HCA Healthcare UK

NHS

Maximizing the donor pool

Optimizing use of organs from infected donors

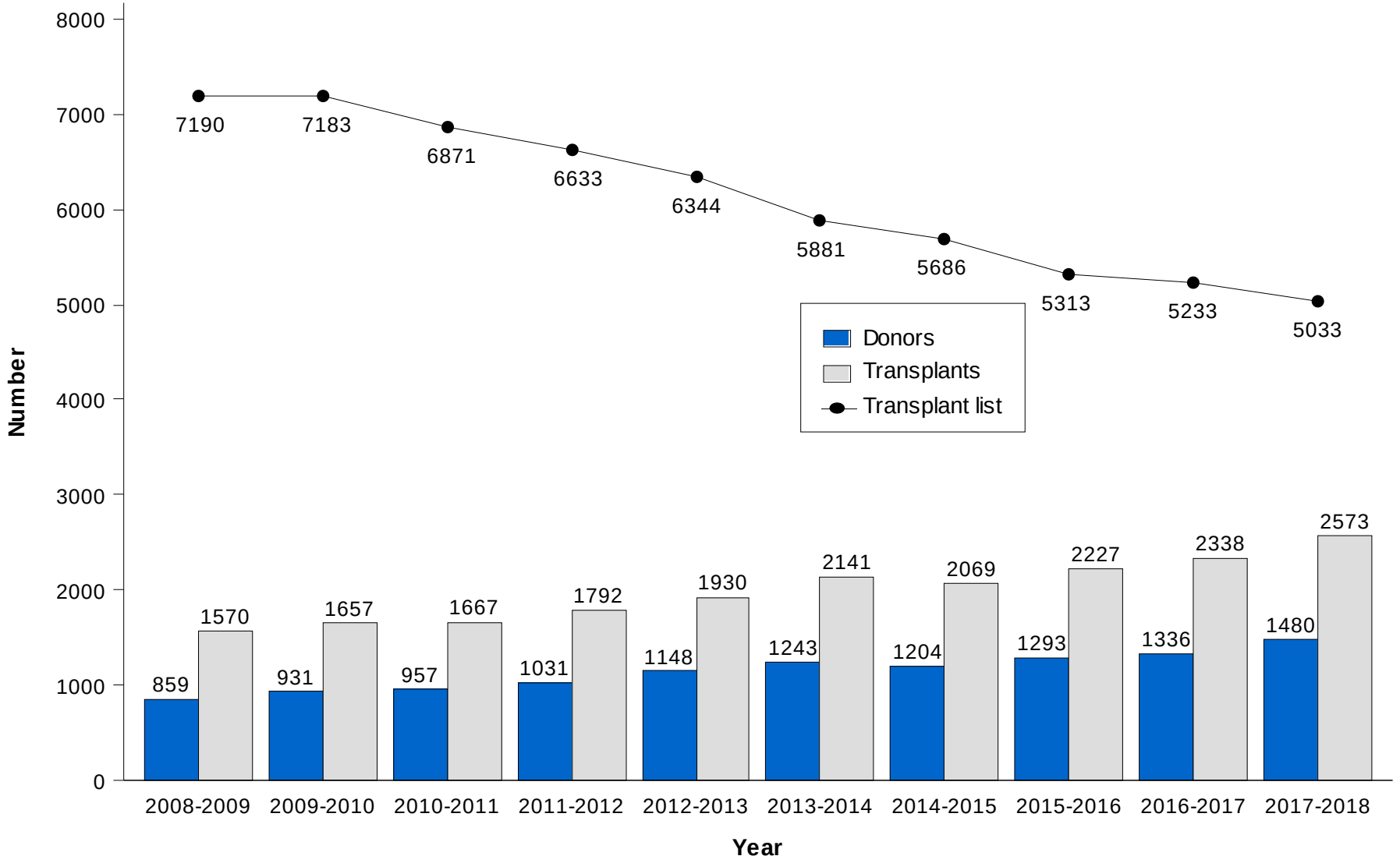
Dr Peter Dupont

Consultant Nephrologist & UCL Honorary Associate Professor
Royal Free Hospital, London, UK

UCLPartners
Academic Health Science Partnership

4th GCC Organ Transplantation & Nephrology Conference

Deceased donor kidney programme in the UK, 1 April 2008 - 31 March 2018,
Number of donors, transplants and patients on the active transplant list at 31 March



Source: Transplant activity in the UK, 2017-2018, NHS Blood and Transplant

Strategies to maximise the donor pool

- Donation after cardiac death (DCD)
- Extended criteria donors
  - Diabetic
  - Hypertensive donors
  - Advanced age
- Dual transplantation
- Living unrelated donation (altruistic) including directed altruistic
- Increased immunological risk
  - ABO incompatible transplantation
  - HLA incompatible transplantation
- Paired donor exchange schemes
- Utilisation of donors with a risk of transmission of infection

How can we maximise donation from donors with increased risk for transmission of infection?

What are the risks?

Transplantation reported to be associated with risk of transmission of:

- Viruses
- Bacteria
- Fungi
- Protozoa
- Nematodes
- Prions

Principles

Risk of infection due to transplantation can never be completely removed

If unusual or extra risks of infection identified

- Should be discussed before transplantation with the person who would receive the organ

E.g. donor was commercial sex worker or IV drug user

Principles

Aim:

Keep risk as low as is reasonably possible

Facilitate maximum clinical benefit from transplantation

A greater degree of risk may be acceptable where organ transplantation is life saving e.g. liver transplantation

Assessing the risk

Full medical history from closest relatives:

Medical

- Blood transfusion
- Risk factors for prion disease

Behavioural

- IVDU
- Unsafe sexual contacts
- Tattoing
- Body piercing

Travel

- To areas endemic for malaria, West Nile Virus, Rabies etc

Case 1

30 y/o male donor

Cause of death:

- Respiratory arrest due to opiate overdose
- Anoxic brain injury

History from family:

- Long history of intravenous drug misuse

Examination:

- Multiple needle tracks both upper limbs
- Needle still in situ when found by paramedics

Investigations

Renal function

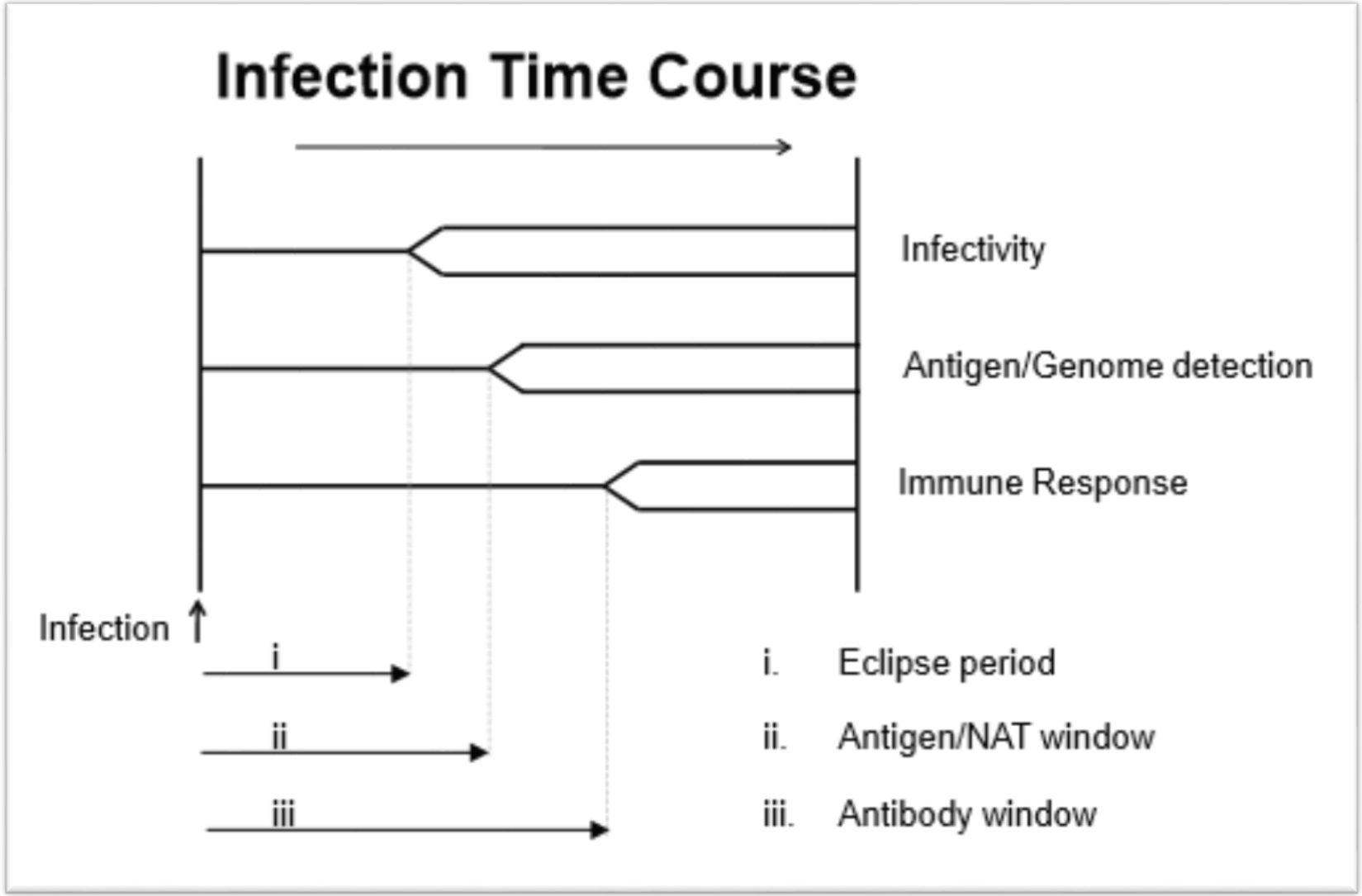
- Creatinine 72mcmol/L
- Urine output 1.5L last 24 hours

Virology

- Hepatitis B surface antigen negative
- Hepatitis C IgG negative
- HIV 1/2 antibody negative; p24 antigen negative

Would you accept these kidneys?

The “window” period



Risk of BBV infection if negative at donation

	Antibody alone	Antibody and antigen	Plus NAT
Hepatitis B	N/A	4.3 (per million donors)	3 (per million donors)
Hepatitis C	59 (per million donors)	7.1 (per million donors)	3 (per million donors)
HIV	N/A	0.8 (per million donors)	0.4 (per million donors)

Outcome

- Kidney accepted
- Primary function
- Creatinine on discharge 98mcmol/L
- Further screening for HIV, Hep B/C negative

Case 2

50 y/o donor

Cause of death:

- Meningo-encephalitis

History from family:

- Recently returned from trip to Australia

Examination:

- Signs raised ICP
- No skin rash

Investigations

CSF

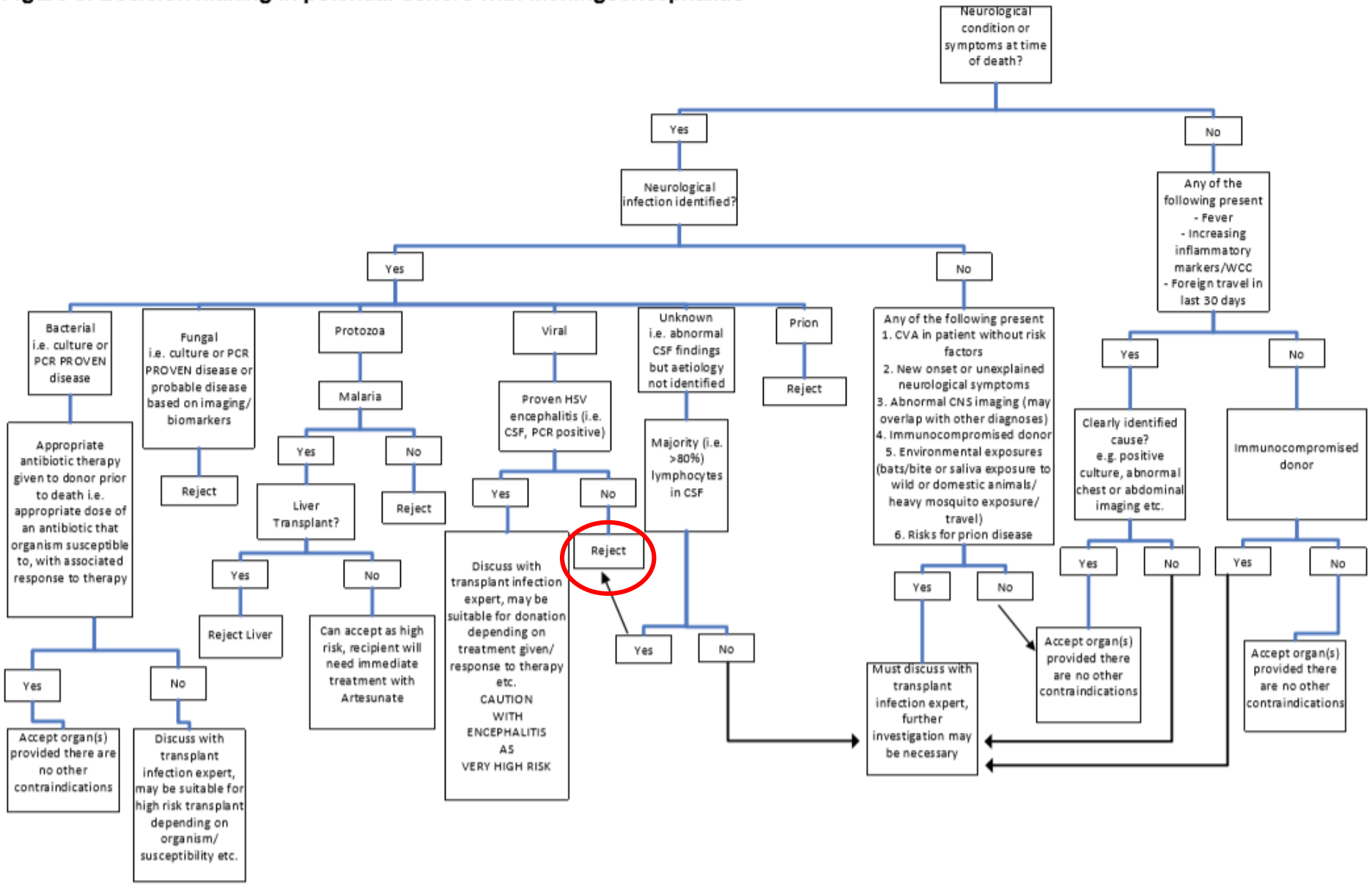
- 200 WBC/ml; 85% lymphocytes
- No organisms on gram stain, ZN stain or initial culture
- HSV PCR negative

Renal function

- Creatinine 86mcmol/L
- Urine output 2L last 24 hours

Would you accept these kidneys?

Figure 3: Decision making in potential donors with meningoencephalitis



UK SaBTO guidelines 2023

Case 3

45 y/o donor

Cause of death:

- RTA with severe head injury

History from family:

- Known hepatitis C carrier – never treated

Examination:

- No signs of chronic liver disease

Investigations

Virology

- Hepatitis C IgG positive
- Hep C RNA 300,000 copies/ml
- Hep B negative
- HIV negative

Renal function

- Creatinine 66mcmol/L
- Urine output 1.2L last 24 hours
- Urinalysis – no blood or protein

Would you accept these kidneys for a HCV negative recipient?

HCV – a historical perspective

Historically organs from hepatitis C positive donors discarded

- High risk of transmission

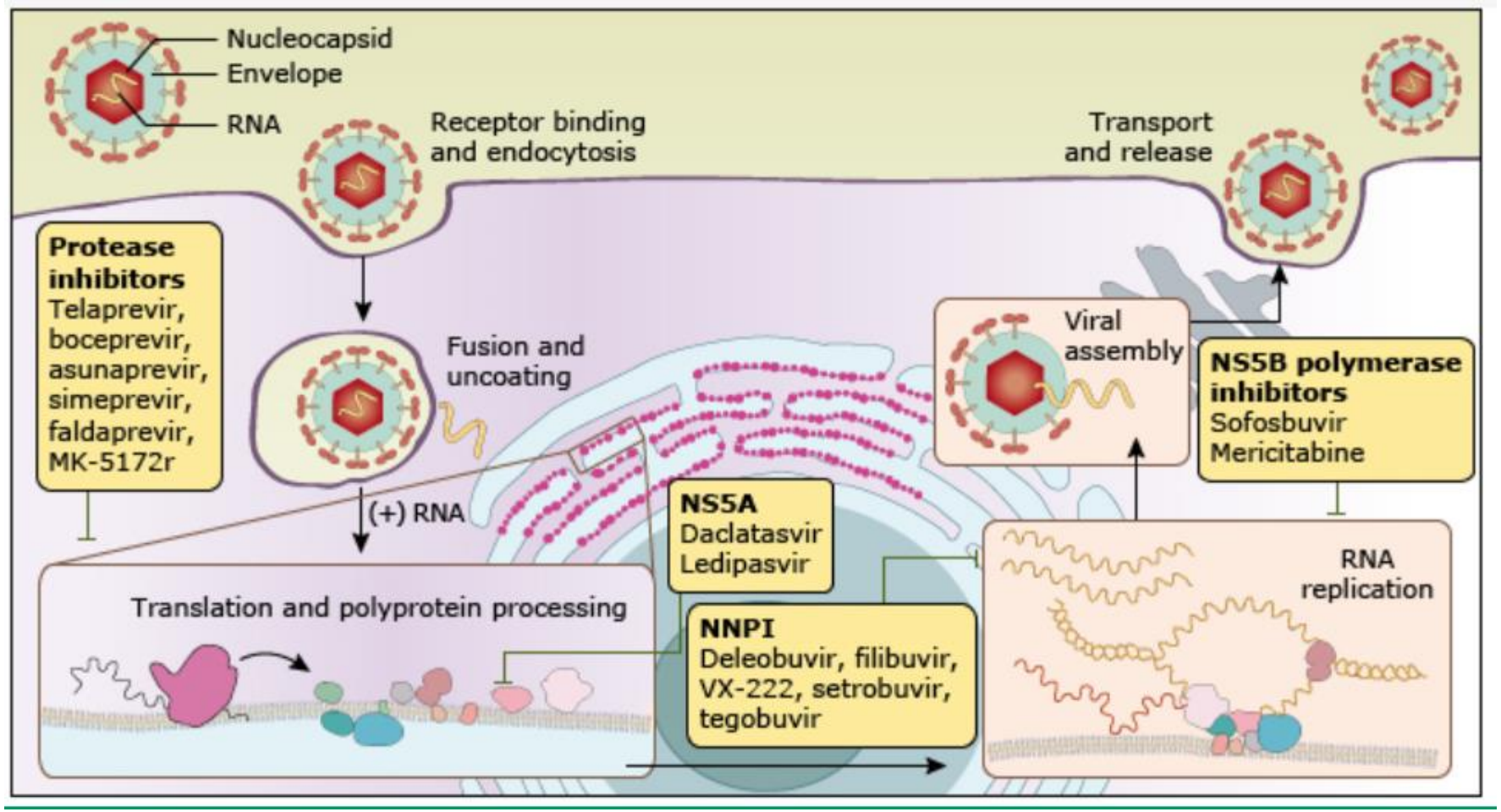
UK experience:

- 2000 – 2015: 168 donors declined due to HCV
- 69% discard rate

USA experience:

- 4% of donors are HCV positive
- 500 HCV positive kidneys discarded annually

HCV - Directly acting antiviral agents (DAA)



Pockros PJ. Clin Pharmacol Ther 2014

HCV – anti-viral therapy

Directly acting antiviral agents

1st generation

- Teleprevir, Boceprevir
- 80% cure rate (combined with interferon and ribavirin)

2nd generation

- Sofosbuvir, Simeprevir, Daclatasvir, Ledipasvir
- Pan-genotypic
- 95% cure at 12 weeks

3rd generation

- E.g. Grazoprevir, Elbasvir
- 95-100% cure rate
- Safe in ESRD (liver metabolized)

Hepatitis C – a curable disease

Directly acting antiviral agents

95% -100% cure rate at 8-12 weeks

Newer agents safe to use in patients with CKD / ESRD

Similar outcome in transplant recipients to general population

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Trial of Transplantation of HCV-Infected Kidneys into Uninfected Recipients

TO THE EDITOR: Waiting times for kidney transplants exceed 3 to 5 years in many parts of the United States.[1] Yet more than 500 high-quality

ness and accuracy of the data and analysis and for the adherence of the trial to the protocol, available with the full text of this letter at

Goldberg et al. NEJM 2017; 376:24

Trial results

10 HCV negative patients received HCV positive kidneys

- Median age 59
- All donors genotype 1

All recipients became viraemic by day 3

- 2/10 had transient transaminitis

All achieved SVR after 12 weeks

- Elbasvir–grazoprevir

Median creatinine at 6 months 97mcmol/L

- eGFR 63ml/min

Median waiting time 58 days!

What are the risks?

Fulminant cholestatic hepatitis

- Usually responds to treatment with DAA

Risk of developing cryoglobulinaemia /MCGN

- Mitigated by early treatment

Risk of treatment failure

- Estimated 1:2500

Case 4

52 y/o female donor

Cause of death:

- RTA

History from family:

- Recently returned from trip to Caribbean

Examination:

- Maculopapular skin rash

Investigations

Investigations

- Zika virus PCR positive

Renal function

- Creatinine 56mcmol/L
- Urine output 3.2L last 24 hours

Would you accept these kidneys?

No!

Acute Zika virus infection is an absolute contra-indication to donation

Neurotropic – risk of encephalitis

Case 5

60 y/o male donor

Cause of death:

- CVA

History from family:

- Nil of note

Examination:

- NAD

Investigations

Investigations

- HTLV1 positive

Renal function

- Creatinine 110mcmol/L
- Urine output 1.7L last 24 hours

Would you accept these kidneys?

Relative contra-indication

Risk is T cell lymphoma and spastic paraparesis

Case 6

36 y/o male donor

Cause of death:

- Haemorrhagic CVA

History from family:

- HIV positive for 10 years
- On HAART

Investigations

Investigations

- HIV RNA undetectable
- CD4 count 400

Renal function

- Creatinine 106mcmol/L
- Urine output 2.1L last 24 hours
- No proteinuria

Would you accept these kidneys?

Relative contra-indication

HIV positive recipient only

Risks

Transmission of resistant strain

"Tropism switching"

- Additional mechanism cellular entry
- Associated with drug resistance and accelerated disease progression

Risk transmission to staff

prosthetic knee-associated infection: evaluation of 40 consecutive episodes at a single centre. Clin Microbiol Infect 2006;12:433-9.
4. Barberan J, Aguilar L, Carroquino G, et al. Conservative treatment of staphylococcal prosthetic joint infections in elderly patients. Am J Med 2006;119(11):993.e7-993.e10.
5. Perlroth J, Kuo M, Tan J, Bayer AS, Miller LG. Adjunctive use of rifampin for the treatment of Staphylococcus aureus infections: a systematic review of the literature. Arch Intern Med 2008;168:805-19.

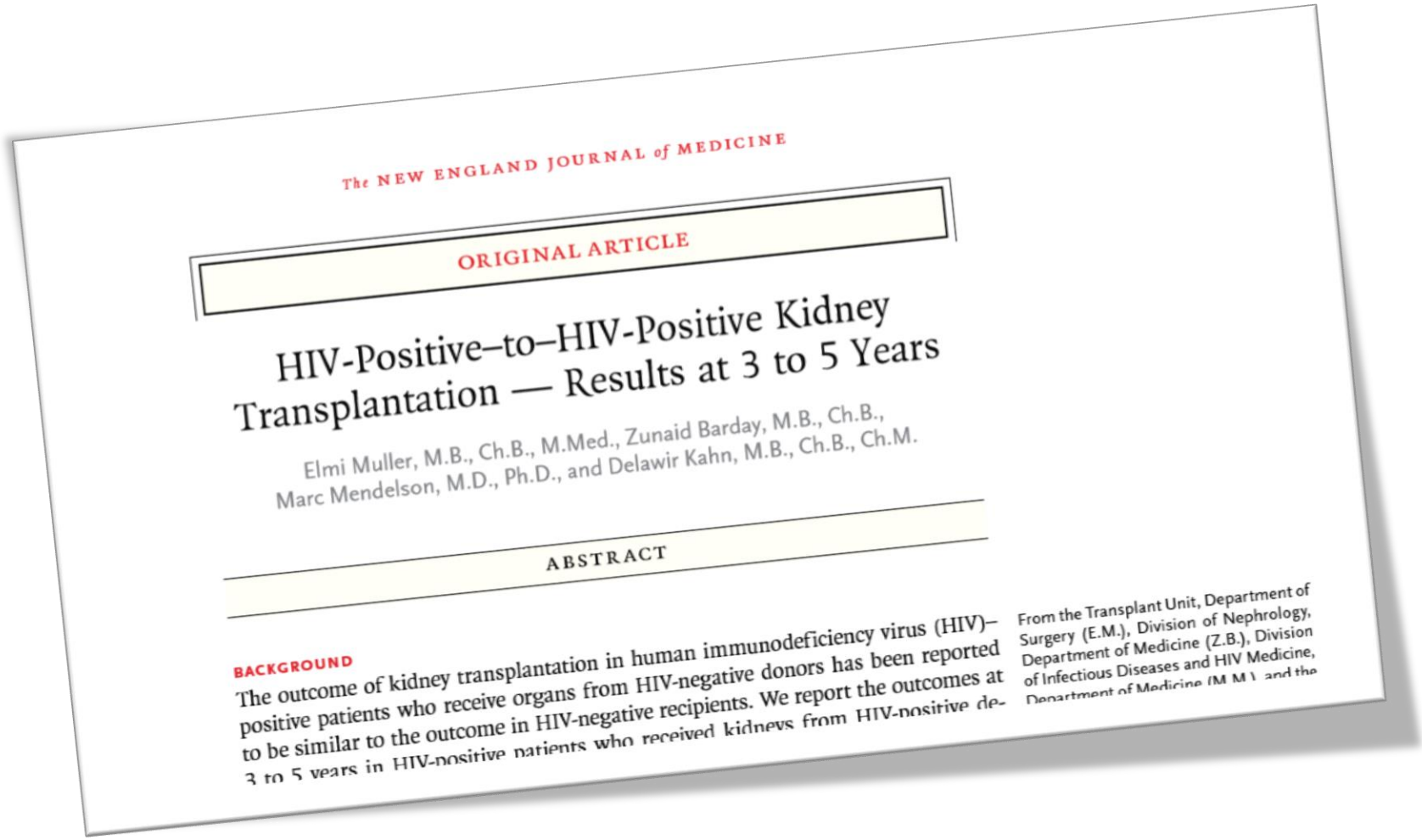
Renal Transplantation between HIV-Positive Donors and Recipients

TO THE EDITOR: Nephropathy associated with infection with the human immunodeficiency virus (HIV) is the leading cause of end-stage renal disease (ESRD) in HIV-infected patients in South Africa.[1,2] We practice in a resource-constrained environment where the use of dialysis is limited;

Table 1. Clinical Characteristics of HIV-Positive Recipients of a Transplant from an HIV-Positive Donor.*

Characteristic	Patient 1	Patient 2	Patient 3	Patient 4
Age (yr)	47	56	37	29
Sex	Male	Male	Male	Female
Before transplantation				
Diagnosis on renal biopsy	HIV-associated nephropathy	HIV-associated nephropathy and hypertensive nephropathy	Malignant hypertension	HIV-associated nephropathy
Creatinine (μmol/liter)	678	582	1712	725
CD4 count (cells/mm³)	288	258	132	147

Muller et al. NEJM 2010; 362:2336-37



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

HIV-Positive–to–HIV-Positive Kidney Transplantation — Results at 3 to 5 Years

Elmi Muller, M.B., Ch.B., M.Med., Zunaid Barday, M.B., Ch.B., Marc Mendelson, M.D., Ph.D., and Delawir Kahn, M.B., Ch.B., Ch.M.

ABSTRACT

BACKGROUND

The outcome of kidney transplantation in human immunodeficiency virus (HIV)–positive patients who receive organs from HIV-negative donors has been reported to be similar to the outcome in HIV-negative recipients. We report the outcomes at 3 to 5 years in HIV-positive patients who received kidneys from HIV-positive de-

From the Transplant Unit, Department of Surgery (E.M.), Division of Nephrology, Department of Medicine (Z.B.), Division of Infectious Diseases and HIV Medicine, Department of Medicine (M.M.), and the

Muller et al. NEJM 2015; 372:613-20

Outcomes

27 recipients HIV+ kidneys

Donors

- Untreated or 1st line ART

Follow-up 3-5 years)

Outcomes

Time post transplant	Patient survival	Graft survival (death-censored)
1 year	84%	93%
3 year	84%	84%
5 year	74%	84%

Outcomes

Rejection rates

- 8% at 1 year
- 22% at 3 years

- HIV remained well-controlled in all

HOPE act

HIV Organ Policy Equity (HOPE) 2013

Permitted utilisation of HIV positive kidneys for HIV positive recipients

Estimated 500-600 HIV positive potential donors annually in USA

Impact:

Rate of transplantation increased x 3

Median waiting time 10 months

Summary of UK guidelines (SaBTO 2023)

Absolute contra-indications

Viruses

Rabies

West Nile Virus

Zika virus

SARS / MERS

Yellow fever

Dengue fever

Viral haemorrhagic fever e.g. Ebola

Chikungunya

Progressive multifocal leucencephalopathy (JC)

Mpox (active infection)

Prion disease

Transmissible spongiform encephalopathy

Bacterial

Active TB or <6 months Rx

Anthrax

Parasites

Active malaria

Fungal

Active fungaemia

Relative contra-indications

Viruses

HIV

[Hepatitis B]

Hepatitis C

Measles

Mumps

Rubella

Viral myocarditis

Bacterial

Lower respiratory tract infection

Localised abscess

Infective endocarditis

Drug-resistant organisms in donor

UTI

Lyme disease

Listeria