Human immunodeficiency virus: epidemiology and transmission risks

General details
The HIV virus was discovered in 1983. There are currently two groups of viruses which have been isolated (HIV type 1 and HIV type 2), collectively known as HIV (human immunodeficiency virus). In general, HIV type 2 is not found outside western and central Africa. HIV type 1 is identified globally. Following infection, the host’s cells transfer the virus to the local immune system, including T-cells, macrophages and dendritic cells. Within 10-12 days of infection, HIV RNA can be detected in blood by PCR.

During this acute infection (also referred to as primary HIV infection, or the seroconversion illness), HIV RNA levels peak, before declining over subsequent weeks. Antibodies to HIV usually develop within 3-5 weeks of becoming infected. The time period between becoming infected and developing antibodies is referred to as the serological “window period.” Following seroconversion, there is an asymptomatic phase of variable duration. During this time, patients are well. Later in the course of the infection, HIV RNA levels tend to drop. Over the subsequent asymptomatic period, of variable duration, CD4+ lymphocyte levels gradually decrease. If levels of CD4+ lymphocytes drop below 200-350 cells/μl, the patient is at increased risk of developing opportunistic infections.

Clinical information
The symptoms of acute HIV infection can last for between 7 and 10 days. The patient may complain of symptoms resembling the “flu,” or mononucleosis infection. Typical symptoms include fever, maculopapular rash, oral ulcers, lymphadenopathy, arthralgia, pharyngitis, malaise, weight loss and myalgia. Once these acute symptoms resolve, most patient enter an asymptomatic phase. This asymptomatic phase can last more than 10 years.

When CD4+ lymphocyte levels drop below 200-350 cells/μl, the patient is at increased risk of developing opportunistic infections, including pneumocystis pneumonia, oesophageal candidiasis, cerebral toxoplasmosis, and cytomegalovirus, amongst others. These infections, along with cancers such as Kaposi sarcoma, are referred to as AIDS defining conditions.

Treatment for patients with HIV infection is with life-long anti-retroviral drugs. This results in a significant reduction in the amount of virus in the blood, usually to undetectable levels, and allows for immune recovery.

Transmission
HIV has been isolated from semen, cervical secretions, lymphocytes, cell-free plasma, cerebrospinal fluid, tears, saliva, urine and breast milk. This does not mean, however, that these fluids all transmit infection since the concentration of virus in them varies considerably. Particularly infectious are semen, blood, and possibly cervical secretions. The risk of transmission increases with the burden of HIV (i.e. the HIV viral load) in the inoculum.

The commonest mode of transmission of the virus throughout the world is by sexual intercourse. Other methods of transmission are through receipt of infected blood or blood products, donated organs, and semen. Transmission also occurs through the sharing or reuse of contaminated needles by people who inject drugs (PWID) or for therapeutic procedures, and from mother to child. The virus is also transmitted through breast milk. Healthcare workers (HCW) can be infected through needlestick injuries, and skin and mucosal exposure to infected blood or body fluids.

Prevalence of HIV infection in Ireland, Europe and the world
Ireland
HIV became a notifiable disease in Ireland in September 2011. Case based reporting of HIV cases has been in place since 2001. In 2014, a total of 377 newly diagnosed cases were reported in Ireland, a rate of 8.2/100,000. The highest proportion was attributed to MSM exposure (49%), followed by heterosexual transmission (33%), and PWID (7%). Of the 377 cases, 36.3% were born in Ireland and 53.8% were born abroad.

Annual numbers of new diagnoses of HIV in Ireland have fluctuated between 300 and 400 over the past decade. In recent years there has been a change in the predominant modes of transmission – the annual number of new cases among PWID has decreased each year since 2004, up to 2013; the annual number of cases attributed to heterosexual transmission has decreased from a peak in 2003; and the number of cases in MSM continues to rise year on year since 2005.
Blood donors
Of 313,019 first time blood donors tested by the IBTS between 1997 and 2015, 14 (0.0045%) were found to be HIV positive. (Personal communication, Dr Joan O’ Riordan, IBTS, July 2016).

Pregnant women
HIV screening is offered routinely to all pregnant women in Ireland under a voluntary antenatal HIV testing programme that was introduced in 1999. In 2014, the national reported uptake of HIV antenatal screening (from 17 hospitals) was 99.9%, the rate was 100% in 16 of the hospitals. The HIV prevalence rate among pregnant women in Ireland was 0.15% in 2014, slightly higher than the rate in 2013 (0.14%). The prevalence of HIV infection among pregnant women varied among HSE areas, ranging from 0.05% in HSE West to 0.23% in HSE Dublin Northeast.9

Prisoners and injecting drug users
In 1997, 17% of a group of PWID in the HSE eastern region, who were attending methadone clinics, tested positive for HIV infection.10 A cross sectional study of 307 opiate users attending 21 addiction treatment centres in the HSE eastern region was carried out in 2001. The prevalence of anti-HIV was 11%.11 In 2001, the largest tertiary centre for HIV infection in Dublin reported a five-fold increase in new HIV diagnoses in PWID between 1995 and 2000.12 A study carried out among socially excluded drug users in 10 European cities in 1998-2000 found a self-reported HIV positive prevalence of 24.6% in Dublin, the second highest of the cities.13

In 2014, 27 new HIV diagnoses (7%) were among people who inject drugs (PWID), representing a 29% increase in the number of diagnoses in 2013 (21). 89% of the cases were resident in HSE East at diagnosis and many of the infections were recently acquired at time of diagnosis. Injection of newer street drugs, including “snow blow”, amongst homeless, chaotic PWID were common factors in these individuals.8

A national cross sectional survey of Irish prisoners in 1998 showed a prevalence of anti-HIV of 2%. The prevalence was 3.5% in prisoners who were PWID.14

Asylum seekers
Screening of asylum seekers in the HSE eastern region 2000-2003 found a prevalence of anti-HIV of 2.2%.15

HIV infection in Europe
In 2013, 29,157 HIV diagnoses were reported by 30 EU/EEA countries with a rate of 5.7 / 100,000 population. The male-to-female ratio was 3.3. Young people aged 15-24 accounted for 11% of all HIV diagnoses reported by this varied widely from 6% in Norway to 25% in Romania.16

MSM accounted for 42% of diagnoses while heterosexual transmission accounted for 32%. Transmission due to injecting drugs accounted for 5% of diagnoses and for nearly 20% of the cases, the transmission mode was unknown.16

Global HIV distribution
At the end of 2010, an estimated 34 million people were living with HIV globally. The annual number of people newly infected with HIV continues to decline, although there is stark regional variation. In sub-Saharan Africa, where most of the people newly infected with HIV live, the incidence peaked in 1996-1998. However, the annual number of people newly infected with HIV has risen in the Middle East and North Africa in the past decade. And in Eastern Europe and Central Asia, where the incidence had slowed drastically in the early 2000s, the incidence has been accelerating again since 2008.17

The prevalence of HIV among adults (15-49 years) by world (WHO) region is estimated to be as follows: Africa (4.5%), Americas (0.5%), Eastern Mediterranean (0.1%), European (0.4%), South-East Asia (0.3%), Western Pacific (0.1%).18

Estimates of HIV prevalence globally among those with a history of PWID vary.19 This paper by Mathers et al presents detailed tables of prevalence of PWID and of HIV in PWID by world region. The largest numbers of injectors were found in China, the USA and Russia, where mid-estimates of HIV prevalence among injectors were 12%, 16% and 37% respectively (see maps, appendix 26).
Transmission risks

Needlestick injuries
Following a needlestick injury with a needle contaminated with blood from a source known to have HIV, the risk of becoming infected with HIV is thought to be between 0.1% and 0.36%.\textsuperscript{20, 21, 22} The risk from needlestick injuries in the community is more difficult to estimate and the exact incidence of needlestick injuries and the transmission rate is unknown. Intravenous drug injections carry a higher risk, with the risk of HIV transmission estimated to be between 0.63% and 2.4% per injection.\textsuperscript{24} The risk from a community needlestick where the source is unknown is estimated to be between 0.003 and 0.05%, if the local PWID seropositivity is approximately 1%.\textsuperscript{25}

Several factors influence the rate of transmission. In a study of occupationally associated needlestick injuries, seroconversion was associated with factors including whether the needle or device was visibly contaminated with blood (odds ratio 10, 95% CI 4.6-23), the injury was deep (OR 15, 95% CI 8-26), or if the injury was sustained by a large gauge hollow bore needle (OR 14, 95% CI 4.9-39).\textsuperscript{22} The health of the source patient is also relevant. If the source patient has AIDS, the odds ratio for transmission of HIV is 1.9 (95% CI 0.8-4.6). It has been demonstrated that if the source patient died within 2 months of the needlestick injury, the odds ratio for transmission increased to 4.8 (95% CI 2.3-10).\textsuperscript{22}

Post-exposure prophylaxis (PEP) is thought to reduce seroconversion by up to 81% (95% CI 48-94%).\textsuperscript{22} Commencing PEP early after the injury provides the greatest benefit. In animal studies, administration of PEP within 36 hours prevented seroconversion. In animals who received PEP at 72 hours after exposure, 25% seroconverted. In contrast, 75% of the animals who did not receive any PEP seroconverted by 4 weeks post exposure.\textsuperscript{26} Additionally, treatment is most effective when continued for 28 days. There are documented case reports of HCWs who have become infected with HIV following occupational exposure, despite use of PEP, which in one case was commenced within 30 minutes.\textsuperscript{27}

Blood splashes
The risk of transmission associated with splash injuries is less than the risk associated with needlestick injuries, and HIV seroconversion following splashes of blood to intact skin has not been reported.\textsuperscript{23} The risk of HIV transmission associated with exposure of non-intact skin and mucous membrane exposure to HIV infected fluid is possible\textsuperscript{27}, but the risk is very low.\textsuperscript{23} Pooled data provided an estimated risk for transmission of HIV via mucous membrane exposure at 0.09%, based on one seroconversion from more than 1000 documented exposures.\textsuperscript{21}

Human bites
Infection with HIV after a bite from a patient with HIV “is biologically possible, but remains unlikely”.\textsuperscript{28} Cases of transmission have been reported in case reports, but the exact risk of transmission is unknown, and thought to be very low.\textsuperscript{29, 30} In the cases reported, blood was present in the mouth of the biter, and the skin of the recipient was broken. PEP is recommended if a patient has been bitten by someone known to be HIV-positive, with a high viral load, if the bite breaks the skin.\textsuperscript{31}

Although there are reports of HIV transmission from a dentist who had AIDS to patients, it has never been demonstrated that the dentist acquired HIV from any of his patients.\textsuperscript{32, 33} Cases of other dentists and dental health practitioners who developed HIV after presumed occupational contact are reported, but no evidence exists to demonstrate the exact mode of transmission.\textsuperscript{34} Given that injuries to dentists during procedures are common, at a reported rate of 0.9 per 1000 procedures\textsuperscript{35}, and there are no documented transmissions of HIV to dentists from patients, the rate of transmission overall is very low.

Sexual exposures
The risk of transmission of HIV following sexual exposure depends on the type of exposure, the viral load of the source, the susceptibility of the host, and the presence of sexually transmitted infections in either the source or the recipient. If the index partner also has a genitourinary infection, for instance, the risk of transmission is approximately doubled.\textsuperscript{36} If the recipient has a genitourinary infection, the risk of acquiring HIV is also elevated.\textsuperscript{37} Effective antiretroviral therapy has been shown to be protective in preventing sexual transmission of HIV in a landmark randomised controlled trial\textsuperscript{38} and a “real world” cohort study.\textsuperscript{39} The PARTNER study has demonstrated this to be true in male/female and male/male sexual encounters across a range of sexual activities, including unprotected receptive vaginal and anal intercourse.

Heterosexual exposures
Overall the risk of transmission of HIV, per unprotected coital act, for receptive vaginal sex and insertive vaginal sex is 1 in 1000 and 1 in 1219 respectively.\textsuperscript{40} Correct use of a condom reduces the risk of transmission by 93%-100%.\textsuperscript{37, 41} Circumcision has been shown to significantly reduce HIV acquisition in heterosexual males in high prevalence settings.\textsuperscript{42} The risk of
transmission is greater during the initial two and a half months of infection.\textsuperscript{36,43} The cumulative incidence of transmission of HIV to females in couples who practice unprotected anal intercourse is reported as 27.8\%, compared to 11.7\% transmission to females who do not report anal intercourse.\textsuperscript{37} Transmission is very unlikely if the source of the exposure is on effective antiretroviral treatment.\textsuperscript{36,39}

**Men who have sex with men (MSM)**

Overall the risk of transmission of HIV, per unprotected coital act, for receptive anal sex and insertive anal sex is 1 in 90 and 1 in 666 respectively.\textsuperscript{40} An Australian cohort study has estimated the per coital risk of HIV to be lower in circumcised MSM (0.11, 95\% CI 0.02 - 0.24) versus uncircumcised MSM (0.62, 95\% CI 0.07 - 1.68).\textsuperscript{44} Transmission is very unlikely if the source of the exposure is on effective antiretroviral treatment.\textsuperscript{39}

**Orogenital exposures**

The risk associated with orogenital contact cannot be accurately predicted, and is considered low, but not zero.\textsuperscript{45}

**Body fluid exposure**

The risk associated with exposures to non-blood stained body fluids is thought to be lower than the risk associated with blood exposures.\textsuperscript{20} HIV has been identified in semen, but this is reduced if the index patient is on treatment and blood HIV RNA is detected at <400 copies/ml.\textsuperscript{46} HIV DNA has been extracted from CSF\textsuperscript{47} and synovial fluid.\textsuperscript{48} Other fluids which it is thought could be implicated in HIV transmission are pericardial fluid, amniotic fluid, peritoneal fluid, human breast milk, vaginal secretions and pleural fluid. Unless there is visible blood present, faeces, vomitus, urine, nasal secretions, saliva, sputum, sweat and tears are not thought to have any infectious potential.\textsuperscript{49}
### HIV transmission risk by exposure type

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Risk per exposure (unless otherwise stated)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Needlestick</strong></td>
<td></td>
</tr>
<tr>
<td>Healthcare setting, source patient (serology) known</td>
<td>Increased risk if large gauge needle, hollow needle, deep injury, visible blood on the device, needle was in patient’s artery/vein, or if the source patient has AIDS (or terminal illness).</td>
</tr>
<tr>
<td>Healthcare setting, source patient unknown, or unable to test source</td>
<td>Risk assessment required of the type of injury and the likely infection status of the source.</td>
</tr>
<tr>
<td>Community needlestick</td>
<td>Overall low risk and requires a risk assessment of the type of injury, location of the discarded needle (for example if discarded in a location where PWID are known to inject), likely age of the discarded needle and the background prevalence of HIV in the local population.</td>
</tr>
<tr>
<td>Mucous membrane exposure to blood</td>
<td>0.09% [21]</td>
</tr>
<tr>
<td>Intact skin exposure to blood</td>
<td>No risk [23]</td>
</tr>
<tr>
<td><strong>Human bite</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Very low risk [29] Only risk if blood in the mouth of the biter, and significant injury. No risk if no blood in mouth of biter, and exposure to saliva only. Case report suggests that if source co-infected with HCV, HCV transmission more likely than HIV transmission [50]</td>
</tr>
<tr>
<td><strong>Sexual exposure</strong></td>
<td></td>
</tr>
<tr>
<td>Heterosexual exposure (general)</td>
<td>If source on antiretroviral therapy with suppressed viral load transmission rate $= 0$ (if viral load $&lt; 400$ copies/ml) [38, 39] Increased risk if source patient has recently seroconverted, e.g. within 2.5 months of seroconversion risk of transmission is estimated to be 0.0082/coital act (95% CI 0.0039-0.015) [36]</td>
</tr>
<tr>
<td>Receptive vaginal intercourse</td>
<td>Overall risk is 1 in 1000, which is increased in the presence of cervical ectopy, genital tract trauma, menstruation, genital ulcerative disease (in either partner), infectious syphilis and pregnancy. Male circumcision reduces HIV acquisition [40]</td>
</tr>
<tr>
<td>Insertive vaginal intercourse</td>
<td>Overall risk is 1 in 1219. [40] The PARTNER study has demonstrated zero transmissions in HIV serodiscordant couples where the HIV positive individual is on effective antiretroviral therapy. [39]</td>
</tr>
<tr>
<td>MSM unprotected receptive anal intercourse</td>
<td>Overall risk is 1 in 90, increased risk if there is ejaculation within the rectum. The PARTNER study has demonstrated zero transmissions in HIV serodiscordant couples where the HIV positive individual is on effective antiretroviral therapy. [39]</td>
</tr>
<tr>
<td>MSM unprotected insertive anal intercourse</td>
<td>Overall risk is 1 in 666. The PARTNER study has demonstrated zero transmissions in HIV serodiscordant couples where the HIV positive individual is on effective antiretroviral therapy. [39]</td>
</tr>
<tr>
<td>Orogenital contact</td>
<td>Overall very low risk, estimated to be &lt;1 in 10,000 for both receptive and insertive oral sex. [45]</td>
</tr>
</tbody>
</table>

**Remember**
- There are only 5 reported cases of confirmed HIV transmission from a patient to a healthcare worker in the UK [51]
- There have been no such transmissions between 2004 and 2013, in the UK [52]
References


