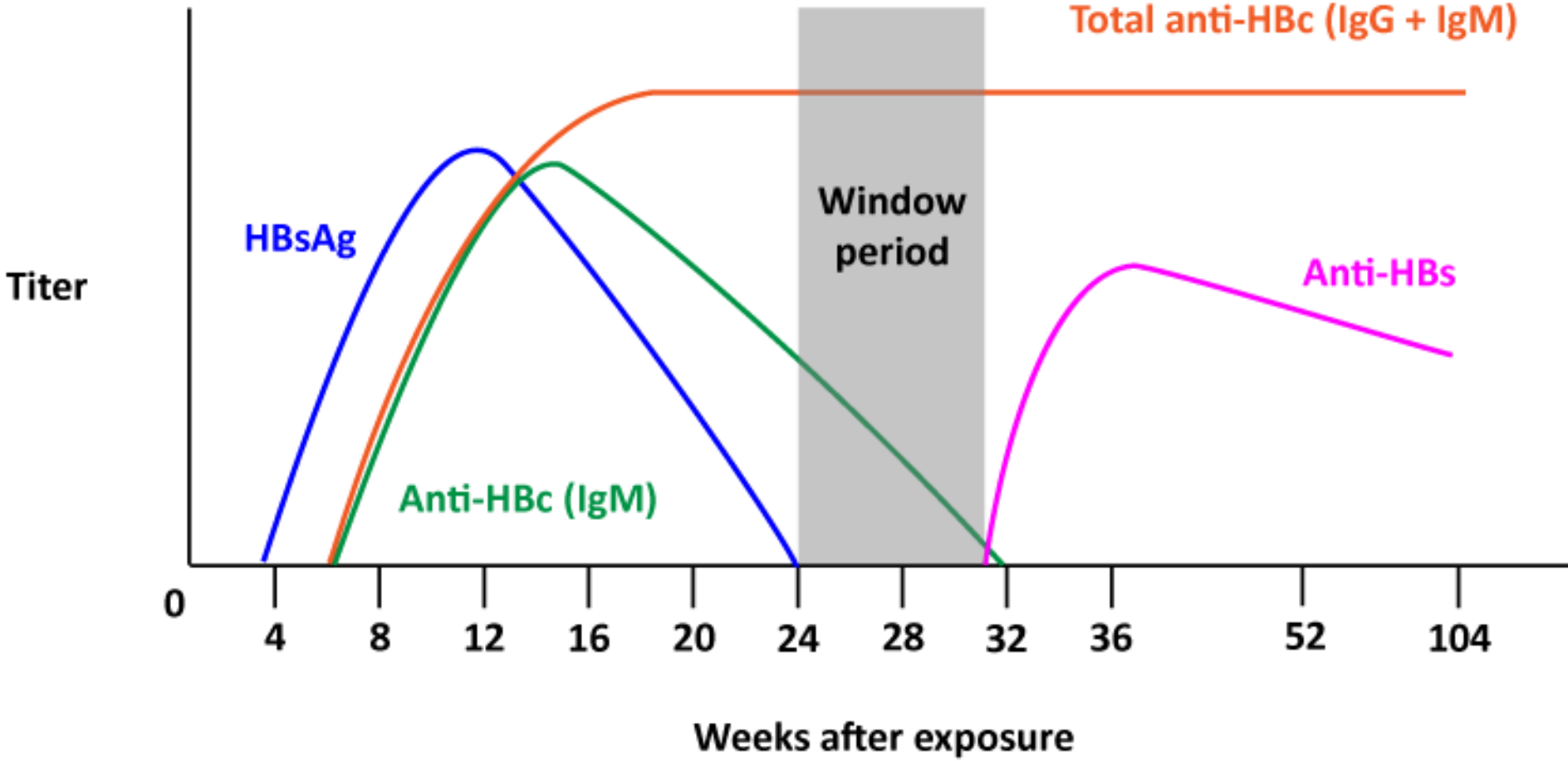
- They are not uniform in their structure, genetics, mode of transmission.
- The symptoms of each disease are similar, but the severity of the disease is different.
- Primarily hepatitis A,B,C,D,E, G virus can cause
- Signs and sypmtoms: tiredness, nausea, vomiting, diarrhea, jaundice, itch, fever, dark urine, clay-colored stools, abdominal pain
- Cause: carrier state, acute and chronic hepatitis, cirrhosis and hepatocellular carcinoma

Hepatitis B virus (HBV)

- double-stranded DNA virus
- Cause: carrier state, acute and chronic hepatitis, cirrhosis and hepatocellular carcinoma
- An estimated 350 million carriers are found worldwide, and about 1 million deaths a year
- Transmission: sexual contact, variety of other percutaneous exposures (accidental needlestick, shared syringes and needles by drug addicts, contaminated needles used in acupuncture, dentistry or tattooing), transfusion, perinatal

Prevention of HBV infection

- Exclude those at risk (donor screening)
- Potential markers to detect HBV status
  - HBsAg, HBeAg
  - anti-HBc IgM/IgG, anti-HBs, anti-Hbe
  - HBV DNA
- For routine screening in Hungary: HBsAg, anti-HBc, HBV DNA



There is an IgM and an IgG core antibody. The presence of IgM anti-HBc generally indicates an acute HBV infection. IgM anti-HBc is the first antibody to appear when fighting a HBV infection. The presence of IgG anti-HBc generally indicates a chronic HBV infection. Once infected with HBV, IgG anti-HBc will generally persist for life. Oftentimes total hepatitis B core antibody will be referenced because the two tests commonly run in the clinical lab are total hepatitis B core antibody and IgM anti-HBc. Total hepatitis B core antibody (anti-HBc) simply means IgM and IgG anti-HBc.

https://www.grepmed.com/images/1910/serologictesting-windowperiod-hepatitisb-diagnosis-antibody

Hepatitis C virus (HCV) infection

- HCV is a single-stranded, enveloped RNA virus
- approximately 180 million people worldwide are chronically infected with HCV
  - most cases mild and non-icterus
  - 50-70%: become chronic
  - 20%: develop cirrhosis
- Transmission: iv. drugs, blood component, incompletely inactivated plasma fractionation products (IVIG, anti-D Ig for iv., factor VIII concentrate), transplants

  Perinatal and sexual transmission low.

Prevention and screening of HCV

- Exclude those at risk (donor screening)
- Markers to detect HCV status:
  - anti-HCV AB
  - HCV RNA

Hepatitis A virus (HAV)

- non-enveloped picornavirus
- agent of epidemic hepatitis
- Transmitted: faecal–oral route
- Incubation time: 15-30 days
- Cause: transient viraemia, rarely post-transfusion hepatitis, does not induce a carrier state

Prevention and screening of HAV

- Vaccination, exclude those at risk (donor screening)
- Marker to detect HAV status:
  - NAT

Other hepatitis viruses

- Hepatitis E virus (HEV)
- Hepatitis D virus (HDV)
- Hepatitis G virus (HGV)
- Transfusion transmitted virus (TT virus)
- SEN virus

Human immunodeficiency virus (HIV)

- Retrovirus
- Two subtypes: HIV-1, HIV-2
- Approximately 36,7 million people worldwide are infected with HIV
- Transmission: men sex with men, unsafe sexual practices, the use of intravenous drugs, blood transfusion or blood product, perinatal

Symptomps, prevention and screening of HIV

- Symptomps:
  - primary HIV infection: fever, joint pain, skin rash, sore throat, tiredness, swollen lymph nodes
  - chronic HIV disease leads to AIDS: opportunistic infections, malignant tumors
- Prevention: donor selection, excludes from blood donation who is at high risk groups
- Screening (also window phase)
  - anti-HIV AB
  - NAT

Human parvovirus B19

- Small single-stranded, non-enveloped, thermostable DNA virus
- Transmission: droplet infection, blood and plasma fractionation products
- Symptomps:
  - in child (usually mild): febrile, rash
  - in adults: fever, rash, polyarthritis, myalgia
  - because of cytotoxic effect on erythroblasts can cause red blood cell aplasia
  - intrauterin infection: hydrops fetalis, heart disorder, spontaneous abortation
- Screening: NAT

West Nile virus

- Mosquito-borne RNS flavivirus
- Incidence: 1:1,4 million
- Humans serve as an incidental host.
- Seasonal (in Hungary july-october), incubation period: 3-14 days
- Transmission: mosquito bite, blood products, organ transplantation, perinatal,breastfeeding
- Symptomps: 80% asymptomatic, 20% symptomatic: headache, weakness, febrile illness (West Nile fever), 0,5% meningoencephalitis
- Screening: NAT

Chikungunya virus

- single-stranded RNA Alpha virus transmitted by Aedes mosquitoes (humans serve as an incidental host)
- Endemic: sub-Saharan Africa, southern India and Pakistan, Southeast Asia, Indonesia, and the Philippines
- Incubation period: 1-12 days
- Symptomps: usually symptomatic: fever, chills, headache, severe arthralgia, rash, photophobia, conjunctival injection, abdominal pain, chronical joint pain. Haemorrhage, meningoencephalitis, myocarditis: rare
- Prevention: defense against mosquitoes bites, exclusion from blood donation of those who returning from an endemic area (30 days)
- Screening: commercial tests are not available

Zika virus

- Mosquito-borne flavivirus
- Transmission: mosquito bite, sexual contact, perinatal, blood product
- Endemic: Brazil, other parts of South and North America, several islands in the Pacific, and Southeast Asia
- Symptomps: fever, rash, headache, joint pain, red eyes, muscle pain, Guillain-Barré sy.
  - Zika infection during pregnancy: microcephaly. It is also linked to other problems, such as miscarriage, stillbirth, and other birth defects
- Prevention: to protect yourself from mosquito bites, exclusion from blood donation of those who returning from an endemic area (30 days)
- Screening: in Hungary no routine screening

Cytomegalovirus

- DNA, beta herpes virus
- Severe in immunocompromised hosts
  - Direct cytotoxic effect on infected cells → ↓cellular immunity→ ↑ bacterial, fungal and protozoa infections
  - parenchymal damage: retinitis, pneumonitis, gastroenteritis, encephalitis
- Donors positive
  - Developed countries: 30-80%
  - Developing countries up to 100%
- Prevention: anti-CMV negative donors, leukocyte-free blood products (CMV is usually found within the leucocytes)

Other viruses

- Human T-cell leukaemia virus type I and type II (HTLV-I/II)
- Epstein-Barr virus (EBV)
- Dengue virus

Treponema pallidum

- Spirochaete bacterium
- Pathogen of syphilis
  - Decreasing prevalence
- Transmission: sexual contact, transfusion, transplacental
- Incubation period: 1- 4 months (averaging 9–10 weeks)
- Symptomps: swelling of the lymph node, fever, typical secondary eruption
- Prevention: exclude risk groups
- Screening: every donor, every blood donation
  - routine antibody screening

Other bacterial infections

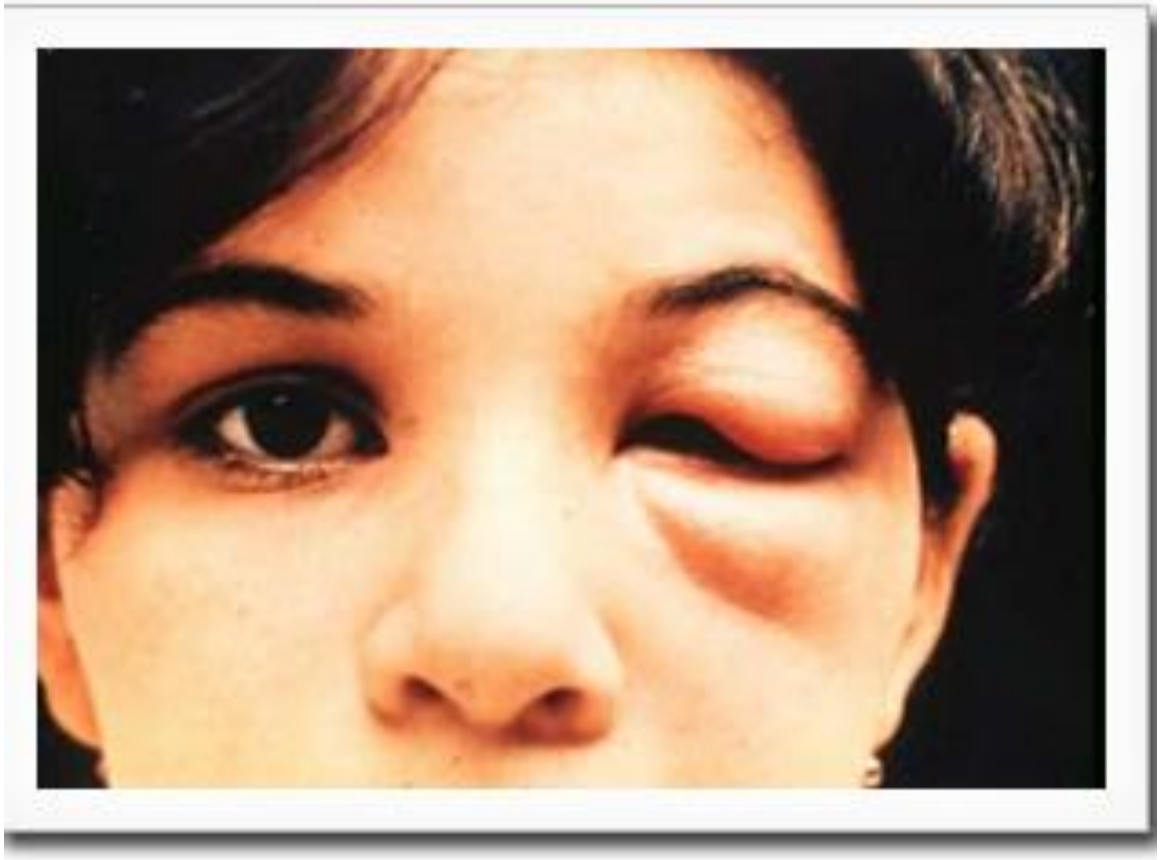
- Borrelia burgdorferi: pathogen of Lyme-disease
- Brucella abortus
- Rickettsia rickettsii: pathogen of Rocky Mountain spotted fever
- Coxiella burnetii: responsible for the development of Q fever
- These infections are rare, no routine screening

Plasmodium genus

- Protozoans, cause malaria
- Endemic: tropical and subtropical countries
- Frequency of post-transfusion malaria:
  - Non-endemic countries: 0,2:1000000 blood transfusion
  - Endemic counrties: 50:1000000 blood transfusion
- Transmission: mosquito bite, transfusion
- Incubation period: 12-30 days
- Symptomps: severe shaking chills, cyclical high fever, headache, profuse sweating, nausea, vomiting, abdominal pain, diarrhea, convulsions, coma, bloody stools, anemia
- Prevention: in non-endemic countries: defer donors who have travelled in endemic regions. Deferral periods vary from six months to permanently depending on the length of time the donor resided in the malaria risk area
- Screening: in Hungary no routine screening

Trypanosoma cruzi

- Cause: Chagas disease
- Endemic: Latin-America (24 million infected people)
- Transmission: Triatomid bug bite, transfusion
- Incubation period: 20-40 days
- Symptomps:
  - acute: fever, flu-like symptoms, rash, lymph nodes enlargement, headache and body aches, fatigue , gastrointestinal symptoms (nausea, vomiting, diarrhea), hepatomegaly , splenomegaly, Romana's sign
  - Chronic: cardiomyopathy, megaoesophagus, megacolon
- Prevention: in non-endemic countries: defer donors who have travelled in endemic regions. Deferral periods vary from six months to permanently depending on the length of time the donor resided in the risk area
- Screening: In USA routine serologic screening, in Hungary no routine screening



Romana's sign (acute unilateral eye swelling)

https://www.cdc.gov/parasites/cme/chagas/lesson_2/3.html

Photo courtesy of WHO/TDR Image Library. TDR photo, Brazil, 1991.

Microfilariae

- Endemic: tropical and subtropical countries
- Transmission: bite of a mediating vector (mosquito, fly)
- Survives well in stored blood (up to 3 weeks)
- Wuchereria bancrofti, Loa loa, Onchocerca volvulus
- Prevention: in non-endemic countries: defer donors who have travelled in endemic regions deferral periods vary from six months to permanently depending on the length of time the donor resided in the risk area
- Screening: in Hungary no routine screening

Prion

- Low molecular weight protein
- 2 different types of prion
- Cellular prion- produced by all healthy cells- normal function of nerve cells
- Scarpie prion protein : abnormal protein- the results of gene mutation or exogenious other abnormal prion- can not be eliminated , cumulated in the central nervous system→cell death

Prion disease

- Classical: gene mutation, familial disease eg: Creutzfeld – Jakob disease (inherited) or iatrogenic (aquired, human pituitary growth hormone and human dura mater grafts)
- Variant CJB (caused by the consumption of infected beef)
- Incubation period: extremely long (may be up to 20 years)
- Symptoms: behavioral and psychiatric problems, gradual mental decline, dementia, which will lead to death within 3-12 months
- Mortality: 100%
- Prions are resistant to the conventional virus neutralizing procedures

Prevention of prion disease

- Prevention:
  - defer donors
    - who have received growth hormone or a dura mater graft
    - with a family history of CJD
    - who were born in or spent more than 1 year in the UK between 1980-1996
  - plasma of blood donors from the UK is not used for pharmaceutical purposes
  - use of prion filter
- Screening: no screening test

Summary

- infections can be transmitted by blood products
- geographical and societal differences in the world
- voluntary, non-remunerated blood donors and it is important to exclude those in the risk group
- tests safety will never reach 100%

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