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Sexually transmitted Infections

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Trinity College Dublin

THE GUIDE CLINIC
ST JAMES'S HOSPITAL

Synergism-STI's increase risk for acquisition and transmission of HIV

number of mechanisms, including breaching of mechanical barriers to infection, increased inflammation and higher levels of HIV cellular targets, and increased genital tract HIV levels[1]

Altered HIV Susceptibility	Altered HIV infectiousness
↓ mechanical barrier to infection	↑ Bleeding during intercourse
↑ Quantity of activated CD4+ cells in genital tract	↑ serum HIV viral load
↑ Ease of entry of HIV into CD+ cells	↑ HIV Viral replication in genital tract

1. Cohen et al Top HIV Med. 2004 Oct-Nov;12(4):104-7.
HIV and sexually transmitted diseases: lethal synergy.

Genital Ulcer Disease and HIV Interactions

↑ Susceptibility and Infectivity

↑ Acquisition

Transmission ↑

GUD

HIV

↑ Frequency and Duration of GUD & Shedding

- Genital ulcer disrupts epithelial / mucosal surface
- Recruitment of inflammatory cells, CD4 lymphocytes and macrophages to site of mucosal break

Case study 1

- Bridget, a 56 year old married lady attended GP with history persistent vaginal discharge.
- Treated for yeast infection, bacterial vaginosis over a period of time with little or no improvement
- After several weeks (reluctantly) referred to GUIDE clinic
- Full STI screen performed

Case study 1

- Results revealed positive chlamydia swab
- Patient horrified
- Sexual history revealed 1 partner in her lifetime – her husband.
- Bridget treated with Azithromycin
- Husband invited in for screening
- His tests came back all clear

‘Healthy degree of suspicion’

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- His sexual history revealed he had recently travelled overseas – work related
- History also revealed recent anti-malarial meds – doxycycline
- Doxycycline also treatment for chlamydia

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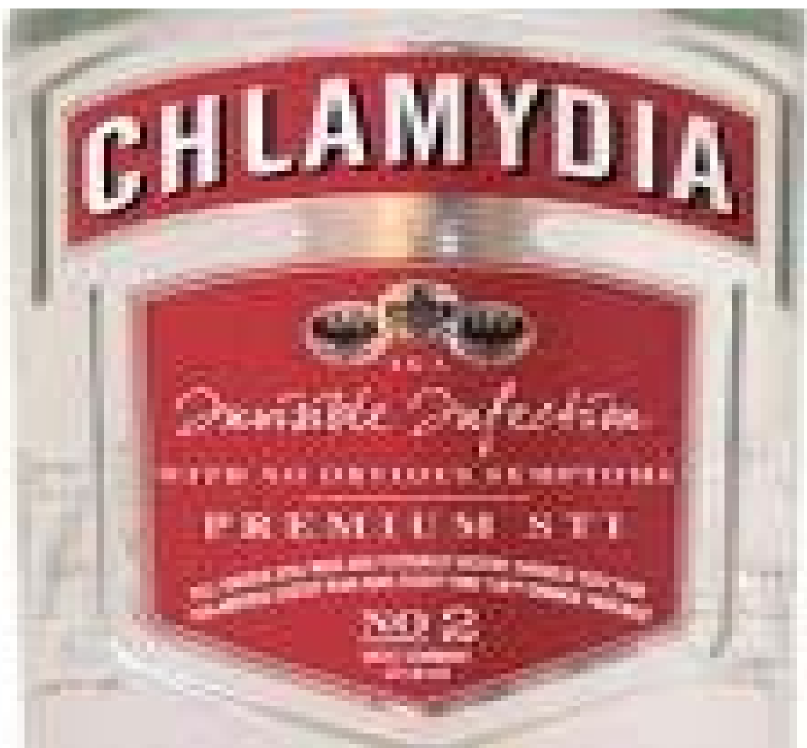

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Symptoms

Male

- Dysuria
- Urethral discharge
- **<u>None</u>**

Female

- IMB
- PCB
- Vaginal discharge
- Dysuria
- Dyspareunia
- Lower abdo pains
- **<u>None</u>**

Untreated Chlamydia Complications

- P I D – Pelvic Inflammatory Disease
- Fitz- Hugh Curtis Syndrome
- Epididimo-orchitis
- Reiters Syndrome / SARA

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Cervicitis

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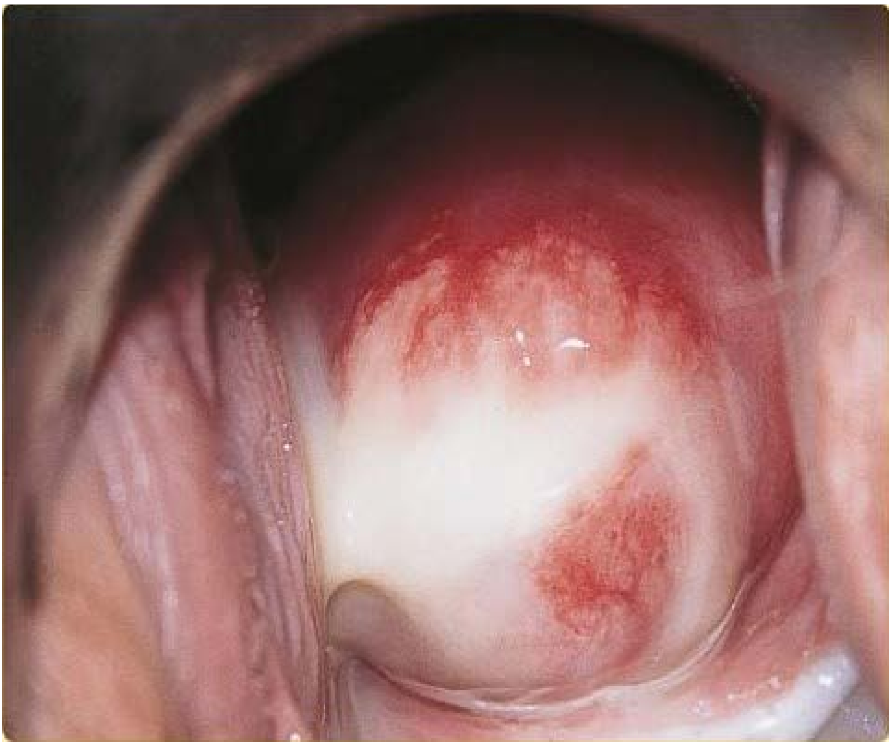

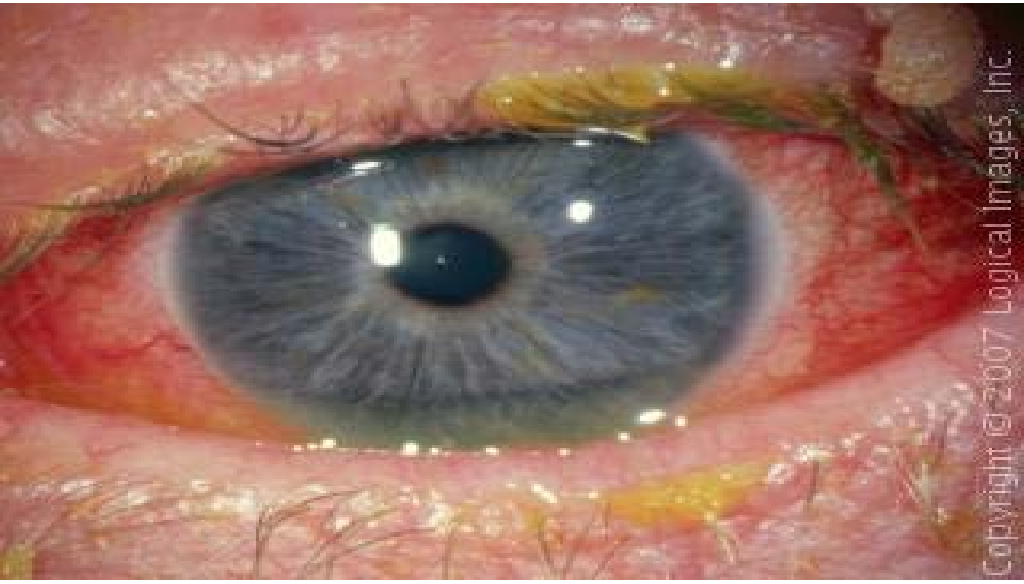

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Diagnosis

- Nucleic acid amplification tests
- Women vulvo-vaginal swab
- Men First Void Urine
- Rectal swab
- Pharyngeal swab

Treatment

- Doxycycline 100mg bd for 7 days

In pregnancy or breast feeding:

- Erythromycin 500mg bd for 14 days
- Azithromycin 1g stat

Contact tracing:

- All partners in the last 6 months if asymptomatic
- 1 month prior to onset in symptomatic

JAMA

COMMENTARY

Questioning Azithromycin for Chlamydial Infection

H. Hunter Handsfield, MD

Sexually Transmitted Diseases ● Volume 38, Number 11, November 2011 1029

- Blind faith in single dose azithromycin
- Many trials done in era of less sensitive tests

" ...the personal health benefits of doxycycline or test of cure might be substantial for many patients while we await confirmatory studies."

Azithromycin antimicrobial resistance and genital *Chlamydia trachomatis* infection: duration of therapy may be the key to improving efficacy

Paddy J Horner[1,2]

Sex Transm Infect
April 2012 Vol 88 No 3

1. “heterotypic resistance
2. the consequence of single dose therapy with a bacteriostatic antibiotic.
3. emergence of homotypic (genetically inherited) resistance to azithromycin”

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What is the first line treatment for asymptomatic rectal Chlamydia at your clinic?

1. Azithromycin 1g stat
2. Doxycycline 100mg bd 7 days
3. Doxycycline 100mg bd 21 days
4. Ofloxacin 400mg od for 10 days
5. No treatment if asymptomatic

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Azithromycin for rectal CT???

- There have been no RCTs for antibiotic therapy of rectal CT
- Observations of poor outcome with Azi 1g – 4 papers now

If meta-analysis:

- Azi 1g – 186/221 = 84.2% (95%CI 78.7-88.4)
- Doxy – 201/205 = 98.0% (95%CI 94.9-99.4)

- RCTs needed
- MSM – good with pills
- Rectal CT - median age 32

Hathorn E, Opie C, Goold P. Sex Transm Infect (2012)

Drummond et al International Journal of STD & AIDS 2011; 22: 478–480.

Steedman N , McMillan A. International Journal of STD & AIDS 2009; 20:16-18

Elgalib A et al. International Journal of STD & AIDS 2011; 22: 474–477

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Question??

Your 20 year old daughter has been diagnosed with asymptomatic Chlamydia. Would you advise her to take ???

1. Azithromycin 1g stat
2. Doxycycline 100mg bd 7 days
3. Azithromycin 1g stat then 500mg qd 4 days
4. Moxifloxacin 400mg od for 10 days
5. Take out a contract on her boyfriend!

Remember……

Case Study 2

23 year old Jane presents with

- Vulval discomfort ? Itching x 2 days
- Self treated with antifungals OTC
- Increased dysuria over next 24hrs
- Painful ulceration

What is your differential diagnoses?

Infective Causes:

Syphilis
Chancroid
Granuloma Inguinale
Lymphogranuloma Venereum

Cytomegalovirus
Tuberculosis and atypical mycobacteria
Histoplasmosis
Schistosomiasis
Tularaemia

Other Causes

GI Crohn's disease, Coeliac disease, Ulcerative colitis

Rheumatology Behcets syndrome

Drug-induced Fixed drug eruptions
Stephen's Johnson Syndrome

Dermatology Pemphigous+pemphigoid
Lichen planus(ulcerative variety)
LS&A
Erosive balanitis/vulvitis/scabies

Neoplasm Local carcinoma/melanoma/mets

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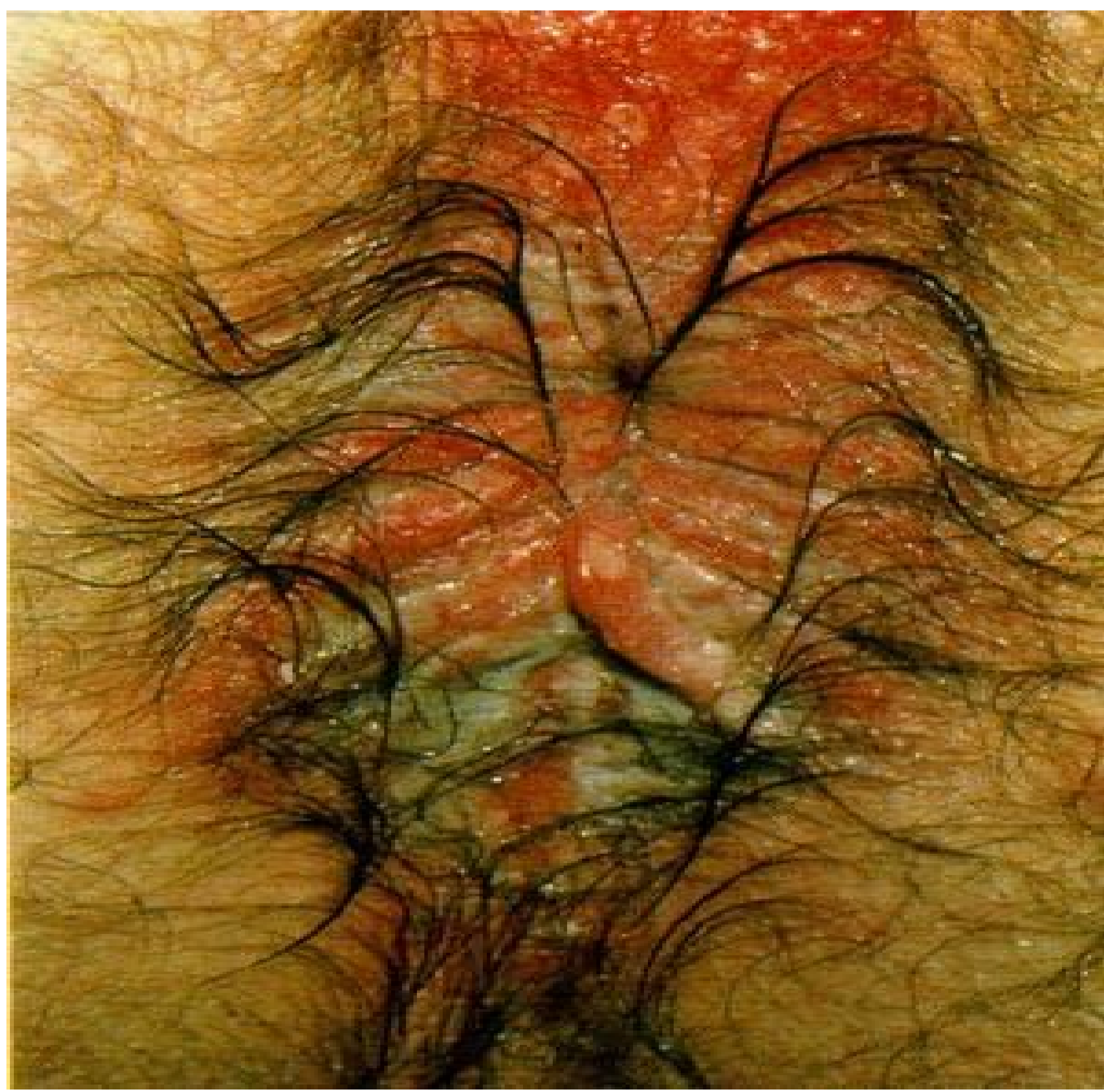

Herpes simplex genitalis

- HSV-1 and 2
- Primary infection…latency in local sensory ganglia…reactivates periodically :
  - 0.34 recurrences/month HSV-2,
  - 0.08 recurrences/month HSV-1
- Symptomatic primary infection in adult life, as likely to be HSV-1 as HSV-2
- Asymptomatic shedding

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Management HSV genitalis

- **Antivirals**
  Valacyclovir 500mg BD x 3/7- acute attack
  Valacyclovir 500mg od x 1 year –suppression

- Saline baths
- Analgesia
- Local anaesthetic
- Counselling

- May require admission and suprapubic catheterisation

Case study 3

Jane's syphilis serology reported

RPR : 64

TPPA : 2568

FTA : IgM +

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History

- Syphilis has many alternate names: Miss Siff, the Pox (or Great pox, to distinguish it from smallpox).

- Symptoms of syphilis are myriad dubbed the "Great-Imitator“ by Sir William Osler

- Syphilis was the leading cause of neurological and cardiovascular disease among middle-aged persons at turn of 20th century.

- Because of the outbreak in the French army (1546), it was first called the “French disease”.

(In that time it is noteworthy that

the Italians: "Spanish disease“

the French: “English”, “Italian” and “Neapolitan- disease”,

the Russians: “Polish disease“

the Arabs: "Disease of the Christians”)

A number of famous historical personages,

Charles VIII **(1470-1498)**

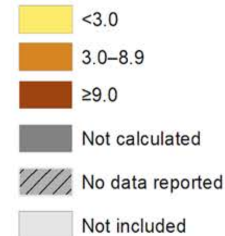
Friedrich Nietzsche **(1844-1900)**

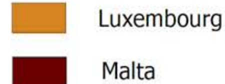
Al Capone **(1899-1947)**

Syphilis epidemiology EU/EEA 2017

Reported cases, rates

- **33 189** cases, 28 countries
- EU/EEA rate **7.1**/100 000
- National rates range: **0.7- 15.4**
- 58% of cases reported from: DE (23%), UK (23%), ES (15%)

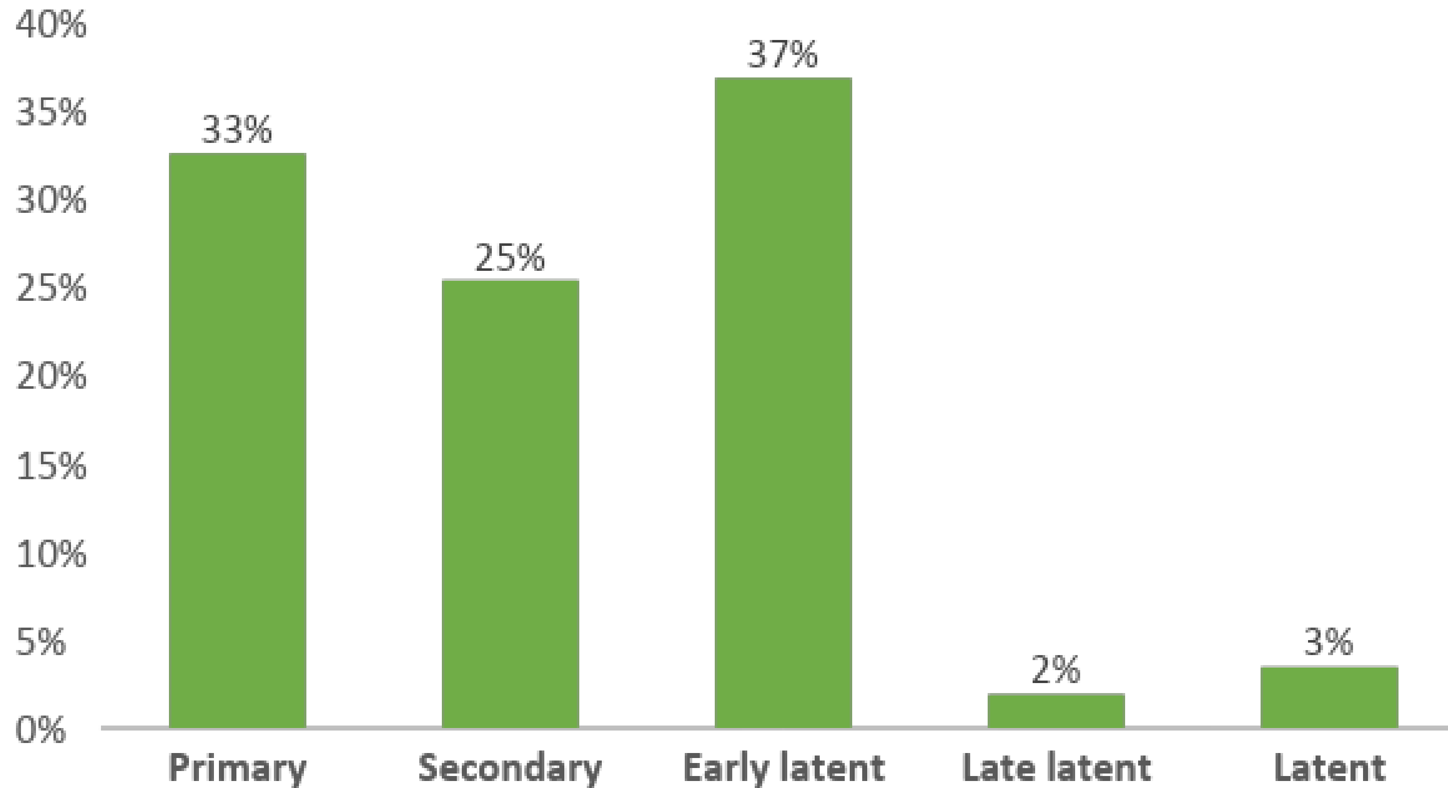


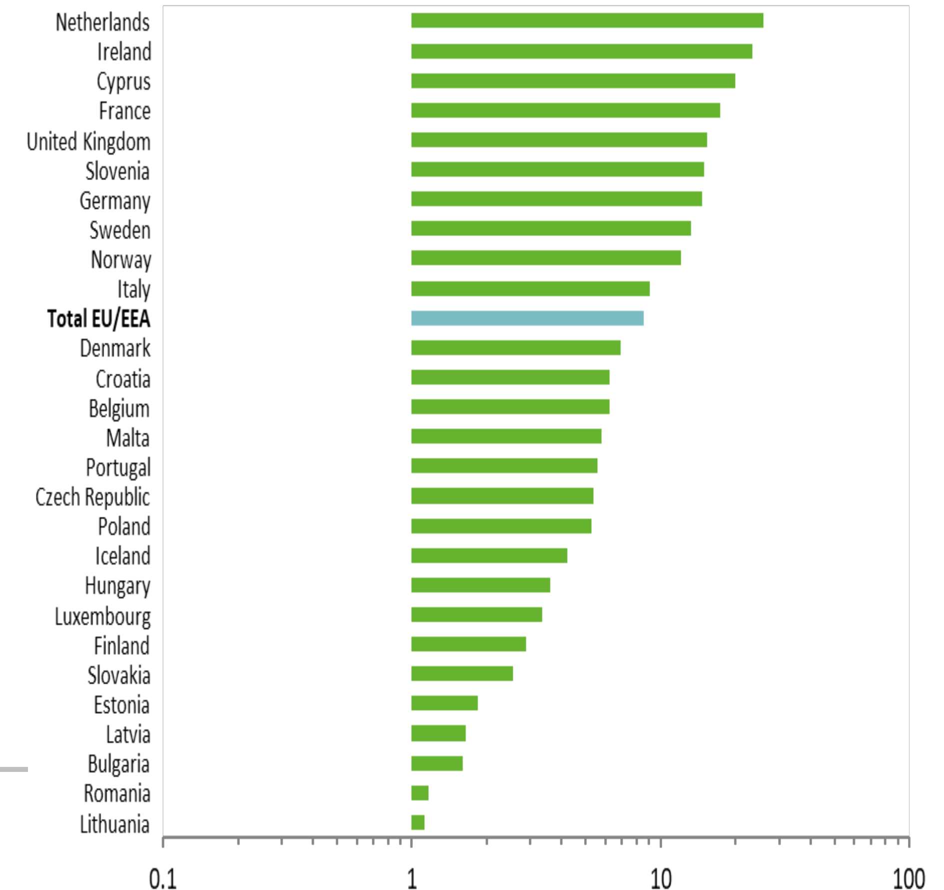


ECDC. Map produced on: 29 Jan 2019

Source: ECDC Surveillance Atlas of Infectious Diseases

Syphilis epidemiology EU/EEA, 2017
Infection stages at diagnosis (n =13 899)



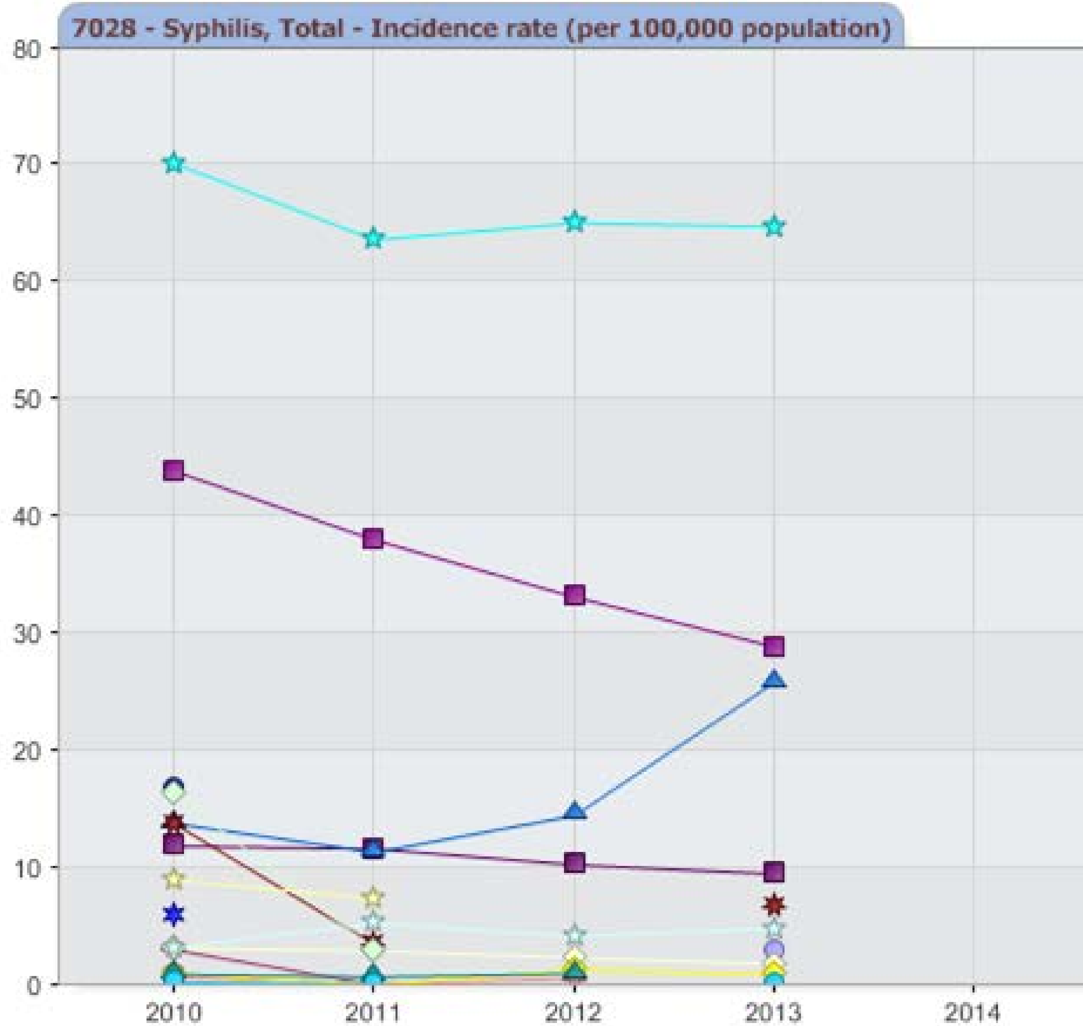


Note: includes country reports from Czech Republic, Estonia, France, Hungary, Iceland, Ireland, Latvia, Lithuania, Malta, Netherlands, Norway, Romania, Slovakia, Slovenia, United Kingdom.

M:F 9:1

Source: ECDC Surveillance Atlas of Infectious Diseases; ECDC Syphilis Annual epidemiological report 2017 (in press)

Syphilis, non-EU countries



World Health Organization

REGIONAL OFFICE FOR Europe

ecdc

7028 - Syphilis, Total - Incidence rate (per 100,000 population)

	2010	2011	2012	2013	2014
Albania	0.81			2.81	
Andorra	2.95	0			
Armenia	3.17	2.87	2.32	1.76	
Azerbaijan	3.2	5.24	4.14	4.8	
Belarus	11.84	11.61	10.24	9.45	
Bosnia and Herzegovina	0.66	0.13	0.51		
Georgia	13.76	11.31	14.45	25.82	
Kazakhstan					
Kyrgyzstan	16.72				
Monaco					
Montenegro	0.95	0	1.26	0.95	
Republic of Moldova	70.11	63.62	65.06	64.74	
Russian Federation	43.84	37.97	33.1	28.86	
San Marino	13.72	3.41		6.75	
Serbia	0.88	0.68	0.95		
Tajikistan	5.84				
North Macedonia	0.24	0.05		0.1	
Turkmenistan					
Ukraine	16.25	2.96			
Uzbekistan	8.95	7.34			

Country	Year	Comment
All	All	Blank cells indicate that data is either unavailable and/or has not yet been reported to WHO

Source: WHO Europe Centralized information system for infectious diseases (CISID)
http://data.euro.who.int/cisid/

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Syphilis Is Back!
Treponema pallidum
causes Syphilis

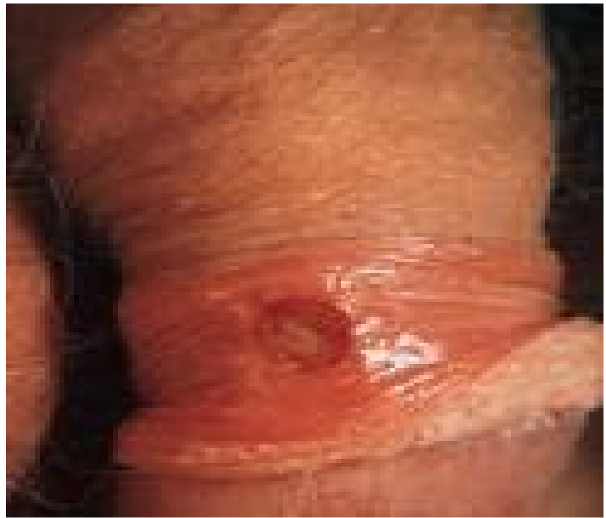
Pathogenesis

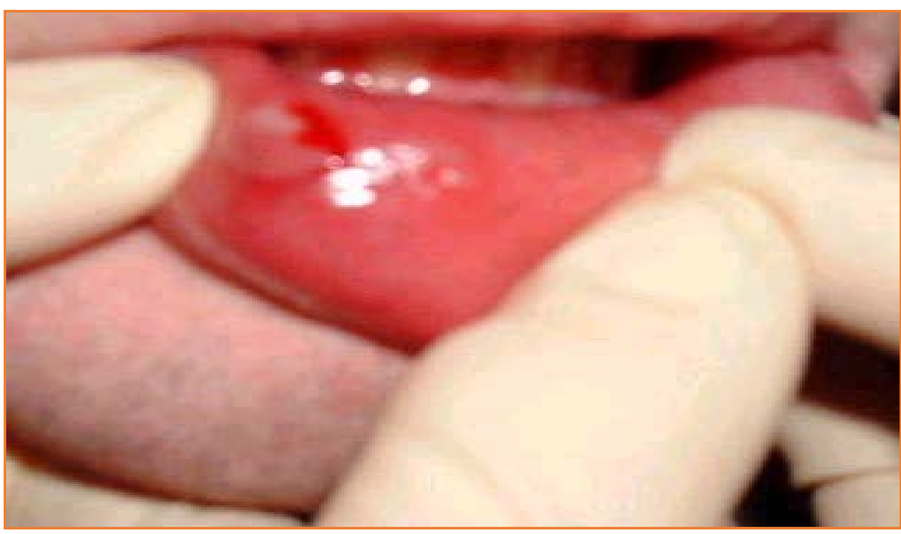
- Patient v infectious during Primary stage
- 50 % of contacts are infected
- Incubation period 3-90 days
- Doubt over total eradication of treponemes following treatment.

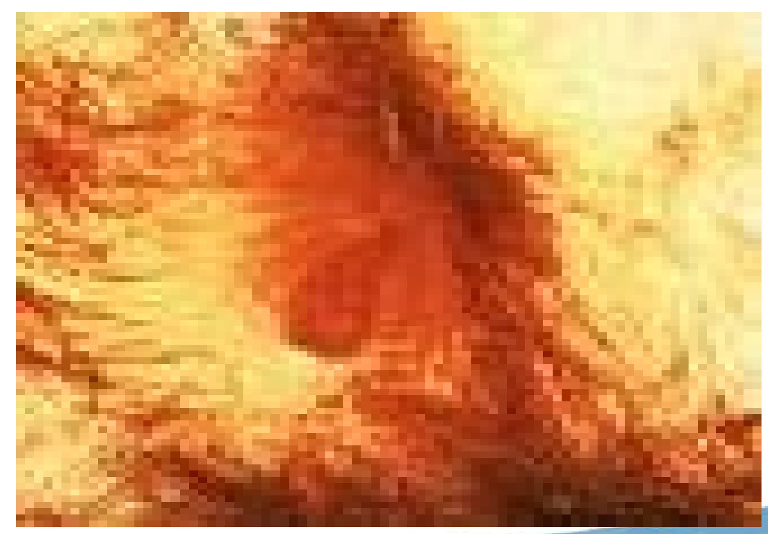
Variation depends on:

- Number of treponemas innoculacted
- Host immune status (e.g HIV)
- Intercurrent antibiotics
- Secondary infection

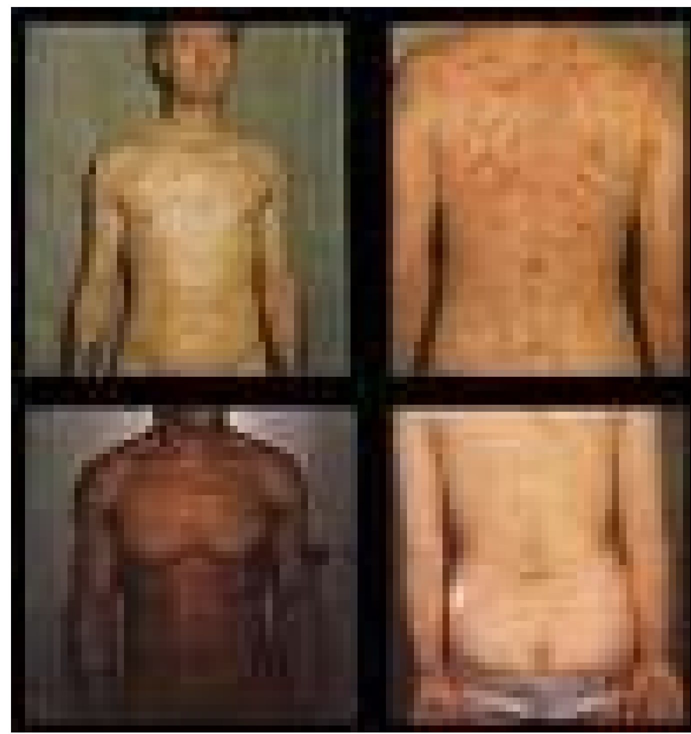
Chancre on Penis, Vulval and Anorectal

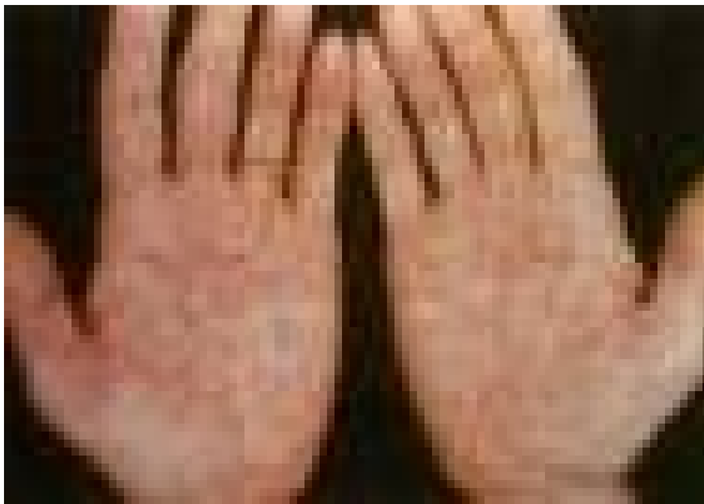


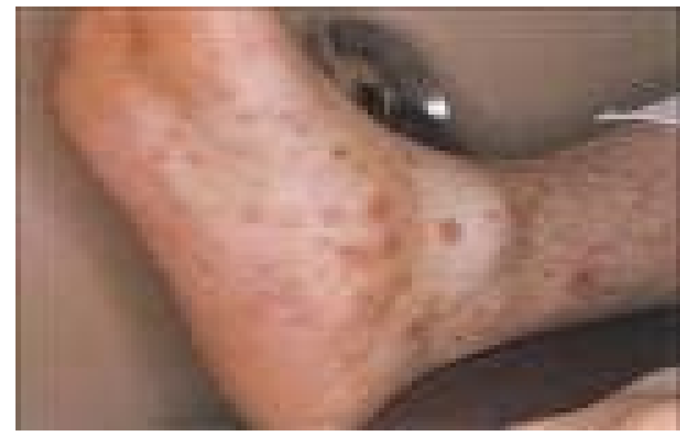




Secondary Syphilis 6 weeks to 6 months post exposure

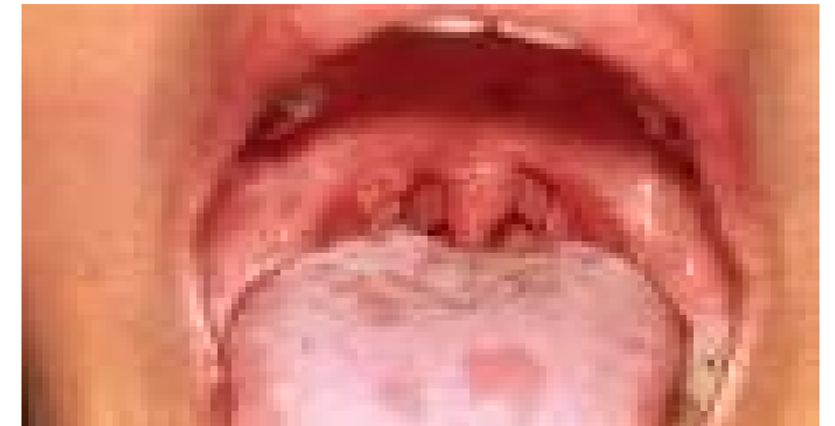






Secondary Syphilis Cont.

- Condyloma lata-Papules enlarge and erode producing moist grey white plaques
- Mucous Patches – typically silver grey superficial erosion with red edges
- Both Highly infectious



Secondary Syphilis

Constitutional symptoms-70 % low grade fever, malaise, pharyngitis, painless lymphadenopathy, weight loss, anorexia

CNS - 40% headache, meningism ,visual disturbances, hearing loss and cranial nerve palsies

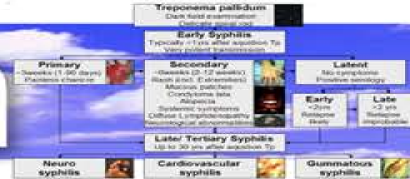
Organs – Hepatitis

Kidneys- Proteinuria

Uveitis

Synovitis

Clinical Manifestation



Early Syphilis
Typically <1yrs after acquisition TP
Very potent transmission

Primary
~3weeks (1-90 days)
Painless chancre

Secondary
~6weeks (2-12 weeks)
Rash (incl. Extremities)
Mucous patches
Condyloma lata
Alopecia
Systemic symptoms
Diffuse Lymphadenopathy
Neurological abnormalities

Latent
No symptoms
Positive serology

Early
<2yrs
Relapse likely

Late
>2 yrs
Relapse improbable

Late/ Tertiary Syphilis
Up to 30 yrs after acquisition TP

Neuro syphilis

Cardiovascular syphilis

Gummatous syphilis

Neurosyphilis

Commonest presentation

- asymptomatic

Caucasians > blacks

8-40% of untreated syphilis

No clinical manifestations but abnormal CSF

- raised WCC,
- raised protein,
- low glucose,
- local CNS production of antibodies to TP

Macrolide Resistance in *T. pallidum*

2 mutations ; A2058G, later A2059G discovererd

Sequence Analysis of 23S rRNA Gene

Geographical distribution of mutation is unknown

–Dublin 2002[1]	88%
–Dublin 2010	93%
–Madagascar 2006	0%
–Nanjing, China 2007	100%

Lukehart et al. NEJM 2004;351:154-8

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2014 European Guideline on the Management of Syphilis, *Janier et al*

First line treatment

- Early syphilis (P, S, EL, i.e. acquired ≤1 year previously)
  Benzathine penicillin G 2.4 m units IM, **single dose**
- Late latent or unknown duration
  Benzathine penicillin G 2.4 m units IM, **weekly on days 1, 8 and 15**
- Neurosyphilis, ocular and auricular syphilis
  Benzyl penicillin 18–24 m units IV daily, 10–14 days

Alternative regimens include doxycycline, tetracycline, and for neurosyphilis, potentially ceftriaxone. Clinical and laboratory follow-up needed!

STI Treatment Pocket European 2018 Guidelines

Case Study 4

Nora, 48 year old admitted
% Generalised aches & pains,
Sore throat and painful joints

O/E looked ill, temp 38.5c

All skeletal joints were tender

Bartholin's abscess

Non blanching purpura, extensor surfaces of both legs

- Hg 14.7,
- WCC 11.6,
- Platelets 205,
- ASOT neg
- Hepatitis A,B,&C neg

Case Study 4

5 days later – a swelling of the right Knee

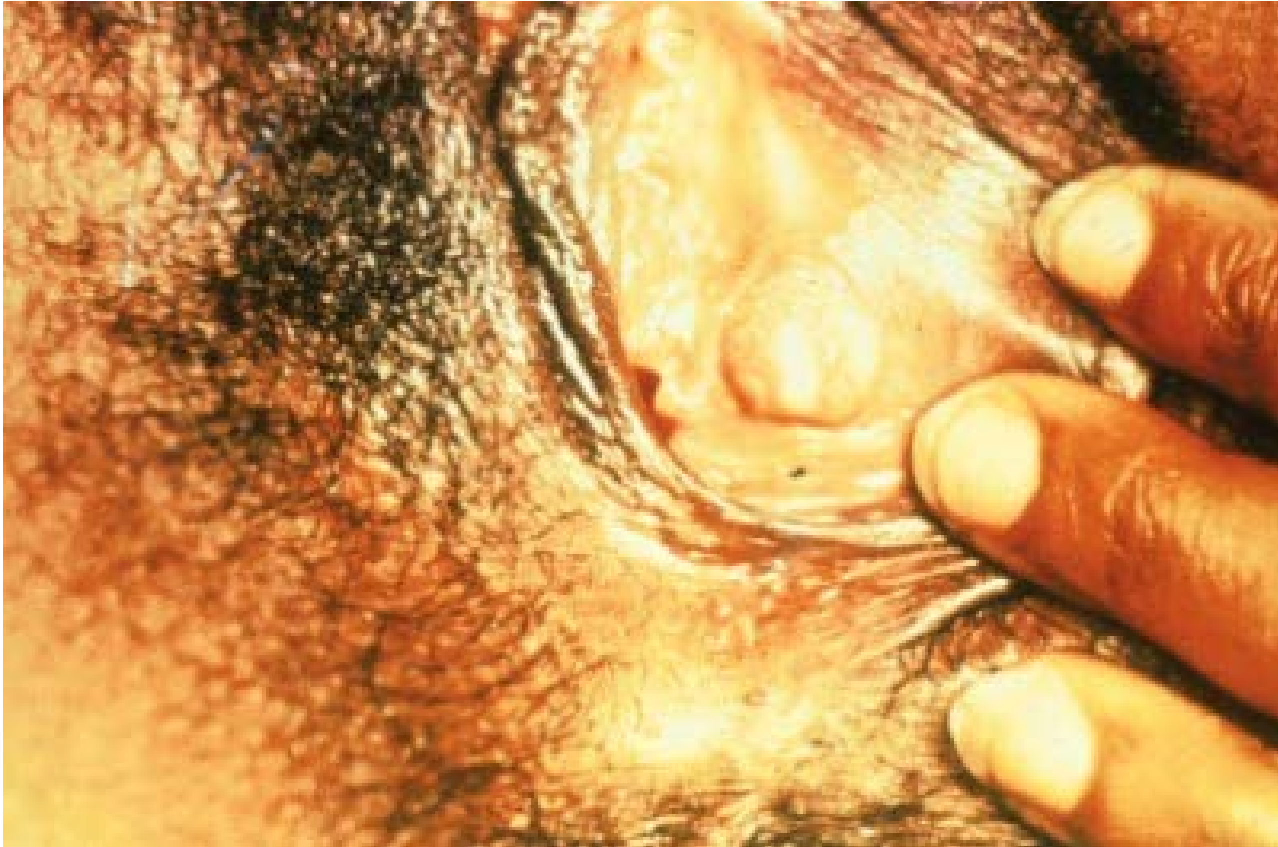
Aspirated – aspirate grew N gonnorhoea

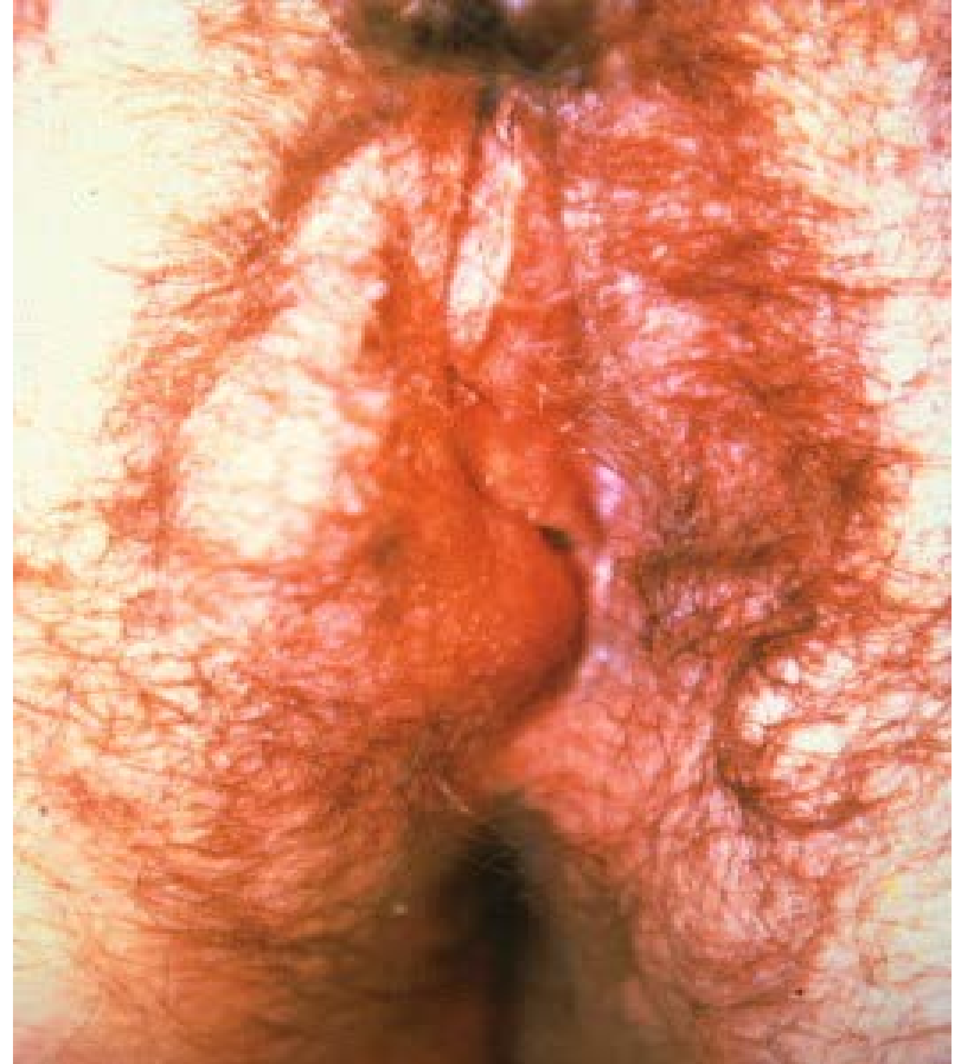
Further hx revealed UPSI with CMP in south east Asia

Rx with ceftriaxone

Recovery was uneventful

Bartholin's abscess

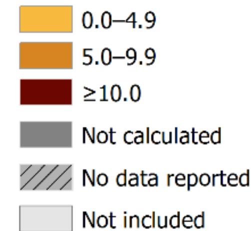




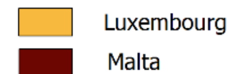
Gonorrhoea epidemiology EU/EEA 2017
Reported cases, rates

- **89 239** cases, 27 countries
- EU/EEA rate: **22.2**/100 000
- National rates range: **0.2- 74.7**
- Rates >25/100 000 in SE, NO, IS, DK, IE, UK
- 55% of cases reported from UK

Notification rate (N/100000)



Countries not visible in the main map extent

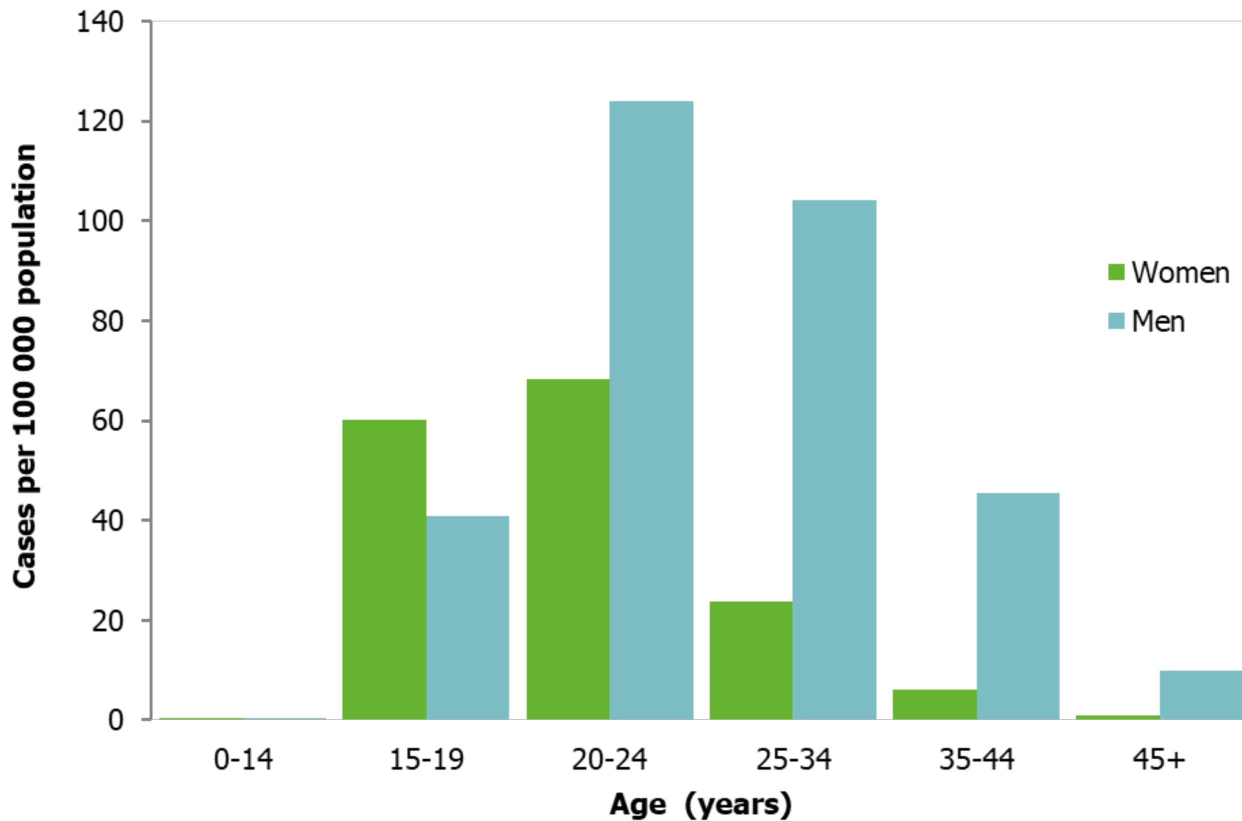


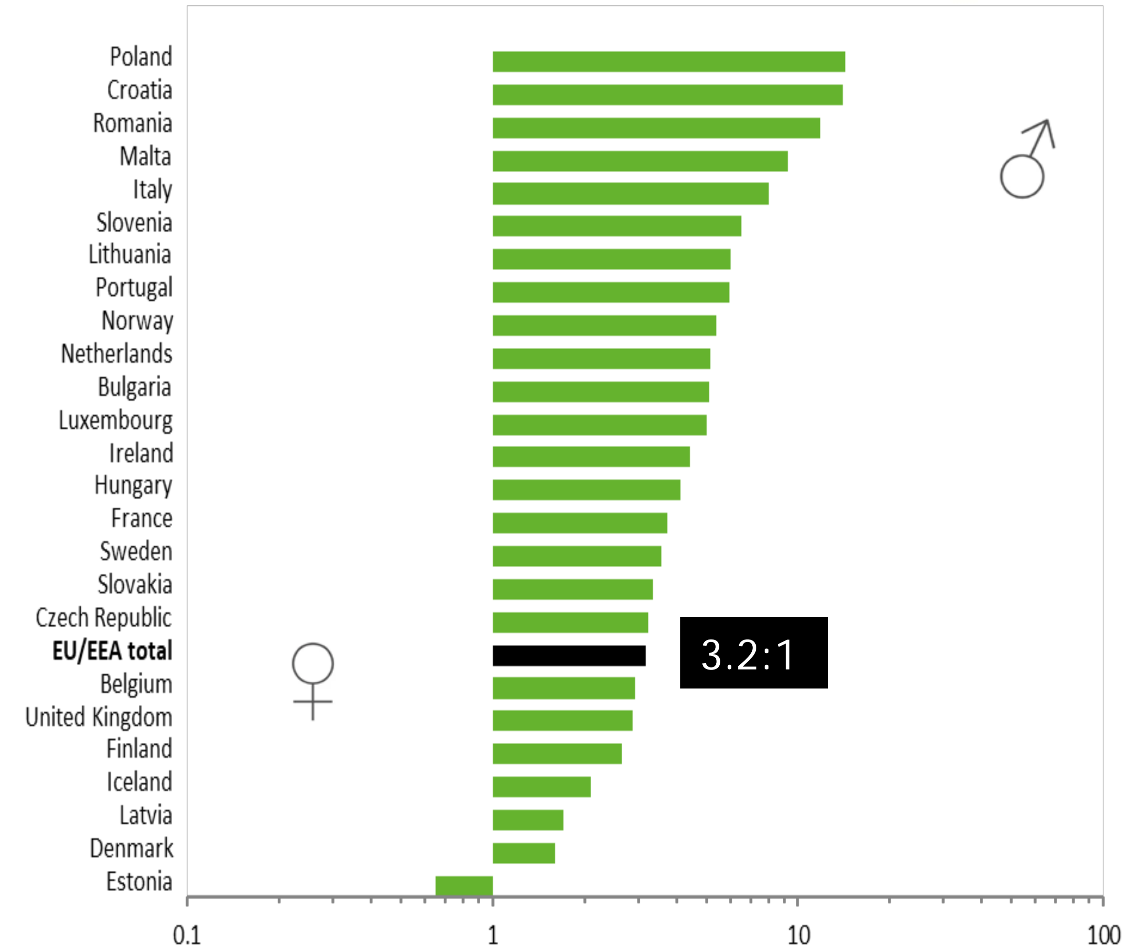
ECDC. Map produced on: 10 Dec 2018

Source: ECDC Surveillance Atlas of Infectious Diseases; ECDC Gonorrhoea Annual epidemiological report
https://ecdc.europa.eu/sites/portal/files/documents/gonorrhoea-annual-epidemiological-report-2017.pdf

Gonorrhoea epidemiology EU/EEA 2017

Rates by age and gender, male-to-female ratio





Source: ECDC Surveillance Atlas of Infectious Diseases; ECDC Gonorrhoea Annual epidemiological report
https://ecdc.europa.eu/sites/portal/files/documents/gonorrhoea-annual-epidemiological-report-2017.pdf

Gonorrhoea, non-EU countries

World Health Organization

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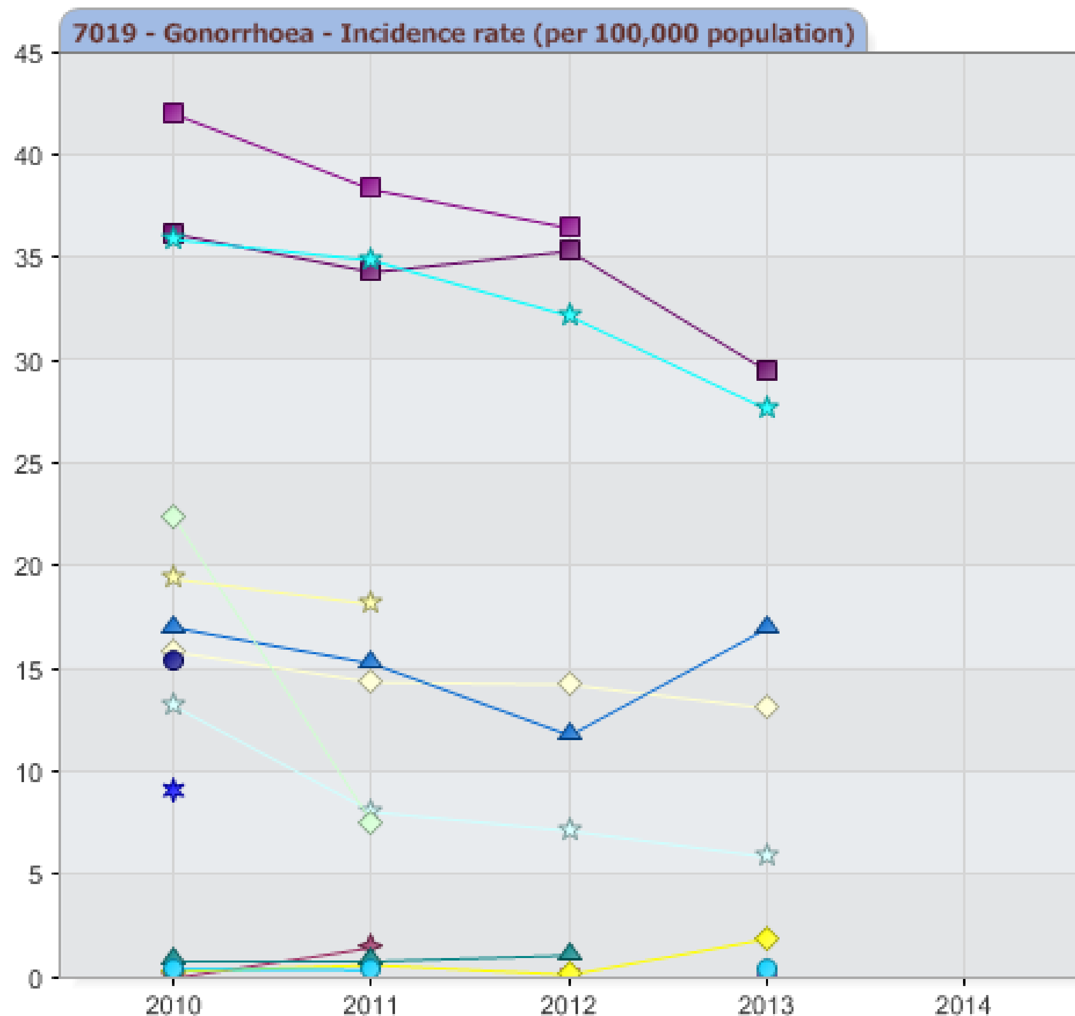

- Albania
- Andorra
- Armenia
- Azerbaijan
- Belarus
- Bosnia and Herzegovina
- Georgia
- Kazakhstan
- Kyrgyzstan
- Monaco
- Montenegro
- Republic of Moldova
- Russian Federation
- San Marino
- Serbia
- Tajikistan
- North Macedonia
- Turkmenistan
- Ukraine
- Uzbekistan

7019 - Gonorrhoea - Incidence rate (per 100,000 population)

	2010	2011	2012	2013	2014
Albania	0.03			0.03	
Andorra	0	1.48			
Armenia	15.85	14.39	14.26	13.12	
Azerbaijan	13.2	8.08	7.15	5.88	
Belarus	36.18	34.33	35.35	29.52	
Bosnia and Herzegovina	0.29		0.11		
Georgia	17.03	15.29	11.8	17.01	
Kazakhstan					
Kyrgyzstan	15.35				
Monaco					
Montenegro	0.32	0.63	0.16	1.9	
Republic of Moldova	35.91	34.9	32.19	27.65	
Russian Federation	42.01	38.35	36.47		
San Marino	0				
Serbia	0.79	0.8	1.1		
Tajikistan	9.09				
North Macedonia	0.44	0.39		0.34	
Turkmenistan					
Ukraine	22.34	7.52			
Uzbekistan	19.4	18.17			

Source: WHO Europe Centralized information system for infectious diseases (CISID)
http://data.euro.who.int/cisid/

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BUY BONDS

PENICILLIN
CURES
GONORRHEA
IN 4 HOURS
SEE YOUR DOCTOR TODAY

2012 European Guideline on the Diagnosis and Treatment of Gonorrhoea in Adults

Bignell C et al. 2012

First-line treatment of uncomplicated *N. gonorrhoea*

- urethra, cervix and rectum infections
  Ceftriaxone 500 mg IM, single dose and **Azithromycin 2 g** oral, single dose.
- infection of the pharynx
  Ceftriaxone 500 mg IM, single dose and **Azithromycin 2 g** oral, single dose.
- infections in pregnancy and during breast feeding
  Ceftriaxone 500 mg IM, single dose.
- genital, anorectal, pharyngeal infection when extended-spectrum cephalosporin resistance identified
  - **Ceftriaxone 1 g** IM, single dose and **Azithromycin 2 g** oral, single dose OR
  - **Gentamicin 240** mg IM, single dose and **Azithromycin 2 g** oral, single dose.

Consider *C. trachomatis* co-infection in young heterosexuals and MSM

Test of cure

- For all patients! Particularly for pharyngeal infections!
- If symptomatic after Tx: culture 3-7 days post treatment; NAAT
- If asymptomatic after Tx: NAAT 2 weeks post treatment.
- Report treatment failures!

Contact management: test and treat all sex partners within preceding 60 days of onset/diagnosis

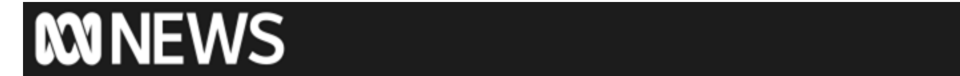
https://journals.sagepub.com/doi/10.1177/0956462412472837

XDR Gonorrhoea – 2018

Live Science > Health

UK Man with 'Worst Ever' Drug-Resistant Gonorrhea Is Now Cured

By Rachael Rettner, Senior Writer | April 20, 2018 02:56pm ET



UK man's super-gonorrhoea cured — but now two Australians have it

Updated 21 Apr 2018, 5:47am

The Telegraph

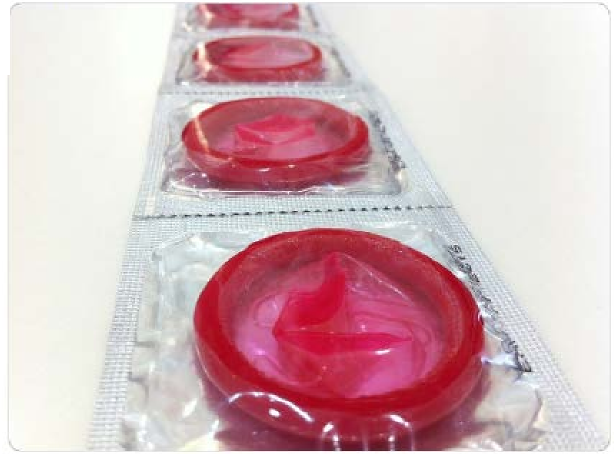
News

UK pledges £5m to fight 'super gonorrhoea'

The £5m will go to the non-profit partnership the Foundation for Innovative New Diagnostics (FIND) for the development of a test that will be ready for use by 2025.

Public Health England
@PHE_uk
Following

Two cases of drug resistant gonorrhoea have been diagnosed in the UK. We're reminding people of the importance of practising safer sex and seeking help if they are worried they may have an STI: bit.ly/2Cd8LzI



12:35 AM - 10 Jan 2019

European Centre for Disease Prevention and Control
An agency of the European Union

Rapid Risk Assessment: Extensively drug-resistant (XDR) Neisseria gonorrhoeae in the United Kingdom and Australia

risk assessment

7 May 2018

2012 European Guideline on the Diagnosis and Treatment of Gonorrhoea in Adults

Bignell C et al. 2012

First-line treatment of uncomplicated *N. gonorrhoea*

- urethra, cervix and rectum infections
  Ceftriaxone 500 mg IM, single dose and **Azithromycin 2 g** oral, single dose.
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  dose.
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  cepha
  - **Ceftriaxone 1 g** IM, si
  - **Gentamicin 240** mg IM, single dose and **Azithromycin 2 g** oral, single dose.

Consider *C. trachomatis* co-infection in young heterosexuals and MSM

Contact management: test and treat all sex partners within preceding 60 days of onset/diagnosis

https://journals.sagepub.com/doi/10.1177/0956462412472837

Test of cure

- For all patients! Particularly for pharyngeal infections!
- If symptomatic after Tx: culture
  3-7 days post treatment: NAAT

2019 BASHH (UK) guidelines

Treatment of uncomplicated ano-genital and pharyngeal infection in adults

- When antimicrobial susceptibility is not known prior to treatment:

Ceftriaxone 1g IM, single dose (Grade 1C)

- When antimicrobial susceptibility is known prior to treatment:

Ciprofloxacin 500mg, single dose, orally (Grade 1A)

https://www.bashhguidelines.org/media/1208/gc-2019.pdf

Key Messages

- CT Treatment may be sub optimal
- LGV an emerging problem
- HSV early diagnosis critical
- Syphilis staging important in treatment management
- GC resistance increasing

If not sure what to do.........

WAVE

EACS European AIDS Clinical Society

Don’t Panic!!!

www.guideclinic.ie