

The Rise and Fall of Syphilis in Renaissance Europe

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Abstract The rapid changes that syphilis underwent after the first major outbreak that occurred in Naples in the mid-1490s are believed to constitute the first well-documented example of a human disease. The new plague was of exceptional virulence, highly contagious and causing severe ulceration at the site of infection. According to medical and other historical sources, the ‘genius epidemics’ changed some years after this onset, and a slower-progressing form of syphilis seems to have replaced the initial severe form, as do many virulent epidemic infectious diseases that appear in devastating forms in a previously uninfected population. But what exactly were the features of the disease at the moment of its appearance in Europe at the end of the fifteenth century? How many years did it take for the early, virulent form to be replaced and become endemic? What was the pace of these changes through the decades following the onset of the epidemic? In this essay, I review these issues through an analysis of a large number of chronologically-ordered primary historical sources.

Keywords Syphilis · Venereal diseases · History · Renaissance Europe · Medical knowledge

Introduction

In the heated controversy on the origin of syphilis, there are two points on which the partisans of the various theories agree: syphilis first appeared in Naples in its epidemic form in 1495, and after several years, the severity of the symptoms began to abate. However, with regards to this, we have only second-hand information reiterated over the centuries by syphilographers and historians of medicine. What is missing is an accurate, chronologically-ordered review of first-hand testimonies. In fact, as one moves further away in time from when the changes were recorded by contemporaries, the information on the early

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symptoms and the evolution of the virulent disease becomes ever less precise. Therefore, what do the firsthand sources really tell us about the new plague, its initial features and the subsequent changes of the disease, and about the timing of this shift to a reduced severity? In this paper, I will focus in particular on these issues through the analysis of a variety of primary and secondary sources, in several languages, of a medical, literary, and annalistic nature, collecting the medical descriptions and the memories of the sufferers, some of which have not been taken into account.

Syphilis appeared in Europe for the first time around 1495. The young king of France, Charles VIII, had invaded Italy the year before with an army of over 30,000 mercenary soldiers hired from all over Europe. On 19 February 1495, his forces reached Naples, which was primarily defended by Spanish soldiers.¹ After holding the town for a few months, Charles VIII demobilized his army. By the summer of that year, mercenaries, infected with a mysterious, serious disease, returned to their native lands or moved elsewhere to wage war, spreading the disease across Europe, initially striking Italy, France, Germany and Switzerland; then Holland and Greece in the following year; England and Scotland within 2 years; and Hungary and Russia within 4 years. In this period of European expansion—the Age of Exploration—syphilis was soon carried by European sailors to the non-European world, reaching India and China by 1504. Scholars used a series of terms to refer to the new plague: ‘French disease’, ‘Disease of Naples’, ‘venereal lues’, ‘Great Pox’ (in contrast to smallpox) and ‘Morbus Gallicus.’ Several decades after the beginning of the epidemic, the famous Veronese physician, poet, and astronomer Girolamo Fracastoro (1478–1553) gave the disease the elegant name of syphilis in his poem, “Syphilis sive morbus gallicus.”²

Ever since the disease first appeared in Europe, the question of the origin of syphilis has been hotly debated.³ After five centuries, the controversy amongst the supporters of the three dominant theories—Colombian, Pre-Colombian and Evolutionary—has still not abated,⁴ but recent advances in a series of fields, especially that of molecular genetics,⁵ have improved our understanding of these events. However, there is still no conclusive proof. The efforts of archaeological medical detectives and paleopathologists in searching for signs of syphilis in mummified or skeletonized human remains both in pre-historical America and the Old World have still not succeeded in conclusively demonstrating that syphilis was unknown in Europe until the end of the fifteenth century or that it existed in Europe before the Middle Ages, reappearing as an epidemic in Renaissance Europe—the result of favourable ecological, biological, and social changes,⁶ newly differentiated at that time from the mass of other diseases with which it had previously been confused. Naturally, this debate covers a wide range of topics involving the history of diseases: the pathocenosis,⁷ the distribution of diseases in the medieval world; the difficulty in obtaining compelling evidence from the often vague descriptions of diseases written in the distant past; the state of medical knowledge at the time and the confusion between syphilis and other transmitted diseases such as chancre and gonorrhoea; and the possibility that the disease diagnosed as syphilis may have been misdiagnosed as leprosy in previous eras.

In reality, many ideas are based on indirect knowledge of the contemporary sources and of the philosophical speculation of the more famous physician-philosophers and exponents of academic medicine.⁸ Careful analysis of the writings of physicians and surgeons closer to the medical practice—to which I will refer in this paper⁹—demonstrates, instead, early understanding of the severity and specificity of the most virulent of venereal infections. It can be said, in fact, that perhaps never in history had a new disease been analyzed by physicians with such rapidity and effectiveness: its venereal character, its high contagiousness, and its low mortality. The clinical signs of the primary phase of the infection (characterized by hard chancres with small erosions or deep ulcers on the genital

organs) and of the secondary phase (in which the principal lesions effect the skin and mucous membrane) were recognized and described with great precision. Highlighting the level of medical knowledge about syphilis that has so far been heavily underestimated is another of the objectives of this article.

Tremendous disease: the accounts of physicians and sufferers

All contemporary sources, from physicians to chroniclers to the sick who left personal stories, are unanimous in emphasizing the violent and malignant character of syphilis when it broke out in Italy and almost simultaneously in the rest of Europe from the summer of 1495 onward (Fig. 1). The first known description is that of the Venetian military surgeon, Marcello Cumano, who had taken his troops to the battle of Fornovo and fought alongside the armies of Charles VIII of France and the League of Venice. His medical account, founded on his observations of the soldiers, is most accurate: the first manifestation of the disease was the appearance of a painless skin ulceration localized on the penis. Sores and pustules then appeared all over the face and the entire body, accompanied by joint pains and pruritus.¹⁰ His contemporary, Giovanni da Vigo, surgeon to Pope Julius II, also describes the primary chancre on the genitalia followed by a latent period and the secondary stage of the disease with skin manifestations and mentions the severe pains occurring especially at night.

In 1498, a notary from the Umbrian town of Orvieto, Tommaso di Silvestro, whose account can be considered one of the first patient narratives in the history of medicine, refers to the same symptoms: a small lesion known as a ‘chancre’ was the first stage. The second involved generalized symptoms, such as skin lesions and pains in the joints:

I remember how I, Ser Tomaso, during the day 27th of April 1498, coming back from the fair in Foligno, started to feel pain in the virga. And then the pain grew in intensity. Then in June I started to feel the pains of the French disease. And all my body filled with pustules and crusts. I had pains in the right and left arms, in the entire arm, from the shoulder to the hand, I was filled with pain to the bones and I never found peace. And then I had pains in the right knee and all my body got full of boils, at the back at the front and behind.¹¹

His relatively unknown personal account of his experiences with syphilis testifies, *inter alia*, to the moral climate of that period, far from the puritanical atmosphere of the Victorian age. It is also important to note that it precedes the classic personal story of the German patriot and satirist Ulrich von Hutten (1488–1523),¹² a supporter of Martin Luther, who is most cited by historians and contains important information about the incubation period. Plagued by a particularly severe form of syphilis, von Hutten stresses the sordidness of the pustules, emphasized by many contemporaries, and describes his repulsive case,¹³ which included ‘boils that stood out like acorns, from whence issued such filthy stinking matter that, whosoever came within the scent believed himself infected’.¹⁴

The descriptions given by syphilis sufferers and the accounts of physicians match perfectly, providing accurate reports of the clinical manifestations of the primary and secondary stages of syphilis. After an incubation period that varied from 10 to 90 days post-contact, the disease manifested itself with a chancre—a single, painless, hardened ulcer—at the site of inoculation. In men, the commonest site affected was the penis. At 40 to 60 days after the appearance of the first ulcer, the second stage involved generalized symptoms, such as fever, headache, sore throat, skin lesions, swollen lymph nodes and terrible pains in

characterised by soft, tumour-like growths in the skin and mucous membranes but could occur almost anywhere in the body, often in the skeleton. The localized tumour outgrowths were called ‘gummas’ by Girolamo Fracastoro as a result of their resemblance to cherry and almond resin. They were composed of hard nodules of different sizes (from the size of a lentil to that of an egg) with a slow accretion rate which, with the passage of time, would soften, fill with a gummy liquid full of spirochaetes, and then ulcerate, creating a nauseous smell. The exceptional wealth of descriptions of venereal syphilis present in medical writings between the fifteenth and sixteenth centuries attests, on one hand, to the knowledge and the understanding of its specificity and severity, and on the other, to the impression elicited by the repulsive external appearance of those suffering from the disease.

The reports are so detailed in describing the appearance, position, and colour of the destructive skin lesions that they are nearly visual impressions, such as this example by Fracastoro in his prose treatise written in about the fourth decade of the sixteenth century:

The infection does not occur the moment you receive it, but it lies dormant; but in a short time it manifests itself. First of all, mainly around the genital region, you can see some small ulceration arise, and a certain decay of the tissues takes place [...] difficult to get rid of, the ulceration recovers only with great difficulty and, often, even if healed on the one side, it starts on the other. After this, in most [of the cases], commonly some pustules covered with crusts [scattered] all over the body [appear], and sometimes they start from the scalp. At first they are small, then they grow little by little reaching the volume and shape of the gland calyx: the crusts are rough and disgusting, with a livid colour verging on yellow. This happens in most of the cases, [but] other times the crust is white, sometimes [black], reddish and hard: but this happens rarely. Hence after a few days the pustule opens and gives off a stinking and mucilaginous mucosa, and it is impossible to say how much filthy material constantly comes out... Therefore the pustules ulcerate and not only twist, but also destroy the tissues and mutate into ulcers that are wide, dirty, corrosive, difficult and very resistant to treatment. The ulcers also spread to the nervous parts and attack the bones: this disease does not attack everyone in the same parts, in fact for some the infection is limited to the head, for others to the upper limbs and for others elsewhere... some people can have the complete destruction of the lips, others of the nose, and others of all their genitals.¹⁵

Fracastoro’s description of the mutilations corresponds exactly with those given before him by other physicians. The military surgeon Alessandro Benedetti (1450–1512) was the most important of the chroniclers of Charles VIII of France’s expedition to Naples in 1494 as well as the forced marches back through Italy the next year. Benedetti reported in 1497, in his *Diaria de bello carolino*, that he had seen sufferers who had lost hands, feet, eyes, and noses to the disease.¹⁶ Syphilis, he reports, made ‘the entire body so repulsive to look at and causes such great suffering’. Leprosy and elephantiasis were indeed horrific, yet syphilis surpassed them in its ability to disfigure and decompose bodies, a feature highlighted by observers who themselves were not physicians, such as, the Bolognese chronicler and author of the famous *Cronica Bianchina*¹⁷ and the noble jurist Francesco Muralti of Como who lived between the fifteenth and sixteenth centuries. Muralti wrote that the disease ‘ate the nose in the middle of the face or the male member (penis)’.¹⁸ A ‘sort of smallpox or leprosy’,¹⁹ wrote another contemporary, the annalist Fileno Dalle Tuade; a disease in which ‘the man becomes full of boils and pains so that he cannot move from the bed and there are no doctors that can find a treatment.’²⁰ This frightening impact on the body is portrayed in an illustration in a work by the scholar and astrologer Joseph Grunpeck, published in 1496, that constitutes the earliest known visual depiction of syphilis (Fig. 2).²¹

Fig. 2 Madonna and Child with Syphallis Sufferers Woodcut from *Tractatus de Pestilentiali Scorra Sive Mala de Francos* (1496) Joseph Grunpeck, 1473–1532



Another unanimously reported feature of this disease was the speed of its spread, ‘like mistletoe’, as one annalist reported:

The above-mentioned disease spread like mistletoe via food and drink and by carnal contact and many people who caught this disease could not see and became crippled and others’ bodies wasted away from boils and pain.²²

Besides the high rate of contagiousness of the disease, this description underlines another fact: that there were non-venereal forms of transmission, even though all contemporaries agreed to the fact that the venereal form prevailed. After noting that this disease could be transmitted among men talking or consulting with someone at a short distance, Pere Pintor, physician to Pope Alexander VI, specified that infection took place mainly through sexual relations.²³

Even the famous doctor and anatomist Niccolò Massa of Padua, in his essay written in 1507 and published in 1527,²⁴ gives his views on the role of coitus in spreading the infection although he affirmed the disease could be transmitted by other forms of contact. After the early years of the epidemic, however, there are no medical descriptions recognizing a non-venereal mode of transmission, except for those that observed the manifestations of congenital syphilis. In his prose treatise, Fracastoro wrote that contagion could not take place at a distance or through ‘intermediary carriers’. As a result of the property of its ‘semen’, which was considered ‘not penetrating’, syphilis could not be transmitted merely by ordinary person-to-person contact: this contact had to be very close ‘as when two bodies

mutually touched in warmth’ that ‘mainly happens during coitus’. The other possibility of contagion, he noted, was infection from the mother via breast-feeding.²⁵ The last observations of the period on possible transmission through other forms of contact appear to be those contained in the first printed medical book written in English, the renowned ‘Breviary of Helthe’ (1547) by the physician, traveller, and writer Andrew Boorde (1490–1549), who visited various European universities in the 1530s. He affirmed that sexual intercourse was the prevalent route of transmission, even if others (common and innocuous practices, such as drinking or eating from a common cup or plate) should not be overlooked:

[...] The cause of these impediments (morbus gallicus) or infyrmytes doth may wayes, it maye come by lyenge in the shetes or bedde there where a pocky person hath the night before lyenin, it may come with lyenge with a pocky person, it maye come by syttenge on a draught or sege where as a pocky person did lately syt, it may come by drynkyng oft with a pocky person, but specially it is taken when a pocky person doth synne in letchery the one with another.²⁶

The decline of virulence: how and over how long a period? Historiographic synthesis and the firsthand witnesses

Some centuries after its appearance in Europe, physicians and medical historians emphasized the differences between past and present in the severity of the disease, such as described by an academic physician and collector of ancient medical writing:

To tell the truth, whether nowadays the so-called secondary or virulent stage of syphilis mostly starts either with no fever or with a very slight one—so that this syphilitic phenomenon is denied by some authors—in the past it was preceded by a very violent fever, and by an intense skin rash; on the contrary, it now starts with a simple “reddening”. Briefly, the syphilis of the end of the fifteenth century and the beginning of the sixteenth century was distinguished by a contagious fever, that abated little by little, without losing the power to injure the inner organs and the deepest functions; and when it became chronic it appeared impetuously outside, in the outward appearance, which plays an important part in acute infections.²⁷

The difference between the manifestation of syphilis at the end of the nineteenth century and its characteristics in the early phase of the epidemic is remarked in nearly all contemporary treatises on venereal diseases:²⁸

Undoubtedly, the greater part of the syphilitic infections does not have today the serious character of those described one or two centuries ago.²⁹

In the first half of the twentieth century—on the eve of the discovery of the syphilis pathogen—Hans Zinsser (1878–1940), the leading bacteriologist and immunologist in the United States, developed the same observations in his classic book, *Rats, Lice, and History*:

There is little doubt that when syphilis first appeared in epidemic form, at the beginning of the sixteenth century, it was a far more virulent, acute, and factual condition than it is now.³⁰

According to the most recent historiographical literature,³¹ these changes in the virulence of the disease were observed in a short time from the initial epidemic, a statement based on

several generations of writers such as Johannes Benedictus (1508), Ulrich von Hutten (1519), Jean de Bordigné (1529), Fracastoro (1546), Ambroise Paré (1568) and Jean Fernet (1579) who naturally had differing perceptions of the transformations depending on whether they were ongoing or had already occurred. Furthermore, many historians fail to distinguish between the dates when the very first changes were observed and the dates when a major decline in virulence could be seen, as well as not giving sufficient attention to the new features the disease presented in the various steps. Yet what do the primary historical sources really tell us about the timing of this shift to a reduced severity? The information from contemporaries tends to be discordant. The best-known and, therefore, most cited is that of von Hutten who talks of 7 years, affirming that in Germany, the characteristic acute skin eruption and fever seen in the first cases did not occur after the disease had been prevalent in the country for approximately this period of time. An unknown physician from Florence mentions a period of about 15 years, and 20 is the estimate given by Girolamo Fracastoro.³² However, other authors indicate an even longer period of transition. Moreover, we have to consider that as we move away from the start of the epidemic at the end of the sixteenth century, not all the information comes only from contemporary observers, either from those who had experienced the disease shifts as physicians in clinical practice or those who were first-person sufferers. It is, therefore, important to classify into periods all the writings at our disposal in order to distinguish between first-hand information and that which arises from books and the oral tradition.

In general, it can be concluded that 10 to 15 years after the start of the epidemic, a decline in its virulence was perceived. Significant, for example, is the mocking comment by a doctor from Florence, dating back to 1513, the year of the election of Cardinal Giovanni de' Medici as Pope, who took the name of Leo X. Observing that God chose the 'new Pope', he jokingly complained that He had also propitiated good health and 'driven away the French disease from Italy'. This loss of potential patients would injure the doctors, who were surely deprived of a substantial part of their income.³³

Many physicians and contemporary observers also confirm the progressive decline in the severity of the disease. Many symptoms were less severe, and the rash, of a reddish colour, did not cause itching. Girolamo Fracastoro talks about some of these transformations in his prose treatise and affirms that 'in the first epidemic periods the pustules were filthier', while they were 'harder and drier' afterwards.³⁴ Even the historian and scholar Bernardino Cirillo dell'Aquila (1500–1575), writing in the 1530s, stated:

... this horrible disease in different periods (1494) till the present had different alterations and different effects depending on the complications, and now many people just lose their hair and nothing else.³⁵

Some years later, conquistador Hernán Cortés' chaplain confirmed that syphilis was less severe than the early form: 'at the beginning this disease was very violent, dirty and indecent; now it is no longer so severe and so indecent'.³⁶ According to the medical literature, the fever, which was always present in the second stage, was less violent, while even the rashes were just a 'reddening'. Moreover, the gummy tumours appeared only in a limited number of cases.

By the middle of the sixteenth century, the generation of physicians born between the end of the fifteenth century and the first decades of the sixteenth century considered the exceptional virulence manifested by syphilis when it first appeared to be ancient history. The physician and botanist Luca Ghini (1490–1555) observed that the appearance of the disease was initially more excruciating ('*primis temporibus fuere atrociora quam nunc*').³⁷

One of his contemporaries, the famous French surgeon Ambroise Paré (1510–1590), says more or less the same thing:³⁸

Today it is much less serious and easier to heal than it was in the past [...]. It is obviously becoming much milder... so that it seems it should disappear in the future.

Antonio Musa Brasavola (1500–1555), personal physician to three popes, gives an idea of the variety of the forms in which syphilis presented itself in the 1530s. He provides a detailed list with 234 types of disease manifestations and their combinations: tumours, pain, loss of hair, body hair, or teeth, injuries to the eyes, and gonorrhoea.³⁹ These manifestations included:⁴⁰

Scabies gallica
Dolores gallici
Deflussio pilorum
Gonorrhoea
Scabies gallica cum doloribus
Scabies gallica cum deflussio pilorum
Scabies gallica cum gonorrhoea
Dolores gallici cum tumoribus
Dolores gallici cum deflusione pilorum
Dolores gallici cum dentium casu
Scabies gallica cum doloribus and gonorrhoea
Scabies gallica cum tumoribus and oculorum aemissione [sic]
Scabies gallica cum tumoribus and gonorrhoea
Dolores gallici cum tumoribus and pilorum deflusione

By the middle of the sixteenth century, as Brasavola recorded in another short work, the symptoms had become milder. If sick people received help from physicians, they healed quite easily and their hair grew back again.⁴¹

In the *De morbis venereis libri sex*, on the basis of hundreds of works on syphilis he had collected, Jean Astruc (1684–1766), a celebrated professor of medicine at Montpellier, divided the ‘varias mutaciones’ of the ‘lues venerea’ into six periods:⁴²

- 1494–1516
- 1516–1526
- 1526–1540
- 1540–1550
- 1550–1562
- 1562–1675

The first period was the most severe for the disease ‘per quam morbus maxime fervit’. In the epidemic stage, all ages were involved, and mouth disorders and pains in the bones were the rule; later, the virulence of the disease decreased, and other symptoms and pathological manifestations such as alopecia (1516–1526) and tinnitus (1550–1562) appeared.

Conclusions

Between the Middle Ages and the Modern Age, an exceptional number of first-hand testimonies and medical writings, either manuscripts or printed in Latin and Italian were produced on the subject of syphilis—more than on any other disease. Detailed descriptions from physicians and contemporary observers confirm that ‘venereal lues’ represented a

completely new affliction when it first appeared in Italy at the end of the fifteenth century, and chroniclers also agreed on its tremendous severity and its frightening impact on the body. Documentary evidence demonstrates that syphilis was much more severe in the first half of the sixteenth century than it has been ever since. However, the disease did not become less virulent in such a short time as 5 to 7 years from the initial outbreak, as asserted by Ulrich von Hutten some years after his direct experience with the disease—an assertion which is a benchmark for many historians, his book being the most famous in the early sixteenth century.

Evidence for the timing of these changes comes from several medical descriptions and first-hand accounts of sufferers; in that initial period, only the earliest signs of the changes in the virulence of the disease were observed. In fact, changes in the ‘genius epidemicus’ took place gradually, over a span of several decades, in which the disease transformed itself from being acute, severe, and debilitating into a milder infection.

By following the chronology of the primary sources—and in accordance with the accurate chronology appointed by Jean Astruc—it appears that different stages in the transformation of syphilis can be distinguished. In the first stage, the disease was highly virulent. Some years after the initial epidemic, the severity began to abate. Then the clinically exuberant primary and secondary phases of the infection arose far more rapidly. The manifestations (pustules and necrotic lesions) became less serious and less feared; the tremendous bone pains and the pruritus (provoked by the cutaneous eruption) lost their severity. The bad smell stressed in the very earliest reports of syphilis, such as von Hutten’s, become rare among the sufferers. After some decades, new manifestations of the disease appeared, including hair loss (alopecia) and tinnitus (ringing in the ears), and syphilis began to exhibit polymorphic phenotypes that could mimic the effects of many other diseases. So protean was its manifestation in the nineteenth century that the eminent clinician Sir William Osler proposed its being described as the ‘Great Imitator’.

In conclusion, this study throws some light on the state of medical knowledge at the time, perhaps underestimated so far. Venereal syphilis was described in great detail from the fifteenth century onwards, and the writings of physicians demonstrate considerable understanding of its specificity and severity, as well as its differentiation from other forms of other sexually transmitted diseases like chancre and gonorrhoea. The evidence presented in this article reveals, once again, the usefulness of a review of the primary sources on syphilis which provides a far fuller and more accurate representation of the evolution of syphilis, contributing to a more precise description of the first example in history of rapid changes occurring in a human disease.

Endnotes

- 1 On the history of syphilis see, Quétel, *History of Syphilis*; Arrizabalaga, Henderson, and French, *The Great Pox: The French Disease in Renaissance Europe*; Watts, *Epidemics and History: Disease, Power and Imperialism* and McNeill, *Plague and Peoples*.
- 2 Fracastoro, *Syphilis: or a Poetical History of the French Disease*. Dedicated to the Cardinal Pietro Bembo, Secretary of Briefs to Leo X, the medical poem, of great formal elegance, was republished in 50 editions and was translated into many languages. It is in Latin and deals with the punishment given by Apollo to the young shepherd Syphilis. In the new lands just discovered by Columbus, he had imprudently attracted the god’s wrath and was suitably punished with a terrible disease that covered his body with pustules and lesions, taking the flesh off, making his teeth fall out and his breath stink and reducing his voice to a tremulous sound. This poem by Fracastoro is the most commonly cited of his works, but his theories on the disease are better reported in the classic *De Contagione et Contagiosis Morbis* (1546) and in his prose treatise on syphilis, dated to around 1530. This book is nearly completely

- unknown in English-speaking world; the translation from Italian of the previous quotation is mine as are all others.
- 3 The standard Renaissance debates about the origins of syphilis and began with the publication in 1539 of a book by the Spanish physician Ruiz Diaz de Isla (1462–1542) in which he asserts that he had treated members of Columbus' crew that had been suffering from a new disease in 1493 and that these sailors had imported syphilis to Europe.
 - 4 The theory of the American origin of syphilis is the most widely accepted. The bibliography on the debate is impressively wide, even considering just the last century. Of the most important studies see Sudhoff, 'The Origin of Syphilis'; Holcomb, 'The Antiquity of Syphilis', Hackett 'On the Origin of the Human Treponematoses', Weisman, 'Syphilis: Was It Endemic in Pre-Columbian America or Was It Brought Here from Europe?'; Crosby, 'The Early History of Syphilis A Reappraisal'; Idem, "The Columbian Exchange: Biological and Cultural Consequences of 1492" McGrew, "Encyclopaedia of Medical History", Guerra, 'The Dispute over Syphilis: Europe versus America'. Livingstone, 'On the Origin of Syphilis: An Alternative Hypothesis', Carmichael, 'Syphilis and the Columbian exchange: was the disease really new?', Malakoff, 'Columbus, Syphilis, and English Monks'.
 - 5 Carl Zimmer, 'Can Genes Solve the Syphilis Mystery?', *Science*, 292 (2001), 1091.
 - 6 At the time, social environmental and biological conditions were ideal for the spread of syphilis: new contacts among people, increasing trade exchanges, movements of armies from one part to the other of the country, prostitution. Promiscuity, overcrowded rooms and extemporaneous refuges, poor personal and collective hygiene, contributed to the diffusion of venereal and non-venereal infection.
 - 7 The concept of pathocenosis is connected with the name of Mirko Dražen Grmek, the eminent historian of medicine and science.
 - 8 The most famous collection of the sixteenth century is that of Luisinus *Aphrodisiacus, siue de lue* published in 1728 and edited by the famous Dutch physician Hermann Boerhaave and continued by Grüner, *Aphrodisiacus sive de lue venerea*. In 1924 Karl Sudhoff edited the edition in facsimile of ten incunabula, *Zehn Syphilis-Drucke aus den Jahren*.
 - 9 See, for example, Scillacio, "De novo morbo"; Leonicensio, "Libellus de epidemia, quam vulgo morbum Gallicum vocant"; De Villalobos, "El sumario de la medicina con un tratado de las pestíferas bubas"; Pintor, "De morbo foedo et occulto"; Grünpeck, *Tractatus de pestilentiali Scorra sive mala de Franzos*; Idem, "Libellus Josephi Grünpeckii de Mentulagra, aliis morbo Gallico"; Da Vigo, "Practica copiosa in artem chirurgica"; de Béthencourt, *Nouveau carême de pénitence, et purgatoire d'expiation à l'usage des malades affectés du mal français ou mal vénérien*; Manardi, "Epistularum medicinalium tomus secundus"; Falloppio, *De morbo gallico*.
 - 10 Cumani, "Curationum et observationum med. centuria una", 186.
 - 11 Memoria come a me ser Tommaso a di 27 di aprile 1498 ritornando dalla fiera di Foligno mi cominciò a dolere la verga. E da poi tuttavia omni si cresceva lo male. Da poi a di giugno mi cominciaro a venire le doglie del male francioso. E tutto lo capo mi si empi di brusciale, ovvero croste come brusciale. E le doglie me vennero allo braccio dritto e allo manco, adeo che tutto lo braccio, dalla spalla insino alla congiuntura della mano, mi dolevano l'ossa che non trovava mai riposo. E da poi mi vennero le doglie al ginocchio dritto e tutto mi empiè di bolle, tutto lo dosso divanti e di dietro'. Di Silvestro, "Diario d'Orvieto", 88.
 - 12 De Hutten, *Of the Wood Called Guaiacum, That Healeth the French Pocks, and Also Helpeth the Goute in the Feet, the Stone, Palsey, Lepre, Dropsy, Fallynge Evyl, and Other Disease*.
 - 13 From private memories and letters it implicitly emerges that these features of the disease conditioned social and intimate relationships.
 - 14 Cited by Major, "Classic Descriptions of Disease: With Biographical Sketches of the Authors," 31.
 - 15 'L'infezione non si manifesta al momento in cui si viene colpiti... In breve (il contagio) butta fuori i segni. Prima di tutto, per la massima parte intorno alle regioni genitali, si vedono sorgere delle piccole ulcerazioni, e (succede) un certo disfacimento dei tessuti molto dissimile da quello che di solito proviene dai lavori manuali: questo infatti è resistente a scomparire e l'ulcerazione non risana se non con difficoltà e, spesso, pur guarita da una parte, ricomincia dall'altra. Dopo di ciò, nella massima parte (dei casi), comunemente (compaiono) alcune pustole ricoperte di crosta (sparse) per il corpo, le quali talvolta hanno inizio nel cuoio capelluto, un'altra altrove. Esse si mostrano piccole dapprima, poi crescono poco a poco raggiungendo anche il volume e la rassomiglianza di un calice di ghianda: le croste sono ruvide e squallide, di colore livido che trae leggermente al giallo. Ciò si verifica nella maggior parte dei casi, (ma) altre volte la crosta è bianca, talora (nera), rossastra e dura: ciò però avviene più raramente. Quindi dopo

pochi giorni la pustola si apre ed emana una mucosa fetida e mucillaginosa, né si può in verità dire quanto di sordido, quanta materia continuamente fuoriesca ...Si ulcerano quindi le pustole e non solo serpeggiano, ma anche distruggono i tessuti e si tramutano in ulcere fagedeniche, sordide, difficili e assai ribelli a curare.... le quali spesso non si impadroniscono dei soli tessuti carnosì, ma si propagano anche alle parti nervose ed attaccano le ossa: non ugualmente in tutti i casi queste parti ammalano, ma in alcuni l'affezione si limita al capo, in altri intorno al dorso, in altri agli arti superiori e in altri altrove. In alcuni casi si ha la distruzione completa delle labbra, in altri del naso, in altri di tutti i genitali'. *Fracastoro's prose treatise*, 154.

16 Benedetti, *Diaria de Bello Carolino*.

17 *Cronica Bianchina*.

18 Annalia Francischi Muralti.

19 At first, people assimilated leprosy and syphilis. See Foa, 'The New and the Old: The Spread of Syphilis (1494–1530)', and Singer, "A Thirteenth Century Clinical Description on Leprosy;" Brody, *The Disease of the Soul: Leprosy in Medieval Literature*; Richards, *The Medieval Leper*.

20 Dalle Tuade, *Historia di Bologna principiante dalla sua origine sino all'anno 1513*.

21 Grünpeck, *Tractatus de pestilentiali Scorra sive mala de Franzos*.

22 'El dito male se apichaua chome fa el uischio per manzare e per beuere e per usare charnalmente et assai persone prexono el dito male che mai più non erano da uedere et remanevano storpie et asidia et altri assai tutti manzati per la persona chon bole e doie'. Degli Ubaldini, *Cronaca dalla creazione del mondo fino all'anno di NS 1518 nella quale non lascia di scrivere tutta l'istoria della sua patria 1518*.

23 Pintor, "De morbo foedo et occulto", 8.

24 Massa, *Liber de morbo Gallico*.

25 *Fracastoro's prose treatise*, 132.

26 Boorde, *The breviary of helthe*, Talking about syphilis, he continues: 'In englyshe Morbus Gallicus is named the french pockes, whan I was yonge they were named the spanyshe pockes the whyche be of many kyndes of pockes, some be moyst, some be waterashe, some be drye, and some be skorvie, some be lyke scabbes, some be lyke ring wormes, some be fistuled, some be festered, some be cankarus, some be lyke wenne, some be lyke biles, some be lyke knobbls or burres, and some be ulcerous havynge a lytle drye scabbe in the middle of the ulcerous skabbe, some hath ache in the jointes and no singe of the pockes yet it may be pockes' 155–6.

27 Corradi, "Nuovi documenti per la storia delle malattie veneree in Italia dalla fine del Quattrocento alla metà del Cinquecento", 301.

28 Fournier, *Collection choisie des anciens syphilitographes*.

29 Patamia, *Trattato teorico-pratico delle malattie veneree e sifilitiche*, 340.

30 Zinsser, *Rats, lice and history*, 56.

31 Quétel, History of Syphilis, Arrizabalaga, Henderson, and French, The Great Pox; Oriel *The scars of venus: a history of venereology*.

32 *Fracastoro's prose treatise*, 152.

33 Penni. In Corradi, "Nuovi documenti per la storia delle malattie veneree in Italia", 370.

34 *Fracastoro's prose treatise*, 154.

35 Aquilano, *Annali della città dell'Aquila, con l'histoire del suo tempo*.

36 Cited by Gamberini, *Cenni storico-scientifici sui precipui scrittori di sifilografia*, 21.

37 Ghini, "Morbi neapolitani curandi ratio perbrevis". In Del Guerra and Mondani. *I primi documenti quattrocenteschi sulla sifilide e le lezioni pisane di Luca Ghini. sec. XVI*, 95.

38 Paré, *Oeuvres. Le seizième livre traitant de la grosse vérole*.

39 Gonorrhea and syphilis were often present together in infected individuals Some physicians assumed that gonorrhoea was a stage of syphilis. Paracelsus thought that gonorrhea was an early symptom of syphilis.

40 Musa Brasavola, "De Lue venereal". In Luisinus, *Aphrodisiacus, siue de lue venerea*, 565.

41 Musa Brasavola, *In Aphorism. Hippocr. et Galeni Comment*, 461.

42 Astruc, *De morbis*, 65–8.

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