Emergency treatment to prevent HIV

Margaret Kingston
Consultant Genitourinary Medicine
Manchester Royal Infirmary

38 year old cardiac surgery assistant

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- Further information needed?
- What needs to be done?

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- The Donor
  - HIV positive 10 years
  - On HAART, centre of care unknown, lives in the Lake District
- The Recipient
  - No previous injuries
  - Fit & well
  - No regular medication
  - No known HIV risk, no previous test
  - Low pregnancy risk

Principles of PEP

- **To abort HIV infection by inhibiting viral replication following exposure**
  - Once through a mucosal/skin barrier it takes up to 48-72 hours for HIV to be detected in the regional lymph nodes and 5 days in blood
  - Taking antiretrovirals during this “window” may prevent the establishment of HIV in the exposed person

Evidence to support the use of PEP

- <u>This is based on:</u>
  - Biological plausibility
  - Expert opinion *(DH, BASHH guidelines etc)*
  - Animal studies
  - Human studies & experience
    - Occupational exposure
    - Vertical transmission
    - Non-occupational exposure
    - Data registries and experiences

Evidence to support the use of PEP

- **Animal studies:**
  - Numerous animal models have used different retroviruses, inoculums, modes of inoculations and drugs
  - Basically show that it is potentially effective and that time to initiation and duration of treatment are important

Evidence to support the use of PEP

- **Human studies:**
  - Prospective RCTs not possible
    - Ethical issues (withholding potentially effective treatment)
    - Recruitment of sufficient numbers
- **Occupational exposure:**
  - Cardo *et al NEJM 1997* retrospective case-control study
    - 28 days AZT found to be protective (OR 0.19, 95% CI 0.06-0.52)
  - Ineffective in at least 21 documented cases
- **Vertical transmission:**
  - Several studies indicate a protective effect of ARVs given following delivery in breastfeeding and non-breastfeeding women

Risk of HIV transmission

Risk of HIV transmission =
Risk that source is HIV positive X
Risk of exposure

- *High plasma viral load in source*
- *Advanced HIV in source*
- *Type of injury:*
  - *Deep injury*
  - *Injury penetrates blood vessel*
  - *Visible blood on penetrating device*

Significant occupational exposures

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  - Penetrating injury (0.3%)
  - Mucous membrane exposure (0.09%)
  - Exposure via broken skin

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- High risk body fluid
  - Blood
  - Amniotic fluid
  - Ascitic/pericardial/synovial/ pleural fluid
  - CSF
  - Other exudative fluids (burns etc)
  - Saliva associated with dentistry or other bloodstained bodily fluids
  - Genital secretions
  - Human breast milk

When the source is of unknown status

Homosexual men		
London	20%	
Scotland	3%	
Elsewhere	4%	
Heterosexuals	MALE	FEMALE
UK	0.5%	0.2%
Rest Europe	2%	0.2%
North America	3%	0.1%
Sub Saharan Africa	6.9%	11.3%
East & SE Asia	0.5%	0.7%
Caribbean	1.2%	1%
Central & S America	2.4%	0.9%
S Asia	0.5%	0.6%
Australasia	0.8%	0.1%
Injecting drug users		
London	2.9%	
Elsewhere in the UK	0.5%	

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When the source is of unknown status

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- Arrange testing
- Start PEP in the meantime

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What HIV Drugs to Use?

- Triple therapy:
  - Combivir & Nelfinavir
  - Truvada & Kaletra meltrex
- Animal studies and Cardo *et al NEJM 1997* suggest 4 weeks, or until donor found to be negative

BUT

Resistant viruses, donor drug treatment history, drug interactions, what if the recipient may be pregnant…….

AND

First Aid, Hepatitis B & C

Follow-up testing & protection of partners

54 year old midwife

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- Risk: 0.09%
- Took HAART for 24 hours and discontinued due to side effects and low risk

26 year old A&E SHO

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- Venflon been in donor's arm slips and goes into his hand
- Donor then leaves the department
- Risk: 0.5%x0.03%=0.015%
- Takes HAART 1 month with considerable side effects

32 year old gay man

- Visiting Manchester meets someone in a bar then goes to a club, can't remember much after that
- Wakes up some hours later in doorway of a Chinese restaurant, wallet missing, cuts & bruises, in following hours noted rectal tenderness and bleeding
- Attends 38 hours after episode ? For PEPSE
- Risk: 10%x3% = 0.3%, probably higher due to trauma

- STI screen & prophylaxis
- Hepatitis B vaccination
- HIV PTD and test
- Disclosure to partner
- Follow up, support & counselling
- Took the month's therapy and DNA'd follow-up

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- Risk: 0.1%x0.09%=0.00009% (1/100,000)
- Reassured, offered Hepatitis B vaccination & STI screen & prophylaxis

PEP following other exposures?

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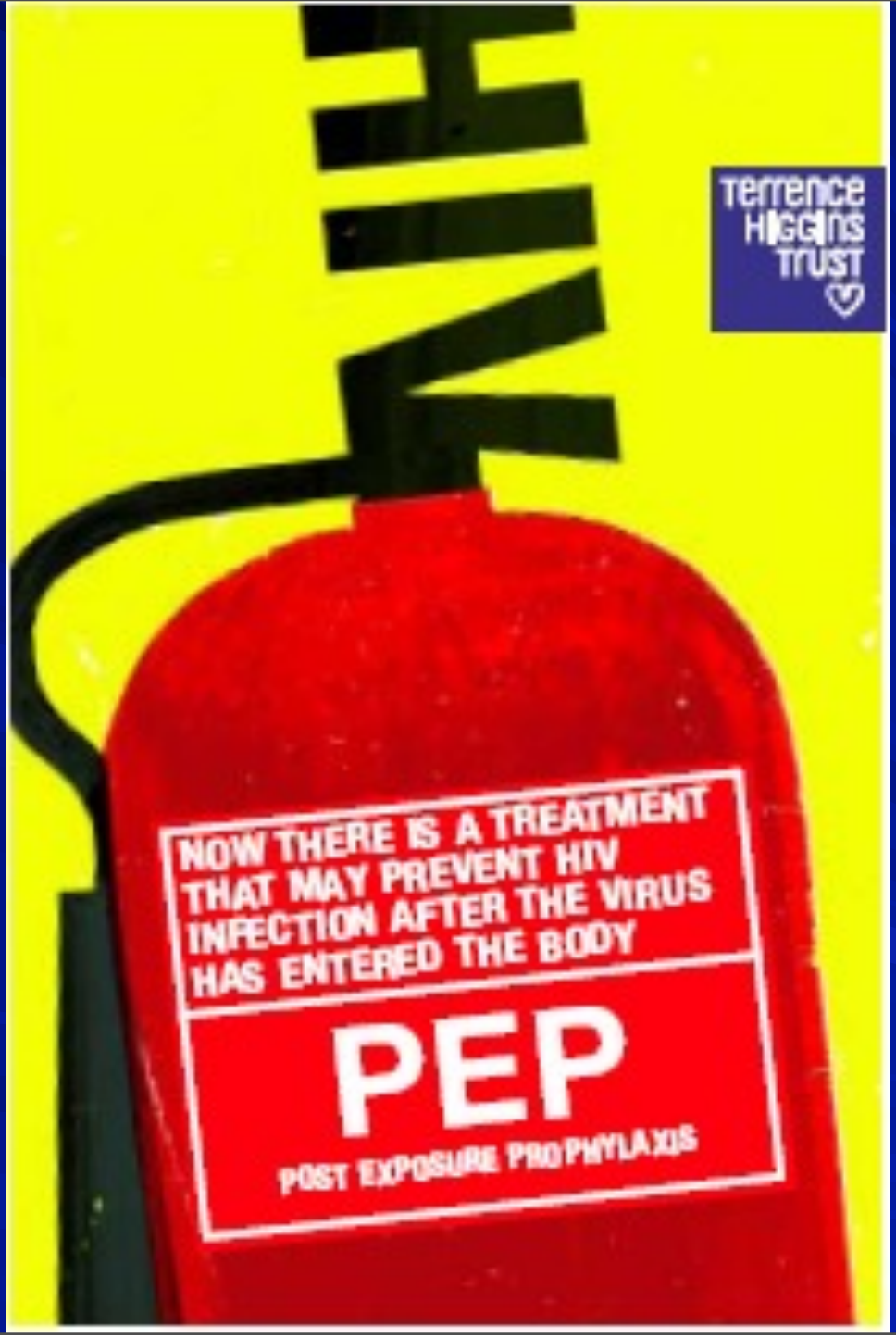
- Condoms not used with casual partner of unknown status?


HIV
Terrence Higgins Trust
NOW THERE IS A TREATMENT THAT MAY PREVENT HIV INFECTION AFTER THE VIRUS HAS ENTERED THE BODY
PEP
POST EXPOSURE PROPHYLAXIS

PEP:

- could stop someone getting HIV
- must be started as soon as possible after unsafe sex or a condom not working - and definitely within 72 hours (3 days)
- involves taking anti-HIV drugs for 4 weeks
- has side effects
- isn't guaranteed to work

Post

- after

Exposure

- a situation where HIV has a chance to get into someone's bloodstrearm

Prophylaxis

- a treatment to stop an infection happening

so...

PEP

- a treatment to stop a person becoming infected with HIV after it's got into their body

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- Campaigns in Australia, Denmark and USA
- THT publicity campaigns in UK

Evidence around the use of PEPSE

- **Data gathered following PEPSE**
  - Prospective data from data registries and non-randomised studies in Europe, North and South America and Australia indicate:
    - Triple drug regimens most frequently used
    - Majority complete 28 days despite considerable side effects
    - Significant reduction in HIV seroconversion rates
    - No increase in risky sexual behaviour and a possible reduction
    - Cost effectiveness depends on appropriate use
    - Some evidence of wasteful use

What constitutes a significant exposure?

Blood transfusion (one unit)	90-100%
Receptive anal intercourse	0.1-3.0%
Receptive vaginal intercourse	0.1%-0.2%
Insertive vaginal intercourse	0.03%-0.09%
Insertive anal intercourse	0.06%
Receptive oral sex (fellatio)	0-0.04%
Needle–stick injury	0.3% (95% CI 0.2%-0.5%)
Sharing injecting equipment	0.67%
Mucous membrane exposure	0.09% (95% CI 0.006%-0.5%)

BASHH Guidance: PEPSE yes or no?

	Source HIV+	Source >10% risk	Source low risk
Passive AI	recommended	recommended	consider
Active AI	recommended	consider	no
Passive VI	recommended	consider	no
Active VI	recommended	consider	no
Oral + Ejac	consider	consider	no
Semen in [illegible]	consider		
Oral - ejac	no		

Possible risks with PEPSE

- Side effects (NNRTIs generally contraindicated, PIs contribute most, ? role for dual NRTI therapy)
- Adherence & resistance
- Psychological effects
- Drug interactions
- ? False reassurance: Younger less well educated gay men with history of drug use report greater intention to use PEP

PEP: Information & Follow-up

- Rationale for PEP
- Limited data to support use
- Risks and side effects of PEP
- HIV follow up:
  - PTD and rapid test
  - 4 weeks PEP if HIV negative
  - HIV test at 3 and 6 months
  - Adherence support and managing side effects
  - Safer sexual practices, risk reduction counselling
  - Issues around disclosure and coping
  - Screening for other STIs
  - Hepatitis vaccinations & possible early treatment
  - PCC in women (IUD may be needed)
  - Risk of pregnancy