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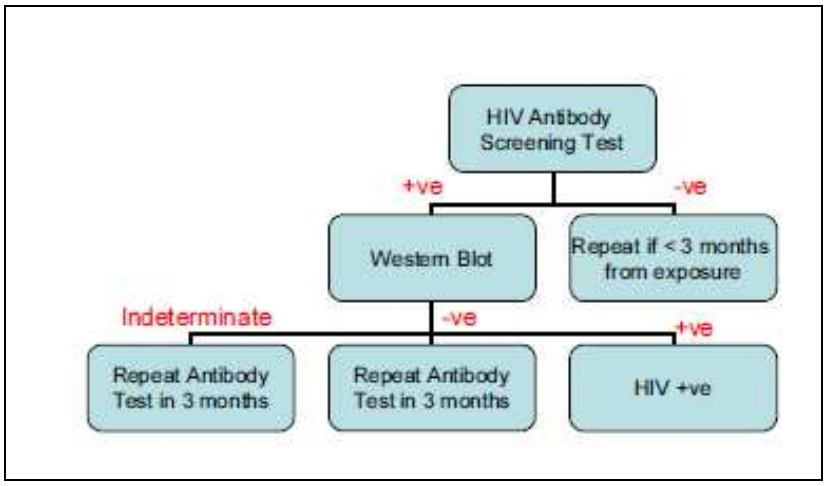
Topic
HIV Screening and Diagnosis

Introduction

Diagnostic tests for HIV have developed at a rapid rate in the past 3 decades. We look at various HIV testing algorithms and the approach to a patient who attends for HIV testing.

Singapore HIV Testing Algorithm

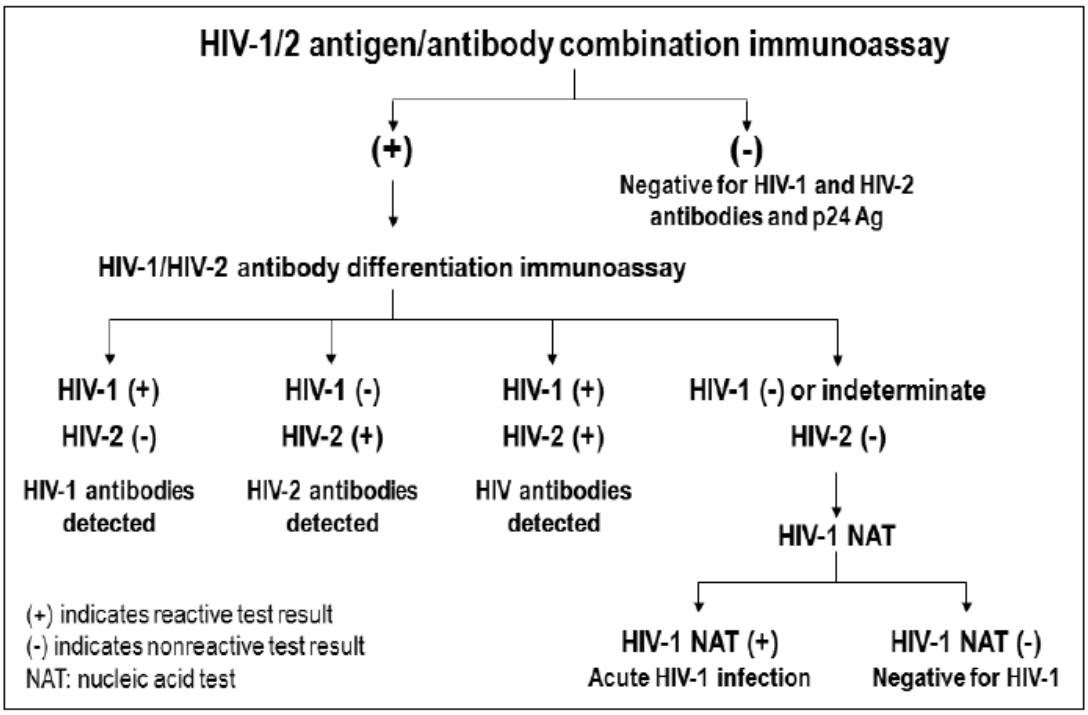
The following algorithm is constructed from known practice at DSC and MOH recommendations.



Limitations

1. Western Blot is very poor at confirming an infection at an early stage
2. Western Blot is very poor at confirming a HIV 2 infection leading to a persistent indeterminate reading
3. Antibody assays have a long window period
4. Antibody assays miss out rare cases of sero-negative infections

US CDC Testing Algorithm



Reproduced from US CDC, Updated recommendations: Laboratory testing for the diagnosis for HIV Infection; 27th June 2014

The UK and European HIV testing guidelines are identical to the above algorithm provided by the US CDC i.e. 1st line assay should be an Antibody and P24 Antigen test (4th Generation screening test) and positive results confirmed by another Antibody and Antigen test which differentiates HIV 1 and 2. A third tie-breaker test, if necessary, should be a HIV NAAT (RNA) test.

WHO/UNAIDS guidelines are not as clear. They generally recommend sequential testing (as opposed to parallel testing) with 1 screening test followed by 1 confirmatory test. A 3rd test is recommended for confirmation of infection in countries with HIV prevalence of < 5%.

Accuracy of tests

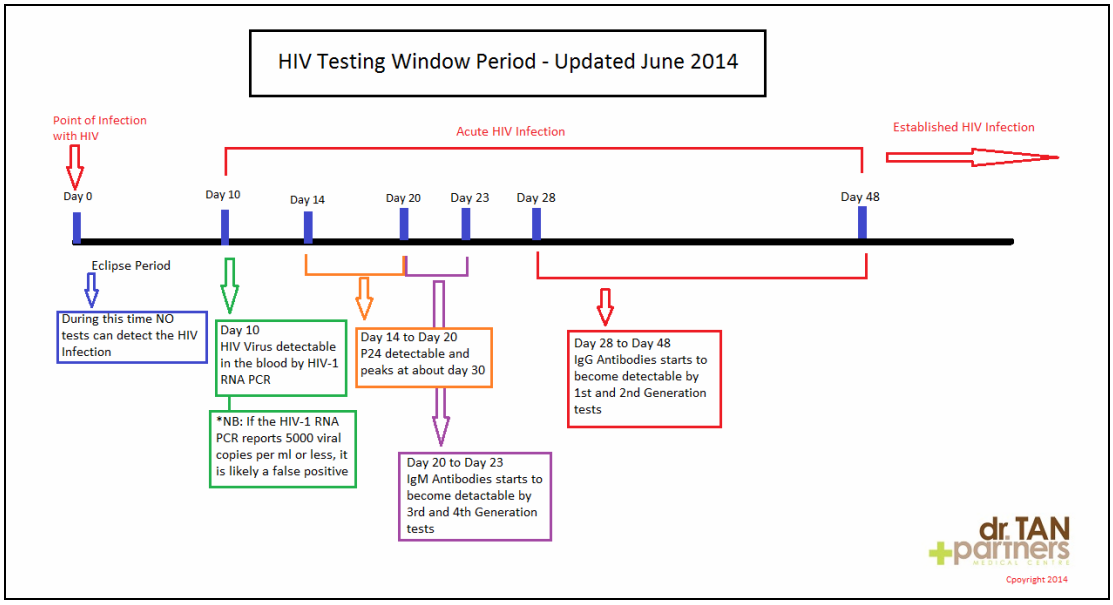


Chart based on data from US CDC, Updated recommendations: Laboratory testing for the diagnosis for HIV Infection; 27th June 2014

US CDC guidelines state that the P24 antigen becomes detectable by 20 days post exposure and IgM antibodies become detectable by 23 days post exposure. This is in keeping with the UK guidelines which state that the HIV Combo test is conclusive at 1 month post exposure.

US CDC guidelines also state that the HIV 1 virus becomes detectable via RNA PCR at day 10 post exposure. The RNA PCR is not recommended as a first line screening test because of its high risk of false positives. That said, studies in New York and Canada using pooled HIV NAAT screening has yielded good results.

Risk Assessment

Risk assessment is a very imperfect science. There are many factors that affect transmission risk. It is not possible to quantify with any accuracy the impact of each individual factor. So we can at best give patients a ballpark figure as to their risk. More often than not, patients find this very useful as many people tend to over-estimate their HIV risk.

Risk assessment can be divided into:

1. Source risk
2. Transmission risk

Source risk

This is based on knowledge of HIV prevalence as well as the individual risk factors of the patient's sexual partner(s).

Singapore's HIV prevalence rate is 0.13% of the general population as reported by UNAIDS GARPR statistics. The same report noted that between 40% to 48% of new cases detected were already in the late stage of HIV infection. This suggests that there is a large pool of undiagnosed HIV +ve people in Singapore.

This hypothesis was given further credence by a study conducted by MOH in 2007. More than 3000 anonymous blood samples were collected from hospitals in Singapore and tested for HIV. The prevalence rate was 0.28%

Singapore's MOH in its Update on the HIV/AIDS situation in Singapore 2013 report stated that there were currently 4,558 people living with HIV in Singapore. With a resident population of 5 million, that puts the prevalence rate at just below 0.1%.

The HIV prevalence if MSMs in Singapore is estimated at 3.14%.

There is no published data on the prevalence of HIV among CSWs in Singapore. Commercial sex is legal in Singapore. CSWs are required to attend monthly screenings for HIV, Syphilis, Chlamydia and Gonorrhoea. Commercial sex is also widely available at massage centres in Singapore. Masseuse are therefore also required to undergo screening for HIV, Syphilis, Chlamydia and Gonorrhoea but only once every 6 months.

Non-licensed CSWs or "street walkers" are common in Singapore. They are unmonitored and therefore do not undergo regular screenings. Anecdotal reports have identified Vietnamese non-licensed CSWs as the highest risk group with prevalence approximately 4%.

If the patient's partner a known injection drug user/abuser, has had organ transplant or blood/blood products transfused prior to 1985 or from an unreliable source, he/she is deemed to be at an increased risk of HIV.

HIV rate in Thailand – The HIV prevalence among MSMs in Thailand ranges from 7.1% to 17.3% with a higher concentration in Bangkok. Reported rates of HIV prevalence among female sex workers range greatly from 2.2% to 20.2%. HIV prevalence rate among male sex workers is reported as 12.2%.

HIV rate in Bali – In 2010, the National AIDS Commission of Indonesia released a report stating that the HIV prevalence rate among CSWs in Bali is 25%.

Table 1. HIV Prevalence estimates in selected Asian countries [1].

Country	Adults and children living with HIV, end 2007		HIV prevalence (%) in adults aged 15-49, end 2007	
	Estimate	[Low estimate - High estimate]	Estimate	[Low estimate - High estimate]
Bangladesh	12,000	7,700-19,000	…	<0.1
Cambodia	75,000	67,000-84,000	0.8	0.7-0.9
China	700,000	450,000-1,000,000	0.1	<0.1-0.2
India	2,400,000	1,800,000-3,200,000	0.3	0.2-0.5
Indonesia	270,000	190,000-400,000	0.2	0.1-0.3
Japan	9,600	7,900-10,000	…	<0.1
Laos PDR	5,500	3,300-13,000	0.2	0.1-0.4
Malaysia	80,000	52,000-120,000	0.5	0.3-0.8
Myanmar	240,000	160,000-370,000	0.7	0.4-1.1
Nepal	70,000	50,000-99,000	0.5	0.4-0.7
Pakistan	96,000	69,000-150,000	0.1	<0.1-0.2
Philippines	8,300	6,000-11,000	…	<0.1
Republic of Korea	13,000	7,500-42,000	<0.1	<0.1-0.1
Singapore	4,200	2,600-7,300	0.2	0.1-0.3
Sri Lanka	3,800	2,800-5,100	…	<0.1
Thailand	610,000	410,000-880,000	1.4	0.9-2.1
Vietnam	290,000	180,000-470,000	0.5	0.3-0.9

Reproduced from An Asian perspective on HIV/AIDS

The above table gives us an idea of the HIV prevalence in various Asian countries. However, we must note that HIV prevalence will vary greatly in specific sub-populations.

Transmission Risk

Assessment of transmission risk only makes sense if the source if known or deemed to be HIV +ve.

TABLE 1. Estimated per-act risk for acquisition of HIV, by exposure route*

Exposure route	Risk per 10,000 exposures to an infected source	Reference
Blood transfusion	9,000	74
Needle-sharing injection-drug use	67	75
Receptive anal intercourse	50	76, 77
Percutaneous needle stick	30	78
Receptive penile-vaginal intercourse	10	76, 77, 79
Insertive anal intercourse	6.5	76, 77
Insertive penile-vaginal intercourse	5	76, 77
Receptive oral intercourse	1	77†
Insertive oral intercourse	0.5	77†

* Estimates of risk for transmission from sexual exposures assume no condom use.
† Source refers to oral intercourse performed on a man.

Reproduced from US CDC MMWR January 21, 2005 / 54(RR02);1-20

Table 2 Risk of HIV transmission following an exposure from a known HIV-positive individual

Type of exposure	Estimated median (range) risk of HIV transmission per exposure (%)
Receptive anal intercourse	1.11 (0.042–3.0%)[9–15]
Insertive anal intercourse	0.06 (0.06–0.065%)[9,11,12,16]
Receptive vaginal intercourse	0.1 (0.004–0.32%)[9,14,17–26]
Insertive vaginal intercourse	0.082 (0.011–0.38%)[13,14,17–20,23,27,28]
Receptive oral sex (giving fellatio)	0.02 (0–0.04%)[12,29]
Insertive oral sex (receiving fellatio)	0[11,29]
Blood transfusion (one unit)	(90–100%)[30]
Needlestick injury	0.3 (95% CI 0.2–0.5%)[31–33]
Sharing injecting equipment	0.67[34]
Mucous membrane exposure	0.63 (95% CI 0.018–3.47%)*[35]

NB: All sexually related risk probabilities are for unprotected sexual exposure; it is assumed similar risks will exist where condom failure has occurred
*The writing committee has concern regarding the risk estimate following mucous membrane exposures, which is derived from a single study including only small numbers of health-care workers exposed to HIV following mucous membrane exposures. This is likely to significantly overestimate the risk

Reproduced from UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure (2011)

Table 1: Probability of Transmission HIV

Exposure (positive source)	Probability of transmission per episode
Blood transfusions (single unit of whole blood)	90% (Donegan, 1990)
Intravenous needle or syringe exposure	0.67% (Kaplan, 1992) [1/150]
Injection drug use – needle sharing	0.67% (Kaplan, 1995) [1/150]
Needlestick	0.3% (95% CI = 0.2 to 0.5%) (Bell, 1997; Cardo, 1997) [1/333] *There have been no reported instances of transmission of HIV from improperly discarded needles outside of the health care setting in either the USA or UK (MG Fowler, CDC, June 15, 2002 cited in Havens, 2003; Robertson, 2001). Another study found no seroconversions in 274 community needlestick injuries in pediatrics indicating that the risk of transmission in these events are very low* (Papenburg, 2008).
Receptive anal intercourse	1 to 30% (CDC, 2005; Powers, 2008; Boily, 2009) [1/100 – 1/3]
Insertive anal intercourse	0.1 to 10% (CDC, 2005; Powers, 2008; Boily, 2009) [1/1000 – 1/10]
Receptive vaginal exposure	0.1 to 10% (CDC, 2005; Powers, 2008; Boily, 2009) [1/1000 – 1/10]
Receptive oral exposure	0.04% (Vittinghoff, 1999; PHAC, 2004) [1/2500]
Mucous membrane exposure to blood or bodily fluids contaminated with blood	0.09% [95% CI, 0.006 to 0.5] (Ippolito, 1993; PHAC, 2004) 0.1% (ANCAHRD, 2001) [1/1000].
Human Milk Exposure (single)	0.001% - 0.004% (Havens, 2003) [1/100,000 – 1/25,000]

Reproduced from the Alberta Guidelines for Non-Occupational, Occupational and Mandatory Testing and Disclosure Act Post-Exposure Management and Prophylaxis

Female-to-Male Transmission	**1 in 700 to 1 in 3,000**
Male-to-Female Transmission	**1 in 200 to 1 in 2,000**
Male-to-Male Transmission	**1 in 10 to 1 in 1,000**
Fellatio	**0 (CDC)**

Reproduced from the Sanford Guide to HIV/AIDS and Hepatitis Therapy 2014

Type of exposure with known HIV positive source	Estimated risk of HIV transmission/exposure[a]
Receptive anal intercourse (RAI) – ejaculation – withdrawal	 1/70 1/155
Contaminated injecting equipment	1/125
Insertive anal intercourse (IAI) uncircumcised	1/160
Insertive anal intercourse (IAI) circumcised	1/900
Receptive vaginal intercourse (RVI)	1/1250* (See next page)
Insertive vaginal intercourse (IVI)	1/2500* (See next page)
Receptive or insertive oral intercourse	Unable to estimate risk – extremely low
Needlestick injury (NSI) or other sharps exposure	1/440
Mucous membrane and non-intact skin exposure	< 1/1000

Reproduced from Australian Society for HIV Medicines, National guidelines for post-exposure prophylaxis after non-occupational and occupational exposure to HIV

Summary of risks

Expoure Route	US CDC MMWR	UK PEP	Alberta PEP	ASHM	New York
Blood Transfusion	90%	90%	90%	-	-
IDU	0.67%	0.67%	0.67%	0.8%	Higher Risk
Receptive ASI	0.50%	1.11%	1 to 30%	1.4%	Higher Risk
Needle Stick	0.3%	0.3%	0.3%	0.2%	Higher Risk
Receptive VSI	0.01%	0.1%	0.1 to 10%	0.08%	Higher Risk
Insertive ASI	0.0065%	0.06%	0.1 to 10%	0.6%	Higher Risk
Insertive VSI	0.005%	0.082%	-	0.04%	Higher Risk
Receptive OSI	0.001%	0.02%	0.04%	-	Lower Risk
Insertive OSI	0.0001%	0%	-	-	Lower Risk
Mucous membrane	-	0.63%	0.09%	<0.1%	Higher Risk

As expected there are large discrepancies in the estimated risks. Receptive anal intercourse is invariably the highest risk sex act.

Factors Influencing Transmission Risks

Condoms – There have been many studies on the effectiveness of condoms in reducing HIV risk. Results range from 60% to 90%. The US CDC Condom Report published in 2001 estimated the average protection rate to be 87%. Condom use should therefore be encouraged for all patients.

Treatment as Prevention – HIV +ve patients on ART are about 90% less likely to transmit HIV. This could be due to the decreased viral load.

Circumcision – Circumcision has been found to reduce the risk of contracting HIV by about 60%. This may be due to the removal of the foreskin which is rich in Langerhan Cells.

Other Factors:

Male-to-Female Transmission	**Relative Risk**
Oral Contraceptives	2.5-4.5
Gonococcal Cervicitis (Gonorrhea infection of the Cervix)	1.8-4.5
Candida Vaginitis	3.3-3.6
Genital Ulcers	2.0-4.0
Bacterial Vaginosis	1.6
HSV 2	2.5
Vitamin A Deficiency	2.5
Female-to-Male Transmission	
Lack of Circumcision	5.4-8.2
Genital Ulcers	2.6-4.7
Sex during Menses	3.4
HSV 2	6-16.8

Reproduced from the Sanford Guide to HIV/AIDS and Hepatitis Therapy 2014

HIV ARS / PHI

HIV ARS is a mononucleosis-like syndrome that may occur during HIV sero-conversion. Only 40% to 70% is people infected with HIV develop ARS.

HIV ARS can develop anytime between 2 to 6 weeks from the date of infection. About 80% of people who do develop ARS will do so between 2 to 4 weeks.

The commonest symptoms (90% of patients with ARS) are fever, rash, pharyngitis and swollen cervical lymph nodes.

The HIV rash usually comes on 2 to 3 days after the onset of the fever and lasts for at least 2 weeks. It is a Morbiliform Exanthem rash consisting of macules and papules up to 1cm in diameter which are pink to red in colour. Each lesion remains discrete and do not become confluent. It is widespread and always (100%) involves the upper thorax and collar region also commonly (60% to 40%) affects the face, arms, scalp, thighs and palms in descending order of frequency.

Because HIV ARS symptoms are so non-specific, they should not be used to determine a patient's HIV status. However, patients with an exposure history who show typical mononucleosis symptoms should be offered a HIV test.

Summary

HIV testing techonology has come a long way since it's development in the 1980's. To ensure the the best standard of care for our patients, we must always recommend the right test at the right time.

Practice Pointers

1. Always treat HIV testing patients with openness, empathy and respect.
2. Always address their concerns factually.
3. Recommend HIV tests according to the duration from the date of exposure.
    a. < 3 days – assess risk and consider PEP
    b. 10 days – HIV RNA PCR
    c. 28 days and above – HIV P24 Ag/Ab Combo
    d. 12 weeks – HIV P24 Ag/Ab Combo test KIV Antibody test
        i. Recommending the Combo test for 1st line screening is supported by all international guidelines.
        ii. We must be conscious of the relatively high cost of the test in Singapore and must counsel the patient accordingly.
        iii. Patients who opt for the Antibody test should be informed of the 1 in 1 million chance of a sero-negative infection.
4. Always discuss screening for other STDs.
5. Always discuss HPV vaccination.

References:

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2. UK National Guidelines for HIV Testing; 2008
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15. Adam M. Spivak et al, Seronegative HIV-1 infection: a review of the literature. AIDS 2010, 24:1407-1414
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