Syphilis and Theories of Contagion

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Abstract

Syphilis provides a useful lens for peering into the history of early modern European medicine. Scholarly arguments about how diseases were transmitted long preceded certain scientific information about the etiology or cause of disease in the late 19th century. Compared to the acute and widely infectious nature of bubonic plague, which ravaged Europe in the mid-15th century, syphilis was characterized by the prolonged chronic suffering of many beginning in the early 16th century. This study reveals the historical anachronisms and the discontinuity of medical science focusing primarily on the role of Girolamo Fracastoro (1478-1553) and others who influenced contagion theory. Examination of contagion theory sheds light on perceptions about disease transmission and provides useful distinctions about descriptive symptoms and pathology.

I. **Introduction**

Treponema pallidum is a long and tightly coiled bacteria discovered to be the cause of syphilis by Schaudinn and Hoffman on March 3, 1905. The theory of contagion, or how the disease was transmitted, was vigorously debated in Europe as early as the sixteenth century. Scholarly arguments about how diseases were transmitted long preceded scientific information about the etiology or cause of disease. The intense debate about syphilis was the result of a fearsome epidemic in Europe that raged from 1495-1540. Compared to the Black Death, which had a short and sudden acute impact on large numbers of people one hundred and fifty years earlier, syphilis was characterized by the prolonged chronic suffering of many. At a time well before the development of a germ theory of disease, or knowledge of the immune system and modes of disease transmission, there was suspicion early in the epidemic that syphilis was contagious through venery. This study reveals the historical anachronisms and the discontinuity of medical science. The examination of contagion theories not only sheds light on perceptions about disease transmission, it provides distinctions about descriptive signs, and whether syphilis was even considered a new disease. When coupled to theories of contagion, syphilis provides a useful lens for peering into the history of early modern European medicine.

The syphilis epidemic at the turn of the fifteenth century sparked a reevaluation of the importance of contagiousness by direct or indirect passage of disease between humans by invisible living, or nonliving entity, or entities. This investigation of contagion theories leads to the conclusion that by the 1540's, several physicians felt strongly that "living and growing" disease entities were responsible for the epidemic. In order to clarify this view, it becomes necessary to discuss competing contagion theories in the first half of the sixteenth century. Physicians at the time especially grappled with ways to express the symptoms and spread of new disease with terms like emanation, foetid breath, poison or virus, putrefaction, and fermentation.

It has proven difficult to distinguish overlapping and interchangeable uses of the terms contagion, infection and miasma. Several primary source translations have been used, but most of the information comes from secondary opinions based on the writings of Gaspar Torrella (1452-1520), Jean Fernel (1506-/7-1558), Pietro Trapolino (1451-1509), Girolamo Fracastoro (1478-1553), and Johann Baptista Montanus (1493-1552). Fernel was a professor of medicine at the University of Paris and an enormously influential writer on syphilis and contagion. Torrella was a Spanish papal physician in Rome who argued early for treating prostitutes who had developed syphilis. Montanus, Trapolino and Fracastoro contributed to the debate about contagion at the University of Padua. By investigating historical translations and interpretations of contagion theories spawned by a dreadful syphilis epidemic from 1495-1540 in Europe, it is possible to determine that leading physicians, most notably, Fracastoro, subscribed to the idea that living grown disease entities were responsible for disease.

This essay attempts to answer the following questions: What were the leading contagion theories in the first half of the sixteenth century and how did these ideas influence Girolamo Fracastoro? Why have there been alternate historical inflation, derision, and revival of Fracastoro's contagion theory in the twentieth century? What explains the contradictions in Fracastoro's writings? Why did syphilis generate unprecedented interest in contagion theory?

II. The Symptoms and Pathology of Syphilis

Medical practitioners often described symptoms of syphilis that were notably more severe at the start of the sixteenth century compared to the middle of the century. This was one of several reasons why there was theoretical discussion as to whether the disease was perhaps caused by a living growing entity or entities responsible for disease consistent with discernable improvements in bodily defenses. Modern medical textbook descriptions of syphilis pathology inform us about the suffering experienced by a large number of Europeans contracting syphilis for the first time, and serves to clarify perceptions about how the disease was transmitted.[1]

Syphilis averages around three weeks from the time the bacteria are contracted until symptoms first arise in the form of a hard painless skin sore generally located in the external groin area when sexually transmitted.[2] The primary stage sore, or chancre, does not cause distress and women may be unaware of a sore hidden on their cervix. In males the chancre sometimes forms in the urethra and may likewise pass undetected. Surprisingly the disease is transmitted only 33% of the time after sexual intercourse during this stage.[3]

Bacteria enter the lymphatic system during the primary stage, and two to ten weeks later a secondary stage develops characterized mainly by painful skin rashes with varying appearances. The rashes are widely distributed on the skin and also found in the mouth, throat and cervix.[4] The disease is most contagious during the secondary stage. Skin rashes soon subside and the disease becomes latent or dormant for about 2-4 years.

Following this latent period syphilis disappears on average 60% of the time with resistance to re-infection.[5] In 40% of the cases, disease reappears as a tertiary stage many years after the onset of the latent stage. Grotesque rubbery masses of tissue, called gummas, appear in many organs and on the skin. The disease is not highly contagious in this stage. The brain is often affected with loss of motor control, personality changes, blindness, seizures and death. It is likely that the syphilis epidemic was caused by a new more virulent strain of *Treponeme* infecting a naive European population and originating from the New World.[6] The result was a fulminating infection where the tertiary stage of syphilis was more frequent and appeared sooner during disease cases in the early sixteenth century than it does today.

III. Earliest Ideas About How Syphilis Was Transmitted

Prior to the epidemic of syphilis in Europe in the sixteenth century, there had been rare discussion about contagion in early modern Latin medical traditions, in Greek, Arabic, Indian and Chinese language medical texts.[7] Traditional theories about the cause of disease varied in emphasis, but the primary causes were based on the alignment of planets or stars, or the wrath of God or god's.[8] Primary causes were believed to trigger other remote earthly events such as volcanic eruptions, exhalations by stagnant marshes and ponds, earthquakes, or bad weather. Remote causes led to atmospheric changes, often referred to as *miasmata*, carrying disease in the form of an invisible cloud.

Making the cause more complex during the sixteenth century was the argument that predisposing causes could overlap into the category of remote causes such as a poor diet, emotional stress, injury, absence of cleanliness, heredity, or exposure to weather. Predisposing causes, referred to as the "non-naturals" were also sometimes called proximate or near causes in connection with the usage of terms such as exciting, efficient, or immediate. Certain references to proximate causes lent to usage of the terms contagion and infection. Miasma tended to describe general local causes, as compared with contagion, which was correlative with "exciting."[9] Infection often was used to

bridge these two levels of cause. However, all three terms could interchange into another word, act singly, or interrelate with any instance of disease.[10] Whether triggered by primary, remote, atmospheric or proximate causes, a disturbance in the distribution and quality of the four humours resulted. An imbalance of the four humours, or *dyscrasia*, in turn, caused a condition known as putridity, or fermentation. It was recognized long ago that fever derived from this putrescence could be conveyed to the circumambient air and infect others.[11]

During the syphilis epidemic the focus tended to be more on the subject of proximate cause of venery rather than remote or primary causes. Different periods in history were distinguished by their choice of emphasis on the many types of disease causality. There has been a tendency for historians to consider the secularization of thought as indicative of a period of conflict between religion and science. This conflict was circumscribed by time periods when primary and remote causes were de-emphasized during commentaries on disease. The new debate over contagion theories took place at the beginning of the general use of printed materials, the discovery of the New World, and the influence of humanist philosophers who increasingly explained human events and vicissitudes by natural laws rather than by direct intervention of supernatural influences. Aside from the concurrent historical developments of the syphilis epidemic, there were four unique aspects of the disease that resulted in more frequent medical discourse. First, it was obvious to many that syphilis was uniquely conveyed from person to person by venery.[12] Second, it was widely debated whether syphilis arrived for the first time in Europe in 1495 and spread during the sixteenth century, but many authorities writing on the subject believed it was a new plague.[13] In this way syphilis captured the attention of a wider audience of commentaries beyond the ordinary cycle of epidemics. Third, since medical therapies actually *appeared* to work on a consistent basis, syphilis especially captured the attention of medical practitioners and society in general.[14] Unfortunately, this feature was an illusion as syphilis is a chronic disease: it portrays an unusual capacity for natural remission only to reappear with new signs after a relatively long period of absence.

It is likely that patients informed their physicians as to how they believed they had acquired the disease as a consequence of relations between venery and the immediate development of primary stage disease signs. These four aspects of the syphilis epidemic are markedly different from the Black Death due to bubonic plague one hundred and fifty years earlier. Since the initial sign of large skin pox in the groin area was relatively unique, obvious, and developed into a chronic rather than acute illness, physicians and patients had ample opportunity to consider the cause. Therefore, syphilis inherently promoted the concept of contagion to a degree no other disease had before.

IV. A Problem of Terminology

The early modern European dialogue about contagion is illustrative of how easy it has been for historians to project an anachronistic view. The word, "contagium" is taken from the Latin word "contactu" which means touching, and was often interchangeable with the Latin term for infection, "infectio." These terms have a clear meaning to us today, since it is know by current microbiologists that certain living pathogenic microbes such as bacteria, viruses, and the microscopic larvae of parasites are contagious. Unfortunately medical historians sometimes interpret "contagious" as passing from one person to another. Likewise, the term infection means establishment of pathogenic microbes in the host by direct contact with another infected person, or through indirect contact with water, food, or contaminated droplets in air or from inanimate objects. In the 16th century contagion did not necessarily mean what passed from person to person was a disease entity. This time period was well before the elucidation of living disease entities in the late nineteenth century. It was, nevertheless, clear early on during the epidemic of syphilis, that the disease was transmitted by venery. Since syphilis was thought to be sexually transmitted contagion theory was kept alive in the early sixteenth century.

The ambiguous concepts of contagion, infection, and miasma developed layers of meaning over time with each time period adding a different nuance. Historians have tended to oversimplify the definitions in retrospective accounts consistent with the spirit of authors writing about the Renaissance and the heroes of science. One difficulty for historians has been in arriving at

workable definitions without over-simplification or discrediting old ideas. The term contagion was not always used in a strictly medical sense. According to Margaret Pelling, contagion was used more in the context of practical folk beliefs in medicine, agriculture, horticulture, animal husbandry and technologies such as dyeing and wine making.[15]

In a purely medical sense, the term was used during epidemics, or when there were changes in the prevalence of endemic diseases. Changing political, economic, or social contexts could also influence usage of the term contagion in relation to medical theory and practice. For example, notions about individual morality in the context of behavior were altered after gaining knowledge about American Indians. Due to the advent of the printing press, there were changes of expression designed to include either a more or less specialized reading audience. Finally, the concept of contagion is difficult to separate from public measures of isolation and quarantine, which in turn influenced ideas about individual morality, new issues in caring for family, and community involvement.[16] Carlo Cipolla's 1976 work on the origin and development of health boards during the Renaissance contributed significantly to an understanding of how northern Italians viewed the incessant cycle of high mortality rates during epidemics.[17] Sometimes medical theories changed local public health policies lending support to practical measures of sanitation and quarantine laws. Likewise, medical practices tended toward confinement for the patient, and refined evaluations of occupational stress for physicians.

A problem of historical mistranslation becomes evident with 'syphilis,' a term not used by physicians before the late eighteenth century. Syphilis can be a confusing historical term since the bacteria discovered to be responsible for veneral syphilis, *Treponema pallidum*, also causes two other diseases that are not veneral, yaws in certain tropical areas, and bejel in Middle Eastern areas. Although I will use the term syphilis in order to be consistent in this paper, from 1496 to the mid-sixteenth century, local Italian laity recorded a disease called Morbus Gallicus, or "French Disease." Most university physicians felt the name was inappropriate. However, they did agree that syphilis traveled to Italy with the mercenary troops of Charles VIII when they invaded Italy and occupied Naples in 1494.[18] In retrospect, it is possible that some of the troops had traveled with Christopher Columbus to the New World and contracted a virulent form of spirochete from Native Americans and transmitted it to Europe.

Italians sometimes called the disease the Neopolitan disease or "Mal de Napolitano" echoing the belief that the disease had first been brought to Italy from Spain.[19] Francesco Guicciardini blamed the "Indies Indians" for having infected the Europeans.[20] An alternative explanation for blaming Spain rested with a Roman chronicler, who had recounted the specific way the disease was transmitted by Jews driven out of Spain by King Ferdinand, and living in Naples. On the other hand, a Genoese chronicler said it came from Ethiopia. In any case, the syphilis epidemic took place during a time of nation-state building. The French blamed the Spanish, the Germans blamed the French, while the Polish blamed the Germans. By the end of the sixteenth century, "Morbus Gallicus" was commonly referred to as *lues venerea*, meaning venereal disease. Medical practitioners like William Clowes, an English surgeon writing about lues venerea in 1594, typify the trend away from nation blaming.[21]

In a time of intense anti-clericalism, humorous jokes about priests with syphilis were used in biting satire during the Reformation.[22] Catholics, in turn, attributed the disease to the Reformation. Erasmus described with levity certain nobility when he said, "unless you're a heavy drinker, a reckless spendthrift, heavily in debt and decorated with pox, hardly anyone will believe you're a knight."[23] The manner of finding fault for syphilis provides an excellent example of cultural relativism and illuminates factors of communication about the origin of infectious disease.[24]

V. Pre-Modern Views of Contagion Theories

It is useful to briefly construct the pre-modern foundation for contagion theories in order to better understand the sixteenth century reaction to syphilis. There are numerous instances where contagious skin diseases are mentioned in the Bible. According to the Elinor Lieber, the widely debated Hebrew term *sâra'at* in Leviticus 13 is only rarely referring to leprosy, and instead means

something more general such an "unclean." Based on extensive studies of Biblical descriptions, and other contemporary writings, Lieber has differentiated four different skin diseases in the Old Testament. The most common skin lesion associated with hair turning white is an early sign of bejel, a highly contagious chronic skin disease endemic to the Near Eastern desert caused by *Treponema pallidum*, the same bacteria responsible for syphilis.[25] From the beginning of Isrealite exodus from Egypt, new and special measures were instituted in the desert to separate those with contagious skin diseases from those with psoriasis. Unfortunately, the context of contagion here is rare, in the desert, and therefore rendered unavailable to early modern interpretations of medicine in Europe.

Greek medicine was highly influential toward Latin based medical traditions, but the Greek focus centered on diseased people rather than on disease itself. Poor diet, or hereditary weakness, age, gender, personal habits and seasons were predisposing conditions for disease. Physician assessment was personal despite the fact that certain diseases had names with similar symptoms in different people. Greek mechanistic theory, later associated with contagion theories in the sixteenth century, was not attractive to Galen. Humoral theory was sufficient to explain the cause of disease.

There were several words that could qualify comparably with the word contagion in the Greek language. According to Vivian Nutton, *synanchrosis* is the closest term to *contagion* as derived from the Greek word translated as "with an intensified touch."[26] However, *synanchrosis* is not common in Greek literature. The Latin word, contagion, was translated by the Greeks as *miasma*. The root derivation for *miasma* involves sharing or polluting. Thus, for Nutton in the context of disease proximity, the Greeks are said to share, or pollute, while the Latins touch. It was rare in ancient Greece for human disease to be transmitted by touch. Those diseases believed caught by proximity were phthisis, opthalmia, rabies, leprosy, and scabies.[27] When rare epidemics did occur in humans, they were often compared with animal epidemics in sheep or goats. Rapid spread of disease through herds evoked the wisdom of segregating infected animals and removing the healthy to a far pasture.[28] There were never consequences for epidemics in humans since authority was not strong enough to break the family bonds of caring for the sick.[29] Most often in ancient Greek medical tradition, diseases were caused by internal body changes to the four humours, the four elements, rarely by so-called atoms, and mostly by external surrounding air.

Vivian Nutton has found Galen (131-201 A.D.) wrote about "seeds" as responsible for the onset of disease in the small book *On Initial Causes*, although this book was not included in the Latin Opera Omnia editions of Galen until after 1490, and rarely cited afterward.[30] Nutton places Galen's view on the far perimeter of a series of speculations that were never organized.[31] Galen's magnetic or electrical hypotheses were alternative models for the spread of disease that were never integrated into his humoral system. For Galen, there was no need for theories of transmissibility since diseases exhibiting fever were either common in summer or winter and therefore considered a part of the humoral cycle.[32] The appearance of seed theory as a part of contagion theory took a back seat in antiquity and during the Renaissance since there were not methods in existence, nor any attempts to identify "seeds" in the atmosphere or in the patient.[33]

In medieval Muslim culture, disease was not generally considered contagious since it came directly from God.[34] As Michael Dols has pointed out, the Muslim society did not affirm that plague was God's punishment, and therefore did not encourage leaving the city during popular religious ceremonies. In this way, Islam did not support a belief in the contagious nature of diseases, an idea more prevalent in Christian Europe. "Adwa" is the closest term to contagion in the Arab language, although more broad in translation.[35] The Andalusian scholar Ibn Qutayba (d. 889) attracted European attention during the Black Death in the mid fourteenth century for his early observations about the contagious nature of disease. It was clear to the pre-Islamic Arab tribes into which Qutayba was born, that a demonic contagion befitted the spread of camel mange.[36] Qutayba extended the idea of contagion beyond popular superstition by arguing that contagion developed from the *odour* of leprosy, and also from sexual intercourse. The idea of contagion was then applied to children who may have contact with people suffering from

consumption or hectic fever. Many arguments in medicine had more leeway in Muslim culture than formulations of legal jurisprudence.[37] The most convincing argument in the context of contagion theory, was that God could use contagion as an instrument of His will. This was a notion Muslims were more readily able to accept. [38]

Avicenna's (980-1037) Canon, is an extraordinarily influential medical text in medieval Europe after being translated into Latin in Toledo in 1187, provided only a brief statement in a vast work about the contagiousness.[39] In Book IV regarding leprosy, Avicenna offers the cause of leprosy in three ways: The first cause was due to an increased flow of black bile from a faulty phlegmatic complexion of the liver. Second, this disease could be caused by anything that prevented the capacities of elimination. Finally, leprosy could be caused by corrupted air by reason of proximity, or by heredity, or hot air, or bad food. The third position of corrupted air created elaborate debate between moralists and physicians at the University of Paris in 1277.[40] However, a vast majority of physicians did not emphasize contagion as a factor in disease. Internal disease took precedent over environment in medieval Europe.

Pietro d 'Abano (d. 1316), in his famous Conciliator, emphasized the terms corruption and pestilential air as important predisposing factors with leprosy. However d'Abano did not specify whether the origin of this corrupt air was natural or human.[41] In d'Abano's commentary on the Aristotelian Problems, the question of contagion was specifically discussed and printed six times before 1525.[42] During the persecution of lepers in 1321, there were no arguments reflecting an awareness of the doctrine of contagion.[43]

The perspective on contagion began to change during the Black Death in the mid thirteenth century. It is generally accepted by historians of science, that the unprecedented epidemic known as, "The Black Death," was caused by a disease known today as bubonic plague, and with an etiology of *Yesinia pestis*. Paradoxically, the prominent French surgeon, Guy de Chauliac (1298-1368), was the first to consider the main cause of leprosy as corrupted air and contact with lepers, but never reasoned the same for the cause of the pestilence.[44] Tommaso del Garbo (d. 1370), professor of medicine and astrology at Padua, tried to explain the speed of disease spread during the Black Death by noting that the pestilence was caught by the sight and by the touch.[45] The significance of his lectures at the University of Bologna, which included the statement that Galen had declared that certain *seminaria* were in bodies already full of superfluities, was commonly extended to the sixteenth century medical classroom.[46] The Florentine chronicler Matteo Villani, was one of the first to suggest the pestilence was spread by a "healthy mixing" of persons, or possibly by conversing with the sick.[47] Jacobus, a royal and papal physician and Chancellor at the University of Montepellier, provided perhaps the most detailed account of the contagious nature of what is today known as bubonic plague, during the Black Death.[48] Certainly the contagious nature of disease was incubating in the minds of mid-fourteenth century medical practitioners.

VI. Syphilis and the Concept of Contagion

One thing has become clear in this analysis: the concept of infection and contagion are metaphors of indefinite strength. Another is how the multi-factorial structure of natural and supernatural causes compounds the theories of contagion. Early modern European physicians had to grapple with many questions. What did it mean to receive the contagion? Why didn't everyone who was exposed to the disease become affected?[49] How was it that diseases occurred in some places more frequently than others? It is pure speculation but it seems likely that nearly everyone who contracted the disease reported to their physicians how right after sexual intercourse large sores or pox in the groin area began to appear.

According to the medical literature of the period, many physicians reported the number of cases of syphilis dropped and leveled off by 1540.[50] The key question was how invisible discrete entities, or entity, could be passed or propagated? Medical historians generally consider contagion in reference to entities or an entity that increased in number.[51] Only when retrospective knowledge of the past is not contingent upon our germ-theory culture can we compare and contrast early modern with contemporary European views on the cause, and signs of disease. Twentieth century

historians of medicine examining germ theory tend to use the idea of an increase to suggest a multiplication of living organisms. It is an anachronism to look at old ideas in this way since the boundaries between living and non-living entities were constantly changing, and biology was not introduced as a term until the late eighteenth century.[52] The concept of spontaneous generation was used to explain the variety of life forms like insects, and worms. Spontaneous generation meant that life could dissolve by putrefaction, and give rise to other forms. Moreover, multiplication did not have to entail a physical process as evidenced by "action at a distance" in the case of the eye transmitting and propagating occult qualities of disease.[53]

Early sixteenth century physicians revived ancient theories of "atomism" and combined them with new theories of contagion that gravitated towards small particles. In some cases swarms of insects or other organisms might better provide an analogy to independent observations of decay. One example was that of rotting fruit and the observation of spread only to the fruit next to it.[54] These types of observable putrefactions and fermentations were fundamental to contagion theories. Other analogies were found in the spread of *odours* from deceased animals, vapors from marshes, caves and mines, or *foetid* animal breath. There were often parallels between the spread of disease and the effects of poisons, or to poisoning of a well where a small amount caused high mortality. Animal poison such as the venom of snakes was referred to as virus. This term was usurped in the twentieth century and used when referring to non-living replicating nucleic acids wrapped in protein.

The terms seed and germ did not have attributes of living organisms in the modern sense although they did refer to growth.[55] It is difficult to separate the cause of disease from the process of disease. This is the same problem with usage of the terms contagion, miasma and infection. Much confusion arises from an inability to distinguish between living or nonliving entities passed between persons or environments, and the process of passing or affecting as being either direct or indirect. The Black Death and epidemic syphilis were perceived as externally imposed disasters that affected many people at the same time. Theories of contagion reached paradigmatic consideration when disease was passed by touch or from little distance.

In Rome, Gaspar Torrella (1452-1520) a Spanish papal physician to Pope Alexander VI, tried to separate his group of rational and learned doctors from the astrologers on the question of the cause of syphilis in the first decade of the epidemic.[56] Experience showed these rational doctors that proximity was responsible for the appearance of syphilis in another person, after the planets had entered new conjunctions, or as God's anger had waned. Torrella's argument had an important intellectual resource, the Disputationes written by the Florentine philosopher Pico della Mirandola in 1496.[57] To argue strongly that astrology was the cause of an epidemic spread of syphilis denied human and divine free will. Torrella believed astrologers were occupying too large a role at the center of a disease that learned physicians knew best how best to cure.

Torrella argued that *contagio*, whether by touch or at little distance, made the disease "a thing." He went further and insisted that after its first appearance, that syphilis was only contagious. He denied any changes in the air being analogous to the corruption thought to cause phthisis and pestilential fever.[58] More explicitly, Torrella said that the agent of transmission was "corrupt vapours" from the uterus entering pores in the male member. He also claimed knowledge of a case of indirect contagion from bed linens in which an older man caught syphilis by sleeping in the same bed as his younger brother who was already infected. By 1500, Torrella believed the disease was also being spread, in rare instances, to infants from the breasts or mouth of wet nurses.[59] Torrella was careful not to deny that syphilis involved an imbalance of the humours, or that the six non-naturals could be predisposing factors. His account was male centered as evidenced by his assertion that men suffered more from the disease, and that men should avoid infected women, but not the reverse.[60] Torrella's language was apparently directed toward fee-paying males. The uterus was cold, dry and dense, and it was only after repeated sexual contact with infected males that women became infected.

Torrella acted as a public health advisor proclaiming the only prevention of syphilis was for authorities to treat all infected prostitutes, and urged that matrons should be given powers to examine prostitutes and commit those who were infect to a special institution with its own doctor.[61] His urgent message was spread throughout Europe, yet nothing was done until later in the century when his advice was put into practice in his own home of Valencia.[62] It is hard to know if Torrella's preventative measures were too difficult to implement, or simply ignored.

Pietro Trapolino (1451-1509), a physician and lecturer at the University of Padua, examined the notion of "seeds of disease" that was another contender in the arena of contagion theory during the syphilis epidemic.[63] He used the term *seminarium* as equivalent to *fomes*, requiring the right conditions for development of disease. Trapolino was convinced that empirics cured better than most learned physicians.[64] He, like a growing number of other physicians, tended to side more with Avicenna than Galen in terms of an essence to disease.[65] He distanced himself from manifest qualities and felt that what made a person likely to contract syphilis was a type of ignitable quality he called fomes generated within that person from its corruption. Wilmer Cave Wright believes Trapolino influenced Girolamo Fracastoro's views on contagion.[66]

The contagious nature of syphilis compelled medical practitioners to find an explanation. It is obvious that physicians had reputations to uphold against the views of empirics, and as educated practitioners had to stop the spread of the disease. Empirics were enjoying as much success as physicians in prescribing cures for syphilis as the disease went into natural remission regardless of treatment. Typically syphilis was explained as a disease of cause and effect. The cause was the sick patient, but there were two explanations for effect. One formulation involved the manifest qualities described by Aristotle of hot, dry, wet and cold, which was widely accepted as the "doctrine of sympathy."[67] However, this doctrine only explained how a part of the body suffered with another, but without a direct local cause. Another was the "doctrine of subtlety", a name invented to cover natural actions that could not be explained by manifest qualities.[68] The use of either of these approaches for explaining contagious disease was dependent on the author's religious orientation, and to the extent they were concerned with natural philosophy taught at the university.

Due to the influence of the physician and philosopher Marsilio Ficino's (1433-1499) Three Books on Life, written in 1489, interest in astral and occult forces as a cause of disease, and as a therapy, increased in the fifteenth century at the University of Padua. Hidden qualities and sympathies defied Aristotelian categories and explained the switch to occult qualities, or what was known as the "whole substance."[69]

Jean Fernel (1506/7-58), a physician and professor at the University of Paris, contributed to the new "doctrine of subtlety" utilizing the debate on how syphilis was caused.[70] The subtle powers Fernel referred to were invisible aspects of the natural world. He had stated that syphilis existed in different people at different states of intensity depending on their constitution.[71] He also called syphilis a contagious disease that was not self-generated but arising from a maligned quality that spread through the body, even to the spirits, from a small point of contact.[72] What was passed was referred to as an efficient cause of disease. Fernel believed that while the most important method of passing syphilis was through venery, it could also be transmitted by skin contact, by the breath, and from mother to unborn child.

One traditional analogy of invisible transfer, described by Fernel, was associated with the electric eel. The eel passed a quality through the trident of the fisherman and numbed his arm. Galen had talked about the action of poisons, certain drugs, and the same shock of the eel as rare actions of a "whole substance." Fernel used Galen's "doctrine of whole substance" and argued that some diseases, like syphilis, acted on the "whole substance" of the parts of the body.[73] These actions were considered "occult" by Fernel, since they were hidden from the senses of the physician. Fernel maintained something divine in his view of the "whole substance" action on organs, particularly in the category of diseases like syphilis. The closest to any mechanism of contagion in Fernel's description of syphilis is an "occult" process hidden by God's actions.[74] According to

Arrizabalaga, Fernel's idea of "whole substance" was closer to the spiritual meaning of the "soul" in Christian religious tradition.

Fernel had developed Galen's doctrine of the "whole substance" of certain drugs into a new theory of medicine where certain diseases act on the whole body. He added this "whole substance" disease category to the traditional categories of constitutional disorder and faults in humoral complexities. De naturali parte medicinae, or The Natural Part of Medicine, was published in 1542 and enormously popular for synthesizing classical, medieval and Renaissance medical thought with Christianity. His speculative dialogue De abditis rerum causis, or On the Hidden Causes of Things was published in 1548. There were ninety-seven complete editions or translations of his writings between 1554 and 1680.[75] Fernel was enormously influential in heightening the debate about the cause of syphilis and about contagion theory among learned physicians at universities in Europe.

Viewed retrospectively the importance of sixteenth century contagion theory rests with the Veronese physician and humanist Girolamo Fracastoro (1478-1553). His famous three-part poem, Syphilis or the French Disease, was completed by 1525 and published in its final form in 1531. It was a tribute to his poem that the disease was named syphilis by historians in the seventeenth century. According to Margaret Pelling, Fracastoro's theory of contagion has alternatively been ignored, eulogized, diminished and merged into context by successive generations of medical historians.[76] For his poem and writing on contagion theory, historians of science like Charles Singer and Karl Sudhoff, in the early twentieth century, considered Fracastoro a pioneer in bacteriology and epidemiology. William Cave Wright has noted biographers who have variously listed Fracastoro as the first to use a sort of telescope;[77] the first to design a planetary model of movement known as an orrery;[78] designing and marketing wooden globes with maps of the New World;[79] and in confirmation of Da Vinci's "discovery" that rock strata at Monte Balca near Verona contained extinct marine fossils.[80] It is not important to debate Fracastoro's precise contributions to these discoveries, however, it does serve to illustrate in how many areas of investigation Fracastoro lived on the cusp of change from natural philosophical principles to those of the early modern scientific revolution.

According to Wilmer Cave Wright, Fracastoro was most influenced by his colleagues at the University of Padua, Pietro Trapolino, and the Aristotelian philosopher Pietro Pomponazzi (1462-1525) of Mantua.[81] She clarifies that Pomponazzi's influence as an astronomer, physician and philosopher is best explained by his pretext that human events were governed by natural laws rather than supernatural intervention. Secular humanism was at a certain peak of influence on medical thinking with Pomponazzi. Arrizabalaga implies less of a connection between Pomponazzi and Fracastoro by omitting comments on the role of Pomponazzi. Trapolino had supported the ideas for categorizing diseases found in writings of Averroes, but Pomponazzi was largely anti-Lucretian and anti-Averroist in medical philosophical contexts.[82]

Fracastoro, who started lecturing on logic at Padua in 1501, was decidedly more cautious and orthodox lecturer than many of his peers. He started his physicians practice in Verona in 1510 under conditions where a foreign garrison of 8,000 soldiers never cleaned the streets.[83] He had warned city officials of an epidemic of pestilence and fled to Incaffi during the outbreak of 1510 since there were no facilities to deal with the epidemic. He stayed at his summer residence on the Lake of Garda during another epidemic where it is said he started to write his poem Syphilis, inspired by his view of the famous ruins of the Latin poet Catullus.

Fracastoro essentially announced himself as a learned humanist composing a rare poem about disease in classical Latin style. In the poem, Fracastoro describes the clinical features of a disease resulting from "the impious wars of the Gauls."[84] He took the name "syphilis" from the legend of *Syphylus*, a young shepherd boy punished by Apollo with a terrible disease that covered his body with sores for neglecting his flocks. The word *syphylus* is from the Greek work syn meaning together, and *philein* meaning to love. In William Van Wyck's translation from 1934, in the fifth paragraph he first refers to the semina or seed of the disease, and its origin from Spanish sailors:

O Muse, reveal to me what seed has grown
The evil that for long remained unknown!
Till Spanish sailors made the west their goal,
And ploughed the seas to find another pole,
Adding to this world a new universe.
Did these men bring to us this latent curse?[85]

William van Wyck translates Fracastoro's use of the term contages as *contagious*, and here finds the suggestion that syphilis cannot be tamed by human power. Fracastoro uses the terms contagion, miasma, and virus become often in his poem.

Ever is it contagious and one sees
It born for common woe. And it appears
Everywhere with such strange diversities,
Changing in every climate through the years
Atlantis-fruit, it adds to human fears.
The womb of centuries has given it birth.
Go, curious mortals, go and seek its worth!
Attempt to seize this all mysterious force.
Explore the surface of the globe, where dwell
All humans stricken in this plague's mad course,
Tracing its origin to heave or hell.
Alas, is not this ill too prompt to fell
Quicker than lightning people everywhere?
Find its source in the water, fire, or air! [86]

In the next paragraph Fracastoro comments on the influential role of air as a corrupting influence.

Is it of air, whose unhealthy wave
Weigh on the body, every breast to lave,
Wherever Nature's atmospheres will spill,
First cause of all calamities that kill?
Creator-Principle of all the living
Is the air, pregnant with its ferments, giving
Corruptions to its fluid mass and, spent,
Striking at humans with vile intent.
Learn how the air gives people each disease,
Air the invincible for centuries [87]

Fracastoro finds that planetary conjunctions are primary causes. The Black Death had been attributed to the conjunction of Saturn, Mars and Jupiter, which took place on March 22, 1345 in the fourteenth degree of Aquarius. Fracastoro attributes the primary cause of syphilis to the same triple conjunction of planets in the sign of Cancer.[88]

Reaching the zenith of heavenly way,
The sun has measure to the centuries
Those hours that rule the fat of earth and skies,
Under the kind of gods'eternal sway.
An ear of calamity restored,
Jupiter calls a congress of the stars,
Evoking and Saturn and the war-god Mars,
Asking their aid and as their overlord.
That he ordain the future's course, he calls
The Crab, the guardian of the sacred walls,
To open the double doors of heaven's walls.[89]

In the second paragraph of another passage, according to Van Wyck, Fracastoro is speaking like a physician who considers astrology a matter of superstition.

….Oceans exhale miasamic miseries
Carried upon the air as well as seas.
Mixing with these new evils and unseen,
Poisons cooperate, on mischief bent,

Contagions following where they have been,
Changing the atmosphere to some extent.
Let me not hide, for all my halting speech,
The difficulties crowding me. For each,
I ask that heaven will link it to those things
That cause it. But a tardy heaven brings
Naught save delays. And, Making no advance,
I find that this hangs on the play of change,
Renewing endlessly mine every doubt,
Scattering many errors on my route.
Secretive in design, like nature too,
These varying poisons fill our earth with gloom…[90]

Fracastoro also describes in Book I the symptoms of the disease as afflicting the pudenda, an uncontrolled corrosion of the groin. Other serious signs are described including gummata, which resembles a resinous exudate from trees.

Book II of the poem describes the treatment of syphilis including phlebotomy twice a year, herbs like aloe vera, and mineral concoctions of myrrh and antimony.[91] In Book III of the poem, Fracastoro describes the virtues of *lignum sanctum*, the holy wood, as a preferential treatment over mercury. Here he recounts the cruelty of the Spaniards towards the Indians in the New World and describes the myth of the shepherd *Syphilus*. Fracastorus said the Spaniards had found syphilis prevalent on an island, later to be known as Hispaniola. At that point, a newly arrived ship brought word that the disease had been raging in Europe. In this way Fracastoro informed his readers how the disease in Europe did not have New World origins.[92]

For all of Fracastoro's uses of contagion in his poem, according to the recent analysis by Saul Jarcho, Fracastoro did not believe syphilis was transmitted by direct contact in 1530.[93] This view was first delivered by, Charles and Dorothea Singer in 1911, who noted in the first issue of the *Annals of Medical History* that Fracastoro used the term miasma in relation to the air as the main cause of the epidemic disease in Syphilis.[94]

Fracastoro enlisted classical Roman humanist beliefs and not a vengeful Old Testament God who inflicted disease upon humans.[95] In giving a prominent place to the *seminaria* of disease in Syphilis, he departs from Galenic and Aristotelian views of medicine and natural philosophy and sided with the ancient atomist views of the Greek atomist Epicurius (342-270 B.C.), and the Roman philosopher and poet Lucretius (95-55 B.C). It was not, however, altogether clear in 1530 whether Fracastoro looked on syphilis as a disease entity like plant seeds that could propagate, and whether this took place in the air or in the infected body.

Vivian Nutton points out that Fracastoro's views on contagious disease were much clearer by 1546 in his seminal work, De Contagion. From 1935 to 1950, Francesco Pelligrini translated several Italian letters regarding contagion from Fracastoro to the astronomer Giovanni Battista della Torre.[96] According to Pelligrini, most of these letters were written between 1530 and 1535. Nutton is convinced by these letters that Fracastoro defined contagion as physical entities passing from one thing or person to another by direct contact.[97]

In 1977, historian Norman Howard-Jones strongly criticized the view that Fracastoro was among the great biologist's of his time. For one thing, Howard-Jones informs us, he did not distinguish between infection and contagion.[98] When Fracastoro said an infection passed from one thing to another, he compared it to the emanations of an onion being peeled causing tears to form. However, for Howard-Jones, tears are not drawn from people at long distances.[99] Howard-Jones further criticizes Fracastoro's use of the term *seminarium* as not having anything to do with a living substance, or with multiplication, and having more to do with asexual reproduction or a chain reaction. Howard-Jones quotes Fracastoro as saying "Typhus was spread more by a taint in the air than by transmission from one person to another.[100] He also believed in the mythical animal called a *catablepha* that could kill from long distances. Finally, he critiques Fracastoro's view that ophthalmia could be passed to everyone the infected looked at. Taken together, Howard-Jones

only emphasizes superstition and tradition in Fracastoro, and closes off his contribution to the progressive development of medical thought found in Nutton, Arrizabalaga, and Jarcho.
Saul Jarcho, who recognized the inadequacy of Fracastoro in using the term contagion in his poem Syphilis, considers his later work, On Contagion a medical classic.[101] He finds Fracastoro very cautious in recognizing the need for philosophical support since the work was dedicated to Alexander Cardinal Farnese who later became Pope Paul III. Fracastoro lived through a popular movement toward secular humanism and also the return of a more traditional Catholicism. Fracastoro had written De Contagione with 24 chapters of explanatory introduction titled De Sympathia. Surprisingly, De Sympathia has not been translated into English, but Wright did provide a still highly regarded analysis in 1930. In De Contagione, Fracastoro references his theory in De Sympathia, and lays out how the concept of contagion was based on selective affinity or analogy between *seminaria* and the four humours present in the patient. Sympathy was a communication of an unknown mechanism, or quality, or subtle action at a distance. The epidemic of syphilis particularly spurred an interest in theories of sympathy as a way to explain contagion.[102] The examples Fracastoro used are not the same as Aristotelian natural philosophy. They include rather bizarre folklore examples such as: Lightening melts the gold, but leaves the cash-box intact; The lion is terrified only of the cock when crowing; Cabbage and rue will never grow when sown together.[103] More notable examples of sympathy were the unknown miracle of the needle for pole in the ship's compass, and the lodestone having sympathy for iron. It was recognized by his contemporaries that some of the folklore examples were taken from the Roman philosopher Pliny the Elder's (23-79 A.D.) Natural History. Although distanced by many centuries, Fracastoro apparently held much regard for Pliny as both had in common, birth in Verona, and erudite interest in plants and herbs and special medical powers.

In The Great Pox, Arrizabalaga and his colleagues provide a detailed analysis of De Sympathia. Fracastoro asks why the material or particle qualities of *odour*, taste and sound have no name. He calls these aspects of the world, spiritual pieces, and is explicit that these species were atomic *simulacra* emerging from the surface of things and either perceptible to the sense, or effecting physical action. [104]

In Fracastoro's book De Contagione, he explores medical applications linking ideas of sympathy with contagion in the context of syphilis.[105] It is evident contagion was a certain infection passed from person to person. A simple infection occurred when a person drank a poison and became ill. This was not contagion in the case of eating contaminated food, milk or water. He breaks from Galen in stipulating that that contagion was not limited to living things, and not just the four elements. Contagion consisted of particles that were invisible, small, and responsible for causing corruption, perhaps due to the introduction of contraries not tolerated by the body, or alternatively, a certain mixing that led to dissolutive putrefaction.[106] His most concise definition of contagion is "a certain similar corruption of a mixed body according to substance, passing from one to another by an infection in insensible particles.[107]

Without doubt, Fracastoro's theory of contagion has proven challenging to translate, is contradictive, and therefore engenders many unanswered questions. The three varieties of contagion Fracastoro describes at length are produced by imperceptible particles. The first form of contagion is by direct contact or touch. These particles are considered hot and sharp when they evaporate, but are moist in combination.[108] The particles are called the *seminaria* of contagious diseases, or *seminaria contagionum*. The second variety of contagion is the most difficult to decipher, but for Nutton simply means "by contact leaving behind fomites which preserved the seeds of contagion and infected by them."[109] Fracastoro starts his discussion of the second variety by mentioning how *seminaria* may in some instances persist in *fomites* for a long time. In his explanation of fomites in clothing, he comes close to the modern English plural noun fomites, which is contact with inanimate objects. Fracastoro next separates descriptions of the *seminaria* into ones produced by contact between humans, although he used the example of fruit, that are not hard and may be viscous and elaborated, and ones that infect by means of *fomites* as viscous and sticky.[110] According to Jarcho, the word fomes has two derivations. One means *touchwood*, a desiccated or decayed fragment of tree useful in conveying fire. It is not far from the inflammation

and suggests the tactile component of contagion.[111] The alternative source comes from the German word *zunder*, akin to tinder and inflammation. Some historians believe this type of contagion is evidence for human-to-human contact transmission.[112]

The third category of contagion is infection at a distance. Here Fracastoro takes from the Islamic idea that ophthalmia, or conjunctivitis, will infect everyone who looks at that person with a beam of light. Infection at a distance also included pestiferous fevers, thought today to mean bubonic plague, and phthisis, believed to be tuberculosis.[113] His third cause of contagion does not involve occult properties, but rather a very subtle material agent that is of a strong viscous composition. Fracastoro's also writes a significant chapter explaining how contagious diseases are spread from a distant object and in a circle. Here according to translation by Jarcho, Fracastoro says:

> One method of penetration is by propagation. The original seminary which have adhered generate and propagate others precisely like themselves, which in turn propagate others, until the entire mass and bulk of the humors is infected.[114]

This is evidence for the concept of contagion by living entities, the *contagium vivum*.
In another chapter Fracastoro writes about how some people were more easily infected than others. He asked, "Is there some way that we accustom ourselves to pestilences, as if they were poisons?"[115] Here Fracastoro asserted that specific *seminaria* had affinities for specific plants or animals. Although Fracastoro promises to return to this residual problem later in his book and never does, historians of medicine have often suggested Fracastoro broached the idea of natural immunity in these passages.[116]

Fracastoro also described diseases such as phthisis where the *seminaria* of contagions developed originally in a person with obstruction and plethora leading to putrefaction. Eventually these *seminaria* were passed to another person of almost perfect health. Fracastoro wrote an entire chapter on phthisis confirming its contagious aspects and makes particular note that it had specificity for no tissue other than lung, based on autopsies that he had conducted.[117] More importantly, he relates cases of phthisis where parts of the lung were found in the sputum, left as wet fluid on bed linens, were dried and still contagious as fomites for another person.[118] For this passage Fracastoro is often credited with having originated the concept of indirect contact transmission. Arrizabalaga and his colleagues play down the significance of this passage since practical people knew empirically that disease could be caught from inanimate objects that had been exposed to disease elsewhere and earlier.[119]

Fracastoro believed that syphilis was not contagious when it first arrived in 1494 in Italy based on statements made in his poem Syphilis. However, twenty years later he observes that most of the cases are contagious *seminaria* obtained by direct sexual contact and on occasion passed by breast-feeding.[120] Further, he correctly assessed that syphilis was not transmitted by *fomites* and caused no infection from a distance. In terms of describing the disease symptoms and signs, Fracastoro misses the primary lesion, or common chancre lesion that occurs with syphilis, but otherwise accurately describes other chronic aspects including time intervals and signs in the most accurate terms.[121] He also observed that during the last two decades the disease had weakened, that the pustules were smaller, and there were smaller and fewer gummata causing less pain.[122]
Perhaps the unusual aspect of Fracastoro is that he left himself wide open for criticism with blatant contradictions in at least three instances of his seminal work, On Contagion. In the first instance he says that syphilis was a rare new disease, and in the very next sentence says that it was common all over the world.[123] In another instance, Fracastoro contradicts an earlier part of his treatise that detailed how syphilis was contagious by direct sexual contact, and then informs that the disease was transmitted by air, adding there could be not other possible explanation for its presence in so many countries. His final contradictions are based on an earlier statement that typhus was contagious by direct contact, and then later stipulates that typhus can only be transmitted by air.

Johann Baptista Montanus (1498-1551), a physician and professor at the University of Padua, was a chief competitor of Fracastoro. Cardinal Farnese once summoned both men to Rome as consultants to advise for a personal illness, but Montanus generally had a better reputation as a doctor in Verona having been the personal physician of Cardinal de Medici in Bologna in 1533.[124] It is difficult to ascertain the origin of strong disagreement with Ficino's "occult cause" in explaining contagion, but both Montanus and Fracastoro were in agreement on this subject. Vivian Nutton has detailed how first Montanus and then Fracastoro strongly attacked explanations of the occult consistent with a physicians admission of ignorance.[125] In lectures given at the University of Padua in 1540, Montanus subscribed to the Galenic idea of a "material poison" produced in part by changes of weather, and partly by vapours arising from the earth.[126] In a lecture regarding Avicenna, he provides a concise opinion:

> Contagion is a Malady which goes from one body into the other, either by means of touching, or without means; by the agreement of the stuff, or by the contrariety of the part of the form, caused by the alteration of the heat, which the moist parts unaptly digests.[127]

Montanus rejected spiritual causes of contagion emphasizing the importance of factors such as the immensity of putrefaction, the sensitivity and receptivity of the part affects, and various types of skin manifestations in the appearance in scabies, opthalmia, and during outbreaks of the plague.[128] His lectures in 1540 were very similar to writings in Fracastoro's De Contagion by virtue of his description of variations in contagion between diseases, and his belief that phthisis was transmitted by infected lung particles, and putrefied blood cast out by spit as they would pass through bare feet.[129] Montanus had also stated that the putrefaction in syphilis, with its thin sharp *vapour*, was not able to penetrate until the opening of pores by the friction of sexual intercourse. According to Nutton, Montanus explained later there were many similarities between what he and Fracastoro were arguing, although his lectures were six years prior to the publication of De Contagion, and eight years prior to Fernel's, De abditis rerum causis. Montanus ideas on contagion were not put into print until his death in 1551, and his own Morbo de Gallico was not published until 1566.

VII. Conclusion

From the general debates that existed in the early sixteenth century and especially during the 1540's, contemporary historians Saul Jarcho and Vivian Nutton favor the view that Girolamo Fracastoro was a key figure in promoting a theory of contagion stipulating invisible living and growing entities spread by direct contact between people. Nutton and Jarcho emphasized the importance of Fracastoro's De Sympathia in understanding his De Contagione, and for Nutton, letters written by Fracastoro and translated by the Italian historian Francesco Pelligrini. Fracastoro's writings on contagion were not new in their formulation at the University of Padua. The contemporaneous lectures of Johann Baptista Montanus at the University of Padua beginning in the 1530's were apparently a major influence on Fracastoro as well as much older Roman humanist writings of Pliny the Elder and Lucretius. More fundamental in influence on Fracastoro were the late fifteenth century writings of Pomponazzi, another contemporary of Fracastoro's at the University of Padua, who regarded human events as being governed by natural laws not supernatural intervention. At the turn of the sixteenth century, Pietro Trapolino's use of *seminarium* as equivalent to fomes may be the source of use of this term, as well as the initiation of a crude system for categorizing diseases.

It is most difficulty to ascertain how Jean Fernel's might have influenced Fracastoro, but he was assuredly the catalyst for a view among physicians that syphilis was transmitted by venery, skin contact and passed from mother to child. Fernel also exposed the idea that syphilis existed in different states in different people, a precursor to the concept of immunity that Fracastoro elaborated on to a minor extent in De Contagion.

While Fracastoro was not clear in his 1530's about whether *seminaria* were transmitted through air, by the 1540's he had pinpointed *seminaria* as living and growing *contagium vivum* transmitted by sexual contact. Fracastoro's writings were most renowned on the subject because of his originality in writing a superb poem on disease. His widespread fame for Syphilis perhaps biased retrospective opinions about his importance to medical history. In his time, Fracastoro was not as

famous for his medical writings about syphilis, or even ideas about contagion, as Jean Fernel. Fracastoro was also less highly regarded in terms of physician advice to the papal court than Montanus in Italy. Perhaps his fame, particularly among the humanists, promoted his writings more expeditiously, and therefore when viewed in retrospect, he appears to have been more original and one of the earliest to publish a large discourse on contagion

It is difficult to interpret contradictions in Fracastoro's De Contagion. Perhaps he was merely arguing for all facets of an idea as was sometimes customary in serious intellectual debates. On the other hand, Fracastoro may have presented intellectual sides of the argument as a precaution against the shifting proving grounds of religious heresy. He was considered more cautious than most lecturers at Padua in trying to avoid absolutist statements contradictory of Church opinion. Ultimately the debate was framed by an urgent need to understand and better treat the terrible epidemic. Fracastoro believed in four *humours*, but his contagious diseases were independent of humoral balance. His ideas about treatment worked on the *seminaria* whether the patient was choleric or phlegmatic.[130] Nevertheless, it was always safest to avoid malodorous miasmata than to treat invisible theoretical seeds.

It is a kind of paradox that in critiques of Galen, Fracastoro had implored all physicians to rely more on observation. After all, no one had ever seen any *seminaria*, poisons, or miasma that were being described so graphically, and these ideas were outside the mainstream Greek world of Galen and Hippocratic medical practice. He lived at a time when astrology was gravitating toward astronomy, and alchemy was moving toward modern chemistry. He lived on the cusp of change from natural philosophy to the modern scientific revolution. For a physician like Fracastoro, this meant a remarkable degree of indirect observation, and theorizing about syphilis.

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