



## Poems, Paintings and Penile Chancres

Tony Worthington talks about Syphilis:  
a maddening disease with history

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**S**YPHILIS, a potentially fatal sexually transmitted disease (STD) caused by the spirochaete *Treponema pallidum* (fig.1), once caused widespread epidemics and continues to remain a major cause of morbidity and mortality worldwide. Once called 'the great imitator' as the signs and symptoms of infection are indistinguishable from many other diseases, syphilis has been with mankind for hundreds, possibly thousands, of years and its origins remain an issue of some debate.

Throughout history, syphilis has been famously portrayed in art and literature and indeed, many renowned names have fallen victim to 'the pox'. Following the sharp decline in the number of cases of syphilis in 1958 after the widespread use of penicillin, levels have fluctuated periodically and have usually been correlated with behavioural changes and

educational campaigns. In 1998, advances in molecular research allowed for complete sequencing of the genome of *T. pallidum*, which will allow for a better understanding of the microorganism, potentially leading to improved diagnosis and treatment of infection. However, in contrast to these recent scientific advances, resurgence in unsafe sexual practices, has led to a recent increase in the number of new cases of syphilis and other STDs. And so the story continues...

### The Origins of Syphilis

*"A mysterious epidemic, hitherto unknown, which struck terror into all hearts by the rapidity of its spread, the ravages it made, and the apparent helplessness of the physicians to cure it."* These were the words used by Sir William Osler (1849-1919), 'the father of modern medicine' and distinguished physician who ended his career as the Regius Chair in

Medicine at Oxford University, to describe the sudden appearance of syphilis in the early sixteenth century. Although the sixteenth century is widely documented in literature to be the era when syphilis caused havoc amongst the sexually privileged, the actual origins of the disease remain a subject of much debate. There are currently three theories related to the origins of syphilis: pre-Columbian, Columbian and evolutionary<sup>1</sup>. The pre-Columbian school of thought believes that the origins of syphilis existed in the Old World before Columbus' discovery of America. Evidence for this theory resides as far back as 600 BC where the tertiary form of the disease appears to be noted in the early writings of Hippocrates in Classical Greece. Further evidence to support this has been found at the site of a fourteenth century Augustian friary in the port of Kingston upon Hull,

which provided palliative care and burial rites for "wretched souls". The bones of approximately two-thirds of the skeletons subsequently discovered at the friary were shown to have lesions highly characteristic of tertiary syphilis<sup>2</sup>.

The Columbian school of thought deems that syphilis arrived from the New World; brought back by Christopher Columbus and his promiscuous crew during their first voyage. Evidence for this theory lies in the finding of bone relics with indications of syphilitic damage throughout the Americas and a lack of paleopathological documentation that syphilis was present in the Old World. Further circumstantial evidence is based upon the fact that several of Columbus' crew joined the army of the French King, Charles VIII, which conquered Naples in 1495; the region where syphilis (or as it was subsequently phrased *Morbus*

# the arms of nus...



Figure 1. *Treponema pallidum* (Darkground Microscopy)

*Gallicus* - the French Disease) first reached epidemic proportions. It is also believed by supporters of this theory that the European spread of syphilis is due to the sexual activities of Charles's large corps of mercenary soldiers, who, upon demobilisation, returned to their homes throughout Europe<sup>2</sup>.

A more recent approach is the evolutionary theory which states that a single microorganism responds to changes in environmental temperature and evolves to form distinct species and subspecies located in different geographical areas throughout the world. This may account for the distinct species of *Treponema* and sub species of *T. Pallidum*, being distributed worldwide. This theory is further supported by research which has demonstrated that experimental syphilis in rabbits can be modified by altering the environmental temperature. In addition, the

recent discovery of a syphilitic skeleton from between 1296 and 1445 in Rivenhall, near Chelmsford further casts doubt over the Columbian school of thought as this finding suggests that syphilis was already present in England before Columbus discovered the new world in 1492<sup>3,4</sup>. *Bones are the memory chips of the body, surviving to tell the tale once everything else has disappeared...* And so the debate continues...

### Syphilis in Art and Literature

Throughout history, syphilis has been frequently portrayed in Art and Literature by many famous names. However the word 'syphilis,' was first introduced into our language in 1530 in a poem by Girolamo Fracastoro, one of the greatest physicians and poets of his generation. Fracastoro could not resolve the origins of syphilis nor indeed identify the venereal

mode of transmission of the disease therefore he wrote a poem entitled '*Syphilis, sive Morbus Gallicus*' and devised a myth, giving the name syphilis to a fictional shepherd. The poem describes how *Syphilus* ('pig lover'), a pastoral shepherd is stricken with syphilis, albeit somewhat harshly given the circumstances, for having 'offended' Apollo:

*A shepherd once (distrust not ancient fame)  
Possess these Downs, and Syphilus his Name;  
Some destin'd Head t'attone the Crimes of all,  
On Syphilus the dreadful Lot did fall.  
Through what adventures this unknown Disease  
So lately did astonisht Europe seize,  
Through Asian coasts and Libyan Cities ran,  
And from what Seeds the Malady began,  
Our Song shall tell: to Naples first it came  
From France, and justly*

*took from France his Name...*

Further historical references to syphilis can also be found in many plays, novels and paintings: in William Shakespeare's play *Measure for Measure* (1601-1606), Lucio refers to "thy hollow bones" — undoubtedly a reference to one of the side effects of mercury which was widely used to treat syphilis; in Voltaire's *Candide* (1759), Pangloss, Candide's mentor and teacher, participated in sexual jovialities with a maidservant and contracted syphilis which ravaged and deformed his body resulting in the loss of an ear and an eye; the Dutch artist Kees van Dongen (1877-1968) produced several illustrations for *Lassiette au Beurre*, an anarchist publication, which depicted the decline of a syphilis-riddled prostitute from poverty to death as a criticism of the social order at the end of the nineteenth century<sup>2</sup>. ▶



Figure 2. Penile chancre in primary syphilis

### Famous Syphilitics

*“And of course Mozart died of syphilis...because every great man dies of syphilis!”*

Faith Fitzgerald, internist and professor at University of California, Davis School of Medicine. Syphilis is no respecter of class, dignity or occupation and many ‘famous’ syphilitics have been documented throughout history. Although many of the diagnoses are made retrospectively from historical data and are therefore questionable, several syphilitics made reference to the disease in personal diaries. Famous documented syphilitics include; Christopher Columbus, King Charles VIII of France, Henry VIII and five wives, Pope Alexander VI, Ivan the Terrible, Voltaire, Wolfgang Amadeus Mozart, Ludwig van Beethoven; Abraham Lincoln, Charles Darwin, Edgar Allan Poe, Vincent van Gogh, Oscar Wilde, Adolf Hitler, and Al Capone to name just a few.

### Syphilis: Clinical Manifestations and Treatment

Syphilis, if untreated is a chronic disease which is characterized by three main stages; primary syphilis, secondary syphilis and tertiary syphilis which are summarized in table 1<sup>1</sup>.

#### Primary Syphilis

Approximately 30% of people who have unprotected sex with an infected partner will develop syphilis<sup>1</sup>. Following contact with the microorganism, the treponemes disseminate throughout the body, however, multiplication occurs predominantly at the point of contact, with the formation of a primary lesion or chancre (figure 2) within 10 to 90 days post contact. The chancre is oedematous, infiltrated with inflammatory cells and serous fluid from the lesion contains numerous treponemes. The patient may also experience lymphadenopathy during primary syphilis. The chancre heals spontaneously within 2-6 weeks.

#### Secondary syphilis

Non specific symptoms of secondary syphilis including fever, headache, sore throat and arthralgias occur approximately 1-5 weeks after the chancre has healed. However, the most characteristic signs of secondary syphilis include a

red maculopapular rash anywhere on the body (figure 3) and moist, pale papules (condylomata lata) in the anogenital region, axillas and mouth, and contain high numbers of treponemes. These symptoms resolve spontaneously within 2-6 weeks, but may recur within 3-5 years post infection if the patient is not treated. In approximately 30% of patients, early syphilitic infection progresses spontaneously to cure without treatment.

In a further 30%, the untreated infection remains latent and the patient is asymptomatic. Duration of infection <1year, which is asymptomatic, is defined as the early latent stage. As lesions are not usually present after the first year, the patient is considered non-infectious and this stage is defined as the late latent stage, however treponemes may still be passed from mother to fetus for up to 4 years post untreated infection (congenital syphilis). In the remaining



Figure 3 Macropapular rash in secondary syphilis

patients, syphilis progresses to the tertiary stage.

#### Tertiary syphilis

Tertiary syphilis is the most acute and destructive stage of the disease characterized by the destruction of tissue from a response to the presence of long-standing treponemal antigens with the development of granulomatous lesions (gummas) in skin, bone, viscera and the eye. The clinical-pathological manifestations are those of vasculitis and chronic inflammation. In cardiovascular syphilis, vasculitis involves the arteries leading to the formation of aortic aneurysms and aortic rupture. Degenerative changes in the central nervous system leading to neurosyphilis is a further complication of tertiary syphilis and may be due to direct invasion of the parenchyma by treponemes or by brain infarction due to vasculitis. Neurosyphilis may present in many forms depending upon the location of the lesions. Involvement of the dorsal columns of the spinal cord results in a loss of position sensation (tabes dorsalis) which may result in trauma to the knee and ankle joints (Charcot’s joint).

Generalised involvement of the brain leads to impaired motor function ( paresis), loss of integrative functions and personality changes. This clinical manifestation is

TABLE 1. Stages of syphilis infection (adapted from Larson et al., 1998)

Stage	Incubation period (post infection)	Clinical Manifestations	Affected site
Primary	10-90 days	Chancre, lymphadenopathy	Skin mucous membranes
Secondary	6 weeks - 6 months	Multiple lesions, lymphadenopathy, fever, condylomata lata	Skin/mucous membranes
		Alopecia	Hair/eyebrows
		CNS involvement (asymptomatic/ symptomatic)	Meninges
Latent	Early: ≤ 1 year Late: > 1 year	Asymptomatic	
Tertiary	Months/years	Gummatous lesion	Tissue
		Aortic aneurysm Tabes dorsalis, dementia, Optical atrophy	Aorta Meningovascular
			Eye

referred to as 'general paralysis of the insane'. A further sign of neurosyphilis is the 'Argyll-Robertson pupil', which is characterized by failure of the pupil to respond to light but reacts to near and distant objects.

#### Treatment of Syphilis

As early as the late fifteenth century mercury was used for the treatment for syphilis and its use gave rise to the saying 'a night in the arms of Venus leads to lifetime on Mercury'. Mercury, along with its associated side-effects, remained the choice of treatment for syphilis for more than three centuries even though it lacked efficacy in the treatment of the tertiary stage.

The development of potassium iodide followed as an important advancement in the treatment of syphilis as it proved effective in treatment of late stages of the disease. However, in 1908, Paul Ehrlich isolated compound 606 (arsphenamine) in an attempt to cure sleeping sickness, and whilst the compound proved to be ineffective in the cure of the disease, it did destroy *T. pallidum*. In 1910, compound 606 was termed Salvarsan and was heralded as the *magic bullet* in treatment of syphilis. However, treatment with salvarsan was both expensive and painful with severe side effects within 6-8 hours following administration. Furthermore, patients thought to be cured of syphilis soon relapsed.

Physicians eventually discovered that treatment with salvarsan had to be supplemented by applications of mercury or bismuth ointments. In 1939, the most effective treatment of early syphilis consisted of alternating eight to twelve week courses of bismuth and salvarsan continuously for 60 weeks. Even then, this augmented treatment did not have ideal results<sup>5</sup>. In 1928,

the discovery of penicillin by Alexander Fleming was about to change the world of modern medicine and by 1945, penicillin became accepted as the treatment of choice for syphilis, although optimal doses were not finalized until 1960. Today, resistance to penicillin and its derivatives has not yet been reported amongst *T. pallidum* and these antibiotics remain the gold standard for the successful treatment of syphilis<sup>6</sup>.

#### Syphilis in the Twenty-First Century: Science versus Sexual Behaviour

Major advances in molecular research have allowed for the genomes of many microorganisms to be sequenced providing the information necessary to fully understand the aetiology of infection. In 1998, scientists sequenced the complete genome of *T. pallidum*<sup>7</sup> generating a plethora of genetic information enabling scientists to enter the twenty-first century with the tools necessary to potentially eliminate a disease whose origins lie as far back as 600BC, if not before. The genetic map of *T. pallidum* identifies specific genes that are present or absent in the microorganism thus providing scientists with the crucial information necessary for the development of improved methods of treatment, diagnostic tests and also vaccines.

However, in sharp contrast to these recent scientific advancements, in 2001, for the first time in a decade, there was an increase in the numbers of cases of primary and secondary syphilis in bisexual and homosexual men in the USA<sup>8,9</sup>. Reported figures in 2001 reached 6,103 which increased a further 12.4% by 2002<sup>10</sup>. The nationwide increase in rates of syphilis and other STDs has been

associated with a resurgence of unsafe sexual practices. Of further concern, is the fact that syphilis increases the risk of transmitting human immunodeficiency virus (HIV) by 3 to 5 fold.

Worryingly, the rise in the number of cases of syphilis is also being seen in the UK. Between 2001 and 2003 the overall diagnoses of infectious syphilis rose by 67% in males and 33% in females<sup>11</sup>. In 2002, 1,163 new diagnoses of primary and secondary syphilis were made in Genitourinary medicine clinics in England, Wales and Northern Ireland.

The increase in syphilis in the UK is punctuated by a series of outbreaks occurring in high incidence areas including Manchester, London, Bristol, Newcastle Nottingham and Northern Ireland.

#### Conclusions

There is no doubt that syphilis has made its mark as one of the major infectious diseases in history, and whilst

it has been poetically captured in verse and colourfully portrayed in paintings, it remains the third most frequently sexually transmitted infectious disease worldwide today. Whilst recent advancements in science may potentially pave the way for reducing the global incidence of the disease, this must be concurrent with changes in sexual practice, particularly amongst high risk groups. Continued worldwide educational programmes promoting safer sexual behaviour are essential in helping to prevent the spread of STDs. Strategies need to include mass media campaigns, special awareness events (e.g. safer sex week), development of educational material, targeted community interventions and condom promotion.

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