Screening donors and donations for transfusion transmissible infectious agents

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Aim

- Not to teach you microbiology
- To provide and awareness of the 'big picture'
- To provide an understanding of what is done to ensure the microbial safety of products:
  - which infectious agents are screened for
  - which screening targets are used
  - how screening is performed
  - outcomes

Basic safety

- The safety of donated products is critical
- There is no such thing as 'absolutely safe'
- The level of safety of the processes which use the donated products must be equally as safe
- Cost must be balanced against benefit

Transmissible infectious agents

- The range of agents potentially transmissible is potentially relatively large
- The agents considered to be the greatest and universal risk is much smaller
- Range of agents transmitted includes:
  - viruses
  - bacteria
  - parasites
  - prions (strong causal evidence)
- Transmissibility depends upon a number of factors

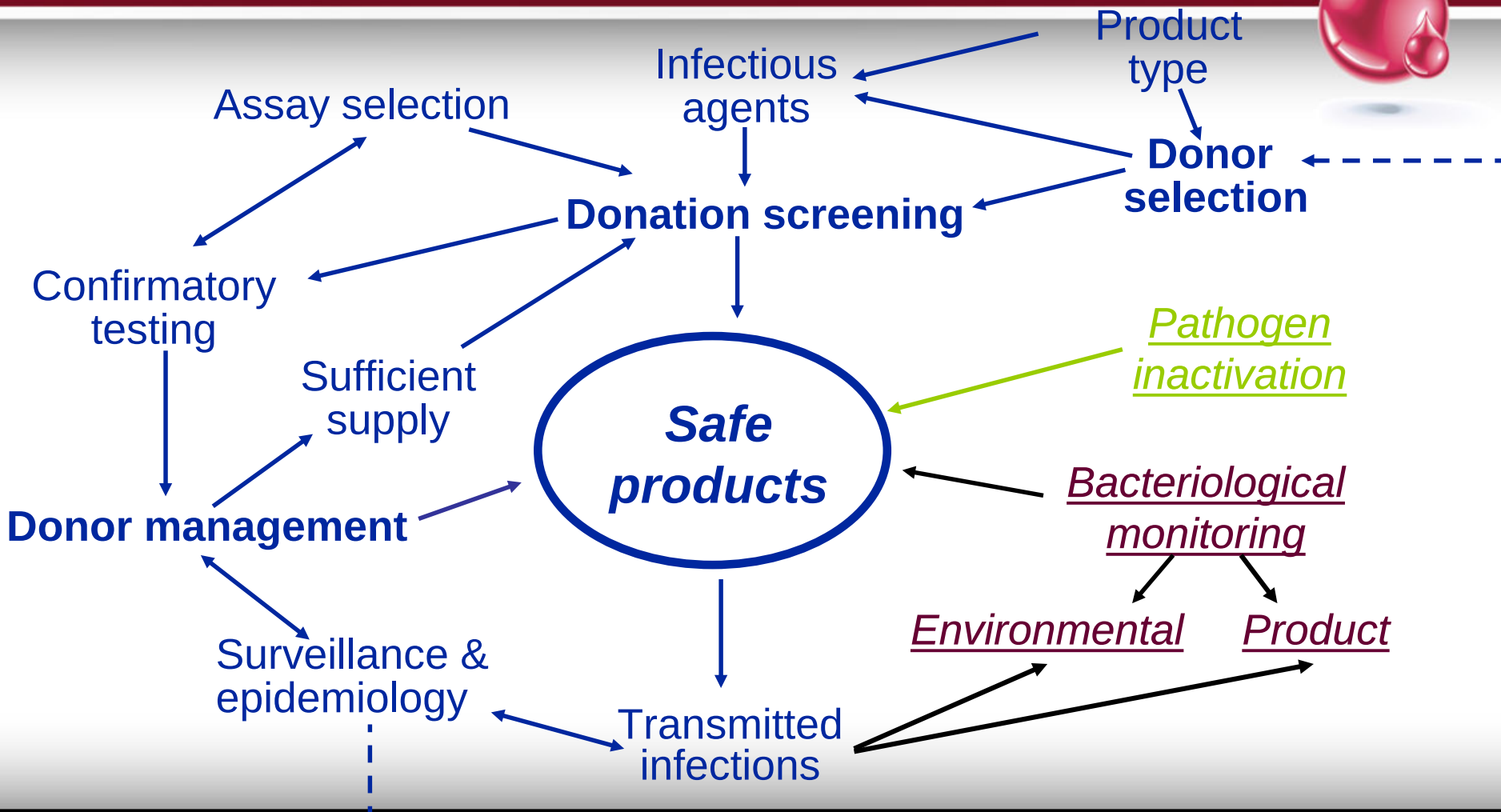
Transmissibility

- Present in the product
  - circulates in blood (sufficient quantity)
  - infectious form
- Asymptomatic infection
  - donor does not have symptoms
  - at least some infectivity whilst asymptomatic
- Parenteral transmission
  - via blood and body fluids
  - direct inoculation into the blood stream
- Stable under storage conditions applied
  - from -196°C to 22 °C

Clinical consequences

- Even if transmissible, is transmission harmful?
- Do all transfusion transmitted infections do harm?
- If not, is there any need to screen for a transmissible agent that does not appear to have any adverse clinical consequences?

Ensuring safe products



Which infectious agents are screened for?

Agents reported to have been T/TT

- Viruses
  - hepatitis viruses A-E
  - HIV 1+2
  - HTLV I+II
  - CMV
  - EBV
  - HHV-8
  - Parvovirus B19
  - GBV-C
  - TTV
  - West Nile Virus
  - Dengue
  - Zika
- Bacteria
  - Treponema pallidum (Syphilis)
  - Brucella melitensis (Brucellosis)
  - Yersinia enterocolitica/Salmonella spp.
  - Rickettsia rickettsii (Rocky Mountain Spotted Fever)
  - Coxiella burnettii (Q fever)
- Protozoa
  - plasmodium spp. (Malaria)
  - *Trypanosoma cruzi* (Chagas' disease)
  - *Toxoplasma gondii* (Toxoplasmosis)
  - *Babesia microti/divergens* (Babesiosis)
  - leishmania spp. (Leishmaniasis)

Infectious agents screened for (UK)

- The infectious agents screened for are defined within the UK Transfusion Guidelines (Red Book)
  - mandatory (all donations)
  - additional (selected donations)
- Mandatory
  - HBV, HIV, HCV, Syphilis, HEV
  - HTLV
- Additional agents/markers
  - HCMV Ab & DNA, HBcAb, Malarial Ab, *T. cruzi* Ab (Chagas disease), WNV RNA

Why do we not screen for all?

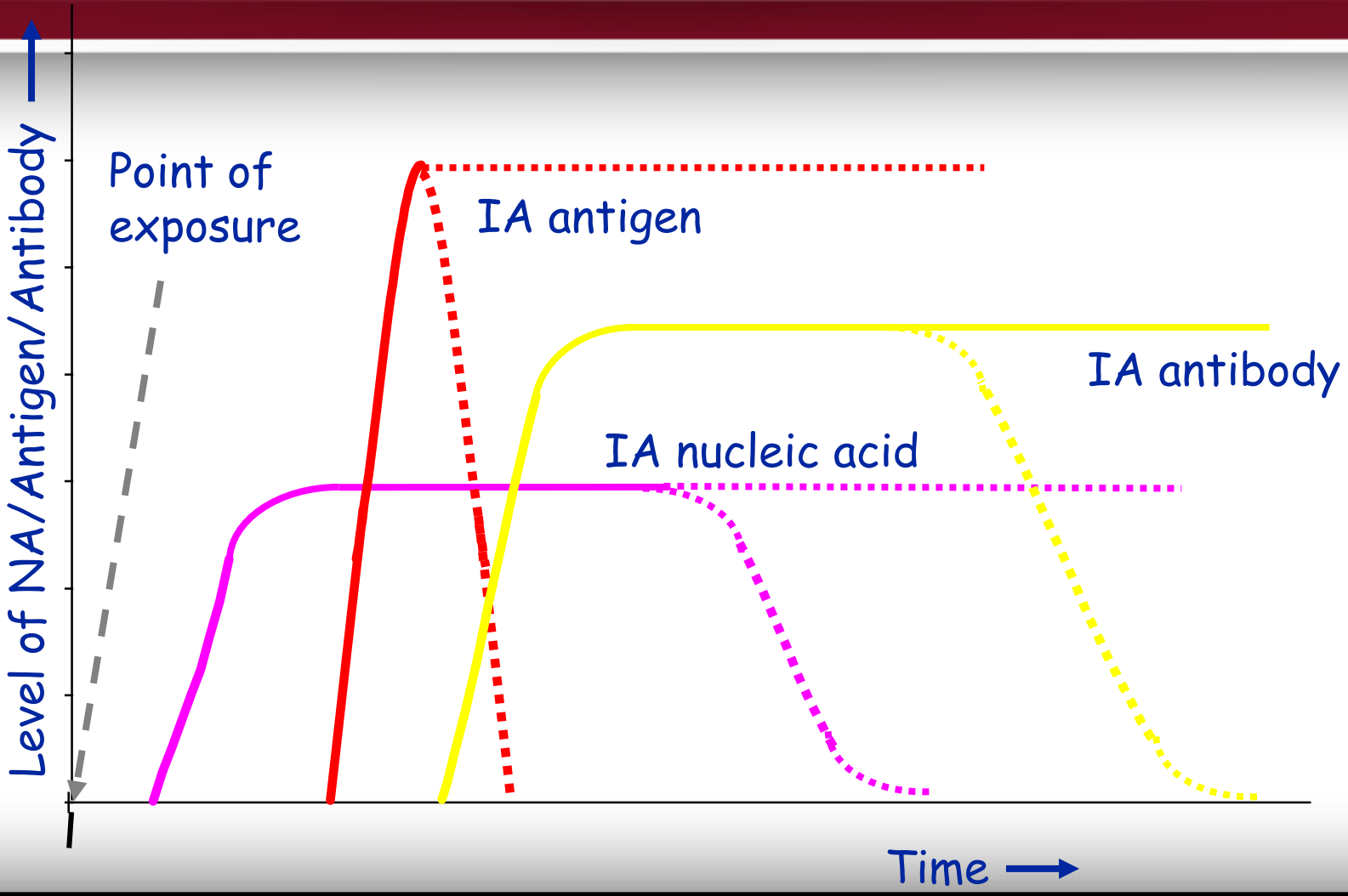
- Not present in donor population
  - prevalence of infection in the general population
  - prevalent/incident infection in donors
- Some present at high level in population
  - significant proportion of the population already exposed
- Not a risk to all recipients
  - selective screening possible
  - do not give rise to clinical consequences
  - transmission but no or limited disease
- Effective screening not always possible
  - serological markers of little use
  - molecular often not practical/appropriate

Which screening targets are used?

Specific screening targets

- For each infectious agent, which target is used?
- The course of an infection
  - exposure to the agent - infection
  - incubation - multiplication of the agent
  - appearance of first circulating marker
  - appearance of subsequent circulating markers
  - resolution of infection

Agent/host/test interaction



Mandatory screening targets

Mandatory screening:

	Blood	Tissues/Stem cells
HBV	HBsAg	HBsAg, HBcAb, HBV DNA*
HIV	Ag/Ab(1+2+O)	Ag/Ab(1+2+O), HIV RNA*
HCV	Ab, RNA	Ab, RNA*
Syphilis	specific Ab	specific Ab
HTLV	Ab (I+II)	Ab (I+II)
HEV	HEV RNA	HEV RNA

Molecular screening of blood donations performed on pools of 24 or 6 samples; tissue and stem cell screening is ID only

* if serology only a f/u sample must be taken at 6/12

Additional screening targets

- HCMV Ab / HCMV DNA - for at risk recipients
- Malarial Ab, *T. cruzi* Ab, WNV RNA - potentially exposed donors

- (HBcAb - piercers, history of jaundice)

How is screening performed?

Screening – donor selection

- First part of the screening process
  - decision point for release of donor
- Is the donor suitable?
  - will donation harm the donor?
  - will donation harm the recipient?
- Requires comprehensive and appropriate donor selection guidelines

Screening - laboratory

- In-vitro screening of donor/donation samples
  - decision point for release of donation/products
- Requires:
  - defined infectious agents and screening targets
  - evaluated and suitable assays and platforms
  - appropriate screening algorithm
  - effective and appropriate confirmation of screen reactivity

Evaluated and suitable assays and platforms

- All assays used for screening are evaluated through the UK kit evaluation groups (NHSBT – KEG, SNBTS – MTEG)
- Automated screening platforms with high levels of process control
- Working within an effective QMS
- Combination of molecular and serology

Appropriate screening algorithm

- The screening algorithm defines how the screening results are generated and used – fate of the donation

- UK screening algorithm is that of initial screen and repeat of any initial reactives in duplicate using the same assay
  - 2 out of 3 rule applied
- Donation fate based upon overall screen result

Effective confirmation

- Screen repeat reactive donors need to be investigated to determine if the reactivity is specific or non-specific
  - clinical intervention for infected donors (public health)
  - management of donor base
- Donor management is important to maintain donor base
  - non-specific reactivity is assay associated
  - non-specific reactivity is cumulative
  - unnecessary loss of donors should be avoided
  - non-specifically reacting donors can still be used
- Donor fate based upon confirmatory result

Screening outcomes

Outcomes

- Screen negative – donation issued
  - residual risk of a 'false negative' screen result
- Screen repeat reactive – blood donation discarded
  - confirmation determines fate of donor
  - re-instatement whenever possible

Residual risk

- Risk of collecting a donation from a donor with a very low level of screening target, not detected on screening
  - does not indicate risk of transmission of infection

Current residual risks

	HBV	HCV	HIV
No. donations tested before a low pos would not be detected ($x10^6$)	2.1	95.8	15.5
No. of years to a miss	1	46	7

TTI incidents (recipients) by infection

	Pre 1996	1996 to 2001	2002 to 2007	2008	2009	2010	2011	2012	2013	2014	2015	Total
HAV	0	2(2)	1(1)	0	0	0	0	0	0	0	0	3(3)
HBV	1(1)	6(7)	3(3)	0	0	0	1(2)	1(1)	0	0	0	12(14)
HCV	0	2(2)	0	0	0	0	0	0	0	0	0	2(2)
HEV	0	0	1(1)	0	0	0	1(2)	1(1)	0	2(2)	2(3)	4(6)
HIV	0	1(3)	1(1)	0	0	0	0	0	0	0	0	2(4)
HTLV	2	0	0	0	0	0	0	0	0	0	0	0
B19	0	0	0	0	0	0	0	1(1)	0	0	0	1(1)
Malaria	0	1(1)	1(1)	0	0	0	0	0	0	0	0	2(2)
vCJD	0	3(4)	0	0	0	0	0	0	0	0	0	3(4)
Bacteria	0	23(23)	11(11)	4(6)	2(3)	0	0	0	0	0	1 (1)	40(43)
Total	3	38	18	4	2	0	2	3	0	2	3	75

2015 cumulative SHOT data