



Donor infection and the impact on transplantation

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**THE INSTITUTE OF
TRANSPLANTATION**


The Newcastle upon Tyne Hospitals
NHS Foundation Trust



Donor derived infection

Organ transplant is a low risk but important route of transmission of infection from donor to recipient.



Agenda

1. Blood born Viruses
 - Hepatitis B
 - Hepatitis C
 - HIV
2. EBV & CMV virus
3. All the others
4. COVID 19



MICROBIOLOGICAL SAFETY GUIDELINES

PREVIOUSLY KNOWN AS

**GUIDANCE ON THE MICROBIOLOGICAL SAFETY
OF HUMAN ORGANS, TISSUES
AND CELLS USED IN TRANSPLANTATION**

The most important
resource for
microbiology guidance
in transplantation in
the UK



What are we dealing with ?

The degree of risk for transmission of infection carried with grafts, notably of viruses, is largely unknown and, for a specific organ, difficult to assess.

When will we see infection?

Days from Transplant to Recognition of Infection					
	0-30 days	31-90 days	91-180 days	>181 days	TOTAL
Viral	11	7	4	8	30
Bacterial	23	1	0	0	24
Fungal	20	5	2	1	27
Mycobacterial	2	2	2	0	6
Parasitic	7	4	6	1	18
TOTAL	63	19	14	10	106
	59%	18%	13%	9%	

Mandatory screening

Table 3– Mandatory and recommended screening of organ, tissue and cell donors

Infection	Serological Test	Organs*	Tissues**	Haematopoietic progenitor cells (HSPC), therapeutic cells (TC) and human embryonic stem cells**	Gametes and embryos***
HIV1/2	Anti-HIV1/2Ab/HIV Ag combo	M	M	M	M
HBV	HBsAg	M	M	M	M
	Anti-HBc	M	M	M	M
HCV	Anti-HCV IgG	M	M	M	M
HTLV1/2	Anti-HTLV1/2****	R	M	M	M
Syphilis	Anti- <i>T. pallidum</i> antibody	R	M	M	R
<i>Toxoplasma gondii</i>	Anti- <i>T. gondii</i> IgG	R	NR	R*****	NR
CMV	Anti-CMV IgG	R	NR	R	R
EBV	Anti-EBV IgG	R	NR	R	NR
HEV	HEV RNA	R	R	R	NR
<i>Chlamydia trachomatis</i>	n/a	NR	NR	NR	M
<i>Neisseria gonorrhoea</i>	n/a	NR	NR	NR	M

M = Mandatory Tests as required by EUODD and EUTCD

R = Recommended tests

NR = not required; n/a = not applicable;



Required Donor Information

- Treatment received in the illness before donation (including duration and dose of antimicrobial and other drug therapy)
- Vaccination history and immunisation status
- History of receipt of blood, blood components, blood products, tissue or organ graft.
- Previous or current immunosuppression (by disease or drugs) as this may affect the interpretation of test results or the donor's suitability.
- Travel History



Required Donor Information

- History of contact with animals and other vectors. Transplantation may transmit zoonotic infections.
- History that may have put the donor at increased risk of transmissible spongiform encephalopathies (TSEs).
- History of malignancy, recent infectious disease or exposure to an infectious disease.
- Behavioural history that could have put the donor at risk of transmissible pathogens This will include questions about risk behaviours such as recreational drug use, men who have sex with men (MSM), sex with commercial sex workers, sex with a partner know to have a sexually transmissible disease, acupuncture, tattooing and body piercing.
- Results of any recent microbiological tests should be reviewed.



Transmission of Blood born virus

- Human immunodeficiency virus (HIV)
- Hepatitis C virus (HCV)
- Hepatitis B virus (HBV)
- CMV and EBV

Blood born virus (Hep B, C & HIV)

Exact rates of transmission are not well understood.

There are certain things from the history however that will give you indications for risk.

Transmission rates

Hepatitis B 100 more transmissible than HIV

Hepatitis C 10 times more transmissible than HIV

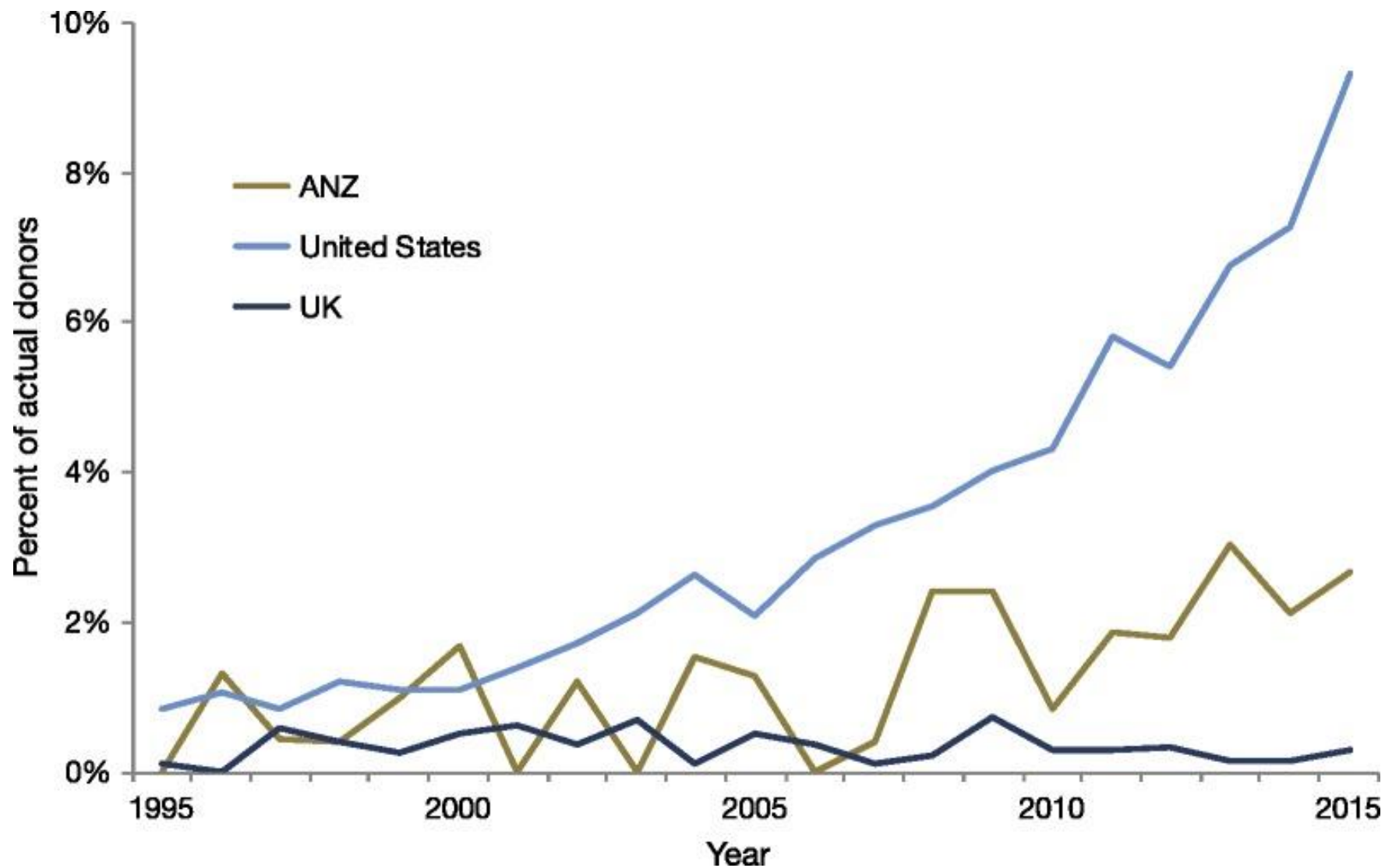
HIV - often has the largest Stigma attached



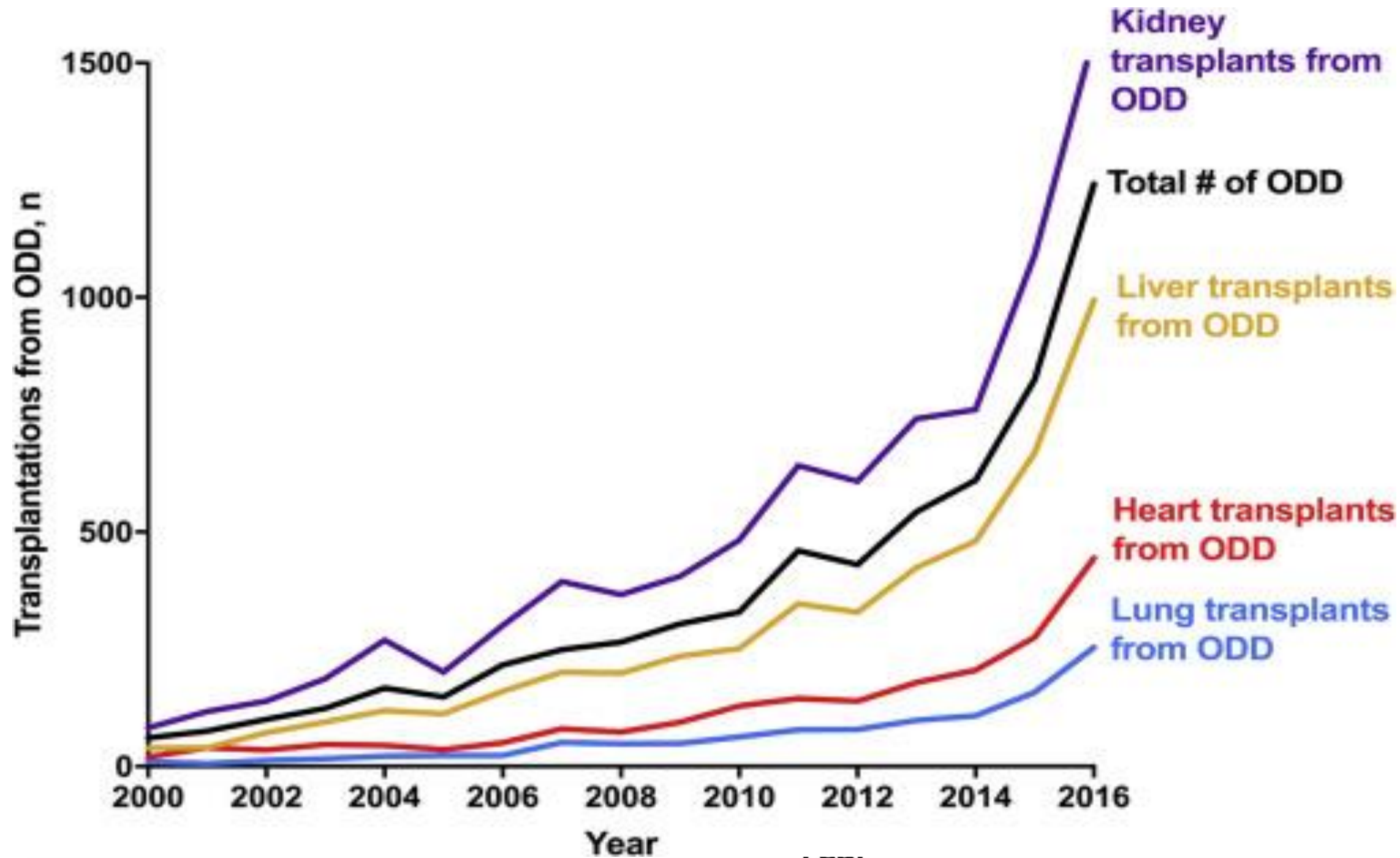
High Risk activity

Pathogens	Behavioral characteristics	Nonbehavioral characteristics
HIV	<ul style="list-style-type: none">• MSM• IVDU• Noninjection illicit drug use• Multiple sex partners• Sex with partner known to be HIV-infected• Age ≤ 18 at first sexual intercourse	<ul style="list-style-type: none">• STI• Marital status
HCV	<ul style="list-style-type: none">• IVDU• Noninjection illicit drug use• Multiple sex partners• Sex worker• Inmates• Age ≤ 18 at first sexual intercourse• Sex with partner known to be HCV-infected• Sex with an injection drug user• Tattooing performed by a nonprofessional	<ul style="list-style-type: none">• Hemodialysis• Receipt of blood transfusion• Signs and symptoms (eg, jaundice, elevated ALT)• STI• Marital status
HBV	<ul style="list-style-type: none">• MSM• IVDU• Multiple sex partners	<ul style="list-style-type: none">• Hemodialysis• STI• Marital status

HIV, human immunodeficiency virus; HCV, hepatitis C virus; HBV, hepatitis B virus; MSM, men who have sex with men; IVDU, injection drug use; STI, sexually transmitted infection.



Twenty-year trends in the percentage of donors with drug overdose (intended or unintended) as a cause of death in Australia and New Zealand (ANZ) compared with the United Kingdom (UK) and United States (data sources: Australia and New Zealand Organ Donation Registry [ANZOD], Organ Procurement and Transplantation Network [OPTN], National Health Service Blood and Transplant [NHSBT]).



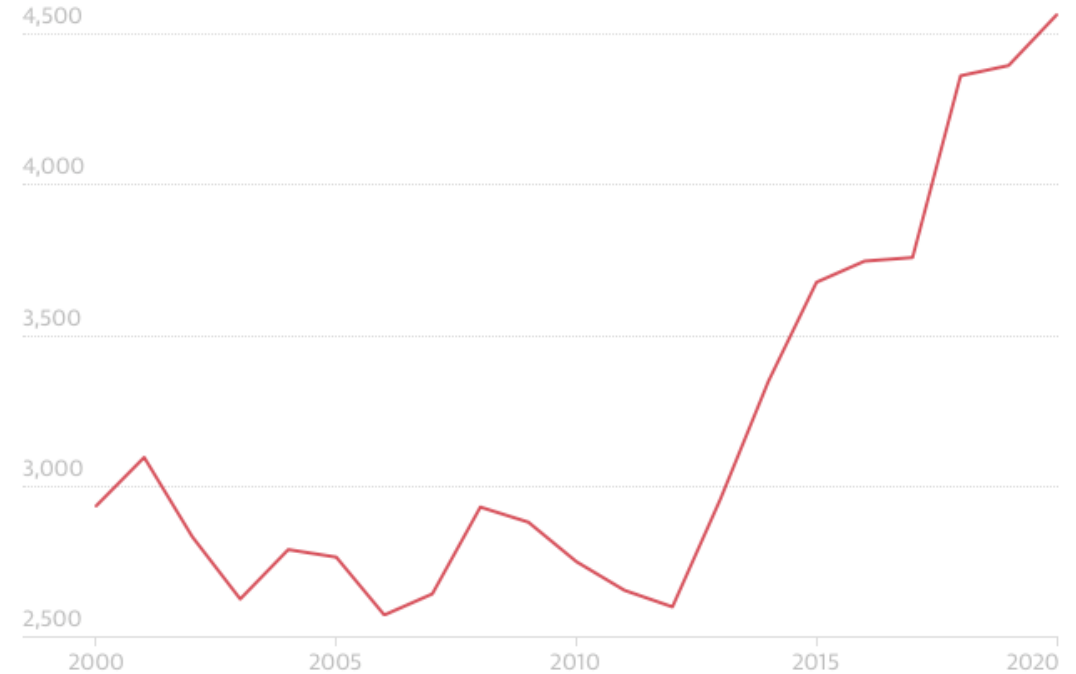
Drug poisonings in England and Wales

The rate of drug poisonings continues to increase

Rates of drug-related poisoning were **60.9%** higher in 2020 (79.5 deaths per million) than they were in 2010 (49.4 per million).

The rate has increased every year since 2012

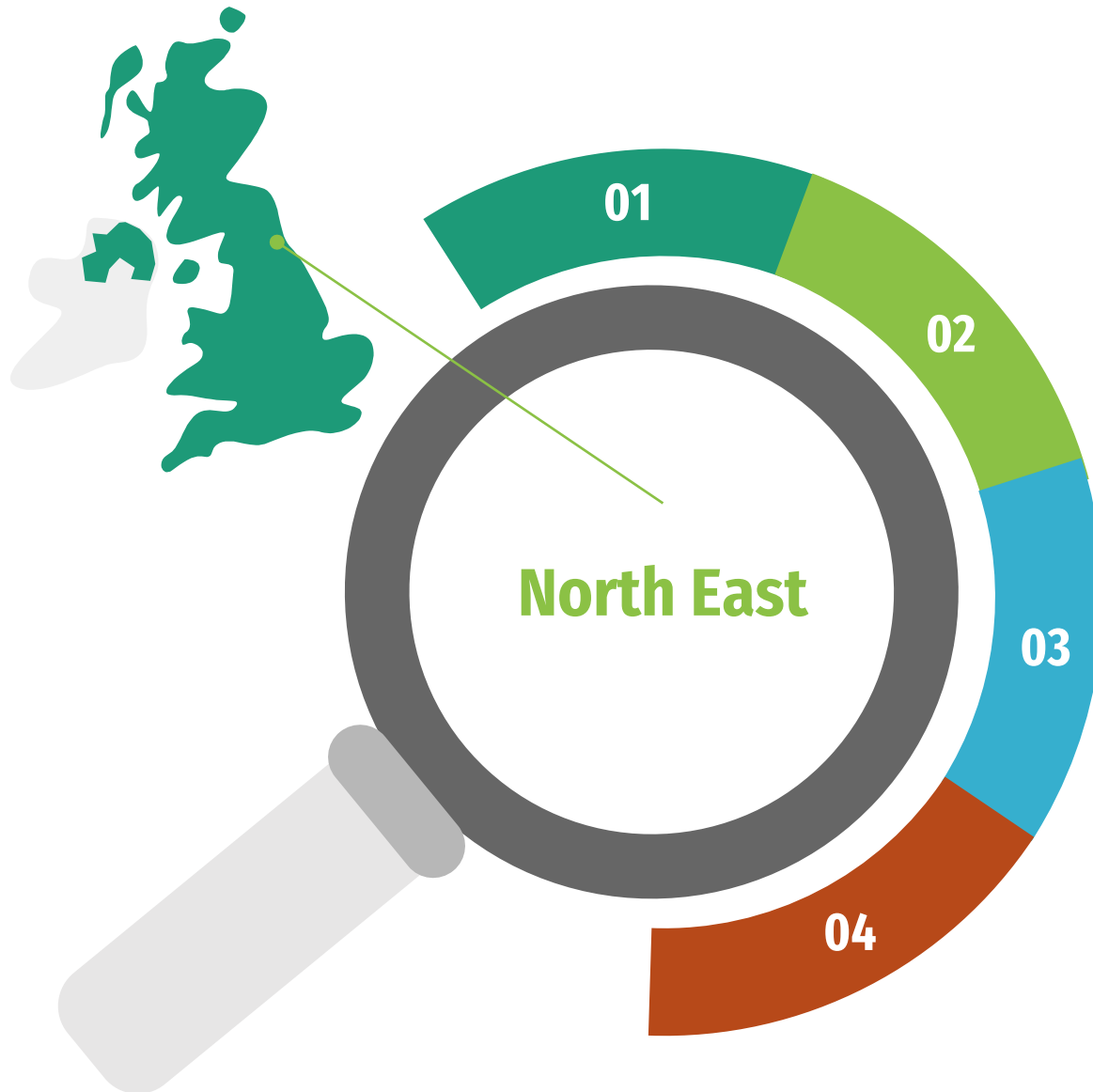
There were 4,561 drug poisoning deaths in England and Wales in 2020 – the eighth consecutive annual rise



Guardian graphic. Source: ONS

ONS:Deaths related to drug poisoning in England and Wales: 2020 registrations

Regional Variation (England and Wales)



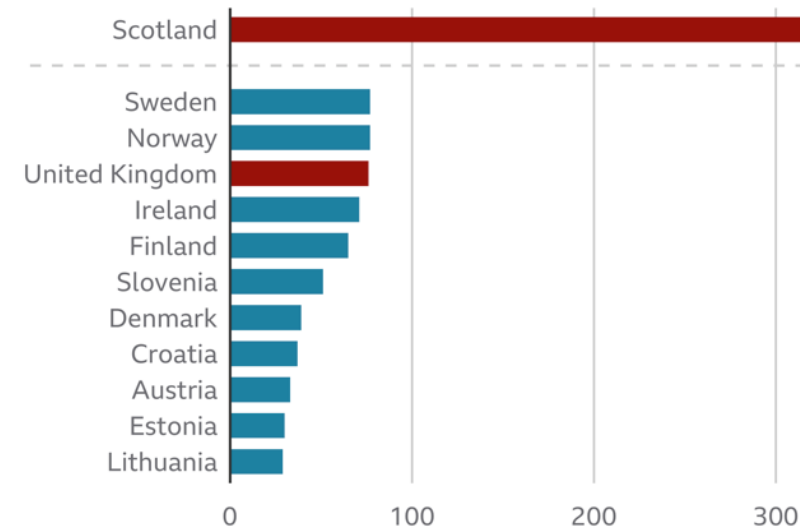
North - South Divide

In 2020, the highest rate of drug misuse deaths was observed in the North East (104.6 deaths per million; 258 registered deaths), while the lowest rate was in London (33.1 deaths per million; 296 deaths).

The North East has had the highest rate of drug misuse for the past eight years and has a statistically significantly higher rate than all other regions of England.

Scotland has far more drug deaths per capita than any European country

Number of deaths per million people, ages 15-64, latest available data



Note: Latest available data for most countries is from 2019, although UK-wide figure is from 2017. Data shown for Scotland is from 2019 for comparison reasons

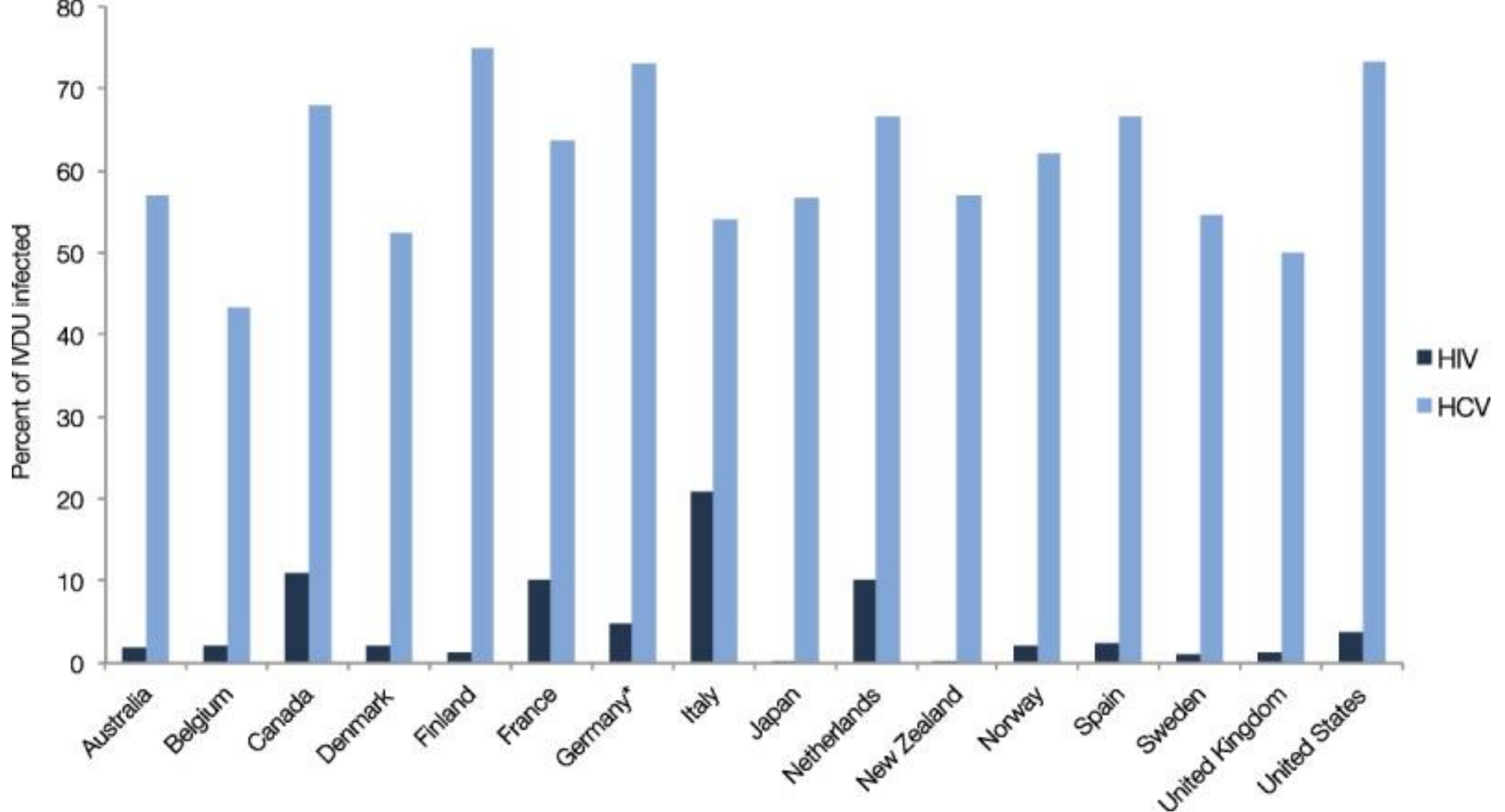
Source: EMCDDA, National Records of Scotland

BBC

Scotland

It means Scotland continues to have by far the highest drug death rate recorded by any country in Europe.

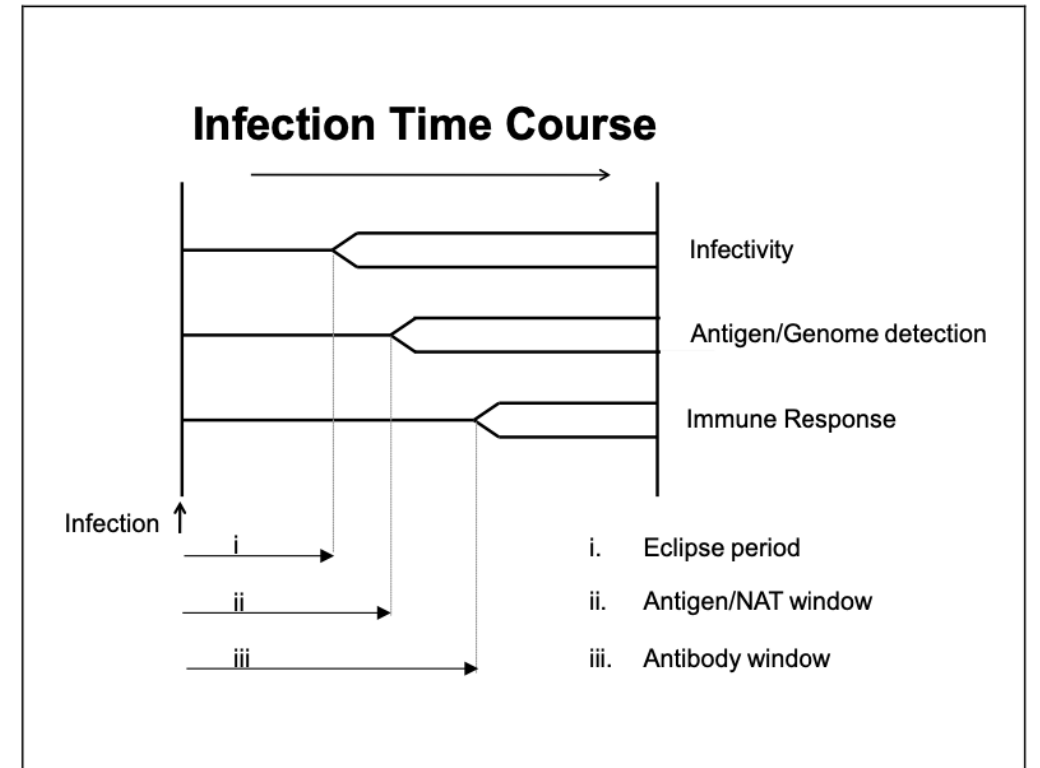
And its rate is more than three-and-a-half times that of England and Wales.



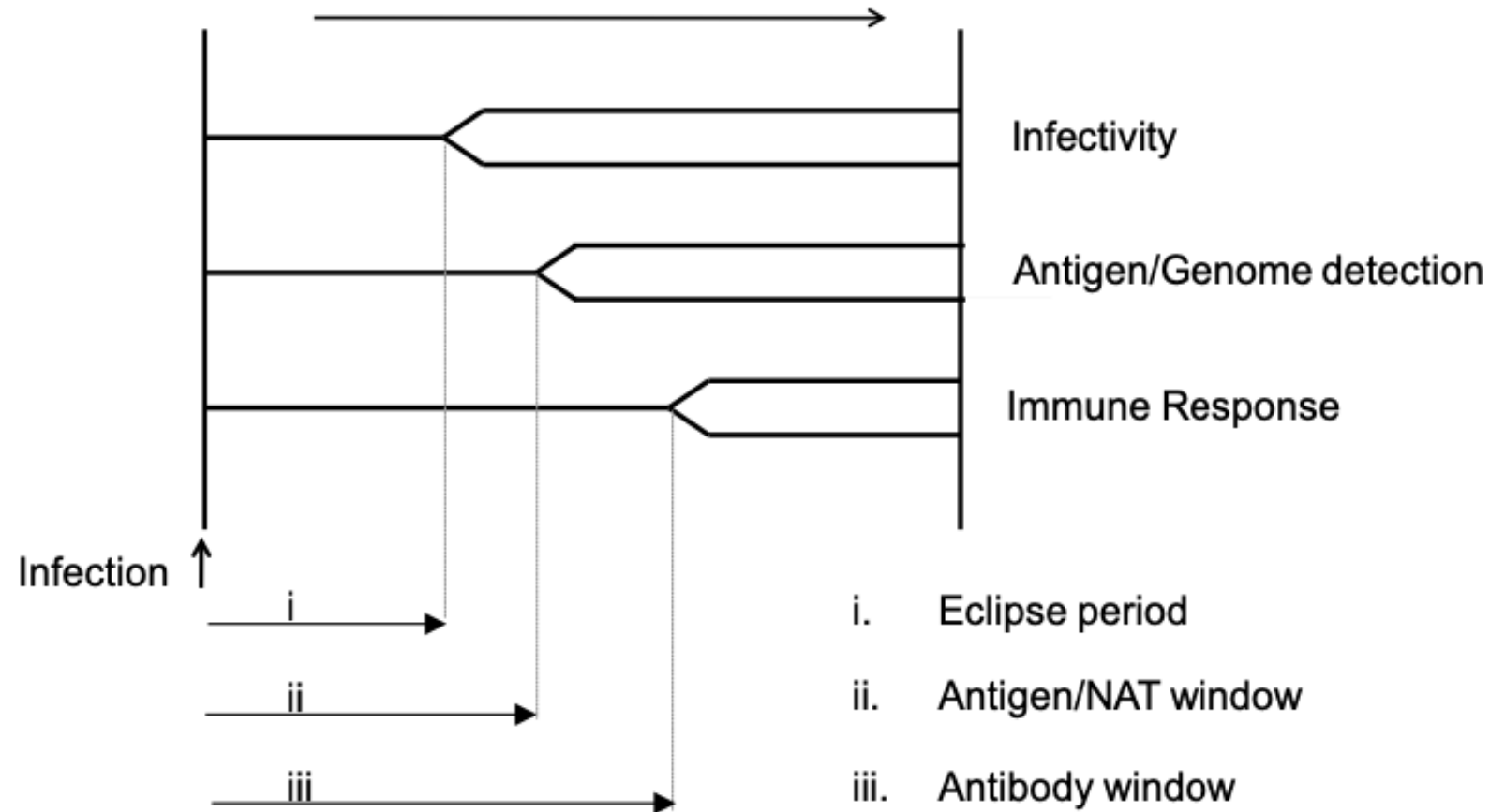
Estimated prevalence of human immunodeficiency virus (HIV) and hepatitis C virus (HCV) among people who inject drugs in selected high-income countries. HCV prevalence estimates represent mid-range estimates (source of HCV data: United Nations Office on Drugs and Crime <http://unodc.org>; source of HIV data: UNAIDS aidsinfo.unaids.org). *HCV estimate for Germany represents high range estimate for the year 2011. IVDU, intravenous drug users.

Interpreting donor test results

- Following exposure to, and infection by, a microbiological agent there is a period of time during which no microbe can be readily recovered from the host; this is classically called the eclipse period.
- Donations taken during this period are unlikely to be infectious but in practice this would not be safe and should be avoided.



Infection Time Course



Window

Table 1: Estimates of window period length for different testing methods*

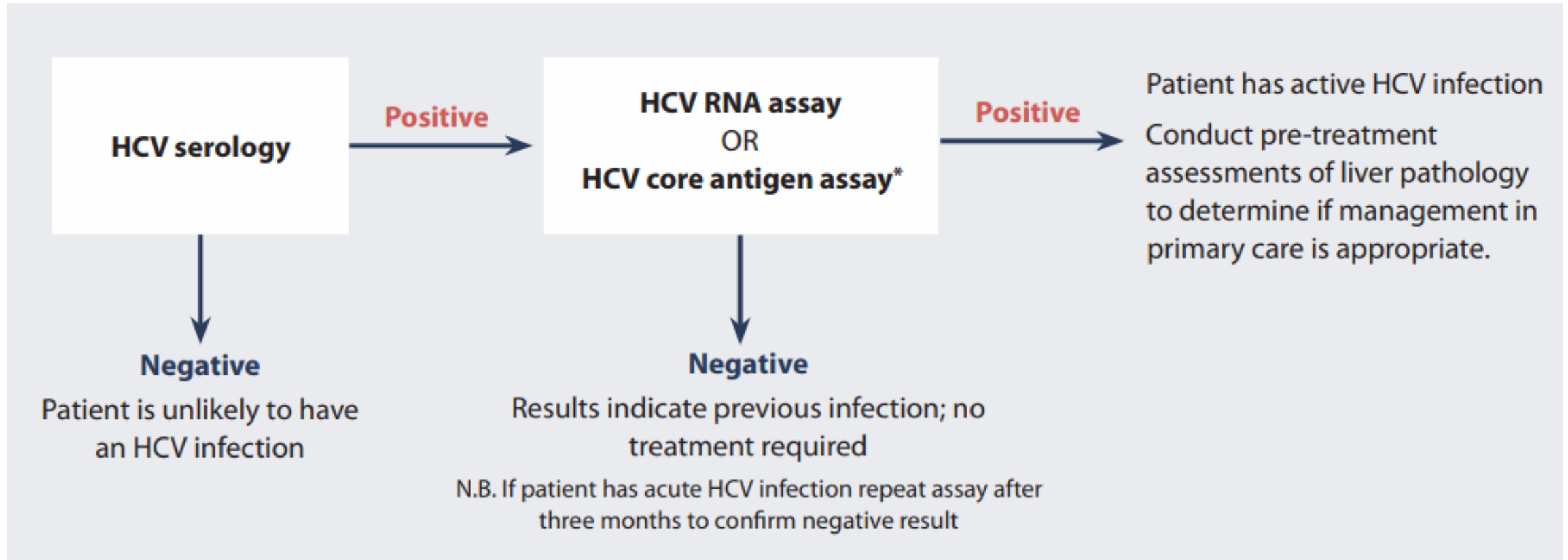
Pathogen	Standard serology	Enhanced serology (fourth generation or combined antibody-antigen tests)	Nucleic acid testing
HIV	17–22 days (5–8)	~7–16 days (9,10)	5–6 days (5,6)
HCV	~70 days (5,8,11)	~40–50 days (12–14)	3–5 days (5,11)
HBV	35–44 days (15,16)	Not applicable	20–22 days (8,15)

Interpreting Hepatitis B Blood Test Results

Interpretation & Action Needed	HBsAg Hepatitis B Surface Antigen	HBsAb (anti-HBs) Hepatitis B Surface Antibody	HBcAb (anti-HBc) Hepatitis B Core Antibody
Not Immune - Not Protected Has not been infected, but still at risk for possible hep B infection. Vaccine is needed.	—	—	—
*Immune Controlled - Protected Surface antibodies present due to natural infection. Has recovered from a prior hep B infection. Cannot infect others. No vaccine is needed.	—	+	+
Immune - Protected Has been vaccinated. Does not have the virus and has never been infected. No vaccine is needed.	—	+	—
Infected Positive HBsAg indicates hep B virus is present. Virus can spread to others. Find a doctor who is knowledgeable about hep B for further evaluation. More Testing Needed.	+	—	+
*Could be Infected Result unclear - possible past or current hep B infection. Find a doctor who is knowledgeable about hep B for further evaluation. More Testing Needed.	—	—	+

*Inform all doctors about a prior or current hepatitis B infection and include this information as part of your health history.
Talk to doctors before taking immune system suppressing medications to understand the risk for possible hep B reactivation.

Hepatitis C tests





HIV

- Screening for HIV infection must include a combined HIV antigen/antibody assay.
- Samples giving repeat reactivity in antibody or combined antigen/antibody assays must undergo additional testing to confirm HIV infection including nucleic acid tests (NAT) for HIV RNA.
- Confirmed detection of specific anti-HIV 1/2 antibodies and/or HIV RNA and/or HIV antigen indicates current infection.
- The use of organ and cells from HIV-infected individuals may be considered in the setting of HIV-infected recipients.



CMV and EBV

- The majority of adult populations worldwide are latently infected with CMV and/or EBV,
- CMV: 20% to 100%
- EBV: 50% to 90%

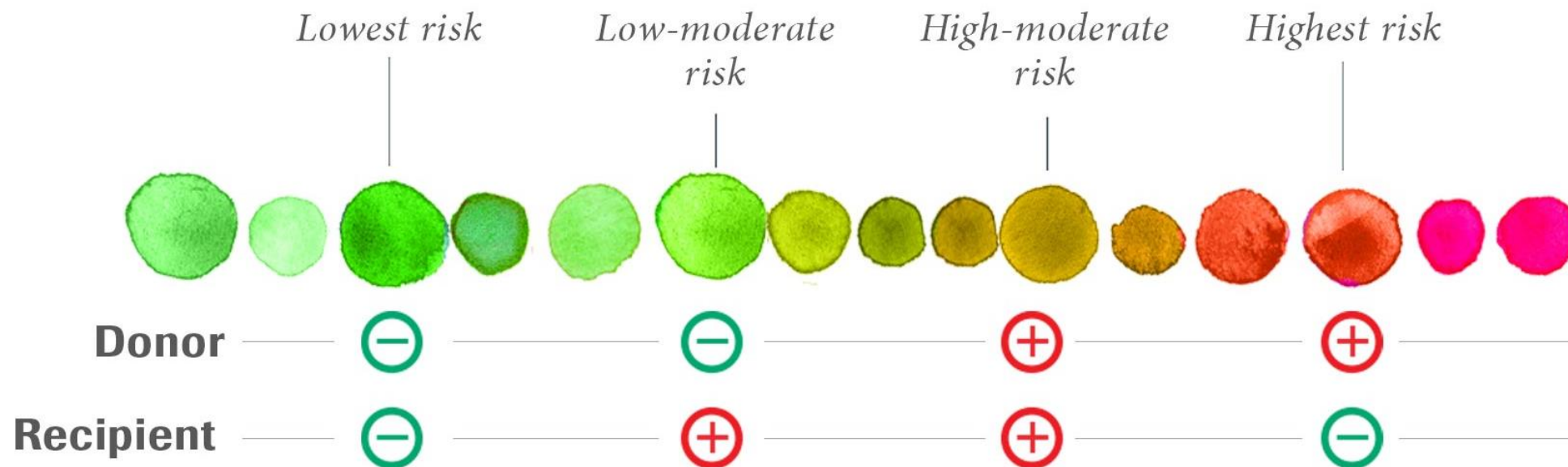
of populations older than 18 years, respectively



CMV and EBV

- CMV and EBV cause lifelong infection, and organs from seropositive donors may transmit infection, potentially causing severe disease in a seronegative recipient.
- Latent CMV and EBV may also reactivate in immunosuppressed seropositive patients post transplantation.
- No contraindications exist for organ donation in the case of donors with latent CMV infection, although recipient morbidity increases in the case of D+/R- combinations.

CMV





EBV - *Epstein-Barr virus*

- Epstein-Barr virus (EBV) infection is associated with the development of post-transplant lymphoproliferative disorders (PTLDs).
- EBV transmission to a seronegative recipient is the greatest risk factor for PTLD
- EBV positive donors does not prevent transplant but monitoring is recommended

Viral infection Tests

Tests for viral infection	
HIV 1/2 antibody	Contraindicated but considered for HIV-positive recipient
Cytomegalovirus IgG antibody	Not contraindicated but essential to define prophylactic strategy after procedure depending on recipient serology
EBV IgG antibody	Not contraindicated but essential to monitor EBV-negative recipients, especially children
HBsAg	Contraindicated but considered for HBsAg+ recipients or HBV protective immunity
HBcAc/'HBc alone'	Not contraindicated but consider antiviral prophylaxis for liver and HBV non-immune recipients
HCV antibody	Contraindicated but considered for HCV+ recipients

Hep C organs are now being excepted into negative recipients by some units who are pre-consenting recipients given how effective treatment for HEP C has become



Human T cell Lymphotropic Virus (HTLV)

- The Human T-cell lymphocytic virus-1 (HTLV-1) is an oncogenic retrovirus that preferentially infects CD4+ T-cells.
- Transmission may occur as a result of breast feeding, IV drug use, sexual intercourse or blood transfusion.
- Although infection is usually asymptomatic in most individuals, approximately 2% to 5% of infected individuals will subsequently develop acute T-cell leukaemia/lymphoma (ATL) around 20 to 30 years after infection.
- A smaller proportion (0.25–4%) will develop HTLV-1–associated myelopathy/tropical spastic paraparesis (HAM/TSP) soon after the initial infection.



Human T cell Lymphotropic Virus (HTLV)

- **The majority of HTLV-1–infected individuals will not develop clinical manifestations of ATL or HAM/TSP in their lifetime.**
- However, infection with HTLV-1 suppresses immune surveillance and increases susceptibility to other infections including parasitic infection with *Strongyloides stercoralis* and scabies, bacterial infections including *Mycobacterium tuberculosis*, *Mycobacterium leprae*, and infectious dermatitis, and viral infections including HIV, HCV, and HBV.

HTLV

- HTLV is not mandatory for all donors of tissues and cells but is for donors living in, or originating from high-prevalence areas, or with sexual partners originating from those areas or where the donor's parents originate from those areas.
- The decision to proceed = based on an assessment of risk



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Toxoplasma gondii

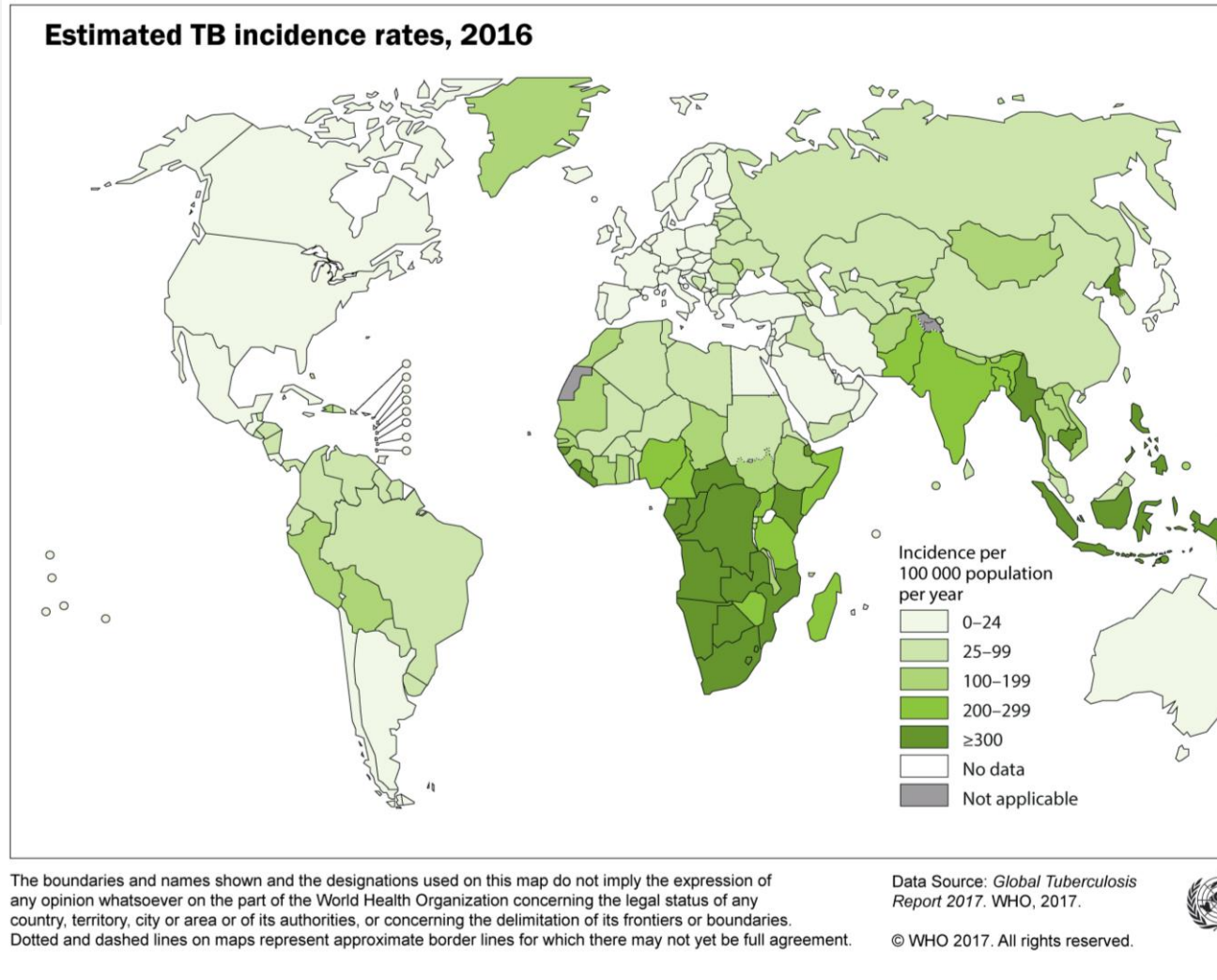
- Transmission of an infection with *T. gondii* occurs most commonly when a seronegative recipient receives an organ from a seropositive donor.
- Whereas the occurrence of toxoplasmosis following non-cardiac organ transplantation is low, the reported prevalence in serologically **mismatched (D+/R–) heart and heart-lung recipients** in the absence of antimicrobial prophylaxis can be as high as 75% due to the transmission of *T. gondii* cysts present within cardiac tissue.

If positive

- Donation permitted
- Informs need for prophylaxis in heart recipients

TB - Tuberculosis

- Donation of organs and tissues is contraindicated from donors with active disease or within the first six months of anti-tuberculosis treatment.
- Previous disease or from a risk area - requires donor prophylaxis.



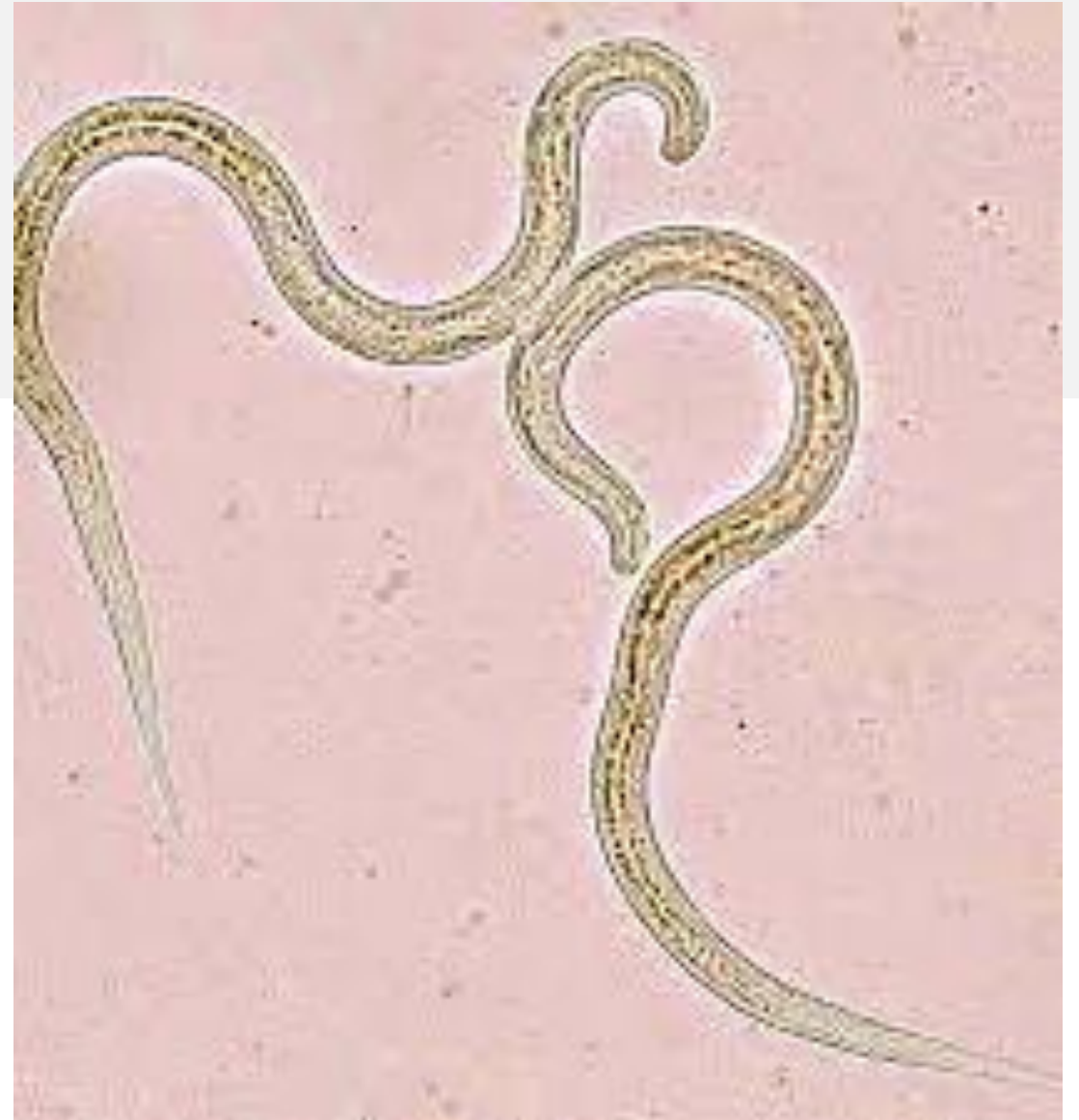


Hepatitis E Virus

- Hepatitis E virus (HEV) is overall the world's most common cause of acute viral hepatitis.
- If positive
- Donation permitted. Informs post transplant management

Strongyloides stercoralis

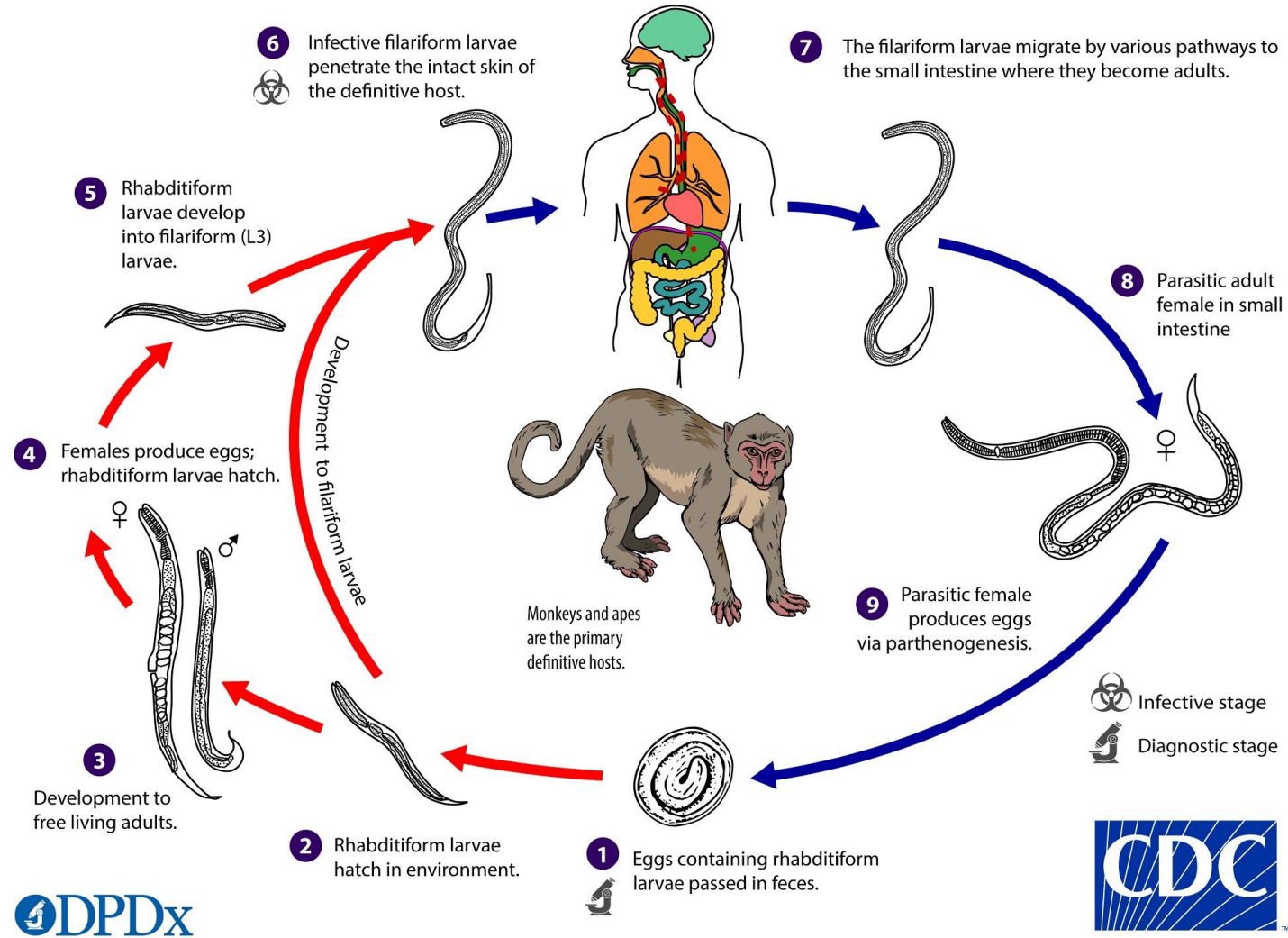
- Asymptomatic carriage with *strongyloides stercoralis* has been reported most often in donors who were both born in and lived for some while in endemic areas which include most of the Tropics and Sub-tropics.
- An Eosinophilia may or may not be present. Transmission to immuno-compromised recipients is often associated with significant morbidity and a high mortality rate.
- Pre-donation identification from stool sampling and serology, most practicable for a live donor allows for effective recipient prophylaxis.



Strongyloides fuelleborni

Free-Living Cycle


Parasitic Cycle



Treponema pallidum (Syphilis)

- Syphilis is never a contraindication for using organs
- Penicillin should be administered to recipients of serologically reactive donors.





Drug resistant bacteria e.g. methicillin resistant *Staphylococcus aureus* (MRSA), vancomycin resistant *Enterococcus* (VRE), carbapenemase-producing *Enterobacteriaceae* (CPE)

Drug resistant bacteria can be transmitted from donor to recipient. Transmitted infections are difficult to treat and are associated with poorer outcome in the recipient.

- The presence of drug resistant bacteria in the donor is a relative contraindication to solid organ transplantation.
- Specialist microbiological advice must be sought.
- Careful consideration of benefits from transplant is required.



Yearly Epidemic Influenza



- UK guidelines state that lungs and bowel should not be used from donors with confirmed influenza infection.
- Other organs may be offered, and the final decision lies with the transplanting surgeon.



Meningoencephalitis of unknown cause

- Donors with undiagnosed meningoencephalitis are an uncommon but potentially lethal source of donor-derived infection.
- Transmission of rabies, LCMV, WNV, *Mycobacterium tuberculosis*, *Cryptococcus*, *Coccidioides immitis*, *Aspergillus*, and *Balamuthia* have occurred when donors with meningitis or encephalitis of unknown cause have been used as organ donors.
- For this reason, any meningitis or encephalitis without a proven cause should be an absolute contraindication to transplantation, according to the international guidelines

Bacterial meningitis

- If bacterial meningitis has been confirmed, and there is no visible damage or local infection in the organ or tissues required at retrieval, the donation of the organs, tissues and cells are acceptable provided appropriate treatment has been administered to the donor.





Transmissible Spongiform Encephalopathies (TSEs) (Prion)

TSEs (otherwise known as prion diseases) are a group of fatal transmissible neurodegenerative disorders that in humans occur in sporadic, genetic and acquired forms.

The commonest human TSE, Creutzfeldt-Jakob disease, occurs in all three forms:

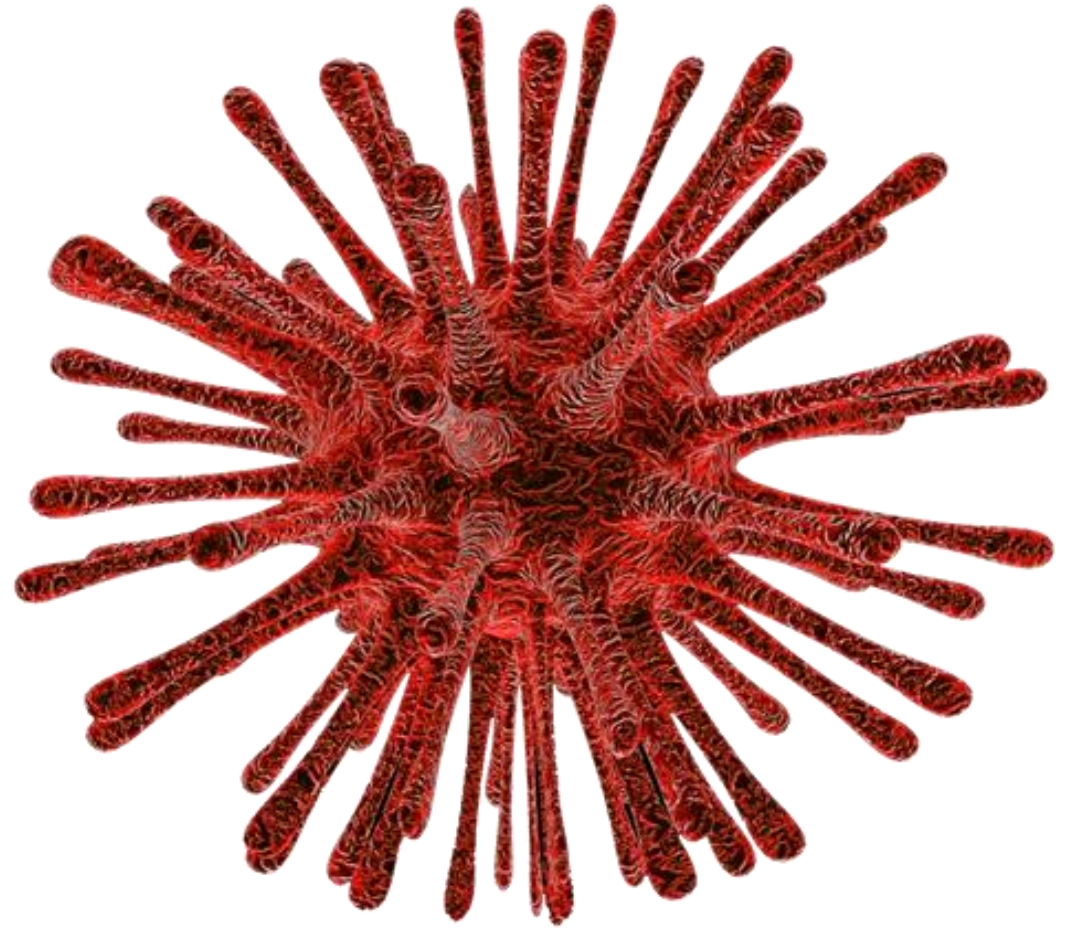
1. Genetic (gCJD),
2. Sporadic (sCJD)
3. Acquired (Variant CJD,vCJD, and iatrogenic CJD,iCJD).

Exclusions from organ and/or tissue donation based on possible TSE exposure

	Solid Organ Donors
Definite, probable or possible case of human TSE, including CJD and vCJD	Absolute contra-indication
Individual with a neurological disease of unknown aetiology	Absolute contra-indication
Individual whose blood relatives have had familial CJD ¹	Absolute contra-indication
Individual "presumed infected" with vCJD ²	Absolute contra-indication
Individual "at increased risk of CJD/vCJD" (for public health purposes) ³	Individual assessment required ⁴
History of definite ⁵ or probable ⁶ blood transfusion since 1980	Individual assessment required ⁴
History of receipt of <i>dura mater</i> graft	Individual assessment required ⁴
History of definite receipt of tissue since 1980	Individual assessment required ⁴
History of receipt of pituitary derived growth hormone and/or gonadotrophin	Individual assessment required ⁴
History of receipt of organ	Individual assessment required ⁴

COVID 19

SARS-CoV-2



SARS-CoV-2

- There is growing experience in the use of organs from donors that are positive for SARS-CoV-2 ribonucleic acid (RNA). Thus far, transmission has only been described through transplantation of lungs where a lower respiratory tract sample was not tested during donor screening and was subsequently shown to be strongly positive for SARS-CoV-2 RNA.
- Patients with a diagnosis of COVID-19 and positive SARS-CoV-2 RNA results, where COVID-19 is felt to contribute to the cause of death, are currently not being considered for deceased organ donation.
- In potential deceased donors with no diagnosis of COVID-19 (where COVID-19 is not felt to contribute to the cause of death) and positive or indeterminate SARS-CoV-2 RNA tests, analysis of the patient's history and consecutive viral RNA results can help with interpretation of the likely stage of infection.
- Where positive screening results are compatible with recent, resolving, or current infection in the upper and/or lower respiratory tract, evidence thus far indicates that transmission of SARS-CoV-2 through the transplantation of (non-lung) organs leading to COVID-19 in the recipient is unlikely. Non-lung organs from these donors will now be offered.

Aide Memoire

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SaBTO Aide Memoire

This tool was last updated on: 09 June 2022 at 16:51.

Aide Memoire

Disease Type

Infection ▼

Category

Viral infection ▼

Specific Infection/Disease Type

Dengue virus (DENV) ▼

Specific Infection/Disease Subtype

Donor with acute illness ▼

Results: Infection, Viral infection, Dengue virus (DENV), Donor with acute illness

Recipient

Urgency:

Exceptional: **DO NOT USE**

Urgent: **DO NOT USE**

Thank You

Questions?