

## Syphilis: old problem, new strategy

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Syphilis is on the increase again. Lorraine Doherty and colleagues report on four recent localised outbreaks and recall the features of infectious syphilis, its treatment, and the public health measures needed to contain it

Infectious syphilis is a disease of considerable public health importance, with overwhelming health effects if it is not treated. These include cardiovascular and neurological disease and adverse pregnancy outcomes, such as stillbirth and congenital syphilis. Further, concurrent infection with syphilis can facilitate transmission of HIV.<sup>1</sup> Syphilis is most infectious through sexual contact during the primary or secondary stages (see box 1), but transmission can also occur during the early latent stage.<sup>2</sup> Syphilis is preventable, and treatable with effective and inexpensive antibiotics. The possible resurgence of infectious syphilis, a disease previously believed to be close to eradication, is a matter of increasing global concern.<sup>3-6</sup>

This article outlines recent changes in the epidemiology of infectious syphilis in England, including the features of a number of outbreaks. It aims to increase health professionals' awareness of the clinical features of infectious syphilis, and to consider approaches to the investigation and control of syphilis and other outbreaks of sexually transmitted infection.

### Recent epidemiology of infectious syphilis in England

Between the 1960s and the late 1970s homosexually acquired syphilitic infection increased, in keeping with liberalisation of attitudes towards homosexual behaviour.<sup>7</sup> Changes in behaviour in response to HIV/AIDS, particularly among homosexual men, may have contributed to dramatic reductions in syphilis in the 1980s. During the 1990s, until 1998, the number of cases of infectious syphilis diagnosed remained stable among both sexes in England, but then more than doubled between 1998 and 2000 (from 172 to 372) in men and rose by 53% (102 to 156) in women (figure).<sup>8</sup> In 2000, 48% of syphilis infections in men were homosexually acquired, rates being highest in London (men 2.9/100 000; women 0.8/100 000) and in north west England (men 2.0/100 000; women 0.2/100 000) regions. The increases that have been observed over recent years are largely due to several localised outbreaks.

### Summary points

Untreated infectious syphilis may have a number of very serious health effects

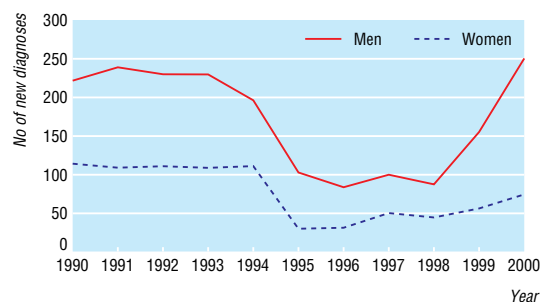
Recently there has been an upward trend in incidence, partly due to several localised outbreaks affecting homosexual men and heterosexual men and women

These outbreaks have emphasised the importance of investigating wider sexual networks as well as tracing individual contacts to identify further cases and prevent further spread

The general public, certain groups at risk, and relevant health professionals should be aware of the risks of acquiring syphilis and the symptoms and signs of acute infection

### Outbreaks in England 1997-2000

Between 1997 and 2000 four outbreaks of infectious syphilis in different areas of England were investigated by a number of departments of genitourinary medicine and of public health in collaboration with the Public Health Laboratory Service Communicable Disease Surveillance Centre.<sup>9-14</sup> They occurred in disparate geographic regions and social groups including



New cases of infectious syphilis in genitourinary medicine clinics in England, 1990-2000<sup>8</sup>

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BMJ 2002;325:153-6

Features of recent outbreaks of syphilis in England

Dates	Bristol	Manchester	Brighton	Peterborough and north Cambridgeshire
	Jan 1997 to May 1998	Feb 1999 to Jan 2002	Jun 1999 to June 2001	Jan 2000 to Jan 2002
No of cases	45	103	64	13
Men	19	100	61	5
Women	26	3	3	8
No (%) of cases in heterosexuals	45 (100)	7 (7)	8 (13)	12 (92)
No (%) of cases in homosexual men	0	96 (93)	56 (87)	1 (8)
No (%) of cases in homosexual men with HIV	0	33 (34)	18 (32)	0

both homosexual men and heterosexual men and women (table). Most patients had acquired their infection in the United Kingdom.

Investigations into the outbreaks showed a number of common features: infection from unprotected intercourse; cases linked to high risk social and sexual networks<sup>9 10 13 14</sup>; high rates of change of partners and of anonymous contacts; unprotected oral sex reported as the sole high risk sexual practice<sup>13</sup>; illicit drug use during sexual intercourse; and concomitant HIV infection.<sup>9 13</sup>

### Box 1: Clinical presentation and recommended treatment regimens for syphilis

#### Primary syphilis

Presents 9-90 days after exposure

One or more chancres (ulcers): "any anogenital ulcer is syphilis until proven otherwise"

Regional lymphadenopathy

#### Secondary syphilis

Presents 6 weeks to 6 months after exposure

Localised or diffuse mucocutaneous ulcers

Generalised lymphadenopathy

Rash may affect palms and soles, and may be itchy

Condylomata lata

Less commonly: alopecia, iritis, uveitis, meningitis, hepatitis, cranial nerve palsies, splenomegaly

#### Early latent syphilis

Presents no more than 2 years after exposure

Positive serology

By definition, there should be no clinical signs

#### Treatment for infectious syphilis (primary, secondary, or early latent)

Jenacillin A 3 ml=750 000 U

or procaine penicillin G 600 000 U intramuscularly daily for 10-14 days

or benzylpenicillin benzathine 2.4 MU intramuscularly weekly for two weeks

*Penicillin allergy:* doxycycline 200 mg twice daily for 14 days

*Parenteral treatment refused:* amoxicillin 500 mg four times a day plus

probenecid 500 mg four times a day for 14 days

#### Treatment for infectious syphilis in those who are HIV positive

Procaine penicillin 2 000 000 U (as 8 ml Jenacillin A = 2 MU)

intramuscularly for 17 days plus probenecid 500 mg four times a day by mouth for 17 days

or penicillin G 4 000 000 U intravenously 4 hourly for 17 days

or penicillin G 5 000 000 U intramuscularly 6 hourly plus probenecid 500 mg four times a day by mouth for 17 days

or second line doxycycline 200 mg twice a day by mouth for 28 days

Jenacillin A is a German proprietary combination of benzylpenicillin and procaine penicillin. Note that procaine penicillin is no longer available

### Clinical features of cases

Patients presented to a variety of health professionals, mainly general practitioners and dermatologists. Clinical presentations of infectious syphilis ranged from asymptomatic disease to overt genital ulceration—sometimes misdiagnosed as genital herpes; oral ulceration was seen in several cases. Overall, a third of cases presented with primary syphilis; more than a third presented with symptoms of secondary syphilis, such as fever, malaise, and pharyngitis, and with skin rashes and lymphadenopathy as well as less common problems such as iritis and uveitis; and the remainder were diagnosed as early latent syphilis on the basis of positive serology in the absence of clinical signs. A case of congenital syphilis was linked to one of the outbreaks.<sup>14</sup> A number of patients had concomitant HIV infection.

### Investigation and control

Similar methods were used in the investigation and control of all the outbreaks. These included enhanced surveillance of patients with syphilis at genitourinary medicine clinics; partner notification; increased efforts to raise awareness; communication with health professionals including general practitioners; increased level of genitourinary medicine services; targeted promotion of sexual health to "at risk" groups, including specific work with homosexual men.<sup>12</sup> The importance of identifying and investigating sexual networks and of involving local voluntary agencies in delivery of targeted promotion of sexual health was emphasised.

Enhanced surveillance of infectious syphilis (where additional demographic, behavioural, and clinical information is collected on each patient and also on their sexual partners identified through the partner notification procedures) was started in genitourinary medicine clinics in affected areas. This was facilitated by the use of a standardised questionnaire, developed by the Communicable Disease Surveillance Centre, which covered the patient's characteristics, sexual orientation, clinical details, history of previous or current sexually transmitted infection, and contact history.

### Diagnosis of syphilis

A good sexual history is essential to determine whether individual patients have been at risk of acquiring syphilis or may be infected. The infectious stages of syphilis and their clinical presentation and current guidelines for effective treatment are summarised in box 1. A diagnosis of syphilis may be suspected on the basis of clinical symptoms as outlined in box 1. In

genitourinary medicine clinics, diagnosis may be made by finding *Treponema pallidum* in material from syphilitic lesions by dark field microscopy.<sup>15</sup> The mainstay of diagnosis is serological testing; detailed guidance is available on this, including a testing algorithm.<sup>2</sup>

## Public health implications of increases in transmission of syphilis

### Impact on health

Recent increases in the incidence of infectious syphilis in England are of public health concern. The case of congenital syphilis linked to one of the recent outbreaks<sup>16</sup> emphasises the serious consequences of untreated syphilis in infected adults and children. Syphilis has disproportionate effects on vulnerable or disadvantaged populations and on people involved in high risk activities such as illicit drug use, sex work, unprotected intercourse, and sex with multiple partners.<sup>15</sup> Failure to intervene early to prevent the spread of infection in these communities may perpetuate and worsen existing health inequalities.

Outbreaks of syphilis in a community may be due to altered immunity, changes in sexual behaviour, the level and effectiveness of intervention, or random fluctuations in composition of the population.<sup>17</sup> In each of the outbreaks we mention here infection was acquired by unprotected sexual intercourse. Although the sexual behaviours of people who attend genitourinary medicine clinics are not necessarily representative of those of the general population,<sup>18</sup> these outbreaks indicate that unsafe sexual behaviour continues among both the heterosexual and homosexual populations in England. This is further substantiated by the documented rise in other sexually transmitted infections<sup>8</sup> and evidence from other studies of high risk sexual behaviour among homosexual men.<sup>19, 20</sup> The failure of sections of the sexually active heterosexual and homosexual populations to protect themselves against sexually transmitted infections is worrying and indicates either lack of knowledge about transmission risks or complacency about individual risk of acquiring a sexually transmitted infection. Some patients in these outbreaks had concurrent HIV infection, which they would be at risk of transmitting if they engage in unprotected intercourse.<sup>13</sup>

### Implications for clinical practice

Increased awareness of the risks of acquiring syphilis and of the symptoms and signs of acute infection among the general public, certain at risk groups, and relevant health professionals is needed (box 2). Few general practitioners will have dealt with a case of infectious syphilis, but they need to consider the diagnosis in appropriate patients presenting with vague symptoms. Doctors should promptly refer suspected cases to genitourinary medicine services. Genitourinary services should be provided at an appropriate level to allow prompt investigation, diagnosis, and treatment of patients. All patients with a new diagnosis of a sexually transmitted infection, or ongoing sexual behaviour which puts them at risk of acquiring a sexually transmitted infection, should be offered testing for syphilis. Treatment of infectious syphilis should follow the most recent guidelines.<sup>15</sup> All patients with

### Box 2: Key messages for health professionals

- “Safer sex” messages need continual reinforcement among the sexually active population
- Unprotected oral sex is a risk factor for transmission of sexually transmitted infections, including syphilis
- Healthcare professionals, particularly general practitioners, should make themselves aware of the symptoms and signs of infectious syphilis
- General practitioners should refer patients suspected of having syphilis to specialist genitourinary medicine services for investigation and treatment

confirmed syphilis should be encouraged to have an HIV test, as a positive result will alter the dosage and duration of treatment, and require lifelong annual follow up. Patients with HIV infection should be routinely tested for syphilis every six months.

In two of the recent outbreaks of syphilis oral sex was associated with transmission of syphilis in homosexual men.<sup>13</sup> The evidence for an association between oral sex and transmission of non-viral sexual infections is documented and implicates oroanogenital sex as a route of transmission of syphilis among men.<sup>21</sup> This evidence, and that produced recently in relation to transmission of HIV associated with oral sex,<sup>22</sup> will require health professionals and others to promote use of condoms by those having oral sex with unknown partners or with those who may have been at risk of sexual infection.

### Investigation and control of outbreaks of sexually transmitted infections

The investigation of these outbreaks of syphilis highlighted a number of methods of identification, investigation, and control specific to an outbreak of sexually transmitted infection. These have informed the development by the Communicable Disease Surveillance Centre of an outline plan for outbreaks of sexually transmitted infections; this has been consulted upon and is currently being updated.<sup>23</sup>

Outbreaks of sexually transmitted disease are difficult to detect, and the genitourinary medicine consultant may be the first to recognise the problem. The timescales within which such outbreaks may be detected, investigated, and controlled may be longer than those for other outbreaks. Investigations of outbreaks of infectious disease are usually led by the local consultant in communicable disease control, but outbreaks of sexually transmitted disease may require different ways of working. Each of the outbreaks of syphilis to which we refer involved a collaborative approach between local genitourinary medicine and public health professionals and their colleagues at the communicable disease surveillance centre at Colindale.

Notification of partners is essential in identifying and treating infected people involved in outbreaks of syphilis.<sup>24</sup> Control of such outbreaks requires complementary strategies, however, in particular the investigation of wider sexual and social networks in addition to tracing of individual sexual contacts. The effectiveness of this approach has been described<sup>25</sup> and observed during investigations of outbreaks elsewhere.<sup>26</sup> Sexual health advisers at genitourinary medicine clinics and

### Box 3: Control of outbreaks of sexually transmitted infections

#### Finding and treating additional cases (secondary prevention)

- Improve access to genitourinary clinic services (including screening and treatment for sexual infections)
- Partner notification to identify sexual contacts at risk
- Publicity campaigns to encourage those at risk to come forward for screening
- Alerting local practitioners (both general practitioners and genitourinary medicine specialists) to improve case detection
- Screening in venues where sexual disease transmission is likely to take place
- Analysis of social and sexual networks

#### Modifying risky sexual behaviours

- General health promotion campaigns—for example, campaigns on awareness of sexual infections and safer sex
- Health promotion campaigns targeted at those at greatest risk
- Targeted outreach work in affected communities by voluntary organisations and health professionals

sexual health promotion professionals are the key in this regard. Interventions used in outbreaks of syphilis and other sexual infections need to be tailored to the needs of the community affected, and they need to be delivered by a range of professionals and community based voluntary organisations. Useful interventions in the control of outbreaks of syphilis or other sexual diseases are summarised in box 3.

### Conclusions

The occurrence of outbreaks of infectious syphilis in England and elsewhere highlights the importance of sustained multidisciplinary public health action in this area.<sup>27</sup> The practice of screening all pregnant women for syphilis in every pregnancy should continue.<sup>28</sup> Clinicians need to be alert to the possibility of patients presenting with syphilis. Regional and national surveillance systems are required to identify increases in incidence of syphilis. Public health and genitourinary medicine professionals need to be given adequate resources to enable them to undertake local investigation and management of acute incidents or outbreaks of sexually transmitted infection.

Funding: None.

Competing interests: None declared.

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(Accepted 15 January 2002)

### Endpiece

#### An Osler aphorism

So long as we have human beings as house officers, ordinary mortals for medical students and modified angels for nurses, we shall have typhoid contagion from one patient to another in the wards of our hospitals.

Sir William Osler.

No 18 of *Collected Aphorisms*

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