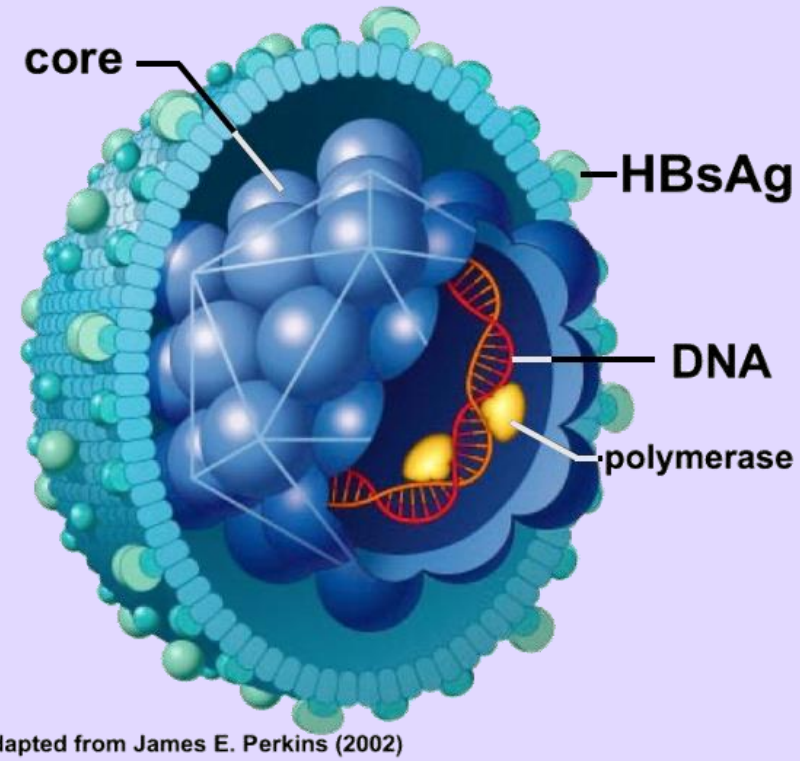
Basics of HBV infection and HBV donorscreening

IPFA/PEI Workshop - Aarhus, May 15th 2024

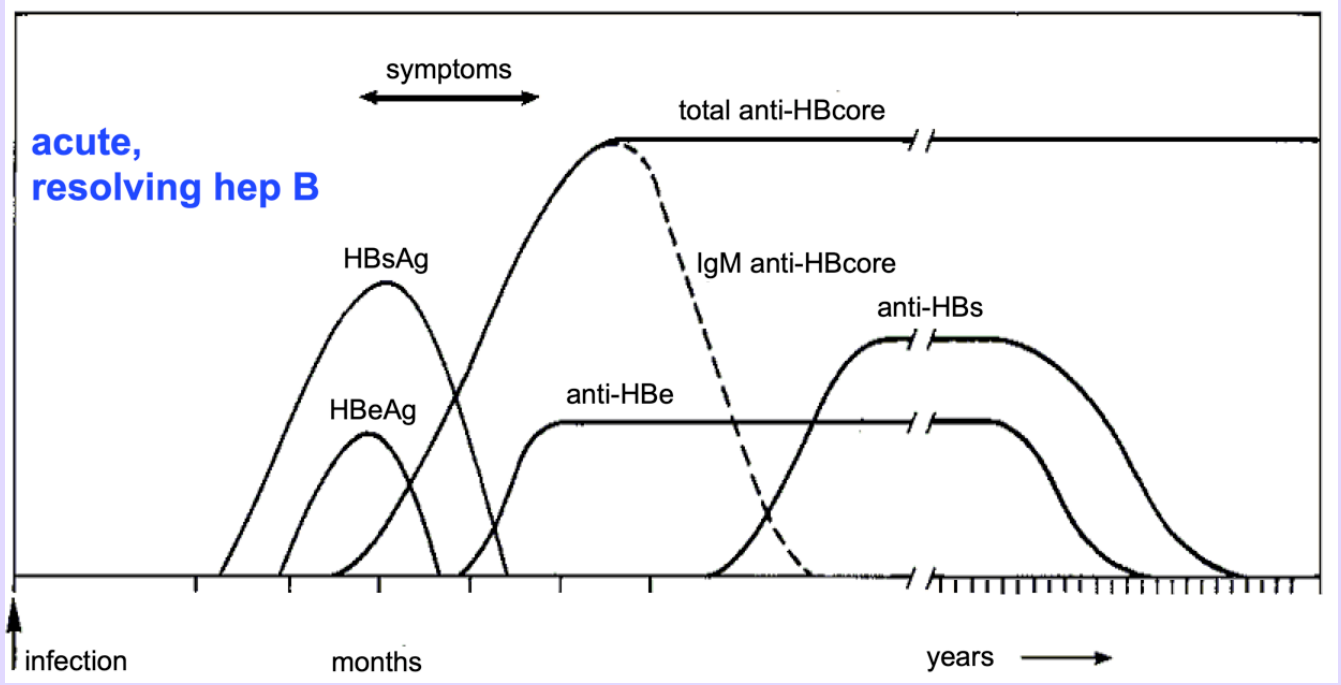
prof.dr. Hans Zaaijer, medical microbiologist
Sanquin Blood Supply Foundation, Amsterdam NL

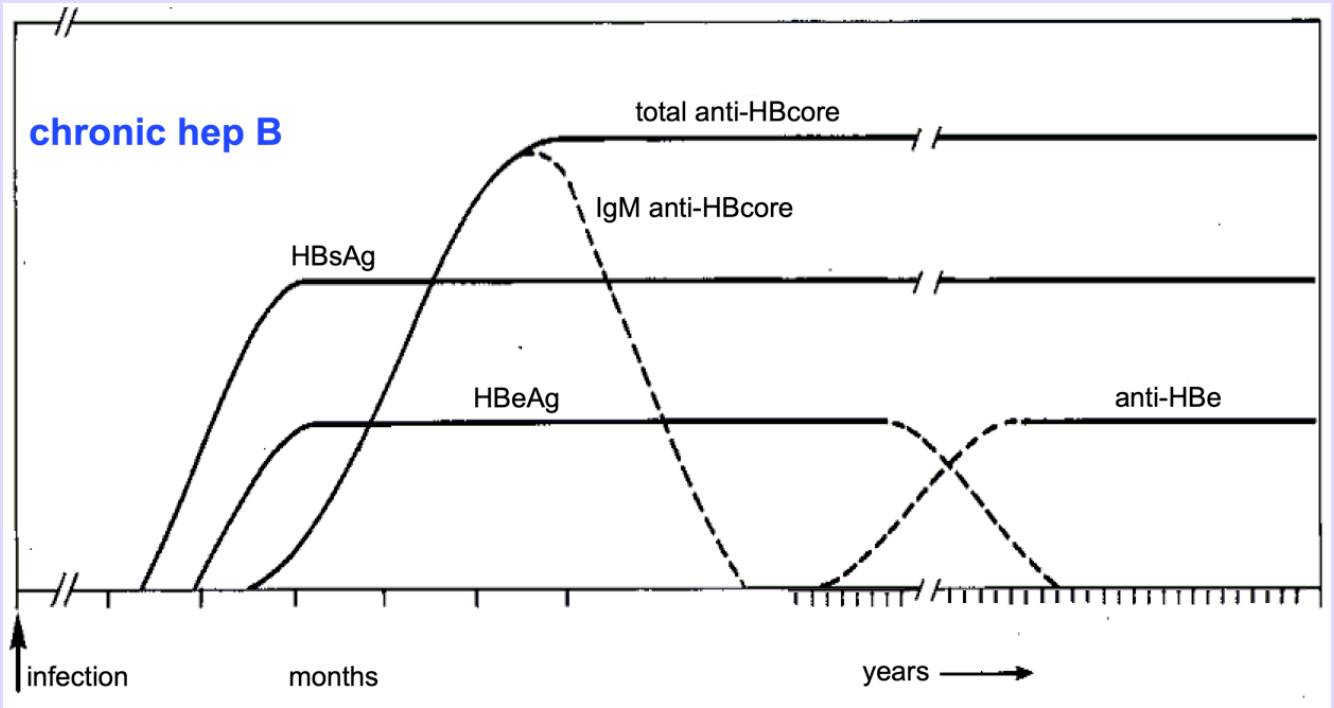
No conflict of interests.



adapted from James E. Perkins (2002)

hepatitis B virus





Hepatitis B serology: the rules of thumb

HBsAg = pos	HBV infection	≥ 6 mo: chronic
anti-HBcore = pos	HBV infection: now or in the past	
anti-HBs = pos	immunity to HBV	≥ 10 IU/L = positive

Hepatitis B serology: the rules of thumb

HBsAg = pos	HBV infection	≥ 6 mo: chronic
anti-HBcore = pos	HBV infection: now or in the past	
anti-HBs = pos	immunity to HBV	≥ 10 IU/L = positive
IgM anti-HBcore = pos	recent HBV infection, or chronic+flare	
IgM anti-HBcore = neg	*no* recent HBV infection	
HBeAg = pos	probably highly viremic and infectious	

eAg = ?

Why "e" ?

What is eAg?

What does eAg do?

eAg = ?

Why "e" ?

THE JOURNAL OF IMMUNOLOGY Vol. 109, No. 5, November 1972

NEW SPECIFICITIES IN AUSTRALIA ANTIGEN POSITIVE SERA DISTINCT FROM THE Le BOUVIER DETERMINANTS

LARS O. MAGNIUS AND J. ÅKE ESPMARK

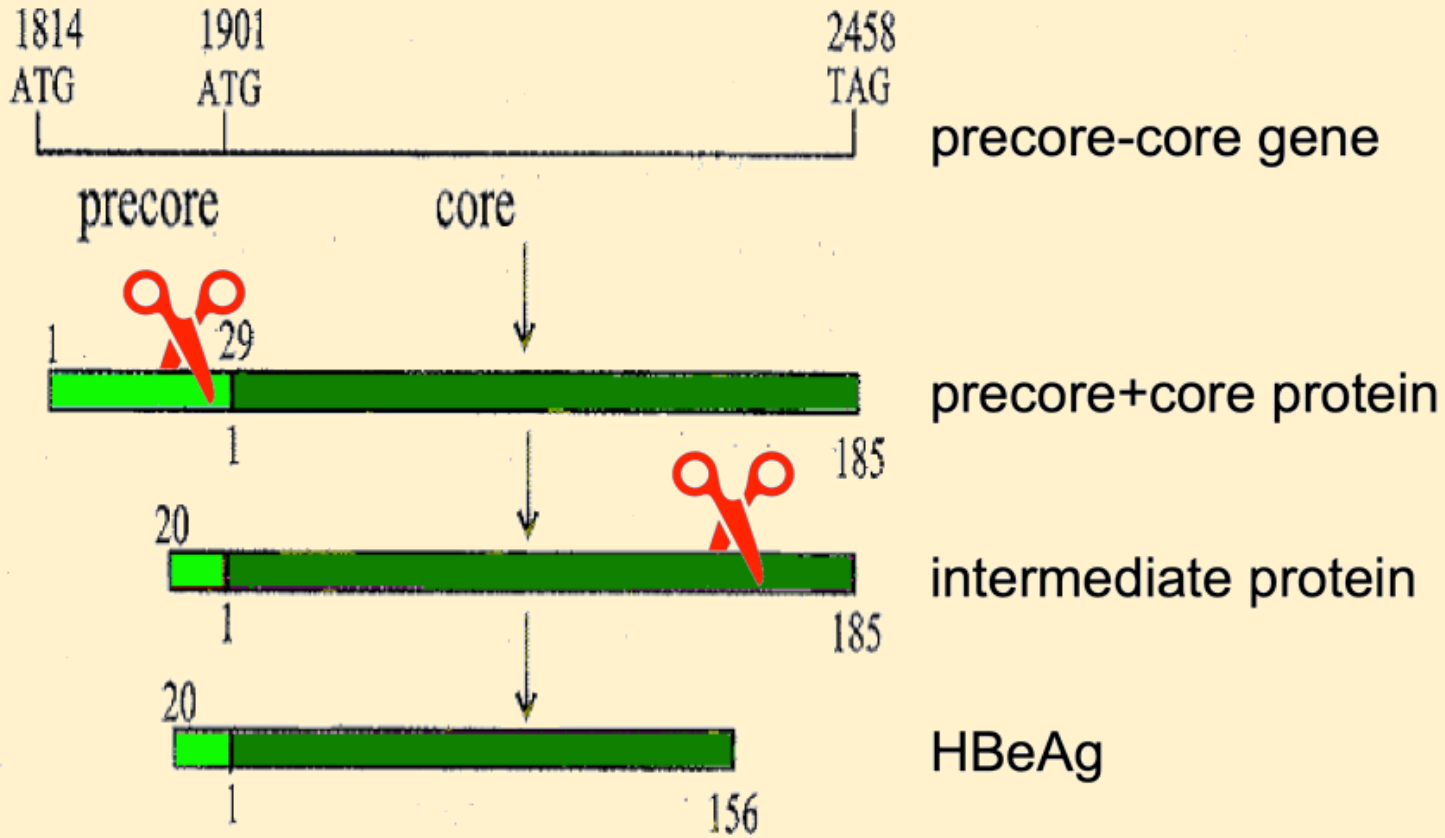
From the Department of Virology, Statens Bakteriologiska Laboratorium, 105 21 Stockholm, Sweden

Evidence for new antigenic specificities in Australia antigen positive sera, for one of which we have proposed the designation e, has been obtained in immunodiffusion tests according to Ouchterlony. These specificities co-occur with Au antigen and are distinct from the a, d, y and x determinants of the Au antigen complex ... Some evidence is presented for the possible association of this antigen complex to contagiousness.

eAg = ?

What is eAg?

= core protein,
plus a head,
minus a tail:



eAg = ?

What does eAg do?

I still don't know

Advanced hepatitis B serology

HBsAg and anti-s are both positive in ~10% of chronic hep B

HBsAg positive some weeks after HBV vaccination, no infection

HBsAg negative but there is HBV infection:

1) latent/occult infection = normal
2) vaccine suppressed infection = normal
3) HIV co-infection
4) delta flare or acute delta
5) HBV genotype G mono-infection

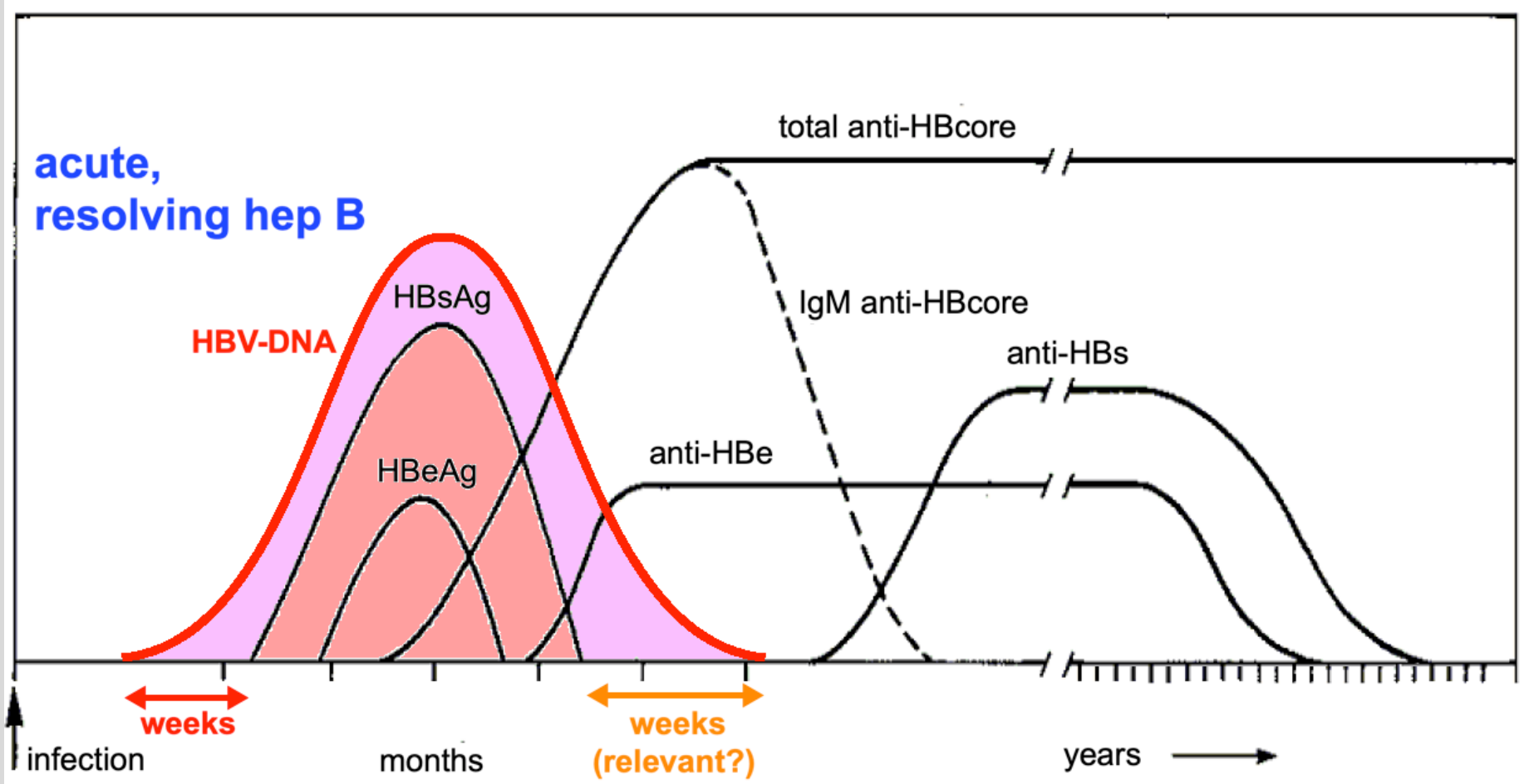
anti-core negative and chronic HBV infection: HIV+ persons ; after stem cell Tx.
latent (occult) blood donors sometimes loose aHBcore.

each assay will produce false-positive test results

3x added value of HBV-NAT for bloodbankers

1.
reduced window

leading and trailing window

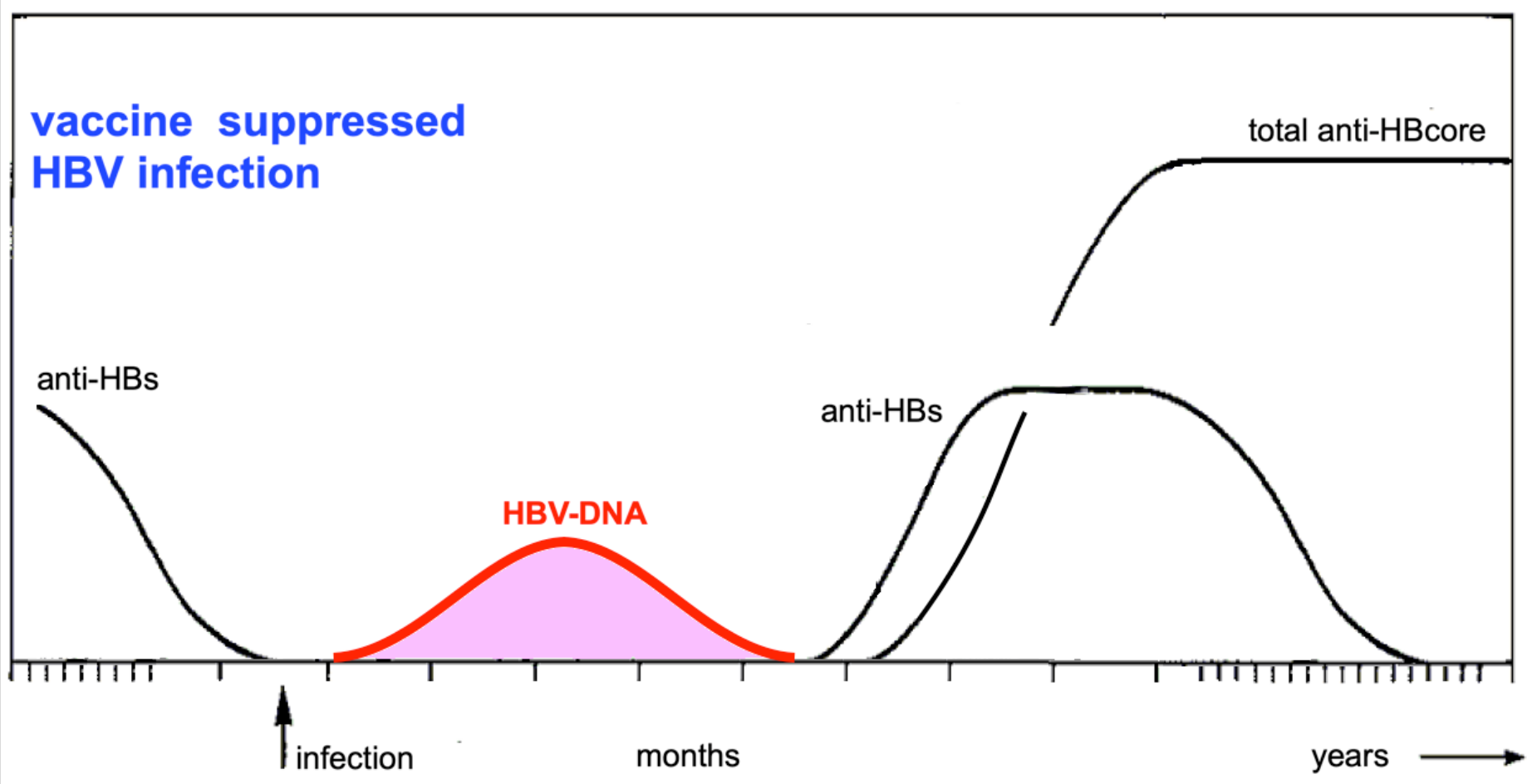


3x added value of HBV-NAT for bloodbankers

2.
detection of vaccine sup-pressed HBV infection

= normal and common

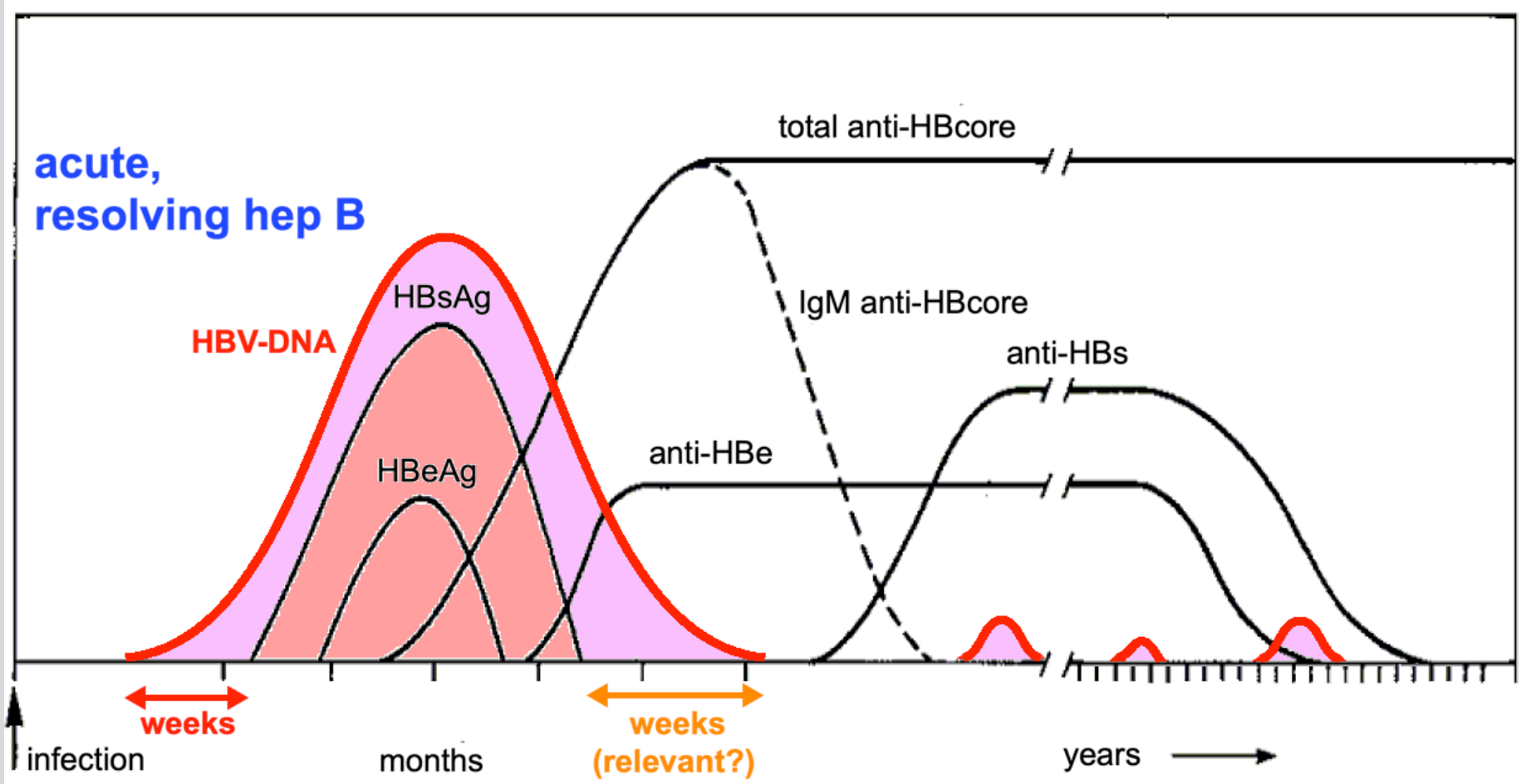
= only threat to trans-fusion, not contagious 'in society'



3x added value of HBV-NAT for bloodbankers

3.
detection of
(some)
latent HBV blips

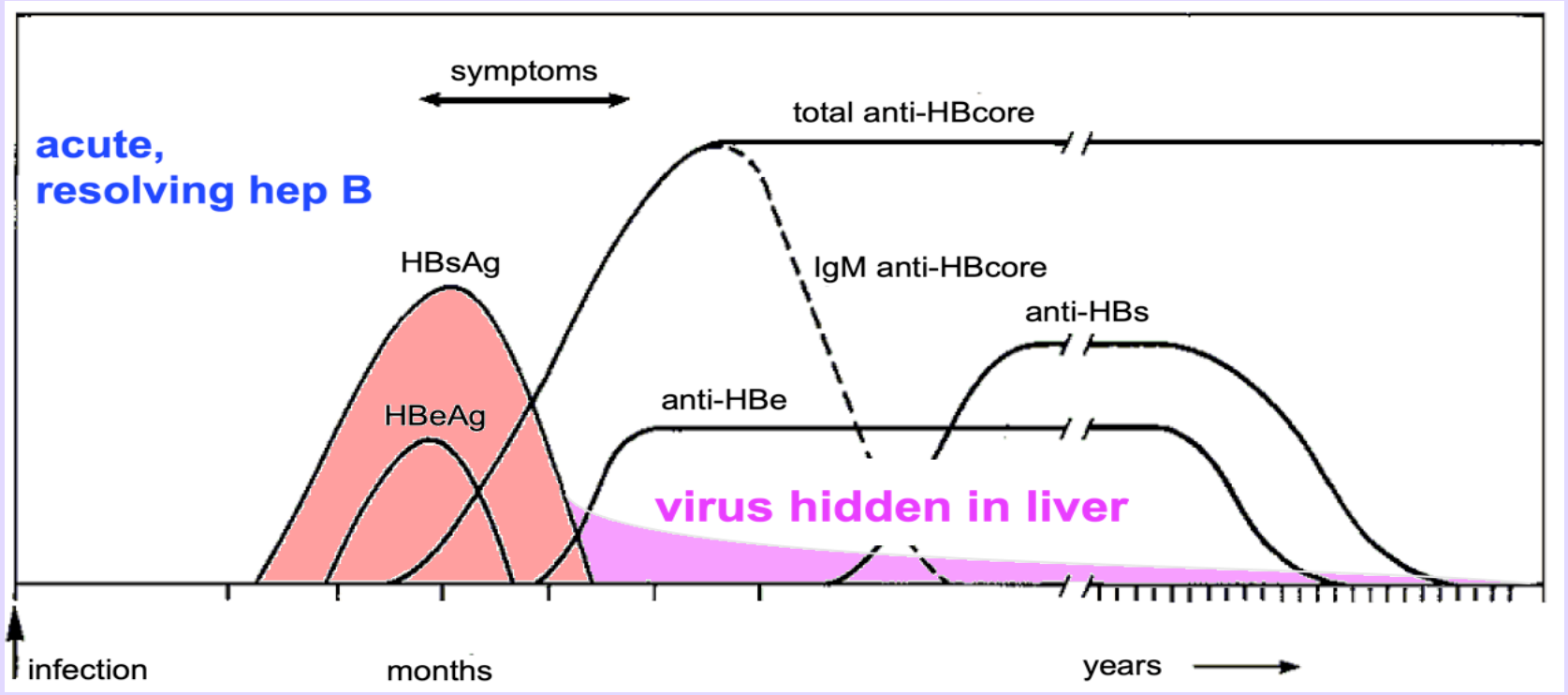
"OBI"



latent HBV infection

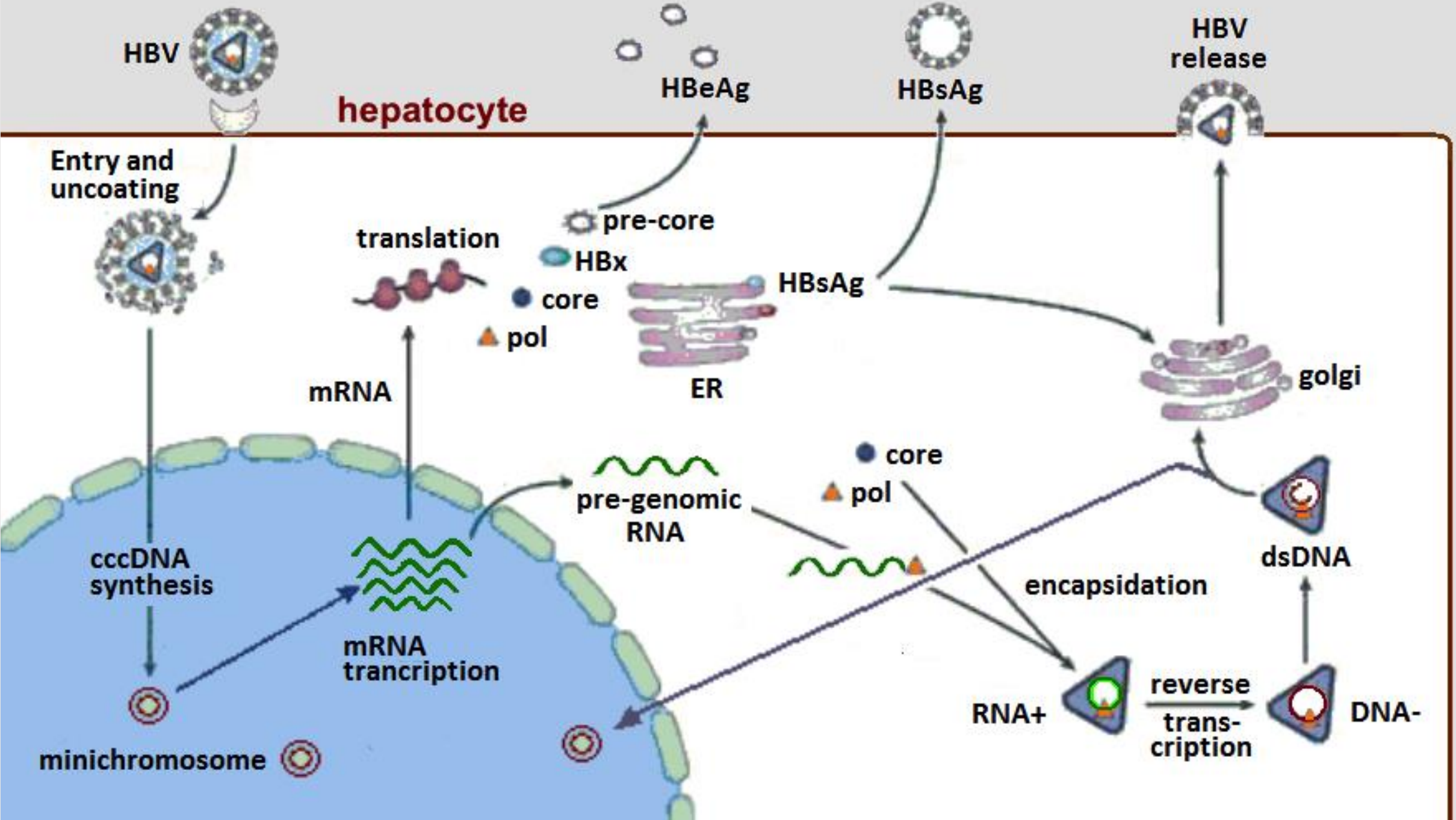
after acute, resolved hepatitis B
HBV often hides in the liver

sometimes for decades



- HBsAg = negative
- sometimes HBV DNA = detectable: "OBI"

- not infectious via sex
- donations sometimes infectious
- chemo or organ Tx: risk of severe hep B reactivation


HBV
HBeAg
HBsAg
HBV release
hepatocyte
Entry and uncoating
translation
pre-core
HBx
core
pol
HBsAg
ER
golgi
mRNA
pre-genomic RNA
core
pol
cccDNA synthesis
mRNA trancription
encapsidation
dsDNA
minichromosome
RNA+
reverse trans-cription
DNA-

"OBI"



OBI = HBV DNA + , HBsAg − , and no recent HBV infection

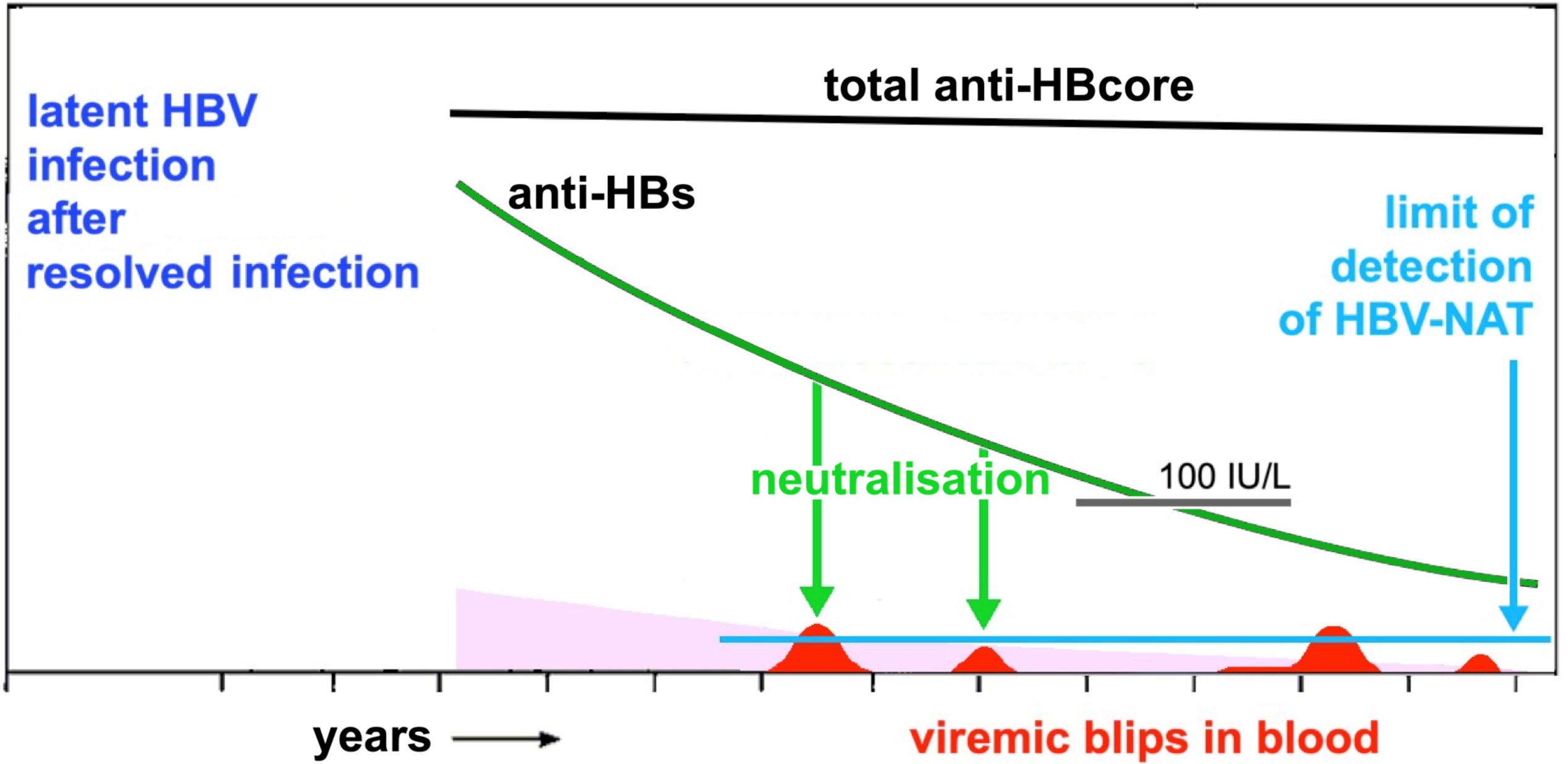
3 problems with "OBI"

problem # 1: HBV-DNA levels in OBI are around level of detection,
"OBI" depends on NAT-sensitivity and pool-size.
➔ OBI is poor marker for OBI.

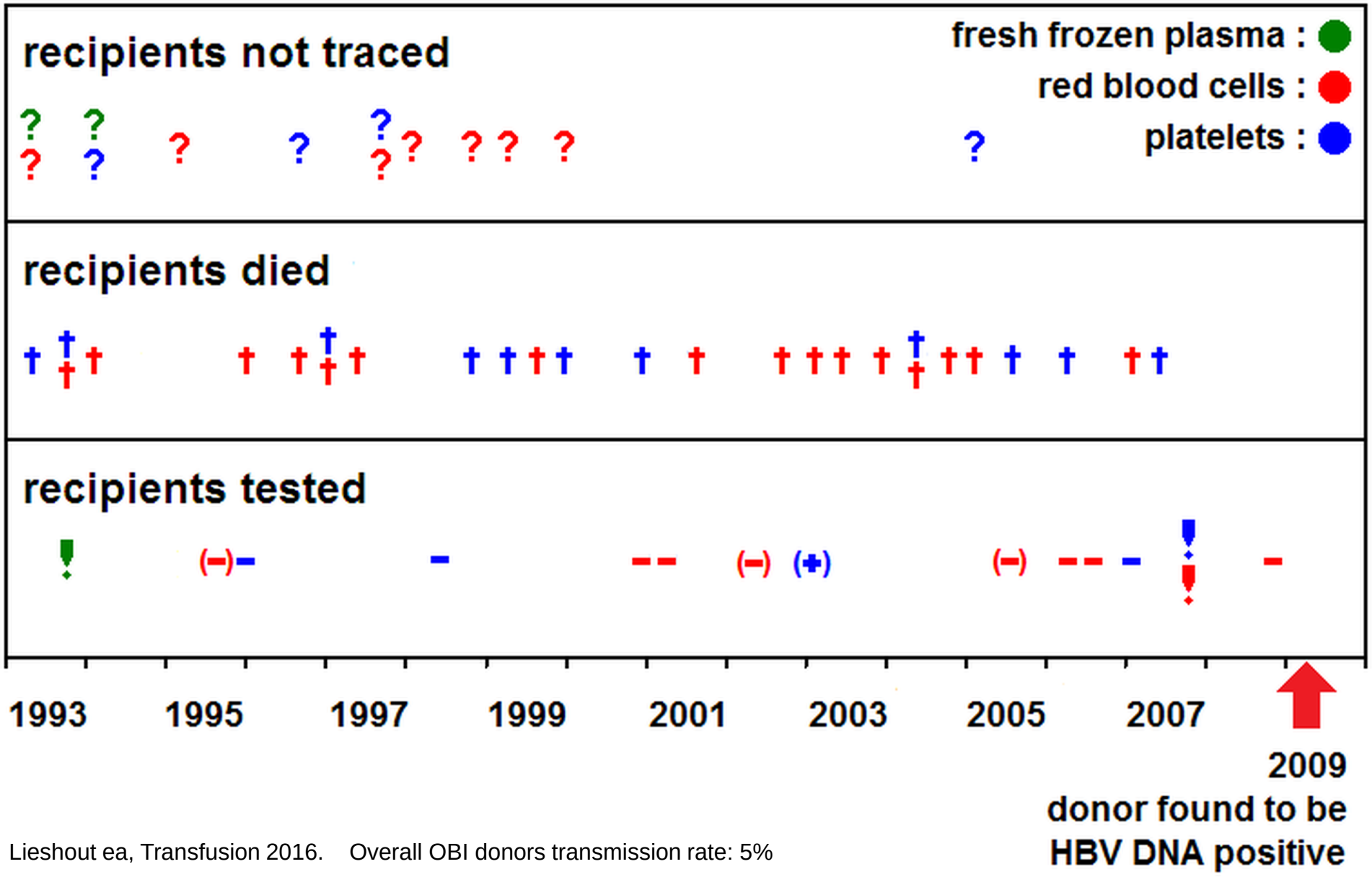
problem #2: Today donor X shows "OBI", tomorrow not (while infectious).
➔ OBI is poor marker for OBI.

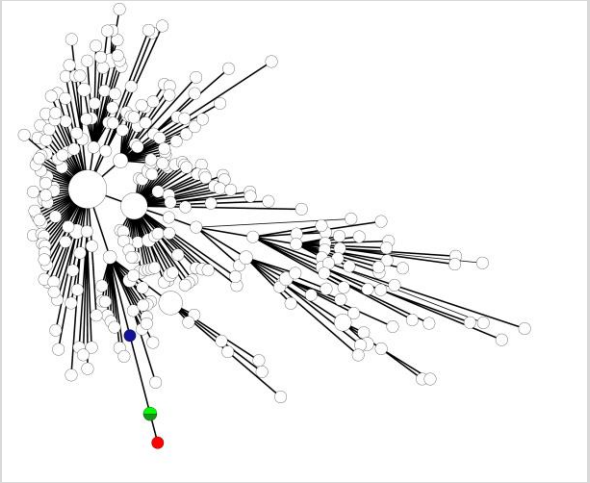
problem #3: Level of anti-HBs determines infectivity.
➔ OBI is poor marker for threat by OBI.

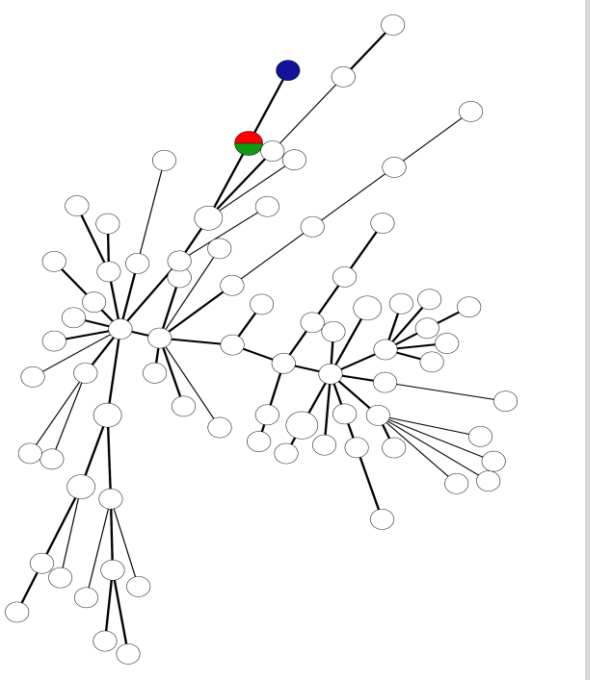
Let's use **"latent HBV infection"**
as in other hidden virus infections.


latent HBV infection after resolved infection
total anti-HBcore
anti-HBs
limit of detection of HBV-NAT
neutralisation
100 IU/L
years
viremic blips in blood

Tracing 55 components from 47 donations from an OBI donor (anti-HBs negative)







Lieshout ea, Transfusion 2016. Overall OBI donors transmission rate: 5%

summary:

HBV in our donors	superior screening assay	alternative screening assay
acute HBV infection	HBV-DNA	HBsAg (longer window period)
chronic HBV infection	HBsAg (cheaper)	HBV-DNA
vaccine suppressed HBV infection	HBV-DNA	-
HBV blips during latent infection	anti-HBcore plus anti-HBs ?	HBV-DNA ?

Detection of latent HBV in our donors

HBsAg test	no use
HBV NAT	- detects part of the HBV blips. - detects irrelevant blips, neutralised by anti-HBs
anti-HBcore	'detects' (includes) 99% of latent HBV, but donor loss is unacceptable
anti-HBcore and anti-HBs < 100 IU/L	'detects' (includes) 99% of latent HBV, but donor loss often unacceptable

Thank you

Blood-borne infections team at Sanquin:

Boris Hogema
Michel Molier
Ed Slot
Mariet Feltkamp
Thijs van de Laar
Ryanne Lieshout
Hans Zaaijer