

Issues facing blood transfusion services in providing infection free products

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(Infectious) issues facing transfusion services

- New/emerging/spreading infections
- Legislation
- Changing priorities

Infections

Infection is different.....
(from other clinical and pathology disciplines).....

.....it spreads!

Risk of transmitted infections

- Transfusion services do more today than ever before to minimise any risk of infection from their products

..... yet despite everything we do, there remains the risk of infection

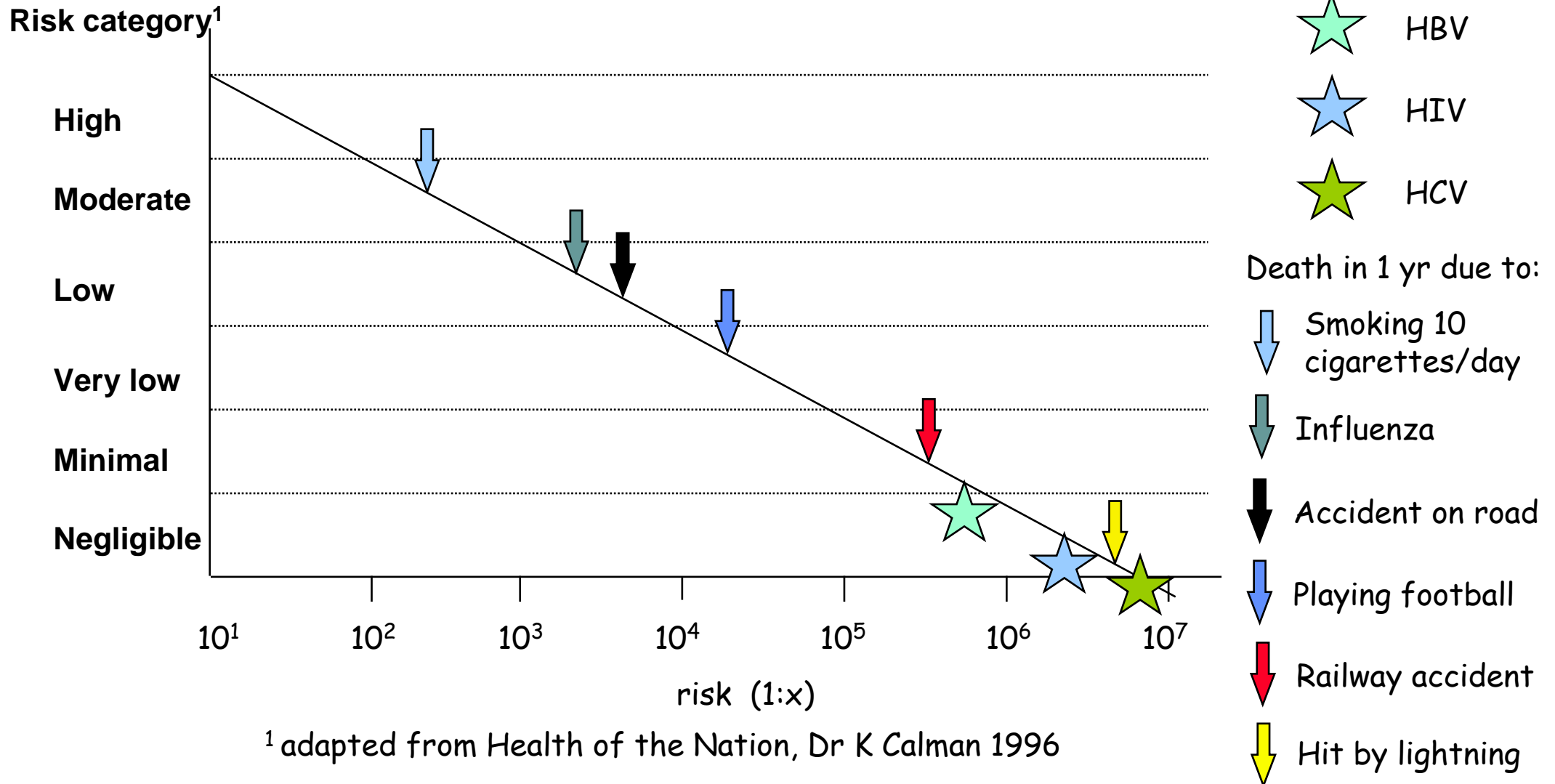
..... why, and can we do anything to reduce it further?

Infection risks

- Failure to detect an infectious agent
 - failure of screening to identify infected donation
 - failure to screen for all transmissible infectious agents
- What is more important - to reduce the numbers of 'misses' or to introduce additional screening?
- Implementation of unnecessary tests
 - loss of focus due to too much screening
 - significant cost of screening

Are we at risk from post transfusion infections?

Provisional estimates (2006) of infection in 1 donation



UK SHOT results

- UK national reporting system for (all) adverse events related to transfusion
- TTI's for 2007 (latest published figures)
 - 25 reports to transfusion centres
 - 3 cases confirmed (all bacterial, 2 rbc, 1 plt)
 - 21 not TTI
 - 1 not concluded (HCMV)

Cumulative SHOT data

<u>SHOT TTIs</u>	<u>1996-2007</u>	
Hepatitis A	3	
Hepatitis B	10	
Hepatitis C	2	
Hepatitis E	1	
HIV	2	
HTLV	2	
Bacteria	34	(8 deaths)
Malaria	2	(1 death)
vCJD/prion	4	(3 deaths)
Total cases	60	(1.4% of all reports)

Failure to identify an infected donation

- Why do transmissions of known infectious agents occur?
- Errors
 - poor systems
 - poor adherence to systems
 - human error
- Poor quality assays
 - EU IVDD CE marking provides only a minimum standard
 - not all CE marked assays are suitable for donation screening
 - operational sensitivity is often poorly understood

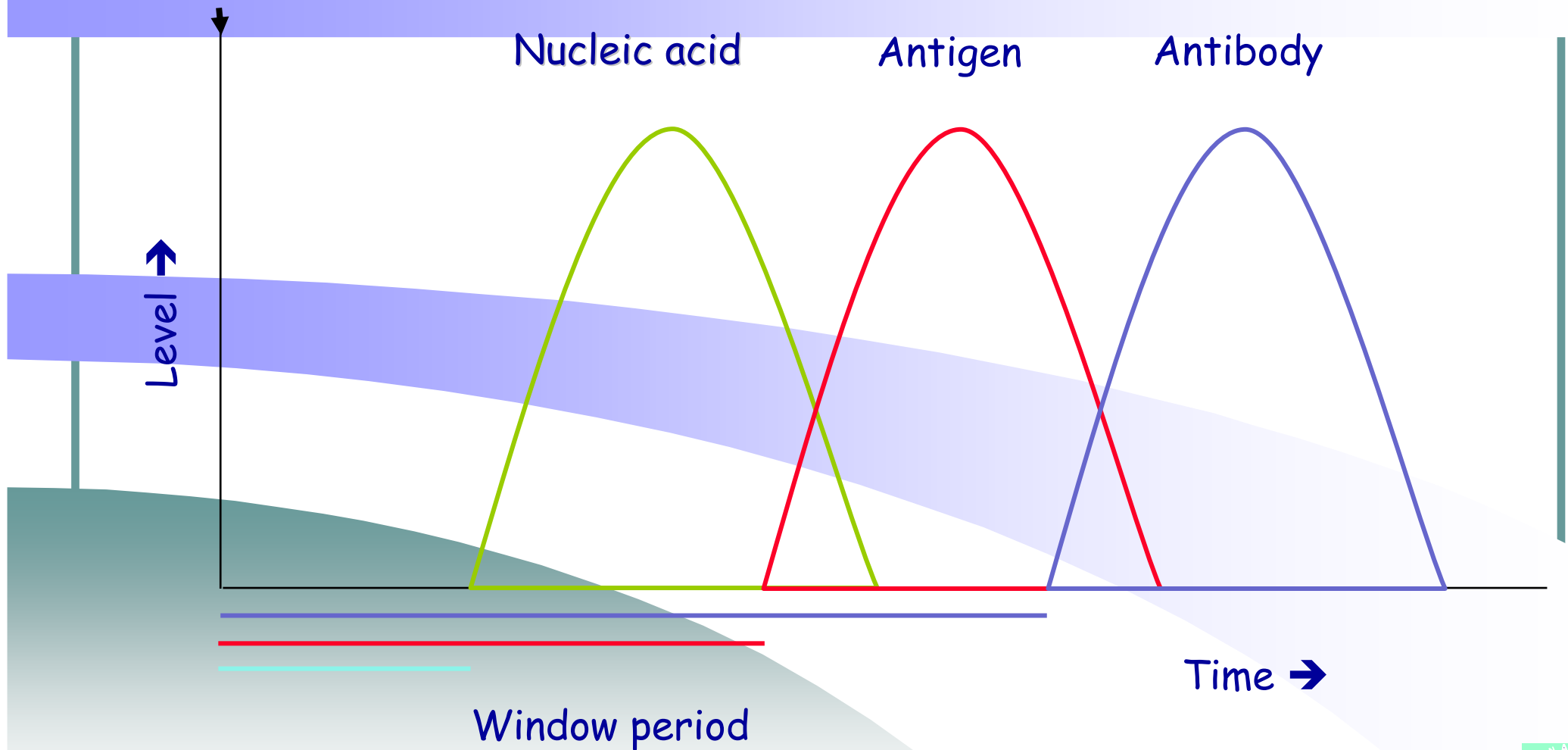
Failure to identify an infected donation

- **Window period**

- the period during which an infected donation is not detectable with the test in use (generally early infection)
- major reason for continual potential for 'missing' a donation infected with a known infectious agent
- biological factor that can only be minimised, not eliminated

Infection in action - window periods

Point of exposure



Residual risk analysis for UK donations

	HIV	HCV	HBV
	1 in x million	1 in x million	1 in x million
Donations from all donors	5.22	29.03 (3.23)	0.50
Donations from new (first time) donors	2.26	6.79	0.16
Donations from repeat donors	6.16	46.99	0.65

SHOT overall risks 1996-2007

Overall risk of serious hazard	1 in 12,000
Risk of IBCT	1 in 20,000
Risk of ABO incompatible	1 in 105,000
Overall risk of major morbidity	1 in 100,000
Risk of major morbidity from IBCT	1 in 300,000
Risk of death from IBCT	1 in 1.3 million
Risk of death (all categories)	1 in 400,000

Failure to identify a new infectious threat

- Why do transfusion services not screen for all potentially transmissible agents?
 - not all present a threat to all countries/services
 - not all present a threat to all patients
 - more screening = more wastage (donations and donors)
 - more screening = more costs

Infectious disease outbreaks



New infections - since 1975

- HIV
- vCJD
- Hepatitis C, E
- HTLV; HHV6, 7, 8
- Lassa, Ebola
- Nipah, Hendra
- Hantavirus (SN)
- Avian flu, SARS
- TT virus
- Legionella
- Campylobacter
- C. difficile
- Helicobacter pylori
- E. coli O157
- Vibrio cholerae O139
- Cryptosporidium
- Chlamydia

Re-emerging and resurgent

- Tuberculosis
- Dengue
- Malaria
- Cholera
- West Nile virus
- Yellow fever
- Chikungunya
- Chagas disease

Why are diseases spreading?

- Modern lifestyle

- travel
- trade
- fast food
- childcare/elderly care
- sexual freedom
- prosperity.....and poverty

Why are diseases spreading?

- Decreased healthcare/public health
 - financial constraints
 - conflict
- Improved healthcare
 - transfusion/transplantation
 - anti-microbial treatments
 - support

Infectious threats to product safety

- What 'new' infections are around the corner, and why?
- What response is needed and what is the trigger?
- Is the target the donor (deferral) or donation (screening)?
- Does the infectious agent actually cause clinical disease?
- Would recipients survive long enough for disease to appear

Responses to infectious agents

- What response should a national transfusion service mount in the face of a new infectious threat?
- Depends on what the agent is!
- What options are there?
 - defer donors
 - screen donations
 - do nothing

Screening donors

- Defer donors
 - all donors or some?
 - temporary or permanent
- What criteria?
- How to deal with losses?
 - recruitment not easy
 - better to make good use of existing donors than try to recruit new ones

Screening donations

- How many tests already performed
 - mandatory/discretionary
- Can we just add another one?
- Is there another one available?
 - different technology e.g. WNV
- All donations or just some
 - mandatory v. discretionary screening
 - how do we identify the 'some'
- Can we stop screening at some time
 - e.g. syphilis and HTLV

Unnecessary testing - an additional risk

- Pressure to adopt 'new technologies' without full consideration of the measurable outcomes
- Implementation of NAT testing is a major problem!
- Why implement NAT
 - new technology
 - increased sensitivity
 - increased safety?
 - legislative requirement

Value of NAT

- What benefit is NAT?
 - does the use of NAT identify any additional infectious donations?
 - does the use of NAT specifically increase the safety of products?
 - is it cost-effective?

No action

- Do nothing
 - watch and wait
 - for how long?
- What to do whilst you are doing nothing?
 - monitor
 - collect data
 - determine the point at which action is needed
- When do you do something?
 - incidence of infection reaches a critical level

Legislation

Legislation

- Transfusion/transplantation becoming more political than clinical
- The safety of the blood and non-blood donations is a major political concern
- Most national transfusion services in countries with developed healthcare system are regulated nationally
 - transfusion services are pharmaceutical manufacturers
 - pharmaceutical regulation is largely appropriate
 - donations are biological not chemical products

Legislative pressures

- Global commercial plasma fractionation is fuelling the need for legislation
- New technologies are influencing legislation
- Legislation is increasing globally
- Legislation is becoming globally harmonised
 - EU
 - countries who use products from other countries

Legislative problems

- EU transfusion services and transfusion practice are regulated both nationally and by EU legislation
 - legislation does not always reflect best practice in every country
 - legislation is different for blood and non-blood donations
 - there is always a risk that legislation may adversely affect patients

Priorities

Priorities

- Transfusion services are developing specific additional areas of involvement/expertise
 - tissue banking
 - stem cell therapy
 - cord blood
- Most transfusion services are focussed on the screening of blood donations
- Screening strategies have to encompass both blood and non-blood donations

Blood and non-blood donations

- The screening needs for non-blood donations are often different (legislative and clinical need)
- The regulation/legislation for blood and non-blood donations are different
- The screening systems in use are not intended/suited for non-blood donations
 - sample detection systems
 - assay validation
 - range of markers/agents available

Mandatory screening within the UK

Marker/ Donation	HBsAg	HIV Ag/Ab	HCV Ab	Syphilis Ab	HTLV Ab	HBc Ab	HCV RNA	HIV RNA	HBV DNA	HCMV Ab	HCMV DNA
Blood	X	X	X	X	X (P)		X (P)				
Surgical tissue (single sample)	X	X	X	X	X (P)	X	X (P)	X (P)	X (S)		
Surgical tissue (2 samples, 180 days apart)	X	X	X	X	X (P)	X					
Cadaveric tissue (adult)	X	X	X	X	X	X	X	X	X		
Cadaveric tissue (neonate)	X	X	X	X	X	X	X	X	X		
	X	X	X	X	X (P)	X	X (P)	X (P)	X (P)		
Cadaveric tissue (maternal)											
Stem cells	X	X	X	X	X	X					
Allogeneic cord blood	X	X	X	X	X	X	X	X	X	X	X (HCMV Ab+)

Screening strategies and algorithms

- Different screening algorithms and strategies may be needed
 - fate of donations and donors may be different
- Cadaveric donations/donors
 - donor deferral process different
- Stem cell donations/donors
 - autologous/related/unrelated
 - recipient may already be infected with BBV

Screening strategies and algorithms

- Significance of screen reactivity may be different
 - blood donations discarded based upon screening result
 - non-blood donations may be issued/used on the basis of reference investigation results

Possible actions

What can be done to reduce risk?

- Implement tighter donor selection procedures
 - already concern in US that donors are lost unnecessarily
- Introduce screening for additional agents
 - needs knowledge and resource
 - needs sufficient donor capacity
- Use more selective screening strategies
 - needs knowledge and understanding

What can be done to reduce risk?

- Improve laboratory screening
 - combination Ag/Ab assays
 - combining serology with molecular
 - strengthen quality management systems
 - ?? other approaches
- Implement pathogen removal/inactivation
 - has limitations

What is without doubt

- Infectious diseases spread and 'new' threats appear (and disappear)
- There are increasing expectations that all products should be 100% safe (zero risk)
 - the product is often safer than the intervention using it
- A measured and balanced response to any potential threat is essential
 - the actual threat needs to be properly understood BEFORE a response is mounted
 - the response should be in proportion to the actual threat

Perspective is everything

