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THE ORIGIN OF SYPHILIS — STILL CONTROVERSIAL?

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Summary: Syphilis is a sexually transmitted disease caused by spiral-shaped bacterium, *Treponema pallidum*. The disease has been known under many names during history, and has had a prominent role in history and literature for the last several hundred years. Since its recognition in 15th-century Europe as a new disease, syphilis has been the subject of great mystery and legend. There are three main theories. These are the Columbian theory, the Pre-Columbian theory and the Evolutionary theory. The Columbian theory is most accepted. Syphilis exists nowadays, the World Health Organization estimates that 12 million new cases of syphilis occur each year. While syphilis eradication seems a biologically plausible goal, the major political, cultural, and logistic difficulties involved make it unlikely. Regrettably, rather than become an infection of historical significance, syphilis in the era of HIV continues to challenge researchers and clinicians.

Key words: syphilis, history of medicine, sexually transmitted infection.

INTRODUCTION

The impact of emerging diseases on current medicine and society suggests there is value to understanding a disease that arose in Europe in the late 15th and early 16th centuries. Understanding how syphilis emerged, spread, and was “contained” by society may provide insights to fighting diseases such as AIDS today (1).

Syphilis is a chronic sexually transmitted infection caused by *Treponema pallidum* subspecies *pallidum*. Syphilis has many synonyms. These include ‘the Great Pox’, Lues, the Great Mimic, the Great Imitator and Morbus Gallicus.

Syphilis is a fascinating and perplexing infection, with protean clinical manifestations and both diagnostic and management ambiguities. It is usually transmitted sexually but congenital infections can occur and, in certain parts of the world, endemic nonvenereal disease due to *T. pallidum* exists (2).

The genus *Treponema* belongs to the order *Spirochaetales*, consisting of spiral-shaped pathogenic bacteria (Fig. 1). Other members of this order are the genera *Borrelia* and *Leptospira*. Apart from *T. pallidum* subspecies *pallidum*, the causative agent of venereal syphilis, other pathogenic treponemes that cause disease in humans include *T. pallidum* subspecies *pertenue*, the causative agent of yaws; *T. pallidum* subspecies *endemicum*, the causative agent of endemic syphilis; and *T. carateum*, the causative agent of pinta (3).

Controversy exists as to the historical origins of venereal syphilis.



Figure 1. Spiral shaped bacteria of the genus *Treponema*

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ORIGIN OF SYPHILIS

The origin and antiquity of syphilis are among the greatest historical and scientific questions in the history of medicine. Did Columbus and his crew bring syphilis from the New World to the Old World in 1493, as suggested by the timing of the first reported epidemic in Europe just years after their return? Or did syphilis originate in the Old World, simply going unrecognized until the early fifteenth century or, perhaps, noticeably increasing in prevalence or virulence at this time?

There is considerable controversy regarding the origin of syphilis. However, there are three main theories. These are the Columbian theory, the Pre-Columbian theory and the Evolutionary theory (4).

The commonly held belief is that syphilis, a gift of the New World to the Old, arrived in Spain with Columbus' sailors in 1493 (Fig. 2). A minority contend that syphilis occurred in Europe before the Christian era and that Augustus Caesar, the first Roman Emperor, had hereditary syphilis (5).

The troops of Charles VIII, King of France, who marched to Naples in 1493, were probably infected by soldiers of King Ferdinand of Naples, who had also hired mercenaries, among them soldiers from Barcelona in Spain. Many of the besieged gave up and succumbed to the French troops, who spread the disease on their way back north. Since 1495, the disease has appeared epidemically and spread explosively over the whole of Europe (6).

Why was virulence so high when syphilis first appeared? We can speculate that the syphilis spirochaete in the New World had evolved to an optimum virulence in a coevolving host population with a variety of resistance mechanisms. On introduction to a European host population with none of these mechanisms in place, the pathogen would have been 'released' from these constraints on virulence, and ironically was then more pathogenic than necessary to give the highest fitness (7).

Due to differences in climate, clothing, and sexual practices, Renaissance Europe would have represented a very different environment than that present in Hispaniola, the location of Columbus's first arrival in the New World. The bacterium responsible for treponemal disease, *Treponema pallidum*, would thus have encountered a very new set of selective pressures upon arrival in the Old World. Perhaps it was exposure to this novel host environment that resulted in the birth of the *T. pallidum* subspecies that causes syphilis (*T. pallidum* subsp. *pallidum*). Thus, in this modified Columbian hypothesis, Columbus and his crew could have transported a New World, nonvenereal treponemal infection to Europe upon their return, which, once there, could have responded to dramatically different selec-



Figure 2. Christopher Columbus (1451–1506)

tion pressures with a new sexual transmission strategy. Today, neither of the major competing hypotheses regarding the origin of syphilis assigns blame or makes moral judgments upon Native Americans, as was suggested by "The Syphilis Enigma" (8).

The Pre-Columbian theory implies that syphilis was present in Europe for several hundred years before Columbus first returned from the New World. It is based on the fact that European medical literature in the 1200–1300s describes clearly certain forms of 'leprosy' which were highly contagious and could be transmitted sexually and also from mother to child in-utero.

The Evolutionary/Unitarian theory is the least well known of the three main theories. The Evolutionary theory postulates that the different members of the genus *Treponema* evolved from a single organism responding to changes in the environment. The original disease was probably pinta, which was prevalent in Africa and Asia (4).

New data, instead of clarifying matters, contribute to an even more intricate scenario. For instance, osseous evidences of syphilis on pre-Columbian individuals from Europe, point against a New World origin of syphilis, while molecular data contradict the Unitarian hypothesis. Consequently, although the issue has been discussed for five centuries, the origin of syphilis is not yet clear (9).

It was soon recognized that different varieties of treponemal disease exist. Unlike syphilis, which is caused by the spirochete *T. pallidum* subspecies *pallidum*, the other types normally strike during childhood and are transmitted through skin-to-skin or oral contact. All are quite similar with regard to symptoms and progression, but endemic syphilis, or bejel, caused by subsp. *endemicum*, has historically affected people living in hot, arid climates and yaws, caused by subsp. *pertenue*, is limited to hot and humid areas. Pinta, caused by *Treponema carateum*, is the most distinct member of this family of diseases. Once found in Central and South America, this mild disease is characterized

solely by alterations in skin color. Today, the debate over the origin of treponemal disease encompasses arguments about whether the four infections are caused by distinct but related pathogens or one protean bacterium with many manifestations (10).

The early names for the new disease reflected its origin and included the Spanish disease, the Neapolitan itch (possibly coinfection with scabies), and the *morbis Gallicus*.

However, the name that was to become part of everyday language was syphilis, derived from the title of an epic Latin poem *Syphilis Sive Morbus Gallicus* (syphilis or the French disease) by Girolamo Fracastoro (1483–1553). This pastoral Latin poem became the most popular medical poem ever written and did much to spread knowledge of the disease across Europe.

In this poem, Syphilus, a shepherd boy who lives in the time of King Acithous of Haiti, loses his sheep because of a drought. He blames the sun god and propagates to render homage to King Acithous, rather than the sun god. The sun god took revenge by sending a plague of a dreadful disease to Haiti, and Syphilus was the very first victim (11).

CLINICAL STAGES OF SYPHILIS

Syphilis is a chronic, multistage disease with diverse and wide-ranging manifestations.

The French venereologist Philippe Ricord differentiated syphilis from gonorrhea through a series of experimental inoculations from syphilitic chancres. He also identified primary, secondary, and tertiary stages of the infection in a monograph in 1838 (*Traite des maladies veneriennes*) (12).

Syphilis, caused by the spirochaete *Treponema pallidum*, occurs in three stages. Primary syphilis is characterized by an indurated ulcer at the point of infection (the ‘chancre’). This is followed by secondary syphilis, typically involving fever, a sore throat and a rash, but other symptoms may occur. Finally, tertiary syphilis occurs after a latent period that usually lasts for many years and has the most severe symptoms. These include the ‘gummas’ or gummy tumours formed in virtually any body tissue, and neurological damage sometimes leading to insanity (13).

PHYLOGENETIC APPROACH

Because of the paucity of samples available for experiments, most comparative studies have included very few non-venereal strains.

The *T. pallidum* genome is small (roughly 1,000 kilobases) and was sequenced in 1998. However, comparative genetic studies of *T. pallidum* have been rare

and relatively small in scope. One reason for this is the difficulty in obtaining nonvenereal strains for study. Today only five known laboratory strains of subsp. *pertenue*, two strains of subsp. *endemicum*, and no strains or samples of *T. carateum* survive. Furthermore, it is uncertain whether the disease pinta still exists. No cases have been reported to the World Health Organization from the former endemic countries Mexico or Colombia since 1979. Similarly, endemic syphilis was eradicated some time ago in its European focus, Bosnia. In Turkey, only one infected family has been reported in the last forty years, and a large survey in the United Arab Emirates revealed only non-active cases of endemic syphilis in the elderly. In the Old World, yaws is still reported but appears limited to a few isolated foci in the Republic of Congo and the Democratic Republic of Congo, as well as Indonesia (10).

Another limitation on comparative studies has been the small amount of variation present in the *T. pallidum* genome. It is possible that most polymorphism in the *T. pallidum* genome may be concentrated in genes with limited phylogenetic informativeness (10).

SYPHILIS AMONG FAMOUS DURING HISTORY

Infectious diseases have led to illness and death for many famous. Venereal disease has been no respecter of persons and many notable figures have been afflicted in the past. Royal personages and politicians have enjoyed no immunity, and poets, musicians, writers, and artists longing for new experiences to inspire new works have ultimately had to face reality and publicity when complications arose in the form of stricture, tabes, insanity, or blindness with the whole world aware of their misfortunes (14).

During history, many famous persons, like political figures (King Charles VIII, Queen Mary I, Catherine the Great, Paul I, Vladimir Lenin), musicians (Mozart, Beethoven, Paganini, Schubert, Schumann, Smetana) and literary greats (Oscar Wilde, William Shakespeare) suffered of syphilis (15). Soldiers and sailors with their extensive leisure and changing domiciles have always seemed to stray, but as they are expected to do so they have generally received adequate treatment with a better prospect of avoiding painful late consequences than is the case for civilians (14).

CONCLUSION

Syphilis is a reemerging disease burden. Although it has been studied for five centuries, its origin and spread is still controversial. Did it accompany the evolution of the genus *Homo* and does it date back to more

than a million years or did it emerge only after Columbus's return to Europe?

Syphilis exist nowadays, the World Health Organization estimates that 12 million new cases of syphilis occur each year (16). While syphilis eradication seems

a biologically plausible goal, the major political, cultural, and logistic difficulties involved make it unlikely. Regrettably, rather than become an infection of historical significance, syphilis in the era of HIV continues to challenge researchers and clinicians.

Sažetak

POREKLO SIFILISA — JOŠ UVEK SPORNO?

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Sifilis je seksualno prenosiva infekcija koju izaziva bakterija spiralnog oblika, *Treponema pallidum*. Bolest se javljala pod različitim nazivima u prošlosti, i imala značajno mesto u istoriji i literaturi tokom poslednjih nekoliko stotina godina. Od pojave prvih slučajeva sifilisa u XV veku u Evropi, ova bolest je tokom prošlosti bila predmet mnogih misterija i legendi. Postoje tri teorije o poreklu ove bolesti — tzv. „Kolumbova teorija“, tzv. „Pre-Kolumbova teorija“ i tzv. „Evolutivna“ teorija. „Kolumbova teorija“ je najšire prihva-

ćena. Sifilis postoji i danas, i Svetska Zdravstvena Organizacija reportuje oko 12 miliona novih slučajeva sifilisa godišnje. Iako je eradikacija sifilisa biološki moguća, političke, kulturne i logističke teškoće je otežavaju i čine manje verovatnom. Na žalost, umesto da bude polno prenosiva infekcija od istorijskog značaja, sifilis još uvek, naročito u eri HIV infekcije, nastavlja da prkosi istraživačima i lekarima.

Cljučne reči: sifilis, istorija medicine, seksualno prenosiva infekcija.

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