Textbook of Venereology

Sri Lanka College of Sexual Health and HIV Medicine (SLCoSHH)

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2025

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This textbook has been developed to provide a comprehensive foundation in venereology and its preventive aspects, tailored for undergraduate medical students and clinicians preparing for postgraduate screening examinations. The editors sincerely acknowledge and appreciate the valuable contributions of all authors whose expertise and dedication made the completion of this work possible.

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Content

Section 1:
History of STI control in Sri Lanka

A short history of sexually transmitted infections (venereal diseases) control in Sri Lanka

Dr Lucian Jayasuriya

It is reasonable to think that sexually transmitted infections (STI), syphilis did occur in ancient Sri Lanka. But their prevalence seems to have been low till the Portuguese reintroduced them in the sixteenth century (1)

Measures to control STI have been in operation for about 180 years. The Vagrants Ordinance No. 4 of 1841, the Contagious Diseases Ordinance No. 17 of 1867 and the Brothels Ordinance No. 5 of 1889 were passed with a view of controlling venereal diseases. By 1886 free VD Clinics and wards were available in Colombo, Kandy and Galle.

As a result of the report of The Venereal Diseases Commission of 1920, STD control was started on an organized basis in 1921. In 1938 a Venereal Diseases Control Programme was initiated, and the Venereal Diseases Ordinance No. 27 was passed. From 1941, doctors who worked in venereal diseases clinics were trained for three months in Colombo before they started work outstations.

In 1949, Professor George Leiby, Professor of Syphilology, of the University of California visited Sri Lanka on a WHO assignment. One of his recommendations was the establishment of 60 venereal diseases clinics, staffed by trained medical officers - a number we have not achieved still.

In 1951 the Chief of the Venereal Diseases and Treponematoses Section of the WHO, Geneva visited Sri Lanka. As a result, the WHO established the Venereal Diseases Control Project (Ceylon 0005) under the leadership of Dr S. M. Laird. The objectives of the project were

- To establish a model venereal diseases clinic in Colombo, which would serve as the chief clinic for the country and the training centre for medical and paramedical personnel.
- To develop a full venereal diseases service with trained staff in the main outstations
- To establish serological tests for syphilis for expectant mothers to control congenital syphilis
- To train local staff in simple serological testing
- To develop diagnosis and treatment facilities for seafarers in the Port of Colombo.

As a result of this project the Anti-Venereal Diseases Campaign (Anti-VD Campaign) was established in 1952. Dr E. D. C. Perera the first Superintendent of the Campaign was a dynamic leader. She was able to achieve most of the objectives very soon. Every OPD building of a provincial hospital had rooms demarcated to the VD clinic with separate access, because of her initiative. Some of these are still used. Dr Laird

revisited Sri Lanka in 1967 and was happy with the progress made (3).

With the 13th Amendment to the Constitution of Sri Lanka implemented in 1989, the Anti-VD Campaign was decentralised. The Director lost control of all the clinics except the Central Clinic in Colombo. With the peripheral clinics going under the management of the provincial health services the quality of the work deteriorated. Some clinics were manned by doctors with no training in venereology. Though there is more coordination now, the problems created by this legislation have not been fully rectified. In 1996 Cabinet approval was granted to take over the peripheral clinics to the Central Health Ministry, some STD clinics which were physically located in hospitals managed by it. However, for this to be effective, concurrence was necessary from the provincial governments (4). That concurrence has been granted only for the STD clinics in Galle (Mahamodera) and Jaffna.

With the advent of HIV/AIDS in the early 1980s, the Anti-VD Campaign was renamed the National STD AIDS Control Programme (NSCAP) in 1985, and more attention was given to prevention of HIV and provision of treatment and care for people infected with HIV. Dr G.N. Jayakuru who was already the Director of the Anti-VD Campaign became the first Director of NSACP.

In 1996, the World Bank committed a major part of its funds under the Health Services Project (IDA/WB/HSP/SL) to strengthen the NSACP. A modern four- storied Central STD Complex in Colombo and 21 upgraded or newly constructed provincial/ base hospital clinics were constructed. The Central STD Complex houses the administrative and financial units, the Central STD and HIV Clinics, the National Reference Laboratory, the Strategic Information Management (SIM) unit and the Multi-sectoral HIV prevention unit.

Administration of NSACP

Up to 2005, all the Superintendents or Directors of the Anti-VD Campaign and the NSACP were specialists in venereology. The post of Director NSACP is considered a senior administrative post, and they were considered as regional experts in the HIV and STI field.

By 2005 the Ministry of Health changed the requirements to be the Director of the NSACP which made it easier for a medical officer who is already in the administrative grade to get the post of Director/NSACP. The first non-venereologist to be the Director/NSACP was Dr N. Edirisinghe (2006-2012).

Postgraduate training in Venereology

From the time of the establishment of the Anti-VD Campaign in 1952, venereology was considered a specialty within public health. There was a separate cadre of specialists in venereology. Doctors were selected for a career in venereology. To apply they had to have at least two years of service as a Medical Officer of Health (MOH). They were trained for three months at the Central VD Clinic and then posted to man the outstation clinics. Then they were sent abroad to UK or USA for DPH (or

equivalent) and further training in venereology at a centre/s of excellence. When they returned, they were appointed as specialists in the Anti-VD Campaign.

With the establishment of the Postgraduate Institute of Medicine (PGIM), from 1980 the specialist qualification became MD in Community Medicine with local and overseas training in venereology. The Sri Lanka College of Venereologists (originally called the College of Genitourinary Physicians) was formed in 1995. The College took a decision to revise the training of a specialist in venereology to accommodate increasing demands in the context of HIV/AIDS epidemic. The College was able to get a Board of Study in Venereology established in the PGIM in 2001. It organized courses for the Postgraduate Diploma in Venereology from 2002 and the MD in Venereology from 2003(5).

Sri Lanka's notable achievements in STI control include maintaining a low prevalence of HIV and receiving certification from the World Health Organization (WHO) in 2019for the elimination of mother-to-child transmission of syphilis and HIV.

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Further Reading

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Section 2:
Overview of Sexually Transmitted Infections

Introduction to STIs

Dr Iyanthi Abeyewickreme

Sexually transmitted infections (STI) or sexually transmitted diseases (STD) previously known as venereal diseases are conditions that can be transmitted or acquired predominantly through unprotected sexual contact. The term "sexually transmitted infection" (STI) refers to a pathogen that causes infection through sexual contact, whereas the term "sexually transmitted disease" (STD) refers to a recognizable disease state that has developed from an infection.

Many STIs are asymptomatic but may progress into a sexually transmitted diseases when symptoms and signs develop. Individuals with an asymptomatic STI may not be aware of their infection but are able to transmit the infection to others and may go on to develop long term and potentially fatal outcomes. Long-term effects of STIs include chronic pelvic pain, infertility, ectopic pregnancies, congenital syphilis, increased risk of HIV infection, neurological complications and genital and oral cancers.

STI s constitute a global public health and economic problem as they can have a profound impact on health affecting the quality of life. STIs also lead to economic problems for countries. Cost of treating STIs and managing their consequences and the days of productivity lost places a significant economic burden on healthcare systems. Costs include medical care, medications, and lost productivity. They are also associated with stigma and domestic violence. The stigma associated with STIs often prevents people from seeking timely testing, treatment, and preventive measures. As a result, stigma can perpetuate the spread of infections.

Transmission or acquisition of STIs could occur during vaginal, anal, and oral sex through exchange of infected body fluids or direct skin-to-skin contact where the infection is active. Some STIs can also be transmitted during pregnancy, delivery, and breastfeeding with potential adverse consequences for the infant. STIs can also be transmitted through infected blood or blood products. One STI may also facilitate the transmission of other STI, thus some individuals may have multiple infections at the same time.

Classical venereal diseases included only five conditions, namely syphilis, gonorrhoea, chancroid, lymphogranuloma venereum and granuloma inguinale. Presently, more than 30 pathogens of varying types including bacteria, viruses, fungi, parasites and arthropods may cause STIs. Eight pathogens are linked to the greatest incidence of STIs[1]. Of these, four are currently curable: syphilis, gonorrhoea, chlamydia and trichomoniasis.

The other four are incurable viral infections: hepatitis B virus, herpes simplex virus (HSV), human immunodeficiency virus (HIV) and human papillomavirus (HPV).

Emerging outbreaks of new infections that can be acquired by sexual contact such as monkeypox, *Shigella sonnei*, *Neisseria meningitidis*, Ebola and Zika[2], as well as re-emergence of neglected STIs such as lymphogranuloma venereum herald increasing challenges in the provision of adequate services for STIs prevention and control. These outbreaks are linked to increased international travel, unprecedented connectivity between people, and social networking that have promoted the dissemination of existing as well as newly emerging STIs at the global level.

Table 1: Pathogens causing STIs

Spectrum of Pathogens				
Parasites	*Trichomonas vaginalis, Sarcoptes scabiei, Pthirus pubis*			
Fungi	*Trichophyton mentagrophytes* subspecies Note: Candida albicans is only facultatively pathogenic and does not cause STIs.			
Bacteria	*Chlamydia trachomatis* (serotypes D-K, serotypes L1–L3), *Klebsiella granulomatosis, Neisseria gonorrhoeae, Treponema pallidum, Haemophilus ducreyi, Mycoplasma genitalium*			
Viruses	Human papillomaviruses, Herpes simplex virus 1 & 2, HIV, Hepatitis B virus, Hepatitis C virus, Molluscum contagiosum virus, monkeypox virus, Zika virus			

Certain risk factors increase the likelihood of acquiring or transmitting STIs. These include unprotected sexual contact, multiple sexual partners, substance users, persons having STIs, sexual abuse and rape. Key population groups at risk include men who have sex with men (MSM), bisexual men, transgenders, sex workers, beach boys (in Sri Lanka), and people in closed settings such as prisoners.

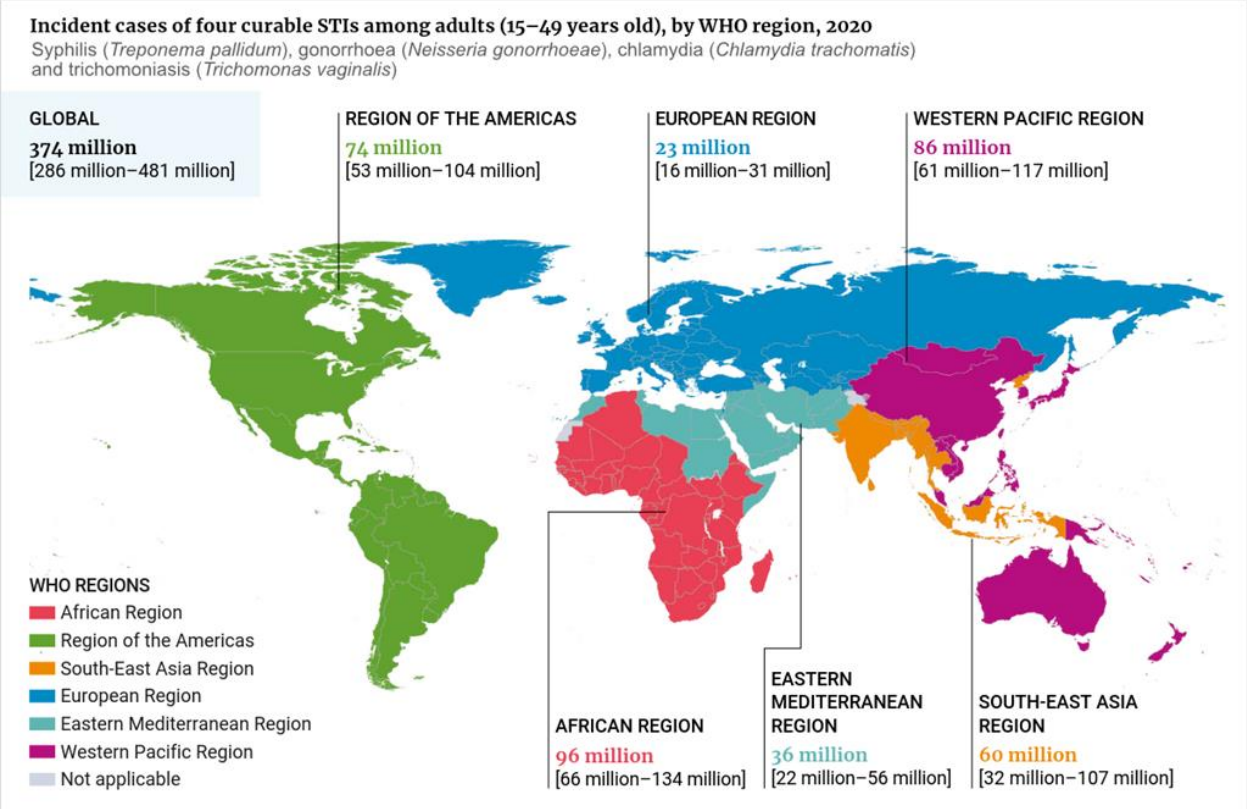
Global Epidemiology

STIs continue to have a profound impact on sexual and reproductive health worldwide. The World Health Organization (WHO) produces global and regional estimates of

the prevalence and incidence of four of the most common curable STIs in adults 15 to 49 years of age: chlamydia (etiological agent: *Chlamydia trachomatis*), gonorrhoea (*Neisseria gonorrhoeae*), trichomoniasis (*Trichomonas vaginalis*) and syphilis (*Treponema pallidum*) every 4-5 years.

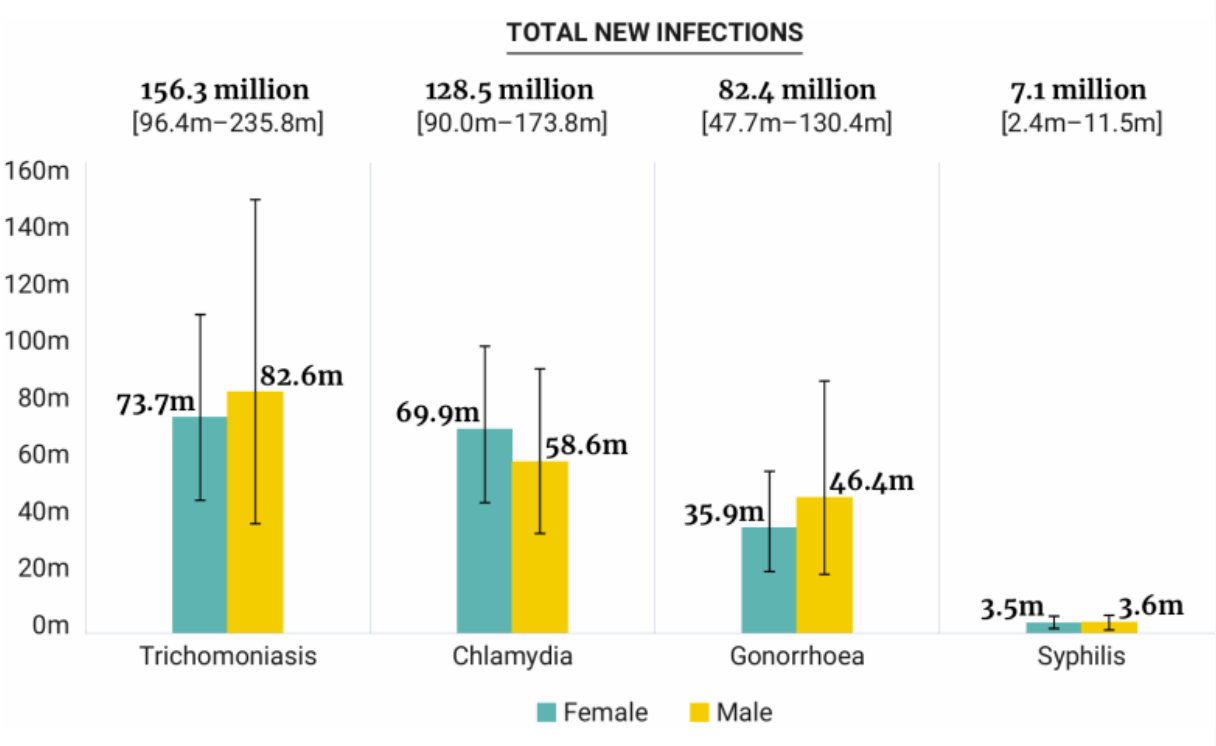
According to the WHO, over 1 million STIs are acquired daily worldwide and the majority of these are asymptomatic 1. In 2020, WHO estimated that on average 374 million new infections are acquired with 1 of 4 STIs: chlamydia (129 million), gonorrhoea (82 million), syphilis (7.1 million) and trichomoniasis (156 million)[1].

Figure 1: Incident cases of four curable STIs among adults (15-49 years old), by WHO region, 2020



Source: WHO 2021

Figure 2: New cases of four curable STIs among adults (15–49 years old) per year, by sex, global, 2020



Source: WHO 2021

Globally HSV is one of the most reported viral STIs. There are two types of herpes simplex virus. Type 1 (HSV-1) mostly spreads by oral contact and causes infections in or around the mouth (oral herpes or cold sores). It can also cause genital herpes. In 2016 (last available estimates), 3.7 billion people under the age of 50, or 67% of the global population, had HSV-1 infection (oral or genital[3]). The 2016 study also estimated 491.5 million people were living with HSV type 2 infection, equivalent to 13.2% of the world's population aged 15-49 years. More women are infected with HSV-2 compared to men since sexual transmission is more efficient from men to women. Prevalence increases with age, though the highest number of new infections are in adolescents.

The WHO does not produce estimates of Human papillomavirus (HPV) prevalence or incidence. The estimated annual incidence of genital warts in developed world populations is about 0.15% of the adult population per year[4]. However, HPV infection is associated with over 311 000 cervical cancer deaths each year[5]. There are effective vaccines to prevent infection with HPV, and they are available in some countries. By the end of 2020, the HPV vaccine had been introduced as part of routine immunization programmes in 111 countries, primarily high- and middle-income countries.

Table 2: Global and regional estimates of the percentage of population (%) among individuals 15 to 49 years of age for the 4 curable STIs, 2020

WHO Region	Chlamydia		Gonorrhoea		Trichomoniasis		Syphilis	
	M	*F*	*M*	*F*	*M*	*F*	*M*	*F*
AMR	3.7	6.8	0.5	0.6	0.8	7.1	1.14	1.12
AFR	4.0	5.5	1.2	1.6	1.3	12.0	1.69	1.70
EUR	2.0	3.4	0.2	0.3	0.2	1.7	0.11	0.11
EMR	3.5	4.4	0.4	0.5	0.5	4.7	0.61	0.65
SEAR	1.2	1.9	0.7	0.8	0.3	2.7	0.13	0.13
WPR	2.3	4.3	0.7	0.9	0.4	3.7	0.32	0.32
GLOBAL	3.8	4.0	0.7	0.8	0.5	4.9	0.56	0.58

AFR – African Region, EUR – European Region, EMR – Eastern Mediterranean Region, SEAR – Southeast Asian Region, WPR – Western Pacific Region M – males, F- Females
Source –WHO Global Health Observatory

WHO Global Gonococcal Antimicrobial Surveillance Program (GASP)

Gonorrhoea remains a major public health concern with an estimated 82.4 million new cases infected among adults and adolescents aged 15-49 years worldwide. Most of the cases were in the WHO African Region and the Western Pacific Region.

Effective management of gonorrhoea depends on the sensitivity of the antimicrobials used. Over the years the gonococcus has acquired resistance to the antibiotics that were used for the treatment of gonorrhoea. This has continued to expand over the past 80 years, and resistance has rapidly emerged to sulphonamides, penicillins, tetracyclines, macrolides, fluoroquinolones and early-generation cephalosporins. Ciprofloxacin resistance is very high among many countries. The WHO GASP is a special programme that has been documenting the emergence and spread of antimicrobial resistance (AMR) in

gonorrhoea globally since 1992. GASP is a worldwide laboratory network coordinated by focal points and regional coordinating centres. In 2017/2018, 73 countries in 6 regions reported N. gonorrhoeae isolate susceptibility data for one or more antimicrobials[7].

Table 3: Number of countries in different WHO regions reporting Neisseria gonorrhoeae isolates with resistance (R) to azithromycin and ciprofloxacin, and decreased susceptibility or resistance (DS/R) to ceftriaxone and/or cefixime to WHO-GASP in 2018

	AFR	AMR	EMR	EUR	SEAR	WPR	Total
Ceftriaxone							
No. countries reporting:	**5**	**8**	**4**	**30**	**4**	**10**	**61**
≥5% DS/R						1	**1**
<5% DS/R	2	2	1	3	2	6	**16**
0% DS/R	3	6	3	27	2	3	**44**
Cefixime							
No. countries reporting:	**4**	**12**	**2**	**30**		**1**	**49**
≥5% DS/R			1	5			**6**
<5% DS/R	1	2		9		1	**13**
0% DS/R	3	10	1	16			**30**
Azithromycin							
No. countries reporting:	**5**	**9**	**3**	**30**	**4**	**7**	**58**
≥5% R	1	8	2	24	1	4	**40**
<5% R		1		1	1	1	**4**
0% R	4		1	5	2	2	**14**
Ciprofloxacin							
No. countries reporting:	**4**	**12**	**5**	**30**	**4**	**10**	**65**
≥90% R	2	2	3		3	2	**12**
≥5% R	4	12	5	29	4	9	**63**
<5% R						1	**1**
0% R				1			**1**

AFR – African Region, AMR - American Region, EMR – Eastern Mediterranean Region, EUR – European Region, SEAR – Southeast Asian Region, WPR – Western Pacific Region

Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP)

Since widespread antimicrobial resistance (AMR) in highly variable strains of *Neisseria gonorrhoeae* continued to cause significant public health concerns and compromise the management and control of gonorrhoea, WHO started the Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP) which aims to strengthen sentinel surveillance for gonococcal AMR in selected countries. The extensively drug-resistant gonorrhoea with high level resistance to the current recommended treatment (ceftriaxone and azithromycin) and to resistance to penicillin, sulphonamides, tetracyclines, fluoroquinolones and macrolides are referred to as super gonorrhoea.

Elimination of mother to child transmission (EMTCT) of syphilis

Syphilis is the second most common infectious cause of stillbirth worldwide. Mother-to-child transmission (MTCT) of syphilis during pregnancy can lead to serious foetal outcomes in the second or third trimester including early foetal death, stillbirth, neonatal death, preterm birth, low birthweight and congenital infection in infants[6]. In 2007 the World Health Organization (WHO) launched the global initiative to eliminate mother-to-child transmission of syphilis (congenital syphilis, or CS).

According to a study on global burden of maternal congenital syphilis conducted in 2016, the estimated global maternal syphilis prevalence in 2016 was 0.69%, resulting in a global CS rate of 473 per 100,000 live births and 661,000 total CS cases, including 355,000 adverse birth outcomes (ABO) and 306,000 non-clinical CS cases (infants without clinical signs born to un-treated mothers)[6].

Epidemiology of STIs in the Southeast Asia Region

World Health Organization's Southeast Asia Region (SEAR) consists of 11 countries that include, Bangladesh, Bhutan, India, Indonesia, Nepal, Democratic Peoples' Republic of Korea (North Korea), Maldives, Myanmar, Sri Lanka, Thailand and Timor-Leste. STIs varies across the Region because most SEAR countries do not have dedicated STI control programmes. STI control efforts have not been sufficiently scaled up or sustained, and evidence of increasing STI incidence and prevalence is appearing in some areas and some population groups.

There were an estimated 60 million new infections of 4 curable STIs in SEAR in 2020. Chlamydia accounted for 15.2 million, gonorrhoea 21.1 million, syphilis 360,000 and trichomoniasis 23.1 million. In addition, 53,000 babies were estimated to have congenital syphilis.

The World Health Organization (WHO) estimates that the Southeast Asia (SEA) region accounted for 16% of the global new STI infections in 2020.

Figure 3: New infections of 4 curable STIs in SEAR-WHO, 2020 (60 million new cases)

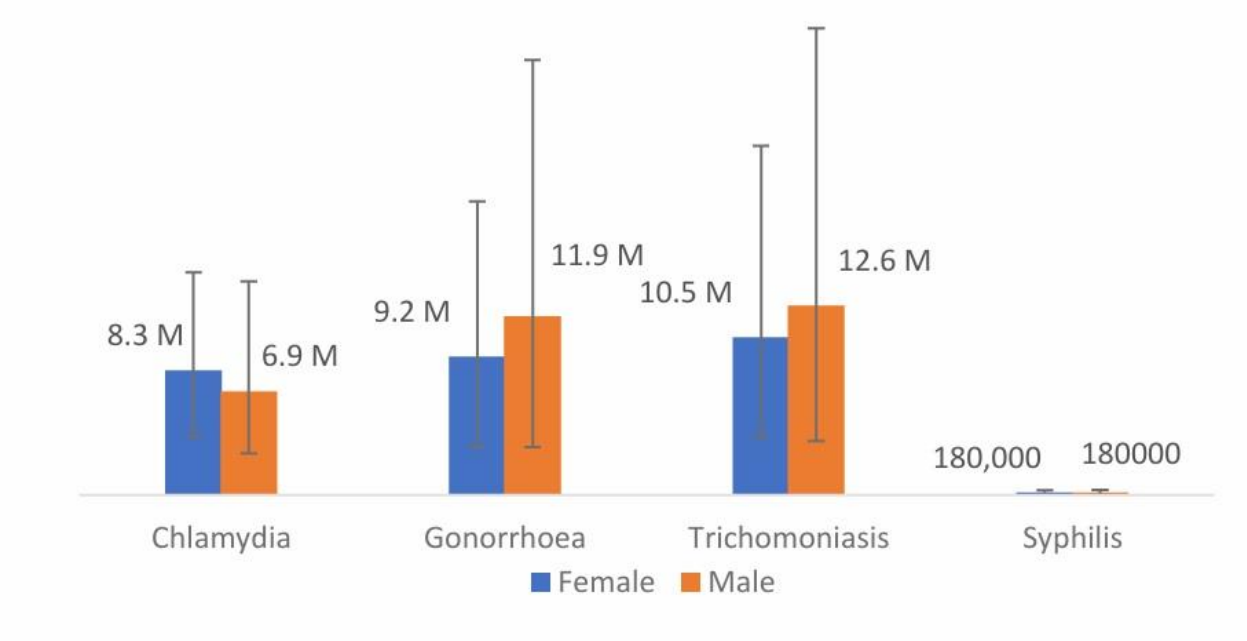
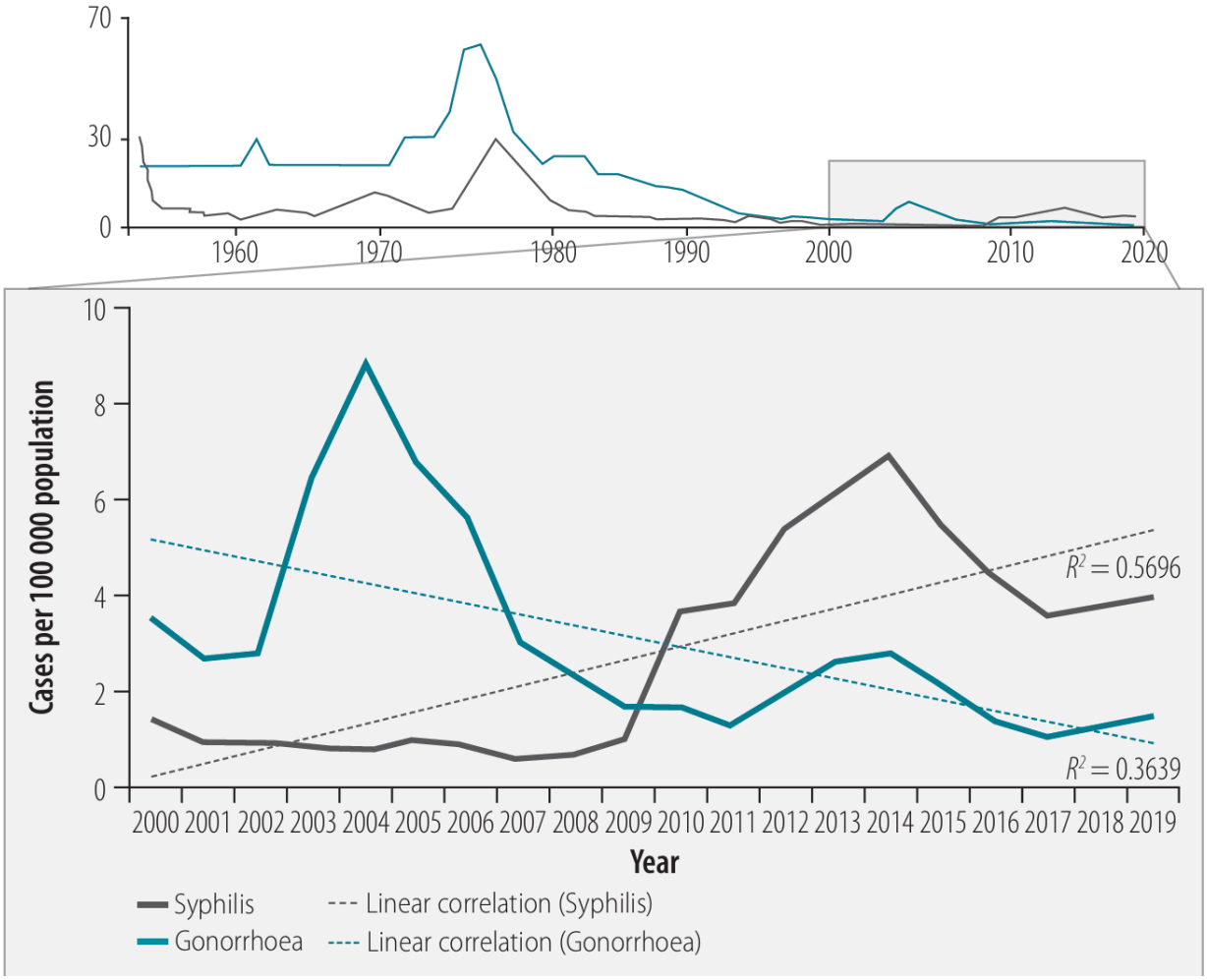


Figure 4: Incidence of 4 curable STIs in SEAR-WHO from 1995 to 2020

Source – WHO SEARO

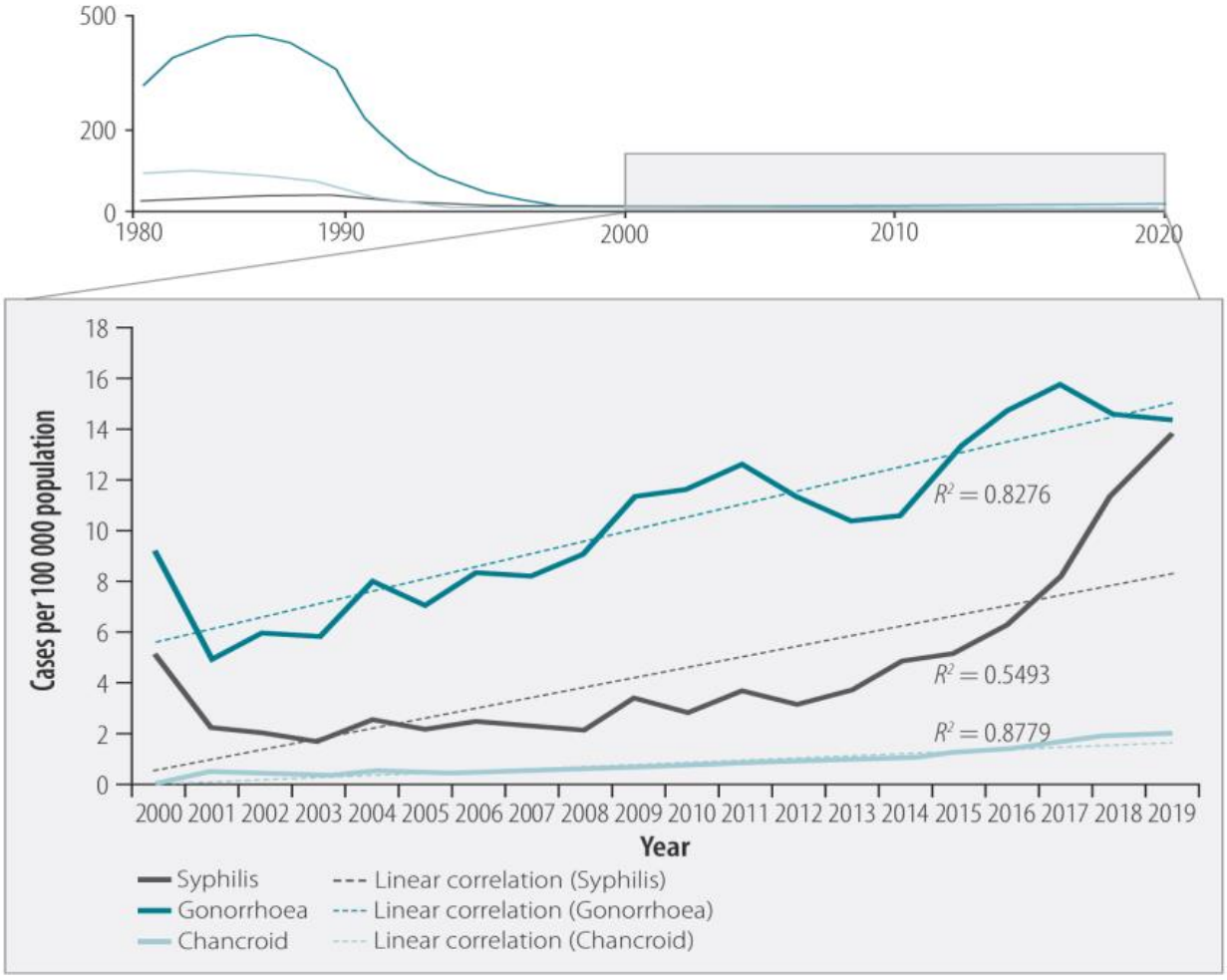
Historically, STIs have been among the most serious public health problems in the WHO SEAR, with associated high morbidity, mortality, disability and adverse pregnancy outcomes. However, large-scale interventions with package of services, including the promotion of condom use in sex work led to large STI declines and slowing of HIV epidemics notably in Thailand, Sri Lanka, Bhutan, Nepal, Maldives and India.

Figure 5: Trends in STIs in Sri Lanka, 1952-2019



Source – Annual reports: National STD/AIDS Control Programme, Sri Lanka

Figure 6:Trends in STIs in Thailand, 1982-2019



Source: Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand

In Thailand and Sri Lanka, reported syphilis cases rose on average 2.4 and 5.1 times, respectively, from 2000–2009 to 2010–2019, while gonorrhoea cases increased 1.7 times in Thailand over the same periods (Fig. 1 and Fig. 2).

Like other Regions of the WHO, Covid pandemic affected the STI programmes across SEAR in 2020-2021, but there has been a rebound of service delivery with resurgence of STI especially syphilis among men who have sex with men and transgender populations. Resurgence of STIs has been observed in all countries including the well-controlled countries like Sri Lanka and Thailand.

Most published STI prevalence data come from key populations (KP), bridge groups or clinic-based samples, which are informative for those sub-populations but cannot be directly extrapolated to derive general population estimates. Insufficient data on STIs and low coverage limit assessment of the epidemiological situation in most other countries of the region.

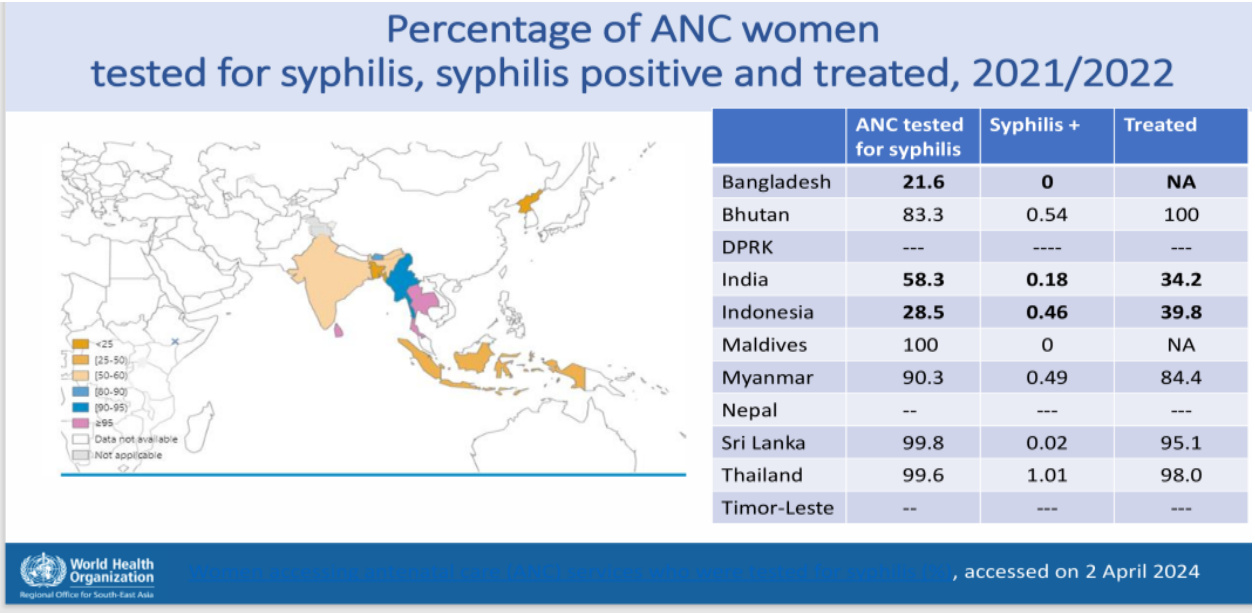
There have been large decreases in sexually transmitted infections documented in several countries of the region from 1980 to 2010. It can be at least partly attributed to comprehensive prevention efforts – in particular, promotion of condom use in targeted high-risk groups and programmes to control sexually transmitted infections in response to the rapidly growing HIV epidemics. During the past decade, however, these trends appear to have levelled off or reversed in at least some populations, with a growing number of outbreaks of sexually transmitted infections being reported or rising trends being seen across the region[9].

Most prominent increase in STI incidence in SEA region is observed in Maldives (297.78%). The largest number of incident cases occurred in India (99.91 million), and Indonesia (32.61 million) in 2019[10].

Reliable data on gonorrhoea come from Sri Lanka and Thailand, which use affordable microscopy with Gram stain and culture to distinguish gonococcal from non-gonococcal infections. Sri Lanka, Thailand and India regularly report antimicrobial resistance data while the rest of the countries are yet to strengthen AMR activity. However, these data are not available.

The situation regarding syphilis among pregnant women in SEAR countries is shown in the slide below. There is no data available from DPRK, Nepal and Timor-Leste.

Figure 7:Percentage of ANC syphilis screening in SEAR-WHO



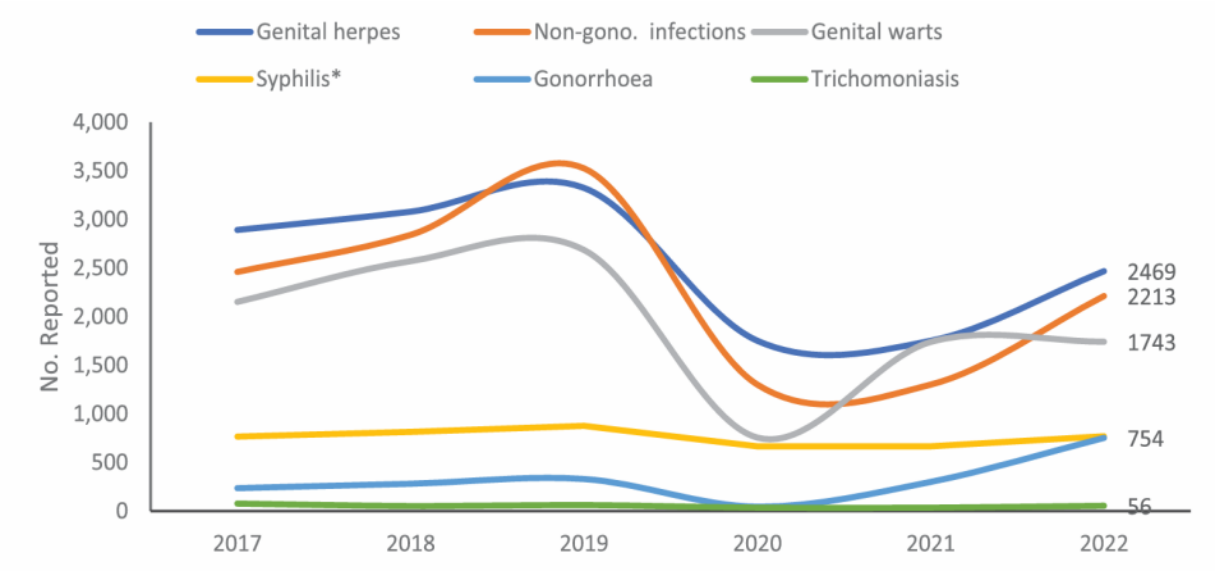
	ANC tested for syphilis	Syphilis +	Treated
Bangladesh	**21.6**	**0**	**NA**
Bhutan	83.3	0.54	100
DPRK	---	----	---
India	**58.3**	**0.18**	**34.2**
Indonesia	**28.5**	**0.46**	**39.8**
Maldives	100	0	NA
Myanmar	90.3	0.49	84.4
Nepal	--	---	---
Sri Lanka	99.8	0.02	95.1
Thailand	99.6	1.01	98.0
Timor-Leste	--	---	---

STI epidemiology in Sri Lanka

In Sri Lanka, STI services are provided mainly by the National STD/AIDS Control Programme (NSACP) of the Ministry of Health. Although other medical practitioners also provide treatment for STIs, they do not report STI data to the NSACP.

In 2022, there were 41 full time and 30 branch STI clinics distributed throughout Sri Lanka. Epidemiological data on STIs collected from all clinics are collated and analysed by the National STD/AIDS Control Programme (NSACP) of the Ministry of Health. These data indicate that Sri Lanka is no exception when it comes to increasing trends in STIs over the years[11].However, it must be noted that although the reported STI indicate an increasing trend they underestimate the full scope of the problem because many cases can be asymptomatic and are therefore, often undiagnosed, untreated and not reported.

Figure 8:Trends of number of reported STIs 2017-2022



Source - Annual reports: National STD/AIDS Control Programme, Sri Lanka

In Sri Lanka too, the Covid-19 epidemic related service accessibility issues caused the decline in STIs during 2020 and 2021. The same pattern was noticed in reported HIV diagnoses in this period. Nevertheless, a rising trend of STIs was seen from 2021 onwards.

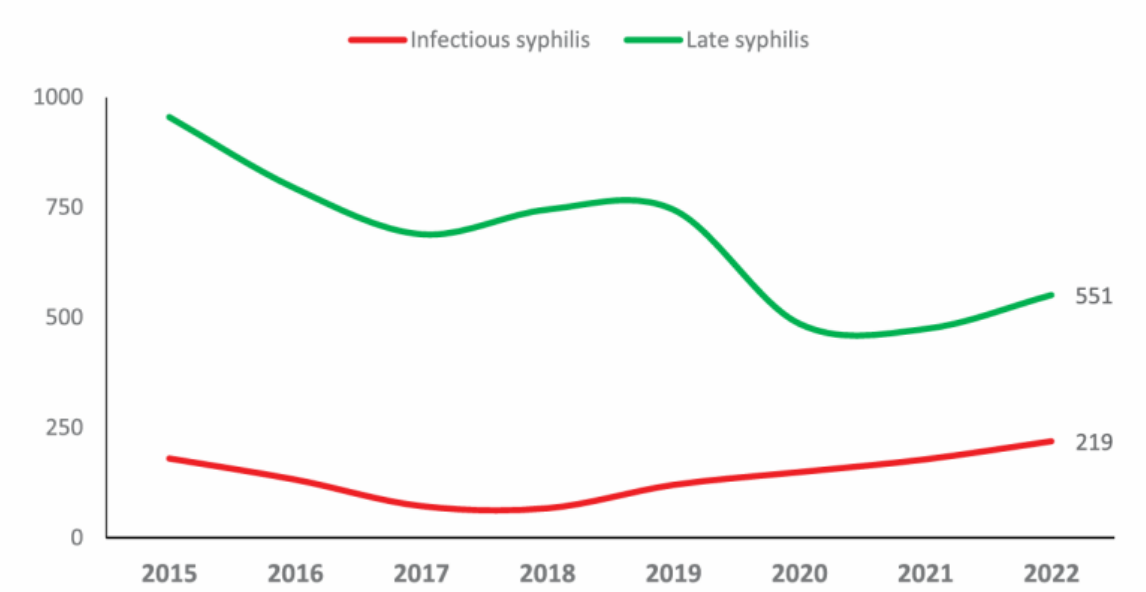
Of a total of 8331 reported STIs in 2022, genital herpes accounted for 30% and more women had genital herpes compared to men. This is in keeping with the global picture.

Table 4: Diagnoses reported from STD clinics during 2022

Diagnosis	Sex				Total	
	Male		Female			
	No.	*%*	*No.*	*%*	*No.*	*%*
Genital herpes	1094	27%	1375	0.32	2469	0.3
Non-gonococcal infections	659	16%	1554	0.36	2213	0.27
Genital warts	883	22%	860	0.2	1743	0.21
Syphilis	587	14%	183	0.04	770	0.09
Gonorrhoea	645	16%	109	0.03	754	0.09
Trichomoniasis	29	1%	27	0.01	56	0.01
Other STIs	171	4%	155	0.04	326	0.04
Total STIs	**4068**	**48.8%**	**4263**	**51.2%**	**8331**	**100%**

Source – 2022 Annual Report, NSACP

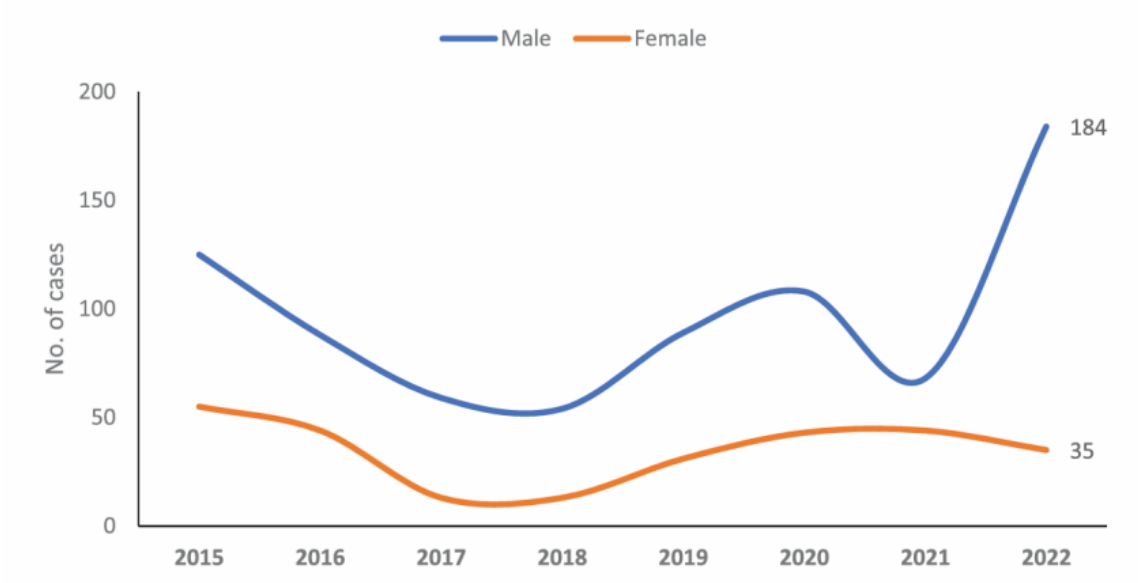
Figure 9:The trend of syphilis cases, by stage, 2015-2022



Source – 2022 Annual Report, NSACP

Although syphilis accounted for only 9 % (n=770) of all STIs reported during 2022, 28.4% were early infections. Males contributed to the majority of (76.2 %) syphilis compared to females. Since 2018, a rising trend of early syphilis cases have been reported even during the Covid-19 affected years.

Figure 10:The trend of infectious syphilis cases by sex 2015-2022



Source – 2022 Annual Report, NSACP

As shown in the above graph, there has been a sudden increase in infectious syphilis among males in 2022. This increase may indicate an in increase in unprotected sex by men or it may have been due to reporting being normalised following the Covid epidemic or both.

Table 5:Status of congenital syphilis, 2020-2022

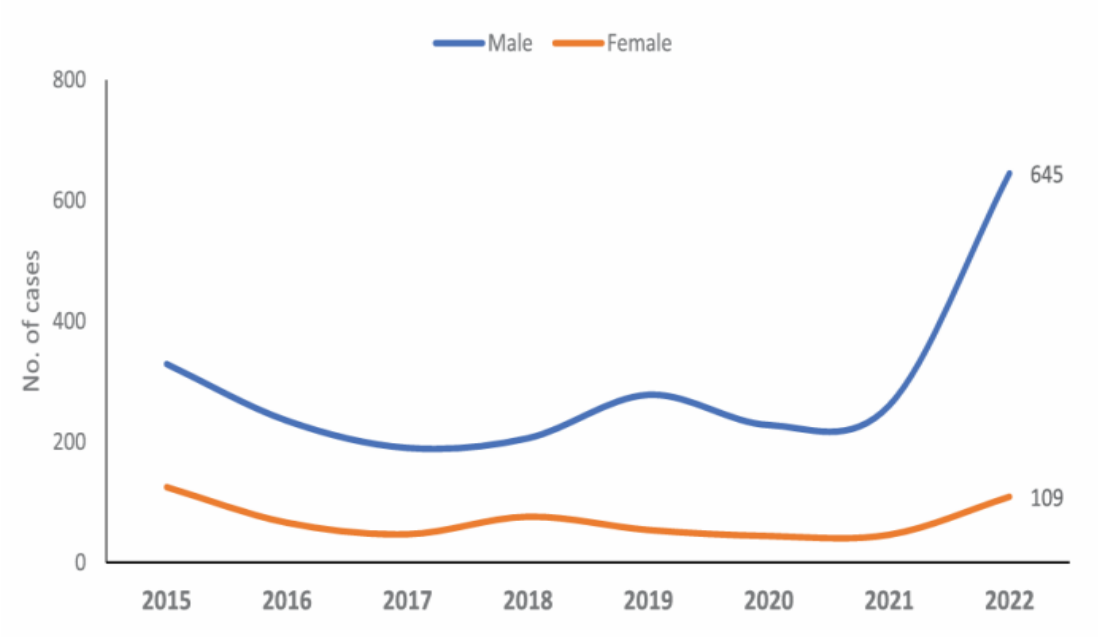
Congenital syphilis per 100,000 live births	**2020**	**2021**	**2022**
Live births	301,706	284,848	275,321
Number of congenital syphilis cases	2	3	1
Annual rate of congenital syphilis per 100,000 live births	0.66	1.05	0.36

WHO's surveillance case definition of congenital syphilis include: (i) a live birth or foetal death at > 20 weeks of gestation or > 500 g (including stillbirth) born to a woman with positive syphilis serology and without adequate syphilis treatment; or (ii) a

live birth, stillbirth or child aged < 2 years born to a woman with positive syphilis serology or with unknown serostatus, and with laboratory and/or radiographic and/or clinical evidence of syphilis infection (regardless of the timing or adequacy of maternal treatment)[12].

According to the WHO case definition, only one case of congenital syphilis was reported in 2022 in Sri Lanka. The number of live births in the country has been declining over the past few years. In 2022, the rate of congenital syphilis per 100,000 live births was 0.36.

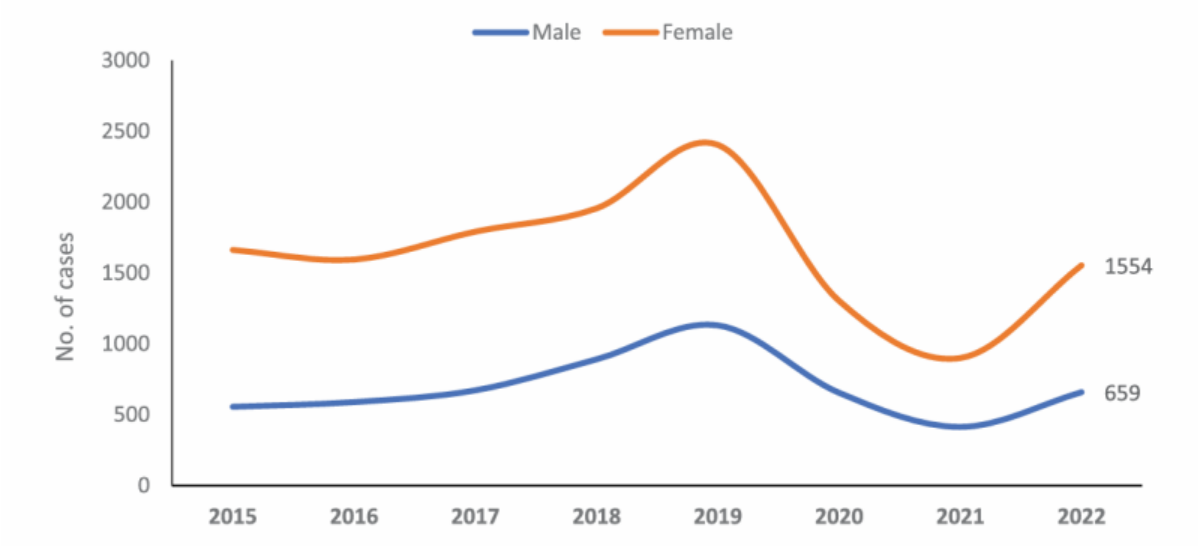
Figure 11: The trends of gonorrhoea cases by sex 2015-2022



Source – NSACP, Annual Report 2022

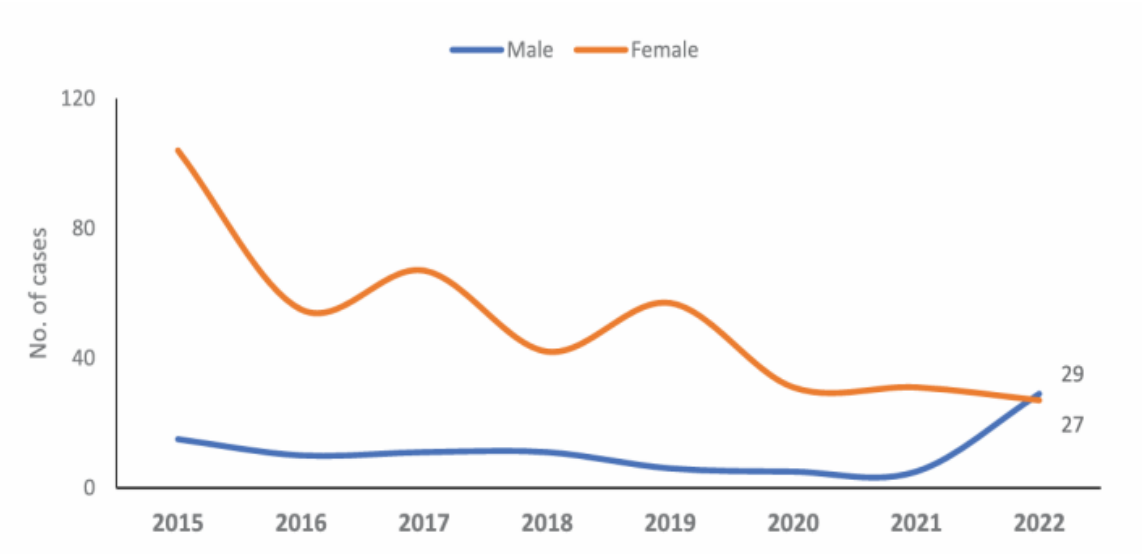
Gonorrhoea is a classic sexually transmitted disease caused by infection with the bacterium *Neisseria gonorrhoeae* (*N. gonorrhoeae*). According to the 2022 data of the NSACP, a significant increase in the number of reported gonorrhoea infections particularly among males accounting for 85.5 % of the total reported cases of gonorrhoea can be observed. Although there was a slight increase among females, it was not found to be significant.

Figure 12: The trend of cases of non-gonococcal infections by sex 2015-2022



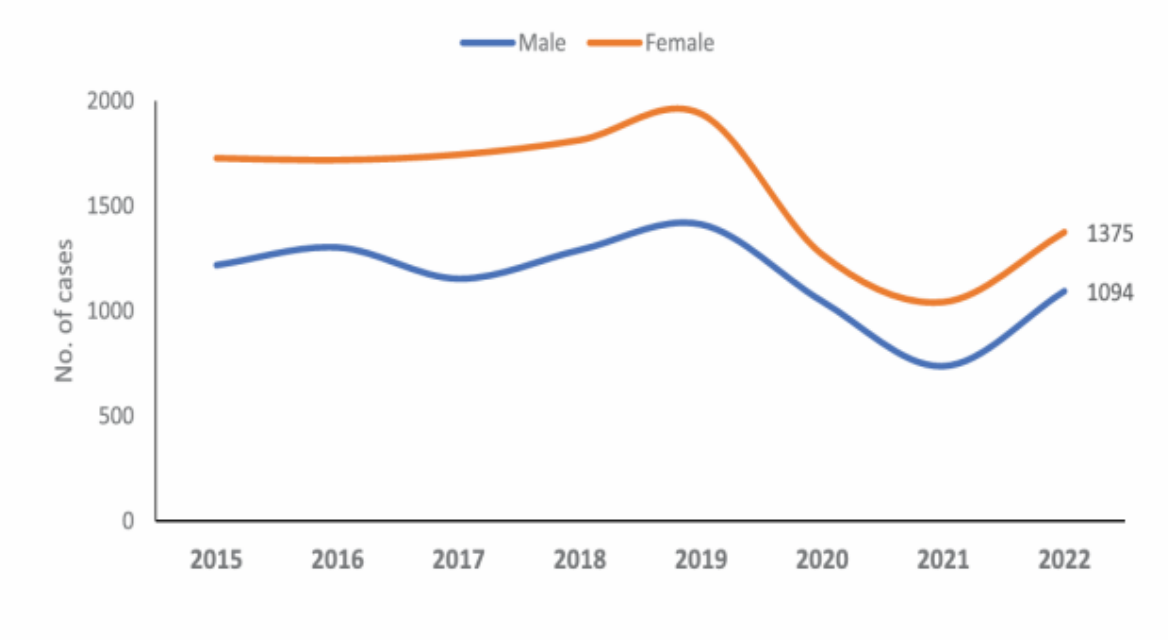
Non-gonococcal infections are those infections caused by pathogens other than by *Neisseria gonorrhoeae*. *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Trichomonas vaginalis*, Herpes Simplex virus, Adenovirus and Haemophilus vaginalis are some of the other pathogens that can cause non-gonococcal infections of the urethra in men and cervix in women. Among the total number of non-gonococcal infections reported in 2022, 70.22% were among female STD clinic attendees, similar to past trends. Non-gonococcal infections were more common among clinic attendees who are over 25 years of age.

Figure 13: The trend of cases of trichomoniasis by sex 2015-2022



Even though infections with *trichomonas vaginalis* is the most common, non-viral sexually transmitted infection (STI) worldwide, trichomoniasis accounted for just 1% of the total STIs reported to the NSACP in 2022. However, an increase in the number of cases among males were noted in 2022 compared to the previous 7 years. It must also be noted that many infected persons may not experience any symptoms[13].

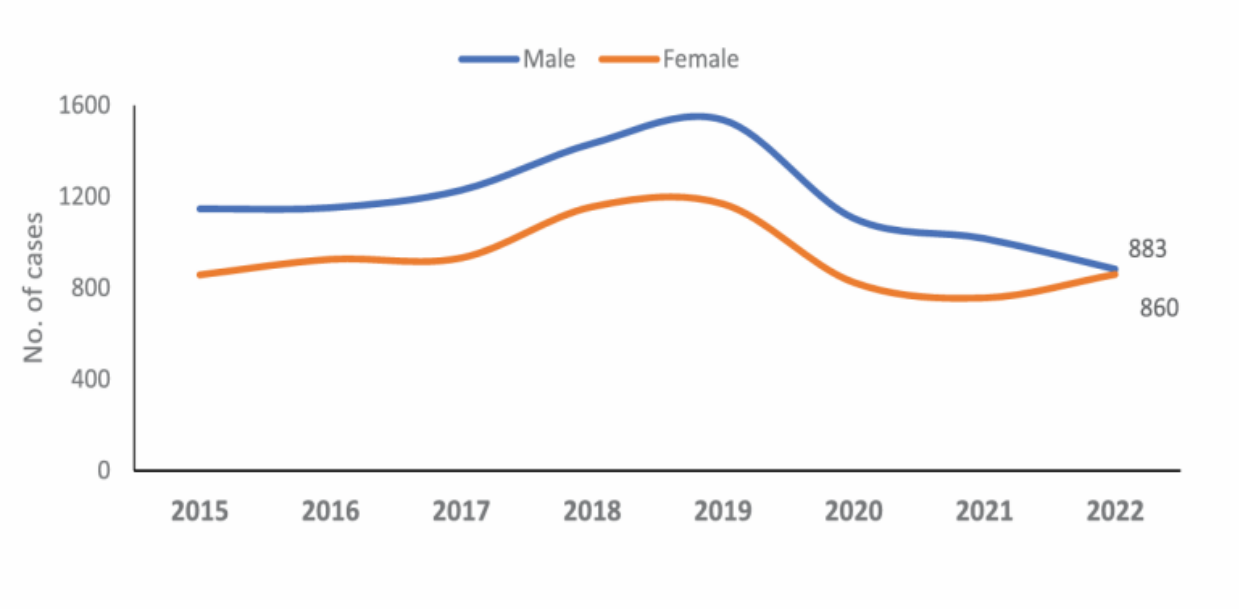
Figure 14: The trend of cases of genital herpes by sex, 2015-2022



Genital herpes is considered a chronic sexually transmitted infection (STI) characterized by recurrent, self-limited genital ulcers, caused by herpes simplex virus. While HSV-1 may cause both oral and genital infection, HSV-2 nearly exclusively causes genital disease. Rates of HSV-2 are highest among women as observed in the Sri Lankan data of 2022 where 55.7% of the total reported cases were among women.

Similar to other STIs, genital herpes (HSV) infections were more commonly reported among clinic attendees over the age of 25. In line with the overall rise in STI cases, genital herpes infections showed an increase during 2022, reflecting the general trend observed for STIs in the country during that period.

Figure 15: The trends of cases of genital warts by sex, 2015-2022



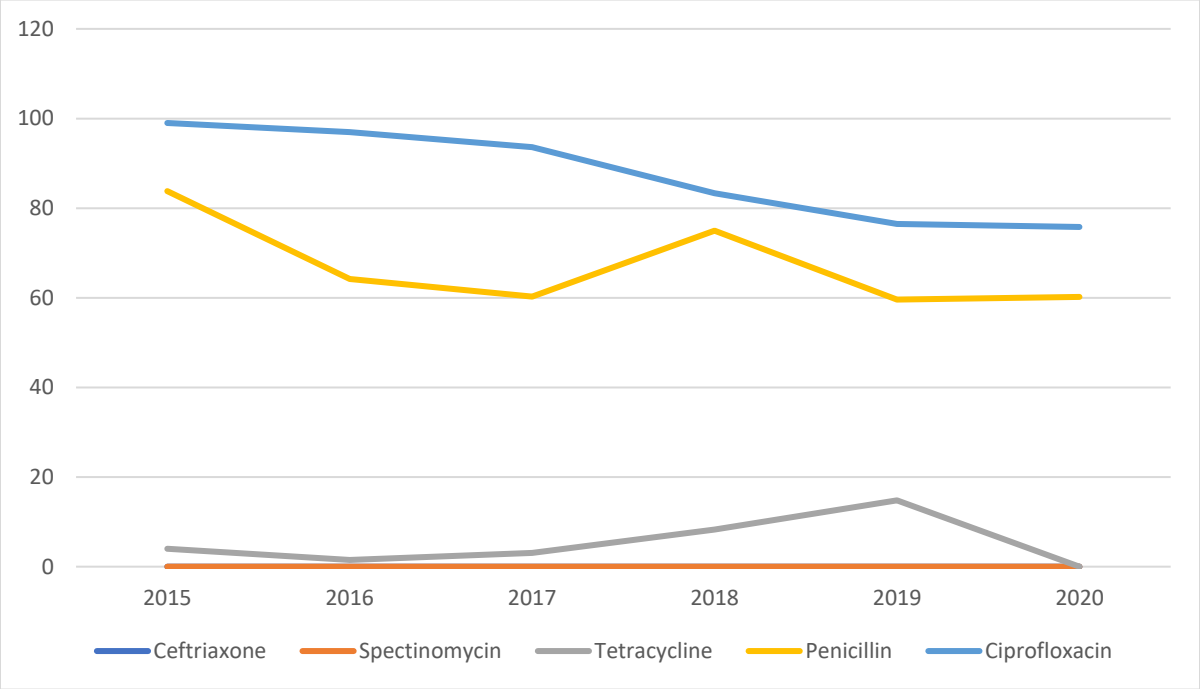
Laboratory services of the NSACP

There are 29 peripheral laboratories in district STD clinics distributed island wide[11]. All STD laboratories have microscopy facilities, VDRL/RPR, TPPA tests, Dual HIV/Syphilis rapid tests and Diagnostic Tests for HIV including ELISA and rapid diagnostic tests. GC culture and antibiotic sensitivity testing (ABST) facilities are available in 7 STD clinics while Nucleic acid amplification testing (NAAT) facilities for chlamydia/gonorrhoea are currently available only at the central STD clinic, Colombo[11].

Sri Lanka is one of the few countries that report gonococcal antimicrobial resistance data. It is fortunate that resistance ceftriaxone has not been detected up to 2020.It is noteworthy that all sexually transmitted infections (STIs), except for genital warts, have shown a rising trend in 2022. Whether the reasons for the increase were due to normalisation of health services that were disrupted during the political upheaval that took place in Sri Lanka in 2021 or whether there has been an increase in unprotected sexual activity among people or a combination of both remains to be seen. The STI trends over the coming years will probably continue to increase unless STI control activities are increased manyfold in the country particularly with newly emerging STIs that are looming on the horizon

Table 6: Antimicrobial resistance patterns for Neisseria gonorrhoeae (%) 2015 - 2020

	2015	2016	2017	2018	2019	2020
Ceftriaxone	0	0	0	0	0	0
Spectinomycin	0	0	0	0	0	0
Tetracycline	4	1.5	3.1	8.3	14.8	NA
Penicillin	83.8	64.2	60.3	75	59.6	60.2
Ciprofloxacin	99	97	93.6	83.3	76.5	75.8



These newly emerging STIs would be more dangerous than the typical STIs because of their unique methodologic and epidemiologic challenges for public health experts and research scientists[14,15].

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Clinical Approach to patient with STIs

Dr Nimali Jayasuriya

The rationale and objectives of the clinical approach for patients with STIs are to diagnose and provide comprehensive treatment and care for specific diseases, detect asymptomatic cases, prevent disease complications, community transmission, and vertical disease transmission, support protective sexual health behaviours, encourage behavioural changes in "at-risk" individuals, promote awareness and linkage to care, and enhance reproductive and sexual health.

Creating a safe and non-judgmental environment for the patient and ensuring the confidentiality of their information is an essential aspect of approaching a patient with an STI. Clinicians should not make assumptions about the gender of partners or about certain sexual behaviours; instead, refer to things in gender-neutral terminology. It's important to use open-ended questions and active listening approaches to explain or confirm the patient's understanding of a particular topic. When actively listening, it's important to focus on instructive, emotional, or missing content. The clinician should be comfortable with the use of a wide range of sexual terms but should not assume the patient knows the meaning of these terms. (e.g. fellatio, anal sex).

History-taking starts with the main complaint and the history of the present complaint. A reason for visiting should always be an open-ended question. The complaint may involve routine STD or HIV screening (such as for a new relationship, unprotected intercourse, or sexual assault), genital or STI-related symptoms, a sexual partner with symptoms or a recent STD diagnosis, a positive test result requiring treatment, follow-up testing or treatment, vaccination, preventive care, counselling, or any other STI-related services or testing. For STI-related symptoms, thoroughly assess and document details of urethral discharge (in males), vaginal discharge (in females), dysuria, urinary frequency or urgency, itching or irritation (affecting the vulvar, anal, penile, pubic, or perineal areas), genital ulcers or lesions, genital warts or lumps, abnormal vaginal bleeding, non-genital skin rashes, pelvic pain, dyspareunia, testicular pain, swelling, or masses. Additionally, include symptoms related to rectal or perianal areas, inguinal lymphadenopathy, and oral lesions or ulcers.

The history of the presenting symptom should be explored in detail to assess the location and characteristics of any lesion, including its onset, duration, progression since onset, recurrence, history of similar symptoms, exacerbating factors, relationship to menstruation or sexual intercourse, and whether any sexual partners are experiencing symptoms.

It is important to ask about the patient's past medical history, as this may influence the investigation, diagnosis and management of a sexually transmitted infection. If the

patient has a medical condition, gather additional details to evaluate how well the disease is managed. Additionally, reviewing the patient's drug history is essential to determine its impact on their sexual health. Some medications are directly relevant to sexual health, like PrEP, PEP, anti-retroviral treatment, and antivirals for recurrent genital herpes. Some medications, such as antibiotics, can cause candidiasis (thrush) or drug eruptions. Understanding the patient's prior history of STIs and previous STI testing simplifies management. Key information includes a history of herpes, genital warts, syphilis, other bacterial STIs, and the date of the most recent HIV test, all of which are crucial when evaluating a patient with an STI.

A gynaecologic history should be taken as part of routine STI care for a female client. Menstrual history, parity (pregnancy history), hygiene practices (douching, shaving, waxing), contraception practices, and about the last pap test need to be assessed.

Obtaining an accurate and detailed sexual history is essential for introducing the comprehensive STI screening package. A sexual history should be obtained at the initial visit, follow-up visit, and whenever a patient presents with a sexual health concern. Reviewing the history at each visit becomes essential since behaviours may change significantly over time, particularly following an important life event like a divorce, moving, or travel. The current recommendation is to use a standardized approach to taking sexual histories to ensure that it is done correctly and completely each time. Generally, a sexual history starts with the question, "Are you currently or have you ever been sexually active?" The CDC has developed a framework called the five P's of Sexual Health, which are five domains that the clinician should consider when eliciting a complete sexual history. These are about: partners; practices; protection from STIs; past history of STIs; and prevention of pregnancy. Details about last sexual exposure, as well as information about the last three months, the last one year, and lifetime sexual behaviours, are among the standard questions of a sexual history. Taking a comprehensive sexual history provides an important opportunity to offer appropriate testing, specific treatment, prophylactic treatment, risk-reduction counselling, partner screening, identifying contraceptive needs, and retesting.

A social history is essential during an assessment for sexually transmitted disease and prevention purposes. Basic social history should include substance abuse, occupation, financial stability, family details, social support, and travel history.

Following a comprehensive history, perform a thorough physical examination, focusing on the genitalia and pelvic area, and look for any signs of infection, such as sores, rashes, discharge, or swelling.

Based on the patient's history, physical examination findings, risk behaviours, and risk category, order appropriate tests for STD screening and identify the sites for sample collection. Common diagnostic tests include nucleic acid amplification tests (NAATs) for detecting chlamydia, gonorrhoea, and trichomoniasis. Blood tests are used to screen for HIV, syphilis, and hepatitis B/C. Swabs and cultures are

recommended for gonorrhoea, herpes simplex virus (HSV), and other infections when lesions are present.

Initiate treatment based on test results and guidelines. Management is based on a laboratory-based diagnosis or syndromic approach. Presumptive treatment is provided based on known contact with the disease, symptoms, signs, and nonspecific laboratory test findings, whereas specific treatment is based on disease-specific laboratory test findings. Antibiotics are commonly used for bacterial infections like chlamydia, gonorrhoea, and syphilis. Antiviral medications are used for viral infections like HIV and HSV. Partner management, treatment, and counselling based on a specific STD diagnosis. Client-centred counselling is initiated on disease-specific, risk-reduction, and partner notification. Patients should be addressed on any psychological or emotional issues related to the diagnosis and provide resources or referrals for counselling if needed. Referrals have to be considered to specialists for complex cases or if specialized care is needed.

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Population at risk and Sexual orientation

Dr Nimali Jayasuriya

Population at risk

HIV can affect anyone regardless of sexual orientation, race, ethnicity, gender, or age. However, certain groups are at higher risk for HIV, categorized into two groups known as key population groups and vulnerable groups. Vulnerable populations are groups of people who are particularly vulnerable to HIV infections due to their living conditions or situations, such as young people, women, migrants, long-distance drivers, displaced populations, men in uniform, and others. Key populations are defined groups that, due to specific higher-risk behaviours, are at increased risk of HIV, irrespective of the epidemic type or local context. They have a higher vulnerability to HIV transmission due to various factors such as social, legal, economic, and structural barriers.

Key population groups are:

1. Men who have sex with men (MSM)
2. Sex workers (female or male)
3. Transgender people
4. People who inject drugs (PWID)
5. People in prisons and other closed settings

***MSM*:** Determinants of HIV transmission among MSMs are multifactorial. Factors related to sexual behaviour play a pivotal role among MSM, including types of sexual practices, multiple partners, anonymous partners, condom less sex, and substance use. HIV transmission occurs much more readily through receptive anal sex compared with penile-vaginal sex.

Sex workers: Persons who exchange sex are at increased risk of getting or transmitting HIV and other sexually transmitted diseases (STDs) because they are more likely to engage in risky sexual behaviours like sex without a condom, sex with multiple partners, and substance use.

Transgender: Transgender people are disproportionately affected by HIV. Particularly transgender women are perceived as the receptive partner during sexual interactions and engage in high-risk sexual activities such as having several partners, having sex in groups, and having sex without condoms.

PWID: Condom less sex and sharing of injection equipment are the behaviours associated with increased risk of HIV acquisition among PWID.

People in prisons and other closed settings: Specific factors responsible for the transmission of HIV in prison settings include injecting drugs with shared, unsterilized needles and syringes; unprotected penetrative sex between men; and tattooing with shared, unsterilized equipment.

In addition to that, Sri Lanka recognizes beach boys (BB) as *a group of key populations in Sri Lanka*. A beach boy is a *male who is a lifeguard or other worker at a* beach. Beach boys act as a bridge for HIV

transmission between higher-risk groups (paying female tourists, men who have sex with men) and the lower-risk heterosexual female population in Sri Lanka.

Sexual orientation

An individual's feelings of romance or sexual attraction to another person are referred to as their sexual orientation. Sexual orientation comes in several forms.

***Heterosexual**:* Individuals who identify as heterosexual have an attraction to people of opposite sex both romantically and physically: heterosexual men are attracted to women, while heterosexual women are attracted to men. Sometimes, heterosexuals are referred to as "straight."

***Homosexual**:* Individuals who identify as homosexual are attracted to other individuals of their own sex both romantically and physically. Lesbians are women who are attracted to other women, whereas gay people are men who are attracted to other men.

Bisexual: Individuals who identify as bisexual have an attraction to people of both genders, both romantically and physically.

***Asexual**:* Individuals who may not be interested in sex, but they have a strong emotional bond with others.

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Syndromic management Vs etiological management of STI

Dr Manjula Rajapakshe

Ideal management of STI involves definitive diagnosis based on clinical signs, symptoms and positive laboratory investigations. However, there may be constrains for laboratory investigations to confirm aetiological diagnoses especially in resource limited settings. Therefore, the concept of syndromic management of STIs was recommended and used in managing common STI syndromes in settings with no or limited laboratory facilities.

Syndromic management of STI involves making clinical decisions based on a patient's symptoms and signs without waiting for the investigation results. It involves using a flowchart (algorithms or decision trees) for the common symptoms and signs of the STD syndrome, such as genital ulcer, urethral discharge, vaginal discharge, lower abdominal pain, scrotal swelling, inguinal bubo and ophthalmia neonatorum (neonatal eye discharge) to

make decisions about the disease management.

In syndromic management the most common pathogens causing syndrome are covered e.g. in the genital ulcer syndrome, most common STIs causing genital ulcers; syphilis, herpes and chancroid are covered while in vaginal discharge syndrome, chlamydia and gonorrhoea causing cervicitis as well as trichomoniasis, candida and bacterial vaginosis causing vaginitis are covered. (details of different syndrome management will be discussed in relevant chapters)

Box 1 Advantages of STI syndromic management

- The algorithms are simple, problem-focused, and based on presenting symptoms.
- Therapy is rapid. Patients can be treated at first visit without need for laboratory confirmation and are therefore not lost to follow-up.
- High cure rates are achievable in the symptomatic groups.
- Money is saved on laboratory tests.
- High coverage rates can be achieved in a population.
- Management can be easily implemented into a primary health care system.
- Even non-medical staff can manage cases with proper guidance.
- Reporting, ordering, and supervision of drugs are simplified.
- Data collection for surveillance and planning is facilitated.
- Reduce ongoing transmission

While in the settings where there is no laboratory support, diseases can be managed fully with syndromic approach while in the settings with microscopic facilities the differential diagnoses can be narrowed down depending on smear results from relevant sites. There are many advantages as well as disadvantages of STI syndromic management. (See Box 1 and 2)

Box 2 Disadvantages of STI syndromic management

- Physicians are reluctant to treat STDs without a definitive diagnosis.
- It is not as effective for women because of low sensitivity and specificity for gonococcal and chlamydial infections.
- Risk assessment is needed to improve effectiveness.
- Even with risk scores, it is not highly sensitive or specific for asymptomatic infections.
- Surveillance of antibiotic susceptibility profiles is required.
- Some algorithms do not provide a second- to third-line treatment.
- Overtreatment may result, with associated increased costs, leading to increased antibiotic resistance.
- Asymptomatic cases are not detected

Due to island wide availability of STD clinics with in-house microscopy and serology facilities in Sri Lanka, it is always preferable to refer patients with STD symptoms to nearest the STD clinic not only to enable aetiological diagnosis and treatment but also to facilitate other important management aspects like screening for HIV and other STI, partner notification, health education, counselling, risk reduction and safe sex promotion.

However, depending on individual patient factors, syndromic management can be used to identify and manage patients in general practice, prison, plantation sector and some primary healthcare settings. Whenever feasible these patients/partners should be referred to STD clinics even after initial treatment for further comprehensive STI management.

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Comprehensive management of patient with STIs

Dr M. K. D. N. Mallikarachchi

Comprehensive management of patients with STIs includes following aspects.

Detail history taking
Physical examination
Investigations
Diagnosis
Treatment
HIV testing and counselling
Health education
Counselling of risk reduction and prevention
Condom promotion and provision
Referral where appropriated
Partner notification
Follow up

Detail history taking and examination.

All patients who present with suspected STI, high risk sexual behaviour or request STI screening should have their full history taken and undergo thorough physical examination. It should be done in a private room with adequate privacy If the patient requests, a clinician of their preferred gender, that should be provided where possible.

Confidentiality needs to be assured before taking the history. The duty of confidentiality to the patient is absolute, except in very specific circumstances, if it is for the best interest of the patient, where another health care worker to be informed, their consent to disclosure should be sorted.

It is important to find out whether patient has any symptoms suggestive of STI. If so, further details of specific symptoms need to be obtained. The clinician needs to ask specifically about any symptoms related to genito-urinary system. The history should also include other associated symptoms to narrow down the diagnosis. (See Box 3)

Box 3 Symptom to be inquired during history taking

○ Stinging /burning when passing urine
○ Urethral discharge and scrotal pain in men
○ Vaginal discharge, lower abdominal pain, painful sexual intercourse, post coital bleeding in women
○ Ulcers around the genital area and anus
○ Painful lumps in groin
○ Rectal discharge, bleeding or painful defecation
○ Itching and/or discomfort in genital area or, peri-anal areas
○ Warty lesion in genital or perianal area
○ Non itchy skin rash, generalized lymphadenopathy, oral mucosal lesions

Furthermore, clinician should get the further information on following aspects.

Sexual history – Aspects relevant to detail sexual history is shown in Box 4.

Previous episodes of STIs – If present what were the previous diagnoses, when was the diagnosis made and were they treated are important points to note down.

Previous and current gynaecological, medical, and surgical history- History of previous blood transfusion and the dates of transfusions and presence of any other significant illnesses

- Menstrual history in females – The first date of the last menstruation and duration, the length of the cycles, regularity and any recent change of the menstruation are some of the important points in the management of the patient.
- Contraception history in females – Information on current use of contraception, any missed pills, previous methods of contraception used, and any associated side effects of contraception will also be helpful in the management of patient.
- Date of last cervical cytology and results, any abnormal previous results and investigations underwent for abnormal smear results
- Details of previous pregnancies and their outcome
- Any medication currently on is needed to be found out to avoid drug interactions and to get an idea about the possibility of having a partially treated STIs. It is important to find out whether patient is already on PrEP to assess the risk for HIV infection
- Known allergies to medication.
- Use of alcohol, recreational drugs, and smoking – This will help to assess the risk behaviours of the patient.

- Social history – knowledge on current living status, social and family support, occupation, education, travelling abroad, recreational activities will be helpful in identifying any vulnerabilities.

Box 4 Components of sexual history

Last sexual exposure (when, with whom, type of sex and use of condoms): Date of the last sexual exposure will be useful in educating the patient on need of repeat testing to cover the incubation period, to give emergency contraception for the female patients and to assess the need of providing post exposure prophylaxis
Sexual history of last three months, one year and lifetime where relevant - To assess the risk of STI /HIV
Possible sites of exposure (oral, vaginal and anal); to identify which sites, need to be sampled and to assess the risk
Number of partners and concurrent partnerships
Gender of sexual partners- same sex, opposite sex, transgender
Types of sexual partners- Marital, regular, casual, or commercial
Sex under the influence of alcohol or any other substances
Involvement in sexual networks
Condom use for different sexual exposures
Details about sexual partners: To facilitating partner notification

Physical examination

Before examination, clinician should explain the patient about the procedure and what to expect. The verbal consent needs to be taken and a chaperon should be offered.

The examination should be carried out in a well-lighted private room to ensure confidentiality. Only the needed parts of the body should be exposed and examined. (Box 5 and 6)

If patient declined the examination after detail explanation, clinician must respect the patient's choice; this should be documented in the notes. The patient may allow examination on a subsequent visit after more trust has been established.

Clean, disposable gloves should be used for all genital examinations.

Box 5 Male genital examination

Observation for any obvious lesions on genital skin
Examination of the inguinal and femoral triangle for the lymph nodes: The inguinal areas and the femoral triangles should be palpated to check for lymphadenopathy.
Examination of the scrotum – Both testicles and epididymis should be carefully palpated for swelling and/or pain
Examination of the penis: The foreskin should first be retracted to look for redness, rash, discharge, warts, and ulcers on the penis.
The meatus should be examined for any inflammation or discharge. If the presenting complaint is urethral discharge and no
obvious discharge is coming from urethral meatus, urethra should be gently milked to see whether discharge is present.
Examination of the perineal area and peri-anal area: The perinium and peri-anal area needs to be visually inspected for any lesions.

Box 6 Female genital examination

Abdominal examination needs to be done beforehand in all women who complaints of lower abdominal pain- Look for guarding rigidity and any tender areas and palpable masses
Look for any lesions on genital skin
Examination of the inguinal and femoral triangle for the lymph nodes: The inguinal areas and the femoral triangles should be palpated to check for lymphadenopathy.
Examination of the vulva: The labia should be separated to visually inspect for any lesions in the vulva eg: erythema, tenderness, ulcers, lumps, warty lesions, inflamed Bartholin's glands.
Examination of the peri-anal area and perineum: The peri-anal area and perineum should be visually inspected for any lesions.
The speculum should be fully inserted and gently opened to visualize the cervix. Assess for increased vaginal discharge, its colour and consistency, lesions in the vagina, cervicitis (swelling, erythema, or contact bleeding), and any lesions on the cervix. After inspection, gently withdraw the speculum while observing the vaginal mucosa
Women with lower abdominal pain should undergo a digital bimanual examination to check for cervical **motion** tenderness or adnexal **tenderness**/masses.

Investigations

Investigations should be tailormade depending on the patients presenting complain and the differential diagnosis. When patients presenting with symptoms the relevant investigations are mentioned in relevant chapters. However, those who are asymptomatic but presenting with high-risk behaviours or requesting STI screening, following investigations are recommended (Box 7)

Box 7 Recommended investigations to identify STIs

Gram stain of urethral smear in males for Gonorrhoea- for the patients who complaints of having urethral discharge, urethral discomfort or dysuria
Gram stain of vaginal smear in females- for the patients with increase vaginal discharge or patients with itching or smelly discharge
Gram stain of cervical smear for Gonorrhoea- when there is evidence of cervicitis
Gram stain of rectal smear for Gonorrhoea- only in patient with evidence of proctitis
Wet smear from vagina to exclude Trichomoniasis in female- patients who have increase itchy discharge
Dark ground microscopy for T. Pallidum- from ano-genital ulcers – (A swab from anal ulcers can also give a false positive on dark ground due to the presence of non-treponemal spirochaetes present in the normal bowel flora).
Urine for CT/GC PCR in males
Urine for Trichomoniasis in males
Urine for *Mycoplasma genitalium* in males
Vulvovaginal swab for CT/GC PCR in women
Vaginal swab for *Mycoplasma genitalium*
Rectal swab for CT/GC PCR (order genotype testing for LGV if positive for Chlamydia)
Faecal specimen for microscopy and culture including ova
Faecal specimen for PCR test of enteric pathogens
A swab for HSV/Syphilis PCR test from any suspicious ulcer
Blood for HIV antibody
Blood for TPPA/RPR/VDRL
Blood for Hepatitis B screening (Hepatitis B surface antigen, Hepatitis B core antibody and Hepatitis B surface antibody- only with a history of vaccination)
Blood for Hepatitis C antibody/antigen
Blood for Hepatitis A screening

Diagnosis

Diagnosis needs to be done based on history, finding of examination and investigation results.

Treatment

Treatment should be given to the identified condition after explaining the condition to the patient. Dose and duration of the medications, possible drug interactions, side effects need to be discussed with the patient.

HIV testing and counselling

- All the clients receiving STI care services should be offered HIV screening following provision of brief pretest information and obtaining informed consent.
- Post test counselling needs to be arranged before provision of HIV test results.
- HIV positive and indeterminate results should be given only in person.
- If Positive or inconclusive HIV results client need to be referred immediately to nearest STD clinic for further investigations and counselling.

Health education

Educating a patient is a very important interactive process that involves assessing what the patient already knows about his/her infection and then discuss more about it to improve the knowledge. The nature of the infection, its consequences, transmission, the importance of complying with treatment and follow up should be discussed. It should promote safer sexual behaviour and educate patients on how to minimise or eliminate the risk of acquiring or transmitting a STI/HIV in future.

Risk assessment and counselling on risk reduction and prevention

Risk assessment, risk reduction and prevention counselling are an important aspect of sexual health care. It will enable the clients to understand and perceive their own risk for STI and HIV transmission. It will also help the client to understand the available risk reduction and prevention options and take informed decisions on how to reduce their risk of acquiring STI and HIV in the future. should give positive health benefits to the individual and their sexual partners and prevent the spread of STIs/ HIV. Counselling may consist of but not limited to practicing safer sex, including the use of condoms, PrEP, PEP, mutual monogamous relationships, reducing number of sexual partners and avoid sex under the influence of recreational drugs or alcohol.

Condom promotion and provision

Condoms should be always promoted even for the patient who are on PrEP to prevent other STIs. Correct method of condom use should be discussed and demonstrated to the patient. Free male/female condoms need to be provided from the clinic. In addition, myths and misconceptions related to

condoms need to be discussed and addressed appropriately.

Referral to other health sectors where appropriated

If patient is having any evidence of any other associated medical problems or he or she needs to be seen by some other speciality due to a complication of STI, the patient should be referred to the relevant unit without a delay with a proper referral letter after discussing with the patient.

Partner notification

Partner notification includes informing sexual partners about possibility of having a STI, encouraging partners to attend for treatment and the provision of presumptive treatment. The patient could inform all his/her partners about the infection and need of treatment (patient referral) and get down for the treatment. If the patient is not willing to inform the partners, the contact details of partners can be collected by the health care providers and trace the partners maintaining the privacy and confidentiality of the index patient (provider referral).

The partners of the index patient should also receive comprehensive case management, (Box 8)

Box 8 Components of partner management

Same treatment as the index patient regardless of negative investigation results when appropriate
Any additional treatment according to the results of investigations
Health education
HIV testing and counselling
Risk reduction counselling.
Condom promotion/ demonstration and provision
If positive for any STIs, information on how their partners can be treated and contact referral slips for their other partners need to be given
Follow up (if needed)

Follow up

Patient follow-up is vital to ensure cure, to identify any side effects of treatment, detect any signs of complications, exclude reinfection, ensure partner treatment and to reinforce STI prevention strategies.

Association of HIV and other STI's

Dr Piyumi Perera

It is proven that there is a relationship between HIV (Human Immunodeficiency Virus) and other sexually transmitted infections (STIs), which is known as "epidemiological synergy", as they share a common mode of transmission. The interplay between HIV and STIs is complex and has significant implications for public health, individual treatment, and prevention strategies.

There is a strong association between "Classical STIs" and both the acquisition and transmission of HIV infection. Classical STIs are bacterial and viral sexually transmitted infections that cause genital ulcers and genital mucosal inflammation. Examples of these conditions are genital herpes which is an ulcerative condition and trichomoniasis which causes chronic genital inflammation.

Biological Interactions Between HIV and STIs

There are two important concepts to consider in the role of STIs in increasing the susceptibility of HIV transmission

- Increased infectiousness of the HIV-positive person
- Increased susceptibility of the HIV negative person

Increased infectiousness can be due to the increased HIV concentration in HIV genital secretions and changes in viral phenotype of HIV variants that favours transmission.

Increased susceptibility can be due to direct mucosal disruption in genital ulcer disease, and recruitment of HIV target cells to the genital tract with chronic inflammation associated with STIs. For example, HSV-2 can contribute to HIV transmission through disrupted epithelium, recruitment of HIV target cells and increased HIV viral load.

Importance of association of STI and HIV

1. Having a classical STI can be regarded as a proxy measure for possible future HIV transmission risk unless intervened
2. Early identification and management of STIs will minimize this biological association with HIV
3. If a patient is presented with a recent bacterial STI (gonorrhoea/chlamydia/syphilis) that person can be offered with pre-exposure prophylaxis for HIV
4. Other HIV preventive methods such as consistent and correct condom use, and safer sexual practices can be introduced to patients presenting with an STI

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Prevention of STI's

Dr Jayadarie Ranatunga

Preventive health means any action taken to keep people healthy and well and prevent or avoid risk of poor health, illness, injury and early death. Preventing such events requires a complete understanding of the complexity of influences on risk behaviours, which interact with each other on the individual, group, and population levels.

The foundation of an effective prevention intervention at any level is the epidemiologic data related to the diseases. Finding the aetiologies must be appropriately designed so we can identify the points in the causal pathway that will yield the greatest reductions in disease.

Risk factors should be measured on an individual, group, or population level, and the diseases of interest measured in individuals, groups, or populations. The target or beneficiary of the intervention may be an individual, group, or a population. Preventive interventions target those risk factors identified in etiologic research that influence the probability of acquiring infection for individuals, the possibility of transmission within the population and the likelihood that complications will result. An example of an identified risk factor for HIV infection is infection with herpes simplex virus (HSV) based on research. This kind of research are needed at individual and population levels to support development of interventions addressing these risk factors for STDs and HIV. Interventions at individual level benefits populations in general.

For example, peer-led interventions that use individuals to implement change from a group of commercial sex workers benefit not only the individual sex workers but also their clients and the wives and other sex partners of their clients so that ultimately the general population benefits.

Communicable diseases in general, and STDs in particular, are transmitted by intimate person-to-person contact, and thus the risk of acquiring an infection depends on the overall prevalence of infection in the population and contacts between infected and susceptible individuals. This essential feature of communicable disease transmission is known as dependent happenings and is illustrated by the fact that a single infected individual with many exposures can cause infection of many others. Because of this, traditional measures of effect such as attributable risk, may be less significant for STDs than for chronic, noncommunicable diseases. For example, infection with a STD may increase both the infectiousness of an HIV-infected individual and the susceptibility of an HIV-uninfected person and thus, such individual level factors may amplify the spread of infection in the population. Prevention measures should take these factors into consideration. Political conflict, economic and social disruption, and migration directly affect the political hierarchy and social networks

which can change the transmission dynamics.

The concepts of primary and secondary prevention developed for non-communicable diseases, apply equally to infectious diseases, although with some adaptation. The term “primary prevention” generally refers to prevention of the first occurrence of disease, and “secondary prevention” refers to prevention of complications or reoccurrence of disease among those who are already affected. Interventions for STD/HIV differ somewhat from those developed for chronic disease. For example, early detection and treatment provides secondary prevention of complications in the individual patient as well as primary prevention at the population level. Reductions in viral load after initiating ART is another example of a primary prevention treatment intervention to reduce the transmission probability. Prevention of STDs also has powerful political, social, and related economic consequences due to severe stigma and discrimination attached to them. Stigmatizing attitudes can lead to nondisclosure of disease status, negotiation on condom use, or reluctance to seek testing and treatment.

Activities for prevention of STI are actions intended for prevention of transmission, acquisition of or complications associated with STI/HIV. For this purpose, HIV and STI are considered together as, HIV is sexually transmitted, and they share similar behavioural goals and because STIs enhance the transmission of HIV.

A comprehensive STI control strategy includes targeted community-based interventions, promotion and provision of the means of prevention and effective clinical services within an enabling environment, as well as reliable data to guide the response. STI reporting, an important marker of sexual transmission trends, has largely collapsed in some high burden countries fuelling the transmission of HIV.

In Sri Lanka, prevention is one of the main strategic directions identified in the national strategic plan. We have integrated HIV/STI services in standalone clinics manned by Consultant Venereologists or trained medical officers

Priority STI control interventions according to the present epidemic in Sri Lanka mainly include screening, treatment of STI/HIV of high-risk sub populations, comprehensive case management of symptomatic STIs, Antenatal screening (syphilis and HIV), condom promotion and risk reduction by behaviour change. The above goals are best reached by a comprehensive approach, sustained over time and tailored to local needs.

An approach combining and integrating biomedical, behavioural and structural interventions aimed at individual, group and community-level would be the best for prevention of STI and HIV.

A combination approach assuring all the above components should be used for achieving significant long-term gains rather than focusing only on one factor or only one type of intervention.

Eg-Biomedical approaches such as PrEP, will not benefit if there are inequities in access to basic health care due to cost, stigma, discrimination, or criminalization.

Individual level interventions are aimed at changing individual level modifiable factors like increased infectivity or increased susceptibility. These may be biological or behavioural.

1. Biological – infections in the genital tract, cervical ectopy, vaginal flora, immunological competence
2. Behavioural- sexual practices, number, type, temporal spacing, use of condoms, vaccines, microbicides etc

Group level is the most evaluated type of intervention because these work with a group of people who share many common factors. They will be very cost effective in countries with HIV epidemics concentrated in specific subpopulations. Youth, Men who have sex with Men (MSM), Injection drug users (IDUs), Persons living with HIV, prisoners, beach boys are some examples. The selection of subpopulations should be based on country epidemic and available data.

Broader community level approaches are aimed at changing community norms, reaching those that do not come into agencies or health clinics for care and to empower community members. They are best conducted through mass media campaigns, social marketing and community mobilization. To achieve the above, structural interventions are necessary.

Examples of structural changes are community mobilization, integration of HIV services with STI and reproductive health services or broader sexual health services, changing of laws and policies and economic and educational interventions. Structural interventions are difficult to implement but long lasting than individual level interventions

Biomedical interventions are scientifically proven and used widely by many countries. Male and female condoms and other barrier methods are the first and most widely used by all populations. With time and considering the factors for non-adherence with condom use, other strategies came into picture lately. Some examples are Pre exposure prophylaxis (PrEP), Post-exposure prophylaxis (PEP and PEPSE), treatment as prevention, diagnosis and treatment of sexually transmitted infections.

Prevention of mother-to-child transmission of HIV, blood safety and injection safety are also biomedical interventions which are in practice.

Combination of prevention strategies are needed to maintain adherence and avoid sexual disinhibition (risk compensation) while on PrEP. Prevention with positives is also very important in HIV prevention. several sexual risk reduction interventions for persons living with HIV have been developed. Behaviour change for HIV risk reduction may be difficult, in part because behaviours that result in HIV transmission are deeply ingrained and highly pleasurable. However, facilitating behaviour change is central to HIV prevention. Clients must have the right information to change HIV risk behaviours.

Section 3: Bacterial STIs

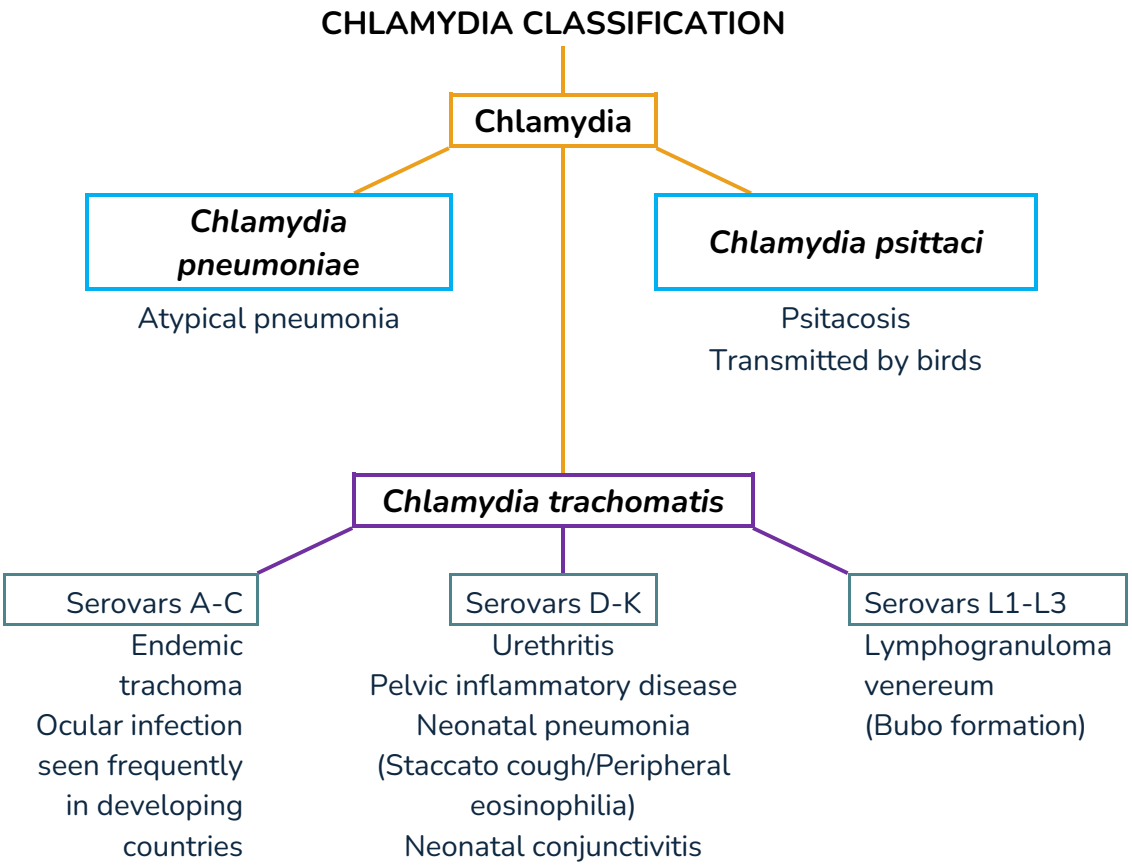
Chlamydial Infection

Dr Kokilanthi Dharmarathne

Introduction

The chlamydiae are a small group of gram-negative, nonmotile, coccoid bacteria that are obligate intracellular parasites of eukaryotic cells. They are entirely dependent on the host cell for ATP and other intermediates, as they are unable to carry out energy metabolism and lack many biosynthetic pathways.

Figure 16: Chlamydia classification



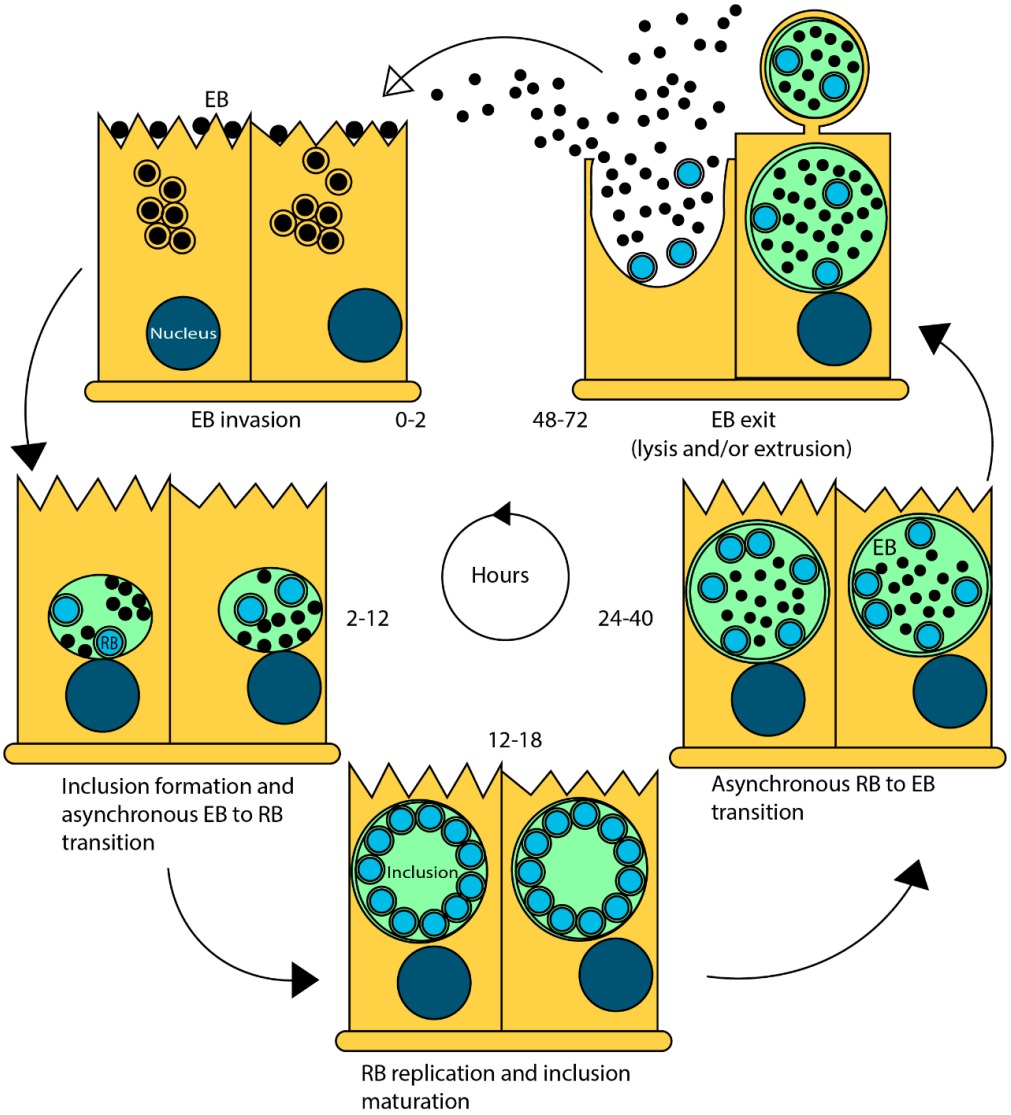
Serovars A-C: A, B, Ba, C (Infect conjunctival epithelial cells)

Serovars D-K: D, Da, E. F, G, Ga, H, I, Ia, J, K (Infect genital tract epithelial cells)
Serovars L1-L3: L1, L2, L2a, L3 (lymphotropic, invasive strains. Infect genital tract epithelial cells and macrophages, causing a more invasive infection than serovars D-K)

The group consists of a single genus, Chlamydia (order Chlamydiales, class Chlamydiaceae) which contains three species, C. trachomatis, C psittaci, and C pneumoniae (TWAR organism). All three species cause disease in humans; C. trachomatis which infects the eye and the genital tract (see Chapter 19), and the two respiratory pathogens C. psittaci and C. pneumoniae. Chlamydia psittaci infects a wide variety of birds and several mammals, whereas C trachomatis is limited largely to humans. Chlamydia pneumoniae has been found only in humans.

Chlamydia life cycle

Figure 17: Chlamydia trachomatis life cycle



All members of the Chlamydia genus cause an intracellular infection with a unique growth cycle, which consist of two alternating, highly specialized morphologic forms. Small (0.3 to 0.6 μm in diameter), metabolically inactive, Elementary Body (EB) is adapted to the extracellular environment, and is the infectious form which is taken up by the host cell. The EB will be differentiated into a much larger (approximately 1 μm in diameter), non-infectious, metabolically active vegetative form known as Reticulate Body (RB), which is adapted to an intracellular environment; hence, this occurs within an intracellular, membrane-bound compartment called the 'chlamydial inclusion', formed within the host cell. Being an obligate intracellular parasite, RB uses energy sources and amino acids of the host cell to replicate. RB re-transform to form new EB, after several replicating cycles producing hundred to a thousand progeny and form new EB to infect additional cells. RB-to-EB conversion is first detected at about 24 h and the developmental cycle ends at 40–48 h.

Chlamydia trachomatis (Serovar D-K) Infection

Pathophysiology

C. trachomatis targets the squamocolumnar epithelial cells of the endocervix and upper genital tract in women, and the conjunctiva, urethra, and rectum in both men and women.

The bacterium is transmitted through direct contact with infected tissue, including vaginal, anal, or oral sex, and can even be passed from an infected mother to the newborn during childbirth.

Clinical features

Approximately 80% of females infected with Chlamydia are asymptomatic, but common clinical findings in those who are symptomatic include dysuria, increased vaginal discharge, post-coital and/or intermenstrual bleeding, and deep dyspareunia.

On examination, signs may include muco-purulent endocervical discharge, erythema and oedema of the cervix, and easily induced cervical bleeding during cervical examination.

Majority (≈80%) of the infected males are also asymptomatic. However, the common clinical features of anterior urethral syndrome among males include dysuria and abnormal urethral discharge characterised by transparent, muco-purulent or purulent urethral discharge.

Complications

In untreated cases, Chlamydia may lead to serious complications, particularly among women. Women may develop pelvic inflammatory disease (PID-endometritis, salpingitis), experiencing acute or chronic abdominal and pelvic pain, which may further progress into pelvic peritonitis and perihepatitis. In later stages, it may cause tubal infertility and ectopic pregnancy as well. Sexually acquired reactive arthritis

(SARA) is a rare complication of chlamydia infection (<1%).

If the infection occurs during the pregnancy, it may lead to perinatal complications including miscarriages, preterm delivery as well as neonatal infection (conjunctivitis/ophthalmia neonatorum, pneumonia as well as oropharyngeal, genital and/or anal mucosal colonisation or infection).

Epididymitis/epididymo-orchitis are not uncommon as complications among untreated males, however, SARA is a rare complication. Subfertility is also a rare complication that may occur in the late stages of the untreated infection.

Lymphogranuloma Venereum (LGV); Chlamydia trachomatis (Serovar L1-L3) Infection

Pathophysiology

Lymphogranuloma venereum (LGV) is caused by one of three lymphotropic, invasive serovars (L1, L2 or L3) of Chlamydia trachomatis, though L2 is the most common strain involved. Serovars L1-L3 do have the ability to infect the genital epithelial cells as well as the macrophages, causing more invasive infection than serovars D-K, which infect only the genital epithelial cells.

LGV generally remains endemic in tropical areas including Southern Africa, West Africa, Madagascar, India, South-East Asia and the Caribbean, however, increasing LGV outbreaks had been reported across Europe since 2003, mainly among HIV-positive MSMs.

Prevalence of LGV in Sri Lanka is not established due to limited diagnostic facilities.

Clinical features

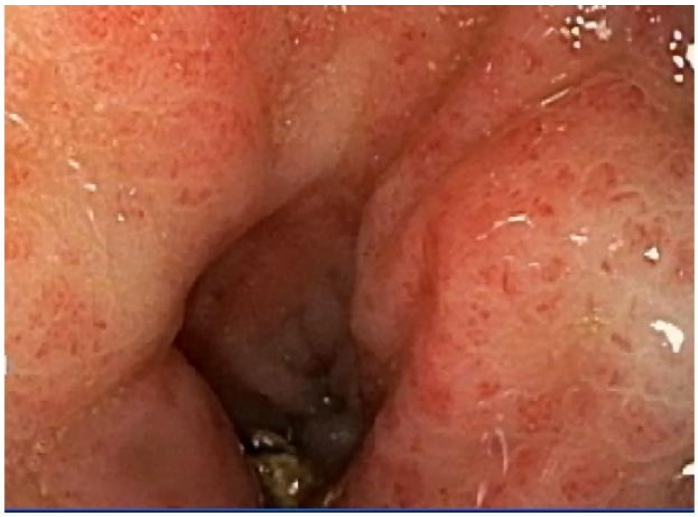
The clinical presentation of LGV can be described in three stages - primary, secondary and tertiary.

Primary LGV

The classic primary lesion is a painless papule or a pustule that may appear following a highly variable incubation period of 3-30 days, which may gradually erode to form a painless, superficial, herpetiform ulcer; the coronal sulcus, prepuce, glans, and scrotum in males and the posterior vaginal wall, posterior cervix, fourchette or vulva of a female are the commonly involved sites. This primary lesion may go unnoticed, due to the painless nature and the involvement of inaccessible anatomical sites. Clinical features of anterior urethritis may rarely occur. The primary ulcer may undergo spontaneous healing without scar formation.

Symptomatic pharyngitis and pharyngeal ulcerations as well as asymptomatic colonisation of the pharynx may occur among both males and females following oro-gental contact with an infected partner.

Figure 18: Haemorrhagic proctitis and/or colitis (Image courtesy: Journal of Investigative Medicine High Impact Case Reports/https://www.researchgate.net and DOI:10.1177/23247096231154649)



Haemorrhagic proctitis and/or colitis characterised by rectal pain, anorectal bleeding/haematochezia, mucoid and/or haemo-purulent rectal discharge, tenesmus, constipation and other symptoms of lower gastro-intestinal inflammation is the common presentation among males having receptive anal exposures. This may also occur among females with or without receptive anal exposures, due to proximity of the genitalia and the anus. Constitutional symptoms such as fever and malaise may also occur in association with proctocolitis. In recent studies, it had been described this haemorrhagic proctocolitis as the more prominent clinical presentation than genital ulceration, markedly affecting HIV infected MSMs.

Although, asymptomatic infection of LGV strains of the rectum is also described, asymptomatic chlamydia trachomatis infection of the rectum is usually due to non-LGV strains; hence it is recommended to treat with doxycycline 100mg BD for 7 days, without routine screening for LGV.

Secondary LGV; lymphadenopathy - Lymphadenitis - Bubo formation

Secondary LGV involves the regional lymph nodes and usually occurs about 2-6 weeks after primary lesion. It may take up to months on rare occasions. Although infrequent, tender inguinal and/or femoral lymphadenopathy is the most common clinical presentation during this stage. It may involve a single node or the entire chain of each group of lymph nodes with considerable peri-adenitis and coalesce to form characteristic 'bubos' (typically unilateral in 2/3 of the cases). The pathognomonic 'groove sign' occurs rarely (10-15%), when both the inguinal and femoral groups of lymph nodes are involved and separated by the inguinal ligament. Bubos may rupture/ulcerate from many sites forming chronic fistulae, otherwise they will

gradually become hardened and undergo resolution.

Inguinal lymphadenopathy occurs among only 20-30% of females, and more commonly observed deep iliac and/or perirectal LN involvement among them may lead to nonspecific abdominal and/or back pain. Pharyngeal involvement may be associated with cervical lymphadenopathy.

Constitutional symptoms such as fever, chills, malaise and myalgia may also be observed in this stage, and the systemic spread may rarely occur giving rise to arthritis, ocular inflammatory disease, cardiac involvement, pulmonary involvement, aseptic meningitis and hepatitis or perihepatitis.

Tertiary LGV; the genito-anorectal syndrome

Most patients recover after the secondary stage without sequelae. The Genito-anorectal syndrome characterised by chronic inflammation and tissue destruction had more commonly been recognised among females secondary to asymptomatic nature of the initial two stages and due to the involvement of deep iliac and retroperitoneal lymph nodes. MSMs are also commonly affected. Chronic inflammation and destruction of tissue may lead to proctitis, proctocolitis mimicking Crohn's disease, fistulae, strictures and chronic granulomatous disfiguring fibrosis and scarring of the vulva with esthiomene.

.

Complications

Destruction of lymph nodes may result in genital lymphoedema (elephantiasis) with persistent suppuration and pyoderma, and an association with rectal cancer has been reported. The two conditions can be confused, and histopathological confirmation may be necessary.

Diagnosis

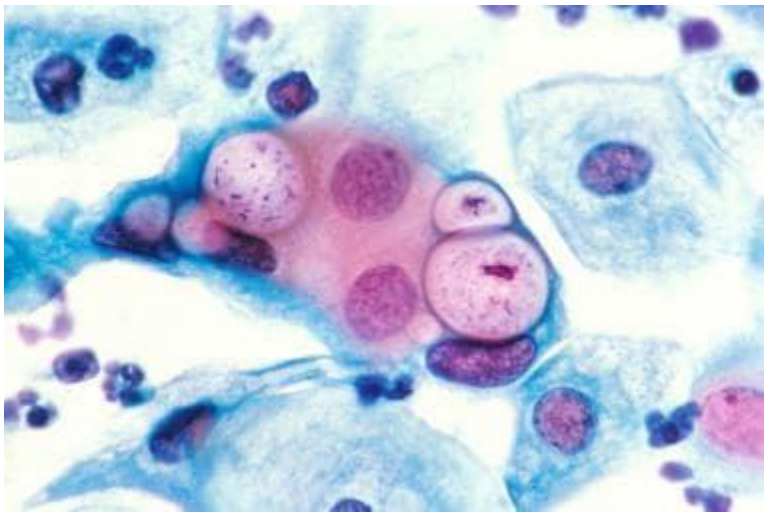
Molecular tests are the gold standard for diagnosing *C. trachomatis* which can be performed in the lab or at the point of care using nucleic acid amplification tests (NAAT).

Urine samples are commonly used for diagnosing chlamydia in men while vaginal swabs are preferred in women. Additionally anal and oropharyngeal swabs are collected according to the exposed sites.

In the presence of chlamydia, tests for other sexually transmitted infections (such as HIV, syphilis and gonorrhoea) are recommended.

The diagnosis of Lymphogranuloma Venereum (LGV) is based on clinical suspicion, epidemiological factors, and the detection of Chlamydia trachomatis through nucleic acid amplification testing (NAAT) at the symptomatic anatomical site. If a rectal swab yields a positive result for Chlamydia NAAT, an LGV-specific NAAT should be performed on the same rectal sample.

Figure 19: Pap smear showing chlamydia in the vacuoles. Magnification, 500x. (Image courtesy of the National Institutes of Health, National Cancer Institute)



Management

Chlamydia anterior urethral syndrome and cervicitis:

The first line treatment for uncomplicated urogenital infection due to chlamydia infection is Doxycycline or Azithromycin. However, Doxycycline is contraindicated in pregnancy, and Erythromycin is recommended.

LGV

The first line therapy for LGV is doxycycline for an extended duration. The second line therapies are Erythromycin and Azithromycin.

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Gonorrhoea

Dr Vino Dharmakulasinghe

Gonorrhoea is a sexually transmitted infection caused by the bacterium *Neisseria gonorrhoeae*, which is classified under the domain Bacteria. It belongs to the phylum Proteobacteria, class Betaproteobacteria, and the order Neisseriales. The bacterium is a member of the family Neisseriaceae and the genus Neisseria, with the specific species being *Neisseria gonorrhoeae*.

Pathogenesis

The pathogenesis of gonorrhoea involves several steps:

Attachment and invasion: The Neisseria gonorrhoea the causative organism initially attach to the mucosal cells of the genital tract and then invade the epithelial cells and replicate within them. The bacteria use specialized appendages called pili to adhere to the mucosal surfaces and then penetrate the epithelial cells.

Inflammatory response: The invasion of the bacteria triggers an inflammatory response in the infected tissues, this response involves the release of cytokines, chemokines, and other inflammatory mediators leading to the recruitment of immune cells such as neutrophils and macrophages to the site of infection. This results in the characteristic symptoms of gonorrhoea, including pain, swelling, and discharge.

Dissemination: In some cases, the bacteria can spread from the initial site of infection to other parts of the body, such as the bloodstream or joints, leading to systemic symptoms and complications.

Immune evasion: N. gonorrhoeae has developed mechanisms to evade the host immune response, including the ability to change its surface antigens, which makes it difficult for the immune system to recognize and eliminate the bacteria.

Clinical features

The clinical features of gonorrhoea can vary depending on the site of infection and the individual's immune response. Common clinical manifestations of gonorrhoea are as follows:

Urethral discharge: In men, gonorrhoea often presents with a purulent or milky discharge from the urethra. This discharge may be accompanied by pain or burning during urination.

Vaginal discharge: Women with gonorrhoea may experience increased vaginal discharge that is often greenish-yellow and accompanied by pelvic pain

Rectal symptoms: Rectal gonorrhoea can cause discomfort, discharge, and pain during bowel movements, particularly in individuals who engage in receptive anal intercourse.

Pharyngeal symptoms: Gonorrhoea can infect the throat, leading to symptoms such as a sore throat, difficulty in swallowing, and swollen lymph nodes in the neck

Asymptomatic infection: It's important to note that many individuals, particularly women, may have asymptomatic gonorrhoea, meaning they do not experience noticeable symptoms. However, they can still transmit the infection to others.

Complications

Gonorrhoea can lead to several complications if left untreated or inadequately treated. Some of the potential complications of gonorrhoea include:

Pelvic inflammatory disease (PID):

Gonorrhoea can ascend into the upper reproductive tract in women, leading to PID. PID is a serious infection of the female reproductive organs, including the uterus, fallopian tubes, and ovaries. It can cause chronic pelvic pain, infertility, and increase the risk of ectopic pregnancy.

Epididymo-orchitis:

Gonorrhoea can ascend and cause the inflammation of the epididymis and the testicle. This condition can present pain, swelling, and redness in the scrotum.

Infertility:

Both men and women can experience infertility because of untreated gonorrhoea. In women, PID can damage the fallopian tubes, leading to infertility. In men, gonorrhoea can cause epididymitis, which can result in scarring and blockages in the reproductive system.

Disseminated gonococcal infection (DGI):

In rare cases, the bacteria can spread through the bloodstream, leading to DGI. This can cause symptoms such as arthritis, skin lesions, and inflammation of the tendons and joints, leading to serious and potentially life-threatening complications.

Diagnosis

Presently, several different techniques are available for Neisseria gonorrhoeae detection as follows

Nucleic Acid Amplification Tests (NAATs):

These tests detect the genetic material of the bacteria in samples collected from the site of infection (e.g., urethra, cervix, throat, rectum). NAATs are highly sensitive and specific for gonorrhoea diagnosis.

Gram Stain:

A gram stain of urethral, cervical, or rectal discharge can reveal the presence of gram-negative intracellular diplococci, which are characteristic of *Neisseria gonorrhoeae*.

Culture:

A culture test involves growing the bacteria in a laboratory setting from samples taken from the infected site. Cultures are less commonly used nowadays due to the higher sensitivity of NAATs.

Antibiotic Susceptibility Testing:

This test determines which antibiotics would be effective in treating the specific strain of Neisseria gonorrhoeae. Given the increasing prevalence of antibiotic-resistant

strains, this test is crucial for guiding appropriate treatment.

The Gonococcal Antimicrobial Susceptibility Programme (GASP) is a global surveillance program that monitors the antimicrobial susceptibility of *Neisseria gonorrhoeae*,

Management

The management of gonorrhoea typically involves a combination of antibiotic therapy, partner notification, and follow-up testing.

Antibiotic therapy

Due to the increasing prevalence of antibiotic-resistant strains, healthcare providers may need to consider the local antimicrobial resistance patterns when selecting the appropriate antibiotic regimen. Commonly used antibiotics for gonorrhoea include ceftriaxone and cefixime.

Follow-up by test of cure (TOC) of patients treated for gonorrhoea is important to ensure that the infection has been successfully treated.

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Syphilis

Dr Priyantha Weerasinghe

Introduction

Syphilis is a sexually transmitted infection caused by the bacterium, *Treponema pallidum*. It can be transmitted vertically from infected mother to foetus. Rarely, transmission other than sexual contact occurs through direct contamination with the organism or via infected blood.

Three subspecies of *Treponema pallidum* are described, and they have been classified as *T. pallidum* subsp. *pallidum* (causative agent of syphilis), *T. pallidum* subsp. *pertenue* (causative agent of yaws), and *T. pallidum* subsp. *endemicum* (causative agent of bejel). *T. carateum* is the agent of pinta. They are morphologically identical. Other than syphilis, other infections are rarely reported today.

Treponema pallidum is a spirochete, slender organism, can be seen through dark ground microscopy. The pathological strains of *Treponema pallidum* cannot be cultured. Commensal species of treponemas could be found in oral cavity, intestine, and genital areas of humans.

Treponema pallidum causes primary skin or mucous membrane lesions. Then disseminated infection and sometimes it can cause recurring lesions. It is known to cause chronic asymptomatic infection in some cases (Box 9). Only in occasional cases can lead to disfiguring and destructive late manifestations after many years.

Transmission of infection and natural history

Syphilis is acquired through unprotected sexual intercourse with an infected partner. The organisms invade the body though minute abrasions in the contact epithelium. Natural course of the illness may follow different stages and may span for many years. Rarely few might show intrinsic resistance to syphilis acquisition, and some may asymptomatic throughout. Infected person with syphilis usually becomes sexually non-infectious after 2 years of infection. However, mother to child transmission remains possible for many years after the infection.

Clinical manifestations of syphilis are generally due to inflammatory and immune response rather than direct cytotoxic effect by *T. pallidum*.

Box 9 Classification of Syphilis

Early acquired syphilis	Late acquired syphilis
• Primary syphilis	• Late latent syphilis
• Secondary syphilis	**Tertiary syphilis**
• Early latent syphilis	• Gummatous
	• Cardiovascular
	• Neurological

Congenital syphilis
- Early: Diagnosed in the first two years of life
- Late: Presenting after two years of life

Primary syphilis

This usually starts 9 to 90 days of primary contact. Primary syphilitic ulcer can occur at the site of initial penetration. It usually starts with red papule resulting from infiltration of lymphocytes and plasma cells.

Later it progresses to form an ulcer classically described as "Chancre" caused by thrombotic obstruction of blood vessels and marked inflammatory changes known as endarteritis obliterans. It is typically a single, painless, indurated clean ulcer discharging clear serum. Non tender bilateral regional lymphadenopathy is commonly seen. However, chancre may be multiple, painful, with purulent discharge, and could occur at extra-genital sites depending on the site of exposure.

In heterosexual males, ulcer often occur at the penis, while in females, they are commonly found on labia, fourchette, or cervix of women. Most of the time primary syphilis go without any notice among females as it is painless and often hidden. Similarly anal or rectal chancre among homosexual males may also go unnoticed.

Secondary Syphilis

Secondary syphilis is due to spread of organism throughout the body and immunological reactions of the host. It generally occurs 7 - 10 weeks after infection or 6 - 8 weeks after the appearance of primary lesions.

This stage is characterized by skin lesions, commonly presenting as maculopapular rash on the trunk, extremities of the body such as palms and soles. Rash could be papular or macular in some cases. The rash is usually non-itchy. Involvement of the mucous membrane can result in mucous patches and generally observed in the buccal, lingual, and genital mucosa. Condylomata lata are hypertrophic lesions occurs in warm moist areas of the body and

are considered as highly infectious with full of spirochetes.

Generalized lymphadenopathy is commonly seen in secondary syphilis. Alopecia and uveitis are less common manifestations of secondary syphilis. Clinically apparent hepatitis or sub clinical hepatitis, glomerulonephritis, splenomegaly are rarely seen.

Asymptomatic CNS involvement may occur during this stage. Some individuals can develop symptomatic neurological complications such as meningitis and cranial nerve palsies.

Latent syphilis

This is defined as having serological evidence of syphilis without clinical manifestations.

Latent syphilis is divided into early latent and late latent stages, considering the time of acquisition of the infection. If the infection is acquired within 2 years, it is called early latent syphilis. If it acquired after more than 2 years, it is called late latent syphilis. Generally early latent syphilis is considered as sexually infectious whereas late latent syphilis is generally considered sexually non-infectious. However, vertical transmission is possible for few years.

Tertiary syphilis

Untreated syphilis may result in late manifestations of illness involving the skin, bones, viscera, central nervous system, heart and great vessels. Time interval may vary from 1 to over 20 years from the acute infection to clinical onset of the late or tertiary stages of disease. However, late syphilis is rarely seen now, except for neurosyphilis, possibly due to the widespread use of antibiotics which may have a treponemicidal action.

Neurosyphilis

Central nervous system could be affected at any stage of the syphilis, and clinical features are varied. Nearly up to one third of patients with primary and secondary syphilis have shown certain features of CSF abnormalities. However, clinical significance of such abnormalities is not evident and routine CSF evaluation is not recommended for patients with primary or secondary syphilis unless neurological manifestations are seen. Only 1 – 2 % of patients with secondary syphilis can manifest clinical features of central nervous system involvement such as acute meningitis and features of uveitis.

Generally, majority of patients with syphilitic meningitis, it is developed within one year of syphilis acquisition. In some patient's, meningitis is the first clinical manifestation. Clinical features of increased intracranial pressure and basilar meningitis which can present as cranial nerve palsies particularly third, sixth, seventh, and eighth are the two common presentations of syphilitic meningitis. Sensory neural deafness can occur in some patients with association of other cranial nerve palsies or as an isolated eighth nerve palsy, and manifest as deafness.

CSF examination shows elevated pressure, mononuclear pleocytosis, elevated protein

levels, and reduction in glucose in some cases. The CSF VDRL is reactive in most, and it is almost diagnostic of neurosyphilis in non-traumatic tap. However, non-reactive CSF VDRL does not exclude the diagnosis. In isolated otosyphilis isolated occulosyphilis CSF VDRL could be entirely normal.

End-arteritis due to extensive inflammation, meningeal infiltrates with plasma cells, and lymphocytes leading to thrombosis, vascular obstruction causing cerebral infraction are the pathophysiological changes seen in syphilitic meningitis. These can lead to basilar meningitis and increased intracranial pressure.

Meningovascular syphilis is a form of vascular syphilis due to underlying endarteritis and infraction. it can occur as early as 3 – 5 years of infection and can go up to 10 years of infection and it can go up to even 25 to 30 years. There are two such presentations.

Focal infectious arteritis resulting infraction and meningeal inflammation in a vascular bed is the main pathophysiology and presentation depends on the vessels involved. The most common involvements are the territory of the middle cerebral artery, but any other artery may be affected.

The most common manifestations are hemiparesis or hemiplegia, aphasia and seizures. The possibility of meningovascular syphilis should be considered in a young adult presenting with cerebro-vascular accident without usual risk factors. They can have features of prodrome prior to manifestation such as headache, memory impairment.

Meningovascular syphilis of the spinal cord could occur as syphilitic meningomyelitis and spinal vascular syphilis.

General paresis and Tabes dorsalis are due to parenchymous involvement of the disease process. Pupillary abnormalities are common with this late manifestation.

General paresis (also named as paretic neurosyphilis, dementia paralytica, and general paralysis of the insane) results in direct invasion of the cerebrum by *T. pallidum*. This occurs usually after a period of 20–25 years of primary illness.

General paresis presents with combination of both psychiatric and neurological manifestations, and the illness is commonly insidious in onset. The clinical manifestations are due to underlying cortical neuronal loss. The early presentation is usually with psychiatric manifestations, and depression may be the predominant presentation. As disease progress gradual memory and cognitive impairment, personality changes, emotional liability, psychosis and dementia are seen. Adult-onset seizures and hemiparesis are late manifestations of GP.

Tabes dorsalis is described as the longest of neurological complication to develop. It is due to inflammatory changes in dorsal column and nerve roots in spinal cord. Clinically present as lightning pains and ataxia. Neurological findings of absent deep tendon reflexes, Argyll Robertson pupils, and a positive Romberg sign are evident. Charcot's joints, and malperforant ulcers are late manifestations due to sensory loss and repetitive trauma.

Cardiovascular syphilis

The cardiovascular system involvement is a late manifestation of syphilis. It can affect up to 10 % or less patients with syphilis. Most common manifestation is aortitis usually in ascending aorta. Underlying pathophysiology is obliterative endarteritis of the coronary arteries near the ostia or vasa vasorum of aorta.

Other manifestations are aortic aneurysms, aortic regurgitation, coronary artery stenosis and myocarditis. Syphilitic aneurysms virtually always involve the thoracic aorta, particularly the ascending aorta immediately at and above the sinuses of Valsalva.

When coronary arteries are involved, it affects almost always only the ostia or the most proximal few millimetres of the coronary arteries. The classical angiographic presentation would be isolated right or left main coronary ostial narrowing with absence of atherosclerosis in the rest of the coronary tree in a person with history of syphilis or other signs of cardiovascular syphilis.

Gummatous syphilis

Generally, after about 15 years of latency, although it can be described even before that. Any organ can be affected but commonly seen in skin and bone. Underlying pathology is proliferative granuloma, with inflammatory response to a few organisms. However, demonstration of *T pallidum* in lesions is difficult in the lesion.

Gummatous syphilis may manifest as osteitis of the nasal bones, hard palate, and nasal septum. It can occur virtually in any organ and manifestations vary with the organ affected. Two forms of skin lesions were described, a nodular or noduloulcerative and a solitary lesion.

Radiological, ultrasonic, and histological assessments are helpful in confirming the diagnosis of the gummatous syphilis.

Diagnosis of Syphilis

Darkfield Examination

The most precise method of confirming the diagnosis of primary syphilis is demonstrating of treponemes with classic characteristic appearance by darkfield microscopic examination of exudate obtained from the surface of the chancre.

T. pallidum is slender, actively motile with sudden bending motions. It is helpful in identification of organism in penile samples by an experienced laboratory staff member. However, it is not ~~very~~ reliable in samples from rectum and not recommended for oral samples where commensal treponemes likely to be present.

No method has been developed for culture outside of animals. PCR-based tests have been developed but are not widely available.

Blood tests to detect infection

Serological tests for syphilis can be divided into two broad categories.

Non-specific / Non treponemal tests: measure antibody to diphosphatidylcholine or cardiolipin. VDRL (Venereal Disease Reference Laboratory Test), and RPR (rapid

plasma reagin) are the widely used tests. Useful as a screening test and assessing the response to treatment.

Non-specific tests can give rise to false positive reactions with many conditions other than syphilitic infection. Once VDRL / RPR is reactive or positive, it needs to be confirmed with treponemal specific test.

Sometimes VDRL / RPR test may remain positive at a low level throughout life even after treatment, this is called sero-fast reaction.

Specific Treponemal Tests: Measure / detect treponemal antibody, and many tests are available. Widely used and available tests are *Treponema pallidum* haem-agglutination assay (TPHA) and *Treponema pallidum* particle agglutination assay (TPPA).

As these are specific tests to detect treponemal infection, positive result indicates the disease. However, these antibodies usually positive for ever once developed, even successfully treated individuals remain positive for life.

Other specific tests not widely available, and usually available in reference laboratory are treponemal enzyme immunoassay (EIA) or treponemal chemiluminescent assay (CLIA), fluorescent treponemal antibody absorption test (FTA-abs) and *Treponema pallidum* immunoblot.

Congenital syphilis (CS)

Congenital syphilis is result from untreated maternal syphilis causing the infection of foetus in-utero. Placental infection with *T. pallidum* occurs during maternal spirochetemia, mostly seen in secondary stage. Nearly almost all foetuses can be affected by untreated primary or secondary syphilis during pregnancy, and many results in preterm delivery or perinatal death. Nearly 40% of untreated early latent syphilis during pregnancy can have adverse foetal outcomes.

When it comes to untreated late latent syphilis, nearly 10% of such infants show signs of congenital syphilis.

Syphilis is generally sexually non-transmissible 2 years after acquisition, but untreated women with syphilis can transmit the infection to foetuses for many years after acquisition.

CS is divided into early (diagnosed in the first two years of life) and late (presenting after two years). Many congenital syphilis cases are asymptomatic at birth, and present with symptoms by five weeks' time.

Early congenital syphilis:

The severity of clinical manifestations is highly variable from severe life-threatening multi-organ involvement to clinically silent radiologic or laboratory abnormalities. Underlying pathophysiology is ongoing active infection with T. pallidum and the inflammatory manifestations of various organs and tissues affected by the organism. Many affected babies are asymptomatic at birth, and most develop clinical manifestations by five weeks. Clinical features include haemorrhagic rhinitis (bloody snuffles), skin rash commonly maculopapular but could be any form and

vesicles or bullae. Generalized lymphadenopathy, hepatosplenomegaly and skeletal abnormalities are commonly seen.

Late congenital syphilis:

Late congenital syphilis, commonly described as stigmata of congenital syphilis corresponds to tertiary syphilis in the adult. This is due to delayed consequences of localized inflammatory process to treponemal infection, and late congenital syphilis is not infectious. Generally cardiovascular system is spared in the child. Manifestations are seen in bones, skin, soft tissues, eye, ear, and central nervous system. Clinical manifestations include interstitial keratitis, Clutton's joints, Hutchinson's incisors, mulberry molars (maldevelopment of cusps of first molars), high palatal arch, rhagades (peri-oral fissures), sensorineural deafness, frontal bossing, short maxilla, protuberance of mandible, saddle nose deformity, sterno-clavicular thickening, paroxysmal cold haemoglobinuria and neurological involvement.

Prevention of CS

Prevention of congenital syphilis depends on identification of maternal syphilis in early pregnancy. All pregnant women should have the screening test for syphilis in early pregnancy and any mothers with added risk need to be offered repeat testing in third trimester. If found to be positive, such mothers need to be identified and confirmed with additional tests. All pregnant mothers with confirmed syphilis should be managed according to the stage of infection and sexual partners need to be managed accordingly. Pregnant mother needs regular follow-up VDRL, and baby should be managed accordingly. By following these measures, congenital syphilis can be prevented successfully. (Refer **Guidelines on Management of Pregnant Women with Syphilis 2024-NSACP publications)**

HIV and Syphilis

Manifestations of syphilis may be altered by concurrent HIV infection.

Treatment

Treatment based on the stage and the involvement of nervous system.

Recommended treatment for primary syphilis, secondary syphilis and early latent syphilis are

- **A single dose of 2.4 million units of benzathine penicillin IM**
- Doxycycline 100 mg twice daily for 14 days is an alternative

Late Latent syphilis or syphilis of unknown duration need to be treated with

- **Benzathine Penicillin 2.4 million units IM weekly for 3 weeks.**
- Doxycycline 100 mg twice daily for 28 days if Benzathine Penicillin cannot be given.

Partner treatment is indicated for primary, secondary and early latent syphilis. For late syphilis, screening of current sexual partner is recommended.

For More details of treatment and partner treatment Please refer STI management guideline

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Chancroid

Dr Dileka Sonnadara

Introduction

Chancroid is sexually transmitted infection caused by *Haemophilus ducreyi*, a Small Gram-negative anaerobic coccobacillus occurring in chains. *H. ducreyi* is a fastidious organism and most clinical isolates are β-lactamase producers.

Epidemiology

Chancroid is gradually disappearing from most countries where *Haemophilus ducreyi* was previously epidemic, except of North India and Malawi. Sporadic cases were reported from Western Europe, often initially misdiagnosed as genital herpes. In contrast to a sustained reduction in the proportion of genital ulcer disease (GUD) caused by *H. ducreyi*, the bacterium is increasingly found in tropical countries– especially, the South pacific region– as a common cause of non-genital cutaneous ulcers, mostly in children. Coinfections of *H. ducreyi with Treponema pallidum* and HSV infection found in over 10% in African studies. In UK, most cases are either acquired abroad or from partners who have travelled. A few sporadic outbreaks have occurred in Europe and the USA.

Transmission

Primarily sexually transmitted including oral sex, but also be auto- inoculated, especially by fingers. Infection rate from male to female 60%. Carriage of *H. ducreyi* without symptoms or signs has been reported in sex workers, who may serve as reservoirs. There is no evidence of congenital or perinatal transmission.

Clinical features

- Incubation period: 3 – 7 days (range 1–14 days).
- Initial tender red papule, which progresses to a pustule then an ulcer after 2– 3 days.
  Pustules, which rupture after a few days and develop into superficial ulcers with ragged and undermined edges. The bases of the ulcers are granulomatous with purulent exudate. The ulcers are soft and painful and may persist for months if left untreated. Secondary superinfection may cause induration. Ulcers can be single or multiple. Multiple ulcers may be facilitated by auto-inoculation — "kissing" lesions. Ulcers may coalesce into giant ulcers.
- Males: prepuce (may cause phimosis), coronal sulcus, frenulum and anus (MSM)
- Females: labia minora, fourchette, rarely vagina, cervix, & perianal region
- Extragenital: very unusual (fingers, breasts, conjunctivae)
- Inguinal lymphadenopathy: usually unilateral occurring in approximately 50% as a tender swelling, which may develop into a unilocular abscess (bubo) in 25%.

Extra anogenital skin ulcers due to *H. ducreyi* (or cutaneous chancroid) have reported in children and adults and may cause diagnostic challenge. Disseminated infection has not been reported.

Complications

- Bacterial superinfection can cause tissue destruction (phagedenic chancroid)
- Chronic suppurative inguinal sinuses.

Diagnosis

NAAT (Nucleic acid amplification techniques)

Most sensitive technique which is 95% sensitive compared with culture. As these methods do not depend on live bacteria, samples may be analysed in laboratories placed remotely from the patient, which is relevant in low facility settings.

The exudate from the ulcer should be collected by vigorous rubbing of the base of the lesion with a sterile cotton-tipped swab and no specific transport medium is required unless special procedures related to individual NAATs indicate otherwise. Specimens taken for culture may also be used for NAAT. Multiplex PCR test is available and detects *H. ducreyi, T. pallidum,* and HSV simultaneously.

Culture

H. ducrei is fastidious bacterium and selective and enriched culture media required for isolation. Material obtained from ulcer base (remove superficial pus) or pus aspirated from the bubo can be inoculated into the culture plates on bed side. When this is not possible Amies or Stuart's transport medium can be used. Many culture media are available and the use of more than one increases sensitivity up to 80%. Even though the definite diagnosis needs positive culture, it was achievable in 75 % of those positive in DNA amplification tests.

Microscopy

Low sensitivity and specificity and not recommended as a diagnostic test. Smear from cleaned ulcer or pus aspirate from bubo by rolling the swab through 180^0 on the slide and stain with Gram stain. Typically, small Gram-positive rods running in parallel and forming chains; 'school of fish' seen (unreliable due to bacterial contamination).

Serology

Only useful for epidemiological studies.

Management

Information, explanation, and advice should be provided to the patient that chancroid is a bacterial infection which is sexually transmitted, but curable with antibiotics and that it is a cofactor for HIV transmission, as genital herpes and syphilis.

First line Treatment

Ceftriaxone 250 mg as a single intramuscular injection or Azithromycin 1 g as a single oral dose

Second line Treatment

For second line treatment, refer latest STI management guideline.

Fluctuant buboes should be aspirated (by needle) from adjacent healthy skin under antibiotic cover. Patients should be re-examined 3– 7 days after treatment to ensure symptomatic improvement. Re-epithelization occurs within 7 days of the onset of therapy. Resolution of fluctuant lymphadenopathy is slower than that of ulcers and may require repeated needle aspiration.

Partner notification

Sexual contacts within 10 days of disease onset should be examined and given epidemiological treatment as for a clinical case.

Follow-up

All patients diagnosed with chancroid should be followed up after treatment, to ensure resolution of symptoms and signs. Successful treatment should improve symptoms within three to seven days. A test of cure is not necessary. Healing might be slower for some HIV-infected patients and uncircumcised men. Consider antibiotic resistance, re-infection, other causes of ano-genital ulcers, or an underlying immunodeficiency in treatment failure.

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Granuloma inguinale

Dr Thanuja Peiris

Granuloma inguinale is a sexually transmitted infection caused by the bacterium *Klebsiella granulomatis* (previously known as *Calymmatobacterium granulomatosis*). It effects skin / mucus membranes of the genital area and considered as a rare cause of genital ulcers. It is a chronic progressive disease.

The endemic regions are South Africa, North America and India. Incidental cases were seen in Australia, mainly among Aboriginal groups. Sexually active groups are at more risk of acquiring the infection and peak incidence is noted between 20 to 40 years age group.

Pathogenesis

The mode of transmission is mainly through sexual contact and due to low pathogenicity of the causative organism, repeated exposures are required to establish the clinical disease. Mother to child transmission is possible during the process of delivery if mother is infected with the causative organism for granuloma inguinale. The infection can spread among children through skin-to-skin contact.

Clinical Features

Incubation period is not well defined, but median is around 50 days, and it can vary from few days up to a year. The initial lesion, a papule or a subcutaneous nodule appear at the site of the skin contact and evolve with progressive destruction leading to an ulcer. In men most common areas affected are corona, glans and prepuce of the penis. Women show involvement of vulva, mainly the labia minora and fourchette. Anal area involvement is mainly seen among males (Box 10).

Box 10 Different clinical presentations of GI

Ulcerogranulomatous - commonest type. Firm papule or subcutaneous nodule formation at the site of skin contact. Then they erode to form soft painless ulcers which tend to bleed easily. The base is beefy red and consist of granulation tissues. The margins are sharp with rolled or heaped up borders. The ulcers enlarge gradually unless treated appropriately.
Nodular
Hypertrophic or Verrucous – large vegetative masses
Necrotic – Deep foul-smelling ulcer
Sclerotic – consists of extensive plaques and scar tissue

Diagnosis

Clinical diagnosis is difficult due to variations in clinical presentations and overlap with other ulcer diseases. Laboratory diagnosis – Microscopy of crushed tissue preparation or biopsy after Giemsa stain to see characteristic dark stained Donovan bodies. Donovan bodies appear as coccobacilli within large vacuoles in the cytoplasm of histiocytes and occasionally in other cells. The organisms are blue purple in colour and surrounded by a prominent capsule. Typical bacteria resemble "closed safety pins".

No FDA approved molecular (NAAT) tests available to detect *Klebsiella granulomatis*. Serology is not useful

Complications

Extra genital infection. Due to direct extension or autoinoculation - Spread to lips/oral, gastro-intestinal mucosa, scalp, abdomen, arms and legs. Haematogenous dissemination involving liver, lung, spleen and orbit.

Secondary infection of nodular lesions can lead to pseudobuboes. Carcinoma (squamous cell /basal cell) will be a possibility in 0.25% of infected patients. Extensive fibrosis, stricture formation and phimosis may result after lesions are healed. Elephantiasis of genitals may occur secondary to destruction of lymphatic system.

Treatment

Treatment stops progression and causes healing of ulcers. Prolonged therapy is required for complete resolution with granulation tissue formation. Relapses are possible for 6 – 18 months after effective treatment.

Recommended Regimen

1. Azithromycin 1g weekly or 500mg daily for >3 weeks and until all lesions are completely healed.

Alternative Regimens

1. Doxycycline 100mg orally twice a day for at least 3 weeks and until all lesions have completely healed.
   Or
2. Erythromycin 100mg 4 times a day for > 3 weeks or until all lesions are completely healed.

   Or

3. Trimethoprim – Sulfamethoxazole one double strength (160mg /800mg) tablet twice a day for > 3 weeks or until all lesions are completely healed.

   Follow up is indicated till lesions are completely healed. Sexual partners need to be checked for any clinical features and treated only if clinically suggestive of infection.

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Section 4:
Viral STI's

Human Immunodeficiency Virus infection

Dr Geethani Samaraweera

Introduction

Acquired immunodeficiency syndrome (AIDS) was first identified in 1981 in United states of America as an outbreak of Pneumocystis pneumonia and Kaposi sarcoma among otherwise healthy men who have sex with men (MSM). The Causative agent for AIDS was identified as a virus belong to retrovirus group in 1983 and it was subsequently named as Human Immunodeficiency virus. In 1986, a second virus causing AIDS was identified and it was named as HIV 2. While HIV 1 is prevalent all over the world HIV 2 is mainly found in western Africa, some parts of India and middle eastern countries. The infection is known to be Zoonotic in origin; HIV 1 is known to be derived from simian immunodeficiency virus in chimpanzee, and the origin of HIV 2 is thought to be through sooty mangabey monkey.

Epidemiology

HIV is one of the most important diseases, causing morbidity and mortality across the globe.

Since the first identification of HIV in 1983, an estimated 91.4 million people globally have been infected and about 44.1 million have died from HIV-related causes.

Globally, by the end of 2024, approximately 40.8 million people were living with HIV, with an adult prevalence of 0.7% among those aged 15–49 years. Of these, about 21.6 million were women and girls, and 1.4 million were children under the age of 15. During 2024, an estimated 1.3 million people newly acquired HIV, and about 630,000 people died from HIV-related causes. The global median HIV prevalence among adults (15–49 years) was 0.7%.

Median prevalence was higher among young women and girls, gay men and other men who have sex with men, sex workers, people who inject drugs, transgender people, and among prison inmates.

The disease burden of HIV varies significantly across the different regions of the world. African region bears the highest burden with an adult prevalence of 3.4% and more than two third of PLHIV worldwide lives within the African region.

By the end of 2024, the South-East Asian region continued to carry the world's second highest HIV burden. According to WHO data, an estimated 3.9 million people were living with HIV in the region, and about 78% of them knew their HIV status.

Sri Lanka is a country with low prevalence of HIV. According to the UNAIDS estimates, there were 4700 people living with HIV in the country by the end of 2023. The adult prevalence is estimated to be < 0.1% and 87% of PLHIV knew their status and of those who knew their status 81% were on anti-retroviral treatment and of those who

were on treatment, 86% were virally supressed. The epidemic is mostly concentrated among six key population groups namely, men who have sex with men (MSM) transgender people (TG), female sex workers (FSW), People who inject drugs (PWID), beach boys (BB) and prison inmates. MSM and TG were identified as the main divers of the HIV epidemic in the country.

Pathogenesis

HIV is a retrovirus which belongs to Lentivirus family which generally cause chronic, indolent infection, that is characterised by long clinical latency period, nervous system involvement and persistent viremia.

Retroviruses consist of an envelope and two single stranded RNA. The virus can translate single stranded RNA into double stranded DNA in the host target cell through the viral enzyme, reverse transcriptase. An additional viral enzyme called integrase, incorporate this DNA copies into the chromosomal structure of the target cell as a provirus.

Modes of transmission

HIV is transmitted through body fluids including blood, semen, vaginal secretions and breast milk.

Transmission can occur only through the following routes:

Unprotected sexual intercourse: This is the most common mode of transmission, and it could occur through unprotected anal, vaginal or oral sex with an infected partner, either heterosexual or homosexual. The risk of sexual HIV transmission is increased by the presence of other sexually transmitted infections, particularly ulcerative types such as herpes or syphilis.

Mother-to-child transmission: HIV could be transmitted from an infected mother to her baby in utero through placenta, during labour or through breastfeeding. Highest risk of transmission is during peri partum period and overall risk of mother to child transmission could varies from 15-45%.

Blood and blood products:

- HIV can be transmitted through transfusion of infected blood or transplanting of infected organs or tissues. However, following the introduction of universal screening of all blood and blood products for HIV, transmission through blood or blood product transfusion has dramatically reduced.
- Sharing of contaminated drug-injecting paraphernalia, such as needles, syringes, or contaminated skin-piercing instruments

HIV cannot enter the body if the skin is intact but can easily enter through an open wound. Prevention therefore involves ensuring that there is a barrier to the virus – condoms or protective means such as gloves and masks, where appropriate – and that needles and other skin-piercing instruments are sterile.

HIV cannot be transmitted by casual physical contact of any kind like:

- Kissing, hugging or shaking hands
- Mosquito or insect bites
- Coughing, sneezing or spitting

- Sharing toilets or washing facilities
- Using utensils or consuming food and drink handled by someone who is infected with HIV

Pathophysiology

The HIV can infect human cells that possess CD4 membrane receptor. The major target cells include T helper cells also known as CD4 cells, monocytes, macrophages and haematologic precursors. The clinical stage of immunodeficiency associated with advanced HIV disease is the direct result of depletion of CD4 lymphocytes.

Once entered the human body, gp120 envelope protein of the HIV virus binds to CD4 receptors. Thereafter the virus fuses into host cell membrane resulting in release of viral particles into the host cell. Within the cytoplasm of the cell, the reverse transcription occurs from viral RNA, and the newly created DNA will either remain in free form or incorporates into host cell DNA. Then the proviral DNA transcribe genomic and messenger RNA. After viral proteins are synthesised, new virions are assembled that bud from the infected cells and circulate in the blood stream until they find a new target cell.

Monocytes and macrophages serve an important role in the pathogenesis of HIV infection. Once infected they are tolerant to the viral replication thus surviving to disseminate the virus to various body sites. Although virus cannot cross the blood brain barrier independently, infected macrophages could carry the virus into CNS and damage through several mechanisms.

Host response to HIV infection.

HIV infection activates both cell mediated and humoral immune response of the host. As a result of activated cell mediated immunity secondary to HIV infection, CD4 lymphocytes decreases in absolute number and in proportion to CD8 cell. Its decrease is gradual in early stages of the infection (Clinical latency period), with more rapid decline observed with the onset of symptoms in late stage. HIV infection not only kills but impair functionality of CD4 lymphocytes. Although HIV does not directly infect B lymphocytes, their function and immunoglobulin production become impaired in HIV infection. This results in poor host response to immunizing agents and increase risk of developing infection from encapsulated organisms such as bacteria.

To neutralise the viral antigen, variety of neutralising antibodies are produced by the human body. Although these antibodies have the capability to impair the structure and function of the virus (causing impaired ability to attach and penetrate the human cell), they are ineffective in eradication of infection once the infection is established.

Natural history of the HIV infection

HIV infection is a chronic illness characterised by evolving clinical and serological manifestations. Soon after the acquisition of infection there is a transient period of intense viral replication even before development of symptoms.

Primary HIV infection

Two to three weeks after acquisition of infection patient could develop flu like illness which is known as acute retroviral syndrome, seroconversion illness or primary HIV infection. The symptoms are generally nonspecific and self-limiting. Table 1 give the common clinical and laboratory findings of primary HIV infection.

Table 7: Clinical and laboratory features of primary HIV infection

Clinical/laboratory feature	Percentage of occurrence (%)	Clinical/laboratory feature	Frequency (%)
Fever	86	**Myalgia**	28
Headache	55	**Nausea**	32
Malaise/Fatigue	59	**Oral ulcers**	37
Rash	38	**Aseptic meningitis**	24
Pharyngitis	52	**Hepatosplenomegaly**	30
Lymphadenopathy	44	**Oral thrush**	24
Diarrhoea	32	**Thrombocytopenia**	45
Weight loss	32	**Leukopenia**	40
Night sweats	14	**Transaminitis**	38

About 30-40 % will not have any symptoms during the initial infection. This acute stage of the infection is self-limiting.

Chronic HIV infection

After the acute stage of the HIV infection many patients will go into a long latent period where they are clinically asymptomatic for 8-12 years and start developing symptoms gradually thereafter.

The chronic HIV infection could be classified into 4 stages according to WHO clinical staging- Stage 1-4.

WHO clinical stage 1

After the acute retroviral syndrome majority of PLHIV will go into long asymptomatic latency. However, about 30% will develop persistent generalise lymphadenopathy (involving at least two sites other than inguinal region which persistent for more than 6 months) but could be otherwise asymptomatic. During this stage patient remain mostly healthy and this stage could

last for 8-10 years. Generally, majority of individuals in clinical stage 1 will have preserved immunity but despite clinically being silent the viral replication and destruction of CD4 cell will continue during this stage.

WHO clinical stage 2

If untreated patients will progress from clinical stage 1 to 2 within 8-10 years but it could vary among different individuals. During this stage the patient will be mildly symptomatic, and the symptoms could be mild weight loss less than 10% of total body weight, recurrent respiratory tract infections such as sinusitis, bronchitis, otitis media and pharyngitis. They could also get variety of dermatological manifestations such as herpes zoster infection, angular cheilitis, recurrent oral ulceration, papular pruritic eruptions, seborrhoea dermatitis and fungal nail infections. During this period majority will show mild immune deficiency but immunological staging could differ from the clinical stage in some patients.

WHO clinical stage 3

As the disease progresses the patient will go into the clinical stage 3 where they will be moderately symptomatic. Patients with weight loss of more than 10% of total body weight, unexplained persistent fever for more than 1-month, unexplained chronic diarrhoea lasting for more than 1-month, pulmonary tuberculosis and severe bacterial infections such as pneumonia, emphysema, pyelonephritis, bone and joint infections, pyomyositis, meningitis and septicaemia are categorised into WHO clinical stage 3. In addition, patients in this stage could also present with mucocutaneous manifestations such as recurrent oral candidiasis, oral hairy leucoplakia, acute necrotising periodontitis, and gingivitis. These patients generally have moderate immunosuppression and if not treated promptly the patients could die of above manifestations or could progress into clinical stage 4. Unexplained anaemia (<8g/dl), and or neutropenia (<500/mm3), and or thrombocytopenia (<50 000/ mm3) for more than one month are also included in WHO clinical stage 3 conditions after HIV status is confirmed.

WHO clinical stage 4

When patients progress into this severely symptomatic stage or end stage, they will develop clinical manifestations called AIDS defining conditions and if not managed promptly can become rapidly fatal. The conditions that are categorised under ADS defining conditions include HIV wasting syndrome, Pneumocystis pneumonia (PJP), recurrent or severe bacterial pneumonia, extrapulmonary tuberculosis, HIV encephalopathy, CNS toxoplasmosis, chronic (more than 1 month) or orolabial herpes simplex infection, oesophageal candidiasis, Kaposi's sarcoma etc.

In addition, a patient in clinical stage 4 could also present with cytomegaloviral (CMV) infections (CMV retinitis or infection of organs other than the liver, spleen or lymph nodes), extrapulmonary cryptococcosis, disseminated endemic mycoses (e.g., coccidiomycosis, penicilliosis, histoplasmosis), cryptosporidiosis, isosporiasis, disseminated non-tuberculous mycobacteria infection, tracheal, bronchial

or pulmonary candida infection, visceral herpes simplex infection, cerebral or B cell non-Hodgkin lymphoma, progressive multifocal leukoencephalopathy (PML), and HIV-associated cardiomyopathy or nephropathy.

Clinical manifestations and staging among children could vary from adults. The clinical staging of children with established HIV infection is shown below after the references.

In addition to the clinical staging, patients could also be categorised according to their CD4 count which is called immunological staging.

Table 8: CD4 levels and the level of immunosuppression in adults and adolescents

Immunological stage	CD4 count (cells/mm^2)
No immunosuppression	>500
Mild immunosuppression	350-500
Moderate immunosuppression	200-350
Severe immunosuppression	<200

According to WHO categorization, advanced HIV disease is defined as any WHO clinical stage 3 and 4 conditions or any clinical stage with CD4 count less than 350 cells/mm^2. On the other hand, if a patient develops a new WHO clinical stage 3 or 4 conditions 24 weeks after initiating ART, this indicates a treatment failure.

Table 9: CD4 levels and the level of immunosuppression in children

HIV associated immunodeficiency	Age related CD4 values			
	<11 months (%CD4+)	12-35 months (%CD4 +)	36-59months (%CD4 +)	>5 years (Absolute number per mm3 or %CD+)
None or not significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-29	20-24	15-19	200-349
Severe	<25	<20	<15	<200 or 15%

Diagnosis

Accurate and rapid diagnosis of HIV infection helps to initiate antiretroviral treatment which is the key to arrest the progression of the disease and prevent transmission to others. Despite the availability of widespread HIV testing, many infections are still undiagnosed until late stage all over the world.

The process of HIV testing should always be voluntary, informed, and free from coercion, with the right to "opt out." For HIV testing verbal consent is adequate thus written separate consent is not required. Detailed pretest counselling is not generally recommended before performing HIV test and brief pre-test information through written, verbal or through short video clips is sufficient.

HIV infection could be diagnosed based on detection of antibodies against HIV proteins, detection of P24 antigen and detection of viral nucleic acid. Culturing of HIV virus need cell culture thus not routinely used for the purpose of diagnosis.

Laboratory diagnosis of HIV starts with screening tests. If the screening test is positive it needs to be further verified with confirmatory tests. Depending on the type of antigen/ antibody detected through the tests, there could be generations of HIV tests. 4th generation tests (tests which could detect HIV antibodies and P24 antigen) are preferred as screening tests due to their high sensitivity. Generally, all commercially available screening tests could detect HIV 1 and 2.

HIV screening tests

The screening tests could be either laboratory-based tests, point of care tests or HIV self-tests. The most widely used laboratory-based HIV screening test is an ELISA, but various other methods such as chem eliminant essay are also used. These tests are usually batch tests thus suitable to test large number of samples at a time. In addition, there are rapid diagnostic tests which are qualified to use in laboratory for diagnosis of HIV.

There are HIV rapid diagnostic tests which are prequalified to use as point of care tests and as field tests. Therse tests are simple to perform and does not need any sophisticated equipment. The advantage of point of care tests is that it could be performed even by trained lay providers, could be done with finger-prick blood samples and the results are usually available within 30 minutes.

In addition, some HIV tests are qualified to be used as self-tests. They could be blood based self-tests or oral fluid based self-tests. These tests are important as they can reach hidden populations who are not willing to attend any other HIV testing facilities.

Molecular diagnostic tests (DNA PCR and RNA PCR) are also used to detect very early cases of HIV, but they are generally not recommended as screening tests because they could miss HIV 2 cases and elite controllers whose plasma virus could be in very low level.

Confirmation of HIV

Once a screening test becomes positive it is essential to confirm it with recommended confirmatory tests before registering into HIV care. This could be done by three test algorithms: performing two recommended rapid tests with high specificity following the initial positive screening tests. This could allow rapid confirmation of HIV even at field level allowing the client to be linked to care immediately without undue delay.

Western blot (WB) and line blot assays which were the gold standard to HIV confirmation earlier are now used only in special cases. The reasons for moving away from Westen blot for routine confirmation is that WB testing needs specialised laboratories, and they have large diagnostic window which delay confirmation and thus delaying the initiation of ART specially in early infections. Furthermore, the decentralising the confirmation of HIV is essential to facilitate early initiation of ART.

Diagnostic window/Window period

The "diagnostic window" referred to the period between acquisition of a pathogen and the first appearance of laboratory measurable infective markers such as antibodies, antigen or nucleic acid. In HIV, the antibody production generally begins at 2 weeks. For 4th generation HIV assays, the safe diagnostic window is 6 weeks whereas for 3rd generation assays which could detect only IgG ad IgM antibodies the safe diagnostic window is 8 weeks. In cases of post exposure prophylaxis, the infection could only be ruled out 12 weeks after the incident. The earliest laboratory marker is HIV RNA which could be detected 2 weeks after the exposure, but negative PCR does not reliably exclude the diagnosis.

Therefore, a negative test result could safely exclude HIV only when there is no re-exposure within the diagnostic window.

Diagnosis in pregnant women and newborns

Timely diagnosis of HIV infection could prevent mother to child transmission of HIV. According to the current Sri Lankan guidelines, HIV testing is recommended for all pregnant women, and it should be done as early as possible during the pregnancy. Repeat testing in 3rd trimester is recommended for pregnant mothers with high-risk behaviours. Only the performance of test date but not the results should be documented in maternity record (H512).

In newborns of HIV positive mothers, maternal antibodies may remain detectable in newborn blood up to 18 months. Therefore, antibody based diagnostic tests are not reliable in detecting HIV infection in newborn babies up to 18 months, thus the national HIV testing guideline recommend molecular testing as the preferred choice for diagnosis of HIV among newborns. At least two negative PCR, 1st one done at birth and second one at 3 months is necessary to exclude HIV in a newborn baby who is born to an HIV positive mother. However, if the baby is receiving breast feeding, the infection could be excluded only 6 weeks after the cessation of breast feeding.

Management

Once the HIV status of an individual is confirmed, the client will be provided with detailed post-test counselling which will enable them to understand about the disease, modes of transmission, availability of treatment, importance of adherence, follow-up and prevention of onward transmission. After the client is registered in HIV care, the client will be evaluated in detail to assess the clinical and immunological stage of the disease, other comorbidities, social and psychological aspects.

Anti-retroviral therapy is the key in managing PLHIV. After initial evaluation, a suitable ART options will be discussed with the client by the caring doctor and if the patent is ready, same day or early initiation (within 1 week of diagnosis of HIV) of ART is the recommended management unless there are reasons to delay initiation of ART. Early initiation is important to reduce mortality and morbidity as well as to prevent onward transmission of HIV. ART will control the viral replication and reduce the viral load in blood to undetectable level while restoration of immunity. However, ART will not completely cure the disease but control the viral replication and bring the viral load to undetectable level mostly within 6 months. Thus, according to the current recommendation, ART needs to be continued for life.

To prevent development of drug resistance and maximise the potency of ART, multi drug therapy consisting of three active ARV is the standard management. The choice of ART depends on the individual patient factors and comorbidities.

The standard anti-retroviral regimens will consist of an NRTI back bone with two drugs and a third drug which is known as anchoring drug which will be commonly chosen from NNRTI, PI or INSTI groups. Detailed description of ART is Available on **National ART guideline – Sri Lanka by NSACP**

After failing the 1st line ART patient will be initiated on 2nd line regimen.

With suitable ART regimen, good adherence and suppressed viral load, patients could live a normal life span like an HIV negative individual. Once the patient is on ART with suppressed viral load for 6 months or more, patient becomes non-infectious to others which is known as **Undetectable equals Untransmissible (U=U)**.

In addition to provision of ART, identification and management of coinfections such as Hepatitis B, Hepatitis C, opportunistic infections such as TB, Toxoplasmosis CMV and comorbidities such as Diabetes mellites, hypertension, renal impairment and heart disease are important aspect in management of PLHIV. Management of psychiatric illnesses and psychosocial issues is also equally important in management of PLHIV. Thus, multi-disciplinary team involvement and management is important.

Mechanism of action of Anti-retroviral agents

Anti-retroviral agents are developed targeting to stop the various steps of the HIV replication cycle, namely viral binding, attachment, fusion, reverse transcription, integration into human genome, viral protein synthesis, viral budding and maturation. Zidovudine is the first antiretroviral agent approved by FDA in 1985 and it acts by inhibiting the action of reverse transcriptase enzyme.

There are 8 different classes of antiretroviral drugs,

1. Nucleotide analogue reverse transcriptase inhibitors (NRTI)
2. Non-nucleotide analogue reverse transcriptase inhibitors (NNRTI)
3. Protease inhibitors (PI)
4. Integrase strand transfer inhibitors (INSTI)
5. Fusion inhibitors
6. Chemokine receptor inhibitors
7. Attachment inhibitors
8. Maturation inhibitors

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WHO CLINICAL STAGING OF INFANTS AND CHILDREN WITH ESTABLISHED HIV INFECTION

Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy
Clinical stage 2
Unexplained persistent hepatosplenomegaly
Papular pruritic eruptions
Extensive wart virus infection
Extensive molluscum contagiosum
Recurrent oral ulcerations
Unexplained persistent parotid enlargement
Lineal gingival erythema
Herpes zoster
Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
Fungal nail infections
Clinical stage 3
Unexplained moderate malnutrition not adequately responding to standard therapy
Unexplained persistent diarrhoea (14 days or more)
Unexplained persistent fever (above 37.5 °C, intermittent or constant, for longer than one month)
Persistent oral Candidiasis (after first 6 weeks of life)
Oral hairy leukoplakia
Acute necrotizing ulcerative gingivitis/periodontitis
Lymph node TB
Pulmonary TB
Severe recurrent bacterial pneumonia
Symptomatic lymphoid interstitial pneumonitis
Chronic HIV-associated lung disease including bronchiectasis
Unexplained anaemia (<8.0 g/dl), neutropenia (<0.5×109/L^3) or chronic thrombocytopenia (<50 × 10^9/L^3)

Clinical stage 4 [a]
Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
Pneumocystis pneumonia
Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site)
Extrapulmonary TB
Kaposi sarcoma
Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
Central nervous system toxoplasmosis (after the neonatal period)
HIV encephalopathy
Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age more than 1 month
Extrapulmonary cryptococcosis including meningitis
Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
Chronic cryptosporidiosis (with diarrhoea)
Chronic isosporiasis
Disseminated non-tuberculous mycobacterial infection
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy
HIV-associated cardiomyopathy or nephropathy

[a] Some additional specific conditions can be included in regional classifications (e.g. penicilliosis in Asia, HIV-associated rectovaginal fistula in Southern Africa, reactivation of typanosomiasis in Latin America).

Ref: http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf

Herpes Simplex infection

Dr Iruka Rajapaksha

Introduction

Herpes simplex virus (HSV), known as herpes, is a common infection that can cause painful blisters or ulcers. Herpes simplex viral infection is characterized by vesicular eruptions that sometimes recurs, occurring on skin and mucosal surfaces of ano-genital and oral areas.

The causative virus is herpes simplex virus. There are two types of herpes simplex viruses.

- **Herpes simplex virus type 1 (HSV-1)**
- **Herpes simplex virus type 2 (HSV-2)**

Both types of HSV can cause genital herpes and most cases of recurrent genital herpes are caused by HSV-2. Herpes simplex virus type 1 is commonly found in oral lesions. Most people infected with HSV have no symptoms or only mild symptoms. The infection can cause painful blisters or ulcers that can recur over time. Medicines can reduce symptoms but can't cure the infection. Most herpes infections are asymptomatic or go undiagnosed, but painful blisters or ulcers that might eventually recur are signs of herpes. The risk of contracting and spreading HIV infection is elevated in individuals with HSV-2 infection[1].

Classification

The Herpesviridae family comprises a group of DNA viruses that cause infections and certain diseases in animals, including humans. These viruses are also known as herpesviruses. It is further divided into three subfamilies:

Table 10: Nine herpesvirus types primarily infect humans

Subfamily	Taxonomic name	Common name
Alpha-herpesvirinae	HHV-1	Herpes simplex virus 1 (HSV-1)
	HHV-2	Herpes simplex virus 2 (HSV-2)
	HHV-3	Varicella zoster virus (VZV)
Beta-herpesvirinae	HHV-5	Human cytomegalovirus (HCMV)
	HHV-6	HHV-6 variant A or B
	HHV-7	HHV-7
Gamma-herpesvirinae	HHV-4	Epstein-Barr virus (EBV)
	HHV-8	Kaposi's sarcoma associated herpesvirus (KSHV)

Pathophysiology

The natural history of HSV infection includes acute or subclinical first episode of mucocutaneous infection, establishment of viral latency and subsequent reactivation. The herpes virus enters the body through the skin or mucous membranes by direct sexual contact with the secretions or mucosal surfaces of an infected person. The virus multiplies at the epithelial layer, where it becomes primary HSV infection.

There may be a prodrome of hours to days consisting of pain, tingling, itching, or burning at the site of exposure. Epithelial damage at the portal of entry leads to eruption of vesicles that open, ulcerate and re-epithelialize during an outbreak that lasts about two weeks. During initial infection, viral DNA ascends along the sensory nerve roots to the dorsal root ganglion, where it persists for life. Reactivation of HSV causes migration back through the axon, its branches to the skin and mucosa[3].

Table 11: Risk Factors for Genital Herpes Infection

Risk factors
1. Advent of sexual activity at or before 17 years of age
2. History of sexually transmitted diseases
3. History of undiagnosed genital lesions or discharge
4. Human immunodeficiency virus infection
5. Multiple sex partners
6. Partner diagnosed with genital HSV infection

Clinical features

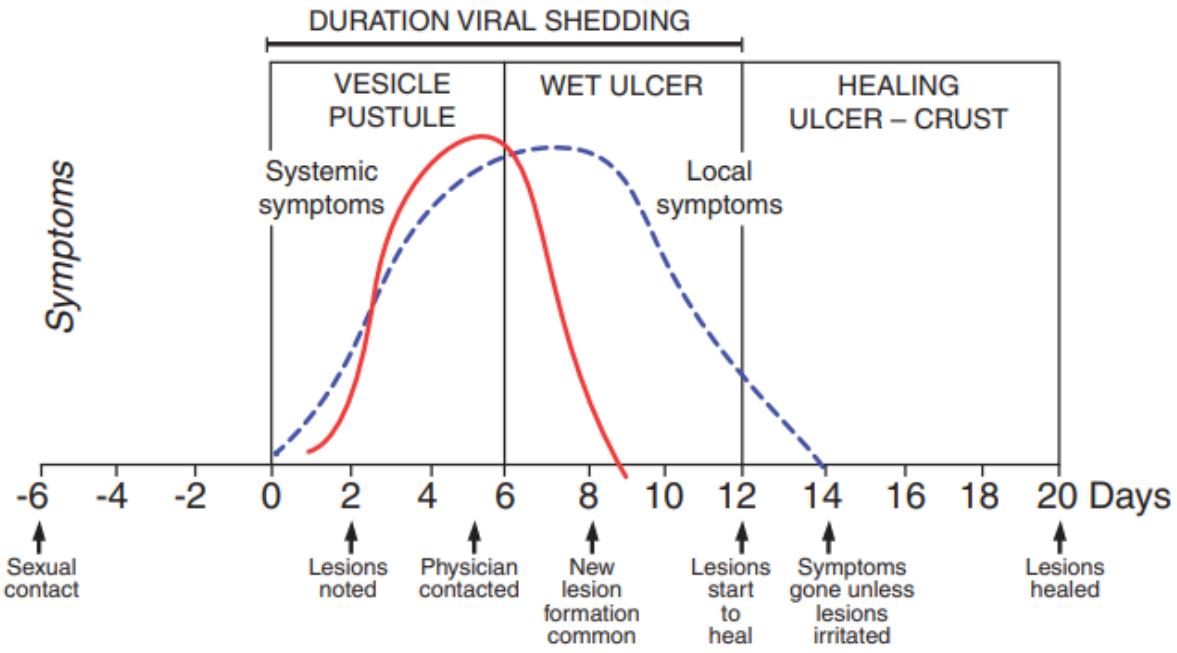
"Classic" outbreaks of primary genital HSV infection begin with a prodrome lasting two to 24 hours that is characterized by localized or regional pain, tingling, and burning. Patients also may have constitutional symptoms such as headache, fever, inguinal lymphadenopathy, anorexia, and malaise. As the disease progresses, papules, vesicles on an erythematous base, and erosions appear over hours to days. Patterns of HSV-1 and HSV-2 infection appear similar. Vesicles usually are uniform in size and the tense centre umbilicate to form a depressed centre. These lesions usually crust and then re-epithelialize and heal without scarring. In women, ulcers can occur on the introitus, urethral meatus, labia and perineum. In men, ulcers often appear on the shaft or glans of the penis. In both men and women, lesions may appear on the perianal area, inner thighs or buttocks. When a person develops clinically apparent painful vesicles for the first time we call it as a first episode. There are two types of first episodes. The first is a nonprimary clinical eruption in a patient who has been infected previously with any type

of HSV. The second type is a true primary infection, which is the first HSV infection in a seronegative patient. Patients with serological evidence of prior HSV-1 infection have less systemic symptoms and have a lower rate of complications and a shorter duration of disease than persons with true primary genital herpes[4].

Table 12: Number of recurrences in the first year after first symptomatic infection

Recurrences	Incidence (%)
Zero	11
1 or more	89
6 or more	38
More than 10	20

Figure 20: Clinical course of primary HSV



First-episode infections have more numerous and scattered vesicles. In contrast to first episodes of genital infection, the symptoms, signs, and affected sites of infection of recurrent genital herpes are localized to the genital region. Compared to the initial genital infection, local symptoms such as pain and itching may be less severe. During initial episodes as well as recurrences symptoms are more painful and more severe in women compared with men.

Around 70% to 90% of women with first-episode HSV-2 infection have HSV cervicitis. This compares to a 15–20% isolation rate of HSV-2 from the cervix among women who present with recurrent external genital lesions. Primary genital HSV cervicitis may be symptomatic (purulent or bloody vaginal discharge) or asymptomatic.

Both external and internal dysuria, appears more frequently in women (83%) than in men (44%). Urethral discharge and dysuria are noted in about one-third of men with primary HSV-2 infection. HSV urethritis and cystitis may account for the higher frequency and longer duration of dysuria in women.

HSV of the pharynx is commonly seen in association with primary genital herpes and may be the presenting complaint in about 20% of patients with either primary HSV-1 or primary HSV-2 infections. Both HSV-1 and HSV-2 may cause pharyngitis and may be associated with oral–genital exposure to the source contact.

HSV has been isolated from rectal mucosal in men and women with symptoms of rectal pain and discharge. HSV proctitis is commonly associated with systemic symptoms such as fever and malaise. Patients usually present with acute onset of rectal pain, discharge, tenesmus, constipation, and bloody or mucoid rectal discharge.

The presence of either HSV-1 or HSV-2 antibody may provide a small degree of protection against developing an infection with the other HSV type at the same or a new site; however, patients should still be counselled on safe sex practices to prevent genital infections[4].

Genital Herpes virus and HIV

Persons with HSV-2 infection have a threefold increase in the risk of acquiring human immunodeficiency virus (HIV) infection. This may be related to open ulcers and lymphocytes at the site of eruptions, facilitating HIV invasion during sexual contact. Concurrent infection with HSV-2 and HIV increases the severity of HSV episodes and the likelihood of atypical presentations. The relationship between genital HSV-1 and HIV infections has not been well studied.

Immunocompromised patients have frequent and prolonged mucocutaneous HSV infection. Mucocutaneous HSV infections in the immunocompromised host may be associated with systemic complaints, prolonged local symptoms and longer durations of viral shedding. Recurrent genital herpes in immunosuppressed patients often results in the development of large numbers of vesicles which coalesce into extensive deep, often necrotic, ulcerative lesions[4].

Complications

Complications of genital herpes are listed in Table 13. However, the predominant morbidity may be the psychological burden attributable to lifelong persistence of virus, recurrences, viral shedding and disclosure to sex partners.

Diagnosis

Although herpes is the most common ulcerative genital disease, the coexistence of multiple aetiologies must be considered.

Table 13: Complications of Genital Herpes

Complications of Genital Herpes
1. Acute urinary retention
2. Super infection with bacterial or fungal pathogens
3. Vulval adhesions in males and phimosis in males
4. Extra genital lesions
5. Disseminate Herpes
6. Aseptic meningitis
7. Encephalitis

Table 14: Differential diagnosis of genital ulcers

Infectious	**Non infectious**
Genital HSV	Aphthous ulcer
Chancroid	Bechet's disease
Lymphogranuloma venereum	Fixed drug eruption
Granuloma inguinale	Psoriasis
Syphilis	Irritant or contact dermatitis
Secondary bacterial infection	Neoplasms
Candidiasis	Sexual trauma
Scabies	

The diagnostic tests outlined below may not be available in all settings because of local facilities or cost.

1. Virus detection and typing by polymerase chain reaction
   In this method directly demonstrate HSV in swabs taken from the base of anogenital lesions or rectal mucosa in the case of proctitis. This method can differentiate HSV 1 and 2. HSV DNA detection increases HSV detection rates by 11–71% compared with virus culture.
2. Virus culture
   HSV culture is still used in some centres but will miss approximately 30% of PCR-positive samples (most significantly patients presenting with late or with mild recurrent disease). Yield of culture is influenced by virus shedding, specimen quality, sample storage and conditions of transport.
3. Serology
   Testing for HSV type-specific antibodies can be used to diagnose HSV infection. The detection of HSV 1 IgG or HSV-2 IgG or both in a single serum sample represents HSV infection with

HSV at some time. It is difficult to say whether the infection is recent as IgM detection is not predictable. Collection of serum samples a few weeks apart can be used to demonstrate seroconversion, due to recent primary infection. HSV-2 antibodies are indicative of genital herpes. HSV-1 antibodies do not differentiate between genital and oropharyngeal infection. Many commercial tests for HSV antibodies are not type-specific and are of no value in the management of genital herpes.

Serology may be helpful in the following situations

A. recurrent genital disease of unknown cause
B. counselling patients with initial episodes of disease (to help identify recent or established infection to aid counselling) including pregnant women
C. investigating asymptomatic partners of patients with genital herpes, including women who are having fertility plans or currently pregnant
D. couples concerned about possible susceptibility to transmission in perhaps discordant relationships.

Management

Episodic and suppressive treatment of herpes is aimed at reducing the severity, duration of episode, recurrence of symptoms and at preventing transmission to uninfected partners. Suppressive treatment may be intermittent or continuous. Nucleoside analogues, which work by inhibiting viral DNA, acyclovir, famciclovir and valacyclovir are approved and well tolerated for treatment of HSV. Regimens are identical for HSV-1 and HSV-2. These agents offer clinical benefit but do not cure the disease. These drugs can be used for episodic treatment or for long-term suppressive therapy.

Acyclovir, a guanosine analogue that inhibits viral DNA synthesis, is the oldest and most-studied medication. It has poor bioavailability and a short half-life, which necessitates frequent dosing. However, acyclovir is cost effective. Valacyclovir, a prodrug that metabolizes to acyclovir, has better bioavailability and requires less frequent dosing than acyclovir. Famciclovir is a purine analogue that has high bioavailability. All have infrequent similar side effects, which include nausea, vomiting, headache and diarrhoea.

Most patients with initial genital HSV infection should receive antiviral therapy. The main goals of initial treatment are to improve symptoms and speed recovery. All the antiviral medications currently used to treat HSV infection have been shown to decrease by several days the time until all lesions are crusted and healed, as well as localized pain, constitutional symptoms and viral shedding.

Episodic therapy is best for HSV-infected patients who have mild and infrequent recurrences. The treatment goal is to diminish symptoms and infectivity during recurrences, rather than reduce the frequency of recurrences. To be effective, treatment should be started during the

prodromal phase or within one day of lesion onset.

Patients with frequent recurrences overwhelmingly choose suppressive therapy. It is recommended for patients with more than six episodes per year, but patient preferences also should be considered. Suppressive therapy reduces recurrences by 70 to 80 percent in patients who have frequent outbreaks (more than six per year). Long-term safety and effectiveness have been well documented in patients receiving daily therapy with acyclovir for as long as six years, and in patients who have taken valacyclovir or famciclovir for one year[6].

The development of drug resistance is rare in immunocompetent patients. treatment is well tolerated and effective and is not associated with significant side effects. Suppressive therapy has been shown to reduce the risk of transmission significantly in heterosexual, HSV-2–discordant couples, though therapy has not been shown to fully eliminate asymptomatic viral shedding. Few studies have compared valacyclovir or famciclovir with acyclovir for suppressive therapy, but the existing studies suggest that all have comparable clinical outcomes[6]. Therefore, cost and dosing frequency are important considerations in selecting a drug for prolong treatment. Because the number of outbreaks may decrease over time, interruption of therapy should be discussed at yearly intervals to assess the need for continued therapy.

Intravenous acyclovir should be considered in patients with severe or disseminated disease (e.g., pneumonitis, hepatitis, central nervous system involvement). The recommended intravenous dosage is 5 to 10 mg per kg every eight hours for two to seven days, or until obvious clinical improvement occurs. The patient then can be switched to oral acyclovir to complete at least 10 days of total therapy.

Box 11 Treatment schedules for HSV infection

1. Episodic Therapy (For Symptomatic HSV Outbreaks)
- Acyclovir: 400 mg TID for 5 days OR 800 mg TID for 2 days
- Valacyclovir: 500 mg BID for 3 days OR 1 g once daily for 5 days
- Famciclovir: 125 mg BID for 5 days OR 1 g BID for 1 day

2. Suppressive Therapy (For Frequent Recurrences, ≥6 Episodes/Year)
- Acyclovir: 400 mg BID daily
- Valacyclovir: 500 mg once daily (for ≤9 recurrences/year) OR 1 g once daily (for ≥10 recurrences/year)
- Famciclovir: 250 mg BID daily

3. Severe or Complicated HSV Infections (e.g., Disseminated Disease, HSV Meningitis)
- Acyclovir IV: 5-10 mg/kg every 8 hours for 2-7 days, followed by oral antivirals to complete 10-14 days

Treatment of HSV in Individuals

During HSV outbreaks, patients should keep the affected area clean and dry to prevent secondary infections. Loose-fitting clothing and cotton underwear are helpful. Patients should avoid touching the lesions and should wash their hands after any contact with the sores. Topical acyclovir is less effective than oral acyclovir[7]. (Box 11)

Future treatments may include immunomodulators such as imiquimod (Aldara) and a variety of microbicides and vaccines to prevent primary infection[6].

Counselling on psychosocial implications is important aspect in management. Although HSV infection is a self-limited disorder, it has a tremendous impact on affected patients and counselling is crucial to management. The principal goals of counselling are to help patients cope with the infection and to prevent sexual and perinatal transmission. Informing the patient of the diagnosis can be a sensitive matter because many patients are in considerable disbelief. It might be beneficial to wait until after the initial outbreak resolves to discuss the chronic aspects of the disease. Many patients may experience a sense of loneliness and isolation, as well as anxiety, diminished self-esteem, reluctance to initiate close relationships as well as fear of initiating sexual relationships and sexual expression. A minority of patients may experience a deepening depression with each recurrence and all aspects of their lives, including job performance, may be affected. By educating the patient about the disease process, the physician can help empower the patient to manage the disease. Patient concerns usually include the severity and frequency of clinical outbreaks, sexual relationships and transmission of the disease to others and whether the disease will affect future childbearing.

Patients with genital Herpes infection need to be advised to abstain from sexual activity when lesions or prodromal symptoms are present and antiviral therapy is available and effective but does not cure the infection. Asymptomatic patients diagnosed by serologic testing should receive the same counselling messages as those with symptomatic infections. Patients should inform current and future sex partners that they have genital herpes. Patients should be informed about the natural history of the disease, including recurrence of episodes. Sexual partners may be infected even without symptoms and serologic testing can determine whether they are at risk. Sexual transmission can occur during asymptomatic periods. When they cover infected areas, latex condoms can reduce the risk of transmission and should be used consistently.

HSV in pregnancy and Neonatal HSV

Herpes simplex virus (HSV) infection during pregnancy can pose significant risks to both the mother and foetus, particularly if it is a primary infection acquired during the third trimester. The risk of neonatal HSV transmission is highest (30-50%) when a mother acquires a primary HSV infection near delivery, as she lacks protective antibodies. In contrast, recurrent maternal HSV infection carries a much lower risk

(<3%) due to existing immunity. Asymptomatic viral shedding at delivery poses a <2% risk, while caesarean section in mothers with active lesions reduces the risk to <1%.

HSV treatment during pregnancy includes episodic therapy with acyclovir (400 mg TID) or valacyclovir (500 mg BID) for 5-7 days to manage outbreaks. Suppressive therapy, starting at 32 weeks gestation, involves daily acyclovir (400 mg TID) or valacyclovir (500 mg BID or 1 g once daily) to reduce recurrence, the need for caesarean section, and the risk of neonatal HSV transmission[5].

Neonatal herpes simplex virus (HSV) infection is a serious condition that can present as localized skin, eye, and mouth (SEM) disease, central nervous system (CNS) disease, or disseminated infection affecting multiple organs. Treatment involves immediate intravenous acyclovir for at least 14 days for SEM disease and 21 days for CNS or disseminated disease. Early diagnosis and prompt treatment are crucial in improving neonatal outcomes.

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HPV and Genital warts

Dr Shanika Jayasena

Introduction

Human Papillomavirus (HPV) infection is a prevalent sexually transmitted infection (STI) with significant clinical implications. It encompasses a diverse group of DNA viruses belonging to the family Papillomaviridae. HPV infection is associated with various clinical manifestations, including genital warts, cervical dysplasia, and HPV-associated cancers.

With over 100 identified types, of which around 40 are sexually transmitted, HPV infection represents a significant global health concern. In heterosexual individuals, HPV infection can lead to genital warts, cervical dysplasia, and HPV-associated cancers such as cervical, vulvar, vaginal, penile, and anal cancers. Cervical cancer is a leading cause of morbidity and mortality among women globally, emphasizing the importance of HPV vaccination and screening programs. In homosexual males, anal HPV and anal cancer precursors are very common and HPV infection is associated with an increased risk of various diseases, including anal cancer, penile cancer, and oropharyngeal cancer. Anal cancer has been recognized as a significant health issue among men who have sex with men (MSM), highlighting the need for targeted prevention and screening efforts in this population.

The classification of HPV

HPV strains are classified into low-risk and high-risk categories based on their oncogenic potential.

Low-risk HPV types, such as HPV 6 and HPV 11, are associated with benign lesions like genital warts.

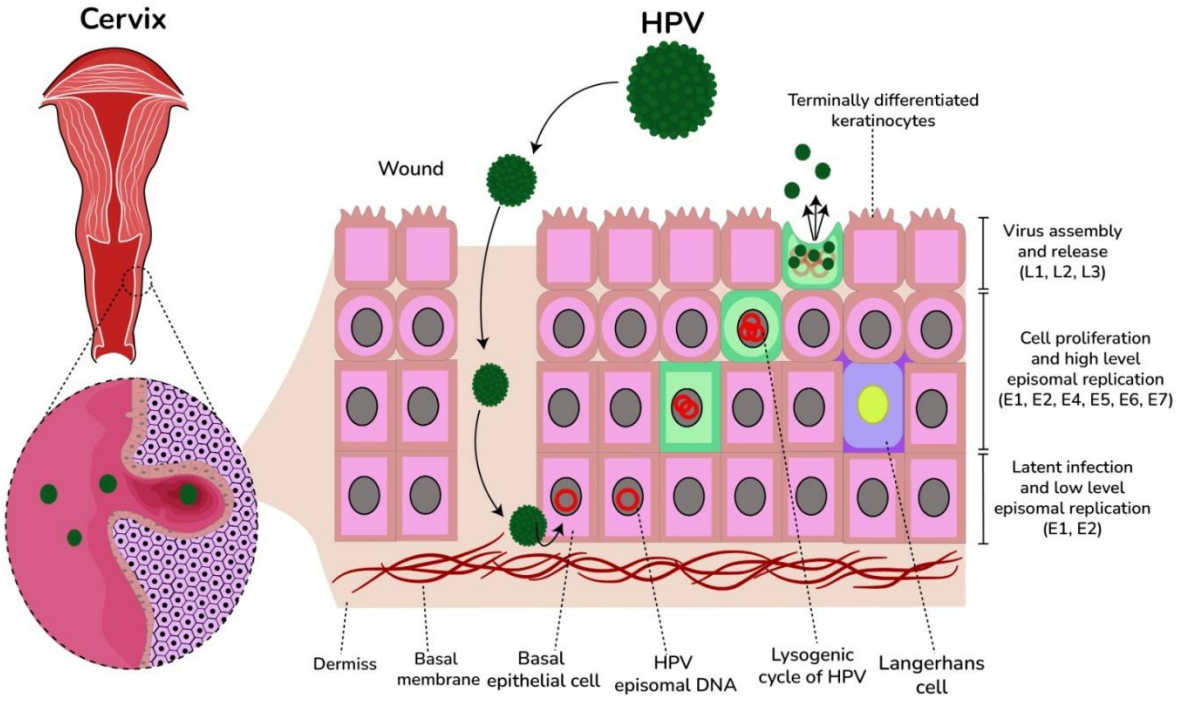
High-risk HPV types, including HPV 16, HPV 18, HPV 31, HPV 33, HPV 45, HPV 52, and HPV 58, have a greater propensity to cause malignancies such as cervical, anal, penile, vulvar, vaginal, and oropharyngeal cancers. HPV types 16 and 18 are responsible for approximately 70% of cervical cancer cases globally. High-risk HPV strains, especially type 16, are strongly associated with anal cancer, particularly among MSM. HPV types 16 and 18 are also implicated in penile, vulvar, vaginal, and oropharyngeal cancers, highlighting the broad spectrum of malignancies associated with these oncogenic strains. The oncogenic potential of other high-risk HPV types, including HPV 31, 33, 45, 52, and 58 are implicated in the development of HPV-associated cancers.

The pathogenesis and pathophysiology of HPV infection

The pathogenesis and pathophysiology of HPV infection intricately involve the

mechanisms underlying the development and progression of HPV-associated diseases, representing a complex interplay between the virus and the host. HPV typically enters basal epithelial cells via micro-abrasions or disruptions in the epithelial barrier, primarily facilitated by sexual contact. Following entry, HPV establishes infection within the cell and undergoes replication, leading to the expression of viral proteins essential for its lifecycle. These viral proteins, including E1, E2, E4, and L1, collectively contribute to facilitating HPV infection, DNA replication and generation of new viral particles, ultimately leading to the development of characteristic wart-like lesions on the skin and mucous membranes. The host immune response plays a critical role in the natural history of HPV infection, with some individuals effectively clearing the virus, while others develop persistent infection. In cases of persistent infection or impaired immune responses, genital warts may develop, and manifest as raised, flesh-coloured lesions with a cauliflower-like appearance.

Figure 21: Pathogenesis of HPV infection



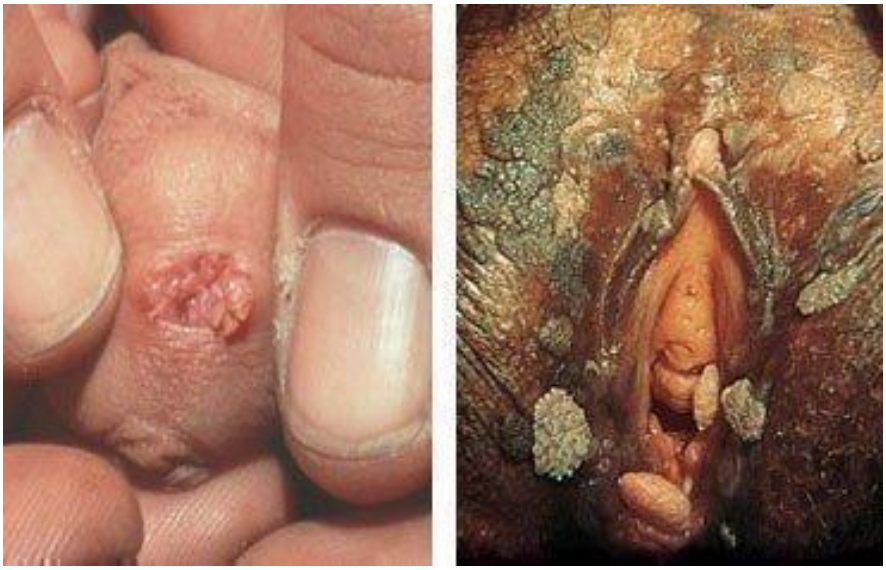
High-risk HPV types, such as HPV 16 and HPV 18, can infect the genital mucosa through mechanisms similar to low-risk types. Once inside the host cell, these high-risk HPV types express viral oncoproteins, notably E6 and E7, which play a pivotal role in cellular transformation and oncogenesis by disrupting key cellular regulatory pathways. E6 and E7 oncoproteins interact with cellular tumour suppressor proteins,

such as p53 and retinoblastoma (Rb), leading to their degradation and aberrant cell cycle control. Dysregulation of cellular regulatory mechanisms by HPV oncoproteins promotes genomic instability and the accumulation of genetic mutations, facilitating the progression of infected cells towards malignancy. High-risk HPV types, particularly HPV 16 and 18, are strongly associated with the development of cervical, anal, and other HPV-related cancers. Persistent HPV infection is influenced by various factors, including viral load, viral genotype, host immune response, and environmental factors, is the strongest risk factor for development of HPV-attributable precancers and cancers.

Clinical Manifestations and Disease Spectrum of HPV infection

Clinical features of HPV infection can vary depending on the type of HPV involved, the site of infection, and individual factors such as immune status. Clinical features of HPV infection encompass a wide range of manifestations, varying from benign genital warts to potentially life-threatening cancers.

Figure 22: Genital Warts (Condylomata Acuminata): (Image courtesy: Habif TP, Campbell JL, Chapman, MS et al. Dermatology DDxDeck. 2006; Mosby Elsevier)



Anogenital warts are common and predominantly caused by non-oncogenic HPV types 6 or 11, accounting for 90% of cases. Occasionally, oncogenic HPV types 16, 18, 31, 33, and 35 may also be detected in anogenital warts, typically in conjunction with HPV 6 or 11 infections, which can be associated with foci of high-grade squamous intraepithelial lesion (HSIL), particularly among persons who have HIV infection. The incubation period for the development of warts typically ranges from 3 weeks to 8 months but can extend up to 18 months.

Anogenital warts manifest as benign epithelial skin tumours with various clinical presentations. These warts can appear as single or multiple lesions, exhibiting soft, non-keratinized texture on moist skin areas and firm, keratinized characteristics on dry, hairy skin surfaces. Clinically, anogenital warts may present as raised, flesh-coloured growths with a cauliflower-like appearance, can be papular or pedunculated, and vary in size from small papules to larger, confluent masses. Although, anogenital warts more commonly appear as soft cauliflower-like growths of varying sizes, and less commonly as flat, plaque-like, or pigmented warts. However, large warts may rarely present with secondary infection and maceration. In some rare cases, warts may grow rapidly, infiltrating local tissue or causing local erosion (Buschke Lowenstein lesion). Although genital warts are often asymptomatic, they can lead to itching, discomfort, or bleeding, particularly during sexual activity or with irritation.

They commonly appear around specific anatomical sites such as the vaginal introitus, beneath the foreskin of the uncircumcised penis, or on the shaft of the circumcised penis. Additionally, warts may manifest at multiple locations within the anogenital epithelium or within the anogenital tract, including the cervix, vagina, urethra, perineum, perianal skin, anus, or scrotum.

Due to the multifocal nature of HPV infection, warts can occur at any genital or peri-genital site. However, lesions commonly occur at the sites of trauma during sexual intercourse. Perianal lesions can occur in both sexes, though not exclusive to anal intercourse, reflecting the regional distribution of HPV infection However, they are more frequently observed in MSM. Additionally, intra-anal warts are typically associated with penetrative anal intercourse. Asymptomatic lesions resulting from genital HPV types may manifest on various sites, including the vagina, cervix, urethral meatus, and anal canal. Additionally, extra-genital lesions attributed to genital HPV types may appear in the oral cavity, larynx, conjunctivae, and nasal cavity.

HPV associated cancers

Persistent infection with oncogenic HPV types is causally linked to nearly all cervical cancers and a significant proportion of other cancers including vulvar, vaginal, penile, anal, and oropharyngeal cancers.

Cervical Dysplasia and Cervical Cancer:

Nearly all cervical cancers are believed to be caused by HPV, with HPV detection reported in about 90% of cervical cancers worldwide. Among HPV types, HPV 16 and 18 are the most common, detected in approximately 70% of cases. Other prevalent types include HPV 31, 33, 45, 52, and 58. In a U.S. study, HPV was found in 91% of cervical cancers, with HPV 16 being the most prevalent at 51%, followed by HPV 18 at 16%, and other oncogenic and rare types at 24%. Besides persistent high-risk HPV infection, other risk factors for cervical precancer and cancer include smoking, higher parity, combine oral contraceptive use and HIV infection or immunodeficiency.

HPV, particularly high-risk strains like HPV 16 and HPV 18, strongly correlates with cervical dysplasia and cancer. Dysplasia, ranging from mild to severe cervical intraepithelial neoplasia (CIN), presents with abnormal vaginal bleeding, post-coital bleeding, or atypical Pap smear result. If untreated, dysplasia can progress to invasive cervical cancer, marked by abnormal vaginal bleeding, pelvic pain, and dyspareunia.

Histological terminology for cervical precursors is evolving, transitioning from CIN grades to cytological designations like LSIL (low-grade squamous intraepithelial lesion) and HSIL (high-grade squamous intraepithelial lesion). HSIL and AIS (adenocarcinoma in situ) are considered cancer precursors requiring treatment, while LSIL often resolves without intervention.

Cervical cancer is the only HPV-associated cancer for which screening is recommended, typically done through exfoliated cytology (Pap tests) combined with clinical HPV testing when appropriate. Abnormalities detected in screening lead to further evaluation, with diagnosis based on histological examination of tissue samples.

Vulvar and Vaginal Precancers and Cancer

Worldwide studies indicate that HPV is detected in a large majority of vulvar intraepithelial neoplasia grade 2 or 3 (VIN2/3) cases (85%) and 40% of invasive vulvar cancer cases. HPV 16 is the most detected type. Similarly, globally, 90% of vaginal intraepithelial neoplasia grade 2 or 3 (VaIN2/3) cases and 70% of invasive vaginal cancers test positive for HPV DNA.

Anal Dysplasia and Anal Cancer:

Anal intraepithelial neoplasia (AIN) grade 2/3 is considered a precursor to anal cancer, although its natural history, including progression and regression rates, is less understood compared to cervical disease. Globally, HPV is detected in 84% of anal cancers, with a higher prevalence in AIN2/3 (94%), with HPV 16 being the most common type detected. Men who have sex with men (MSM) and individuals with HIV infection face elevated risks, where HPV infection, particularly in receptive anal intercourse, contributes to anal dysplasia and cancer. Symptoms include anal bleeding, pain, pruritus ani, or discharge, with untreated dysplasia progressing to invasive anal cancer, characterized by rectal bleeding, anal pain, and changes in bowel habits. However, routine anal cancer screening with anal cytology is not universally recommended due to insufficient evidence regarding screening methods, target populations, and treatment response. However, some clinical centres screen high-risk populations using anal cytology followed by high-resolution anoscopy for those with abnormal results.

Oropharyngeal Cancer

Oropharyngeal cancers can be linked to HPV infection, alongside traditional risk factors like tobacco and alcohol use. Worldwide, HPV DNA is detected in a significant proportion of oropharyngeal cancers, with HPV 16 being the predominant type. HPV-associated

oropharyngeal cancers, including cancers of the tonsils and base of the tongue, are increasingly recognized because of oral HPV infection, particularly with high-risk HPV types.

Penile Cancer

Penile cancer is relatively uncommon, but HPV is associated with a significant proportion of cases globally, accounting for 40%-50% of penile squamous cell cancers. Among HPV-positive penile cancers, HPV 16 is commonly detected. Apart from HPV, independent risk factors for penile cancer include cigarette smoking and lack of circumcision.

HPV associated Other Manifestations

Recurrent Respiratory Papillomatosis (RRP):

Recurrent Respiratory Papillomatosis (RRP) is a rare condition characterized by the growth of benign HPV-associated papillomas in the respiratory tract, particularly the larynx and trachea. Clinical features of RRP may include hoarseness, stridor, dysphonia, and respiratory distress, particularly in children. HPV types 6 and 11 are commonly implicated in RRP cases.

Other Cutaneous Manifestations:

HPV infection can also lead to various cutaneous manifestations beyond genital warts, including common warts (verrucae vulgaris), plantar warts, and flat warts (verrucae plana). These lesions typically occur on non-genital skin surfaces and may present as hyperkeratotic papules or plaques with a rough texture.

Diagnosis

Accurate diagnosis is crucial for effectively managing anogenital warts. While many warts can be identified through clinical examination, certain lesions may necessitate magnified examination, such as with a colposcope, to differentiate them from other genital lumps like vestibular papillomatosis or molluscum contagiosum.

Although visual inspection is the primary method for diagnosing anogenital warts, biopsy may be necessary for atypical lesions or when uncertainty arises. Biopsy becomes even more crucial for immunocompromised individuals or when standard therapy proves ineffective. If lesions exhibit unusual characteristics like pigmentation, induration, affixed to underlying tissue, bleeding, or ulceration, or if diagnosis remains uncertain despite initial inspection, biopsy is warranted. Acetowhite testing is not recommended routinely for diagnosis of AGW. Evaluation of the genitalia and perianal skin is crucial for identifying the complete scope of warts. When perianal warts are present, it's common for patients to also have warts in the anal canal. Therefore, if patients exhibit anal symptoms like irritation or discharge, it's advisable to conduct an examination of the anal canal.

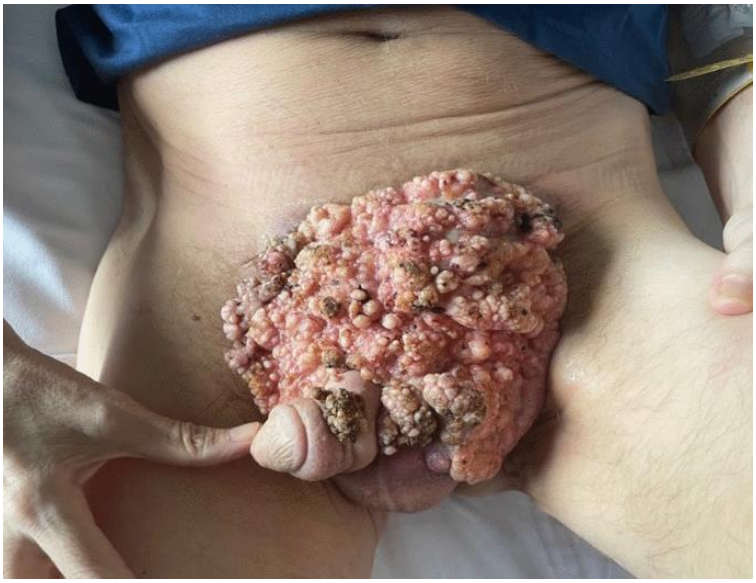
In some cases, patients may have intraepithelial neoplastic lesions in the anogenital area, with or without concurrent benign warts. These neoplastic lesions can affect various regions, including the vulva (VIN), vagina (ValN), perianal area (PAIN), anus (AIN), and penis (PIN). Diagnosis of

intraepithelial neoplasia is typically confirmed through histological examination. Certain factors such as pigmentation, depigmentation, pruritus, underlying immune deficiency, or a history of intraepithelial neoplasia in the same or different anogenital sites may raise suspicion of anogenital neoplasia. HPV testing is not recommended for anogenital wart diagnosis because test results are not confirmatory and do not guide genital wart management.

The differential diagnosis of AGW can include several different skin conditions such as condyloma latum, seborrheic keratoses, dysplastic and benign nevi, molluscum contagiosum, pearly penile papules, and neoplasms

In addition to these skin conditions, high-grade intraepithelial lesions and cancers can mimic AGWs, posing challenges in diagnosis. Bowen's disease, an in situ squamous cell carcinoma, typically remains confined to the epidermis and only rarely becomes invasive. Associations between Bowen's disease and both low- and high-risk HPV types have been documented. Bowenoid papulosis often presents similarly to AGWs, but histological examination typically reveals squamous cell carcinoma in situ. Buschke-Lowenstein tumours, a rare form of highly differentiated genital carcinoma, are associated with specific subtypes of low-risk HPV.

Figure 23: Buschke-Lowenstein tumour



Treatment

The main objective of treatment for anogenital warts is the removal of the warts and improvement of associated symptoms, if present, and treatment results in relieve cosmetic concerns. Anogenital warts may

resolve spontaneously, remain stable, or proliferate if left untreated. Given that spontaneous resolution can occur in less than a year, one option is to observe and wait for natural resolution. However, available therapies for anogenital warts can help reduce the size and number of warts, although they are unlikely to eliminate HPV infectivity. It is currently unclear whether reducing HPV viral DNA through treatment leads to a decrease in future transmission.

Treatment of anogenital warts should consider factors such as wart size, number, and location, as well as patient preferences, treatment costs, convenience, adverse effects, and provider expertise. There is no conclusive evidence indicating the superiority of any single recommended treatment over others, and no one treatment is universally ideal for all patients or all warts. Shared decision-making between patients and providers regarding treatment strategies has been linked to improved clinical outcomes and should be promoted. Given the limitations of individual treatments, clinicians may opt for combination therapy, such as provider-administered cryotherapy combined with patient-applied topical therapy between visits, although there is limited data on its efficacy and risk of complications. Treatment regimens are classified as either patient-applied or provider-administered modalities.

Patient-applied treatments are favoured by some individuals. It's crucial to ensure the effectiveness of these treatments by providing clear instructions to patients and identifying all accessible anogenital warts during clinic visits. Follow-up appointments, typically scheduled after a few weeks of therapy, allow providers to address any questions or concerns about medication usage, manage any side effects, and evaluate the treatment's response.

Imiquimod

Imiquimod, a patient-applied topical treatment, functions as an immune enhancer by stimulating the production of interferon and other cytokines. Acting as a toll-like receptor-7 (TLR7) agonist, it triggers local tissue macrophages to release interferon-alpha and other cytokines, initiating a local cell-mediated response. However, the response to imiquimod treatment may be delayed for several weeks. It is not approved for use in pregnancy due to lack of data.

Imiquimod 5% cream is typically applied once at bedtime, three times a week, for a duration of 16 weeks. Similarly, imiquimod 3.75% cream is applied once at bedtime every night for fewer than 8 weeks. After application, the treatment area should be washed with soap and water 6-10 hours later. However, it's important to note that imiquimod 3.75% cream is not currently available in Sri Lanka.

Imiquimod use can lead to local inflammatory reactions, such as redness, irritation, induration, ulceration or erosion, and vesicles, may need to undergo temporary cessation of treatment. Additionally, hypopigmentation has been reported as a potential side effect.

Clinical trials comparing Imiquimod to placebo have demonstrated response rates similar to those of other topical agents. While some studies suggest a lower relapse rate with Imiquimod, direct comparisons with other therapies are lacking.

It's important to avoid unprotected sexual contact soon after applying Imiquimod due to potential irritant effects on partners, and latex condoms may be weakened by contact with the cream. Immune deficiency may not preclude the use of Imiquimod for anogenital warts, and it has been used in HIV-positive individuals. Imiquimod may exacerbate inflammatory skin conditions and should be used cautiously in patients with autoimmune conditions such as psoriasis, vitiligo, or lichenoid dermatoses, although systemic absorption is minimal. Non-responders after 12-16 weeks should switch to alternative therapies.

Podophyllotoxin

Podophyllotoxin, a purified extract derived from podophyllin, is a patient-applied antimitotic drug known to induce necrosis in warts. It is available in two formulations: a 0.15% cream and a 0.5% solution, both of which are effective against genital warts. While both formulations exhibit similar efficacy, the cream may be more convenient for patients to apply, especially for warts in less accessible areas.

Treatment with podofilox solution (Condyline®) or podofilox gel (Warticon) involves twice-daily application for three consecutive days, followed by a four-day break. This treatment regimen can be repeated for up to four or five cycles, depending on the product used. Medical supervision is recommended, especially if the treated area exceeds 4cmx2cm. The total wart area treated should not exceed 10cm^2, and the daily volume of podofilox should not exceed 0.5 mL.

Podophyllotoxin is licensed for use on warts affecting the penis and female external genitalia but is commonly used for anogenital lesions at all sites. Mild to moderate pain or local irritation may occur after treatment, and patients should allow the gel or solution to dry after each application. Treatment should be discontinued if significant side effects such as soreness or ulceration occur.

While podophyllotoxin treatment cycles are typically limited to four or five cycles, repeat cycles may be considered if the warts are responding to treatment. However, caution should be exercised to avoid unprotected sexual contact immediately after application due to potential irritant effects on partners. Additionally, podophyllotoxin is contraindicated during pregnancy. Patient applied Podophyllotoxin preparations are currently not available in Sri Lanka.

Provider-administered therapy

Cryotherapy

Cryotherapy, a provider-administered therapy, is utilized to destroy warts through thermal-induced cytolysis. This technique involves using a liquid nitrogen spray or a cryoprobe to induce cytolysis at the dermal/epidermal junction, leading to necrosis. Proper training of healthcare providers is essential to ensure the correct administration of cryotherapy, as both overtreatment and undertreatment can lead to complications or reduced efficacy.

During cryotherapy, treatment should be applied until a "halo" of freezing has been established a few millimetres around the

treated lesion. The procedure may involve a single freeze or a double freeze-thaw technique, with no experimental evidence indicating that the technique used or the duration of freezing affects the response rate. However, achieving a complete freeze of the lesion is essential for optimal efficacy, even if it takes longer than the typical 15-30 seconds, limited by patient tolerability.

For benign skin lesions like genital warts, a single treatment session may be sufficient. Cryotherapy is typically repeated at weekly intervals, and lack of response after four weeks may necessitate consideration of alternative treatment modalities.

Pain during and after cryotherapy application is common, often followed by necrosis and blistering. In cases where warts are present in multiple areas or the wart area is extensive, local anaesthesia (topical or injected) may be used to facilitate therapy.

Surgical excision

Surgical excision offers the advantage of eliminating most warts in a single visit, although recurrence remains possible. Excision, a surgical approach, involves the removal of warts under local anaesthetic injection and may be suitable for pedunculated or large warts, as well as for small numbers of keratinised lesions at accessible anatomical sites. Haemostasis can be achieved using electrosurgery or the application of a haemostatic solution or paste, such as ferric subsulphate (Monsel's solution). Surgical treatment can be repeated as necessary, making it a viable option for managing small numbers of warts, although it may be underused.

Electrosurgery

Electrosurgery provides three distinct methods for addressing anogenital warts

Electrocautery: Utilizes controlled burning to target both the warts and adjacent tissue.

1. Hyfrecation: Involves the controlled application of electrical current to produce superficial charring, with potential for deeper tissue treatment.
2. Monopolar surgery: Offers versatility through the generation of different waveforms, facilitating precise desiccation, cutting, or coagulation while minimizing collateral tissue damage.

To mitigate scarring and optimize healing, maintaining skin bridges between treated areas is advised, alongside ensuring proper ventilation during procedures.

Laser treatment

Laser treatment offers benefits in managing large-volume warts and addressing warts in anatomically challenging areas such as the urethral meatus or anal canal. Laser treatment may also prove effective for intraurethral warts, particularly for those who have not responded well to other treatment options.

External lesions are commonly treated with carbon dioxide lasers, while internal lesions may require carbon dioxide or diode lasers. However, laser therapy is more costly

compared to topical or other ablative methods. During laser procedures, there is a risk of generating a smoke plume containing HPV DNA, which can potentially infect the respiratory tract of operating personnel. Therefore, Treatment of anogenital and oral warts should be performed in well-ventilated areas following standard precautions like wearing masks and using local exhaust ventilation.

Trichloroacetic acid (TCA)

Trichloroacetic acid (TCA) is a caustic agent which is used as a provider applied treatment option available to treat AGW, which destroy warts through chemical coagulation, causing cellular necrosis of proteins. It's typically applied weekly in a specialist clinic setting using an 80-90% solution, but careful application is crucial due to its extreme corrosiveness. TCA solution has a low viscosity, so it can spread rapidly and damage adjacent tissues if applied excessively. To protect surrounding skin, petroleum jelly can be applied, and only a small amount should be used directly on the warts and allowed to dry before the patient moves. TCA can cause intense burning for 5-10 minutes after application and may lead to dermal ulceration, making it unsuitable for large volume warts. It can be used at most anatomical sites, and neutralizing agents like sodium bicarbonate should be readily available in case of excess application or spills. Liquid soap preparations or talc powder can also be used to neutralize or remove unreacted acid.

Alternative regimes

Alternative regimens for treating external genital warts, including podophyllin resin, intralesional interferon, photodynamic therapy, and topical cidofovir, have less documented efficacy compared to standard treatments. Shared decision-making between patients and providers is important to assess the benefits and risks of these regimens, which may have more side effects.

Podophyllin resin

Podophyllin resin is no longer recommended due to safety concerns, such as severe systemic toxicity, especially when not washed off within 4 hours. However, in certain cases following strict guidelines, podophyllin resin 10%-25% in a compound tincture of benzoin might be considered for provider-administered treatment. Application should be restricted to less than 0.5 mL of podophyllin or an area smaller than 10cm^2 of warts per session and washing off within 1-4 hours is necessary to avoid local irritation and systemic toxicity. Further, treatment should not be applied to areas with open lesions, wounds, or friable tissue. The safety of podophyllin resin during pregnancy has not been established.

5-Fluorouracil,

5-Fluorouracil, available as a 5% cream, acts as a DNA anti-metabolite but is restricted in its use due to local adverse effects such as chronic neovascularisation and vulval burning. It is also contraindicated during pregnancy due to its potential teratogenic effects. Despite being recognized for its potential in treatment by a Cochrane review, its inferior cure rates compared to combination therapies have resulted in its exclusion from the routine management of anogenital warts.

Interferons

Interferons, including alfa, beta, and gamma, are available in various regimens such as creams, intra-lesional, or systemic injections, but their utility is limited by cost, systemic side effects, and variable response rates. While low dose injection cycles alongside laser therapy have shown promise in reducing relapse rates, interferons are not endorsed for routine anogenital wart management and should only be used under expert guidance.

Other Management considerations

Follow up

Anogenital warts typically show improvement within 3 months of treatment, with factors like immunosuppression and treatment adherence influencing response. If no significant improvement after a full course of treatment or severe side effects occurs, a new therapy should be considered. Throughout the treatment process, continuous evaluation of both treatment response and therapy-associated side effects is essential. Complications from treatment are infrequent when administered correctly but may include, persistent hypopigmentation or hyperpigmentation, particularly with ablative modalities like cryotherapy and electrocautery, or with immune modulating therapies such as imiquimod cream. Scarring, though rare, may occur, especially if insufficient time is allowed for healing between treatments. In some cases, treatment may lead to chronic pain syndromes such as vulvodynia or hyperesthesia at the treatment site, and in instances involving anal warts, it can cause painful defecation or the formation of fistulas.

Counselling

When providing counselling to individuals with anogenital warts, healthcare providers should cover a comprehensive set of points.

Firstly, it's important to clarify that if left untreated, genital warts may resolve spontaneously, remain stable, or increase in size or number over time. Additionally, it's crucial to emphasize that the HPV types responsible for genital warts are distinct from those that can cause cancer, and women with genital warts do not require more frequent Pap tests.

Moreover, it's essential to communicate that the timing of HPV acquisition cannot be definitively determined, and genital warts may appear months or even years after contracting HPV. It is also important to highlight that HPV types causing genital warts can be transmitted to others, even without visible signs of warts, and sexual partners often share the virus.

Furthermore, despite being common and benign, receiving a diagnosis of genital warts may have a significant psychosocial impact on individuals. Treatment for genital warts can address the visible warts, but it does not eliminate the virus itself. Therefore, recurrence of genital warts is common, especially within the first three months after treatment.

Given the sexual transmission of HPV, individuals with genital warts should undergo testing for other sexually transmitted infections (STIs). It's also crucial

to discuss that HPV may persist and can still be transmitted to sexual partners even after the warts have been treated.

While consistent and correct condom use can reduce the risk of transmitting genital warts, it is important to note that they may not provide complete protection as HPV can infect areas not covered by a condom, potentially limiting their efficacy against HPV transmission.

Lastly, individuals should be informed that an effective vaccine is available for both males and females to prevent HPV infection including genital warts. However, this vaccine does not treat existing HPV infections or genital warts but can prevent most cases among those not yet exposed to wart-causing HPV types.

Management of Partners

Current sexual partners may benefit from evaluation for undetected genital warts, other sexually transmitted infections (STIs), or the need for HPV-related information or guidance. Partners should be informed that they could already harbour HPV even in the absence of visible warts, thus HPV testing for partners of individuals with genital warts is not advised. Notification of past sexual partners is not recommended.

Special Considerations in Pregnancy and breast feeding

During pregnancy, caution should be exercised with certain treatments for anogenital warts due to potential teratogenicity or lack of safety data, such as podophyllotoxin, 5-fluorouracil, and imiquimod. Safer options include TCA, cryotherapy, excision, and ablative methods.

While wart removal during pregnancy is possible, complete resolution may be challenging until after delivery. Treatment aims to minimize lesions at delivery to reduce neonatal exposure to the virus.

There is a rare risk of respiratory papillomatosis in infants and children caused by HPV types 6 and 11, although the exact transmission route (i.e., transplacental, perinatal, or postnatal) is not fully understood. Caesarean delivery is not recommended solely to prevent HPV transmission to the newborn, but it is indicated for pregnant women with anogenital warts if there is pelvic obstruction or excessive bleeding risk during vaginal delivery (Gilson et al., 2015; Hazra et al., 2022). Pregnant women with anogenital warts should also be informed about the very low risk (4:100,000 births) of warts on the larynx of their infants or children (recurrent respiratory papillomatosis).

The safety of certain treatments for anogenital warts during breastfeeding is uncertain. Imiquimod, despite undetectable levels in serum post-topical application, lacks specific guidance for lactating mothers and is therefore not recommended. Similarly, due to insufficient data on the excretion of topically applied podophyllotoxin in human milk and the potential risk to breastfed infants, its use is not recommended.

HIV and Other Causes of Immunosuppression

Individuals with HIV infection or other forms of immunosuppression with impaired cell mediated immunity are at increased risk of

developing anogenital warts compared to immunocompetent individuals. Additionally, they may present with larger or more numerous lesions, exhibit reduced responsiveness to therapy, and experience more frequent recurrences after treatment. While altered treatment approaches for immunocompromised individuals are not supported by current data, they may necessitate longer treatment courses and require careful monitoring. Moreover, due to a potentially increased risk of squamous cell carcinomas resembling anogenital warts among immunosuppressed individuals, biopsy for confirmation of diagnosis may be warranted in suspicious cases.

Prophylactic HPV vaccination

The first HPV vaccine was licenced in 2006, and presently 6 prophylactic HPV vaccines are licensed (Box 12). These vaccines are designed to be administered before the onset of sexual activity among adolescents to maximize their efficacy. They are manufactured using recombinant DNA and cell-culture technology from the purified L1 structural protein, that self-assembled to produce virus-like particles (VLPs) of HPV types, without live biological products or viral DNA and are therefore non-infectious. They are designed for prophylactic use only, not for clearing existing HPV infection or treating HPV-related diseases. Currently, three types of HPV vaccines exist: bivalent, quadrivalent, and 9-valent (nonavalent). Currently in Sri Lanka, only the bivalent and quadrivalent vaccines are available.

Bivalent HPV vaccines contain VLPs targeting high-risk HPV types 16 and 18. Quadrivalent vaccines additionally protect against anogenital warts caused by types 6 and 11, with the nonavalent vaccine offering further coverage for types 31, 33, 45, 52, and 58.

Box 12 Different HPV vaccine types

Bivalent HPV vaccine: Protection against HPV 16,18
Quadrivalent HPV vaccine: Protection against HPV 16,18,6,11
Nonavalent HPV vaccine: Contains the same protection as Gardasil, plus additional protection against five additional HPV types: 31, 33, 45, 52, and 58. (Currently not available in Sri Lanka).

Prophylactic HPV vaccines are available in several types and recommended for use globally in females and males from 9 years to 26 years of age. They offer protection against various HPV-related conditions. They effectively prevent cervical, vulvar, and vaginal precancers and cancers, as well as anal precancers and cancers. Additionally,

the quadrivalent vaccine and nonavalent vaccine provide specific protection against ano-genital warts (condylomata acuminata) caused by HPV genotypes 6 and 11. These vaccines offer significant benefits, particularly for individuals who have not yet been sexually exposed to HPV.

Vaccine schedule in Sri Lanka

Two vaccination schedules are recommended based on age groups. All HPV vaccines are non-live and non-infectious. They can be administered concurrently with other vaccines, using separate syringes and injection sites. (Box 13)

Box 13 HPV vaccine schedule - Sri Lanka

0.5 mL is administered intramuscularly
2 doses for children 9 -14 years of age • At 0 and 6 months
3 doses for 15- 26 years of age: • 0, 1 month and 6 months for bivalent HPV vaccine • 0, 2 months and 6 months for quadrivalent HPV vaccine

Immunogenicity

HPV vaccines are highly immunogenic, eliciting a strong humoral response with robust memory. They are delivered via the intramuscular route, allowing rapid access to draining lymph nodes. Vaccine-induced antibodies reach the site of infection through active IgG transudation and exudation of interstitial antibodies.

Efficacy

Clinical trials have demonstrated the high efficacy of HPV vaccines in preventing cervical precancer lesions in young adult women, as well as genital warts and anal neoplasia in men. The vaccines have shown to be effective in preventing HPV infection and associated diseases.

Effectiveness

HPV vaccines were initially licensed based on their demonstrated clinical efficacy. Subsequent immunobridging studies have shown that antibody responses in adolescents are non-inferior to those in adults, supporting their efficacy in younger age groups. The vaccines have been effective in preventing HPV-related diseases in both genders, leading to their widespread use for adolescents and pre-adolescents.

Duration of protection

HPV vaccines offer prolonged protection, with antibodies remaining robust for up to 12 years. Studies confirm sustained effectiveness against HPV16/18 infections and related conditions for at least a decade

after vaccination, irrespective of the dose regimen. While there's no current recommendation for booster doses, ongoing research is assessing this aspect further.

Cross protection

Licensed HPV vaccines offer significant protection against HPV16 and HPV18, with the nonavalent vaccine additionally safeguarding against HPV types 31, 33, 45, 52, and 58. While certain bivalent and quadrivalent vaccines provide partial cross-protection against these non-vaccine HPV types, the extent varies. Studies have shown that the bivalent vaccine can offer cross-protection against HPV31/33/45, HPV35, and HPV58 for up to 11 years, even with a single dose, while the quadrivalent vaccine's cross-protection is statistically significant mainly for HPV31.

Adverse effects

Local reactions

Local adverse events, including pain, redness, and swelling at the injection site, are common following HPV vaccination.

Systemic reactions

Systemic adverse events following HPV vaccination, including headache, dizziness, myalgia, and gastrointestinal symptoms, are generally mild and self-limiting, with little difference observed between bivalent and quadrivalent vaccines.

Pregnancy and Breast feeding

HPV vaccines are not recommended during pregnancy.

HPV vaccines can be safely administered to breastfeeding women. Studies have shown that HPV vaccination does not affect the safety of breastfeeding for either the mother or the infant.

Vaccination of HIV patients

Immunocompromised individuals, including those living with HIV, should be prioritized for HPV vaccination and HPV vaccines in 3-dose schedules are considered safe for HIV-infected individuals. In HIV positive patients HPV vaccination has shown high immunogenicity, with a high proportion seroconverting for HPV vaccine types, particularly after receiving three doses of various HPV vaccines. Despite some declines in antibody titres over time, seropositivity remains high for at least 2-4 years post-vaccination. Lower antibody titres and seroconversion rates were observed in PLWHIV with lower CD4 cell counts or detectable HIV viral loads.

Prevention other than vaccination

Prevention sexual transmission

The most effective way to prevent genital HPV infection is to abstain from sexual activity. However, individuals can also reduce their risk by being in a monogamous relationship, limiting the number of sexual partners.

Consistent and correct condom use can significantly lower the risk of HPV and associated diseases. Studies show a 70% reduction in HPV infection among women whose partners used condoms consistently and correctly. Male circumcision has also been associated with a lower risk of HPV

infection in males and their female partners. Routine surveillance for HPV infection or partner notification is not considered useful for HPV prevention due to the high prevalence of the infection.

Cervical Cancer Screening

Cervical cancer screening, while not preventing HPV infection directly, can effectively prevent most cervical cancer cases and deaths by ensuring appropriate follow-up and treatment for women with abnormal screening results. WHO recommends cervical cancer screening to start at age 30 and continue until age 65. In Sri Lanka, screening targets women aged 35 and 45, but sexually active women can start screening 3 to 5 years after their first sexual intercourse due to rising cervical cancer rates.

Healthcare and Research Laboratory Workers

Healthcare and research lab workers face HPV-related risks during procedures and research. Proper ventilation and biosafety measures are crucial. However, the effectiveness of HPV vaccination in these settings is uncertain due to limited data on transmission risk and vaccine efficacy.

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Molluscum contagiosum

Dr Subhashini Jayasuriya

Introduction

Molluscum infection is a benign epidermal eruption of the skin caused by the DNA virus *Molluscum contagiosum*. Severe molluscum infection can occur in immunocompromised individuals.

Box 14 Transmission modes of Molluscum

Physical contact, fomites and autoinoculation which is commonly seen among children where lesion may affect face, trunk, neck or limbs.
Sexual contact as a STI affecting young adults where lesions occur in genital region, lower abdomen, upper thighs and buttocks.

Clinical Features

Molluscum contagiosum lesions exhibit distinctive features, typically presenting as smooth, firm papules with a central umbilication. These lesions range from 2 to 5 mm in diameter and vary in colour from pearly white to yellow. They often appear as clusters of multiple lesions. The lesions contain a cheesy material, which harbours infectious viral particles.

In cases of immunocompromise, larger molluscum lesions, often referred to as "giant molluscum" (exceeding 15 mm), may emerge. Molluscum contagiosum can affect any area of the body, depending on the mode of transmission. Autoinoculation, the transfer of the virus to different body regions, is a recognized phenomenon. While molluscum lesions are generally painless, they may occasionally be accompanied by pruritus, discomfort, or secondary bacterial infections. (Box 14)

In individuals with normal immune function, molluscum lesions typically resolve spontaneously within 6 to 18 months.

Diagnosis

The diagnosis of molluscum contagiosum is primarily clinical, relying on the distinctive appearance of the lesions. In cases of atypical presentations, dermoscopy and biopsy may be employed as adjunctive diagnostic tools to aid in confirming the diagnosis.

Management

General Advice

Patients should be informed that molluscum contagiosum typically resolves spontaneously within 6 to 18 months, and treatment is generally not necessary. However, they should be counselled regarding the risk of autoinoculation. It is recommended that patients refrain from shaving or waxing the affected areas. Squeezing the lesions should also be avoided, as it may lead to further spread of the infection and increase the risk of secondary bacterial infection. Additionally, patients should be advised against sharing towels, bed linens, or clothing while lesions are present to prevent transmission.

Treatment

Expectant management is recommended for immunocompetent patients.

Patients may seek treatment due to cosmetic reasons or associated symptoms of lesions (itching, secondary bacterial infection).

Box 15 Different treatment options for molluscum

Liquid nitrogen weekly application
0.5% Podophyllotoxin application twice daily for three consecutive days per week followed by a pause for 4 days for 4 weeks duration
Cauterization of lesions (If only small number of lesions are present)
Curettage (Only for small number of non-facial and non-genital lesions)
Imiquimod is no longer recommended as a treatment option for genital molluscum infection.

When patients seek active treatment for genital molluscum infection, liquid nitrogen therapy and topical podophyllotoxin are preferred. (Box 15)

Viral Hepatitis

Dr Ajith Karawita

Dr Nalaka Kulathunge

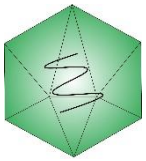
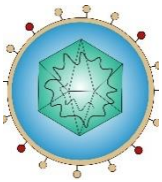
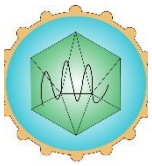
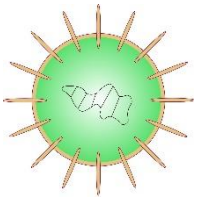
Introduction

Viral hepatitis is a preventable serious infection that puts infected people at higher risk for liver disease, cancer, and death. Viral hepatitis is an inflammation of the liver that is caused by five main strains of the hepatitis virus, referred to as types A, B, C, D and E. They all cause liver disease; however, they differ in disease distribution, modes of transmission, structurally, severity of the illness, treatment and care and prevention methods. Viral hepatitis types B, C and D (usually co-infected or super infected in hepatitis B infection), lead to chronic disease while hepatitis A and E are predominantly acute infections. After the initial infection, the spontaneous immune clearance rate is different by type of infection. Almost all recovers fully from hepatitis A and E with a lifelong immunity. However, hepatitis B and C may progress to chronic state.

Infections with hepatitis viruses, especially HBV and HCV, have been associated with a wide variety of extrahepatic manifestations. The five main viruses which cause hepatitis are summarized in the table 15 and shows important characteristics of different viral hepatitis.

However, there are many other viruses that can cause viral hepatitis. Infrequent causes of viral hepatitis may include Adenovirus, Cytomegalovirus (CMV), Epstein-Barr virus (EBV) and, rarely, Herpes simplex virus (HSV). Other pathogens (eg: virus SEN-V) may account for additional cases of non-A/non-E hepatitis.

Table 15: Classification of Viral hepatitis by types and other important characteristics

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
					
Structure	Non-enveloped, single stranded (ssRNA) virus in the Picornavirus group	Enveloped, partially double stranded DNA virus in the Hepadnavirus group.	Enveloped, single stranded RNA virus (ssRNA) belongs to Flavivirus group	Enveloped, incomplete single-stranded circular RNA virus with HBV surface antigen and hepatitis delta antigen (HDAg). It is the only member of the Deltaviridae group	Non-enveloped, single-stranded positive-sense RNA virus (ssRNA) classified within the Herpeviridae family
Target cells, attachment, and entry	Liver cells	Liver cells	Liver cells	Liver cells	Liver cells
Incubation period	15-50 days; average 28 days (CDC, 2023)	30-180 days (WHO, 2023)	15-150 days	30-60 days, Survival needs HBV as coinfection or superinfection	Ranges from 2-10 weeks, with an average of 5 to 6 weeks.

Pathogenesis

Five main types of viruses and their identified modes of transmissions and populations at risk of viral transmission are tabulated below.

Type of the virus	Infectious materials	Identified modes of transmission	Risk factors for transmission
Hepatitis A	Faeces of an infected individual	The virus is primarily spread when an uninfected (and unvaccinated) person ingests food or water that is contaminated with the faeces of an infected person (WHO, 2023)	● Poor sanitation, lack of safe water, living in a household with an infected person, being a sexual partner of someone with acute hepatitis A infection, use of recreational drugs, sex between men; and travelling to areas of high endemicity without immunization (WHO, 2023).

Type of the virus	Infectious materials	Identified modes of transmission	Risk factors for transmission
Hepatitis B	Infected body fluids like blood, saliva, vaginal fluids, and semen	**In high prevalence areas**: Vertical (mother-to-child) transmission is the primary mode, with horizontal (child-to-child, especially <5 years) transmission also significant. Bloodborne and sexual transmission are less common. **In intermediate prevalence areas**: Horizontal transmission remains important, with increasing concerns about sexual and bloodborne transmission. Vertical transmission is less common than in high-prevalence areas. **In low prevalence areas**: Sexual and bloodborne transmission (e.g., through injection drug use, unsafe tattooing/piercing, or healthcare settings) are more prominent. Vertical transmission is rare, due to effective vaccination programs. *The virus can survive outside the body for at least 7 days.	• Unprotected Sexual Activity: Increased risk for those with multiple partners or unprotected sex • Intravenous Drug Use: Sharing needles or paraphernalia heightens HBV risk. • Healthcare Workers: Higher exposure risk due to blood and needle contact. • Living in Endemic Areas: Higher transmission rates in regions like sub-Saharan Africa and parts of Asia. • Infants Born to Infected Mothers: Newborns are at risk without proper vaccination and immunoglobulin treatment. • Low Vaccination Rates: Unsatisfactory vaccination coverage increases infection risk

Type of the virus	Infectious materials	Identified modes of transmission	Risk factors for transmission
Hepatitis C	Infected blood	Bloodborne transmission: The most efficient route for HCV transmission is percutaneous exposure • Injection drug use – Contaminated needles or drug paraphernalia are the primary global transmission method. • Health care-associated – Transmission can occur in substandard settings (transfusion related) or due to rare breaches in infection control practices (occupational). • Other percutaneous exposures – Rare transmission can occur through blood exposure during rituals, tattooing, body piercing, or commercial barbering. Sexual transmission – Can be transmitted sexually, with higher risk among men who have sex with men (MSM), especially those also infected with HIV Perinatal transmission – About 5-6% of infants born to HCV-positive mothers contract the virus, with a higher risk if the mother is also HIV-positive.	• Injection Drug Use: The most common risk factor for HCV, with 50-90% of people who inject drugs showing evidence of infection. • Intranasal Drug Use: Users of intranasal drugs also have higher HCV prevalence, especially with "chem sex." • Incarcerated/Unstably Housed Populations: Higher HCV rates due to past or current injection drug use. • People with HIV: Co-infection is common, especially among people who inject drugs. HIV increases HCV risk, and the prevalence of HCV in people with HIV varies by geographic region. • Sexual Exposure: MSM have higher HCV prevalence, especially if HIV-positive. HCV is less common among heterosexual HIV-positive individuals. • Perinatal Transmission: HIV co-infection doubles the risk of vertical HCV transmission from mother to child. • Dialysis: HCV infection rates are higher among dialysis patients, despite a decline in incidence. • Healthcare Workers: Risk through percutaneous sharps injury. • Alcohol Use Disorder: Increased HCV infection rates (about 30%) among individuals with alcohol use disorder, potentially worsening liver damage. • Children Exposed Perinatally: HCV prevalence in children is addressed separately.

Type of the virus	Infectious materials	Identified modes of transmission	Risk factors for transmission
Hepatitis D	Infected blood	HDV transmission, similar to HBV, occurs through broken skin (such as through injections, tattooing, etc.) or contact with infected blood or blood products. While mother-to-child transmission is possible, it is rare.	HDV primarily affects high-risk groups, including people who inject drugs, individuals with a history of multiple transfusions/hemodialysis, men who have sex with men engaging in unsafe sex, people with hepatitis C virus or HIV infection and those from countries with high HDV prevalence. • Mediterranean Basin: HDV is endemic, with declining prevalence due to reduced chronic infections and HBV vaccination. • Mongolia and parts of Central Asia have high rates (up to 60% among HBV carriers), while Japan has low rates • HDV is uncommon in western countries Chronic HBV carriers are at risk of infection with HDV
Hepatitis E	Fecal material	HEV transmission occurs through contaminated food and water, blood transfusions, and potentially from mother to child. Person-to-person transmission is rare, but patients can spread the virus during fecal shedding. • Contaminated food and water: HEV genotypes 1 and 2 spread via fecal contaminated water, in areas with poor sanitation. Genotypes 3 and 4 are zoonotic, transmitted through contaminated food like undercooked meat, shellfish, and swine products. • Blood transfusions: HEV can be transmitted through blood transfusions, especially in endemic regions. • Perinatal transmission: HEV can be transmitted from mother to child, though it contributes minimally to the overall disease burden. • Breastfeeding: The role of breast milk in HEV transmission is unclear, though there is concern, and breastfeeding is discouraged for infected mothers until further data is available.	• Contaminated water: In regions with inadequate sanitation, drinking water may be contaminated with fecal matter. • Consumption of undercooked meat: Eating undercooked meat, especially from animals like pigs, can lead to infection. • Vulnerable populations: Pregnant women, individuals with pre-existing liver conditions, and those with weakened immune systems are at higher risk. • Conflict zones: Hepatitis E outbreaks are more common in conflict areas, such as war zones and refugee camps, where access to safe water and proper sanitation is limited.

Clinical features and management

Hepatitis A

Incubation period: 28 days (15-50 days)

Natural history:

- Contagious during the incubation period and one week of appearing the jaundice. (three weeks before to one week after onset of clinical illness).
- 85% of patients recover within two to three months, with nearly all fully recovering by six months

Table 16: Symptoms and signs of hepatitis A

Symptoms: 70% symptomatic	Signs
• <5yrs – mostly asymptomatic • Abrupt onset of nausea, vomiting, anorexia, fever, malaise, and abdominal pain • Within days to a week, dark urine (bilirubinuria) and pale stools (lack of bile pigment) • Followed by jaundice and itching (pruritus) in 40-70% of cases • Jaundice peaks in 2 weeks • Early symptoms lessen once jaundice develops	• Common: Jaundice, scleral icterus, hepatomegaly (80% of cases), and right upper quadrant tenderness. • Less common: splenomegaly, skin rash and arthralgias

Table 17: Hepatitis A different manifestations

Fulminant hepatic failure	Cholestatic hepatitis	Relapsing hepatitis	Autoimmune hepatitis
• Severe acute liver injury with encephalopathy and impaired liver function (INR ≥1.5) • Common in those over 50 or with liver diseases like hepatitis B or C • May require a liver transplant.	• Prolonged cholestasis, affecting <5% of acute hepatitis, is marked by jaundice lasting >3 months, pruritus, fever, weight loss, diarrhoea, and malaise. • High bilirubin (>10 mg/dL) and alkaline phosphatase, mild aminotransferase elevation, and increased cholesterol seen.	• Up to 10% of patients experience symptom relapse within six months, lasting less than three weeks clinically but up to 12 months biochemically. • No known cause and predisposing factors • Initial recovery, followed by milder symptoms and elevated serum aminotransferases.	•Rarely, HAV can trigger autoimmune hepatitis in susceptible individuals •characterized by hyperglobulinemia, autoantibodies (e.g., anti-nuclear, anti-smooth muscle), and liver inflammation.

	• Peak bilirubin occurs by week 8. • Usually resolves without complications • ultrasonography to rule out biliary obstruction. • Treatment is supportive, with cholestyramine for pruritus. • No corticosteroids are needed.	• Anti-HAV IgM antibodies persist, and HAV can be detected in stool, indicating infectivity. • Multiple and asymptomatic relapses may occur • Extrahepatic manifestations are possible. • Complete recovery is typical, and avoid unnecessary tests • Ultrasonography to rule out biliary obstruction needed.	

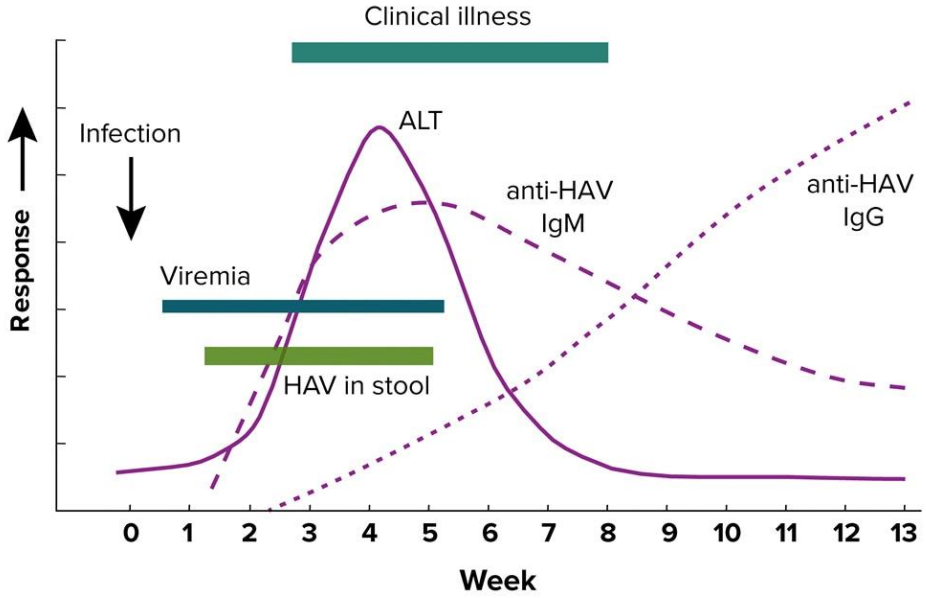
Complications

Extrahepatic manifestations — Specially seen in patients who have relapsing or cholestatic hepatitis. Evanescent rash and arthralgias are seen commonly. Other extrahepatic manifestations include: Leukocytoclastic vasculitis (often on the legs and buttocks), arthritis, glomerulonephritis, cryoglobulinemia, Optic neuritis, transverse myelitis, toxic epidermal necrolysis, myocarditis, thrombocytopenia, aplastic anaemia, red cell aplasia.

Diagnosis

Diagnosis of Hepatitis A
• Compatible clinical history • Presence of risk factors* • Serum IgM anti-HAV antibodies are detectable at symptom onset, peak during acute or early convalescence, and remain for 3-6 months. • In relapsing hepatitis, IgM persists throughout the disease.
Laboratory findings
Elevations of serum aminotransferases (>1000 iu/dL), bilirubin (≤10 mg/dL) & alkaline phosphatase (up to 400 U/L) • The serum aminotransferase elevations precede the bilirubin elevation. • ALT > AST • Serum aminotransferases peak one month after exposure, then decline (rate: 75% per week). • Serum bilirubin declines within two weeks of peak levels. • Elevations of acute-phase reactants and inflammatory markers.

Figure 24: Serology of Hepatitis A



Management

Table 18: Treatment outline of Hepatitis A

Treatment of Hepatitis A
• Usually self-limited, requiring supportive care. • Caution with liver-metabolized medications. • Fulminant hepatic failure requires aggressive support and liver transplantation. • No follow-up is needed

* Person-to-person contact (within households, institutional, daycare centres, military & sexual transmission), contact with/consumption of contaminated food or water, blood transfusion, Illicit drug use.

Prevention

Table 19: Summary of Prevention Methods for Hepatitis A

Protection prior to exposure	Protection following exposure
Vaccine is the primary tool for protection • For all >1year age, 6-12 months age if going to endemic areas, MSM, PWUD/PWID, CLD patients • Single-antigen vaccine (2 doses for children/adults) or Combination vaccine (3 doses for adults) • For travelers ≤40 years, at least first dose before departure • For travelers >40yrs/immunocompromised/with chronic diseases, first dose to be paired with immunoglobulins **Passive immunization with immune globulin** • Individuals who are allergic to the hepatitis A vaccine • Children <12 months of age.	**Vaccination and immunoglobulin** • Close contacts of confirmed HAV infection • Contacts in childcare centers with ≥1 case or ≥2 household cases • Food handlers **Not needed for exposure of a solitary case in schools, offices, or hospitals**

- **Hygienic practices to prevent HAV - handwashing, avoiding unsafe water and raw foods, heating food to >185°F (>85°C) for 1 minute.**

Hepatitis B

Table 20: Acute Hepatitis B clinical features and laboratory findings

Symptoms & signs	Laboratory findings	Diagnosis
• 30% show icteric hepatitis • <1% may go into fulminant hepatitis (due to massive immune-mediated lysis of infected hepatocytes) • Serum sickness-like syndrome during the prodrome (fever, skin rashes, arthralgia, and arthritis) • Followed by anorexia, nausea, jaundice, right upper quadrant discomfort, and constitutional symptoms, lasting 1-3 months. • Fatigue may persist after aminotransferase normalization.	• In acute phase - elevations of ALT and AST seen (up to 1000 to 2000 u/L & ALT > AST). • If anicteric hepatitis, bilirubin will be normal • Prothrombin time is one of the best indicators of prognosis. • If recovered, serum aminotransferases normalize within 1-4 months. • Persistent ALT elevation for >6 months indicates chronic hepatitis.	• Compatible clinical history • Presence of risk factors • **HBsAg - Positive** • Anti-HBs - Negative • **HBeAg - Positive** • Anti HBe -Negative **Anti HBc - IgM positive.**

Incubation period: 30 – 180 days (1-4 months)

Natural history: Majority recover by their own. However, HBV eradication rarely occurs and latent infection in hepatocytes can persist for decades, maintaining under T cell control. Liver damage may occur in latent infection and Immunosuppression can trigger reactivation.

Clinical features and Diagnosis

Acute hepatitis

70% has subclinical or anicteric hepatitis

Management

Table 21: Summary of acute hepatitis B infections management

Treatment
• Supportive treatment with measures to prevent transmission to contacts. • Hospitalization in coagulopathy, severe jaundice, encephalopathy, older patients, or those with comorbidities, poor social support, or difficulty with oral intake. • Poor prognostic factors: immunocompromised, concomitant infection with HCV or HIV, have pre-existing liver disease, older adults. • Indication for treatment: **Patients with severe disease** (coagulopathy - INR >1.5, persistent symptoms for > 4/52, marked jaundice - bilirubin >3 mg/dL for more than four weeks after presentation) **Patients with acute liver failure** Sometimes in fulminant hepatitis and immunocompromised statuses. • Short course of entecavir or tenofovir monotherapy is preferred (avoid interferon) • Stop treatment when 2 consecutive tests 4 weeks apart show HBsAg clearance

Chronic infection (CHB)

A history of acute hepatitis is found only in 30-50% of patients in low/intermediate prevalence areas, but most in high-prevalence areas lack this history due to perinatal infection.

Natural history: The progression from acute to chronic hepatitis B depends on age: 90% for perinatal infection, 20-50% for 1-5 years, and 5-10% for adults. In chronic HBV infection, about 30% may progress to cirrhosis and later liver cancer (HCC). However, some individuals may develop HCC directly without cirrhosis, while others may experience liver failure, with or without cirrhosis.

Table 22: Chronic Hepatitis B; clinical features and laboratory findings

Symptoms & signs	Laboratory findings	Extrahepatic manifestations
• Majority asymptomatic or have nonspecific symptoms like fatigue. • Exacerbations: -asymptomatic -can mimic acute hepatitis -can cause hepatic failure • Signs: (can be absent) -stigmata of chronic liver disease -features of decompensated cirrhosis	• May be normal LFT. • Most have a mild to moderate rise in AST and ALT. • During exacerbations: ALT can be fifty times the ULN, and AFP around 1000 ng/mL. • Low WBC & platelet in hypersplenism • Impaired hepatic synthetic function (hypoalbuminemia, prolonged prothrombin time, hyperbilirubinemia)	• Due to circulating immune complexes • Polyarteritis nodosa • Membranous nephropathy and glomerulonephritis, especially in children, with remission during HBe seroconversion • Sometimes aplastic anemia

Serology and phases of chronic hepatitis B infection

Principles in hepatitis B serology

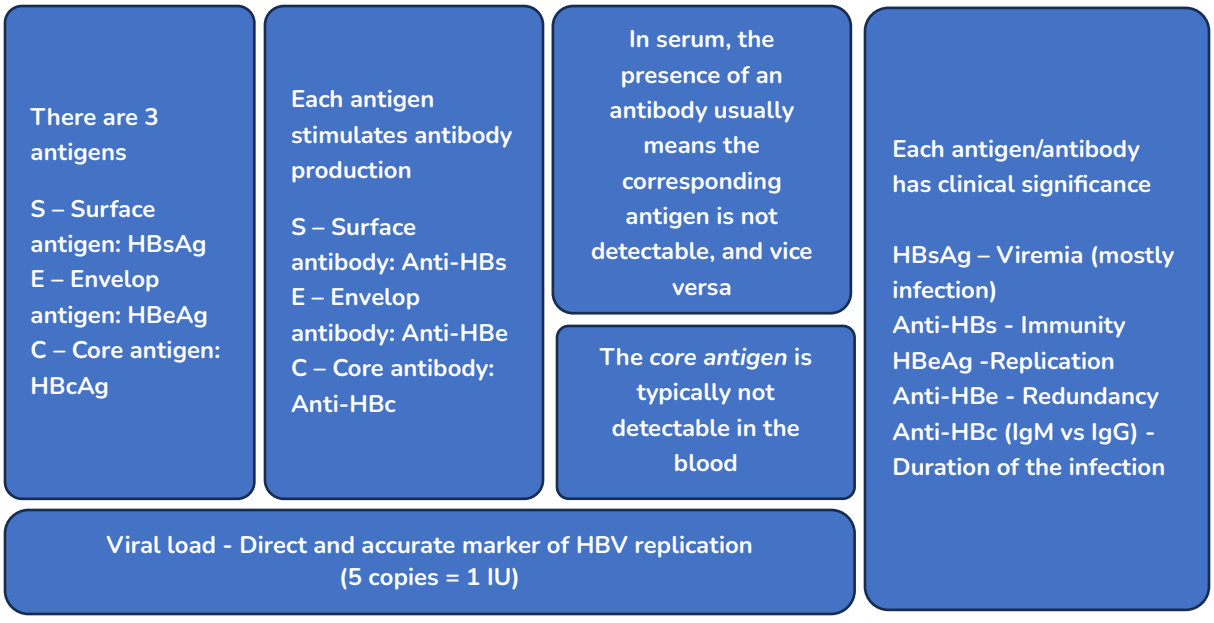


Figure 25: Serology pattern of acute hepatitis B infection (Adapted from WHO)

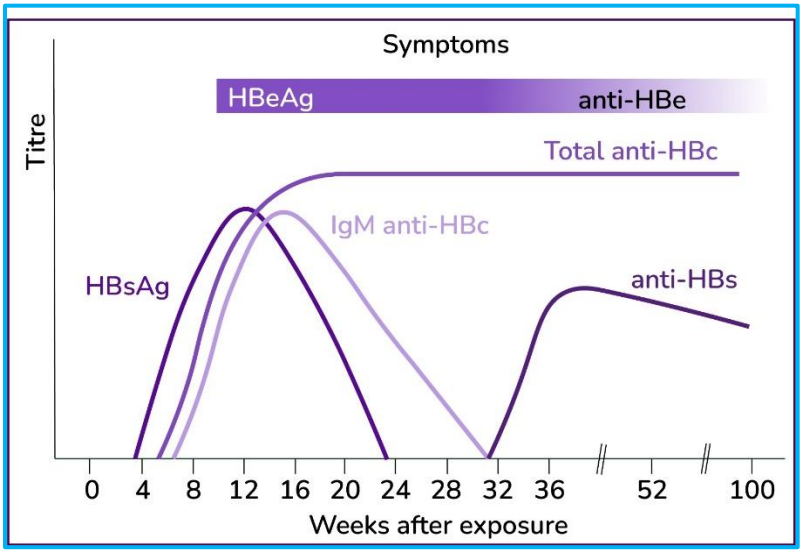
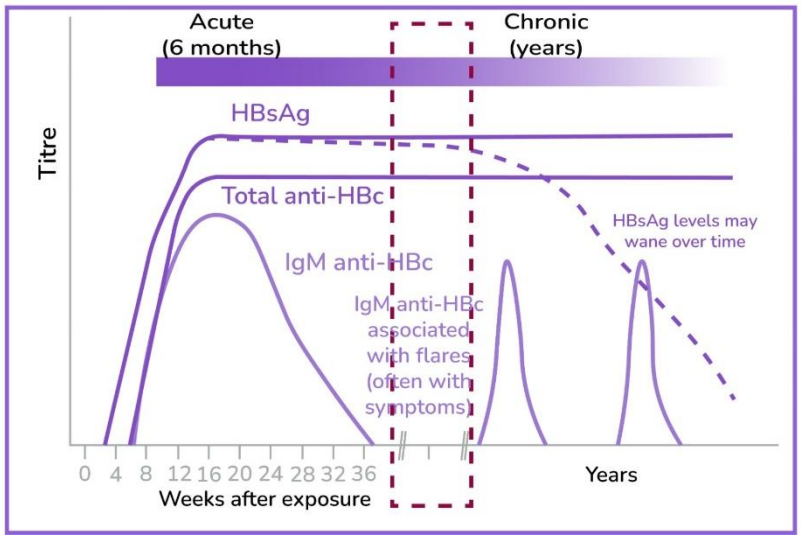


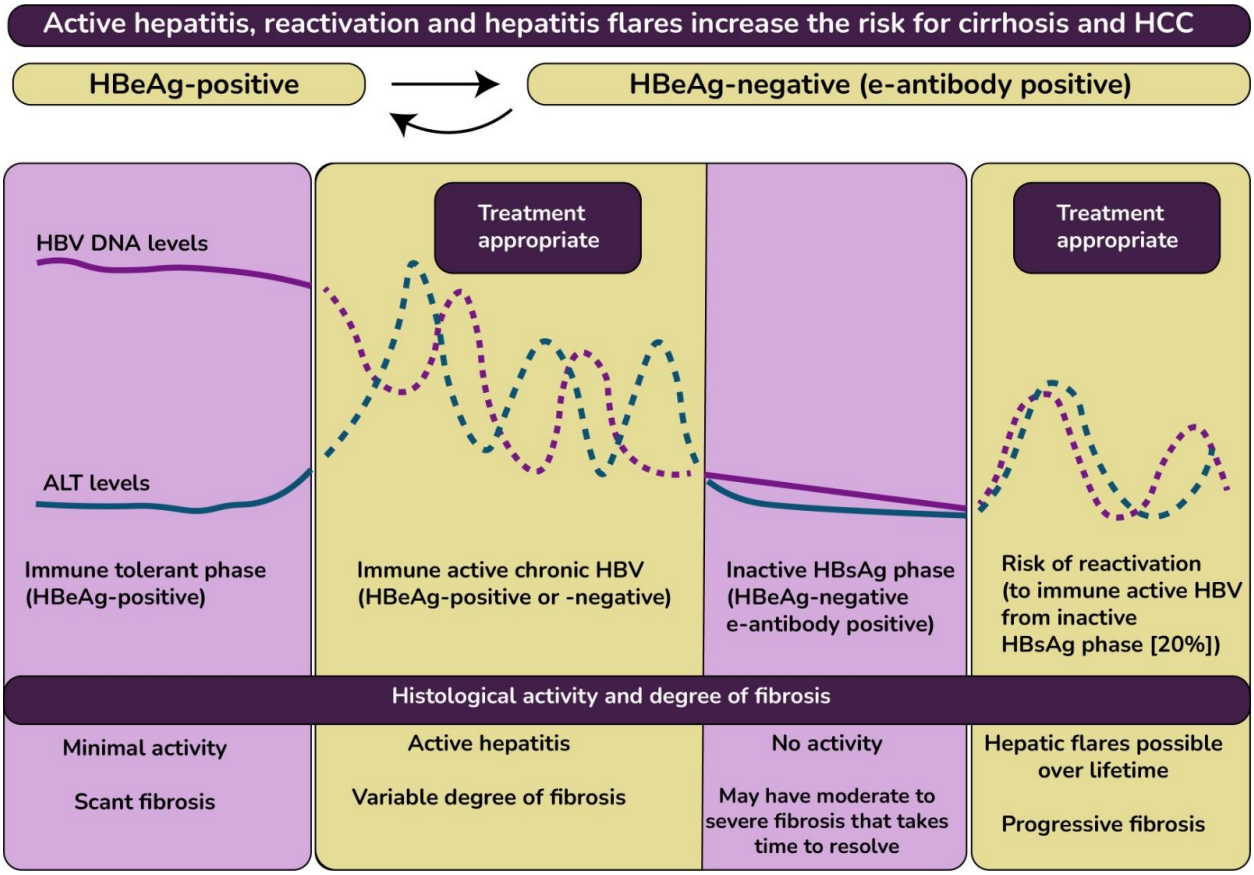
Figure 26: Serology pattern of chronic hepatitis B infection (Adapted from WHO)



The course of chronic HBV infection is influenced by virus replication, immune response, gender, alcohol use, co-infections, and factors like obesity and fatty liver, which may accelerate liver disease progression.

Chronic HBV typically has four phases, though not all patients go through all of them, and **phase reversal can occur**. The phases are named according to HBeAg positivity and presence of liver inflammation i.e. hepatitis (See below)

Figure 27: Different stages of Chronic hepatitis B infection



HBeAg+ve CHB infection (Immune tolerance)	**HBeAg+ve chronic hepatitis (Immune-active, HBeAg+ve)**	**HBeAg-ve CHB infection (Inactive chronic HBV)**	**HBeAg-ve chronic hepatitis (Immune-active, HBeAg-Ve)**

HBeAg+ve CHB infection (Immune tolerance)	HBeAg+ve chronic hepatitis (Immune-active, HBeAg+ve)	HBeAg-ve CHB infection (Inactive chronic HBV)	HBeAg-ve chronic hepatitis (Immune-active, HBeAg-Ve)
• Usually seen in MTCT patients. (almost always vertical transmission occur during delivery) • High HBV replication (HBeAg positive, high HBV DNA) • No liver disease symptoms • Normal ALT, and minimal liver biopsy changes. • Due to transplacental transfer of maternal HBeAg, T cells develop unresponsiveness to HBV antigens. • It can last 10-30 years, with very low HBeAg clearance rates of 2% in the first 3 years and 15% after 20 years.	• The immune tolerance to immune-active phase transition in perinatally acquired HBV typically occurs in the second and third decades (HBeAg clearance increases to 10-20% annually) • In adults with HBV, 70% achieve seroconversion within 10 years. • Exacerbations during this phase, often asymptomatic, can raise ALT, HBV DNA, anti-HBc IgM and AFP, potentially misdiagnosed as acute HBV or HCC. • Exacerbations are more common in men • Severe exacerbations can lead to liver decompensation. • Severe exacerbations need nucleos(ide) analogues & liver transplantation; interferon is contraindicated. • Not all exacerbations lead to HBeAg seroconversion (termed abortive immune clearance), and some may result in recurrent flares and increased cirrhosis/HCC risk	• A low/non-replicating phase with undetectable HBV DNA, normal ALT, and remission of liver disease. • Still significant inflammation or fibrosis can occur despite normal ALT. • Significant liver disease is rare if persistently normal ALT and HBV DNA ≤20,000 IU/mL. • Inactive carrier status should be based on at least three ALT and two to three HBV DNA levels over 12 months. • Combining HBsAg <1000 IU/mL and HBV DNA <2000 IU/mL accurately identifies the inactive carrier phase.	• Some with moderate HBV replication and active liver disease remain HBeAg-negative due to pre-core or core promoter mutations. • They are older patients & advanced liver disease with fluctuating HBV DNA and ALT levels seen. • Flares are linked to age ≥30, male sex, and pre-core mutations. • Majority with post-HBeAg seroconversion, has sustained remission, with negligible cirrhosis and HCC risk

Some chronic HBV patients become HBsAg-negative, with an annual clearance rate of 0.5-2%. This is often preceded by a decrease in HBV DNA. Those who clear HBsAg typically have a good prognosis, with rare progression to cirrhosis or hepatic decompensation. However, HCC risk persists, especially in patients with HCV/HDV coinfection, cirrhosis, or those older than 50. Occult HBV infection occurs when HBV DNA is present in the liver or blood without detectable HBsAg, often with anti-HBc antibodies. These individuals may be asymptomatic but can experience reactivation, especially during immunosuppression.

Important facts:

- Alcoholic patients with HBV infection experience faster liver damage,

increased risk of cirrhosis and HCC, and reduced survival
- Acute HCV-HBV coinfection can reduce HBV replication, hence liver damage
- But in some, co-infection or superinfection with HCV may increase the risk of severe hepatitis and fulminant hepatic failure.
- Dual HBV-HCV infections can lead to more severe liver disease and higher HCC rates. HCV treatment with peginterferon or DAAs may achieve sustained virologic response, but HBV replication could increase post-HCV clearance.
- HDV-HBV infection has worsened outcomes and accelerated cirrhosis.
- Triple infection with HBV, HCV, and HDV shows varied viral replication dominance.
- Hepatitis A vaccination is recommended for patients with chronic liver disease, including those with HBV.

Table 23: Diagnosis and treatment of CHB - a summary

<table>
<tr><th>Diagnosis</th><th colspan="4">Treatment</th></tr>
<tr><td rowspan="3">Initial evaluation
FBC, AST/ALT, total bilirubin, alkaline phosphatase, albumin, INR
HBeAg, anti-HBe, HBV DNA
Screen for fibrosis & HCC
Screen for HCV, HDV & HIV
Liver biopsy is not essential</td><td colspan="2">Patients without cirrhosis</td><td colspan="2">Patients with cirrhosis</td></tr>
<tr><td>HBeAg+</td><td>HBeAg-</td><td>HBeAg+/-</td><td>HBeAg+/-</td></tr>
<tr><td>VL >20,000 iu/mL
ALT ≤2 × ULN
Generally, no treatment
Monitor lifelong</td><td>VL >2000 iu/mL
ALT >2 × ULN or 1 x ULN with biopsy+
Treat till HBsAg loss</td><td rowspan="2">Detectable VL
Any ALT

Compensated:
Treat with ETV, TAF, or TDF indefinitely
Decompensated:
Treat immediately, regardless of ALT or HBV DNA levels with ETV or TAF</td><td rowspan="2">Undetectable VL
Any ALT
Compensated:
Observe and monitor lifelong with VL/ALT
Decompensated:
Refer for liver transplant and monitor.</td></tr>
<tr><td>VL >20,000 iu/mL
ALT >2 × ULN
If not severe observe for 6/12. Otherwise treat*</td><td>VL ≤2000 iu/mL
ALT ≤ULN
Monitor lifelong</td></tr>
<tr><td colspan="5">Monitoring
HBV DNA every three months until undetectable and every six months thereafter
Aminotransferases every three months until ALT is normal and then every six months in patients with an undetectable HBV DNA
HBeAg and anti-HBe annually in patients who are HBeAg positive to determine seroconversion
Screening for HCC (+/- AFP) every six month</td></tr>
</table>

*ETV, TAF, TDF, or PegIFN alfa are preferred | End-point – Seroconversion to anti-HBe | Duration: PegIFN alfa: 48 weeks, ETV, TAF, or TDF: at least 12 months after HBeAg seroconversion.

HCC: All HCC patients should receive nucleos(t)ide analogues to reduce recurrence risk and improve prognosis.

HCV Coinfection: For HBsAg-positive patients, initiate HBV therapy **with or before** HCV treatment. Monitor ALT and HBV markers in HBsAg-negative, anti-HBc-positive patients during HCV therapy.

Table 24: Hepatitis B management in pregnancy

Acute HBV in pregnancy	Chronic HBV in pregnancy	MTCT
Usually not severe need supportive treatment only Can give rise to MTCT	Usually uneventful pregnancy Monitor closely – flares possible Cirrhotic mothers-IUGR, intrauterine infection, premature delivery, foetal death	Highest if mother HBeAg+ Booking visit HBV screening needed If HBsAg+, do HBV and liver profile Repeat HBV VL, AST/ALT at POA 28 1. VL >200000 IU/ml: Antivirals for mother and HBIG & HBV vaccine within 12hrs of birth to the baby (0, 2, 4 and 6 months) 2. VL <200000 IU/mL: HBIG & HBV vaccine within 12hrs of birth to the baby (0, 2, 4 and 6 months)

Management of persistent viremia

- After interferon failure: can switch to entecavir or tenofovir
- While receiving tenofovir/entecavir: A virologic response is considered as undetectable HBV DNA after 96 weeks of treatment. Check adherence since resistance is rare in naïve patients
- If resistance is suspected, resistance testing is done. For entecavir failure, add tenofovir until undetectable HBV DNA, then discontinue entecavir. For tenofovir failure, add entecavir until undetectable HBV DNA, then discontinue tenofovir. While receiving other nucleos(t)ide analogues: Switch to tenofovir. Entecavir should be avoided

Advice:

- Alcohol: Advise abstinence. It worsens liver disease and increases HCC risk.
- Immunizations: Specially for hepatitis A.
- Transmission prevention: Counsel on preventing sexual transmission (e.g., vaccination for partners, safe sex), perinatal transmission, and blood exposure risks.
- Healthy lifestyle: To prevent hepatic steatosis and reduce cirrhosis/HCC risk.

Hepatitis B in Pregnancy

Indication for antiviral is the same as non-pregnant but for high viral loads (>2 x 105 IU/mL), initiate antiviral therapy in late second or early third trimester to prevent MTCT transmission. (TDF is preferred). Breast feeding is safe. (Table 24)

Post exposure process of Hepatitis B

For immune people (>10 IU/ml), specific prophylaxis is not needed. (Table 25)

Table 25: Hepatitis B PEP overview

Occupational exposure	HBIG 400IU IM within 72 hrs of exposure Vaccine at 0 (within 7 days), 1 and 6 months
Sexual exposure	HBIG 400IU IM within 72 hrs of exposure (can be up to 14 days) Vaccine at 0 (within 14 days), 1 and 6 months

Documented vaccine non-responders will not be benefited with vaccination

Hepatitis C

Incubation period: 50 days (15 – 150 days)

Acute hepatitis C infection

Majority have asymptomatic infection. Acute infection usually lasts for 2-12 weeks. (Table 26 and 27)

Table 26: Clinical and laboratory features of acute Hepatitis C

Symptoms & signs	Laboratory findings
• Jaundice, nausea, dark urine, pale stools Right upper quadrant pain • Uncommonly LOA, dyspepsia, fatigue, low-grade fever, chills, pruritus, muscle aches, joint pain • Fulminant hepatic failure-very rare	• Aminotransferase >10-20 ULN (start to rise before symptoms and normalize while still having the infection) – appears before anti-HCV antibodies • Elevated total bilirubin levels

Natural history: Approximately 20-50% of acute HCV infections clear spontaneously within 12 weeks (but can be up to 2 years). Symptomatic patients, younger age, female sex, HCV genotype 1, and prior hepatitis B infection is linked to higher clearance rates, while HIV co-infection reduces clearance likelihood. Reinfection is typically shorter and less severe. Once chronic infection develops, spontaneous clearance is rare.

Management

Acute hepatitis C management focuses on early diagnosis, supportive care, and antiviral therapy. While most cases are asymptomatic or mild, prompt treatment with direct-acting antivirals (DAAs) can prevent chronic infection and liver damage. Regular monitoring for liver function and potential complications is also essential for optimal outcomes.

Chronic Hepatitis C infection (CHC):

Chronic hepatitis C infection is a long-term viral infection that can lead to significant liver damage, including cirrhosis, liver failure, and hepatocellular carcinoma. Many individuals with chronic hepatitis C are asymptomatic for years, making early diagnosis crucial. Regular monitoring of liver function, viral load, and potential complications is essential for managing the condition effectively.

Natural history: Approximately 50-80% go into chronic disease and of that around 70% develop chronic fibrosis of the liver ultimately leading to cirrhosis. Rapid viral mutation allows HCV to escape immune recognition. Presence of specific alleles, female gender, childhood acquisition, white race and symptomatic acute stage tend to cause more spontaneous clearance and less likelihood for chronic infection. Acute exacerbation of chronic HCV infection is possible and manifest as significant elevation of ALT/AST and may accelerate liver disease progression. HCC almost exclusively occur in patients with cirrhosis. Alcohol use, comorbidities (e.g., Diabetes, insulin resistance, obesity and co-infections

with HIV or HBV) and vitamin D deficiency accelerate the fibrosis while coffee, younger age and female gender may slow the progression.

Table 27: Diagnosis and treatment of acute hepatitis C

<table>
<tr><th colspan="3">Diagnosis</th><th>Treatment</th></tr>
<tr><td colspan="3">• +/- Signs and symptoms
• +/- Suggestive history
• HCV RNA &/or Anti HCV within 48 hrs of exposure</td><td rowspan="3">• Harm-reduction strategies
• Standard hygienic practices
• Avoid alcohol and high-dose and paracetamol
• If there is ongoing risk, screen every 6-12 monthly
• Start treatment immediately for Acute HCV
Sofosbuvir-velpatasvir for 12 weeks
Glecaprevir-pibrentasvir for 8 weeks
• Contact screening</td></tr>
<tr><td colspan="2">• HCV RNA +ve</td><td>• HCV RNA -ve</td></tr>
<tr><td>• Anti HCV ab +ve</td><td>• Anti HCV ab -ve</td><td>• If anti HCV ab positive: prior resolved infection
Recheck HIV RNA at 4 weeks*
Recheck HIV RNA and Anti HCV ab at 12 weeks*
Recheck HIV RNA and Anti HCV ab at 6 months*
* If at any point, positive RNA VL, consider as acute HCV (re-infection)</td></tr>
<tr><td>Pre-existing HCV infection (High chance to be a chronic HCV)</td><td>Acute HCV infection</td><td>• If RNA negative: No infection now
Recheck HIV RNA at 4 weeks*
Recheck HIV RNA and Anti HCV ab at 12 weeks*
Recheck HIV RNA and Anti HCV ab at 6 months*
*+ If at any point, positive RNA VL, consider as acute HCV (re-infection)</td></tr>
</table>

Table 28: Signs and symptoms of chronic Hepatis C infection

Symptoms & signs	Laboratory findings
• Most patients are symptomatic but nonspecific: Commonest - fatigue and sleep disturbances Other - nausea, diarrhoea, abdominal pain, anorexia, myalgia, arthralgia, weakness, weight loss, neuropsychiatric symptoms • Rarely, extrahepatic findings Eg: Mixed cryoglobulinemia, idiopathic thrombocytopenic purpura, B-cell non-Hodgkin and primary hepatic lymphomas, Renal (sp membranoproliferative GN), Autoimmune (eg, thyroiditis, the presence of autoantibodies), Dermatologic conditions (porphyria cutanea tarda, lichen planus, Necrolytic acral erythema), Diabetes mellitus, Sjögren's/sicca symptoms	• Aminotransferase: Majority has normal ALT; others may be twice ULN • Elevated but relatively stable HCV RNA levels (85% has <1log viral load fluctuations in chronic HCV) • Due to extrahepatic manifestations: low platelets, rheumatoid factor, high autoantibodies, proteinuria and microscopic haematuria • serum bilirubin concentration, hypoalbuminemia, or a decrease in the platelet count in cirrhosis • mildly elevated serum AFP

Management

Early and accurate diagnosis is crucial, as false positive and false negative laboratory results can occur in some cases.

False negative antibody tests: On haemodialysis, transplant recipients, advanced HIV infection – therefor HCV RNA is preferred in these patients

False positive antibody test: Passively acquired from recent blood transfusions, maternal anti-HCV antibodies in babies- recurrent infection with viruses similar to HCV

Table 29: Diagnosis and management of chronic hepatitis C infection

Diagnosis	Management
Screening test – HCV antibody test • Negative anti HCV ab: No chronic HCV • Positive/equivocal or indetermined anti HCV ab: do quantitative HCV RNA Positive HCV RNA: HCV infection present Negative HCV RNA: past HCV infection now cleared 6-12 month regularly screening for HCV if ongoing risk is present	• Control alcohol use, obesity and insulin resistance, NSAIDS use and marijuana use (Control statins if unstable liver) • Vaccinate for hepatitis A, B & pneumococcal infections • If no decompensated cirrhosis – Start on DAAs (Please refer acute management schedule) • If decompensation present- DAA after expert opinion • Check the viral load 12 weeks **after the cessation of therapy**

Hepatitis C in Pregnancy

Most women with chronic HCV have uneventful pregnancies but rarely can have adverse outcomes Eg: low birth weight, small for gestational age, need for neonatal intensive care and intrahepatic cholestasis of pregnancy. Vertical transmission of HCV to the newborn occurs in 3-10% of cases, with higher viral loads increasing transmission risk. Most transmissions occur perinatally but intrauterine is also possible

Risk factors for MTCT:

- HCV Viral load
- HIV coinfection
- Presence of peripheral blood mononuclear cell (PBMC) infection
- Maternal intravenous drug use (maybe due to increase PBMC rates)
- Invasive prenatal testing and obstetric procedures
- Prolonged rupture of membranes

There is no MTCT association with mode of delivery, breast feeding or HCV genotypes

HCV mono-infection does not affect the delivery route. Postpartum, women can breastfeed unless their nipples are cracked or bleeding. The safety and efficacy of HCV antiviral agents during pregnancy are unknown, so treatment should be delayed until after delivery or considered only on an individual basis. Women treated with ribavirin-containing regimens should avoid

pregnancy for at least nine months after treatment.

Babies born to HCV positive mothers should be tested with HCV RNA at the age of 2 months and then with anti HCV antibody test at the age of 18 months. Even positive treatment is not available till the age of 3 years, and around 25%-50% of infected infants resolve the infection by age 4.

Post exposure process of Hepatitis C

As baseline (preferably within 72 hrs): HCV RNA, HCV Ab, and serum aminotransferases

- HCV RNA may remain detectable in the liver even with serum undetectable viral load - uncertain clinical significance
- HCV RNA will be detectable in blood within days (days to 8 weeks)
- Anti HCV ab will be detectable around 8 weeks post exposure (2-6 months)
- Immunocompromised and chronic dialysis patients may not mount a detectable anti-HCV antibody
- With time anti-HCV ab levels will fall to an undetectable level

Table 30: Summary of Hepatitis C PEP

Negative baseline HCV RNA	Positive baseline HCV RNA
At 1 month: HCV RNA and AST/ALT At 3 months: HCV RNA, Ant HCV Ab and AST/ALT At 6 months: HCV RNA and Ant HCV Ab	anti-HCV ab also positive- favours pre-existing chronic HCV anti-HCV ab is negative – Acute HCV infection: recheck anti HCV in 3 months & viral load to see spontaneous clearance (at month 1, at month 3, and at 6 months)

Hepatitis E

Incubation period: 15-60 days

Natural history: Genotype 1 & 2 sporadic outbreaks related to consumption of contaminated water (and food) while genotype 3 and 4 is due to undercooked meat or close contact with infected animals (zoonotic nature). Most patients spontaneously clear the virus, but 60% may have prolonged cholestasis. Acute hepatic failure is more likely in those who are pregnant and in those who are malnourished or have pre-existing liver disease. Chronic HEV (defined as detection of HEV RNA in serum or stool for longer than six months) has been described almost exclusively in immunocompromised patients.

Prevention of Hepatitis E infection

Good hygienic practice is the mainstay. Vaccine is also available

Table 31: Summary of Hepatitis E clinical features and management

Symptoms & Signs	Laboratory findings	Management
Majority either asymptomatic or subclinical Jaundice is typically accompanied by malaise, anorexia, nausea, vomiting, abdominal pain, fever, and hepatomegaly common symptoms: diarrhoea, arthralgia, pruritus, and urticarial rash.	• Anti HEV IgM • HEV RNA PCR	• Mainly supportive • If chronic HEV, may need ribavirin therapy

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Section 5:
Other STIs and related conditions

Trichomoniasis

Dr Sampath Mahagamage

Introduction

Trichomoniasis is one of the common sexually transmitted infections which is caused by the protozoa, *Trichomonas vaginalis* and it is also a known cause of symptomatic vaginitis in women. *Trichomonas vaginalis* is a motile organism that lives in the lower genitourinary tract of females and the prostate and urethra of men. Often, the infection in men by *T. vaginalis* is asymptomatic (1). Trichomoniasis is believed to increase the risk of transmission of Human Immunodeficiency Virus (HIV) in both women and men (1). In addition, the infection is also associated with adverse outcomes during pregnancy.

Classification & Pathogenesis

Trichomonas vaginalis, a flagellated protozoan parasite, is the causative agent of trichomoniasis. In the scientific classification, the organism belongs to Class-Parabasilia, Family-Trichomonadida, Genus-Trichomonas, Species-*Trichomonas vaginalis*.

T vaginalis trichomonads are approximately the size of a white blood cell (about 10-20 µm long and 2-14 µm wide), although this may vary. Trichomonads have 4 flagella that project from the organism's anterior and 1 flagellum that extends backward across the middle of the organism, forming an undulating membrane. An axostyle, a rigid structure, extends from the organism's posterior (18).

Figure 28: Schematic representation of T. vaginalis

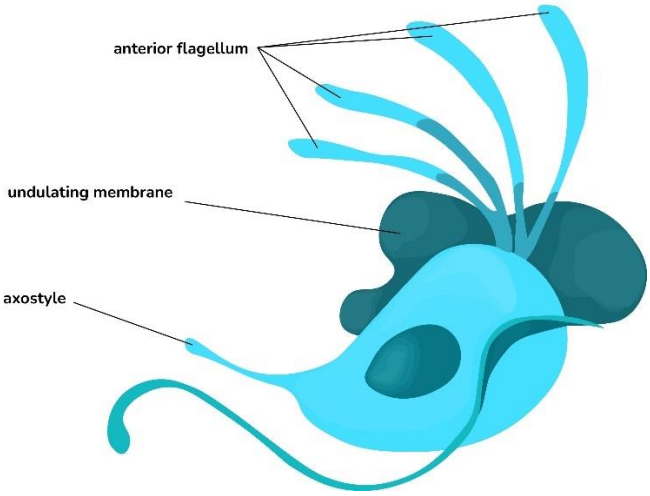
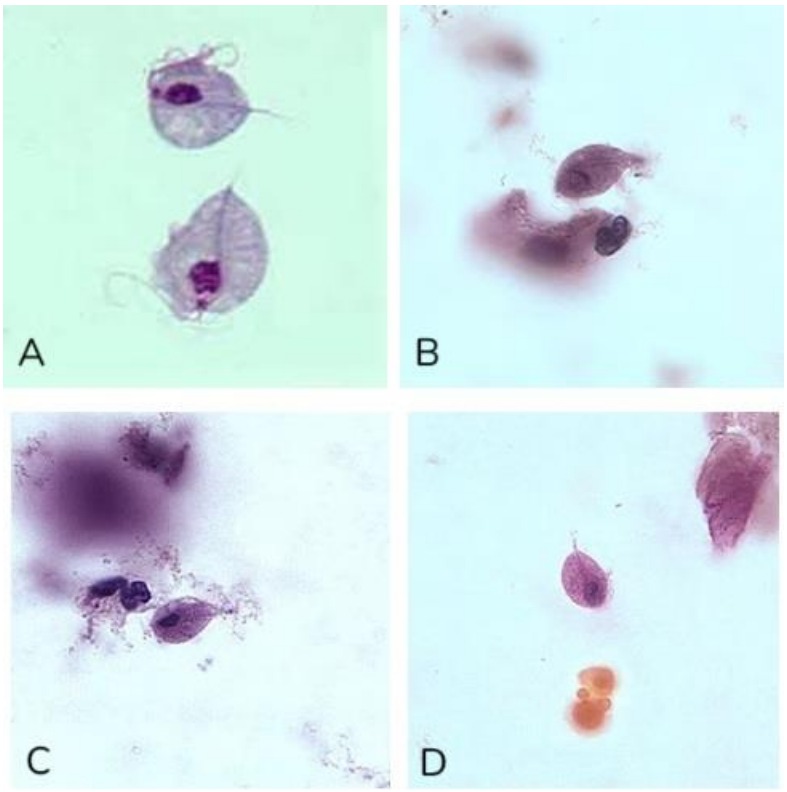


Figure 29: T. vaginalis in different stains under the microscope (image courtesy - CDC)



A: Two trophozoites of T. vaginalis obtained from in vitro culture, stained with Giemsa.
B: Trophozoite of T. vaginalis in a vaginal smear, stained with Giemsa.
C: Trophozoite of T. vaginalis in a vaginal smear, stained with Giemsa.
D: Trophozoite of T. vaginalis in a vaginal smear, stained with Giemsa.

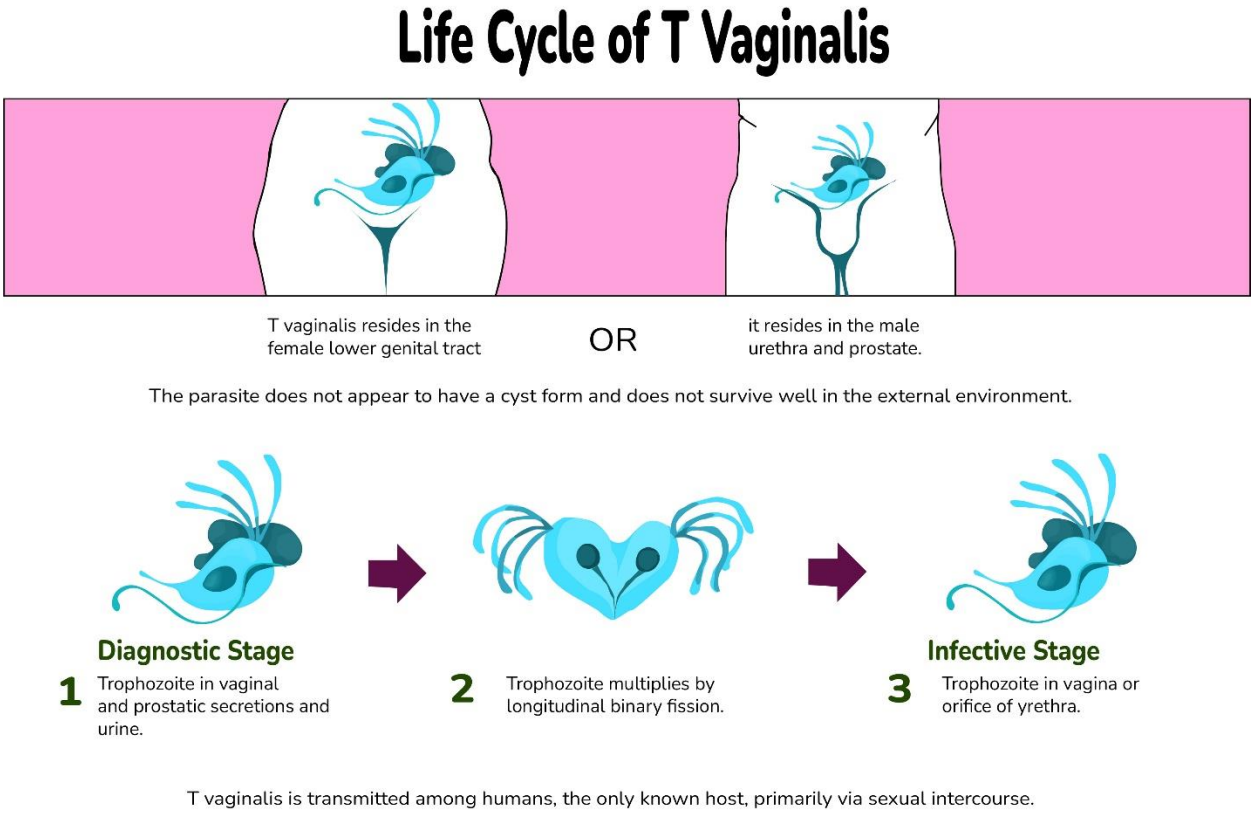
Humans are the only known host of *T. vaginalis*. Transmission occurs predominantly via sexual intercourse. The organism is most isolated from vaginal secretions in women and urethral secretions in men. The rectal prevalence of *T vaginalis* among men who have sex with men (MSM) appears low (17). Although *T vaginalis* has not been isolated from oral sites, evidence suggests that it may cause sexually transmitted oral infection in rare cases (18).

In women, *T. vaginalis* can be isolated from the vagina, cervix, urethra, bladder, and Bartholin and Skene glands. In men, the organism is found in the anterior urethra, external genitalia, prostate, epididymis, and semen. It resides both in the lumen and on the mucosal surfaces of the urogenital tract and uses flagella to move around vaginal and urethral tissues (18). *T vaginalis* has also been isolated from the rectum and detected via molecular techniques in the respiratory tract, although these are not common areas of infection (18). In cases of vertical transmission, *T vaginalis* may infect the respiratory systems of infants; however, not much evidence is revealed about this condition (18).

Life cycle

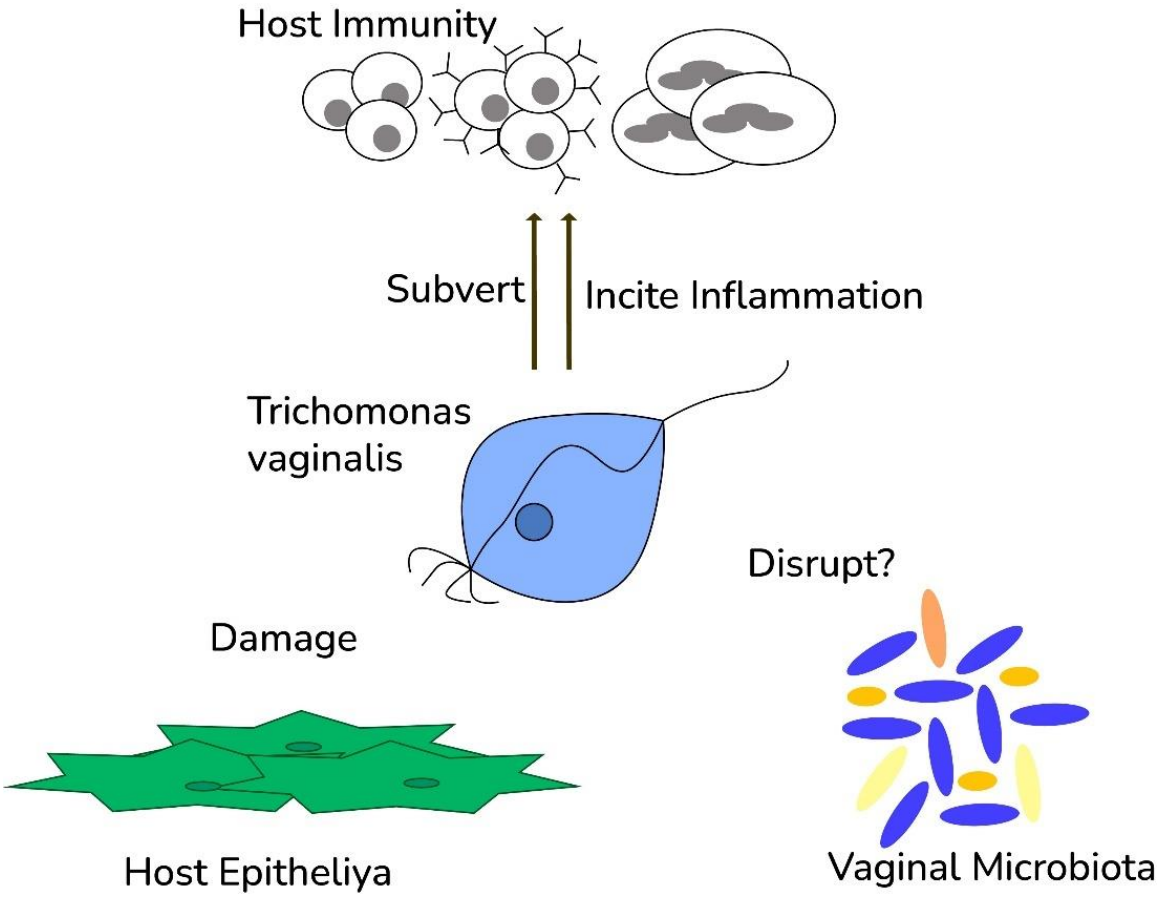
T. vaginalis trophozoite resides in female lower genital tract and in male urethra and prostate, where it replicates by binary fission. The parasite does not appear to have a cyst form and does not survive well in the external environment.

Figure 30: T. vaginalis transmission among humans (Recreated - Image courtesy of Centres for Disease Control and Prevention)



Trichomonas vaginalis mainly causes lesions on the cervicovaginal mucosa in women; however, its pathogenesis remains unclear. What has understood was, this is an extracellular pathogen, mediates adherence to epithelial cells to colonize the human host. In addition, the parasite interfaces with the host immune system and the vaginal microbiota. Modes of TV pathogenesis include damage to host tissue mediated by parasite killing of host cells, disruption of steady-state vaginal microbial ecology, and eliciting inflammation by activating the host immune response. Recent TV research has revealed that multifactorial mechanisms of host-parasite adherence and killing and has examined the relationship between TV and vaginal bacteria. Mechanisms that may lead to parasite recognition and killing, or the evasion of host immune cells, have also been uncovered (15).

Figure 31: Conceptual immunopathogenesis diagram of Trichomonas vaginalis infection



Further to above, some studies investigated the involvement of the endoplasmic reticulum (ER) in the induction of apoptosis by *T. vaginalis* and its molecular mechanisms in human cervical cancer SiHa cells (16).

Clinical features

T vaginalis is transmitted mainly via sexual intercourse, hence it is typically found in sexually active individuals. *This infection* is also transmitted vertically and can be asymptomatic for long durations (19). Nearly half of infected females and nearly all infected males are asymptomatic (18). One third of asymptomatic women become symptomatic within 6 months (20). Because of this, a lack of sexual history per se should not rule out *T vaginalis* infection as a possible diagnosis (18). (Box 16 and 17))

Box 16 Clinical features of *T vaginalis* in females

Symptoms in female

1. Abnormal vaginal discharge, which may be purulent, grey or yellow green with an offensive odour. Can also be frothy, or bloody.
2. Vulval itching, dysuria- but these are not specific for TV.
3. Occasionally lower abdominal discomfort or vulval ulceration.

Signs in female

1. Vaginal discharge is present in up to 70%- varying in consistency from thin and scanty to profuse and thick; the classical frothy yellow discharge occurs in 10–30% of women.
2. Vulvitis and vaginitis are associated with trichomoniasis.
3. Approximately 2% of patients will have strawberry cervix appearance to the naked eye. Higher rates are seen on colposcopic examination.
4. 5–15% will have no abnormalities on examination.

Box 17 Clinical features of *T vaginalis* in males

Symptoms in male

1. 15–50% diagnosed with TV are asymptomatic and men usually present as the sexual partners of infected women.
2. The commonest symptomatic presentation is with urethral discharge and/or dysuria.
3. Other symptoms include urethral irritation and urinary frequency.
4. Rarely, the patient may complain of a copious purulent urethral discharge, or symptoms of complications such as prostatitis

Signs in male

1. Urethral discharge (20–60%)- usually small or moderate amounts only.
2. No signs, even in the presence of symptoms suggesting urethritis: prospective study of infected TV contacts found 77.3% were asymptomatic.
3. Rarely, balanoposthitis.

Complications and associations

Pregnancy and TV

There is increasing evidence that TV infection can have a harmful outcome on pregnancy and is associated with preterm delivery and low birth weight (21). However, further research is needed to confirm these associations and to prove that the association is causal (21). Neonatal trichomoniasis, usually presenting as a genital infection, has been described in some studies (22). A meta-analysis done in 2020 concluded that rigorous studies are needed to determine the impact of universal trichomoniasis screening and treatment during pregnancy on reducing perinatal morbidity (23). Screening of asymptomatic individuals for TV infection in pregnancy is therefore not currently recommended. (Grade 1B) (21). TV infection at delivery may predispose to maternal postpartum sepsis (21). Some studies have shown treatment of TV infection in pregnancy to have a negative impact on the pregnancy, but others have shown no association between treatment for TV and pre-term delivery or low birth weight (21). An observational study done in South Carolina in 1996-2000 found that treatment with oral metronidazole was not associated with increased risk of preterm birth in women diagnosed with trichomoniasis (24).

PID and TV

T. vaginalis was frequently isolated from the lower genital tract of women with clinically suspected PID (25). Generally, TV can be complicated into cervicitis and infection of the adnexa, endometrium, and Skene and Bartholin glands. It is believed that Pelvic inflammatory disease and tubo-ovarian abscess may also occur. A study done in USA in 2019 using secondary data from PEACH cohort found that the women testing positive for vaginal T. vaginalis had twice the odds of histologically confirmed endometritis at baseline compared with those without, and persistent endometritis was highly prevalent (52.1%) at 30 days (25).

HIV and TV

Multiple reports suggest an epidemiological association between HIV and trichomoniasis. There is evidence that trichomonas infection may enhance HIV transmission and there may be an increased risk of TV infection in those that are HIV positive (21). It is estimated that, in women alone, 747 new HIV cases per year result from the facilitative effects of *T vaginalis* on the transmission of HIV (26).

Other viruses and TV

T. vaginalis infection also increases the susceptibility to other viruses, including herpes and human papillomavirus (HPV). *T vaginalis* may increase the rate of infection or reactivation of HPV, although it may also shorten the duration of infection (27).

In addition to above, certain other conditions also been identified as associations to TV.

- Cervical intraepithelial neoplasia (28)

- Post-hysterectomy infection, including cuff cellulitis, cuff abscess, and wound infection (29)
- Trichomonal peritonitis (rare)

Diagnosis

1. Testing for TV should be undertaken in patients complaining of vaginal discharge or vulvitis, or found to have evidence of vulvitis, and/or vaginitis on examination (Grade 1A).
2. Testing is recommended for TV contacts and should be considered in those with persistent penile urethritis (Grade 2B).
3. Screening of asymptomatic women may be appropriate in settings such as sexual health services in geographical areas of high prevalence and/or in women with associated risk factors (Grade 2B).

Sites for sampling

Females

- If the patient is symptomatic and microscopy is available, then a swab taken from the posterior fornix of the vagina at the time of speculum examination is recommended (Grade 1A).
- Self-administered vaginal swabs are likely to give equivalent results to clinician-taken swabs when using nucleic acid amplification tests (NAATs) and are the test of choice if microscopy is not being performed (Grade 1A).
- Urine testing has been evaluated with some NAATs and has shown acceptable sensitivity in the range of 88–90%.

Males

- Clinician taken urethral swabs or self-taken penile-meatal swabs will diagnose approximately 80% cases using NAATs and is the recommended sample (Grade 1A).
- Urine is currently approved for only one NAAT.

Laboratory investigations

Microscopy

Microscopy is a simple and rapid test to perform at any clinic that has access to a microscope and a microscopist (Grade 1A) (21). The specificity with trained personnel is high, although the sensitivity is reported to be as low as 40–60% in vaginal samples in some studies and lower in men, and so a negative result should be interpreted with caution (21). Detection of motile trichomonads by light microscopy can be achieved by collection of vaginal discharge using a loop, which is then mixed with a drop of saline on a glass slide and a coverslip placed on top. The wet preparation should be read within 10 minutes of collection, as the trichomonads will quickly lose motility and could be hardly identified later. The slide should be scanned, firstly at low magnification (×100), and then at a higher magnification (×400) to confirm the morphology of any trichomonads and to visualise the flagella. Microscopy has the advantage that it can be performed near to the patient and in a clinic setting. The sensitivity is highest in patients presenting with vaginal discharge and a visualisation of motile trichomonads in these patients indicates the presence of infection.

Detection of TV by staining dead organisms with acridine orange can give a higher sensitivity than wet microscopy but is not widely used (21).

Point of care tests.

Point of care tests for the detection of TV have been described of which the OSOM® Trichomonas Rapid Test (Sekisui Diagnostics, USA) has demonstrated a high sensitivity (80–94%) and specificity (>95%) (depending on the comparator). Advantages of these tests are no need of instrumentation, provides a result within 30 minutes and is a suitable alternative to culture or molecular testing. Although these tests are more sensitive than those requiring vaginal wet preparation, false positive might occur, especially in populations with a low prevalence of disease. Consideration should be given to confirming positive results in that situation. Whilst local validation may recommend use of the OSOM® assay for specimen types other than vaginal swabs this assay should not be used to test urine from male patients, as low sensitivity (38%) and specificity (83%) has been demonstrated when compared with NAAT. (21)

Molecular detection.

Nucleic acid amplification tests (NAAT) offer the highest sensitivity for the detection of TV. They should be the test of choice where resources available and are the current 'gold standard' (Grade 1A). US Federal Drug Agency (FDA) approved commercial assays which can detect TV nucleic material in samples from women with sensitivities of 88%–100% and specificities of 95–100%, depending on the specimen and reference standard. The site sampled should be that recommended by the manufacturer of the NAAT kit in use by the local laboratory. Detection of TV in specimens from male patients (urine, penile-meatal and urethral swabs) is currently outside of most commercial NAAT assay scope therefore local validation would be necessary. However, sensitivities of 90– 100% and specificities of >99% have been reported depending on the specimen and reference standard. In addition to offering superior detection of the organism, use of NAAT assays may be more cost-effective than other diagnostic methods (21).

Culture.

In the past which was 'the gold standard', culture has proven less sensitive than molecular testing. It has a higher sensitivity (88%) compared to microscopy and can detect TV in men. A commercially available culture system (InPouch TV; BioMed Diagnostics, USA), offers many advantages over previous culture media such as Diamond's medium. Once inoculated the pouches can be transferred to the laboratory for incubation and the entire pouch read microscopically each day for 5 days, negating the need to prepare wet preparations every day that only sample a portion of the culture medium (21).

Management

Please refer Box 18.

Box 18 Treatment for *T vaginalis*

Recommended regimen (Grade 1A)
• Metronidazole 400 mg twice daily for 7 days.
Or
• Metronidazole 500 mg twice daily for 7 days. (In countries where 500 mg tablets are available)
The combination of alcohol and metronidazole has been said to cause disulfiram type reactions in about 10% of individuals (metronidazole SmPC) and should be avoided for 48 hours post-last dose (21)

Alternative regimens
• Metronidazole 2 g orally in a single dose (Grade 2A)

Pregnancy and breast feeding

- 400 mg oral metronidazole twice daily for 7 days in preference to the use of short high-dose regimens which are not recommended during pregnancy (Grade 1A).
- No evidence of teratogenicity from the use of metronidazole during the first trimester of pregnancy.
- Metronidazole can be used in all stages of pregnancy and during breast feeding.
- Symptomatic patients should be treated at diagnosis, although some clinicians have preferred to defer treatment until the second trimester.
- Metronidazole enters breast milk and may affect its taste. The manufacturers recommend avoiding high doses if breastfeeding.
- Tinidazole is FDA pregnancy category C
- The manufacturer states that the use of tinidazole in the first trimester is contraindicated.

People living with HIV (Grade 1A)

- The recommended treatment regimen should also be used in those living with HIV.

Treatment failure

Persistent or recurrent TV can occur due to

- Inadequate therapy
- Re infection
- Resistance.

In cases of persistent or recurrent trichomoniasis, it is crucial to evaluate factors that may contribute to treatment failure. This includes assessing patient compliance with the prescribed therapy and ruling out the possibility of metronidazole vomiting, which could impair treatment

efficacy. Additionally, a comprehensive sexual history should be obtained to identify potential re-infection and determine whether sexual partners have been appropriately treated. Addressing these factors is essential to managing recurrent infections and preventing ongoing transmission. (Box 19)

Box 19 Treatment protocol for non-response to standard TV therapy

Need to exclude re-infection and non-adherence before initiating this protocol
1. Repeat course of 7-days standard therapy
2. For patients failing this second regimen: Higher dose course of nitroimidazole (Grade 2B) ● Metronidazole 2g daily for 5–7days or ● Metronidazole 800 mg three times daily for 7days.
3. Very high dose course of nitroimidazole and very high dose course of nitroimidazole with intravaginal nitroimidazole or paromomycin cream (Grade 2D) ● Metronidazole 2g twice daily for 14days with metronidazole vaginal gel 5g twice daily for 14days
If very high dose tinidazole plus intravaginal cream has been unsuccessful or are unavailable, it is difficult to recommend further treatments at present.

Follow up

Tests of cure are recommended only in cases where the patient continues to exhibit symptoms after treatment or experiences a recurrence of symptoms (Grade 2C). The optimal timing for performing a nucleic acid amplification test (NAAT) to confirm the cure of *Trichomonas vaginalis* (TV) is typically four weeks following the initiation of treatment.

Management of sexual partners

Current and recent sexual partners, including any partner(s) within the four weeks preceding the patient's presentation, should be offered comprehensive STI screening, including HIV testing, and strongly encouraged to undergo screening and treatment for *Trichomonas vaginalis* (TV), regardless of the results of their investigations (21). In cases where a contact of a TV-infected individual is found to have urethritis during screening, it is considered appropriate to initiate treatment for TV and perform a repeat urethral smear before pursuing additional treatment for non-gonococcal urethritis (21).

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Bacterial Vaginosis

By Dr Waruni Pannala

Introduction

Bacterial Vaginosis (BV) is one of the most common causes of vaginal discharge among women of reproductive age with a general population prevalence ranging from 23% to 29% across all regions globally. It is considered as a condition resulting from bacterial overgrowth of the vagina and replacement of normal hydrogen peroxide and lactic-acid–producing Lactobacillus species in the vagina with high concentrations of anaerobic bacteria, including Gardnerella *vaginalis*, *Prevotella* species, *Mobiluncus* species, *Atopobium vaginae*, and other BV-associated bacteria (BVAB). (1) The most common clinical manifestation of BV is fishy smelling vaginal discharge, often of little thickness grey or milky. Women with BV have an additional risk of contracting other sexually transmitted infections including HIV. Although BV is not considered as sexually transmitted infection, those who have multiple sexual partners are at higher risk of developing BV.

Pathogenesis

The normal vaginal microbiota primarily consists of Lactobacillus species, which maintain vaginal pH by processing glycogen and its breakdown products to produce lactic acid, resulting in a remarkably low vaginal pH of ≤4.5. (2)

In cases of bacterial vaginosis (BV), there is a massive overgrowth of mixed complex flora or microbiota, including *Bacteroides* spp., *Gardnerella vaginalis*, *Mobiluncus* spp., genital mycoplasma. Therefore, the disorder represents a disturbance of the vaginal microbial ecosystem rather than a true infection of tissues. The overgrowth of mixed flora is associated with a loss of the normal Lactobacillus spp. dominated vaginal flora, leading to an increase in vaginal pH > 4.5. However, the mechanism by which normal flora is replaced by pathogenic flora remains unclear. Epidemiologic data suggest that the introduction of a particular set of organisms via sexual intercourse may initiate the change in vaginal flora characteristic of BV. (3)

A recent hypothesis explains the aetiology of BV having four main steps which are:

1. Invasion of “early or primary colonizer species,” e.g., *Gardnerella* spp. and *Prevotella* spp which adhere to the vaginal microbiome and alters the pH from 4.5 to 6–7.
2. Characteristic polymicrobial biofilm formation which protects the pathogenic bacteria from the anti-bacterial effects of *Lactobacilli* species.
3. Maturation of the biofilm and coaggregation of “secondary colonizers” such as *Atopobium* spp., *Megasphaera* spp., *Mycoplasma* spp., etc.

4. Dispersion of vaginal epithelial cells covered with pathogenic bacteria (Clue cells), and vaginal discharge induced by hydrolytic enzymes produced by the pathogenic bacteria.

Biofilm is a systematic community of organisms embedded in a self-made extracellular matrix adherent to the vaginal epithelial layer. *G. vaginalis*-associated biofilm adheres to vaginal epithelial cells and provides the needs of the microorganisms including optimal pH gradient nutrients and oxygen. They also protect organisms from H_2O_2, and lactic acid produced by lactobacilli and tolerance to the host immune response facilitating their colonization and persistence in the vaginal environment.

The characteristic abnormal fishy odour of BV is thought to be due to the production of amines by the microbial flora via the action of microbial decarboxylases.

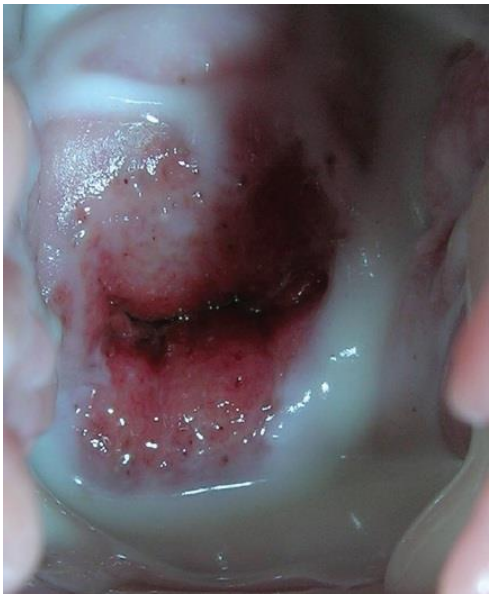
So far, there are no host factors identified that increase susceptibility to BV. However, Cu-IUD use is a possible exception although the mechanisms by which IUD increase the risk of BV is not understood. (3) BV is associated with having multiple sex partners, a new sex partner, recent antibiotic use, decreased oestrogen production of the host and douching.

Clinical features

Symptoms

- Offensive fishy-smelling vaginal discharge, which may be thin, and light grey or white.
- Itching or irritation around the vagina (less common)
- burning during urination (rare)
- Approximately 50% are asymptomatic.

Figure 32: BV discharge (Image courtesy: Richard P Usatine, Mindy Ann Smith, Heidi S Chumley, Camille SAbella, E J Mayeaux, Jr., Elumalai Appachi: The Color Atlas of Pediatrics)



Signs

- Thin homogeneous discharge, coating the walls of the vagina and the vestibule.
- A fishy odour when vaginal fluid is mixed with 10% KOH ("whiff test").
- BV is not usually associated with signs of inflammation.

The main differential diagnosis

- Trichomoniasis
- Candidiasis
- Cervicitis due to chlamydia or gonorrhoea
- But BV can co-exist with all of these.

Complications

Although BV usually does not result in complications, the following potential complications have been identified:

1. Increased Risk of Sexually Transmitted Infections (STIs)
   Women with BV may be at higher risk of contracting sexually transmitted infections such as HIV, *N. gonorrhoeae*, *C. trachomatis*, *T. vaginalis*, *M. genitalium*, HPV and HSV-2 (1)
2. Pelvic Inflammatory Disease (PID):
   prevalence of BV is high in women with pelvic inflammatory
   disease. However, there haven't been any prospective studies examining whether treating asymptomatic women for BV reduces their risk of developing PID afterward. (4)

Pregnancy Complications:

BV affects 6.4 to 16% of pregnant women and is associated with late miscarriage, preterm birth, preterm prelabour rupture of membranes, intra-amniotic infection, postpartum endometritis as well as neonatal complications like respiratory distress syndrome. (5)

Post-operative complications risk

BV is associated with vaginal cuff cellulitis in women who underwent abdominal Hysterectomy. In women who underwent other gynaecological surgeries post-operative fever is more common among those with BV. There is an increased incidence of pelvic inflammatory disease among who underwent first-trimester termination of pregnancy. (6)

Recurrent BV

Individuals with three or more documented BV episodes in one year are defined as having recurrent BV. More than 50% of BV cases may recur at least once within the following 12 months. (7) Post-treatment persistence of BV-associated bacteria or biofilm, repeated exposure to sexual partners carrying BV-associated bacteria, use of certain medications or products that disrupt the balance of vaginal bacteria (such as antibiotics or vaginal douches), failure to recolonize with lactobacillus species, and altered host immune response are potential contributing factors to recurrence. (8)

Diagnosis

Various diagnostic approaches are available for BV, including clinical criteria, Gram-

stained vaginal smear evaluation, point-of-care (POC) tests, and nucleic acid amplification tests (NAATs).

Clinical Criteria:

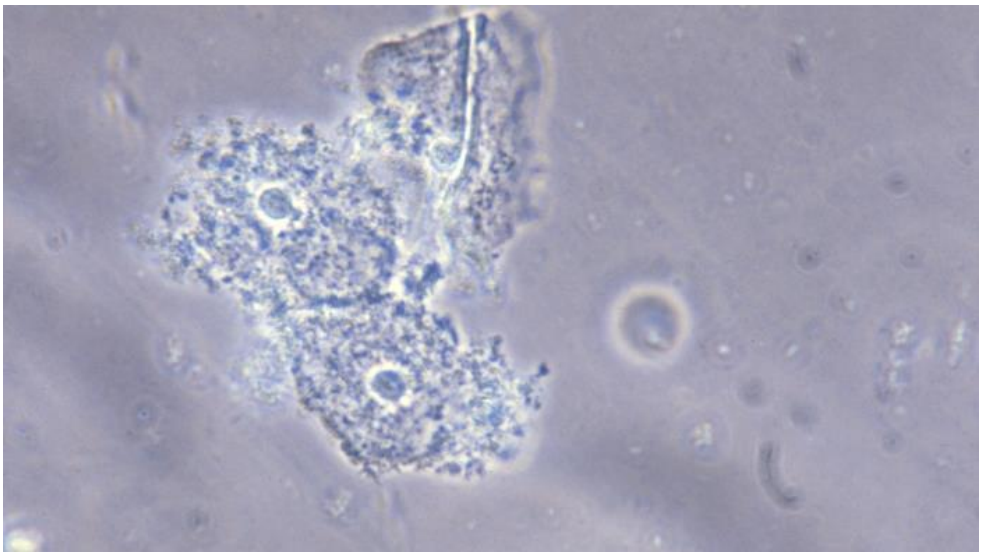
Amsel's Diagnostic Criteria:

At least three of the four criteria should be present to confirm the diagnosis.

Criteria:

1. Thin, homogeneous vaginal discharge
2. Presence of clue cells (vaginal epithelial cells studded with adherent bacteria) on microscopic examination of vaginal smear.
3. Vaginal fluid pH > 4.5
4. Fishy odour of vaginal discharge on adding alkali (10% KOH) or without KOH addition.

Figure 33: A clue cell seen in BV (Image courtesy - Public Health Image Library (PHIL): CDC)



Gram-Stained Vaginal Smear Evaluation

Hay/Ison Criteria:

Grade 1 (Normal): Lactobacillus morphotypes predominate

Grade 2 (Intermediate): Mixed flora with presence of some Lactobacilli, but Gardnerella or Mobiluncus morphotypes are also present.

Grade 3 (BV): Predominantly Gardnerella and/or Mobiluncus morphotypes. Few or absent Lactobacilli.

Nugent criteria

Nugent criteria are another method for evaluating Gram-stained vaginal smears to diagnose BV, employing a scoring system. The score is derived from estimating the relative proportions of bacterial morphotypes to give a score between 0 and 10. A score of 0-3 is consistent with a

Lactobacillus-predominant vaginal microbiota and is normal. 4-6 is with intermediate microbiota with the emergence of G. vaginalis and intermediate, and 7-10 is BV.

Point-of-Care (POC) Tests.

Multiple POC tests are available for the BV diagnosis.

Osom BV Blue test detects vaginal sialidase activity while Affirm VP III an oligonucleotide probe test that detects high concentrations of G. vaginalis nucleic acids. Another test call FemExam Test Card measures vaginal pH, the presence of trimethylamine (a metabolic by-product of G. vaginalis), and proline aminopeptidase.

BV Nucleic Acid Amplification Tests (NAATs):

Several nucleic acid amplification tests (NAATs) are available for the diagnosis of BV. These tests rely on identifying bacterial nucleic acids targeting organisms like *Gardnerella vaginalis*, *Atopobium vaginae*, BV-associated bacterium 2 (BVAB2), or Megasphaera type 1 and therefore have high sensitivity and specificity for BV. NAATs should be reserved for symptomatic women since their accuracy has not been well-defined in asymptomatic cases.

Management

Principles of Management

The goals of treatment include relief of symptoms, restoration of normal vaginal flora, and prevention of recurrence. Patient education plays a crucial role, emphasizing the importance of adhering to the prescribed treatment regimen. Patients should be advised to avoid risk factors for recurrence, such as vaginal douching, using shower gel, or applying antiseptic agents or shampoo during baths. Additionally, smoking cessation is recommended, along with the use of barrier methods of contraception, particularly for those with recurrent bacterial vaginosis.

Treatment Options

Treatment is indicated for women experiencing symptoms, and those undergoing certain surgical procedures. Treatment may be offered to asymptomatic women who do not volunteer symptoms. (4)

Box 20 **Antibiotic therapy for BV**

Recommended regimens
1. Metronidazole 400mg twice daily for 5-7 days
2. Metronidazole 2 g single dose
3. Intravaginal metronidazole gel (0.75%) once daily for 5 days.
4. Intravaginal clindamycin cream (2%) once daily for 7 days.

Several studies evaluating different therapies for BV consistently demonstrate that only antimicrobial agents with broad activity against most anaerobic bacteria are highly effective for treating this condition. All the above treatment regimens have similar efficacy and are effective for the short-term resolution of the infection. (3) (Box 20 and 21))

The use of intravaginal metronidazole has resulted in fewer side effects than the use of oral metronidazole. Intravaginal metronidazole gel and clindamycin cream have similar efficacy, but metronidazole is less expensive compared to clindamycin. Theoretically, metronidazole holds an advantage due to its lower activity against lactobacilli compared to clindamycin. However, clindamycin exhibits greater activity against most of the bacteria associated with BV than metronidazole. (4)

Box 21 Antibiotic therapy for BV

Alternative regimens
1. Tinidazole 2G single dose.
2. Clindamycin 300 mg twice daily for 7 days.
3. Tinidazole 1 g orally once daily for 5 days

Cautions

In clinical practice, healthcare providers often advise patients to avoid alcohol while taking metronidazole to minimize the risk of Disulfiram like reactions. However, the literature raises doubts about this recommendation as interaction occurs with unclear frequency, and, when it occurs, it happens with varying severity among different individuals. (9)

Metronidazole does not directly inhibit acetaldehyde dehydrogenase, as disulfiram does. Instead, the suspicion of disulfiram-like effects with metronidazole arises from the potential for ethanol-dependent or ethanol-independent side effects of metronidazole. These effects, when combined with alcohol consumption, can lead to symptoms similar to those experienced with disulfiram, such as flushing, nausea, vomiting, headache, and rapid heartbeat. Current CDC recommendations suggest that refraining from alcohol use while taking metronidazole (or tinidazole) is unnecessary, as there is suspicion but no confirmed evidence of disulfiram-like effects. (1)

Clindamycin cream is oil-based and might weaken latex condoms and diaphragms for 5 days after use. Pseudomembranous colitis

has been reported with both oral clindamycin and clindamycin cream.

Treatment of recurrent BV (1,4)

Recurrence of bacterial vaginosis (BV) is a common challenge associated with current treatment options. Studies indicate that within 6 to 12 months after completing antibiotic therapy, 50% to 80% of women may experience a recurrence of BV. (10)

However, limited data are available regarding the optimal management of women with persistent or recurrent BV. Following treatment regimens can be used for the management of recurrences although the cure rate is variable.

1. Retreatment with the same recommended regimen is considered an acceptable approach for managing persistent or recurrent bacterial vaginosis (BV) after the initial occurrence.
2. For women experiencing multiple recurrences of bacterial vaginosis (BV) after completing a recommended regimen, a regimen involving 0.75% metronidazole vaginal gel administered twice weekly for more than three months has been reported to reduce the frequency of recurrences.
3. A monthly regimen of oral metronidazole 2 g administered alongside fluconazole 150 mg has been assessed as suppressive therapy for bacterial vaginosis (BV). This approach was found to reduce the incidence of BV and facilitate colonization with normal vaginal microbiota.

Alternative therapies:

Most of the alternative therapies are also targeted for recurrences of BV rather than treatment of the first episode. (10)

- Probiotics (both vaginal and oral):

Lactobacillus-containing probiotics are often used and marketed for the management of BV. and may be beneficial in preventing recurrent BV through recolonization of the vaginal microbiota.

- Vaginal microbiome transplantation

Vaginal microbiome transplantation (VMT) is an emerging therapeutic approach being investigated for preventing recurrent bacterial vaginosis (BV). It involves administering vaginal fluid collected from healthy donors to women with BV.

- Vaginal pH modulators:

It is hypothesised that lactic acid, and other pH modulators like acetic acid and vitamin C, could offer protective effects against vaginal infections by reducing intra-vaginal PH. However, currently, there is insufficient evidence to support their effectiveness as a stand-alone treatment for BV.

- Biofilm disruptors

One proposed explanation for the high recurrence rates of bacterial vaginosis (BV) is the presence of a polymicrobial biofilm. While various agents targeting biofilms exist, dequalinium chloride stands out with the most evidence of benefit in BV.

Treatment of partners

Several placebo-controlled trials have demonstrated that treatment of the male partner(s) does not improve the clinical outcome of treatment of BV or reduce recurrence (3)

Treatment considerations during pregnancy:

Treatment for bacterial vaginosis (BV) is recommended for all symptomatic pregnant women due to its association with adverse pregnancy outcomes, including premature rupture of membranes, preterm birth, intra-amniotic infection, and postpartum endometritis. Meta-analyses have concluded that there is no evidence of teratogenicity associated with metronidazole use during the first trimester of pregnancy. While older studies suggested a possible link between vaginal clindamycin use during pregnancy and adverse newborn outcomes, newer data indicate that this treatment approach is safe for pregnant women. Routine treatment of asymptomatic pregnant women found to have BV in genitourinary clinics is not recommended due to insufficient evidence. However, women with additional risk factors for preterm birth may benefit from treatment before 20 weeks of gestation. (4)

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Candidiasis

Dr Inoka Munasinghe

Introduction

Candidiasis is a common fungal infection caused by Candida, a polymorphic fungus. While many Candida species are harmless and normally colonize the body, overgrowth can lead to infections, ranging from mucosal issues to systemic infections like sepsis. Commonly affected areas include the oral cavity, vagina, and penis. Vaginal infections are often referred to as yeast infections, and candidemia, a bloodstream infection, occurs mainly among hospitalized patients. Systemic infections generally don't stem from genital Candida infections.

Classification

Candida is classified within the domain Eukaryota and the kingdom Fungi. It is part of the Saccharomycetaceae family and the order Saccharomycetales, which are yeasts that reproduce through budding. The Candida genus includes approximately 200 species [1].

Among these, *Candida albicans* is the most common causative agent of candidiasis, responsible for 80% to 90% of Candida infections. It is a natural component of the microbiota in 50% of the population [2]. However, infections can also be caused by non-albicans species such as *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. pseudotropicalis*, *C. stellatoidea*, and *C. tropicalis*. Understanding non-albicans candidiasis is crucial, as these species may exhibit resistance to commonly used antifungal treatments.

Epidemiology

Candidiasis predominantly affects elderly individuals, immunocompromised populations, and infants. In the United States, approximately 37% of neonates develop thrush within the initial months of life [4]. Paediatric patients utilizing inhaled corticosteroids also exhibit an elevated prevalence of oral candidiasis. Vaginal candidiasis is frequently observed during pregnancy. Thrush is one of the earliest and most common clinical indicators of HIV infection and is prevalent worldwide, with higher occurrence in malnourished populations. It affects both males and females equally [2]. The global incidence of invasive and disseminated candidiasis has increased significantly, with immunocompromised individuals being at the greatest risk [4].

Pathophysiology

Candida albicans causes symptomatic infections when host immunity is compromised. Vulvovaginal candidiasis (VVC), a common mucosal infection of the lower female reproductive tract, often involves asymptomatic colonization of the vaginal lumen by *C. albicans* [5]. Candidiasis can be triggered by antimicrobial therapy, hormonal contraceptives, steroids, cytotoxic medications, weakened immunity, uncontrolled diabetes, elevated

endogenous oestrogen (e.g., obesity, pregnancy), or changes in vaginal pH and microbiota.

C. albicans is a polymorphic fungus existing as blastospores, pseudo hyphae, and hyphae (Figure 1). Polymorphism enables its transition from commensal to pathogenic forms, driven by environmental changes.

Blastospores reproduce asexually through budding [6,7]. A small blastospore forms the new bud, which then grows. Once the growth phase is complete, the cell divides, and the daughter cell separates from the parent by forming a partition [8]. Pseudo hyphae are characterized by chains of elongated yeast cells, while hyphae consist of branched chains of tubular cells with no narrowing at the septation sites [8]. Filamentation is promoted by temperatures above 37 °C, alkaline pH, serum, and high CO2 concentrations [9].

The hyphal form is invasive, and in this form, the cells enter the host tissue by active penetration and induced endocytosis [10] (Figure 2). Induced endocytosis is mediated by hyphae invasion and depends on host activity, whereas active penetration depends on the fungal activity [11]. Factors that contribute to the pathogenic potential of Candida albicans are the expression of proteins important for adhesion and invasion. The process of adhesion is affected by various factors, such as the types of protein in the cell wall, and the physical and chemical properties of the cell surface.

Figure 34: The morphological switches and transitions of Candida albicans during the infection process. The morphological transitions from blastospore to pseudo hyphae and hyphae are reversible.

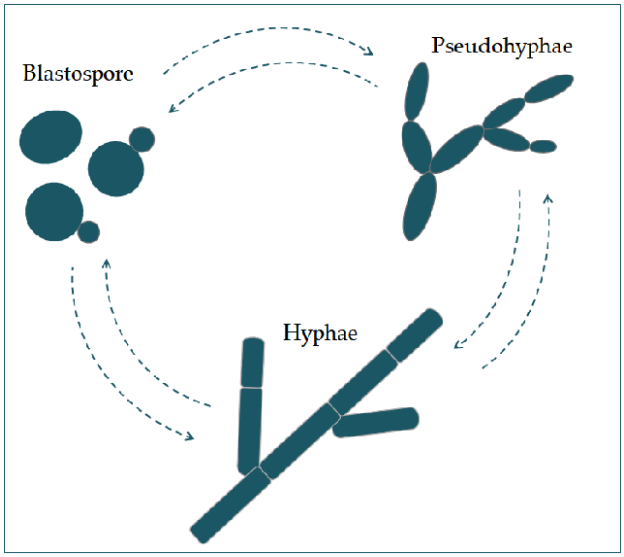
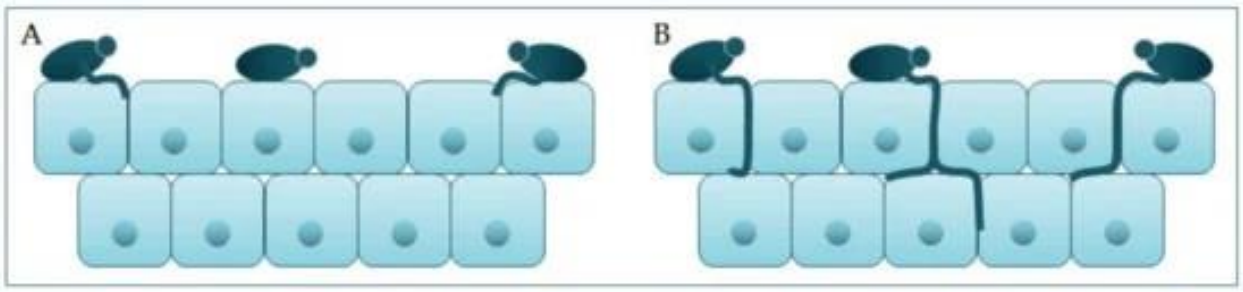


Figure 35: Schematic presentation of (A) adherence and colonization, and (B) penetration and invasion of C. albicans.



It has been shown that a hypha-specific toxin, candidalysin, is crucial for the occurrence of candidiasis [12,13] It is produced by the C. albicans hyphae, and it is crucial in damaging the host cells. The dominant host inflammatory cells are typically polymorphonuclear cells and macrophages. Pathogenesis includes desquamation of epithelial cells and accumulation of keratin, immune cells, fungi and necrotic tissue. This debris forms a pseudo-membrane, which adheres closely to the mucosa. This membrane may rarely involve extensive areas of oedema, ulceration, and necrosis of underlying mucosa.

Clinical features

Both males and females are equally affected by genital candidiasis. However, symptomatic infection can result from exuberant mucosal inflammation that is caused primarily by fungal overgrowth in the vagina, glans penis or on the undersurface of the foreskin and subsequent epithelial invasion and production of virulence effectors.

In Females:

VVC is the most prevalent human candidal infection, estimated to afflict approximately 75% of all women at least once in their lifetime, and 40–45% will have two or more episodes [14].

Common disease symptoms in vulvovaginal candidiasis include vaginal itching, burning, pain and redness. Often, these are accompanied by a vaginal discharge consisting of sloughed epithelium, immune cells, yeast, and vaginal fluid. Vaginal discharge is described as a non-offensive whitish “Curd-like” or "cottage cheese-like" discharge from the vagina. VVC is usually accompanied by an itchy skin rash of the vulva and sometimes there can be an external dysuria which can be mistaken for urinary tract infection. Superficial dyspareunia and vaginal dryness are also some presenting symptoms of vulvovaginal candidiasis. Vulval oedema, erythema, fissuring with excoriation, satellite lesions and characteristic discharge can be elicited during the genital examination. All these signs and symptoms are not pathognomonic

as other dermatological conditions also can mimic the same presentations.

In Males:

Candida balanitis is the most common cause of balanitis. Candida balanitis may present as pain, tenderness with foreskin fissuring, itching, scaly skin rash, erythematous lesions on the glans and/or the foreskin. An exudate may also be present under the foreskin with an odour. Though the candidiasis is not considered as a sexually transmitted infection many males may get the symptoms of candida balanitis after a sexual encounter. Careful examination is needed to exclude any other dermatological conditions with similar symptoms.

In men who are uncircumcised, the mobility of the foreskin should be assessed to exclude the complications of phimosis and paraphimosis. Paraphimosis requires urgent urologic consultation.

Complicated Candidiasis is considered where the single dose of treatment is not appropriate and repeated doses of antifungal medication is needed.

Vulvo-vaginal candidiasis during pregnancy is considered a complicated case of candidiasis. Pregnant women have higher chances of colonizing Candida in the vagina during pregnancy, and prevalence studies shows vaginal Candida colonization up to 30% during pregnancy by culture, especially in the last trimester. Recent studies have considered it a severe problem due to the emerging evidence showing the association of VVC with a higher chance of pregnancy-related complexities (e.g., preterm labour, premature rupture of membranes, congenital cutaneous candidiasis, and chorioamnionitis) [15]. Topical azoles are recommended for the treatment and prolong antifungal treatment courses may be needed during pregnancy.

Recurrent vulvo-vaginal candidiasis is considered if there are four or more symptomatic episodes of candidiasis over 12 months period. Studies have reported that approximately 6% of women of reproductive age will develop recurrent disease [14]. Sometimes, recurrent symptoms can be cyclical. Exclusion of underlying causative factors (eg, diabetes mellitus, frequent antibiotic use or underlying immunodeficiency) in the management of recurrent vulvovaginal candidiasis is important.

Diagnosis

Both fungal balanitis and vulvovaginal candidiasis (VVC) are clinical diagnoses based on typical features supported by laboratory confirmation of Candida sp.

A high vaginal swab (HVS) or a swab taken from lateral vaginal walls of the discharge should be examined for microscopy with Gram stain and wet mount of 10% KOH preparation. Presence of blastospores, pseudo hyphae and hyphae can be seen by both gram stain and 10% KOH preparation in candida albicans infection. Presence of neutrophils can be seen only in gram stain as by addition of KOH would dissolve other cell structures in the wet mount.

Presence of blastospores only and neutrophils in Gram stain may reflect infection caused by *C. glabrata*. Neutrophils

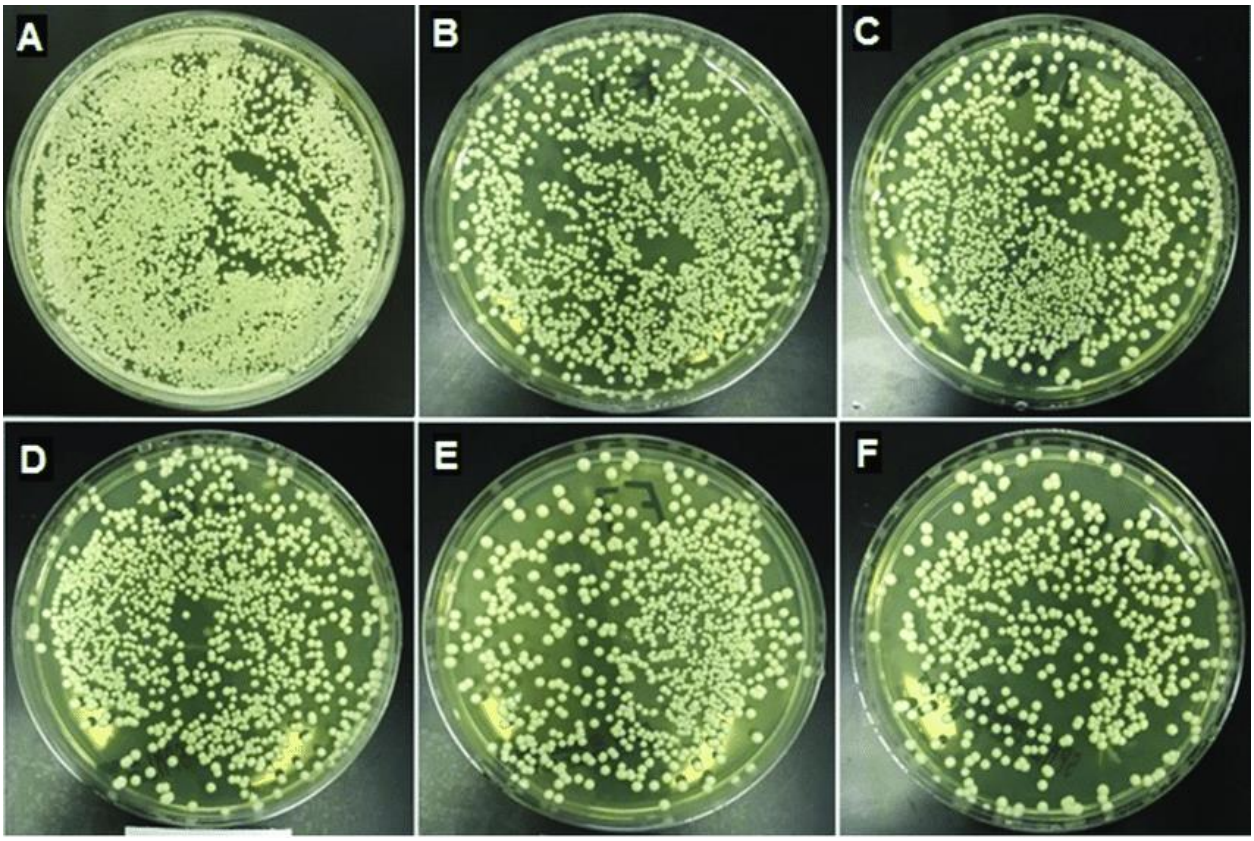
in vaginal secretions suggest an inflammatory response and therefore presence of infection which may or may not be due to Candida seen on microscopy. But absence of neutrophils in the presence of Candida is likely to represent colonisation [14].

Fungal culture is no longer considered a cost-effective addition to microscopy nor a reliable test on its own for the diagnosis of acute VVC due to its inability to differentiate colonisation from infection [14]. However, in recurrent VVC fungal culture and sensitivity testing is important. An HVS of the discharge should be taken for direct plating onto solid fungal growth medium (Sabouraud plate). If direct plating

is not available sending an HVS in a transport medium appropriate for fungal culture is a suitable alternative.

Figure 36: Microscopy picture of candida

Figure 37: Cultures of Candida albicans colonies based on different neem concentrations (image courtesy Journal of Clinical and Experimental Dentistry 11(2): e170-e178 DOI: 10.4317/jced.55458)



Management

Management of VVC include general health advises and specific treatment of the candidiasis.

Patients should be provided with information about the importance of good genital skin care including avoiding the use of local irritants such as perfumed soaps or wipes, the use of an emollient for personal hygiene as a soap substitute, as a moisturiser and a barrier cream and avoid wearing tight fitting synthetic undergarments. This general health advice may help to prevent recurrent VVC.

Specific treatment of VVC include treatment with azoles. In uncomplicated vulvo-vaginal candidiasis, clinical and mycological cure rate of over 80% with all. (Box 22)

topical and oral Azole therapy. The choice is a matter of personal preference, availability and affordability. Following recommended treatment options are available according to the National Guideline of Sexually Transmitted Infections of Sri Lanka for acute VVC

Box 22 Treatment for candidiasis

Topical Therapies

- Clotrimazole* Pessary 500mg single dose at night
- Clotrimazole* Pessary 200mg x3nights
- Clotrimazole* Pessary 100mg x6nights
- Clotrimazole* Vaginal cream (10%) 5g stat
- Miconazole cream 2% 5g intra vaginally x 7 nights 73
- Miconazole$^{\Delta}$ Ovule 1.2g stat
- Miconazole$^{\Delta}$ Pessary 100mg x14nights
- Nystatin Pessary (100,000 units) 1-2x14nights
- Nystatin vaginal cream (100,000units) 4g x 14 nights

NB: *Effect on latex condoms and diaphragms not known

$^{\Delta}$Product damages latex condoms and diaphragm

Oral Therapies

- Fluconazole* Capsule 150mg single dose
- Itraconazole* Capsule 200mg bdx1day

NB: *Avoid in pregnancy/risk of pregnancy and breast feeding

Treatment for recurrent candidiasis

Principles of therapy include induction using one of the above-mentioned regimens or a 100 mg, 150 mg, or 200 mg oral dose of fluconazole every third day for total of 3 doses [day 1, 4, and 7]) followed by a maintenance regime for 6 months. Cessation of therapy may result in relapse. For the induction, topical imidazole therapy can be increased to 10-14 days according to symptomatic response [16] and refer National Guideline of Sexually Transmitted Infections of Sri Lanka for further management options

Non-Albicans Species

Majority are Candida glabrata and are still susceptible to available azoles, although most nonalbicans species have higher MICs. Candida krusei is intrinsically resistant to fluconazole. For non-albicans infection longer courses may be needed although there is no data on optimum duration; two weeks is suggested. For non- albicans infection first line of treatment is the

- Nystatin pessaries 100,000 units daily for 14 nights.

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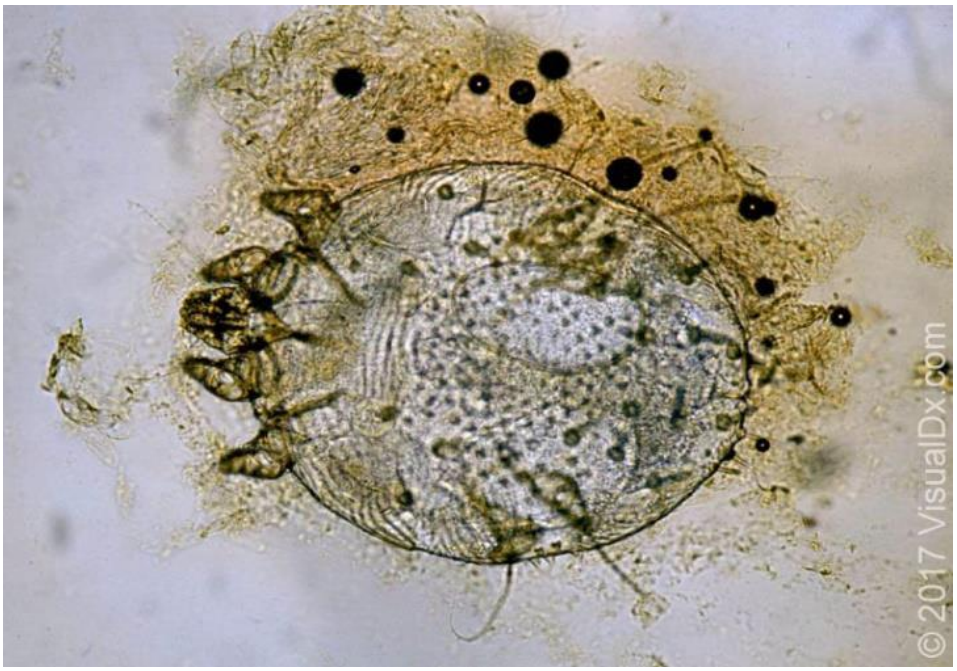
Scabies Infestation

Dr Iresh Jayaweera

Introduction

Scabies is an infestation of the skin by the mite *Sarcoptes scabiei*. Classic scabies typically manifests as an intensely pruritic eruption with a characteristic distribution. The sides and webs of the fingers, wrists, axillae, areolae, and genitalia are among the common sites of involvement. Crusted scabies, a less common variant that primarily occurs in the setting of impaired cellular immunity and is associated with a heavy mite burden, is characterized by thick scale, crusts, and fissures. The diagnosis of scabies is confirmed through the detection of scabies mites, eggs, or faecal pellets with microscopic examination.

Figure 38: Microscopic picture of Sarcoptes scabieii



Aetiology

Scabies is caused by the human itch mite Sarcoptes scabiei var hominis. The lifecycle of the sarcoptes lasts for 4-6 weeks. Mites burrow into human skin and lay their eggs, which later hatch and grow into adults. The female lays about 25 eggs and dies. The eggs develop into adults after moulting in 10-15 days. Less than 10% of the eggs develop into mature adults. The average number of mites in a person with an initial infestation is 10-15 and about half this number with a subsequent infestation.

Transmission

Transmission occurs from person to person through close skin contact. In young adults, scabies is frequently sexually acquired. Transmission of infestation through casual contact such as a handshake is unlikely. The mites can live off a host for 24-36 hours. Fomite transmission is uncommon but can occur in those wearing heavily contaminated clothing or using a bed recently occupied by an infested person. It is more likely to occur with crusted scabies due to the greater number of mites associated with and because mites can survive longer for up to 7 days.

Crowded conditions increase risk for scabies infestation. Epidemics can occur in institutional settings, such as long-term care facilities and prisons.

Clinical Manifestations

The major clinical variants of scabies are classic scabies and crusted scabies.

Classic scabies

Classic scabies presents as pruritus in association with small, often excoriated papules and burrows. Prominent scale, crusts, and fissures are absent.

The main clinical feature of scabies is intense generalised pruritus that is usually worse at night.

Pruritus results from a delayed-type hypersensitivity reaction to the mite, mite faeces, and mite eggs. Symptoms typically begin 3-6 weeks after primary infestation. However, in previously infested patient's symptoms occur earlier, within 1-3 days after infestation (probably due to prior sensitization). History of itching in family members or close contacts more in favour with the diagnosis of scabies.

The most common lesions are erythematous papules, often excoriated, seen in a characteristic distribution. Burrows may be visible as 2 to 15 mm, thin, grey, red, or brown, serpiginous lines. Burrows are a characteristic finding but often are not visible due to excoriation or secondary infection.

The distribution of cutaneous findings usually involves more than one of the following areas.

- Sides and webs of the fingers
- Flexor aspects of the wrists
- Extensor aspects of the elbows
- Anterior and posterior axillary folds
- Peri areolar skin (especially in women)
- Periumbilical skin
- Waist
- Male genitalia (scrotum, penile shaft, and glans)
- Extensor surface of the knees
- Lower buttocks and adjacent thighs
- Lateral and posterior aspects of the feet

The back is relatively not involved, and the head is spared except in children. Palms and soles are also affected in infants, young children and elderly.

Figure 39: Common scabies infestation sites

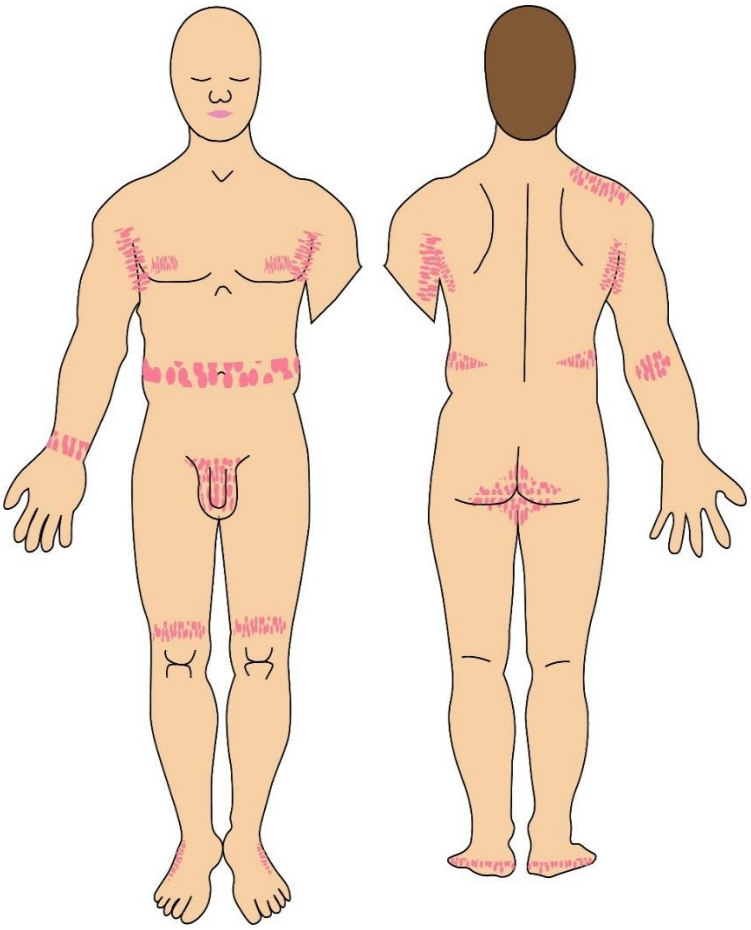
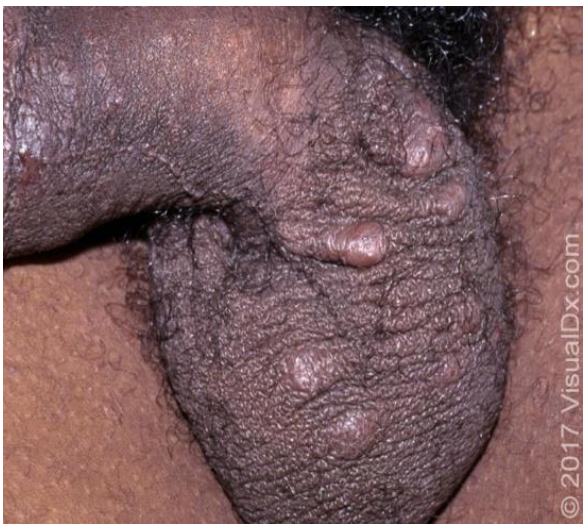


Figure 40: Scabies affecting scrotumFigure:



Nodular scabies is a less common manifestation of classic scabies. Nodular lesions may also be seen especially on the penis and scrotum in men, buttocks, groin and the axillary regions and these are intensely pruritic. They tend to persist after treatment and are thought to result from a hypersensitivity reaction to the mite. Urticarial lesions may rarely occur. Presence of itchy papules and nodules on the penis and scrotum are indicative of sexually acquired scabies.

Crusted scabies

A less common clinical variant, typically presents with scaly, crusted, fissured plaques and primarily occurs in immunocompromised individuals.

Crusted scabies (Scabies crustosa, Norwegian scabies) occur in immunocompromised states: e.g. in AIDS, leprosy, lymphoma, those receiving systemic or potent topical steroids, organ transplant recipients, in the elderly and in physically incapacitated persons or in patients with Down syndrome. However, a fair proportion (about 40%) have no identifiable risk factor suggesting possible genetic susceptibility. It is characterized by erythematous scaly crusted lesions that can be malodorous and associated with fissuring and can affect any part of the body including the face and scalp. However, itching may be mild or absent. Scabies contracted by a healthy person from a patient with crusted scabies is no different from classical scabies. Sepsis is a frequent complication as fissures associated with this condition provide an entry point for bacteria.

Diagnosis

Scabies should be suspected in any patient with a clinical history of itch, worse at night, affecting other family members or close contacts. Diagnosis can be made based on the clinical distribution and appearance of the skin lesions. Definite diagnosis relies on microscopic identification of the mites, eggs or faecal pellets (scybala) from the scrapings of the skin burrows with a scalpel blade and placing the specimen on a glass slide with 10% potassium hydroxide. This dissolves excess keratin (particularly seen in crusted scabies) and thereby permits better visualization of the mite and mite products. Alternatively, a drop of mineral oil is applied to the selected lesion or on the scalpel blade. The entire lesion is scraped away with the scalpel blade. The oil and the skin scrapings are then transferred to the microscopic slide and examined under the microscope.

Burrow ink test (BIT) allows identification of the burrows. Apply black or blue ink to the suspected papule and then wipe off with alcohol to remove surface ink. A positive BIT occurs when a characteristic dark zigzagged line running across and away from the lesion due to ink tracking down the mite burrow.

Other methods used for diagnosis of scabies include in vivo techniques such as dermoscopy, optical coherence tomography and detecting S. Scabiei DNA from cutaneous scales using PCR or ELISA.

Differential diagnosis

Scabies frequently imitates other skin diseases. It is important to have a high degree of suspicion to recognise symptoms

and signs of scabies. Differential diagnosis for scabies includes Impetigo, folliculitis, papular urticaria, atopic dermatitis, contact dermatitis, dermatitis herpetiformis, psoriasis, seborrhoeic dermatitis, pityriasis rosea, secondary syphilis and lymphoma and pseudo lymphoma (if scabies presents with nodules).

Complications

Secondary bacterial infection due to Staphylococcus aureus, group A β-haemolytic streptococci, or Pepto streptococci resulting in impetigo, folliculitis, furunculosis, ecthyma, and abscesses. Secondary eczematisation due to constant scratching, and due to irritant effects of topical medication can occur. Other reported complications include glomerulonephritis and leukocytoclastic vasculitis.

Management

The successful management of scabies involves:

- Eradication of the infestation
- Management of pruritus
- Management of complications
- Treatment of close personal contacts
- Implementation of environmental measures to minimize transmission and recurrence of infestation

Eradication of infestation

The approach to the eradication of scabies mites is dependent upon the clinical presentation (classic or crusted scabies) and patient population (children/pregnant women). Treatment of both the patient and close personal contacts is suggested to prevent recurrent infestation.

Treatment options for classic scabies

The availability of anti-scabietic agents for classic scabies varies worldwide. Treatment can be topical or oral. Topical Permethrin is the preferred initial therapy. Other topical therapeutic options include benzyl benzoate, malathion, sulphur, crotamiton and topical lindane. High efficacy and safety support the preferred use of permethrin therapy rather than benzyl benzoate, malathion, sulphur, crotamiton and topical lindane. Topical benzyl benzoate (10 or 25%) is commonly used in resource-limited countries because of its low cost.

Oral ivermectin is an alternative initial treatment for nonpregnant adults who prefer oral treatment, cannot tolerate permethrin, or are unable to apply topical therapy.

Special considerations are warranted for young children and pregnant individuals.

Permethrin 5% cream

Permethrin is a topical synthetic pyrethroid agent that impairs function of voltage-gated sodium channels in insects, leading to disruption of neurotransmission.

Permethrin is considered safe for use in infants as young as two months of age, children, adults, and pregnant or lactating individuals.

Benzyl Benzoate

Treatment regimens vary. Benzyl benzoate may be applied once daily at night on two consecutive days, with a repeat treatment cycle after seven days. Typical treatment

concentrations for benzyl benzoate are 25% for adults and 10 or 12.5% for children over the age of one year

Malathion 0.5% aqueous lotion

Can be used if permethrin cream is inappropriate [e.g. allergy to chrysanthemums.]

Topical sulphur

Topical sulphur is relatively inexpensive and primarily used for the treatment of neonates and pregnant individuals. The mechanism of action is thought to involve keratolytic effects and scabicidal properties.

Oral ivermectin

Oral ivermectin is an antiparasitic alternative to permethrin that has the advantage of ease of administration. This mode of treatment may be particularly useful for large scabies outbreaks in nursing homes and other facilities where topical therapy can be impractical.

Treatment for crusted scabies

Combination treatment with permethrin and oral ivermectin is the preferred first-line treatment for crusted scabies.

All household members and other potentially exposed persons should be treated at the same time as the infested person.

Management of pruritus

Antihistamines may improve pruritus, which may persist for up to 2-4 weeks after successful treatment for scabies. However, treatment failure should be suspected if new burrows appear or if the itching persists for longer than 2-4 weeks after the last application of scabicide.

Treat post-scabietic itch with crotamiton 10% cream (2-3 times a day) or, if the scabies mites have been eradicated, with topical hydrocortisone 1%. Nighttime use of a sedative antihistamine (e.g. chlorpheniramine) may help with sleep and reduce scratching.

Dry skin/eczema can be treated with emollients.

Sexual partners

Current sexual partners as well as members of the household and those that have had close personal contact should be examined and treated at the same time. Contact tracing of partners from the previous one month should be undertaken.

Follow-up

No clear evidence exists as to optimal follow-up but is not generally required for people with classical scabies.

Pruritus persisting more than 2 weeks after treatment may reflect treatment failure, reinfection or drug allergy to anti-scabietics.

HIV Infection

Patients who have uncomplicated scabies and are infected with HIV should receive the same treatment regimens as those who are HIV negative. HIV-infected patients and others who are immunosuppressed are at increased risk of crusted scabies, for which ivermectin has been reported to be effective.

Phthirus Pubis Infestation

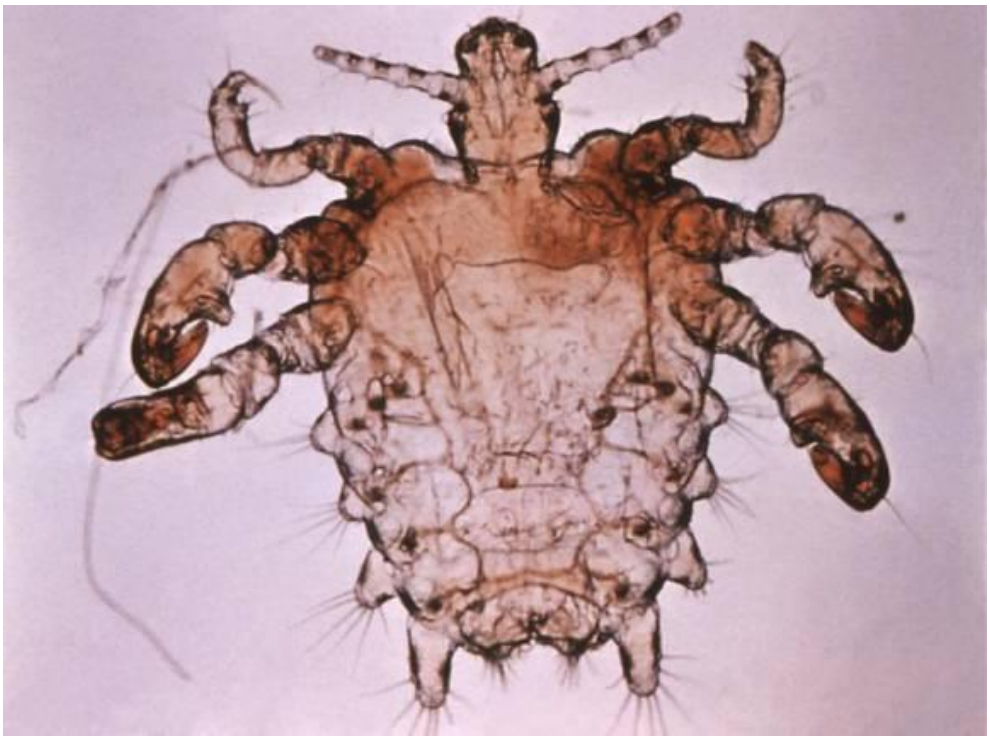
Dr Shalinie Nanayakkara

Introduction

Pubic lice infestation, also known as pediculosis pubis, is caused by the crab louse, *Phthirus pubis*. This human ectoparasite primarily infests coarse pubic hair but can also affect other hairy areas like the axillae, beard, eyebrows, and eyelashes. The louse has a five-stage life cycle, spending its entire life on the human host. It requires frequent blood meals and rarely survives more than 24 hours off the host.

The *Phthirus pubis* has a three-part body: head (with eyes), a thorax (with three legs per side), and a segmented abdomen. Hook-like claws on each leg grasp hair for a secure hold.

Figure 41: Microscopic picture of a Phthirus pubis (Image courtesy CDC)



It is mainly transmitted from person to person via sexual contact. However, fomites (bedding, clothing, toilet seats) may play a minor role in transmission. The incubation period usually ranges from 5 days to several weeks. However, some individuals may have a more prolonged, asymptomatic infestation.

Clinical manifestation

Initially, bites may cause no symptoms or a mild, transient sting. Itching, the primary symptom, typically develops after at least 5 days due to allergic sensitization. Scratching can lead to erythema, irritation, and inflammation. Individuals bitten by many lice in a short period may experience mild fever, malaise, and increased irritability. Pubic lice on the head (eyelashes or eyebrows) of a child are a potential indicator of sexual exposure or abuse.

Examination findings

Adult lice, which resemble small crabs, and/or eggs (nits) firmly attached to pubic hairs can be identified with the naked eye. Blue macules (maculae caeruleae) may be visible at the lice feeding sites. There may be evidence of secondary bacterial skin infections due to excoriations (scratches).

Diagnosis

Diagnosis of pubic lice infestation relies primarily on visual examination of the pubic hair. Adult lice, with their crab-like bodies, and/or eggs (nits) firmly attached to the hair shafts are identifiable with the naked eye. However, a magnifying lens can aid in visualization, particularly for nits or lice in less accessible areas. In rare cases, if there's any doubt about the morphology, examination under a light microscope can definitively confirm the presence of pubic lice.

Management

Effective pubic lice treatment relies on using a pediculicide that kills both adult lice and eggs. Lotions are generally considered more effective than shampoos. A second application of the medication is typically advised after 3-7 days to ensure complete eradication of lice and eggs.

Treatment

Recommended Regimens

- Permethrin 1% cream
- Pyrethrin with piperonyl butoxide

Alternative Regimens

- Malathion 0.5% lotion (Consider using this if resistance to permethrin or pyrethrin is suspected.)
- Ivermectin 250 µg/kg body weight orally

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Section 6:
Clinical presentations

Genital Ulcer disease

Dr Gayani Nanayakkara

Introduction

Genital ulcers may be located on the vagina, penis, and anorectal or perineal areas in males and females and may be infectious or non-infectious aetiology. (Table 1)

Genital ulcer disease commonly refers to ulcerations associated with sexually transmitted infections (STIs), but other than STIs, non-sexually transmitted infective causes of genital ulcer include fungal infections, and secondary bacterial infections. Genital ulcerations have also been reported as rare sequelae of mononucleosis (Epstein -Barr virus).

There are numerus non-infectious aetiologies such as psoriasis, sexual trauma, Behçet syndrome, fixed drug eruptions etc.

The most common cause of STI related genital ulcers includes genital herpes simplex virus types 1 and 2 (HSV-1, HSV-2). The second most common STI related genital ulceration is due to Syphilis (Treponema pallidum) and other rare causes include, chancroid (*Haemophilus ducreyi*), granuloma inguinale or Donovanosis (*Klebsiella granulomatis*, formerly known as *Calymmatobacterium granulomatis*), and lymphogranuloma venereum (*Chlamydia trachomatis* serovars L1, L2, and L3).

There is an increased risk of acquiring HIV, as well as transmission of HIV in the presence of genital ulcerations. Increased shedding of HIV in the presence of a genital ulcer in people living with HIV has been identified.

Some features of genital ulcerations are important in narrowing down the differential diagnosis. It is helpful to divide them into acute and chronic types.

Acute genital ulcerations:

Other than the ulcers of infectious aetiology, there are benign aphthae ulcerations of unknown aetiology, or ulcers in Bechet's syndrome, vulval ulcers appear in stevens Johnsons syndrome and bullous fixed drug eruption in genitalia appear as acute genital ulcers.

Chronic genital ulcerations:

Any chronic genital ulcer of genital mucosa, malignancy must be excluded. Causes of chronic genital ulcerations include:

Genetic: Epidermolysis bullosa, Hailey-Haley disease, Darier's disease causes chronic recurrent ulcerations.

External trauma: sexual trauma, dermatitis artefacta and radiation damage leave chronic genital ulcers

Malignancy: most common malignant ulcers are squamous cell carcinoma and basal cell carcinoma. Melanoma also can present as amelanotic ulcerative nodule.

Infection: Chronic infective ulcers occur in Tuberculosis. Actinomycosis and late stage of Lymphogranuloma venereum

Inflammatory: Lichen planus, Lichen sclerosus, Lupus erythematosus can cause genital ulcerations. Several of auto immune bullous diseases like Juvenile pemphigoid, Pemphigus vulgaris may present with vulval ulcers in females.

Diagnostic Evaluation

Diagnosing the specific cause of genital ulcer disease is based on

- Detailed history
- Physical examination
- Laboratory findings

History and Physical examination

In the history, to identify the genital ulcers of sexuality transmitted aetiology, evaluate the presence of risk factors which are of like other STIs, including unprotected sexual contact, multiple sex partners, alcohol or illicit drug use, etc.

Inquire about common STI symptoms (e.g., urethral discharge, dysuria, genital and perianal ulcers, regional lymphadenopathy, proctitis) and proceed with diagnostic testing when indicated.

Risk factors for non-infectious causes of genital ulcers include a history of inflammatory disease (e.g., psoriasis) and exposure to sexual trauma or medications with ulcerative adverse effects or drug eruptions such as nonsteroidal anti-inflammatory drugs, antimalarials, angiotensin-converting enzyme inhibitors, beta blockers, lithium, salicylates, etc.

Symptoms and signs – Genital ulcers of STI aetiology

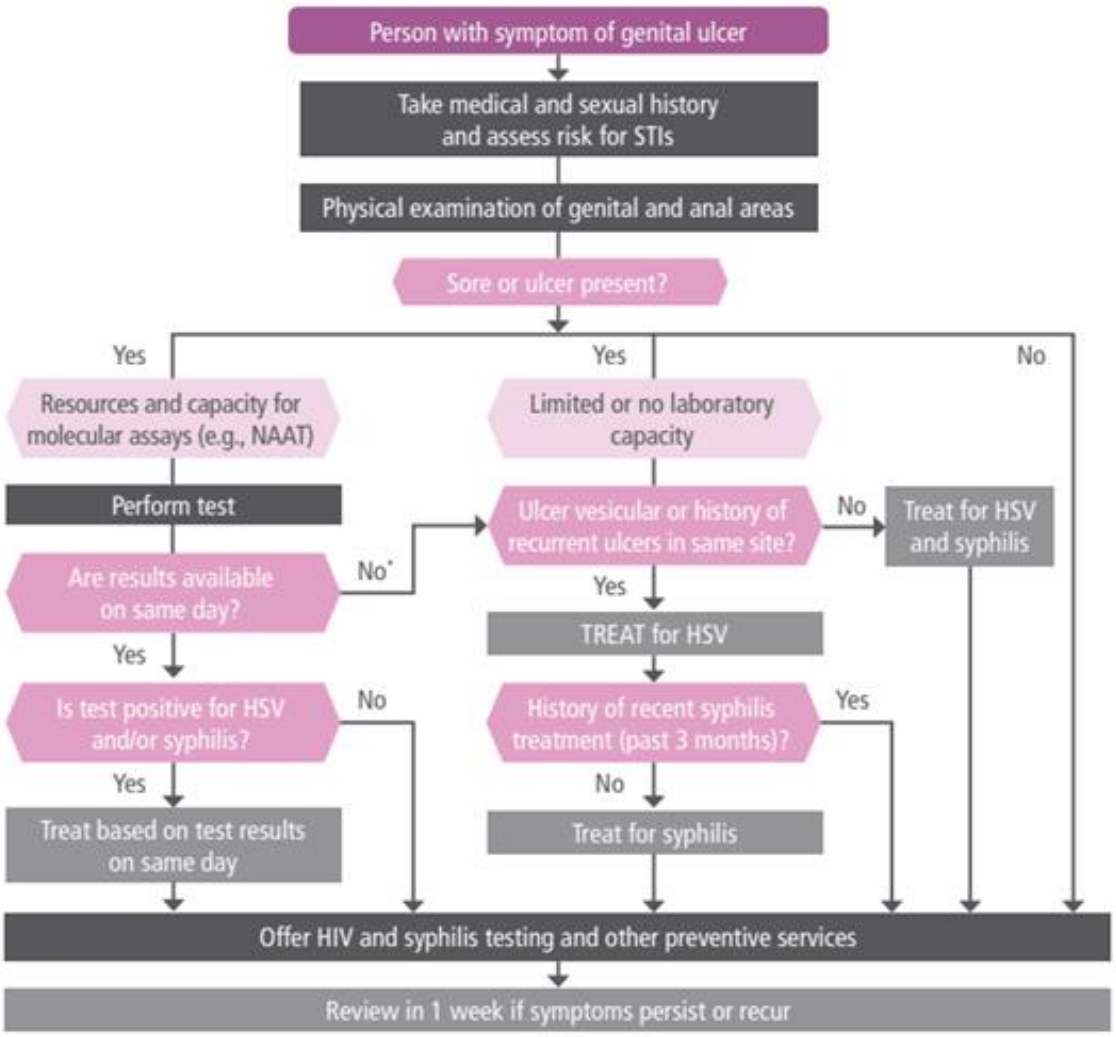
Genital HSV infection is most reliably diagnosed through observation of characteristic genital lesions. HSV lesions are commonly painful, are preceded by prodromal symptoms tingling before vesicular eruptions, and may be found inside the foreskin, labia, vagina, rectum or perianal region.

Initial lesions are usually multiple vesicles; lesions may spontaneously rupture in, leaving a shallow, painful ulcers. First-time infections may cause constitutional symptoms and inguinal lymphadenopathy. Genital HSV infection is most reliably diagnosed through observation of characteristic genital lesions.

Primary syphilis ulcer is known as primary chancre; a single, painless, indurated well demarcated ulcer with a clean base and is caused by active infection with *T. pallidum* and associated with painless, non-tender or minimally tender, rubbery, mattered inguinal lymphadenopathy.

Chancroid causes non indurated, painful ulcers and may be single or multiple. They are characterized by a serpiginous border surrounding a friable base covered with a necrotic and often purulent exudate, bleeds when touched. Painful, unilateral inguinal adenitis is present in one-half of cases, and these can develop into buboes, which can become fluctuant and rupture releasing thick pus.

Figure 42: WHO flow chart for the management of genital ulcer disease including the anorectal ulcers



HSV, herpes simplex virus

* If molecular assay was performed and results were not available on same day, revise the syndromic treatment initially provided according to the test results when available

Granuloma Inguinale (Donovanosis) presents as a firm papule or sub cutaneous nodule initially and ulcerate later with minor trauma. Lesions are highly vascularized, and the lesions are progressive in an outward direction from the centre. Due to high vascularity lesions tend to bleed easily. Self-inoculation is possible and may create

mirror-image lesions in the same general location, usually across skin folds.

Lymphogranuloma venereum (LGV) is a systemic disease and have 3 stages. *Primary stage* is characterized with a painless papule/pustule mostly un-noticeable by the patient, the lesions resolve or heal spontaneously after few days. The secondary stage presents with the development of unilateral or bilateral tender inguinal and/or femoral lymphadenopathy (also called buboes), with fistula. An anorectal syndrome also presents which is characterized by proctitis or proctocolitis-like symptoms. Generalized symptoms like body aches, headache, and fever can occur during this stage. Late stage usually, occur when the disease is left untreated. Necrosis and rupture of the lymph nodes, fibrosis, stricture formation occurs. Elephantiasis of the genital organs can also occur in some cases.

Management of genital ulcer syndrome

Please refer to the specific sections for the specific laboratory diagnosis and management of individual STIs.

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Urethritis

Dr Shyama Somawardhena

Introduction

Urethritis, as characterized by urethral inflammation, can result from either infectious or non-infectious conditions. Although *N. gonorrhoeae* and *C. trachomatis* are well established as clinically important infectious causes of urethritis, *M. genitalium* has been strongly associated with urethritis. Other aetiologies include organisms, such as *Haemophilus* species, *N. meningitidis*, HSV, *Trichomonas vaginalis* and adenovirus. However, even when extensive testing is performed, no pathogens are identified in approximately half of the cases.

Clinical presentation

Symptoms, if present, include dysuria, urethral pruritus, and mucoid, mucopurulent, or purulent discharge. Occasionally, dysuria or itching at the tip of the urethra may be the only symptoms.

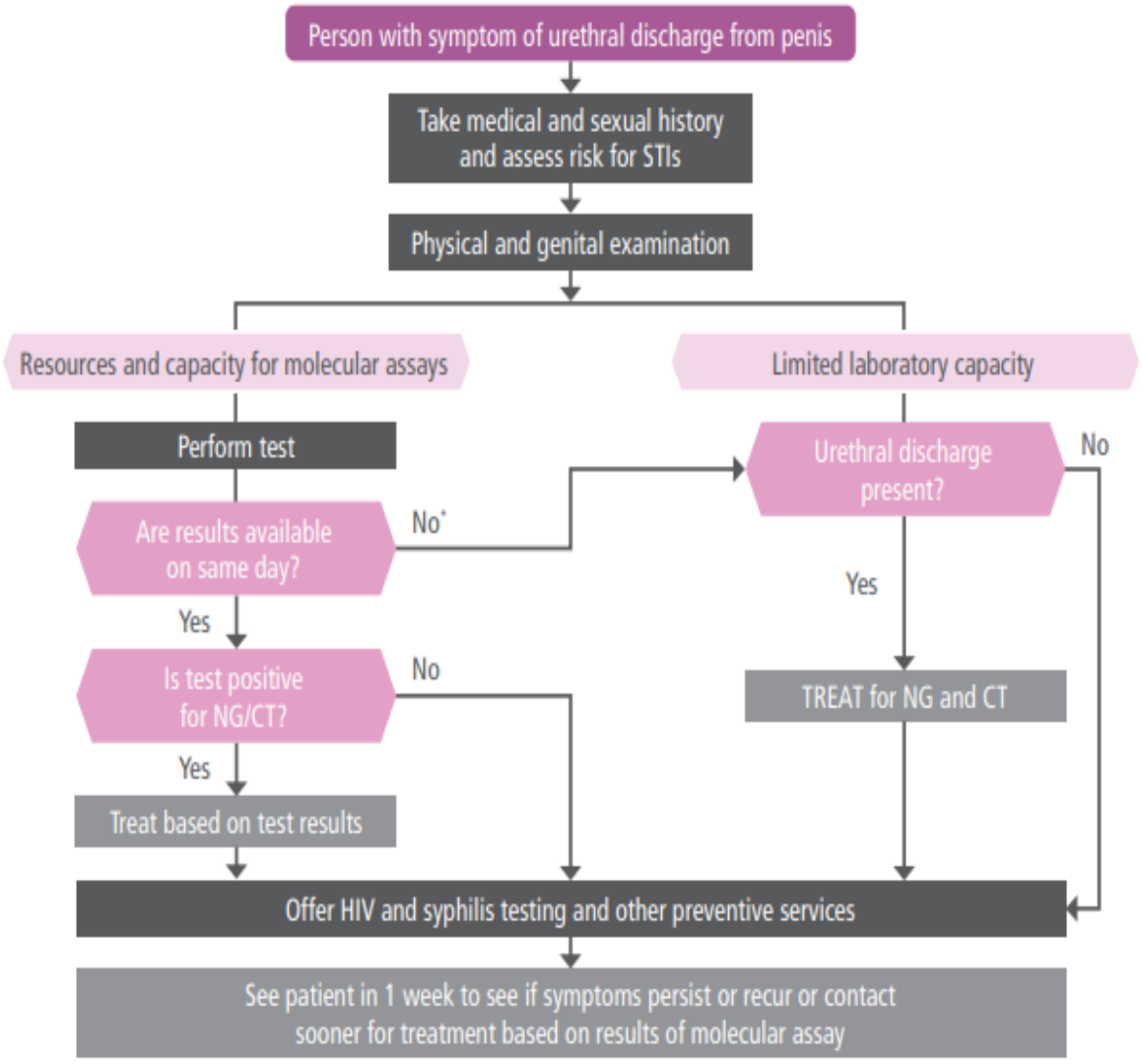
Examination findings – signs

Most men with urethritis have no clinical findings on examination. If urethral discharge is present, it may range in quantity from being scanty to copious and in character from being clear to purulent. Distinguishing between discharge caused by gonorrhoea, chlamydia or any other cause of urethritis is not clinically possible. Sometimes meatitis and balanoposthitis can be seen.

Management

Please refer to the specific sections for the specific laboratory diagnosis and management of individual STIs

Figure 43: WHO flow chart for the management of urethral discharge syndrome



Vaginal discharge

Dr Thilani Ratnayake

Introduction

Vaginal discharge is a common clinical presentation in females in sexual health and could be a normal physiology or pathological.

Pathophysiology

Normal vaginal discharge:

Normal Vaginal discharge also known as leukorrhoea refer to whitish or clear fluid from vagina which is a normal physiological function in female reproductive system. Leukorrhoea consists of secretions from glands inside vagina, cervix, uterus contains dead cells and bacteria. (1)

Amount, colour and odour of vaginal discharge can vary depending on the physiological status and time of the menstrual cycle. Most females in reproductive age experience excess vaginal discharge during midcycle with ovulation. During pregnancy and breast feeding most women experience excess of normal discharge. Sexual arousal also increases the amount of discharge. Females in premenarche and post-menopausal stages get less vaginal discharge with low oestrogen level. (2)

Pathological or abnormal vaginal discharge

Pathological or abnormal vaginal discharge is due to infections or other conditions such as foreign bodies, benign or malignancies related to lower genital tract, vaginal atrophy etc. Pathological vaginal discharge could be excessive, altered in colour and associated with offensive odour, itching and soreness, lower abdominal pain, post coital bleeding etc (1)

Gonococcal infection (GC)

Neisseria gonorrhoea is a sexually transmitted bacteria which causes cervical infection in women resulting excessive and yellowish vaginal discharge as a presenting symptom. Vaginal discharge can be associated with other symptoms like intermenstrual bleeding, post coital bleeding and lower abdominal pain and deep dyspareunia in complicated GC but most females up to 50% can be asymptomatic (3).

Chlamydia

Chlamydia trachomatis (CT) is a common sexually transmitted intracellular bacteria and a cause for cervical infection in women. Like gonococcal infection majority of females with CT remain asymptomatic. when symptomatic they can present with excessive yellowish vaginal discharge because of cervical infection (4).

Table 32: Vaginal Discharge in Females

Physiological vaginal discharge	
	Pregnancy Breast feeding Mid cycle Contraceptive pill
Pathological or abnormal vaginal discharge	
Infections	**Sexually Transmitted Infections (STI)** Gonorrhoea Chlamydia Trichomoniasis **Non STIs** Bacterial Vaginosis Candida
Non-infectious causes	Cervical Ectropion Cervical polyps Foreign bodies inside vagina Cervical cancer Vaginal fistulae Vaginal atrophy

Trichomoniasis

Is a sexually transmitted infection caused by a flagellated protozoon, *Trichomoniasis vaginalis (TV)*. Most women present with excessive vaginal discharge (70%) and typical yellowish frothy vaginal discharge is seen in 30% of women.

Bacterial Vaginosis (BV)

Is the commonest cause for vaginal discharge in women in reproductive age group. Women with BV present with thin whitish vaginal discharge with typical fishy odor or change of smell.

Vaginal candidiasis

Is a common cause for vaginal discharge caused by fungi, *candida* spp mainly *candida albican*. Women with candida have whitish thick discharge typically described as “curd like” discharge and associated with itching and soreness.

Cervical ectopy (cervical erosion)

Is an anatomical variation in some women causing excess vaginal discharge where inner mucosa of cervical canal extends more than usual to the outer surface of cervix more than usual containing more glandular epithelium. This can be seen during speculum examination as erythematous circular area around the os. Most women

with cervical ectropion do not have symptoms but some may have excess vaginal discharge which may contains blood or mucus without itching or odour. Ectropion is associated with oestrogen level and common in young women, pregnancy and women on oestrogen containing contraception. (8)

Cervical polyps

Is an uncommon cause for vaginal discharge and reported in 2-5% of the women. Polyps appear as soft lumps at the cervix and can be ectocervical or endocervical. Symptoms associated with polyps are bleeding after sex, heavy menstruation and whitish or yellowish vaginal discharge. Mostly they are benign but rarely can be malignant especially in post-menopausal women.

Foreign bodies

Foreign bodies inside vagina can cause abnormal vaginal discharge with yellowish or purulent discharge associated with an odour. Most common foreign objects known to retained in vagina are condoms and tampons. Speculum examination with good lighting is essential to detect and remove the retained object fully.

Other rare causes of vaginal discharge

- Cervical cancer
- Vaginal fistula
- Vaginal cancers
- Vaginal atrophy

Vaginal discharge syndrome

In sexual health syndromic management is useful approach to treat and prevent sexually transmitted infections especially at primary health care levels where all laboratory facilities are not available. The basic principle in syndromic management is to treat all possible pathogens responsible for common clinical symptoms and signs using standard algorithms. In vaginal discharge syndrome all possible infections including gonorrhoea, chlamydia, bacterial vaginosis. Trichomoniasis and candidiasis that can cause vaginal syndrome should be covered.

Management of vaginal discharge syndrome

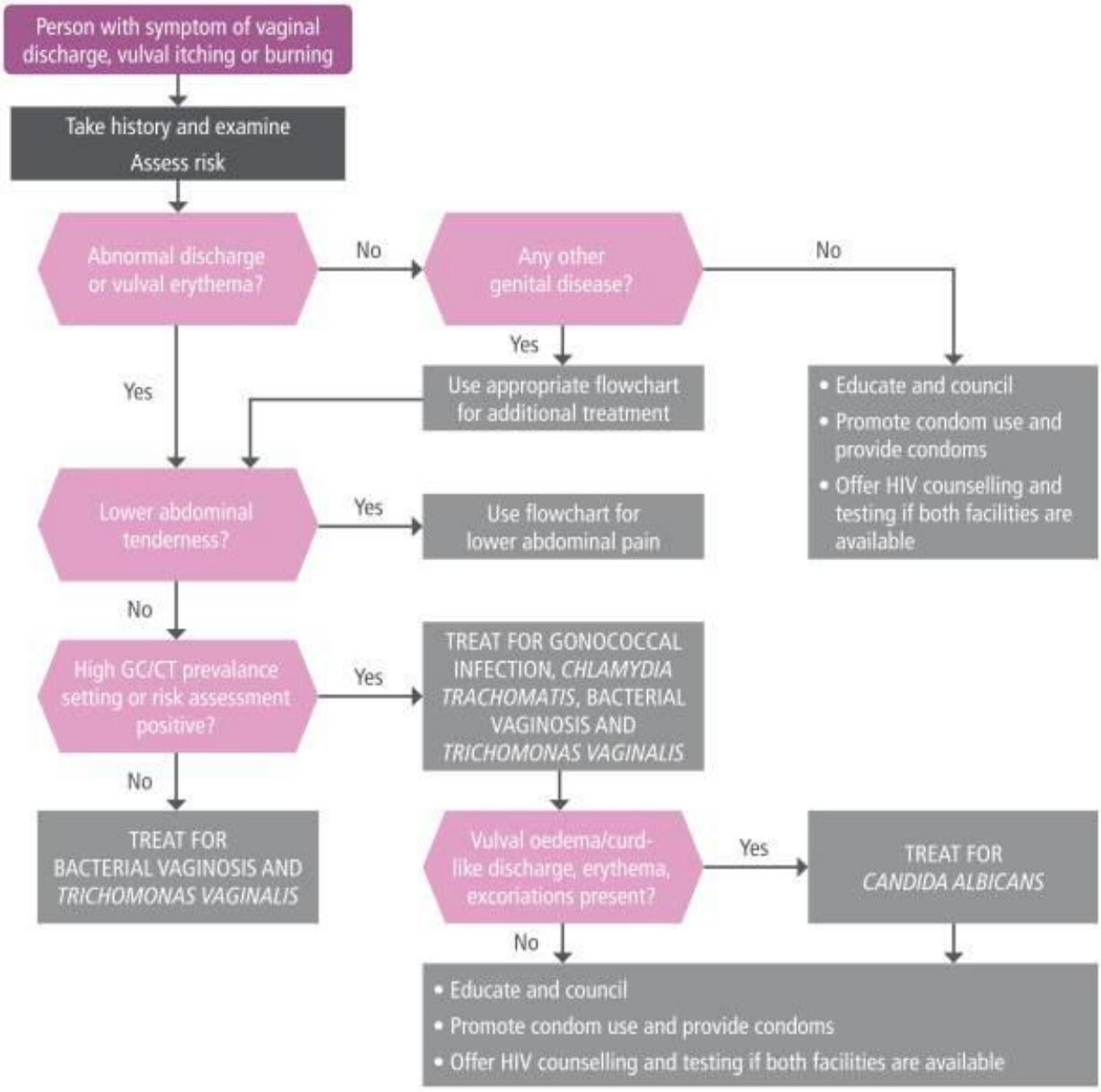
Management of vaginal discharge at primary care level requires a structured approach to distinguish sexually transmitted infections (STIs) from non-STI causes, while often initiating syndromic treatment. A focused history (sexual exposure, symptoms, menstrual and hygiene practices) and examination should be followed by basic investigations where available (vaginal pH, microscopy, NAATs).

STI-related causes commonly include Chlamydia trachomatis infection, Neisseria gonorrhoeae infection, and Trichomoniasis; these are managed with appropriate antibiotics (e.g., ceftriaxone plus doxycycline or azithromycin for gonorrhea/chlamydia, and metronidazole for trichomoniasis), along with partner notification and treatment, counseling, and screening for co-infections including HIV and syphilis.

Other causes include Bacterial vaginosis and Vulvovaginal candidiasis, treated with metronidazole/clindamycin and antifungal agents (e.g., fluconazole or topical azoles)

respectively; recurrence and contributing factors such as diabetes, antibiotic use, or hormonal influences should be addressed. Patient education on genital hygiene, avoidance of douching, and adherence to therapy is essential. Follow-up is advised for persistent or recurrent symptoms, and referral is warranted if complications or atypical features are present.

Figure 44: WHO algorithm for vaginal discharge syndrome



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Pelvic Inflammatory Disease

Dr Nadeera Kumarasinghe

Introduction

PID is usually result of the ascending infection from endocervix to upper genital tract and sometimes to pelvis. Neisseria gonorrhoeae, and Chlamydia trachomatis are the main causative organisms, and organisms associated with bacterial vaginosis may also be contributors.

Acute symptomatic PID — characterized by the acute onset of lower abdominal or pelvic pain, pelvic organ tenderness, and evidence of inflammation of the genital tract. The findings may be subtle and nonspecific.

Clinical Manifestations

Symptoms

1. Lower abdominal pain is the cardinal presenting symptom in females with PID. The abdominal pain is usually bilateral. The recent onset of pain with deep dyspareunia may be the only presenting symptom of PID. The onset of pain during or shortly after menstruation is particularly suggestive.
2. Most females with PID have mild to moderate disease and only a minority develop peritonitis or pelvic abscess, which usually manifest by more severe pain, greater tenderness on examination, and systemic features such as fever.
2. Abnormal uterine bleeding (post-coital bleeding, inter-menstrual bleeding, menorrhagia) occurs in one-third or more of patients with PID.
3. Other non-specific complaints include fever, urinary frequency and abnormal vaginal discharge.

Examination findings

1. Lower abdominal tenderness on palpation, rebound tenderness, fever, and decreased bowel sounds are usually limited to females with more severe PID.
2. Acute cervical motion, uterine, and adnexal tenderness on bimanual pelvic examination are the defining characteristic of acute symptomatic PID.
3. Purulent endocervical discharge and/or vaginal discharge is common.

Complications of PID

Tubo-ovarian abscess

A tubo-ovarian abscess is an inflammatory mass involving the fallopian tube, ovary, and, occasionally, other adjacent pelvic organs. Females with a tubo-ovarian abscess may have a palpable adnexal mass on examination.

Subclinical PID

Subclinical infection of the upper reproductive tract that does not prompt a

woman to present to medical care but is severe enough to produce significant sequelae appears to be relatively common. Females with tubal factor infertility that appears likely to have been a result of past episodes of PID often give no history of PID.

Perihepatitis

Perihepatitis (Fitz-Hugh Curtis Syndrome) rarely occurs in the setting of PID when there is inflammation of the liver capsule and peritoneal surfaces of the anterior right upper quadrant. The syndrome was first associated with gonococcal salpingitis in 1920 and subsequently with *Chlamydia trachomatis* and possibly *Mycoplasma genitalium*.

Diagnostic criteria for PID

Minimum diagnostic criteria: Cervical motion tenderness, uterine tenderness, or adnexal tenderness on pelvic exam. These physical signs should prompt empirical treatment in sexually active young women or those at increased STI risk when no other cause is found.

Supportive tests:

Oral temperature >38.3°C, mucopurulent cervical discharge, friability, presence of abundant WBCs on wet preparation, elevated ESR or CRP, positive cervical *Neisseria gonorrhoeae* or *Chlamydia trachomatis*.

Recommended Laboratory Investigations

Vulvovaginal NAAT swabs for chlamydia and gonorrhoea, bloods for HIV and syphilis, pregnancy test (to exclude ectopic pregnancy), FBC, CRP (for inpatients), urine analysis as indicated.

Imaging: TV (transvaginal) ultrasound when tubo-ovarian abscess is suspected or severe disease is present.

Further tests in severe/refractory cases: NAAT for Mycoplasma genitalium, endocervical swabs for gonorrhoea culture, high vaginal swabs for microscopy/culture; consider endometrial biopsy, MRI, or laparoscopy for diagnostic uncertainty or non-response to treatment.

Differential Diagnoses

- Gynaecologic: Ectopic pregnancy, ovarian cyst or torsion, endometriosis.
- Non-gynaecologic: Urinary tract infection, appendicitis, gastrointestinal disease.
- Other: Functional or unexplained pelvic pain.

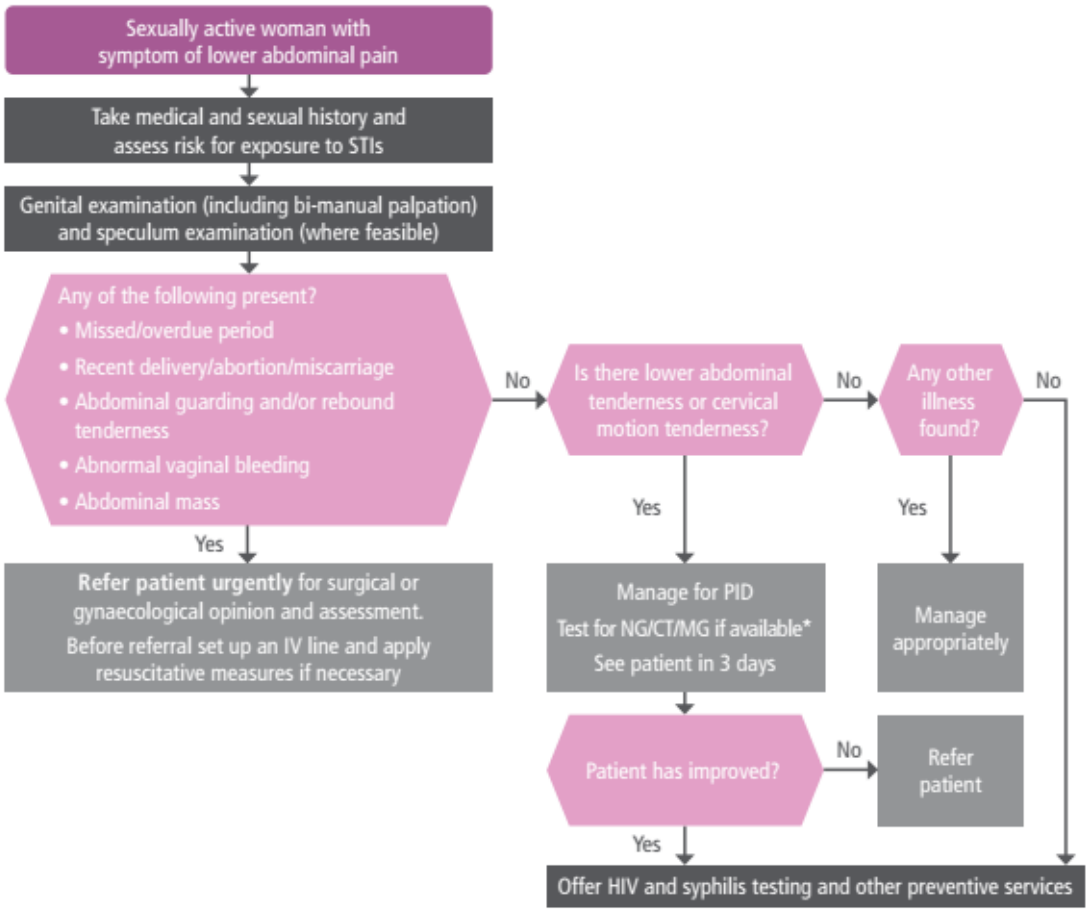
Management

Assess severity:

Outpatient (mild/moderate): Most non-severe PID can be treated as outpatient.

Inpatient (severe or complicated): Indications for hospital admission include inability to exclude surgical emergency, clinical severe disease (pyrexia >38°C, tubo-ovarian abscess, peritonitis), pregnancy, lack of response to oral therapy, or confirmed abscess.

Figure 45: WHO algorithm for lower abdominal pain



*to support partner notification.
NG, *N.gonorrhoeae*; CT, *C. trachomatis*; MG, *M. genitalium*.

ANTIBIOTIC THERAPY:

- Outpatient (mild/moderate): IM ceftriaxone 1g stat, doxycycline 100 mg orally twice daily for 14 days, with metronidazole 500 mg orally twice daily for 14 days.
- Severe/inpatient: IV ceftriaxone 2g daily plus IV or oral doxycycline, switch to oral doxycycline with metronidazole after clinical improvement, for a total of 14 days; alternatives include clindamycin/gentamicin combinations.

SEXUAL PARTNER MANAGEMENT: All recent partners within the last 60 days should be

notified, tested, and empirically treated for chlamydia and gonorrhoea.

FOLLOW-UP: Clinical improvement expected within 48-72 hours, with further review or admission if not improving.

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Epididymo-orchitis

Dr Udari Gallage

Introduction

Patients with Epididymitis characteristically complain of testicular or scrotal pain and sometimes pain on the inguinal area. In severe cases, some patients experience flank pain due to the obstruction of the ureter caused by acute swelling of the spermatic cord. Onset of the pain is gradual on 2/3 of patients while 1/3 have sudden onset pain. Pain is usually located on one side. Orchitis found in association with acute epididymitis in 20-40% of cases.

Epididymo- orchitis following bacteriuria may have symptoms suggestive of urinary tract infection such as frequency, urgency, or dysuria. There may be a history suggestive of urinary tract obstruction such as poor stream of urine and hesitancy or indications for predisposing conditions for urinary tract infections such as benign prostatic hyperplasia or strictures.

Epididymo- orchitis following sexually transmitted infections usually have a history of recent sexual exposure, urethral discharges, and dysuria.

Clinical manifestations

On examination, the scrotum on the affected side may be red and oedematous. Tenderness and induration usually first occur on the epididymal tail and spread to the body and spermatic cord. Acute epididymitis is bilateral in only 5-10% of patients.

Testicular torsion which is an important differential diagnosis, and a urological emergency needs to be excluded during examination. Positive Prehn sign (exacerbation of pain when affected hemi-scrotum is elevated) is seen in testicular torsion while in epididymitis, elevation of the hemi-scrotum relieves pain as it takes the weight off the epididymal suspension. Normal cremasteric reflex indicates that the testicular torsion is unlikely.

In epididymo-orchitis, testes may tend to lie in the normal position in the scrotum. Urethral discharge may present if the patient has not voided recently. Erythema and mild scrotal cellulitis may present and there could be reactive hydrocele in patients with advanced epididymo- orchitis.

Diagnosis

Generally, epididymo-orchitis among men younger than 35 years is most often caused by STI pathogens whereas older men most often non-STI pathogens are very likely.

Diagnosis of epididymo-orchitis is generally clinical. If diagnosis is uncertain urgent ultrasound scan and surgical referral is recommended.

Patient with STI related epididymo-orchitis could be positive for urethral smear for urethritis and may have evidence of STI

pathogens in the urethra. Mid-stream urine microscopy and culture are recommended for patient suspected with non STI origin.

Ultrasound of the scrotum is crucial in the diagnosis of epididymo-orchitis as it helps confirm the diagnosis by demonstrating an enlarged, hypoechoic or hyperechoic epididymis with increased blood flow on Doppler imaging, which indicates inflammation. It also differentiates epididymo-orchitis from testicular torsion as torsion typically shows absent blood flow. Additionally, ultrasound can detect complications such as abscess formation and reactive hydrocele, aiding in comprehensive management.

Management

General management of epididymo-orchitis includes recommendations for bed rest, scrotal support, and the use of analgesics for pain relief. In cases of suspected STI-related epididymo-orchitis, treatment should include coverage for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*. The most up-to-date STI guidelines should be consulted for the specific recommended drug treatments. Additionally, sexual partners should be evaluated and provided with appropriate epidemiological treatment in cases where the epididymo-orchitis is likely related to a sexually transmitted infection.

Sexually Acquired Reactive Arthritis

Dr Randima Kodithuwakku

Introduction

The term "reactive arthritis" (ReA) emerged in the 1960s, where patients are exhibiting acute arthritis with significant synovial inflammation in association with a preceding enteric or genitourinary infection. However, the joint effusions in these patients are constantly sterile.

Reactive Arthritis is a predominantly young adult disease with a peak incidence between 16 and 35 years of age. While more prevalent in males, it can also significantly impact females. In young men, it's the most common cause of acute peripheral arthritis (1).

When ReA is triggered by a sexually transmitted infection (STI), it's specifically termed sexually acquired reactive arthritis (SARA). This encompasses the historical description of sexually acquired Reiter's syndrome, characterized by the triad of urethritis, arthritis, and conjunctivitis. Additionally, other cutaneous and mucosal manifestations may be present, such as keratoderma blennorrhagica, circinate balanitis/vulvitis, uveitis, oral ulcerations, and even cardiac or neurological involvement.

Given the potential for SARA, a high index of suspicion should be maintained for any presentation of acute arthritis, particularly in young adults. In such cases, a thorough evaluation of STIs is crucial, followed by appropriate treatment.

Aetiology

Since the early 1990s, growing evidence suggests the presence of viable but difficult-to-culture Chlamydia in the joints of patients with reactive arthritis (ReA) (1). Synovial tissues from patients with acute ReA have yielded structures indicative of Chlamydia, including whole organisms, as well as Chlamydial DNA and RNA. The development of ReA appears to involve an immune response to the pathogen that undergoes a transformation, allowing it to persist in the synovium in an atypical form while triggering inflammation. Factors influencing individual susceptibility to sexually transmitted infection (STI) complications like ReA, and the limited association of ReA with specific STIs, remain unclear.

Lower genital tract infections, such as urethritis or cervicitis, are the most frequent predisposing factors for ReA. While older studies suggested a prevalence of 0.8-4% for clinically diagnosed ReA in patients with these infections, the actual rate appears to be lower in contemporary practice (2).

Chlamydia trachomatis is the most implicated infectious agent, found in up to two-thirds of ReA cases. *Neisseria gonorrhoeae* has also been reported in up to 16% of cases, independent of its potential to cause septic arthritis (3).

Mycoplasma genitalium and *Ureaplasma urealyticum*, both known to cause urethritis,

have been identified in a limited number of ReA cases. However, a definitive causal role for these organisms in ReA development remains unestablished.

Pathogenesis

The pathogenesis of Sexually Acquired Reactive Arthritis (SARA) remains poorly elucidated. The susceptibility factors leading to the development of SARA following a Sexually Transmitted Infection (STI) are unclear. However, a dysregulated immune response to urogenital pathogens appears to be implicated (2).

DNA and/or surface antigens of *Chlamydia trachomatis*, *Ureaplasma urealyticum*, and other *Mycoplasmas* have been identified within synovial fluid aspirates from SARA patients. The persistence of viable organisms within the joint cavity is likely a crucial factor in initiating and continuing arthritis.

In Chlamydia infections, the organism has been shown to transform into an atypical, persistent form within the synovium. This aberrant form exhibits suppressed expression of the major outer membrane protein (MOMP) and enhanced production of heat shock proteins (HSP), contributing to the inflammatory process.

Several predisposing factors are associated with SARA: A significantly higher prevalence is observed in males compared to females. However, underdiagnosis or less severe presentations in women might contribute to this disparity (4).

The presence of the HLA-B27 gene is a significant risk factor for SARA, particularly for a more severe disease course. It is observed to be ten times more common in individuals with SARA.

An increased incidence of spondyloarthritis, including rheumatoid arthritis (RA), has been documented in sub-Saharan Africa among HIV-positive individuals. This association is not evident in Caucasian populations.

A known association exists with other spondyloarthritis, most notably ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease (IBD)-associated arthritis, and SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, and osteitis). This suggests a potential for a personal or family history of spondyloarthritis, iritis, psoriasis, IBD, or SAPHO syndrome (4).

Clinical presentation

Genitourinary Manifestations: A history of sexual activity, often with a new partner, is typically reported within 3 months of developing joint symptoms. Males frequently experience recent genital symptoms like urethral discharge, dysuria, and/or testicular pain/swelling. These symptoms usually precede arthritis by an average of 14 days (2).

Females may be asymptomatic but might report changes in vaginal discharge (mucopurulent), inter-menstrual or post-coital bleeding, pelvic pain, or deep dyspareunia.

The classic triad of arthritis, urethritis, and conjunctivitis is not always present. Urogenital symptoms can be absent or limited to a mild, painless urethral discharge. More severe infections may occur,

presenting as prostatitis in men and cervicitis (marked by vaginal discharge) in women.

Rectal Manifestations: Rectal sexually transmitted infections (STIs) like gonorrhea and chlamydia can be asymptomatic but might cause rectal discharge, bleeding, discomfort, and tenesmus

Musculoskeletal Manifestations**:** Acute synovitis typically starts 1-3 weeks after the initial urethritis. It predominantly affects the lower limbs in an asymmetrical oligoarthritis pattern. Knee effusions are frequent and can be quite tense. Fusiform dactylitis ("sausage digits") is a characteristic feature of spondyloarthritides, where fingers or toes appear swollen like sausages.

Enthesitis (inflammation at tendon/ligament attachments to bone) is common, often presenting as Achilles tendonitis or plantar fasciitis (heel pain). In addition to peripheral arthritis, patients may experience thoracic and lumbar spine pain along with buttock pain (indicative of sacroiliitis, and inflammation of the sacroiliac joints). Disability can be significant, worsened by fatigue, sweating, and loss of appetite.

Mucocutaneous Manifestations: While less frequent, some specific mucocutaneous lesions can occur. Circinate balanitis is a painless, reddened lesion on the glans penis. Similar lesions might appear on the hard and soft palate, gums, tongue (geographic tongue), and inner cheek lining. These lesions are often overlooked and require a thorough examination.

The less common keratoderma blenorrhagica, resembling pustular psoriasis, can affect the palms and soles. If dermatitis is present, a differential diagnosis of gonococcal arthritis should be considered, as roughly 75% of these patients have skin lesions on the torso and limbs.

Ocular Manifestations: Conjunctivitis can be mild or more severe, with a sterile discharge. In rare cases, serious eye complications like keratitis, corneal ulceration, or even uveitis can develop, with uveitis being more common in recurrent or late disease.

Systemic Manifestations: Some patients (10%) experience systemic symptoms like malaise, fatigue, weight loss, and fever (2).

Electrocardiographic abnormalities, including conduction delays, can be seen in 5-14% of cases (2)

Renal involvement is common (50%), manifesting as proteinuria, microscopic hematuria, and aseptic pyuria which might be due to concurrent urethritis. These are usually asymptomatic.

Diagnosis

SARA diagnosis is a three-pronged approach. It involves confirming a genitourinary infection, identifying typical clinical features of spondyloarthropathy, and evaluating any extragenital manifestations. Additionally, laboratory investigations are necessary. (Box 23)

Box 23 Laboratory investigations in suspected SARA

1. Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP):
• High levels indicate significant inflammation in the body.

2. Leukocytosis:
• May be present, suggesting the body's response to infection.

3. Anemia:
• Normochromic or normocytic anemia may be seen in some cases.

4. HLA-B27 Testing:
• Not essential for diagnosis, but helpful in uncertain cases.
• 80% of ankylosing spondylitis patients test positive for HLA-B27.
• A positive test can influence prognosis

5. Synovial Fluid Analysis and Culture:
• Essential to rule out septic arthritis.
• Analysis typically shows high polymorphonuclear leukocytes (PMNs), indicating inflammation.
• Protein levels in synovial fluid are high.
• Cultures from fluid and tissue should be negative for bacteria.

6. Sexually Transmitted Infection (STI) Testing:
• NAAT *for Chlamydia trachomatis* and *Neisseria gonorrhoeae*:
  o Vulvovaginal sample for women, urine sample for men, throat/rectal samples depending on sexual history/symptoms.
• If N. gonorrhoeae NAAT is positive, further samples for culture and antibiotic sensitivity are required.
• NAAT for *Mycoplasma genitalium*:
  o Particularly important for men with urethritis (endocervical sample for women, urine for men).
• Gram staining and culture:
  o Urethral (men) or endocervical (women) samples if genital symptoms are present.

7. HIV Testing:
• Considered due to the potential link between HIV and reactive arthritis.

Complications

SARA is a self-limiting condition with a full recovery within 4-6 months for most of the patients. However, about half of those affected experience flare-ups (recurrent episodes) at unpredictable times.

The main concern with SARA complications comes from aggressive arthritis. This risk is

higher for people who carry the HLA-B27 gene. Long-term effects (chronicity): Roughly 17% of patients have symptoms lasting over a year. The disease can damage small joints in the feet, causing deformities in 12% of cases. However, severe deformities are uncommon unless psoriasis is also present (4).

Around 15% of individuals develop persistent difficulty in moving (locomotor disability). This is mainly due to joint deformity from erosion, particularly in the toes (metatarsophalangeal joints), ankles, or knees. Inflammation in the lower back (sacroiliitis) or spine (spondylitis) can also contribute.

In rare cases, untreated or repeated inflammation in the front of the eye (acute anterior uveitis) can quickly lead to cataracts and blindness.

Management

Therapeutic goals for established reactive arthritis focus on alleviating arthralgia and synovitis, ultimately aiming to enhance functional capacity until the disease undergoes spontaneous remission. The management strategy should incorporate rest, potentially including immobilization with splints and/or physical therapy interventions.

Early and targeted antimicrobial therapy for uncomplicated genital tract infections is crucial. This approach may potentially mitigate the development of subsequent joint involvement, known as reactive arthritis (ReA).

The impact of antimicrobial therapy on the extra-articular manifestations of ReA remains a topic of debate. Current evidence suggests minimal influence on established arthritis. Extended antibiotic courses (3-12 months) and combination regimens have been explored, but definitive benefits regarding joint disease are inconclusive. Cases of sexually acquired reactive arthritis necessitate referral to a genitourinary medicine clinic for evaluation and contact tracing.

Nonsteroidal anti-inflammatory drugs (NSAIDs) at therapeutic doses are essential. For individuals with a history of peptic ulcer disease, proton pump inhibitors (PPIs) might also be necessary. Following the exclusion of septic arthritis, intra-articular corticosteroid injections into larger joints are generally advantageous. However, if septic arthritis remains a possibility, it's prudent to postpone steroid injection until culture results are available (3).

Unlike in rheumatoid arthritis, there's no evidence supporting the efficacy of oral prednisolone. Therefore, better to avoid its routine use, although intravenous methylprednisolone can be valuable in severe joint inflammation. For patients who cannot tolerate NSAIDs, intramuscular steroids offer an alternative.

In patients with persistent arthritis exceeding 6 months, sulfasalazine might demonstrate disease-modifying antirheumatic drug (DMARD) activity. Additionally, methotrexate and azathioprine may be beneficial in cases of resistant disease.

Prognosis

Sexually acquired reactive arthritis (SARA) exhibits a self-limited course, typically resolves in 4-6 months, though 50% may experience recurrences and 17% may develop chronic symptoms persisting beyond one year (2). Aggressive arthritis is the main joint complication, more common in those positive for the HLA-B27 gene, with 15% of patients facing persistent movement difficulty (1). Up to 23% of SARA patients may also have ankylosing spondylitis, though the link remains unclear. Recurrent uveitis, if untreated, can lead to cataracts and permanent vision loss.

Follow up

Post-treatment management should be directed by the pertinent specialist, dependent on the severity of clinical presentation and the identified genitourinary tract infection.

It is crucial to promote patient engagement in their healthcare plan, incorporating self-care strategies. Patients should be counselled on risk factor reduction for future nosocomial infections, including both genital and enteric sources. Therefore, a discussion on safer sexual practices and appropriate food hygiene techniques is warranted.

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Anal discharge

Dr A B P Perera

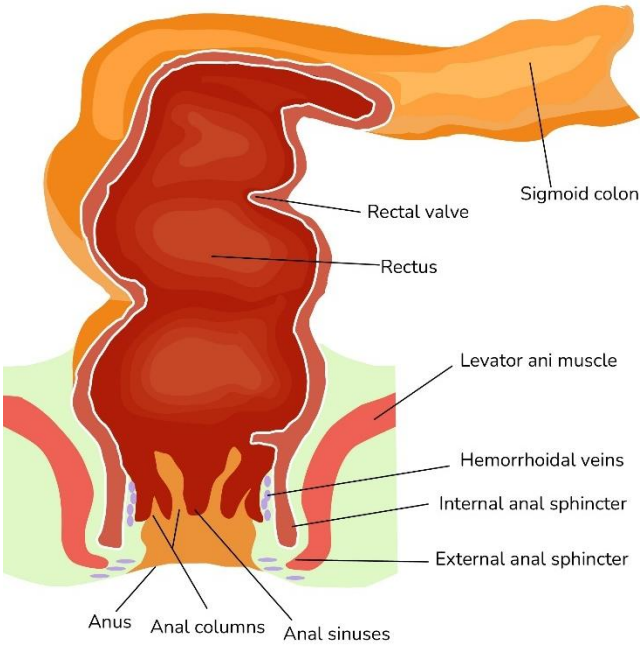
Introduction

Ano-rectal discharge is a recognized symptom of many conditions involving the anal and rectal region or the gastro-intestinal tract. Ano-rectal discharge is caused by the excessive secretions from the anorectal epithelium due to an irritation. Depending on the cause of irritation the appearance of the discharge may vary making it mucoid, purulent or blood stained. Among the many etiological causes of ano-rectal discharge, the commonest causes are:

1. Haemorrhoids
2. Anal fissures
3. Proctitis and procto-colitis with diverse aetiologies including bacterial, viral and protozoal infection, inflammatory bowel disease, intestinal ischemic syndromes, radiation induced procto-colitis, and traumatic colitis
4. Anal/ colorectal growths – including ano-rectal polyps, ano-genital warts caused my Human Papillomavirus, anal and anorectal carcinoma.

In understanding the pathology of ano-rectal discharge, it is important to be thorough with the basic anatomy of the rectum and anal canal to appreciate the sites affected as well as to describe the other associated symptoms due to various aetiologies causing anal discharge. The picture below will explain the basic anatomy of the rectum and anal canal.

Figure 46: Anatomy of anal canal



The rectum is mainly lined by a simple columnar epithelium. Apart from the columnar epithelial cells the rectal mucosa has goblet cells and microfold cells (M cells). The main function of goblet cells is to secrete mucus, and the M cells are specialized cells overlying the gut associated lymphoid tissue in the rectum, both playing crucial roles in the pathogenesis of ano-rectal discharge.

The columnar epithelium in the rectum transforms into a stratified non- keratinized squamous epithelium at the anorectal junction, which merges with the stratified keratinized squamous epithelium at the opening of the anus.

Sexually Transmissible Infections causing ano-rectal discharge

Though there are many causes for ano-rectal discharges we will focus on Sexually transmissible Infections (STIs) causing ano-rectal discharge in this chapter. Ano-rectal symptoms and anorectal STIs are more prevalent among men who have sex with men (MSMs), female sex workers (FSWs), transgender people and heterosexual women engage in unprotected anal intercourse [1]

There are two main mechanisms that STIs can causes anal discharge. Those are,

- Inflammation of the ano-rectal area leading to proctitis or procto- colitis following infection
- Abnormal growth in the ano- rectal area such as warts and/or ano-rectal carcinomas

STIs causing inflammation of the ano-rectal region

Sexually transmissible infections are known to cause proctitis and procto-colitis leading the infected patients to present with anal discharge. Proctitis is defined as inflammation of the rectum which is the distal 10-12 cm of the canal from the dentate line to the rectosigmoid junction, while colitis is defined as inflammation of the colon. Proctitis can be characterized by anal discharge with or without blood, ano-rectal pain and sensation of rectal fullness or incomplete defecation, tenesmus and constipation while procto-colitis can be present with diarrhoea and abdominal cramps in additions to the symptoms of proctitis [2]

STIs can cause enteritis as well and usually presents with diarrhoea and abdominal cramps without the signs of procto-colitis. Hence not discussed in this chapter.

Table 33: STIs causing proctitis and proctocolitis [2, 3, 4, 5]

	Proctitis	Proctocolitis
Bacteria	*Neisseria gonorrhoeae* *Chlamydia trachomatis* (Genotype D-K and L1-3) *Treponema pallidum* *Mycoplasma genitalium*	*Shigella spp* *Campylobactor spp* *Salmonella spp* *Escherichia coli* *Chlamydia trachomatis* (Genotype L1-3) Intestinal spirochetes
Virus	*Herpes simplex* Virus (1/2) Mpox	Cytomegalovirus
Protozoa		*Entamoeba histolytica* *Cryptosporidium spp*

Neisseria gonorrhoea

Neisseria gonorrhoea is a gram-negative diplococcus recognized as one of the most common causes of proctitis transmitted sexually. It is transmitted mainly through direct contact of the rectal mucosa with an infected mucosal surface hence seen among MSMs and women having receptive anal intercourse. Transluminal spread of N. gonorrhoeae from urethra and cervix into the ano-rectal region causing proctitis also have been described [6]. It has been found that one third of females presenting with urogenital gonococcal infection do have rectal infection as well although they do not report anal intercourse [6]. The prevalence of rectal infection among MSMs attending STD clinics attending in USA in the Pre-AIDS era was reported to be between 13-45% [7] and declined after the introduction of ARV. The prevalence of gonococcal proctitis and gonorrhoea prevalence in general has shown an increase in many countries during the past few years.

N. gonorrrhoeae infects the columnar epithelium and the incubation period can range from 5-7 days from the exposure. Majority of the ano-rectal infections for gonococci can remain asymptomatic [3]. When symptomatic, they can present with constipation, ano-rectal discomfort, tenesmus and mucopurulent discharge with occasional blood. The discharge can cause subsequent skin irritation resulting in peri-anal itching and erythema. Gonococcal proctitis presents commonly as asymptomatic or milder form of proctitis, but complications such as anal fistulae, abscesses, strictures and disseminated gonococcal infection has been reported with certain auxo types of *N. gonorrhoea*.

Proctoscopy findings may include presence of mucopurulent discharge in the rectal canal and generalized erythema in the mucosa with areas of easily induced bleeding if the patient is symptomatic. Normal proctoscopy findings cannot exclude gonococcal proctitis as majority remains asymptomatic.

Light microscopy from a rectal swab obtained from a symptomatic patient with *N. gonorrhoea* proctitis will show a field full of pus cells with gram negative cocci arranged in paired within the pus cells. Gram stain can be sensitive for rectal swabs obtained from a symptomatic patient up to 79% when obtained through proctoscopy and 53% when obtained blindly [7]. A positive microscopy finding on a gram-stained rectal swab could be used a reasonable diagnostic tool in diagnosing gonococcal proctitis, though the specificity of this method could be compromised due to presence of other commensal Neisseria species in the rectum. As the sensitivity of microscopy in asymptomatic patients is very low, it is not recommended [6]. Nucleic acid amplification tests (NAAT) shows > 95% sensitivity in both asymptomatic and symptomatic infections in diagnosis of N. gonorrhoeae. Therefore, it is recommended to perform NAAT in diagnosis of gonococcal proctitis though it is not licensed for extra-genital sites.

Information of the actual sensitivity of a single gonococcal culture from an anorectal sample is not known but expected to be less than the estimated sensitivity of a cervical gonococcal culture which is around 80% [7]. The specificity of a positive gonococcal culture from an ano-rectal sample is 100%. The culture is used as a tool for obtaining the ani-microbial sensitivity of the gonococcal strain under investigation rather than a diagnostic tool in the current context of gonococcal antimicrobial resistance [6].

The first line treatment includes Intramuscular injection of Ceftriaxone with or without oral azithromycin 2g stat depending on the local resistant pattern [2,6,8] in many parts of the world. Oral ciprofloxacin 500 mg stat and oral azithromycin 2g stat also has been recommended depending on the antimicrobial sensitivity pattern of the individual patients. The increased trend of antimicrobial resistance of gonococci globally has increased the importance of performing a culture prior to treatment. As the N. gonorrhoeae is known to be resistant to many classes of antibiotics including penicillins, sulphonamides, tetracyclines, quinolones and macrolides (including azithromycin), as well as some of the cephalosporins it is crucial to know the local patterns of resistance, update the local guidance and adhere to them as much as possible.

All patients treated for gonococcal proctitis should be offered a test of cure (TOC) after treatment. The duration from the treatment completion and the TOC and the test used for TOC may differ according to the presence of symptoms at the time of TOC. If the patient is asymptomatic, a NAAT should be used for test of cure (TOC) 2 weeks after completing treatment. If the patient is symptomatic, or if the NAAT done at TOC is positive, performing a culture is recommended [6].

All partners who had sex with a patient diagnosed with gonococcal proctitis within 3 months of the diagnosis needs screening with or without treatment according to the local guidance.

Chlamydia trachomatis

Chlamydia proctitis rates among MSMs are known to range from 3-10.5% [0] and some studies has shown rectal infection can co-exist with uro-genital infections up to 77.3%. C. trachomatis has a predilection for the sqaumo-columnar epithelium, making the rectum a target among many other sites. Though the main mode of action is direct contact of rectal mucosa with an infected mucosal surface, not all patients with rectal infections report anal sex.

Proctitis caused by biovar trachomatis (genotype D-K)

The incubation period may vary between 2-6 weeks, and majority are asymptomatic. If become symptomatic, the patients may present with mild proctitis characterized by ano-rectal discharge, tenesmus and ano-rectal pain. Proctoscopic findings may range from normal rectal mucosa to mild inflammatory changes with small erosions or follicles in the ano-rectal area [7].

A gram-stained rectal swab may reveal leukocytes but no other organisms within the cells as the C. trachomatis would not take the stains due to the lack of cell wall. NAAT specific for C. trachomatis is recommended by many international guidelines due to its superiority in sensitivity, specificity and speed of diagnosing C. trachomatis infection in comparison to other diagnostic methods. Direct immunofluorescence assay (DFA) can be used if NAAT facilities are not available.

The recommended first line treatment for *C. trachomatis* proctitis (with serovars D-K) is oral doxycycline 100 mg 12 hourly for 7 days. The alternative treatment is oral azithromycin 1g single dose followed by 500 mg daily for 2 days. Oral doxycycline remains as the preferable regimen on majority of international guidance due to the evidence confirming that doxycycline treatment is superior to azithromycin treatment for rectal Chlamydia infection and the emergence of macrolide resistance of *Mycoplasma genitalium* which is a common co-infection found with Chlamydia infection [9]. Spontaneous clearance of C. trachomatis also has been reported if left untreated [9], but the mechanism of spontaneous clearance has not been described well.

TOC is recommended for *C. trachomatis* proctitis and it is advised to defer the TOC at least 3-5 weeks from the treatment as the NAATs can give positive results due to the dead inactive bacteria [9].

All sexual partners of patients diagnosed with Chlamydia proctitis within 6 months of the diagnosis should receive testing with or without treatment depending on the clinical scenario [9,10].

Proctitis/ Proctocolitis caused by biovar LGV (genotype L1-3)

The incubation period ranges from 3-30 days for LGV and can be divided into three clinical stages as primary, secondary and tertiary. The primary lesion usually a transient painless papule, pustule an

erosion or an ulcer. Another presentation was described among MSMs (and heterosexual women having anal intercourse) where LGV can cause a haemorrhagic proctitis following direct transmission of the bacteria on the rectal mucosa. These patients presented with anorectal bleeding, mucoid and/or haemo-purulent anorectal discharge, anorectal pain, tenesmus and constipation which is more severe than the proctitis with C. trachomatis genotype D-K. Proctoscopy findings of LGV proctitis includes, erythematous friable rectal mucosa with multiple ulceration. Sigmoidoscopy has shown these signs extending to the descending colon [7] hence it's described as procto-colitis.

These strains having a preference to invade the lymphatic system, leading to the second stage of the infection. The common findings in this stage would be inguinal lymphadenopathy and bubo formation. Involvement of the rectal and colon lymphoid tissue can lead to chronic fistulae and perianal abscess formation.

If left untreated the infection will progress to a destructive granulomatous lesion and scarring of the lymph nodes, as well as in the rectal and colon lymphoid tissue which is defined as the third stage of the LGV infection. The scarring of the lymphoid tissue in the rectal canal causes anal strictures often 2-5 cm proximally form the muco-cutaneous margin of the anus where there is rich supply of lymphatics [7]. Obstruction to the lymphatic and venous drainage due to these strictures may lead to perianal outgrowths of lymphatic tissue called lymphorhoids or perianal condylomas [7]. An association of LGV with rectal cancer has been reported too [11].

Diagnosis of LGV needs high clinical suspicion and appropriate testing. In the past this was a diagnosis of exclusion, but in the current context NAAT for C. trachomatis LGV strains could make a positive diagnosis of LGV. The guidelines recommend all males and females presenting with proctitis and all HIV positive MSMs attending for screening (with or without symptoms of proctitis) to be screened for C. trachomatis LGV strains [9]. In the absence of LGV genovar-specific C. trachomatis NAAT, a presumptive LGV diagnosis can be made using validated and quality-assured Chlamydia genus-specific serological assays. A high antibody titre (particularly IgA anti-MOMP antibodies) in a patient with symptoms suggestive of LGV [12].

Oral doxycycline 100 mg 12 hourly for 21 days remains the first line treatment [9,12]

Routine TOC is not recommended if adequately treated with first line treatment. TOC is suggested after if treated with alternative regimens. The time suggested for LGV TOC varies from 2-6 weeks after completing treatment in different guidelines [11, 12].

All the partners who had sex with a patient diagnosed with LGV within 4 weeks of onset of the symptoms or within 3 months of diagnosis if asymptomatic should receive presumptive treatment with oral doxycycline 100 mg 12 hourly till exclusion of LGV infection in them or complete 21 days [11,12].

Treponema pallidum

The anorectal involvement is more commonly seen in primary and secondary stages of the disease than the tertiary stage. Primary syphilis is characterized by a single painless indurated ulcer in the ano-genital area which is called a syphilitic chancre. Chancre usually occurs at the point of the Treponemal spirochetes enter the body. Therefore, chancres involving the ano-rectal region indicates direct contact of the point of the lesion with an infected mucosa or lesion hence, more commonly seen among MSMs and heterosexual women who are engaging in anal intercourse. Commonly appears after 2-6 weeks of the exposure though it can be delayed up to 90 days [7]. The primary chancres are usually painless as the cutaneous nerves innervating the area is destroyed due to lack of blood supply as the arteritis caused by the treponemes affects the vasa nervorum of the cutaneous nerves. It is easily missed due to the painless nature of the lesion. The discharge caused at the base of the ulcer due to tissue necrosis can be seen as a mucoid ano-rectal discharge. They also may present with mild anal discomfort and rectal bleeding. Careful examination including digital rectal examination and proctoscopy may be helpful in identifying the chancres in the rectal canal. Even though chancres are usually single, they may appear multiple, and places as mirror image (kissing) ulcers in the rectal mucosa, or even ulcerated masses.

Chancres can heal spontaneously, and the patient can go into a latent phase, or some patients can get symptomatic with secondary syphilis. The secondary syphilitic lesions such as mucosal patches and condylomata lata lesions can involve the ano-rectal region. The mucosal lesions in secondary syphilis may appear as discrete polyps, smooth lobulated masses, mucosal ulceration, nonspecific erythema or bleeding [7]. The involvement of the submucosal lymphoid tissue in secondary syphilis may be felt as a rubbery irregularity during examination. The condylomata lata lesions appears in the secondary stage may be found near the entrance of the anal canal most, flat topped warty growths smoother than the ano genital warts producing a foul-smelling discharge and causing peri anal pruritus.

Very rarely late or tertiary syphilis can affect the ano-rectal region in the forms of infiltrative, constrictive or polypoidal masses. Tabes dorsalis which is a manifestation of neurosyphilis can cause severe anal pain and anal sphincter paralysis [7].

Diagnosis, treatment, follow up and partner management is same as syphilis in general which is discussed in the syphilis chapter.

Mycoplasma genitalium

Mycoplasma genitalium belongs to Mollicutes class and it's the smallest self-replicating bacteria and lacks a cell wall. Lacking the cell wall, *M. genitalium* cannot be identified by gram stain and being a very fastidious organism, the growth of the bacteria requires months [13].

Transmission of *M. gentialium* is primarily by genital contact but has been detected in the ano-rectal region and has been identified as a being transmitted through peno-anal

contact [13]. Rectal infection with *M. genitalium* has been reported among 1%–26% of MSM and among 3% of women [15].

Majority of the infections can be asymptomatic but can cause symptoms of proctitis including rectal pain and ano-genital discharge. Examination findings are similar to that of C. trachomatis (non-LGV) proctitis.

Testing for *M. gentalium* is not recommended in asymptomatic patients and guidelines suggests testing to be considered in individuals presenting with proctitis specially if gonococcal and chlamydial proctitis has been excluded [13.14]. The recommended test is *Mycoplasma genitalium* specific NAATS preferable with macrolide resistance mutation detection though there are no FDA approved tests in the market yet.

Different regimens have been recommended by different academic bodies across the globe. According to the British Association of Sexual Health and HIV recommended treatment for *M. genitalium* is oral Doxycycline 100 mg orally 12 hourly for 7 days, followed by azithromycin 1 g orally initial dose, followed by 500 mg orally once daily for 2 additional days if macrolide sensitive [13] or oral moxifloxacin 400 mg orally once daily for 7 days if macrolide resistant.

TOC after treatment of *M. genitalium* is recommended after 5 weeks of treatment [13].

Only current partner (including non-regular partners where there is likely to be further sexual contact) should be tested and treated if positive [13].

Herpes simplex virus

Herpes simplex virus (HSV) 1 and 2 belongs to herpes group of viruses and transmitted by direct contact of the infected mucous membrane on the anorectal region causing proctitis. The incubation period may vary from 2 days to 2 weeks and one third of the infection may remain asymptomatic [14]. If they become symptomatic multiple painful vesicles develop in the ano-rectal regions which will progress into pustules and later rupture form superficial ulcers. Virus leads to ballooning of the cells and lead to lysis of plasma membranes forming multinucleated giant cells. With large amount of cell lysis, fluid collections appear between the epidermis and dermis of the ano-rectal lining forming the vesicles. Apart from the painful vesicles and ulcers, they can present with ano-rectal discharge, tenesmus and haematochezia [7]. Primary infection with HSV will also cause fever, chills, malaise and headaches apart from the ano-rectal symptoms. HSV 1 and 2 can stay latent in neural tissue and when infect the ano-rectal area, they enter the sensory ganglia in the sacral plexus. Involvement of the sacral plexus can lead to constipation, urinary retention, anorectal pain and erectile dysfunction in men [7].

Both HSV 1 and 2 can lay dormant in the sacral plexus after the initial ano-rectal infection and HSV 2 infection is more common to cause recurrences than HSV 1 [15]. Recurrent HSV episodes are milder than the primary infection due to formation of antibodies in the body.

On examination, small vesicles or clusters of vesicles can be seen surrounded by a red areola in the initial infection which soon

become ulcerative and confluent. Rectal epithelium can be more friable diffusely in Herpetic proctitis than in other causes of proctitis [7].

Diagnosis, treatment and follow up of patients with ano-genital infection with Herpes is discussed in detail in the herpes simplex virus chapter and it will be applicable to ano-rectal Herpes as well.

In immunocompetent patients the initial infection can be spontaneously resolved, unlike in immunocompromised patients where the initial infection can be progressed into chronic, large and destructive perianal ulceration.

Monkeypox

The monkeypox virus is an orthopoxvirus causing mpox, a disease like smallpox. Smallpox was irradicated in 1980, while mpox continued to occur in African continent. Since 2022 there have been reported cases on mpox outside the African region [17].

Even though monkeypox is known as a zoonosis, human to human transmission through close contact with body fluids, lesions on the skin or mucosa and contaminated objects were reported during this recent epidemic [17].

The incubation period can vary from 5 to 21 days, and the prodromal symptoms include fever, headache, lymphadenopathy. The muco-cutaneous lesions can range from macules to papules to vesicles to pustules which later become crusted and scabbed [17]. Rectal symptoms include purulent or bloody stools, rectal pain and rectal bleeding [18]. Illness can last 2-4 weeks. When patients presenting with perianal lesions suggesting of M pox it is important to look for lesions elsewhere in the body.

Diagnosis is by performing mpox specific NAAT on the specimens obtained from the lesions. Treatment is recommended for severe diseases, involvement of anatomical sites which might result in scarring or strictures which included ano-rectal lesions and for people who are at high risk of severe disease. Currently there are no treatment approved specifically for mpox. Tecovirimat, and brincidofovir which were antivirals used against human smallpox, vaccinia immune globulins used as a treatment of complications due to vaccinia vaccination and cidofovir, which is an antiviral used against cytomegalovirus are recommended to use where treatment is indicated in mpox infection [18].

Enteric bacteria causing proctocolitis.

There are many *Shigella* spp, *Campylobacter* spp, *Salmonella* spp and *Escherichia coli* causing procto-colitis transmitted sexually due to oro-anal exposure more commonly among MSMs [3]. Anal play (rimming, fingering) or handling contaminated sex toys, used condoms and douching materials is also described as possible modes of transmission of enteric organisms causing procto-colitis.

Pathology of enteric bacteria causing proctocolitis

Shigella spp

Shigella dysenteriae with *Shigella sonnei* and *Shigella flexneri* are known to cause

clinical disease. Incubation period can vary from 12 hours to 7 days but typically 2- 4 days from exposure [19]. Once the epithelium is exposed to the bacteria it will lead to massive destruction of the colon mucosa, entering through the M cells. This will lead to abdominal pain, fever, vomiting, and large volume of watery stools in the early part of the infection and causing tenesmus, urgency, faecal incontinence and small volumes of mucoid diarrhoea with frank blood.

Table 34: Diagnosis and treatment of enteric bacteria causing proctocolitis

Enteric pathogen	Diagnosis	Recommended Treatment
Shigella spp.	Stool culture, Rapid diagnostic test with PCR*, Blood culture	• Majority of the cases do not need treatment. • Treatment is indicated if the patient is hospitalized, pyrexial, the diarrhoea has been present for at least 7 days and/or there are significant comorbidities (frailty, inflammatory bowel disease, immunocompromised, including advanced HIV). • If indicated antibiotics needs to be decided on the local resistant pattern and the sensitivity results for the individual Oral ciprofloxacin/ azithromycin is used as common empirical antibiotics
Salmonella spp	Blood culture, Rapid diagnostic test with PCR *	• Ciprofloxacin, azithromycin, ceftriaxone and co-trimoxazole are used commonly as first line empirical therapy
Campylobactor Spp	Stool culture, Rapid diagnostic with PCR	• Most recover without antimicrobial treatment. If treatment is indicated (65 years or older, pregnant women, and people with weakened immune systems including HIV) • Oral erythromycin or azithromycin would be the primary choices • Parenteral antibiotics may need in severe cases and may need to use according to the sensitivity results

* Multiplex PCR tests are commercially available to diagnose many enteric pathogens

Colonic epithelium can become oedematous, friable with superficial ulceration with focal mucosal bleeding, though this can only be seen with colonoscopy.

Most patients recover without treatment, and the career state usually ceases within 4 weeks. There are occasions where some people can have gastro-intestinal complications such as rectal prolapse, toxic megacolon, cholestatic hepatitis or systemic complications like seizures, syndrome of inappropriate secretions of antidiuretic hormone, encephalopathy, haemolytic uraemic syndrome, septicaemia, disseminated intravascular coagulation and arthritis [19].

Salmonella spp

Salmonellae are gram negative bacilli mainly transmitted via feco-oral route. Salmonella species can be responsible for many clinical syndromes in human including nontyphoidal entero-colitis, nontyphoidal focal disease and typhoid fever. Outbreaks with Salmonella typhi has been described among small clusters in United states, but the role of STI causing proctocolitis is thought to be minimum [21].

Campylobacter spp

Campylobacter spp are curved or spiral, motile, non–spore-forming, gram-negative rods and known to be one of the commonest bacterial among humans. While *Campylobacter jejuni* being the most common organism to cause infection, *Helicobacter cinaedi* and *Helicobacter fennelliae* are recognized as causative organisms of proctocolitis among MSMs which belong to this group. *C. jejuni* is known to cause sever bacteraemic conditions among people with severe immune deficiency with HIV infection [21].

The usual incubation period for Campylobacter infection is reported to be 7 days. Once exposed, the bacteria adhere to the epithelium, invade the epithelium and destroy while releasing enterotoxins causing cramping abdominal pain, fever, frequent watery or blood-stained diarrhoea and tenesmus. On examination patients may appear ill with diffuse abdominal tenderness.

Rarely it can lead to complications like irritable bowel syndrome, temporary paralysis and arthritis,

Apart from these Shiga toxins producing *Escherichia coli* strains are also known to cause proctocolitis transmitted via sexual activity [21].

Entamoeba histolytica

Entamoeba histolytica is a known protozoal parasite causing proctocolitis and recognized to be transmitted sexually among MSMs as well as heterosexual men and women [21]. The incubation period ranges from 1-3 weeks, and majority remains asymptomatic. Nearly 10% of the infected, can be symptomatic. Once the infective form of the *E. histolytica* (trophozoites) gets in contact with the colon mucosa, it will invade the epithelial barrier leading to tissue destruction. This will lead to symptoms such as secretary bloody diarrhoea, tenesmus and lower abdominal pain. The symptoms are usually gradual in onset and may wax and wane for weeks to months making the diagnosis difficult [7,23]. On examination they may have lower quadrant abdominal tenderness with dehydration. Some may have ano-genital

ulceration with punched out appearance with profuse discharge [23]. Complications such as liver abscesses, peritonitis, anorectal and sigmoid colon strictures, lung involvement, pericarditis and cerebral involvement has also been reported [7, 23].

Identification of the amoebic antigens using PCR would be the preferable method of diagnosis [21]. Amoebic cysts can be demonstrated in stools under light microscope but less specific. Examination of a single stool sample has a sensitivity of only 33-35 % which can be improved up to 95 % my examining 3 stool samples over 10 days as the cyst shedding is episodic [23]. Stool and rectal biopsy culture as well as antigen detection with enzyme linked immunosorbent assay (ELISA), rapid diagnostic test with PCR, serum antibody detection are other diagnostic tools when having anorectal symptoms.

While oral Tinidazole 2G daily for 3 days is the preferred treatment for amoebic procto-colitis, oral metronidazole 800 mg TDS for 5 days or oral paromomycin 500mg TDS for 7 days are considered as effective well [21].

Cryptosporidium spp

Cryptosporidium species are small protozoal parasite which can cause cryptosporidiosis. *C. hominis* and *C. parvum* are the common species associated with human disease specially among the immunocompromised. They do not multiply outside the host cells. The incubation period is usually 5-10 days but can vary between 2-28 days. When the oocysts are in the gastro-intestinal tract, gets activated and releases the sporozoites which is the infective stage. It can cause copious amount of watery diarrhoea by increasing the permeability of the intestinal epithelium and rarely cause blood and mucous diarrhoea. In immunocompetent persons this can lead a self-limiting disease which lasts 7-10 days [7] and with immunocompromised persons this can lead to sever or chronic disease with frequent, foul smelling, bulky stools with weight loss.

Cryptosporidium was traditionally diagnosed with microscopic examination of sample with specific staining techniques such as acid-fast staining, direct fluorescent antibody, enzyme immunoassay or immunochromatographic detection of cryptosporidium antigens, but now multiplex PCR tests are available with high sensitivity and specificity [23]. Various samples such as stools, biopsies and lavage from the gastro-intestinal tract can be used for diagnosis.

While nitazoxanides remains, the only medication approved to be used against cryptosporidium, paromomycin and azithromycin also has shown antiparasitic action against cryptosporidium. However, in immunocompromised patient with HIV infection, immune reconstitution with ARV remains the mainstay of treatment.

Cytomegalovirus (CMV)

Cytomegalovirus belongs to the herpes group of viruses and can cause 'latent' infection like the other members in that family. CMV transmission occur from close contact including sexual contact with a person who carries it. Typically, the initial infection can pass unnoticed clinically and

can enter the chronic latent period in the myeloid compartment of the blood cells. It can cause target organ involvement including the colon by re-activation commonly in immunocompromised including patient with HIV, and rarely in immunocompetent individuals.

They can present with abdominal pain, constipation or diarrhoea which can be either watery or bloody and worsening symptoms of inflammatory bowel disease [24]. Complications with toxic megacolon, necrotizing colitis, bowel perforation, peritonitis and sepsis are seen in severe disease. Abdominal signs may not be there in early disease and may develop with the complications.

Diagnosis can be supported with the antigen or viral DNA detection by direct immunofluorescent antibodies. There are studies to support that these methods have high specificity but low sensitivity in diagnosing CMV colitis. Typical histological finding of intranuclear inclusion bodies in rectal or colonic biopsies stained with immunohistochemical staining are considered diagnostic while culture with shell viral assay has also been used as a supportive diagnostic tool.

Antivirals like ganciclovir and foscarnet have been shown effective against CMV colitis which has been more explored in treating CMV retinitis.

Abnormal growths causing ano-rectal discharge

Human Papillomavirus (HPV) causing ano-rectal warts

HPV is a DNA virus which contains about 100 genotypes out of which 90% of ano-genital warts are caused by type 6 or 11. HPV is transmitted usually by sexual contact and studies has shown that 15-64% of the infected people can be symptomatic with these genotypes [25]. The time lapse between the infection and appearance of warts is highly variable but demonstrated shorter in females which is around 3 months as opposed to 11 months in males.

The skin lesions are usually multiple cauliflower like lesions which are fleshy when occurs in the rectal mucosa and can be keratinized when occur in the peri anal skin. When occur in the rectal mucosa it can cause rectal discharge due to the increased formation of the mucins by the epithelial cells due to increase surface area in the warty growth. Warts can cause blood-stained discharge due to the easy bleeding tendency due to the high vascularity of the lesion.

Diagnosis of ano-rectal warts is usually clinical and may need proctoscopy as sometimes it may not be visible in external examination. The soft fleshy warts may be missed during digital examination. Biopsy and histology can confirm the diagnosis.

Treatment of ano-genital warts is described in HPV and genital warts chapter.

Ano-rectal carcinoma

Although most HPV infections are asymptomatic and clear spontaneously, some oncogenic strains can progress into pre-cancer or cancerous lesions in the ano-rectal region. Commonly HPV genotype 16 and 18 and to a lesser degree genotypes 31, 22, 45, 52 and 58 are associated with ano-rectal carcinomas.

These malignant growths can cause mucoid blood-stained discharge due to rapid proliferation of cells and the high blood supply to the area.

Other management principles

Hospital admission

Hospital admission needs to be considered if the person is systemically unwell and /or there are clinical features of severe dehydration, severe vomiting with high-output diarrhoea or there is suspected serious complication such as sepsis or acute kidney injury [26].

Partner screening and treatment

All bacterial STIs needs partner assessment within the specific look back period. Some may need treatment epidemiologically and some may need treatment depending on the outcome of their screening.

Screening for other STIS

All patients diagnosed with one STI need to be offered screening for other STIs specially syphilis and HIV screening.

HIV infection and ano-rectal disease

Majority of the ano-rectal diseases due to STIs follow the same natural course of the disease in all patients with or without HIV if the immune suppression is not severe, and the management principals remains the same. In sever immunosuppression the presentations may become severe, prolonged with more systemic dissemination and complications which may necessitate more intense management with using higher doses of treatment for prolonged durations.

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Ophthalmia neonatorum

Dr Umedha Jayasinghe

Introduction

Ophthalmia neonatorum refers to conjunctival inflammation that occurs in neonates, typically within the first 28 days of life. This condition is primarily caused by infections acquired during passage through an infected birth canal, with the aetiology being either bacterial or viral in nature. The infectious agents responsible for ophthalmia neonatorum include sexually transmitted pathogens such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, which are transmitted from the mother to the neonate during delivery. Additionally, non-sexually transmitted pathogens, including various bacteria and viruses, may also contribute to the development of this condition. The diverse range of potential infectious causes necessitates careful diagnosis and targeted treatment to prevent complications and protect the neonate's vision.

Clinical features

Co-infection with *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is not uncommon in cases of ophthalmia neonatorum. Both pathogens are significant causes of conjunctival inflammation in neonates and are typically acquired during passage through an infected birth canal. Given the asymptomatic nature of many maternal infections, both *N. gonorrhoeae* and *C. trachomatis* can be present simultaneously, leading to a co-infection in the neonate.

Table 35: Clinical features of Ophthalmia neonatorum

Gonococcal ON	Chlamydial ON
Incubation period – 2-6 days	Incubation period - 5-12 days
Typically, bilateral	Unilateral
Purulent discharge	Mucopurulent/Sticky/Serous discharge
Pseudomembranous and membranous reaction	Follicular conjunctival reaction
Oedema of eye Lids	Diffuse infection, milder than GC
Conjunctival infection	

If left untreated, gonococcal and chlamydial ophthalmia neonatorum can result in significant ocular complications. Gonococcal ophthalmia neonatorum, caused by *Neisseria gonorrhoeae*, can rapidly progress to pan ophthalmitis, a severe inflammation involving all layers of the eye, which may lead to corneal perforation and subsequent

scarring. These complications can severely compromise vision and may result in blindness if not addressed promptly. On the other hand, chlamydial ophthalmia neonatorum, caused by *Chlamydia trachomatis*, while generally less aggressive, can still lead to chronic conjunctival scarring, which can impair vision and affect visual development. Timely diagnosis and treatment are essential to prevent these potentially debilitating outcomes and to preserve the neonate's vision.

Diagnosis

To accurately diagnose ophthalmia neonatorum and identify the underlying aetiology, relevant specimens should be collected for laboratory analysis. To exclude gonococcal infection, the following diagnostic steps are recommended:

1. A Gram-stained smear and gonococcal culture should be obtained from the conjunctival discharge to identify *Neisseria gonorrhoeae*.
2. Gonococcal culture should also be performed on specimens from the nasopharynx and rectum, as these sites can harbour the bacteria.
3. Culture for gonorrhoea is essential for a definitive diagnosis, as other Neisseria species and commensals, such as *Moraxella catarrhalis*, may present similarly on Gram stain, making differentiation difficult.
4. Concurrent testing for *Chlamydia trachomatis* should be conducted, as it is a common cause of neonatal conjunctivitis. Given that *Chlamydia* is an intracellular organism, specimens must include conjunctival cells, which can best be collected from the everted eyelid.
5. Additional investigations, such as herpes simplex virus (HSV) PCR, should be considered to exclude other potential causes of neonatal conjunctivitis.

These diagnostic procedures are crucial for ensuring appropriate treatment and management, given the varied aetiologies of neonatal ophthalmia.

Management

Gonococcal ophthalmia should be strongly suspected when intracellular gram-negative diplococci are identified in the conjunctival exudate, which justifies initiating presumptive treatment for *Neisseria gonorrhoeae* while awaiting culture results. In neonates who are at increased risk for gonococcal ophthalmia and present with conjunctivitis, presumptive treatment may still be indicated even in the absence of *Neisseria gonorrhoeae* in the Gram-stained smear of the conjunctival exudate. Management of infants with gonococcal ophthalmia requires consultation with an ophthalmologist, and these infants should be hospitalized for further evaluation, including screening for potential disseminated disease such as arthritis, sepsis, or meningitis. Additionally, the infant’s mother, as well as her sexual partners, should be treated for gonorrhoea to prevent reinfection and further transmission. (Box 24)

Box 24 Treatment for Gonococcal Ophthalmia Neonatorum

Recommended Treatment for Gonococcal Ophthalmia Neonatorum

- Ceftriaxone: Single dose of 50 mg/kg IM (maximum 250 mg per day)
- Caution: Use carefully in infants with hyperbilirubinemia, especially preterm infants
- Topical antibiotics: Not necessary
- Chlamydia aetiology: Should be considered for all infants <30 days with conjunctivitis

Alternative Regimens

- Cefotaxime: 100 mg/kg IV/IM as a single dose

The recommended treatment for chlamydial ophthalmia neonatorum involves oral administration of erythromycin at a dose of 50 mg/kg/day, divided into four doses daily, for a duration of 14 days. Topical therapy is not indicated for this condition.

Follow-Up

Follow-up care for infants with ophthalmia neonatorum is essential to assess the effectiveness of initial treatment. A Test of Cure (TOC) is particularly necessary in cases of gonococcal ophthalmia neonatorum to ensure that the infection has been eradicated. In the case of chlamydial ophthalmia neonatorum, the efficacy of erythromycin treatment is approximately 80%, and therefore, a second course of therapy may be required if symptoms persist. If the duration of the ophthalmia exceeds three weeks, clinicians should consider the possibility of concomitant chlamydial pneumonia, which may necessitate further investigation and management.

Section 7:
Introduction to genital dermatosis

Introduction to genital dermatoses and other genital conditions

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Introduction

Lesions on the external genitalia could be venereal or non-venereal. Non-venereal genital dermatoses are common and may cause considerable anxiety to patients, particularly if noticed after sexual intercourse. Careful dermatological evaluation, including a full history and complete examination, usually allows confident clinical differential diagnosis. A biopsy and other investigations are sometimes indicated. Itching, rashes and tumours are the major components of general dermatology and the genitocrural area is not spared (1).

Dermatoses of the male genitalia

Inflammatory dermatoses

Psoriasis

This is a common condition that can affect the male genital region in isolation or as part of widely distributed disease.

Figure 47: Extensive genital and groin psoriasis

It is not usually itchy; significant itch should arouse suspicions of another dermatosis such as an eczematous dermatitis or tinea. Soreness occurs with superinfection, especially with Candida. Other typically affected sites should be examined for signs of the disease. Genital appearances may be challenging to interpret, especially in the uncircumcised patient, because a mucosal site is affected rather than keratinized skin. The diagnosis is usually easier in the circumcised male where the morphology is similar to extragenital lesions. Topical treatment includes emollients, soap substitutes, corticosteroids combined with antibiotic and antifungal agents or weak tar solutions.

Eczematous dermatoses

- Irritant contact dermatitis
- Allergic contact dermatitis
- Atopic eczema
- Radiodermatitis
- Seborrhoeic dermatitis

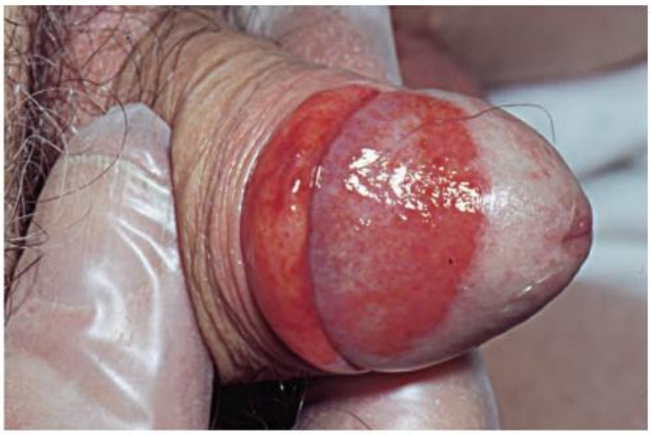
The broad principle of managing allergic contact dermatitis on genital skin is the identification of the potential allergen and its likely source, and then its elimination. Allergic contact dermatitis can persist even after withdrawal of the trigger allergen. Management relating to irritants, with emphasis on the relief of scratching, soap substitution and moisturization, and occlusion of the area, if possible, with a bland dressing – wet if the skin is fiercely eczematized. A potent topical corticosteroid ointment can be used for a few days and then tailed off. Preparations containing tar or combinations of antibacterial, anticandidal and antifungal agents are also useful (1). Oral antihistamines are useful too. Topical local anaesthetics should be avoided because of the risk of sensitization. Occasionally, secondary infection may be severe; a swab should be taken and oral antibiotics and oral antifungals prescribed.

Zoon balanitis

An inflammatory and irritant condition of the glans and mucosal prepuce that is probably over diagnosed. Well demarcated, glistening, moist, bright red or autumn brown patches involve the glans and visceral prepuce, with sparing of the keratinized penile shaft and foreskin (Figure 2). The navicular fossa may be involved. Other signs include dark red stippling – ‘cayenne pepper spots’ – and purpura with haemosiderin deposition, solitary or multiple lesions of differing sizes (guttate or nummular), characteristically symmetrical about the axis of the coronal sulcus and ‘kissing’

Although Zoon balanitis can improve with altered washing habits and the intermittent application of a mild or potent topical corticosteroid (with or without an antibiotic and anticandidal agent), it usually persists or relapses. Circumcision is curative.

Figure 48: Zoon balanitis. Symmetrical moist erythema of the glans and prepuce



Lichen sclerosus

The development of secondary phimosis in school-age boys is highly suggestive of lichen sclerosus. In the older male, persistent primary phimosis or the secondary development of phimosis in a previously retractable foreskin may be related to lichen sclerosus. Lichen sclerosus of the penis may be asymptomatic, but diverse, sometimes vague, symptomatology is usually encountered at rest or during or after sexual intercourse. Patients may describe itching, burning, bleeding, tearing, splitting, rash, haemorrhagic blisters, any manner of symptoms signifying sexual dysfunction or dyspareunia, discomfort with urination and narrowing of the urinary stream, and/or they may be concerned about the changing anatomy of their genitalia. Genital, just like extragenital, lichen sclerosus can manifest as atrophic leucodermic patches or plaques, or lilac, slightly scaly patches with telangiectasia and sparse purpura (Figure 3, 4)

Figure 49: Lichen sclerosus. White plaques and hemorrhagic areas on the glans.

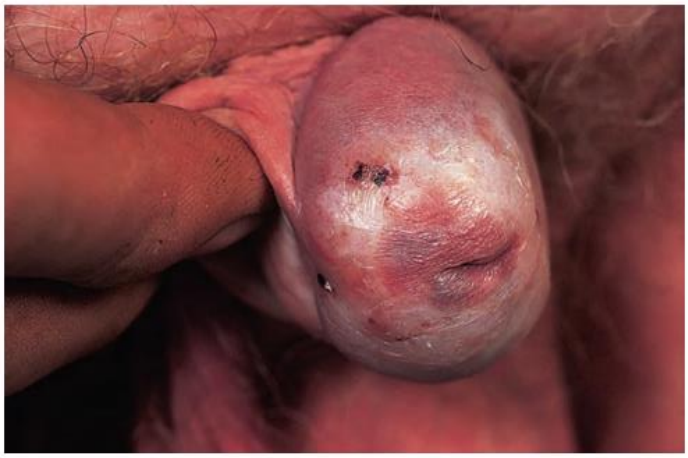
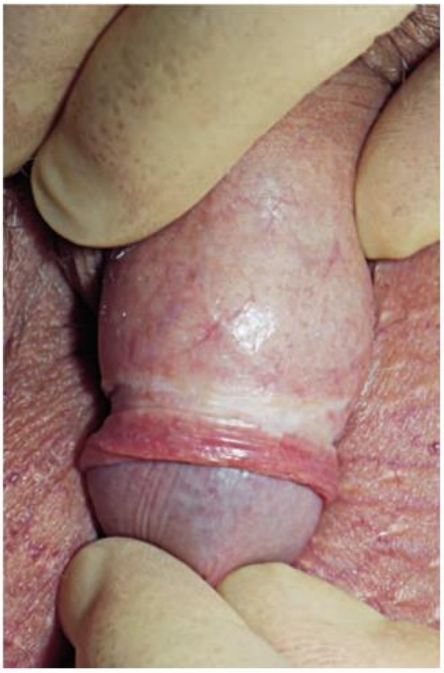


Figure 50: Lichen sclerosus. Sclerotic band of the prepuce causing 'waisting'

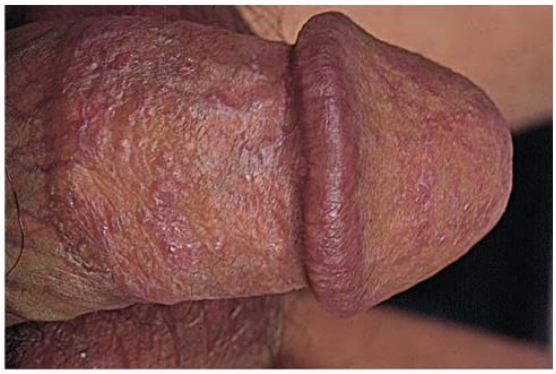


The aims are early diagnosis and effective treatment to obtain normalization of sexual function, reverse or check urinary dysfunction and limit urethral disease and reduce, if not abolish, the risk of penile cancer. Contact with soap, urine and pubic hair should be avoided by use of a soap substitute and a barrier preparation. An ultrapotent topical corticosteroid (usually clobetasol propionate) used under supervision for a finite course is effective. In boys, complete circumcision is the treatment of choice because all affected tissue is removed, and any secondary involvement of the glans probably regresses or resolves.

Lichen planus

Lichen planus can present in, and remain localized to, the ano-genital area, including the groins and perianal skin. Like the classical disease at other sites, it presents as itchy red-purple papules, patches, plaques and annular lesions (Figure 50). Potent and ultrapotent topical corticosteroids usually suffice for treatment.

Figure 51: Lichen planus. Papules and annular lesions with striae of Wickham on the glans and shaft



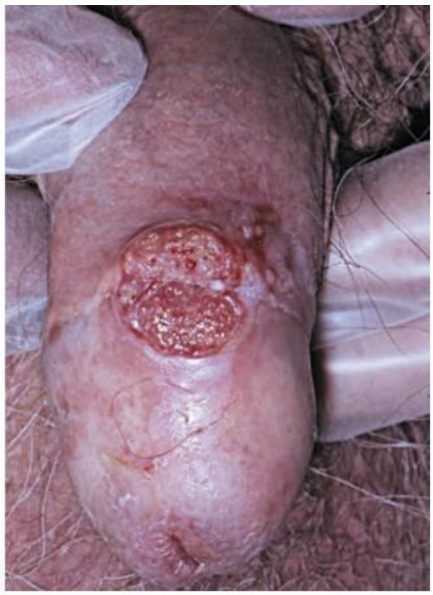
Drug reactions

The penis is a site of predilection for fixed drug eruption. The symptoms are itch or burning. The eruption is acute, with an erythematous plaque, sometimes with central blister formation, erosion and ulceration.

Carcinoma of the penis

Itch, irritation, pain, bleeding, discharge, ulceration or the discovery of a mass are the presenting symptoms of squamous carcinoma. There is often a long history of preceding problems with the penis and foreskin, manifest as dyspareunia, balanoposthitis or phimosis and dysuria. Irregular nodular and ulcerative morphology is found on examination (Figure 51) and there may be background erythroplasia of Queyrat, lichen sclerosus or lichen planus.

Figure 52: Squamous carcinoma. Severe background lichen sclerosus



Dermatoses of the Female Genitalia

Common dermatoses that are easily recognized elsewhere may have a modified appearance on the vulva, where the typical clinical features are often altered significantly. The ano-genital skin is vulnerable, with the local environmental influences of heat, moisture and friction all acting as irritants; changes in the normal bacterial flora are also important.

Inflammatory dermatoses of the vulva

Lichen sclerosus

The presenting symptom is usually itching, which is often severe and distressing. Patients may also complain of discomfort and dyspareunia if there is introital narrowing. Constipation is a common feature in girls with prepubertal disease.

Ano-genital disease tends to be characterized by atrophic, whitened epithelium (Figure 7), which may become confluent, extending around the vulval and perianal skin in a figure-of-eight configuration. There may also be oedema, purpura, bullae, erosions, fissures (Figure 8) and ulceration. The sites most commonly affected are the genito-crural folds, the inner aspects of the labia majora, labia minora, clitoris and clitoral hood.

The super-potent topical corticosteroid, clobetasol propionate 0.05%, is first line treatment.

Figure 53: Lichen sclerosus showing white sclerotic plaques and architectural change

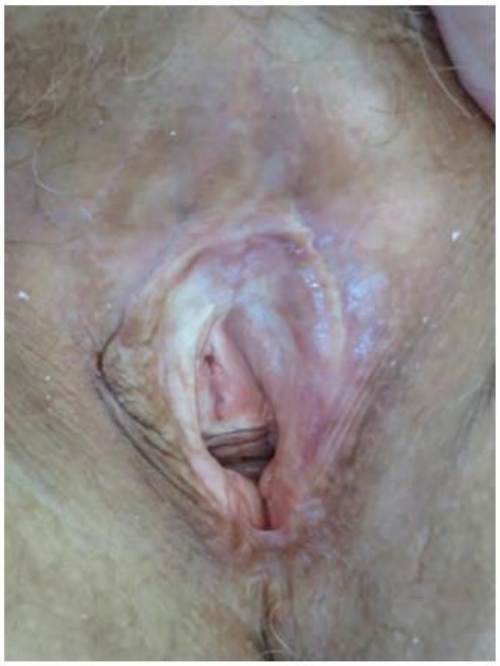
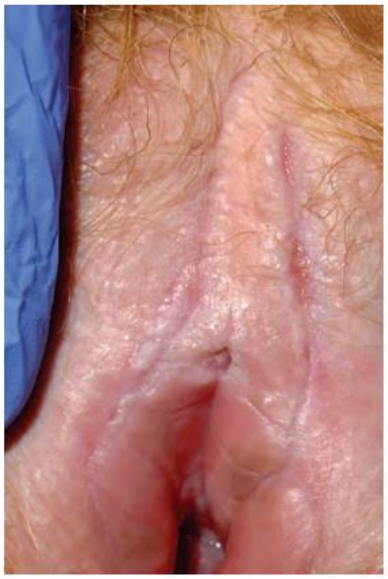


Figure 54: Fissuring in lichen sclerosus



Lichen planus

The clinical features vary with clinical type. Three clinical forms are recognized but there may sometimes be overlapping features.

Classic/papular lichen planus

This type can occur with cutaneous lesions. The typical violaceous papules are seen on the outer labia majora, interlabial sulci and clitoral hood. These may coalesce into small plaques or annular lesions.

Hypertrophic lichen planus

This is the least common form of LP seen on the genital skin. Thickened, intensely pruritic plaques, sometimes with a violaceous edge, are seen on the labia majora, perineum and perianal skin.

Erosive lichen planus

Erosive LP is the commonest type to affect the female genital area. On the vulva, symmetrical erosions are most seen at the fourchette and vestibule. These may have an irregular lacy edge with Wickham striae.

Super-potent topical steroid ointment for vulva and intravaginal foam preparations for vaginal disease. Emollients are also used as first-line treatment.

Seborrhoeic eczema

The signs may be subtle but scaling and erythema are seen on the inguinal folds, labia majora, perineum and perianal skin. Keratin debris may build up in the interlabial sulci and sometimes under the clitoral hood.

Irritant eczema

Erythema is most pronounced on the convex areas – the outer labia majora, perianal skin and buttocks – which are the sites most in contact with external irritants.

Allergic contact dermatitis

An allergic contact dermatitis most commonly presents with pruritus but, if acute, an erosive eruption may be seen which frequently extends down the thighs.

Lichen simplex

There are localized, thickened plaques, most commonly affecting the outer labia majora.

Psoriasis

Well-demarcated erythematous plaques are seen on the labia majora, and extension on to the mons pubis, inguinal folds, perianal skin and gluteal cleft is common. The typical silvery scale seen elsewhere is lost but may be seen on the mons.

Premalignant conditions of the vulva

Vulval intraepithelial neoplasia

The lesions of VIN can be solitary or multiple. The morphology of the lesions is also diverse, with lesions that resemble viral warts, plaques that may be shiny and smooth, skin-coloured, red or white, or others that are warty and pigmented and resemble seborrhoeic keratoses (Figure 9).

Figure 55: Vulval intraepithelial neoplasia

Malignant neoplasms of the vulva

Squamous cell carcinoma

The common symptoms are soreness and pruritus. The patient may present because of the presence of a nodule or plaque that causes few symptoms. Bleeding can occur if the tumour has ulcerated.

Extramammary Paget disease

The lesions are typically moist, erythematous plaques. The site of the

lesions is important as disease involving the urethra and perianal skin is more likely to be associated with an underlying malignancy of the urinary or gastrointestinal tract, respectively.

Vulval melanoma

Vulval melanoma is often asymptomatic until it ulcerates or becomes nodular. Bleeding may occur. The labia majora and clitoris are the most common sites involved.

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