

Syphilis and HIV Co-infection. Old and new dangers combine

Marsh Gelbart 2010





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Learning outcomes

- To understand the historical parallels between syphilis and HIV
- To examine different theories of origin
- To understand the epidemiological footprint of co-infection
- To understand how the infections interact
- To examine the implications for treatment when there is co-infection



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So where did syphilis come from?

Theories for the origin of syphilis

- **The Columbian theory involving trans-oceanic exchange. Two population groups which had no previous exposure to each others illnesses “swapped” infections.**
- **The Unitarian theory states that Yaws-like diseases were endemic to Mediaeval Europe and evolved into syphilis.**



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And HIV hit like a star burst, but from where?

- **Theories for the origin of HIV**
- Most likely an emerging disease, previously confined to the great apes, which arose from the natural transfer of simian immunodeficiency virus to humans through butchering “bush meat”.
- Although doubtful, possibly through iatrogenic means. Perhaps the administration in Africa of vaccines made in substrates of primate kidney, may have been the initial means whereby the precursor simian viruses were transferred to humans.



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Syphilis generates fear and stigma



- Historically, minority groups, women, or outside powers, were blamed by various cultures as the originators of syphilis.
- For example, in Britain it was known as the the French Pox, in France, the Italian Disease etc.



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As does HIV.....



- Things changed little in the era of HIV.
- Sentinel populations; Gay men, Black Africans, in other words those first and most heavily affected by HIV were blamed for its advent.
- Research into co-infection focuses on the self-same groups.*
- This can lead to the danger of further stigmatisation



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Both HIV and syphilis have visible stigmata.....





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Similar footprints of infection

- 33.2 million currently are living with HIV.
- The worst effected areas are sub-Saharan Africa and Southeast Asia
- It is estimated by the WHO that there around 12 million new cases of syphilis each year.
- 90% of syphilis cases are in developing countries predominantly in Southeast Asia followed closely by sub-Saharan Africa
- Both infections are a growing problem in Eastern Europe and both have focal points in the developed West



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The great mimics

- Both Syphilis and HIV can mimic other diseases and of course each other
- Although both are associated with a seroconversion illness, it is not uncommon for early stages of the disease to be asymptomatic.
- Both illnesses have a waxing and waning course





Diagnoses of infectious syphilis (primary, secondary and early latent) by sex and sexual orientation, England and Wales: Jan 2002 – Dec 2008

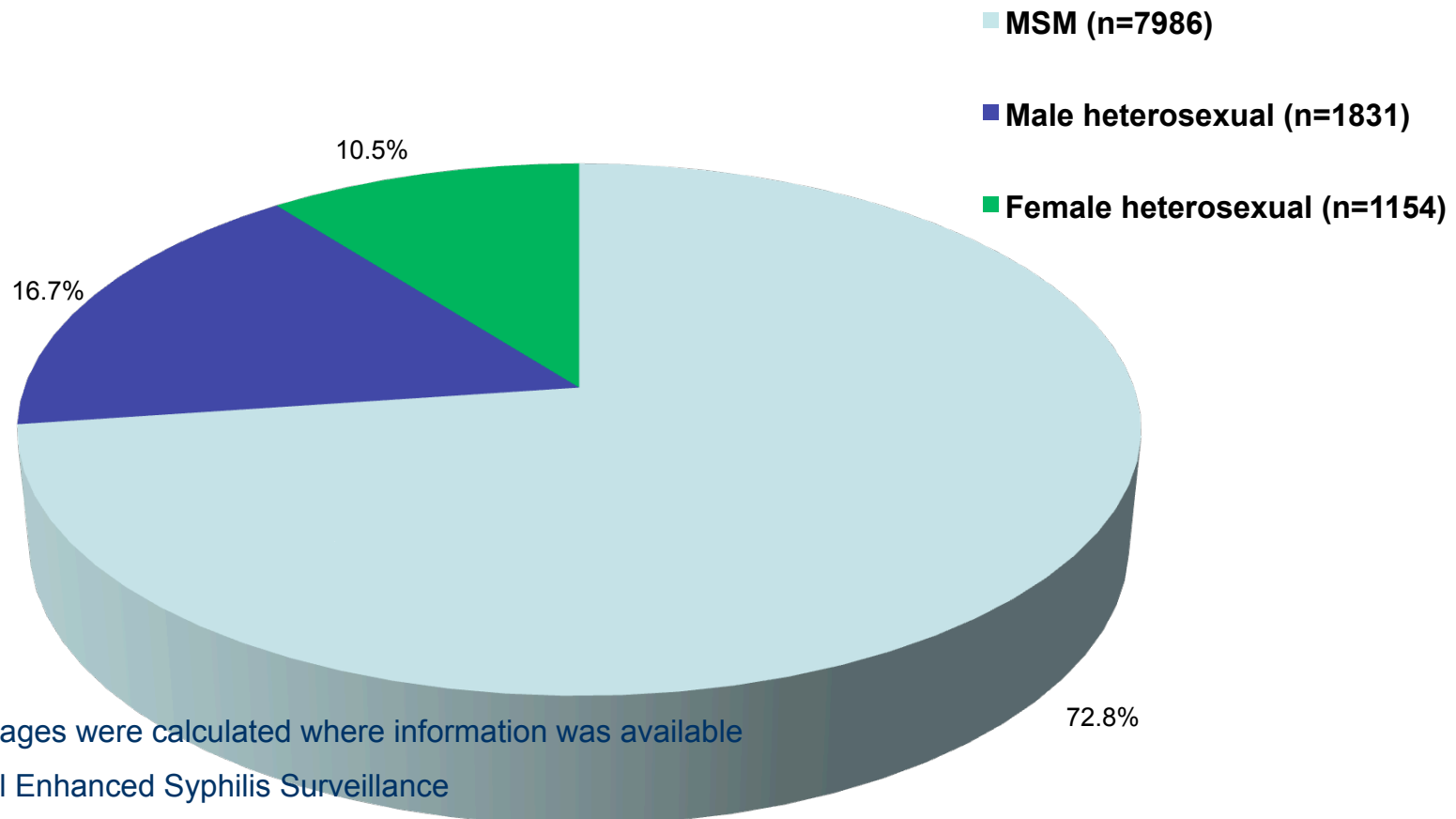

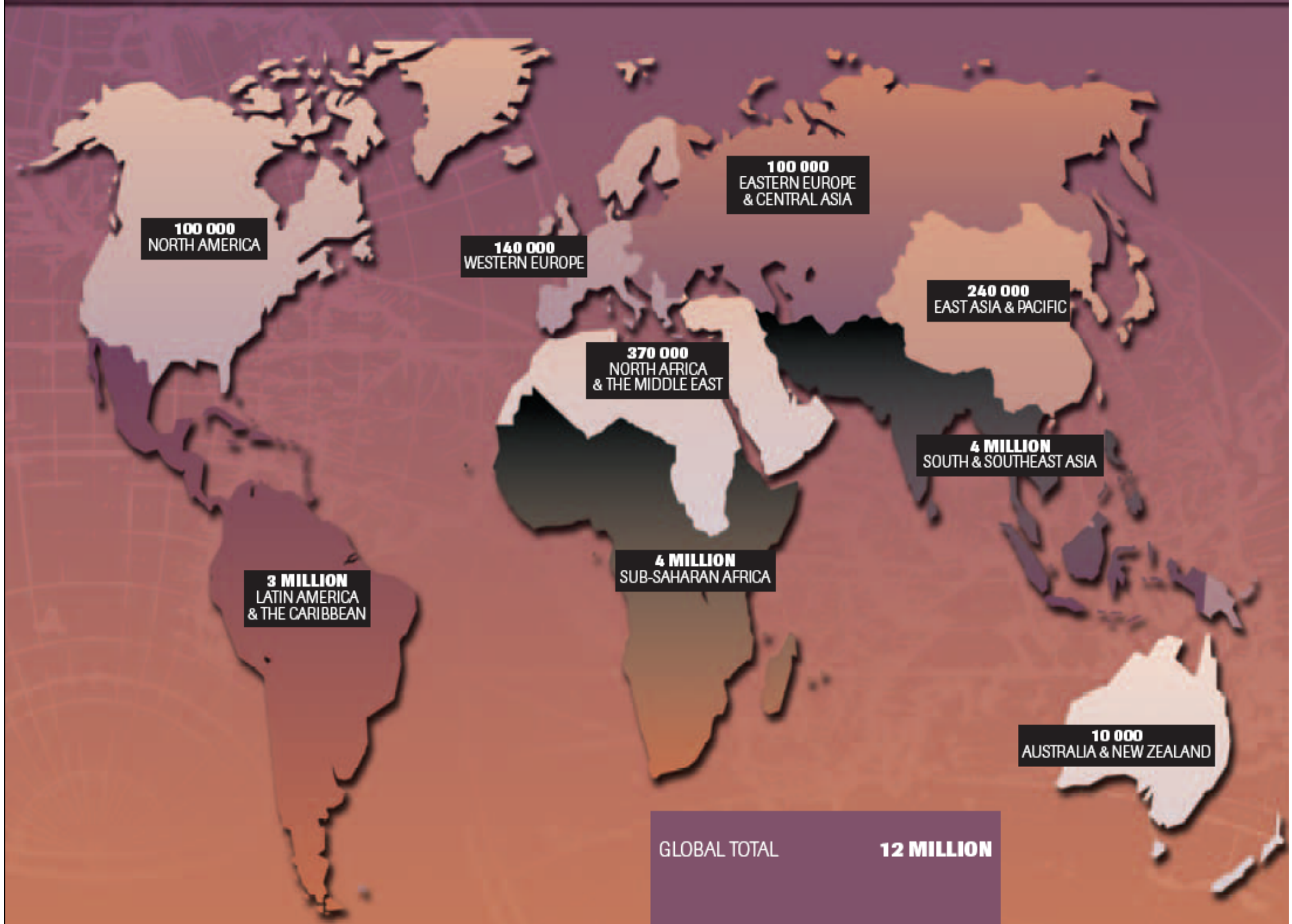
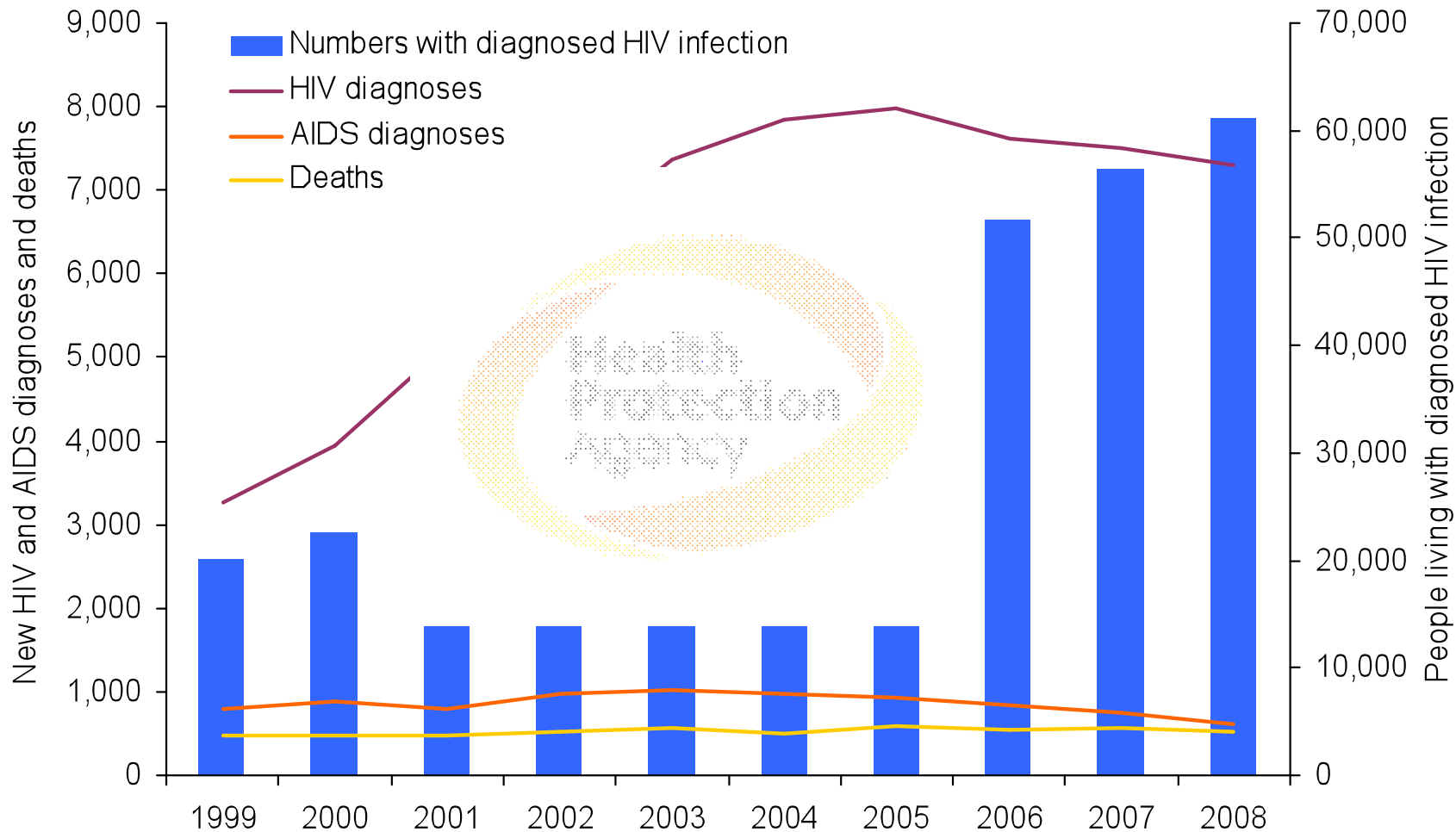


FIGURE 9. ESTIMATED NEW CASES OF SYPHILIS AMONG ADULTS, 1999 





New HIV and AIDS diagnoses, people living with diagnosed HIV, and deaths, among HIV-infected people, UK: 1999-2008

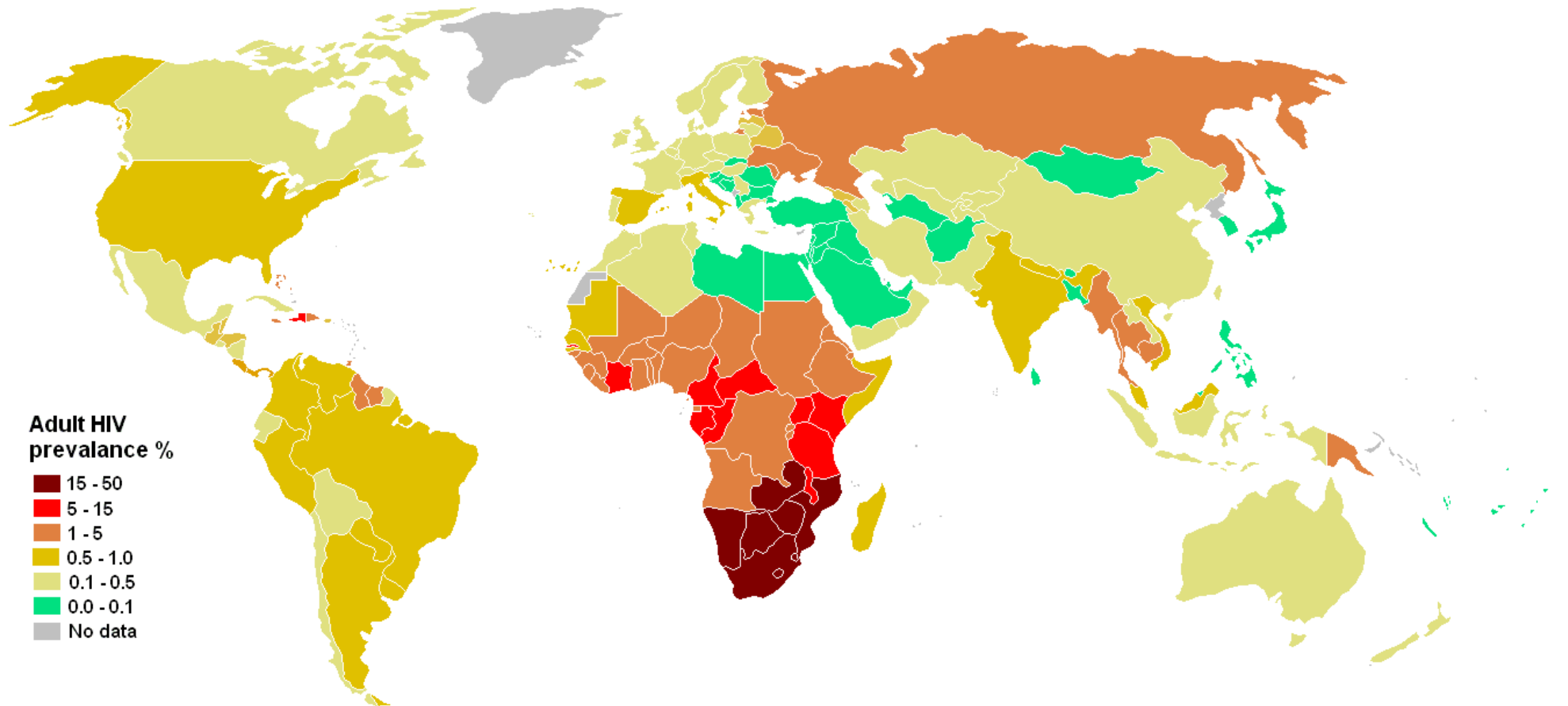




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HIV Prevalence 2007





Incidence of co-infection, local data

- Between April 2001 and December 2002, 770 diagnoses of infectious syphilis had been reported (690 males, 80 females) since the introduction of the London surveillance programme. Enhanced surveillance extended to the rest of England in June 2002
- Of these cases, 81% were amongst men who have sex with men
- Over 50% of syphilis cases reported among men who have sex with men in London were among individuals co-infected with HIV.
- In 2004 alone, 845 new diagnosis of syphilis in London, 732 in men and 113 in females



Data from Up North

- Total of 414 cases of syphilis were diagnosed in Manchester between 1999 and 2002, with 93% of cases being in men: 83% of cases were amongst Gay men.
- A sexually transmitted infection other than syphilis was detected in 30% of these individuals and 37% of Gay men with syphilis were also HIV-positive.
- Unprotected oral sex was identified as the key transmission route, and although 61% of men said they knew oral sex without a condom risked syphilis transmission, only 7% using condoms for oral sex.
- *The irony is that people practising a form of safer sex (i.e. oral sex) to reduce HIV transmission, are proving vulnerable to infection by syphilis.*



Data from the near-abroad

- The number of syphilis cases in the French city of Lyon increased from zero to 28 in 2002. The majority of cases, (18), involved HIV-positive individuals.
- Between March 2000 and October 2001, 182 cases of infectious syphilis were diagnosed in Dublin. The overwhelming majority (92%) of cases occurred among Gay or bisexual men. Of these, 23 were known to be HIV-positive.
- In the following six months, 15 Dublin patients were co-diagnosed with early infectious syphilis and HIV. These patients had a documented negative HIV test in the previous 1 month to 3 years



Data from further afield

- Amongst women working in the vicinity of Tanzanian gold mines in 2003, 42% were HIV positive and 24% had infectious syphilis. Syphilis was thought to be an important co-factor in HIV transmission.
- In 2000, an estimated 545 new cases of HIV infection among African Americans could be attributed to infectious syphilis, at a cost of about \$113 million.
- In Germany in 1996, a large multi-centre study looked at active syphilis in HIV infection. Syphilis was found in 151 of 11,368 people living with HIV, a low rate of 1.33%. Of the 151 people with co-infection, 93% were male of whom 76% were gay or bisexual



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Vital questions

- Does syphilis modify the risks of acquiring or transmitting HIV?
- Does co-infection with HIV modify the natural course, clinical signs or laboratory findings for syphilis?
- Do current regimes for treating syphilis prove sufficient, if there is co-infection with HIV?



Some answers... the effect of syphilis on HIV

- There appears to be evidence that there is a close association with a previous history of syphilis and the risk of contracting HIV
- If a patient has a reactive syphilis serology and/or a history of genital ulceration, there is an increased likelihood of contracting HIV
- The presence of an untreated sexually transmitted infection can increase the risk of contracting HIV by between two and fivefold
- Syphilis infection has been associated with a significant increase in the plasma viral load and a marked decrease in CD4 cell counts in HIV-infected men



HIV impact on syphilis screening

- The presence of HIV increases the chance of a false positive result when being screened for syphilis.
- The number of people having a false positive or rising rapid plasma reagin (RPR) results for syphilis, increases from 0.2%-0.8% to 1%-5.8% in cases where HIV is present
- Very rarely the presence of HIV can lead to a false negative RPR

Syphilis Stages and Time Line

Primary Stage

Contract Disease

90 days
(average 3 weeks)

Painless sore or ulcer called a chancre appears. This chancre contains a clear fluid that is full of syphilis-causing bacteria making you highly contagious. The chancre will heal even without treatment within a few weeks.

Some move directly from Primary to Secondary Stages

Secondary Stage

Indicates Contagious Period

Secondary symptoms can include multiple sores on the penis, anus or around the mouth, a copper-colored rash on the trunk of the body, or larger spots on the palms of the hands and the soles of the feet, hair loss, white patches on your tongue or multiple wart-like growths called condylomata lata. All of these symptoms will go away on their own without treatment within a few weeks.

Occurs over the next 10 - 20 years

Tertiary Stage

Usually one month later

If untreated, 1/3 of those infected with syphilis progress to tertiary syphilis. Although no longer contagious, the disease can prove lethal. Syphilis commonly attacks the brain and spinal cord (neurosyphilis), leading to blindness, paralysis, and insanity, or the heart and major blood vessels in the chest (cardiovascular syphilis) leading to heart failure, aortic aneurysm, and death.

Latent Stage

After the chancre heals, usually you will go through a short period of time when you don't have any symptoms

If you were infected with syphilis in the past year and do not have symptoms, you will be diagnosed with early latent syphilis

If you were infected with syphilis more than a year ago and do not have symptoms, you will be diagnosed with late latent syphilis.



How HIV effects clinical presentation of syphilis? 1

- Effects are related to the level of immunosuppression
- In primary syphilis the chancres can be multiple and extensive. Unlike classic presentations of syphilis, these chancres can be painful.
- The rash of secondary syphilis can be severe, with ulceration and keratoderma, leading to the description “malignant syphilis”



How HIV effects clinical presentation of syphilis? 2

- There is a greater chance of neurosyphilis
- More chance of ocular involvement
- Gummateous syphilis more likely
- An increased possibility of syphilitic aortitis
- *Although information is inconclusive, there is a chance that in treated syphilis, the treponemes may reactivate as immunosuppression progresses*



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Potential pitfalls

- Some treponemes persist even after effective treatment. They can be found in the CSF, fibroblasts and lymph nodes. Thus syphilis might be clinically cured but still present microbiologically
- If a patient with co-infection starts to become resistant to successive HAART regimes, if their immune system deteriorates further, will syphilis reactivate?



Treating syphilis in cases of co-infection 1

- Different opinions as to how primary syphilis with HIV co-infection should be treated. Some centres treat in the same manner as “ordinary” primary syphilis.
- E.g. Benzathine 2.4 megunits stat 1.M.Or Procaine Penicillin 600,000 MIU x 10 If there is a penicillin allergy, then doxycycline 100 mgs BD 10 days





Treating syphilis in cases of co-infection 2

- A trend towards treating all cases of primary syphilis where there is co-infection, with the same more intensive regimes, used to treat neurosyphilis in cases where there is no co-infection. E.g.
- Procaine penicillin 2 gm IM OD - 17 days + Probenecid 500 mg QDS - 17 days or Doxycycline 200 mg BD 28 days if penicillin allergy or refusal to have IM RX.



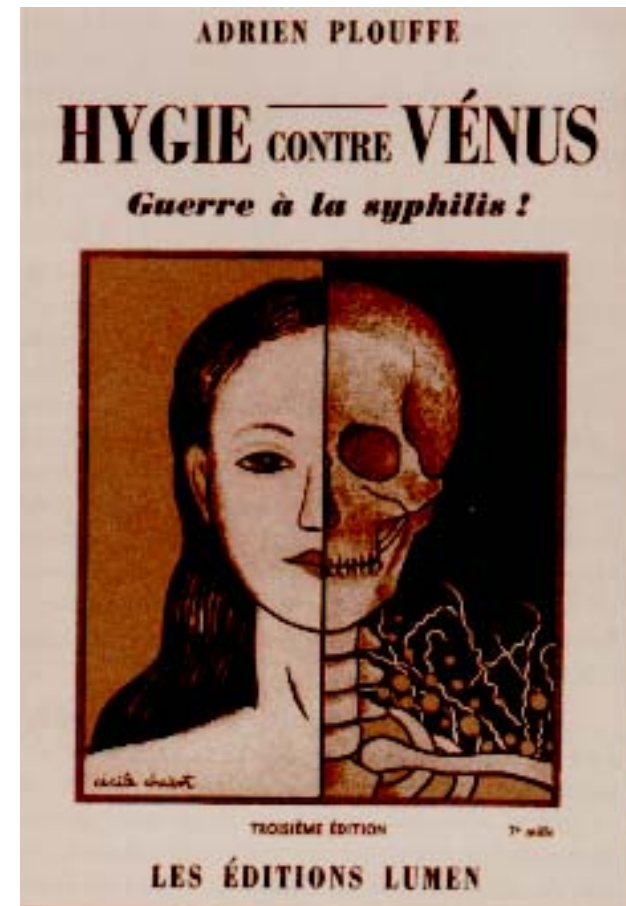


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Treating secondary syphilis when there is co-infection

- The same as when there is no co-infection. E.g.
- Procaine Penicillin
IM 600 mg
(600,000 U) x 17
days





Vertical transmission issues in co-infection

- Half a million babies die of syphilis each year in sub-Saharan Africa alone. The figure rivals that of HIV amongst neonates
- In developing countries with a high prevalence of HIV, a mother if lucky, may be treated with drugs worth hundreds of dollars in order to prevent the transmission of HIV to the child
-*only to see the child die some weeks after birth of syphilis, as there has been no attempt to screen and treat for the disease.*
- In the near future screening tests that cost less than 50 cents will become readily available – if political will and funding is available



Treating in Pregnancy

- Prognosis of *treated* babies not affected by co-infection is relatively good
- Benzathine 2.4 megaunits IM Stat or Procaine Penicillin 600,000MIU x 10
- If there is a penicillin allergy, then erythromycin may be used, but it doesn't readily cross the placental barrier. Thus the baby will need to be considered to have untreated congenital syphilis.
- Ceftriaxone is being considered as an alternative treatment in pregnancy when there is penicillin allergy



Congenital syphilis 1

- Untreated or inadequately treated syphilis in pregnant women can lead to congenital infection, prematurity, or perinatal death.
- Necrotizing funisitis – the umbilical cord has a characteristic appearance, with red and blue "barber pole" stripes. This permits the presumptive diagnosis of congenital syphilis at the time of birth.
- Of infants born to mothers with primary or secondary syphilis, up to 50% will be premature, stillborn, or die in the neonatal period, with most of the remainder developing signs of congenital disease





Congenital syphilis 2

- Most infants born with congenital syphilis are free of clinical symptoms at the time of birth, the problem may not appear for more than 2 years.
- Congenital disease has been divided into 2 categories:
 - early (occurring within the first 2 years of life) most often within the first 3 to 7 weeks after birth
 - late (recognized 2 or more years after birth).





Treating congenital syphilis

- Despite appropriate treatment, as many as 14% of women with infected fetuses will have a foetal death or deliver infected infants.
- If the baby is under 1 month of age, then treatment for congenital syphilis is aqueous crystalline penicillin G, 100,000-150,000 U/kg/day. Administered as 50,000 U/kg dose IV every 12 hours for the first 7 days of life and every 8 hours thereafter for a total of 10 days.
- If over 1 month, then aqueous crystalline penicillin G, 200,000-300,000 U/kg/day IV administered as 50,000 units every 4-6 hours for 10 days.



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Neurosyphilis is more problematical when there is co-infection

- Diagnosing neurosyphilis is harder as even without the presence of syphilis 40-60% of people with HIV may have CSF abnormalities such as elevated protein levels
- Where there is co-infection, there is a greater chance of the patient developing syphilitic meningitis
- More chance of treatment failure on standard regimes – modified treatment required



Neurological complications in case of co-infection

- HIV positive patients who manifest neurological complications of syphilis (neurosyphilis) are less likely to clear *T. pallidum*.
- 31% of patients with neurosyphilis fail to respond to benzathine penicillin.
- Subclinical abnormalities in the cerebro-spinal fluid (CSF) are seen in 70-80 per cent of primary syphilis cases, and *T. pallidum* establishes a chronic infection of the central nervous system (CNS) in 25 per cent of cases.



Treating Neurosyphilis in cases of co-infection

- The only sure diagnosis hitherto has been to perform a lumbar puncture to look for leukocytes indicating infection in the CSF. Many patients decline this invasive procedure.
- The US Centre For Disease Control (CDC) recommends aqueous crystalline penicillin G 2 -4 million units IV every four hours for 10-14 days in cases of co-infection
- An alternate used in the UK is Procaine penicillin 2 gm OD - 17 days + Probenecid 500 mg QDS for 17 days, or Doxycycline 200 mg BD 28 days + Prednisolone 20 mg OD - 3 days



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Implications for partner notification.

- GUM departments have a duty to ensure that cycles of sexual infection and re-infection are closed.
- The sexual partners of those index patients who attend should be notified, (preferably by the index patient) screened and if required treated
- What about in cases of co-infection? Should the same process be implemented?



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This lecture can be found at -

- <http://www.staff.city.ac.uk/m.j.jones>



Resources

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