8-2009

The Puzzle of Syphilis: A Literature Review on Putting the Pieces Together

Tabatha Anne Boekhout
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To the Graduate Council:

I am submitting herewith a thesis written by Tabatha Anne Boekhout entitled "The Puzzle of Syphilis: A Literature Review on Putting the Pieces Together." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts, with a major in Anthropology.

Murray K. Marks, Major Professor

We have read this thesis and recommend its acceptance:

Walter Klippel, Michael Logan

Accepted for the Council:
Dixie L. Thompson

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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The Puzzle of Syphilis:
A Literature Review on Putting the Pieces Together

A Thesis
Presented for the
Master of Arts
Degree
The University of Tennessee, Knoxville

Tabatha Anne Boekhout
August 2009

ACKNOWLEDGEMENTS

I would like to thank all those who had a hand in helping me to complete my Master of Arts degree in Anthropology. I would like to thank Dr. Murray Marks for serving as my committee chair and helping me choose this topic, as well as for overseeing and guiding me toward the finish line. I would also like to thank Dr. Michael Logan for his detailed and supportive critiques of the many drafts of this thesis, and Dr. Walter Klippel for serving on my committee. Finally I would like to thank my husband Travis for his unwavering encouragement and for being my advocate and cheerleader.

ABSTRACT

As culture changes, so does disease. This change has been seen in a variety of diseases, but none are so hotly debated and researched as the treponematoses, the four diseases related to and including venereal syphilis. There have been decades of debate on every aspect of syphilis: where it came from, who gave it to whom, how it evolved, and what the distribution was at various points in time. Herein, the four types of treponematoses will be examined along with the clinical pathology of each. The skeletal evidence will be examined carefully, taking into account the distribution of lesions for each of the treponematoses in order to discern whether they can be distinguished. The debate over the Columbian/pre-Columbian origin of venereal syphilis will be discussed, along with the equally rampant debate over the unitarian/nonunitarian hypotheses for the evolution of the disease. In order to draw conclusions on the origin of the treponematoses, the area of first contact between Spanish explorers and the New World inhabitants will be examined. Next, the problem of differential diagnoses will be discussed, followed by the examination of DNA techniques being employed to trace the origins and distribution of the treponematoses. From the beginning of its recognition as a disease of humans, debate has surrounded syphilis and its cousins, making it one of the most argued over diseases in human history.

Syphilis has long held a place in the forefront of researchers' minds in various disciplines: medical anthropology, paleopathology, epidemiology, virology, and DNA research. Because of the mysterious beginnings and often virulent pathology, decades of debate and ideas about the disease have gained more and less popularity in scientific fields. Unfortunately, there is still no clear winner to any of the debates. For all the research that has been done, more questions

arise. What is the ultimate origin of the treponematoses? Is it a single disease manifesting itself in different ways based on location and social standards? Is it a quartet of closely related syndromes that evolved their virulence in their respective environments? These and other questions will be examined through many different aspects of research.

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CHAPTER 1
Introduction to Disease Processes

To understand the complex nature of diseases like syphilis, one must first understand the processes of disease change. "Infectious diseases are complex bioecological puzzles reflecting a range of interactions among biological, environmental, and social forces" (Saunders 1988:727). Disease has coexisted with humans for the entire length of our history (Inhorn and Brown 1990:89). As society has changed and adapted, so too have the diseases that affect us. As Inhorn and Brown put it, "human groups have often unwittingly facilitated the spread of infectious diseases through culturally coded patterns of behavior or through changes in the crucial relationships among infectious disease agents, their human and animal hosts, and the environments in which the host-agent interaction takes place" (1990:89-90). This chapter will trace these changes from hunter-gatherers to modern times, with a special emphasis on venereal syphilis and the changes the pathogen went through as it adapted to survive amidst the changes through which humans went. Understanding disease processes in the midst of change will have benefits not only for those studying syphilis, but for epidemiologists and those working to cure a multitude of diseases that affect us today. The discussion on change will lead to an examination of epidemiological transitions throughout human history as well.

The first thing that needs to be done is to define the treponematoses. The treponematoses are a series of four closely related diseases that are caused by the *Treponema* genus of bacteria. The bacteria are spirochetes, corkscrew-shaped bacteria shown in figure 1. The bacteria taxonomically identified as *Treponema cariteum* causes

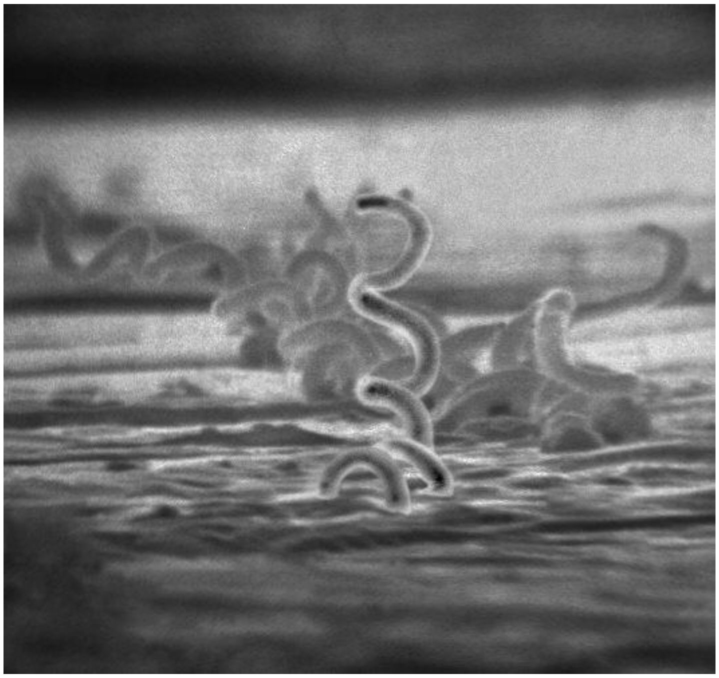

Figure 1. Electron micrograph of *Treponema pallidum* bacteria. [Public Health Image Library (http://phil.cdc.gov/phil), PHIL ID#1977; original image provided by Centers for Disease Control/Dr. David Cox.]

pinta, the least virulent of the four diseases, while the other three are all classified as *Treponema pallidum* subspecies *pertenue* (yaws), subspecies *endemecium* (endemic syphilis), and subspecies *pallidum* (venereal syphilis) (Aufderheide and Rodriguez-Martin 1998:154). Each of these diseases will be examined in more detail in chapter two. According to Myr (1996:264), biological “species are groups of interbreeding natural populations that are reproductively isolated from other such groups”. Taxonomically, three of the diseases are described as subspecies. Traditionally, subspecies are able to interbreed but usually do not due to distance, so in this case, the geographic distance plays a role in the categorization of these diseases. Since yaws, endemic syphilis, and venereal syphilis all seem to confer some degree of resistance to the others, this is evidence of their genetic similarities. Pinta is classified taxonomically as a separate species than the other three diseases. This reflects the difference in the virulence that pinta shows compared to the others as well as its separate path of mutation, a theory that will be discussed in chapter 3.

Another distinction that must be made is the differences between the words endemic, epidemic, pandemic, as well as syndrome and disease. According to Webster’s Dictionary, endemic means “indigenous to a region or people”, epidemic means “affecting a large number of people”, and pandemic is broader, and refers to an “entire country or continent, or to the world”. Hudson defines endemic as the antonym of sporadic (1965:885). In a more basic sense, syndrome is defined as “a set of symptoms that characterize a certain disease or condition”, while disease is defined as “a condition of ill health; malady”. Understanding the nuances between the meanings of these terms is essential to understanding disease theory.

As Hackett describes, there are three ways through which most human infectious diseases arose: "(1) Free-living or saprophytic organisms; (2) Commensals of infections of insects; or (3) Infections of warm-blooded animals" (1963:21). Hackett makes the argument that the human treponematoses probably arose from an animal infection rather than a saprophyte or a commensal, due to the existing animal treponemes like *Treponema paraluiscuniculi* in rabbits and yaws-like infections in apes (Cockburn 1971:46, Hackett 1963:24). In fact, Cockburn hypothesizes that the treponematoses may have come from a non-human primate ancestor from millions of years ago, and Mitchell places the *Treponema* species as far back as six million years ago at the emergence of the hominin lineage (1971:46, see also Mitchell 2003:173). Mitchell supports this with evidence of yaws on a 1.7-1.6 million year old *Homo ergaster* skeleton found in Kenya, which would make the treponematoses one of the oldest existing family of infectious diseases (2003:175). If the *Treponema* family of bacteria is this ancient, it has shown a remarkable ability to adapt not only to different climates and social environments but to different species as well. The study of this bacterium could contribute greatly to our knowledge of infectious diseases and how they change and adapt.

The Epidemiological Transitions

The concept of the three epidemiological transitions was formulated by Omran in 1971 to model demographic and epidemiological changes in human populations (Barrett et al. 1998:249). Omran's model "focuses on the complex change in patterns of health and disease and on the interactions between these patterns and the demographic, economic, and sociological determinants and consequences" (Barrett et al. 1998:249). Although the model was criticized at first for focusing mainly on industrialized nations, the basic premise is still useful for understanding disease change. This model can be applied to human disease changes with a special emphasis on the treponematoses and the changes it went through.

A discussion of the epidemiological transitions begins with the Paleolithic baseline. During this time, the earliest modern human groups likely existed in small family groups of hunter gatherers. Low population density and wild food sources would have created a picture of disease very different from what we see today (Barrett et al. 1998:251). This low population density would not have allowed sustained or epidemic diseases to survive (Inhorn and Brown 1990:94). A few diseases or parasites would have come in contact with these humans during their daily food gathering activities, and those with different host vectors would probably have been present as well (Barrett et al. 1998:251). Smith (2006) has researched the existence of the treponematoses in the Tennessee River valley in the time periods prior to agriculture. She points out that the pottery found in these horizons are markers of sedentism while in a hunter-collector subsistence economy. This information is important as Smith shows that a large population, like those dependent on agriculture, may not be necessary to maintain endemic treponematoses, although sedentism may be. It was probably not until the transition to agriculture and a more sedentary lifestyle that a variety of diseases began to affect humans more and more (Barrett et al. 1998:251).

According to Omran, the first epidemiological transition occurred at the time of the agricultural revolution (Barrett et al. 1998:252). This transition was the result of a massive change in the demography and epidemiology in the life structure of humans. Sedentary life meant a higher population being fed by food with arguably less quality and variety than wild resources. At this time, some groups began living in close proximity to animals, as in pastoralism, which led to various zoonoses, diseases that are communicable from animals to humans (Barrett et al. 1998:252). Their new diet may have made them more susceptible to disease and new agricultural practices did as well. Irrigation, the use of feces as fertilizer and the advent of food storage would have created more opportunities for people to become sickened (Barrett et al. 1998:252-253). As populations grew, people were living closer together and living conditions became more unsanitary, allowing for the spread of infectious diseases. When syphilis moved with human migrations to the cooler areas of Europe it is thought that the disease made its transition to a venereal form because a cooler climate, the wearing of more clothes and more sanitary conditions caused the disease to find a new mode of transmission (Baker and Armelagos 1988:708).

The second epidemiological transition occurred at the time of the Industrial Revolution. Pandemic diseases began to decline at this time due to effective treatments and higher standards of hygiene and cleanliness. This was also the time of a decline in infant mortality and the eradication of smallpox, polio, and other epidemic diseases. It is late in this time period that the use of antibiotics began to cause a decline in the number of syphilis cases in many parts of the world (Barnes 2005:218, Tramont 1995:1362). As nutrition and health improved, "diseases of civilization" began to replace the pandemic diseases. The increase in life expectancy brought about an increase in chronic diseases such as cancer, diabetes, chronic obstructive pulmonary diseases and coronary artery disease (Barrett et al. 1998:255). In addition, the increasing pollution from industrialization caused higher numbers of chronic diseases like allergies, cancer, and birth defects (Barrett et al. 1998:255). Increasing urbanization of the world led to increased hypertension, depression, and anxiety as well.

We are now living in the time of the third epidemiological transition. This is a unique time period marked by three different factors that make the last three decades a time of great concern to epidemiologists and disease researchers. First, we have seen a remarkable increase in newly described diseases, a situation that has not been seen in modern times, especially in a time of such great hygiene and modern medicine. The Centers for Disease Control (CDC) has reported that 29 new pathogens have been identified since 1973 (Barrett et al. 1998:257). These newly emerging diseases include several hemorrhagic fevers like Ebola and Hantavirus and, of course, AIDS. Next, there has been a worrisome increase in reemerging "controlled" infectious diseases. Ecological destruction and climatic change seems to be at fault in the increasing reproduction of malaria vectors and the increase in cholera. Another example is from Africa, where dengue fever has had a dramatic resurgence due to human factors such as poor urban planning in underprivileged areas, leading to standing pools of water beneficial to the life cycle of the mosquito. Finally, there has been a rise in drug-resistant strains of several diseases (Barrett et al. 1998:256). Tuberculosis is the most well-known of these, which has been found to have multiple drug-resistant strains. These strains have emerged due to indiscriminate use of antibiotics, allowing the disease to survive initial onslaughts of medication and mutate. Interestingly, the treponematoses have not become drug-resistant like some of their counterparts, despite all the other mutations they must have gone through to follow humans for millions of years, although resistance to penicillin has been experimentally induced in animals (Tramont 1995:1361). Syphilis has also seen resurgence in numbers that coincides with the emergence of AIDS (Tramont 1995:1361). All these factors (despite scientists who believed the end of infectious diseases was imminent) have shown the scientific community that more work has to be done to understand and eradicate infectious disease.

Paleopathology

Paleopathology has played an important part in the research and documentation of disease in ancient populations (e.g. Buikstra and Cook 1980; Rothschild et al. 2007; Smith 2006). The study of human skeletal remains (e.g. El-Najjar 1979; Lefort and Bennike 2007; Reichs 1989), mummified remains (e.g. Gray 1973; Salo et al. 1994), and coprolites (e.g. Chavez and Reinhard 2006; Reinhard et al. 1973) continues to play an important part in disease theory. Although only a small fraction of human skeletal remains show evidence of infectious disease, each skeleton studied contributes to our knowledge base and helps to complete the picture of ancient disease. Larsen stresses the importance of osteological samples in paleopathological research in order to understand and document the human condition (1994:143). Inhorn and Brown summarize the research objectives of paleopathology in two parts: "(a) to establish the antiquity and evolution of various infectious diseases in human populations through examination of prehistoric osteological and, in some cases, soft-tissue evidence; and (b) to contextualize these findings to the physical and cultural circumstances of the human populations involved" (1990:93). Ortner recognizes that scholarly and scientific reasons for studying paleopathology include identifying the antiquity of diseases, following the transmission of disease between populations and geographic areas and learning the evolutionary dynamics between humans and disease agents (2003:109).

Paleopathology has undergone some scrutiny in the past, as researchers were accused of paying undue attention to individuals instead of populations and focusing on racial differences and typology (Armelagos and Van Gerven 2003:51). Armelagos and Van Gerven suggest that researchers move forward by working with other disciplines and focusing on issues that are relevant to our society today (2003:60). I would argue that studying the effect of a disease like syphilis on populations fulfills both of these obligations.

There are several factors that affect the expression of disease on the skeleton and treponematosis illustrates several of these through one or each of the four different types. Some of these include age of onset, individual immune response, the biology of the disease, portal of entry, effectiveness of treatment, and social conditions that affect immune response and transmission (Ortner 1992:8). In the treponematoses, the age of onset differs from childhood in the non-venereal forms to adulthood in venereal syphilis. This leads to congenital transmission being a possibility in the venereal form and absent in all others. In addition, the longer an individual lives with the disease the more chance there is that the skeleton will be affected. Individual immune response accounts for the fact that not all individuals show a skeletal response. Since the treponematoses are understood to be hematogenous, the portal of entry does not seem to change the skeletal elements affected between the syndromes. In regard to the effectiveness of treatment, syphilis can be cured by penicillin and does not develop drug-resistant strains. All of these factors are central in paleopathological research of all diseases that affect the skeleton, and especially syphilis.

To facilitate paleopathological research and comparability of studies, there are several issues that must be recognized and remedied. First, there must be standardization of descriptive terms and diagnostic criteria so researchers from around the world can compare results. Buikstra and Ubelaker (1994) have published standards that should be used in the description of pathological remains. Also, it is important that research be published with more photos included in these publications so other paleopathologists have an opportunity to offer constructive criticism and differential diagnoses. Another important aspect of research is working toward better training for paleopathologists and future paleopathologists. Finally, for certainty in dating, such as radiocarbon dating, more lines of evidence are required and maintaining provenance is crucial when unearthing remains (Armelagos and Van Gerven 2003). When paleopathologists are aware of these issues and work to resolve them, we will be more able to create a complete picture of disease migration and mutation in populations.

All this information can help us understand the picture of health in past populations although we have to be careful about making assumptions. Wood and others point out the danger of the "osteological paradox," which cautions paleopathologists and paleodemographers about inferring the health of a population by looking at the percentage of skeletal lesions found and the age at death (Wood et al. 1992:343). The authors remind us that skeletal lesions take many years to develop and that the individuals displaying lesions may actually be healthier and living to a greater age, while those dying younger and with fewer lesions may have succumbed to diseases before lesions could develop, meaning they were the least healthy group. As the authors put it, "better health makes for worse skeletons" (Wood et al. 1992:356), although Wilkinson disagrees with this statement in the context of virulent pathological conditions like the treponematoses (Wilkinson 1992:364). An individual with tertiary syphilis would most likely agree with Wilkinson about the state of their health and the toll the disease was taking on their skeleton.

From a standpoint of medical anthropology, the study of infectious disease is important because all human societies have been affected by them and each has their own way of understanding and curing disease. In addition, all societies have a hand in the manufacturing of the diseases that affect them through changes in cultural practices (Inhorn and Brown 1990:110). Since infectious disease is such a universal part of culture, it is important that researchers continue to work to understand all aspects of disease. Inhorn and Brown assert that medical anthropologists should pay attention to research being done by those in other disease research fields for several reasons: that infectious disease has been the most important cause of suffering and death in human societies, that cultural actions have affected the distribution of disease, and that understanding these factors helps to treat people and form control programs today (1990:109).

Disease has had a long history of change and mutation alongside humans (Barnes 2005). Through actions like farming and the wearing of more clothing, humans have forced infectious disease to change and adapt in order to survive. The epidemiological transitions may have changed the picture of human disease, but infectious agents continue to affect all human populations. Disease research and paleopathology have seen a reawakening and there is an expectation that more must be done to understand disease processes. Armelagos and Van Gerven (2003) caution us about the direction that paleopathological research is heading, warning against purely descriptive studies and instead reminding us to focus on interdisciplinary research to form a more complete picture of past populations. This is the reason for this work on syphilis. When we understand our disease history, it will help us understand the diseases that are affecting us today and what we can do to cure them. Syphilis remains a major health problem in much of the world even though treatment exists, so every bit of information gleaned is essential to our understanding of it.

CHAPTER 2
The Treponematoses: Alike but Different

The treponematoses are manifested in humans as four different syndromes, each with unique distribution, clinical symptoms and bodily affectations. Venereal syphilis, endemic syphilis, yaws, and pinta are all caused by bacterial microorganisms of the genus *Treponema* (Singh and Romanowski 1999:188). The bacteria are indistinguishable from one another under a microscope and "cannot be cultured continuously in vitro", which has caused difficulty in study and impossibility in creating a vaccine (Fraser et al. 1998:375). Each of the diseases, save venereal syphilis, is found in a specific region of the world, as shown in figure 2. In this chapter, this family of diseases will be examined closely, as both the clinical pathology and paleopathology of each of the four syndromes will be examined as a background to the discussion to come.

Clinical Pathology of the Treponematoses

Pinta

Pinta is the least virulent of the four syndromes and also has the most limited geographic distribution. It is only found in the tropics of the Americas from Mexico to Ecuador (Aufderheide and Rodriguez-Martin 1998:154, Powell and Cook 2005:11). It is the most distinct from the other treponemal diseases (Hackett 1963). Pinta is spread mainly by children through skin-to-skin contact, and is caused by the bacteria *Treponema cariteum* (Powell and Cook 2005:9). The disease results in sores and plaques mainly on the shin and sometimes the face that leave discolorations when the sores heal, hence the name pinta, which is Spanish for 'spot.' Pinta is the only one of the four treponematoses

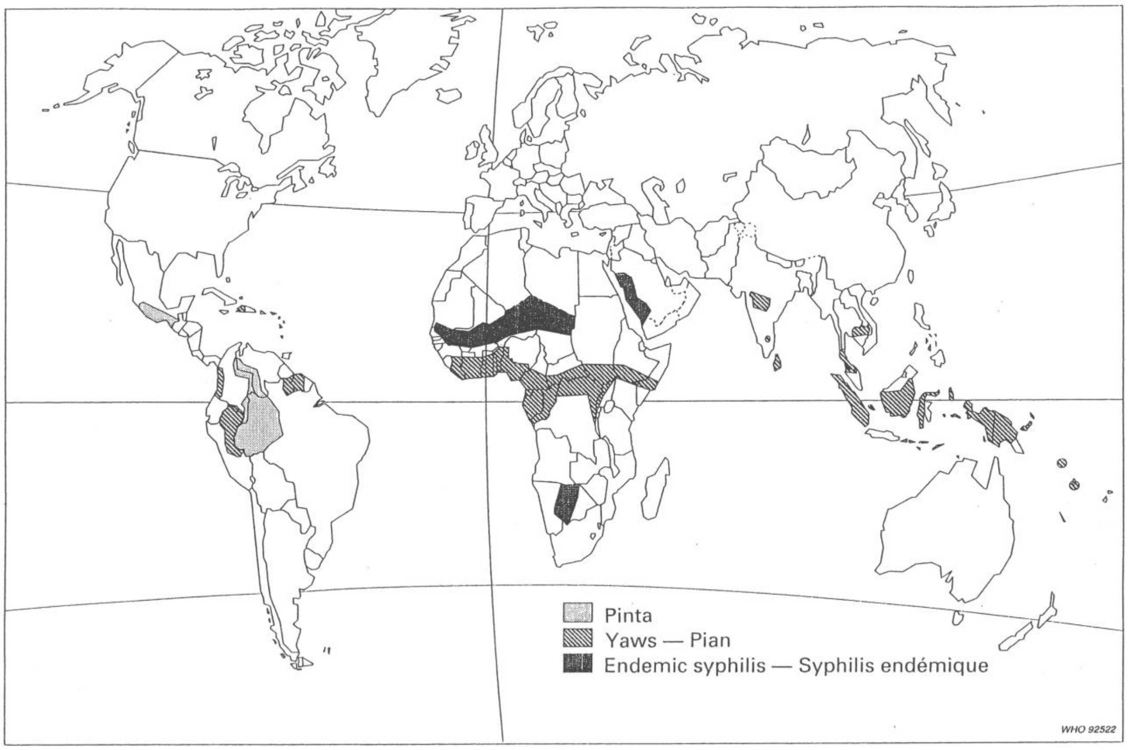

Figure 2. Geographic distribution of the endemic treponematoses in the early 1990s. Courtesy of the World Health Organization.

that does not affect the skeletal system or organs (Hackett 1963:9). There has not been a reported case of pinta in the world since 1979, so it is possible that it has died out (Harper et al. 2008:e148). It is more likely that the disease is still affecting people in remote areas of Central and South America. Consequently, pinta has become more difficult to study, especially with DNA techniques that require specimens for typing and comparison.

Yaws

Yaws is the form of treponemal disease caused by the bacterium *Treponema pallidum* subspecies *pertenue* (Powell and Cook 2005:9). This disease is geographically limited to "tropical and subtropical humid areas" of Africa and Central America, northern Australia and some Pacific islands (Aufderheide and Rodriguez-Martin 1998:154). Yaws has traditionally been linked with societies with poor personal hygiene and low population density. Yaws remains endemic in many tropical parts of the world because of its long period of infectiousness, in some areas affecting 10-25 % of a population (Aufderheide and Rodriguez-Martin 1998:155).

Yaws, like venereal syphilis, is clinically separated into three stages. Yaws begins its primary stage with the appearance of the 'mother yaw,' a granulomatous skin lesion at the site of first infection, usually on the leg and usually in children. These lesions heal and others may reoccur and heal throughout a secondary stage. Each lesion is infectious for a few months at a time (Hackett 1963:9). The lesions may be very large and teeming with spirochetes, facilitating easy transmission, and may become ulcerated (figure 3).

Figure 3. Yaws: ulcerative papillomas. [Public Health Image Library (http://phil.cdc.gov/phil), PHIL ID#3841; original image provided by Centers for Disease Control/Dr. Peter Perine, 1979.]

Lesions can be found on all parts of the body, even on palmar and plantar surfaces of the hands and feet. Yaws often affects the joints, causing pain and swelling (Ortner 2003:227). Tertiary yaws may be diagnosed based on bone destruction of the face or hands and feet, as well as destructive lesions that are non-contagious (Aufderheide and Rodriguez-Martin 1998:155).

Bone lesions occur more frequently in yaws than in either endemic or venereal syphilis. Between 5 and 15% of patients with yaws will show skeletal involvement (Ortner 2003:275, contra Ortner and Putschar 1981:180, Aufderheide and Rodriguez-Martin 1998:156). During the secondary stage, some bone thinning and periosteal reaction may be seen resulting in cortical thickening. Skeletal lesions are normally bilateral. Secondary stage lesions resolve spontaneously after a few months (Aufderheide and Rodriguez-Martin 1998:156). The tertiary stage begins 5-10 years after the initial infection. The tibia is most commonly affected bone, often resulting in saber shin. Saber shin occurs as a result of reoccurring inflammation of the periosteum over the anterior tibial crest, which then has bone remodeled over it until the crest becomes rounded and bowed out, as shown in figure 4. Late stage yaws may cause destructive dactylitis, and rarely skull and nasal deformation (Ortner and Putschar 1981:180). In comparison to venereal syphilis, the lesions found in yaws are often very similar with only quantitative differences, for example, dactylitis, the inflammation of the fingers or toes, is found much more often in yaws than syphilis (Aufderheide and Rodriguez-Martin 1998:156). Yaws is usually not congenitally transmitted due to the long duration between first contact with the disease in childhood and conception at young adulthood, and the low

Figure 4. Saber shin as a result of yaws. [Public Health Image Library (http://phil.cdc.gov/phil), PHIL ID# 3823; original image provided by Centers for Disease Control/Dr. Peter Perine, 1979.]

numbers of bacteria by that time in the host's system (Aufderheide and Rodriguez-Martin 1998:155, 157), although rare cases have been documented.

Endemic Syphilis

Endemic syphilis is also known as bejel or treponarid and is caused by *Treponema pallidum* subspecies *endemecium* (Powell and Cook 2005:9). Some have proposed that the causative agent of endemic syphilis be classified as *Treponema pertenue* instead because the clinical symptoms are so similar to yaws (Mann 1990:144). This treponeme is limited to the more arid subtropical regions of the world. Although endemic syphilis is more virulent than yaws, often affecting the bones and always the skin, it has a low mortality rate and rarely affects the nervous or cardiovascular systems (Aufderheide and Rodriguez-Martin 1998:157). Endemic syphilis is spread through "shared eating and drinking vessels, pipes, toothpicks, cigarettes" or through skin-to-skin contact and transmissibility is high (Powell and Cook 2005:18). It is generally found among societies with poor hygiene and low socioeconomic levels (Aufderheide and Rodriguez-Martin 1998:157). Endemic syphilis is not congenitally transmitted due to the long period of time between first infection and childbearing in women and the low numbers of spirochetes remaining in the system by then.

The earliest lesions of endemic syphilis are often not observed because they are small and painless. Since the disease is often spread by shared eating and drinking vessels the initial sores are often in the mouth. These will be followed by other sores in the mouth, axillae, rectum, and vulva (Hackett 1963:9). The treponeme appears to be drawn to the areas of the body that remain moist most of the time. Like in yaws, lesions occur and heal spontaneously with periodic recurrence (Aufderheide and Rodriguez-Martin 1998:157). Frequently palmar and plantar hyperkeratoses, thickened patches of the epidermis, are reported as well. Late stage endemic syphilis may lead to gummatous lesions similar to those seen in yaws, including nasopalatal destruction of bone or soft tissue.

Endemic syphilis causes lesions of the bones similar to venereal syphilis, including the classic saber tibia and periostitis of the hands and feet. The frequency of bone lesions seems to be somewhat less than in venereal syphilis, perhaps found only 1-5% of those infected (Baker and Armelagos 1988:705). In addition, destructive nasal lesions do occur, but are rare (Ortner 2003:278). Charcot's joint is not reported in bejel but is found in venereal syphilis in the tertiary stage if the spinal cord is affected (Aufderheide and Rodriguez-Martin 1998:160).

Endemic syphilis made its mark around the world in the centuries before Columbus (Powell and Cook 2005:18). The disease became known by local names in different places. It is thought to have been the disease called *sibbens* in Scotland, *button scurvy* in Ireland, *spirocolon* in Greece and Russia, and *irkintja* in Australia, among many other names (Powell and Cook 2005:18, 20). This is a prime example of the spread of the disease with human migration. Today endemic syphilis is on the way to becoming eradicated in these and other areas due to education, medication, and better hygiene. There are only a few pockets of groups that maintain endemic syphilis in their population today, mostly in the arid Middle East and central and southern Africa (Powell and Cook 2005:20).

Venereal Syphilis

Venereal syphilis is the final of the four treponematoses, and is the most severe in clinical pathology. Syphilis, as it is most commonly called, is caused by the bacterium *Treponema pallidum* subspecies *pallidum* (LaFond and Lukehart 2006:29). The bacterium was first recognized and described in 1905 by a German bacteriologist named Fritz Schaudinn (Singh and Romanowski 1999:188). The disease can be found the world over, mainly in societies with good hygiene and higher population density (Aufderheide and Rodriguez-Martin 1998:158). Venereal syphilis has been known as "the great imitator" because of its varied clinical manifestations and sometimes difficult diagnosis (Singh and Romanowski 1999:191). The mode of transmission is venereal in adults as well as congenital.

The picture of syphilis today is dire in some underdeveloped countries. With testing and other prophylactic measures, accidental transmission is rare in cases such as transfusions. Recent reports show that since 2000, the United States has had an increase in the number of new venereal syphilis cases, especially among men who have sex with men or MSM (LaFond and Lukehart 2006:30). The state of syphilis worldwide is even more severe. It is estimated by the World Health Organization that over 12 million new cases are reported each year (LaFond and Lukehart 2006:30). In addition, congenital syphilis is of particular concern as there is little prenatal treatment in many developing countries and babies can be stillborn or diseased (LaFond and Lukehart 2006:30). These factors make syphilis a continuing public health concern.

Venereal syphilis is divided into stages, each of which is characterized by specific clinical symptoms. The first stage of venereal syphilis, primary syphilis, develops about 3 weeks after exposure and consists of a primary chancre like the one shown in figure 5,which usually occurs on the genitals, that is painless and clears on its own within a few weeks if left untreated (LaFond and Lukehart 2006:30). The chancre is often undiscovered by the patient and syphilis may not be diagnosed until the symptoms of secondary syphilis begin. The primary stage lasts until the chancre heals, usually about four to six weeks (LaFond and Lukehart 2006:31).

Secondary syphilis is the next stage of the disease. This stage usually begins within three months after the primary stage (LaFond and Lukehart 2006:31). The secondary stage is characterized by a more generalized rash, low grade fever, malaise, macular and papular lesions, and generalized lymphadenopathy, or lymph node enlargement (Baughn and Musher 2005:209). This stage can also present many other diffuse symptoms with a range of virulence. The highly varied symptoms are sometimes so mild that a patient will not seek medical treatment. On the other hand, in some patients, secondary syphilis can be the beginning of manifestations of neurosyphilis and cardiovascular syphilis (Singh and Romanowski 1999:193). There are many different types of lesions attributed to secondary syphilis; Baughn and Musher describe fourteen different lesions and their distribution on the body, as well as the differential diagnosis for each (2005:207-8).

After the secondary stage, the disease usually enters a latent stage, where it can remain almost dormant in an individual’s system for 10 to 20 years or more, and in some

Figure 5. Primary syphilis chancre in right inguinal region. [Public Health Image Library (http://phil.cdc.gov/phil), PHIL ID# 3484; original image provided by Centers for Disease Control/Joe Miller/Dr. N.J. Fiumara, 1976.]

patients, indefinitely. Latent syphilis is divided into early and late stages based on the percentage of people who relapse and at within what time period. Early latent syphilis is defined as the period of asymptomatic syphilis for up to one year, while late latent syphilis is the period after one year (Singh and Romanowski 1999:193). Patients in the latent syphilis stages can relapse to secondary syphilis, remain asymptomatic in a latent stage, or progress to tertiary syphilis.

The final stage of venereal syphilis is the tertiary stage, the symptoms of which can occur up to 40 years after initial infection. Only about one-fourth of those with untreated syphilis will progress to tertiary syphilis, and it is even less likely to develop today in most areas of the world where antibiotics are readily available (LaFond and Lukehart 2006:30). This stage comes with very serious and life-threatening symptoms. The most common manifestations of tertiary syphilis are neurosyphilis and cardiovascular syphilis. Neurosyphilis occurs when treponemes invade the cerebrospinal fluid. At that point, a patient may develop no further symptoms, but some may develop syphilitic meningitis (Singh and Romanowski 1999:193). From there, patients may progress to meningovascular syphilis, tabes dorsalis, or paresis (Singh and Romanowski 1999:193). Paresis presents clinical symptoms of dementia and psychosis, irritability and personality changes. Cardiovascular syphilis used to make up a significant percentage of clinical cardiovascular disease in general and a large percentage of syphilitics were found to have cardiovascular changes at autopsy (Singh and Romanowski 1999:193). The most common occurrence is syphilitic aortitis, inflammation of the aorta, and aortic regurgitation, leakage of blood from the aorta back into the left ventricle. This can lead to pain and discomfort and heart failure (Singh and Romanowski 1999:193).

Secondary syphilis marks the beginning of signs of bone involvement in some patients, usually in 10 – 20% of untreated cases (Baker and Armelagos 1988:704, Mann 1990:144). The most commonly affected bones are the tibiae, the cranial vault and the nasal bones, the three of which make up 70% of syphilitic lesions (Baker and Armelagos 1988:704). Other areas of the skeleton can be affected as well, such as the clavicles, femora, ulnae, hands and feet (Buckley and Dias 2002:180). The most diagnostic and well known of the lesions of syphilis is found on the cranium. *Caries sicca* scars are usually found on the frontal and parietals and consist of stellate scarring, nodes, and cavitations that do not perforate the inner table of the skull, as shown in figure 6 (Mann 1990:144). This often results in a "worm-eaten" appearance on the skull. Tertiary syphilis can also bring with it Charcot's joints, which are characterized by excessive bone growth from the center of the joint caused by loss of deep tissue sensation through the central nervous system and resulting trauma caused by repetitive use of the joint (Powell and Cook 2005:21, Rodriguez-Martin 2003:161). It has been suggested by Buckley and Dias (2002) that the lymphatic system may be responsible for the particular distribution of skeletal lesions in syphilis, although most others (Ortner 2003:274, Hackett 1963:11) believe the treponemes to be hematogenous, or disseminated through the bloodstream. Either (or both) of these theories may be correct and each has its merits.

Figure 6. Caries sicca scarring on frontal and parietals on an historic adult. [Research slide of Dr. DJ Ortner NMNH 280095, slide 106-492.]

Congenital Syphilis

Congenital syphilis is transmitted through the placenta to the fetus from the bloodstream of the mother, who is infected with spirochetes. It is estimated that 84% of the children of mothers with syphilis are infected congenitally (Bogdan and Weaver 1992:158). Venereal syphilis is usually the form of the disease that is congenitally transmitted. The spirochetes then may cause fetal death, spontaneous abortion, stillbirth, or birth of an infected infant. With the amount we know about congenital syphilis and the relatively easy prevention and treatment of both syphilis and congenital syphilis, it seems like this should not be a major health concern. Unfortunately, congenital syphilis remains a problem in both the United States and worldwide. In fact, it is estimated that in Tanzania, 50% of stillbirths are the result of syphilis (LaFond and Lukehart 2006:30).

The clinical pathology of congenital syphilis is highly varied and may take months or years to manifest in a patient fully. Some researchers have been working to understand how the transmissibility varies depending on the stage of syphilis the mother is in and during which trimester of pregnancy the fetus is infected (Wicher and Wicher 2001:355). As mentioned, any number of outcomes can beset the fetus of an untreated mother. The fetus can be born uninfected, have few symptoms, may have no symptoms until months to years later, or can be stillborn or spontaneously aborted. Some of the symptoms that may be present are bone changes, persistent sniffling indicative of palate problems, syphilitic lesions that can lead to deafness or other problems, and neurologic impairment (Li and Gonik 2006:1). More problems may arise over the course of the child’s life. Lesions may occur on the skull and scapula and slowly resolve spontaneously (Aufderheide and Rodriguez-Martin 1998:165). When the permanent teeth come in, the maxillary central incisors may be notched and barrel shaped, a condition called Hutchinson's incisors (shown in figure 7), or the molars may have a rounded cusp, a condition known as Mulberry molars (Aufderheide and Rodriguez-Martin 1998:166). Fortunately, treatment of syphilis in the mother with penicillin prevents 98% of congenital infections, so screening and treatment are of utmost importance, especially in developing countries (Li and Gonik 2006:1).

There are several paleopathological indicators of congenital syphilis in infant skeletal remains such as osteochondritis and osteomyelitis in the developing bone (Ortner 2003:291). Hutchinson's teeth and mulberry molars would be highly visible signs if found in an archaeological assemblage, although these on their own have been questioned in their specificity to syphilis (Ortner 2003:291). Saber tibia results from periostitis on the anterior tibia which has bone remodeled over it until the tibial crest becomes rounded and bowed out anteriorly as seen earlier. If older children are found, Hutchinson's and Moon's teeth may be discernible. When all these are present, it may be possible to make a diagnosis of congenital syphilis. In paleopathology and bioarchaeology, however, often there are few infant or fetal remains found in archaeological assemblages due to their fragility and differential burial practices that separated babies from adult burial sites.

Although congenital syphilis has long been thought to accompany only venereal syphilis, there have been documented cases of congenital yaws, which can occur if the mother is infected in young adulthood rather than in childhood (Ortner 2003:277). In addition, studies have found that only a small percentage of children with diagnosed

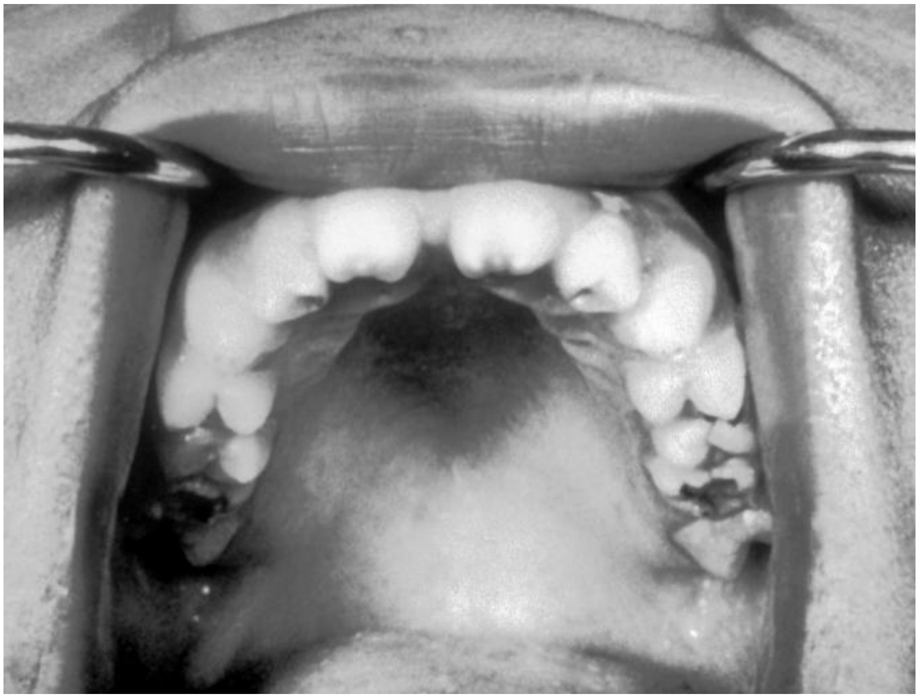

Figure 7. Hutchinson's incisors. [Public Health Image Library (http://phil.cdc.gov/phil), PHIL ID#2385; original image provided by Centers for Disease Control/Susan Lindsley, 1971.]

congenital syphilis actually show any skeletal and tooth involvement (Rothschild and Rothschild 1997:41). Congenital syphilis is an important aspect in the research of the treponematoses because of the debate on the type of syphilis found in the New World at the time of contact, a subject that will be further discussed in the next chapter.

Discussion

When distinguishing the types of syphilis from one another on skeletal remains, pathologists often refer to a biological gradient of affectation, where pinta and yaws occupy one side at the least virulent, endemic syphilis in the middle ground, and venereal syphilis as the most virulent (Hudson 1965:888). The gradient is also geographical, with yaws and pinta occupying tropical humid areas, endemic syphilis in arid tropical zones, and venereal syphilis in the urban temperate zones at the other end of the spectrum (Hudson 1965:888). The gradients in both biology and geography are often used in diagnosing treponematosis in skeletal remains based on where they were found and how severe the skeletal lesions are, although such a diagnosis is often probable and not perfect, as has been shown in several studies (i.e. Rothschild and Rothschild 1995). In contrast, Baker and Armelagos are of the belief that the treponematoses have identical skeletal manifestations and therefore cannot be distinguished from one another, except for quantitatively (1988:705).

Change has played a significant part in the roles of human lives and societies. When humans make changes, whether it be from hunting and gathering to agriculture or from tropical to temperate climates, diseases that rely on humans for transmission must also adapt (Barnes 2005). Treponematosis is no exception. Humankind has seen a series of significant changes from prehistoric times. It is still speculated how the treponemes originally found their way into the human disease system and when this occurred. It has been hypothesized that the disease began in a weaker, less virulent form, and after societies began changing and moving toward more hygienic ways, the disease mutated and the bacterium became transmitted sexually and became more virulent. In the tropical areas where yaws and pinta are found, society and weather dictate the wearing of less clothing, and personal hygiene is often poor. The diseases are most easily transmitted by skin-to-skin contact, especially among children. When a disease with this kind of transmission is introduced into a colder climate, where people are fully clothed and hygiene is better, a new mode of transmission must come about in order for the bacteria to survive (Baker and Armelagos 1998:703, Hudson 1965:885, Hackett 1963:22). This scenario seems to be what happened in the case of the treponematoses, although there is still debate on the subject, as will be shown in the next chapter. The treponematoses enjoy a long and varied range and Aufderheide and Rodriguez-Martin maintain that “every human population has the kind of treponematosis that is adapted to its physical environment and sociocultural status” (1998:155). For a disease to enjoy such a long history alongside humans in every imaginable environment and every imaginable social condition, it must be a successful pathogen worthy of study.

CHAPTER 3
Competing Hypotheses

A hotly debated subject among the researchers of venereal syphilis is the geographical origin of the disease. The camps have divided themselves into subscribers of the Columbian or pre-Columbian theories. In addition, there is debate about the evolutionary history of the treponematoses. These are shown in either the unitarian or nonunitarian hypotheses. Although there have been decades of debate there still is no clear winner. Each of these hypotheses will be examined in detail, along with the skeletal and anecdotal evidence that will support each side.

The Columbian Hypothesis

The Columbian hypothesis is named after Christopher Columbus, the celebrated "discoverer" of the New World. This hypothesis posits that Columbus' crew became infected with syphilis by contact with the Native Americans and brought the disease back to Europe where it proceeded to spread to epidemic proportions in only a few short years (El-Najjar 1979:599-600). There are several pieces of evidence that this camp uses to prove its theory. First, nothing like syphilis was described in Old World medical or historical texts until the epidemic of 1495, soon after Columbus and crew returned from their second voyage to the New World (Crosby 1969:219). The syphilis outbreak of 1495 was well-documented by doctors of the time who claimed to be unfamiliar with the virulent and rapidly spreading disease. The first to fall ill were soldiers from France, Italy, and Spain, and within five years of their demobilization from the military, syphilis was reported all over Western Europe (Powell and Cook 2005:31-32). It has been suggested that the extreme virulence shown during these outbreaks in Europe reflected the fact that the population had no previous contact and, therefore, no immunity to the disease

(Bogdan and Weaver 1992:155, Crosby 1969:219). Additionally, when the epidemic was going on, every group had different names for the disease; names that placed the blame either on the Italians, the French, the Polish, the Chinese, and virtually every other nationality (Crosby 1969:219). Powell and Cook also point out that a concoction made with wood from the guiac tree, *Guaiacum officinale*, native to the West Indies, began to be imported to Europe as a treatment for syphilis; a treatment that was allegedly learned from the natives of the island of Hispaniola (2005:33-34).

A final clue, and perhaps the most illuminating, is the lack of definitive skeletal evidence for syphilis found in pre-contact remains in the Old World. Although the diagnostic sensitivity of skeletal lesions is characteristically insensitive, a fact that will be explored in more detail in chapter 4, there is a suite of lesions that is known to accompany syphilis. There have been few complete skeletal remains found in the Old World that have been analyzed by paleopathologists and found to possess signs of syphilis, and there is always a question of dating attached to purported syphilitic remains (Baker and Armelagos 1988:710). Many leprosy cemeteries have been excavated in the hopes of finding syphilitic remains mixed in, but so far this has not been the case (Baker and Armelagos 1988:710-11). Cemeteries were often used for many centuries, and multiple burials of the same plot can make estimating the date of interment difficult. In addition, radiocarbon dating is fallible and this makes estimating the pre-Columbian status of many remains difficult as well.

On the other hand, there are many definitively syphilitic remains found in the New World that have been dated to Pre-Columbian times. It has been thought that the form found on these New World remains is probably not venereal syphilis but a non-venereal form, perhaps endemic syphilis, that mutated when the bacterium was introduced by Spanish sailors upon their return home to the Old World. This is supported by the paucity of evidence of congenital syphilis in New World skeletal remains. Powell and Cook (2005) bring together research from across North America of syphilitic skeletal remains. Their synthesis makes it clear that they believe treponematosis was present in the New World for at least 2,000 years prior to the arrival of Columbus (Powell and Cook 2005:1), although there is no evidence that the form found there was venereal at the time of contact (Cook and Powel 2005:477). Larsen also believes that treponematosis was endemic in North America prior to European contact (1994:116). There is also evidence of syphilis on skeletal remains in the Dominican Republic, the place where Columbus landed first on his journey (Rothschild et al. 2000:936). The thing that has not been proven is the existence of congenital syphilis in the New World. If evidence of congenital syphilis was found, it would mean that the form of syphilis that inhabited the New World originally was venereal in transmission. Since this is not the case, it is thought that endemic syphilis was the New World culprit, and that the disease had to have mutated after it reached Europe.

If the Columbian hypothesis is correct, it must also be wondered where and when the New World inhabitants incurred the treponematoses, and which type affected them. As no evidence of congenital syphilis has been found in skeletal remains, for now it is thought that venereal syphilis was not the culprit. The most likely scenario would be that the disease accompanied the first travelers into the New World when they crossed the Bering land bridge; however, this is not a given (Hackett 1963:24). Many researchers believe that the cold filter would have made it impossible for the treponematoses (and many other diseases as well) to survive in such a harsh climate. The cold filter of Beringia, the land bridge that once connected present-day Russia and Alaska, is thought to have filtered out diseases from the human population that crossed into the Americas (Merbs 1992:6). Merbs hypothesizes that the diseases that survived this cold climate with the original colonizers of the New World were the ones that had a long period of time to live with humans, and the treponematoses are one of the oldest human diseases (1992:6). Hudson believes that the form that crossed the Bering land bridge was endemic syphilis (1965:899). In addition, Barnes (2005) mentions that lesions suggestive of syphilis have been found in the trans-Baikal region of Siberia from two thousand years ago. Several researchers have hypothesized about alternate methods for the treponematoses to reach the New World. Hackett, for example, has suggested that yaws may have been transmitted to the New World by the transatlantic slave trade from Africa, but that prior to that, the original treponeme was pinta (Hackett 1963:15). Unfortunately, the difficulty in differentiating the skeletal lesions of yaws and endemic or venereal syphilis has made it impossible to be sure, as will be discussed later, and pinta leaves no skeletal evidence.

The Pre-Columbian Hypothesis

In contrast, the pre-Columbian hypothesis posits that the disease was present in the Old World long before the Age of Exploration. The proponents of this theory believe that the syphilis was not medically differentiated from leprosy in the time before more modern medical diagnosis and treatment. Coincidentally, the disease became known to be different from leprosy at the same time as the return of the first ships from the New World (Aufderheide and Rodriguez-Martin 1998:167). As evidence, supporters cite the treatment given for leprosy in these times: mercury ointment, which we now know is effective in treating syphilis but has no effect on leprosy (Aufderheide and Rodriguez-Martin 1998:167). At this time, leprosy was becoming scarce and being treated effectively, so many leper asylums were releasing their wards. Some researchers believe that syphilitics could have been housed with lepers and were released back into society in the fifteenth and early sixteenth century (Barnes 2005:215). There are also several pre-Columbian medical texts that describe diseases resembling venereal syphilis from as far away as China (Powell and Cook 2005:34). Some of these texts describe a form of leprosy that was transmitted venereally, but we know now that leprosy is not transmitted in that way. In addition, there have been several reports of probable evidence of syphilis on skeletal remains in Europe that predate the journeys of Columbus, although the dates on this material have been questioned (Baker and Armelagos 1988:710).

Livingstone (1991) puts forth another interesting hypothesis: perhaps syphilis was not introduced to Europe by Columbus' crew but came from Africa, where explorers had contact for fifteen years prior to Columbus. This would have given ample time for the disease to spread across Europe and become epidemic. Livingstone suggests that the virulence of the syphilis outbreak is because it is one of the youngest infectious diseases known to humankind, since there is no skeletal evidence of syphilis before 2000 years ago in the New World (1991:589). Unfortunately, this idea has not been expanded upon by the syphilitic research community.

Livingstone has a valid argument that merits closer observation. The areas of western Africa that were visited by Portuguese sailors are known to have been home to large kingdoms of people. Populations of this size would have easily been capable of maintaining syphilis endemically and perhaps even venereally. In addition, Africa has been known to be a major reservoir for diseases of all kinds, including AIDS, malaria, and Ebola (Wolfe et al. 2007). The timing and location of Africa as the origin of the virulent outbreak of venereal syphilis seems to fit better. Future research and collaboration with our African colleagues will perhaps yield skeletal evidence of syphilis in the areas of first European contact. This hypothesis has been ignored for too long and it is time that more research is done.

The Unitarian Hypothesis

The next hypothesis on the origin of the treponematoses is more about the evolution of the organisms than their geographic origin. The unitarians, led by Hudson (1965), are of the belief that the different diseases are all caused by the same organism that changed based on the areas and social conventions it found in the population. This theory was supported for a long time by the fact that even under the highest powered microscopes the organisms were all identical and indistinguishable. Rothschild and Rothschild point out that there is still an "inability to distinguish biochemically, histologically, microbiologically, immunologically, or even with sophisticated DNA techniques among yaws, bejel, and venereal syphilis" (1996:556). There is also evidence that contracting one strain confers some resistance to other strains in an individual. As Ortner points out, leprosy is caused by one organism, *Mycobacterium leprae*, which can cause a range of responses in an individual. Therefore, syphilis may have the possibility of "population-based, genetic variation in the immune response resulting in different patterns of skeletal involvement in different human groups" (Ortner 2003:273). Hudson (1965) believes that yaws was probably the first treponemal infection in central Africa, which then spread around the world with human migrations and changed clinical manifestations based on geographical area and social conditions, although the aforementioned cold filter of Beringia may cause problems for this hypothesis (Aufderheide and Rodriguez-Martin 1998:166). It has been suggested that endemic syphilis was the form of treponematosis found in the New World at the time of European contact, and that perhaps the move to Europe facilitated mutation into a venereal form (Stirland 1991:40, Baker and Armelagos 1988:704). Crosby instead maintains that the form of the disease changed according to the social environment even in the New World. He even believes that the disease could have manifested a venereal form in the larger cities (Crosby 1969:218). According to the unitarian hypothesis, the treponematoses would have been present on both sides of the Atlantic at the time of European contact with the Americas; as such, it is idle to speak of Columbus's crew bringing the disease to Europe.

The Nonunitarian Hypothesis

In contrast to the unitarian hypothesis, there is a cohort of scientists that subscribe to a so-called nonunitarian theory on the evolution of the treponemes. The most prolific of the supporters of the nonunitarian theory is Hackett (1963). Those on this side of the debate believe that mutations occurred to change a single original treponeme into four different organisms, each manifesting different clinical characteristics. Each mutational change took place at a different time in response to changing geography and population densities. The nonunitarians believe the first of these changes took place at around 10,000 B.C. and transformed the initial disease, probably pinta, into yaws (Aufderheide and Rodriguez-Martin 1988:166, Powell and Cook 2005:34, Hackett 1963:7). The reason for this mutation was the change to a warmer, more humid environment. The next change is supposed to have taken place at around 7,000 B.C. and this occurred in a more arid environment, resulting in a mutation to endemic syphilis, or bejel (Powell and Cook 2005:34). The final mutation took place because of cultural changes such as denser settlements and more clothing in the Middle East around 3,000 B.C., which produced venereal syphilis. This hypothesis can be connected to the pre-Columbian hypothesis as well, because both assume that the disease was present in the Old World prior to the Age of Exploration (Hackett 1963:7). A problem with Hackett's hypothesis should be mentioned here. The earliest skeletal evidence of treponemal disease has been found on a 1.6-1.7 million year old Homo ergaster skeleton, but the evidence points to yaws, not pinta, which suggests that pinta is not the earliest form of treponematosis (Mitchell 2003:175). This evidence is controversial, though, and it is not certain that yaws was the causative disease for the abnormal bone growth seen on the skeleton.

Discussion

The four different theories discussed here make up the bulk of the debate surrounding the ultimate origin of the virulent venereal syphilis outbreak in sixteenth century Europe. Unfortunately, the evidence to support any of these theories is scanty and slow in coming. The theories with the most support behind them seem to be the Columbian hypothesis and the nonunitarian hypothesis, although I believe Livingstone's alternative hypothesis is plausible and merits further research, especially in West Africa. The skeletal evidence needed for the continued study of the treponematoses and other diseases is sometimes difficult to find. Today, most researchers and scientists are committed to curation and preservation methods and want to learn as much as possible from our ancestors, so they are coming together to help preserve skeletal specimens. Paleopathologists and bioarchaeologists also need to remember to look at the bigger picture in societies under study as the epidemiology of the treponematoses is important. Perhaps recent and future advances in DNA technology can paint a clearer picture of the movement and mutation of the disease around the world, as we will see in chapter 6.

CHAPTER 4
First Contact

The most controversial aspect of the treponematoses is their ultimate origin. There are several researchers (Rothschild et al. 2000) that believe that the most information can be gleaned from learning about the area of first contact for Columbus and his crew. The island of Hispaniola today is the location of the countries Haiti and the Dominican Republic, but in 1492, a native group called the Taino called the island home. In this chapter I will explore the clues that have been gleaned from the Taino and Columbus' expedition. A comparison will be made to the Micronesian island of Yap to explore the possibility that the Taino were the original reservoir for the European syphilis outbreak. In addition, the evolution of the syphilis bacteria in the New World will also be examined in accordance with the Columbian theory, the view that has the most lines of evidence to support it. Most important, hypotheses about the entry of the treponematoses into the New World will be examined as well. All of this information will create a more complete picture of the disease that seems to have affected Columbus' crew at the turn of the sixteenth century.

The Taino are the native people that inhabited the island of Hispaniola at the time of Columbus' "discovery" of the Americas. If the Columbian hypothesis is correct, these people would be the most likely source of the treponemal disease that soon would devastate Europe. As seen in the previous chapter, a part of the debate on the origin of the treponematoses is which form of the disease was found in the Americas: venereal or nonvenereal. Some paleopathological research has been done on the subject on the island of Hispaniola, namely by Rothschild and colleagues (2000). Unfortunately, as the researchers point out, there is a paucity of evidence at the actual sites of interaction. Rothschild and colleagues (2000) did examine skeletal remains from several sites in the Dominican Republic. The type and frequency of lesions were compared with the Rothschilds' previous research so it could ostensibly be determined which form of treponematosis affected the prehistoric Taino (although there are problems with this methodology, which will be discussed in Chapter 5). The authors found that skeletons interred up to 1200 years before present had signs of treponemal disease. According to the researchers, the type and distribution of the lesions found reflected venereal syphilis better than yaws or bejel, causing them to assert that Columbus' crew took this disease back to Europe with them on one of their voyages (Rothschild et al. 2000:938). There is a chance that this information is being interpreted incorrectly considering the small numbers of skeletal remains examined and available for study. In addition, some parallels may be drawn to the island population of the Yap described by Hunt and colleagues which makes it difficult to believe that venereal syphilis was present on the island of Hispaniola (1954).

The island of Yap in Micronesia experienced a rapid decline in population that was studied by Hunt, Kidder, and Schneider (1954). During the occupations of Germany, Japan, and the United States the population decline was documented several times. Hunt and colleagues attempted to discern the reasons for this decline, as well as the increase in birthrates that occurred just prior to their study. Several disease outbreaks such as tuberculosis and influenza reduced some of the population, but the birthrate was too low to bring the numbers back up. The authors come to the conclusion that one of the reasons for this rapid depopulation may be venereal disease, which led to infertility and spontaneous abortion (Hunt et al. 1954:48). On such a small set of islands with little internal or external migration, a venereal disease like gonorrhea was able to spread rapidly. After penicillin was introduced to the Yapese in the 1930s to combat yaws infections, the rate of gonorrhea dropped as well, leading to an increase in birthrates.

The similarities between the two island populations lead me to believe that a venereal disease could not be maintained in such a small population. In addition, little or no information is known about the children and juvenile populations of the Dominican Republic and Haiti before European contact. Rothschild and colleagues found that there was no juvenile affectation in the skeletal populations they examined (2000:937). This information shows that there is no evidence of congenital syphilis in this area. This could be evidence that venereal syphilis is not the disease that was affecting the Taino. On the other hand, lack of juvenile affectation could mean that people were contracting a disease later in life, and venereal syphilis is the only treponemal disease that could be responsible. Hudson makes the argument that there have been many documented cases of the progression of one form of treponematosis into another depending on the climate and cultural practices (1965:889). In this vein, it is possible that the disease was present in an endemic form in the Taino and changed to adapt to the cooler climate of Europe in Columbus' crew. Much more research needs to be done at this important location that lies at the crossroads of the debate on the origin of the virulent venereal disease that swept Europe around the turn of the sixteenth century.

Where did the Taino acquire treponemal disease from in the first place? We know that the original inhabitants of the New World probably entered through the Bering land bridge around 12,000 years ago. It is thought that the cold filter of the freezing temperatures at this high latitude kept diseases such as syphilis from being transmitted and may have even killed the bacteria, as discussed earlier (Merbs 1992:6). If this is the case, how did Native Americans come to contract the disease and what form of the disease affected them?

The treponemal bacterium that causes syphilis is a fragile one. The spirochete is dependent on a host to survive and will die if it gets too dry, too hot or too cold (Barnes 2005:203). In order for researchers to study the treponemes, the bacteria must be propagated in rabbits (LaFond and Lukehart 2006:33). The fragility of the bacteria to environmental factors leads researchers to believe that the disease has no environmental reservoir. It is more likely that the disease has an animal origin, as nonvenereal treponematoses are found in multiple primate species (Wolfe et al. 2007: Note 9). Another animal that has a pathogenic treponeme is the rabbit. As humans and nonhuman primates are so closely related, syphilis may have derived from the disease primates carried, or perhaps the disease has followed us in our evolution from our closest primate ancestor (Cockburn 1971:46). Although Hudson (1965:899) has suggested that the disease, in the form of endemic syphilis, came with the original inhabitants as they migrated across Beringia, this hypothesis is still open for debate. However, it seems unlikely that migratory bands in northeast Asia would have harbored treponemal infections which are, save for venereal syphilis, tropical and subtropical in distribution.

Another issue that has yet to be resolved but is getting little attention is the question of where pinta came from. Pinta is only found in Central and South America and it is not clear why it is so different from the other treponematoses. The form of treponematosis found in the tropics is yaws, so how did the New World tropics get a less virulent form? Some hypotheses for the origin of pinta include an environmental reservoir, a zoonose obtained from New World monkeys, or a mutation of an existing treponemal disease. We have already discussed the reasons why the treponematoses would not have an environmental reservoir, as the bacteria cannot survive outside a host. There are New World monkeys that may have been the animal reservoir for the New World peoples, but there is little research that has been done on the state of treponemal disease in these monkeys. Cockburn (1971) points out that the difference between Old World monkeys and New World monkeys is their primary environment: Old World monkeys live partially or entirely on the ground while their New World counterparts are arboreal. This would not necessarily make it more difficult for the New World monkeys to transmit diseases to humans as these animals were widely hunted as an important food source for indigenous peoples. A type of treponematosis is found in rabbits, though, and humans have been known to contract tularemia from rabbits, so there is a possibility that humans could have originally contracted pinta from rabbits. The final hypothesis is that the disease that traveled with the New World colonizers and through a mutation or evolution it changed into a less virulent and more easily spread disease.

Archaeological evidence of treponemal disease has been documented on skeletons from both North and South America, encompassing a long temporal span (see Powell and Cook 2005). Unfortunately, it is often difficult or impossible to diagnose one type of treponematosis on prehistoric skeletal remains. So although we do know that Native Americans across the continent were affected by treponematosis, we cannot be sure which type was the first to affect them. More research needs to be done on the possibility of rabbits or monkeys being reservoirs for pinta. In addition, paleopathologists subscribing to the Columbian theory should focus paleopathological research efforts on Hispaniola and other areas of early European contact with the New World.

CHAPTER 5
The Issue of Differential Diagnoses

The diagnostic insensitivity of skeletal lesions is recognized by paleopathologists. When examining a case, a researcher must take into account various differential diagnoses. Skeletal lesions are manifested in only a few ways, so in order to make a presumptive diagnosis on prehistoric remains, the distribution and type of lesions found and the systems affected are examined. Without medical records, it can be impossible to guess which disease was the culprit, so paleopathologists must provide detailed reports and examine the variety of infections that could have created similar skeletal stress. Some diseases are more visible on skeletons than others. Bogdan and Weaver point out that "very few infections provoke as much formation of excess bone along with bone destruction as in the bone regeneration reaction of syphilis" (1992:158). With treponematosis, the difficulty lies in deciding which of the treponemes affected the individual. Some argue that this is not possible while others believe the differences are only quantitative. It is also difficult to make a diagnosis of syphilis without an entire skeleton available for study. The standards by which pathology should be coded will be addressed first to establish a baseline for this research. The distribution and types of lesions found in syphilis will be examined, followed by several diseases that may be confused with syphilis as well.

Standards of Recording Paleopathological Data

The standards for recording and coding paleopathological evidence on skeletons are set out by Buikstra and Ubelaker (1994). Many researchers found difficulty in comparing data between different sites so Buikstra and Ubelaker's volume was presented as the standard for paleopathologists and archaeologists to use to record data about human skeletons (1994). They set out methods and forms for recording everything from the number of bones found to the estimated height and sex to any and all pathologies found on each bone. By the use of their coding methods, any other paleopathologist looking at research should be able to decipher the type and quantity of lesions found on a skeleton or skeletal population (Buikstra and Ubelaker 1994:107). The authors stress standardized terminology that is descriptive and detailed. They also stress the importance for paleopathologists to be familiar and comfortable with the range of variation in normal bone.

These standards focus on quantifying skeletal lesions rather than searching for specific differential diagnoses. The coding forms provided as Attachment 25 and 26 allow the researcher to record each bone and the specific type of pathology found on each, if present (Buikstra and Ubelaker 1994). There are codes listed to specify the bone, portion of bone present, side, and nine different categories of pathological bone conditions. Although the coding system can take some time to get used to, having a common set of definitions and a numbered system, comparisons of data between skeletal populations become more easily accessible.

Types and Distribution of Lesions

The most skeletally destructive of the treponemes, venereal syphilis, does not actually affect the bones in all individuals who contract it. Estimates vary, but syphilis is generally believed to affect the skeleton in 10-20 % of untreated cases (Aufderheide and Rodriguez-Martin 1998:158). The most pathognomic of the skeletal evidence in syphilis is *caries sicca*, the pitting and stellate scars found on the frontal and parietal bones that result in a worm-eaten appearance. The tibiae are also commonly affected, along with, somewhat less often, the sternum, clavicles, vertebrae, femora, fibulae, humeri, ulnae, and radii (Aufderheide and Rodriguez-Martin 1998:158). Syphilis creates both nongummatous and gummatous lesions. Nongummatous lesions include periostitis, osteitis, and osteoperiostitis, usually affecting the long bones bilaterally in tertiary syphilis (Aufderheide and Rodriguez-Martin 1998:158). This type of lesion would create the classic "saber" tibia found in some cases of syphilis. Saber tibia is an anterior-posterior bowing of the tibia which creates a rounded, thickened surface on the anterior crest of the shin due to repeated deposition of bone after periosteal inflammation (Powell and Cook 2005:15). Gummatous lesions in syphilis are areas of necrotic tissue that affect the facial bones and cranial vault and sometimes long bones in the more advanced cases of syphilis, creating depressions full of crumbling bone (Aufderheide and Rodriguez-Martin 1998:158). Gummatous lesions are often responsible for the naso-palatal destruction found in endemic syphilis. On the skull, these depressions intermixed with bone reformation create the *caries sicca* sequence (Aufderheide and Rodriguez-Martin 1998:160). There is a large variety of lesion types found in syphilis, but the disease affects individuals in different ways and all these types of lesions may not be present in every case.

Because of the unspecific nature of lesions like periostitis, it can be difficult or even impossible to diagnose syphilis in a fragmented or partial skeleton. Periostitis is a generalized infection of the periosteum, which is the thin covering of the bone. Other diseases affecting bone, such as tuberculosis, leprosy, and tumors, have been known to cause skeletal markings similar to those of syphilis. The distribution of lesions can help confirm a diagnosis. Whereas tuberculosis will leave lesions on the ribs and vertebrae most often, it is not likely to cause bilateral lesions of the extremities like syphilis. Leprosy can also be confused with syphilis because both can cause facial destruction, but leprosy can cause destruction of the fingers and toes as well, whereas syphilis usually does not. In the case of tumors or metastatic carcinoma, lesions are usually completely lytic with no bone healing or resorption (Aufderheide and Rodriguez-Martin 1998:163, Marks and Hamilton 2007). Reichs points out the danger in making a “unidimensional and specific diagnosis” on any particular individual (Reichs 1989:300). Because any systemic infection may allow the individual to be more susceptible to other diseases, all of the skeletal destruction found may not represent a single disease such as treponematosis. These complications may mask any one disease diagnosis with uncharacteristic lesions or unusual distribution. Buikstra and Cook (1980) also point out the danger in assuming that ancient disease leaves identical skeletal markers as their modern counterparts. We have seen that the treponematoses have gone through many changes throughout the centuries, so this is highly likely in this case.

An interesting case that illustrates the difficulty of differential diagnosis is presented by Lefort and Bennike (2007) on a partial skeleton from a Danish cemetery that was once thought to have leprosy, or perhaps ergotism, a destruction of the extremities due to ingestion of the fungus *Claviceps purpurea* on grain, especially rye (344). The authors examined the skeleton and described the lesions present on it. All that remained were the skull, scapulae, clavicles and all arm bones on both sides. Unfortunately, the tibiae were not present. The authors presented the lesions and described the pathology that would be expected for tuberculosis, treponematosis, sarcoidosis, ergotism, leprosy, and smallpox, ending in a discussion that either discounted or accounted for each disease based on what they saw. In the end, the authors believed that treponematosis would be the most likely diagnosis, although they could not rule out sarcoidosis or smallpox. This study shows the difficulty paleopathologists can have making an unambiguous diagnosis even when a large portion of the skeleton remains.

Once a tentative diagnosis of syphilis is made, a paleopathologist will sometimes attempt to decide which form of syphilis was the culprit. Pinta can always be ruled out immediately, as it does not affect the skeletal system. First, the temporal affiliation of the remains must be established. Then, the geographic location must be taken into account. If the remains are from the New World, it may be yaws or endemic syphilis, although endemic syphilis is more likely. If the remains are from the Middle East, the probable diagnosis is endemic syphilis. When all of these questions are answered, it may be possible to make a diagnosis with greater certainty. It also may be possible that no such diagnosis can be made. In the case that a probable diagnosis cannot be made, most paleopathologists prefer not to assume that one disease or another is responsible, instead reserving judgment.

Employing Diagnostic Criteria

Some recent work has been done by paleopathologists to create a set of diagnostic criteria to make a definitive diagnosis among the treponematoses. Because the diseases seem to lie along a gradient, it can be difficult or impossible to differentiate between them. Rothschild and Rothschild (1995) created a set of standards under the acronym SPIRAL after examining syphilis, yaws, and endemic syphilis in three different populations. The venereal syphilis population came from those diagnosed with syphilis in the Todd collection, the yaws skeletal population came from Guam and dated to 500 years before present, and the endemic syphilis population consisted of Bedouins from Israel dated to 150 years before present (Rothschild and Rothschild 1995:1403). Each skeletal population is supposed to have only one type of treponematosis, to control for the type being examined. Unfortunately, there are few skeletal populations with significant numbers of treponemal disease available for study, so the number of individuals studied was quite small for the populations with endemic syphilis and yaws. The SPIRAL acronym stands for: Sabre shin without periostitis; Prepubescent; Involvement of tibia unilaterally; Routinely affected hand or foot; Average number of bone groups affected is greater than or equal to three; and Lacking periostitis but flattened (Rothschild and Rothschild 1995:1405). Each of the standards is answered with a yes or no and the pattern discerned is supposed to point to one of the three treponemal diseases as a diagnosis. This method is to be used in the study of individuals or populations with unknown treponemal affectations.

Several problems with this methodology have been raised. Three of the six characteristics deal solely with the tibia, while none of them deal with lesions of the skull, thought to be the most pathognomic of the bones in diagnosing syphilis (Cook and Powell 2005:471). In addition, other paleopathologists raise issues with the SPIRAL criteria being difficult to interpret, especially the final standard, lacking periostitis but flattened, which refers to the tibia as well. Some issues have been raised with the populations examined as well, as the venereal syphilis population was taken from the Todd skeletal collection, in which the individuals had been diagnosed with syphilis, while the other populations were not diagnosed by medical professionals before death. The populations also differed in several important ways: climate, diet, population structure and density, and all would have the presence of different diseases as well (Cook and Powell 2005:471). In addition, Rothschild and Rothschild do not mention any differential diagnoses for these remains. Although this was a good idea for research, it does not seem that syphilis will let us unravel its secrets that easily.

The distribution and frequency of lesions on a skeleton can be an important indicator of disease or trauma, and especially with syphilis it is important to examine the entire skeleton to make a positive identification. Diseased bone is a nonspecific indicator, so the system as a whole must be examined. A paleopathologist must take into account the differential diagnoses for the lesions, and also must remember that the individual may have been afflicted with other diseases concurrently. While it is not an exact science, researchers should not discard this important aspect of paleopathology.

CHAPTER 6
The Future of Syphilis Research: DNA Analysis

Recent advances in DNA technology are making it possible for researchers to diagnose disease in people who have been dead for centuries. The fields of ancient and modern DNA studies have scientists working to understand every aspect of the lives of our ancestors. Several recent studies have attempted to understand the progression of the treponematoses into the diseases that we see today. A couple of interesting studies have looked at the probable mutation of the treponemes into different forms of the disease. Another aspect to be researched is the geographic origin and the types of syphilis found in different areas of the world at different times. As DNA technology progresses, these and other questions can be asked and answered to make a complete picture of the disease.

The earliest DNA research on treponematosis was undertaken to discern whether the four forms of the disease were identical or were different strains of related bacteria. Researchers began looking for the slight differences between the subspecies of the *Treponema* genus (Noordhoek et al. 1990:2011). Early on, researchers recognized that laboratory animals showed differential sensitivity to syphilis, yaws, and endemic syphilis (Rothschild et al. 2000:936). The *Treponema pallidum* genome was sequenced in 1998 and consists of about 1,000 kilobases, making it one of the smallest prokaryotic genomes (Fraser et al. 1998:375). It has been found that the differences between the genomes of the three *T. pallidum* strains are very small as well (Harper et al. 2008:e148). The small differences between the bacteria disprove the unitarian hypothesis that the diseases are caused by the same organism.

A recent study by Harper and colleagues (2008) used DNA and a phylogenetic approach to trace the mutation of the treponemes by typing the DNA of 22 different strains of yaws, endemic syphilis, venereal syphilis, and animal syphilis. Unfortunately, there are only five yaws strains available for testing in the world, only two of endemic syphilis, and no pinta strains (Harper et al. 2008:e148). To differentiate between the subspecies, the acidic repeat protein gene was examined. Each type of syphilis was found to have differing numbers of repeat units. Harper and her colleagues found that the venereal syphilis strains tested were the most recent mutations and were most closely related to a yaws strain from South America on the phylogenetic tree as shown in figure 8 (Harper et al. 2008:e148). The strains are identified by place and year they were collected, for example, Dallas 1 (1991), and the pathogen types are color coded by subspecies. Interestingly, the Old World yaws strains were found at the base of the tree, meaning they were the earliest to arise. Harper et al. (2008:e148) report that "the pattern of substitutions suggest that a hypothetical intermediate strain, arising from either the [African] *pertenue* strains or *endemecium* strains, once existed and was a progenitor to both New World subsp. *pertenue* and all subsp. *pallidum* strains". These findings seem to support the Columbian hypothesis because it shows that non-venereal strains seem to have originated earlier in the Old World and migrated with humans, changing as it moved into different environments and met with different social conventions (Harper et al. 2008:e148). After it made its way to the New World, the disease eventually returned to the Old World and then the rest of the world as venereal syphilis. The authors felt there

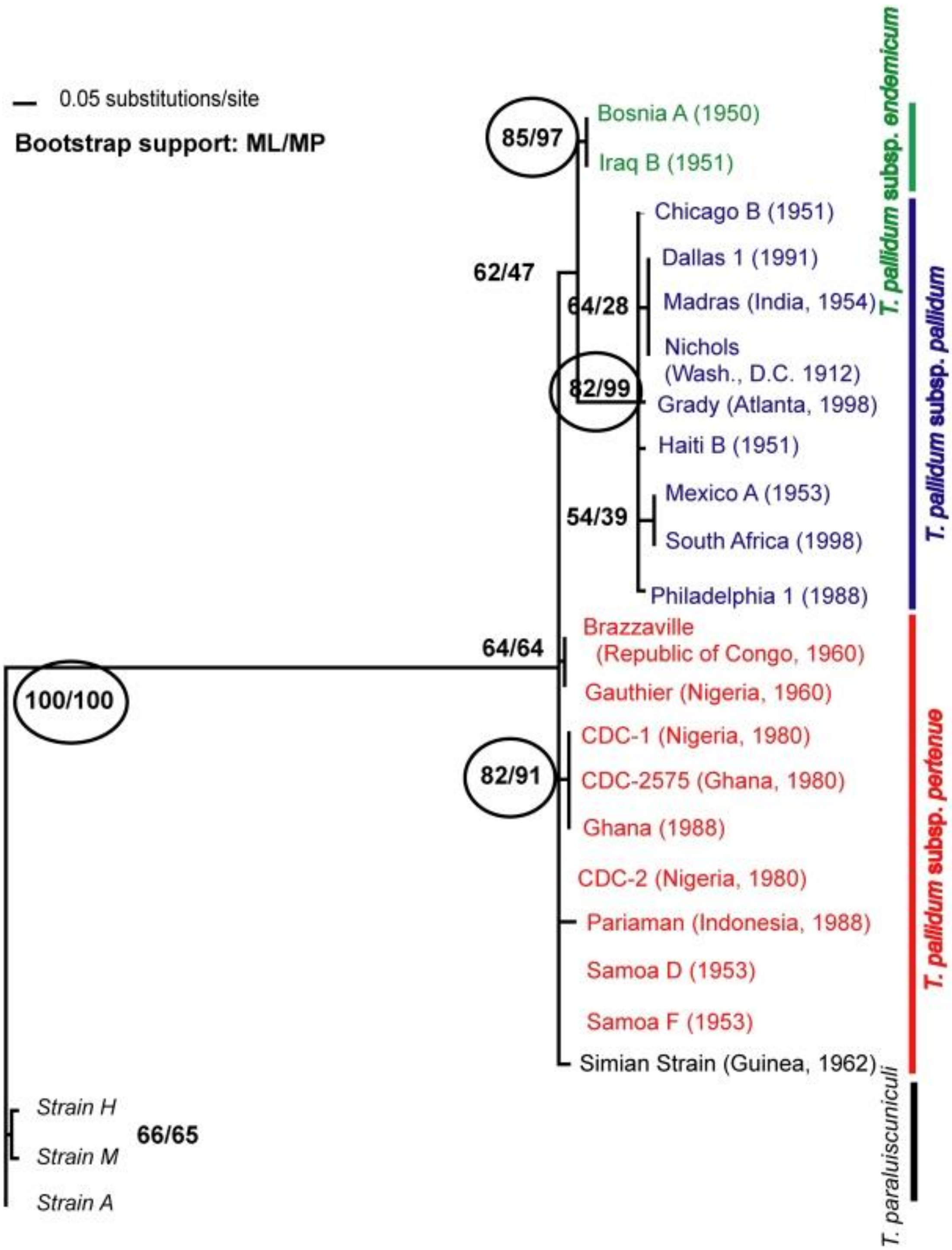

Figure 8. Phylogenetic tree depicting the relationships between *T. pallidum* subspecies. [From Harper et al. 2008:e148.]

was no way to know what the mode of transmission was for the disease that was spread to Europe. As mentioned before, it is unlikely that the Taino, the native inhabitants of Hispaniola, harbored the venereal form of the disease. If Hudson's hypothesis is correct, the non-venereal form found in the New World could have been transmitted to the sailors and then changed to a venereal form upon arrival in Europe.

Another interesting study from recent years was done by Kolman and colleagues in 1999. Venereal syphilis was found in extracted DNA in 200-year old skeletal remains from Easter Island (Kolman et al. 1999:2060). This study "represents the first nucleic acid-based confirmation of a morphologically identified treponemal infection" (Kolman et al. 1999:2063). It is an interesting combination of both types of DNA studies: ancient and modern. The researchers compared ancient DNA from the skeletal specimen with modern DNA from the recent strains kept by the Centers for Disease Control. Ancient DNA research is still difficult and expensive, but if the technology continues to advance, it would be interesting to research the presence of treponematosis in individuals from locations around the world. The study from Easter Island represents the direction ancient DNA studies of the treponematoses must go in order to paint a more complete picture of ancient health and our disease history.

There are some ethical considerations to make in ancient DNA research. The extraction is destructive and therefore not acceptable in some situations and for some sets of remains. In addition, the extraction is not guaranteed to produce DNA results, so if there is a possibility that DNA will be too degraded, destructive analysis should not be undertaken. DNA research should also not be undertaken at the expense of other, less destructive research, and destruction should not take place on samples that are needed for other research (Kaestle and Horsburgh 2002:106). Another consideration must be made with respect to native groups. In North America, researchers must be respectful of Public Law 101-601, the Native American Graves Protection and Repatriation Act, also known as NAGPRA, which requires them to contact the tribes of culturally affiliated remains for repatriation. In some cases, the beliefs of many tribes require that no destruction or study be done on the remains (Armelagos and Van Gerven 2003:58). It is important for researchers to respect the wishes of the tribes they are dealing with.

For the future of ancient DNA studies in treponematosis, attention must be paid to recent work being done on isolating tuberculosis DNA from mummies and skeletal remains. The amplification of *Mycobacterium tuberculosis* in pre-contact Native Americans proved the existence of the disease in the New World before European contact (Kaestle and Horsburgh 2002:105). Now that more sophisticated techniques for DNA extraction are available, the next step should be attempting to find the syphilis bacterium in pre-contact skeletal remains on both sides of the ocean, and discerning the types of syphilis found. This will be the only way to conclusively end the debate on the origins and evolution of syphilis. Exact diagnosis of the type of syphilis with DNA technology can be compared to the skeletal manifestations so that a more exact suite of lesions can be associated with each. Understanding the globalization of disease in the past will give us insight on past populations and what we can expect in terms of disease change and mutation in a more transnational world.

CHAPTER 7
Conclusions

What is the point of this research? Why should scientists spend time and money learning about a disease that affected people hundreds and thousands of years ago? Of course, syphilis still exists today, but there is a cure for it now and eradication programs have been fairly successful in ridding the world of the nonvenereal forms of the disease. Unfortunately, the AIDS epidemic seems to have increased the number of venereal syphilis cases, as having either disease increases the risk of contracting the other (Singh and Romanowski 1999:200). Why is everyone fighting about whether or not syphilis was present in the New World or in the Old World? As the old adage tells us, if we don't study it, history is doomed to repeat itself.

Paleopathologists and bioarchaeologists are interested in reconstructing past health and lifeways of societies through the remains of both their skeletons and their material possessions. Infectious diseases have played a huge part in the history of human life, from the bubonic plague, which wiped out a significant part of the population in Europe, to smallpox, which was also a virulent killer until a vaccine was developed to eradicate the disease. There is no vaccine to guard against syphilis, although penicillin is an easy cure in the early stages of the disease. Eradication efforts have, for the most part, been effective in controlling the non-venereal forms of the treponematoses. In venereal form, syphilis still poses a problem especially in industrialized nations. Because syphilis has been living and mutating alongside us for so long, it is hard to imagine a time in the future when humans will be without the disease.

Understanding the movement and evolution of the treponematoses will give us insight into the evolution and movement of other diseases. These studies will also help us understand our past, and how the actions of our ancestors changed our lives today. We have seen that as human society changes, disease must change along with it to maintain itself. Human populations have gone through a multitude of change, many of which made our lives very different and made the lives of the pathogens very different as well. Everything from changing climates and changing social interactions and diets has made it imperative for pathogens to change as well.

There are still debates over the origins of the treponematoses, so much so that researchers have divided themselves into camps based on their beliefs. The Columbian hypothesis maintains that after his discovery of the New World, Columbus' crew unwittingly picked up and spread syphilis to the entire continent of Europe. In contrast, the pre-Columbian theory maintains that the treponematoses were present in Europe for a long time before the Age of Discovery, but that it was not distinguished from leprosy. In addition, the unitarian and nonunitarian hypotheses deal with the evolution of the bacteria from one form to another. The unitarians believe that only one organism that affects humans differently based on the social and environmental conditions it is found in, while the nonunitarian hypothesis posits that there are four distinct organisms that mutated to survive in new environments. As more information becomes available and more researchers turn their attention to this subject, perhaps we will be able to end the debate and find the true origin and migration of the treponematoses.

An important aspect of the treponematoses that ties in to these hypotheses is the area and timing of humans' first contact with the disease. Researchers hope to understand how the pathogen arose in the New World and how it mutated into the forms that we know today. We also want to know which form of the disease was contracted by the Spaniards, since it is the Columbian hypothesis that has the most evidence behind it. By comparing the island population of Yap to the Taino, the native inhabitants of Hispaniola, it may be postulated that the Taino could not have maintained a venereal form of the disease due to their small population size as well as the disease's negative impact on human fertility. This does not mean, however, that the Taino were not affected with New World yaws, which according to Harper et al. (2008) is most closely related to the venereal form. It should be recalled here that Hudson (1965:889) reported that medical history is full of examples of transition from nonvenereal to venereal syphilis and vice versa. Livingstone's alternative hypothesis, that the disease was spread from Africa, may be an equally plausible scenario for the origins of venereal syphilis and warrants further study.

Another aspect of paleopathology that must be addressed in research is differential diagnosis. Skeletal lesions are usually nonspecific indicators of disease and trauma. Any disease that causes skeletal distress must be looked at as possibly contributing to lesions found on a skeleton when we have no medical records. Syphilis is systemic, causing lesions on several different bones, often bilaterally. There are few other diseases that cause this kind of extensive damage, but there are some that researchers need to compare before making a diagnosis. In some cases, a complete skeleton will not be found, or there may be a non-traditional set of lesions, making a definitive diagnosis difficult or impossible. It is important that researchers understand the limitations of paleopathology and construct their studies to facilitate peer review.

Another avenue of future research may be found by looking at the AIDS epidemic. There has been much speculation about the similarities between the two diseases. AIDS has only recently been diagnosed and differentiated from the multitude of diseases that affect AIDS patients after they are immunocompromised. Researchers feel that AIDS was affecting people long before it was finally identified, which relates to the problems doctors had with diagnosing syphilis in the late 1400s. In addition, syphilis and AIDS have both had a social stigma that placed blame and distrust on the afflicted. It has been discovered that a history of syphilis in men is significantly associated with seropositivity for HIV, and syphilis has experienced a revival in numbers of individuals affected (Baker and Armelagos 1988:720). Despite the pathogen's inability to mutate into a drug-resistant form, and despite the relatively easy and inexpensive treatment for syphilis, and despite the availability of protective measures to be used during sexual contact, syphilis remains a daunting and destructive pathogen.

New research in the field of ancient DNA studies is helping to clarify the origins of this difficult disease. Technology has advanced so far in the past ten years and it will only get better. With greater technology comes greater responsibility to understand our past and help future generations. We have been able to learn that there are genetic differences between the four treponematoses and that the disease has traveled around the world. Researchers can now extract DNA from ancient remains, although there is still a long way to go. The research is still expensive and sometimes destructive. As technology advances further, many new avenues of research will open up and more information will be gleaned from skeletal remains around the world. This avenue of evidence will be perhaps the most accurate and has the potential of ending the debate on the treponematoses once and for all.

Some other avenues of research may be useful in helping to complete the picture of syphilis. As new technology becomes available, old questions may be answered. Soon DNA testing may be less destructive and more powerful, able to isolate DNA of diseases where previously it would have been impossible. Just as researchers have done with tuberculosis, soon we may find out if many supposed syphilitic remains are truly syphilitic, and perhaps even which form of the disease affected them. More detailed and specific diagnoses may allow us to gain more knowledge on the quantitative aspects of lesions to expand upon the research done by Rothschild and colleagues.

Finding information about disease in general and syphilis in particular is a daunting task. The best way to learn the most we can about syphilis is to use interdisciplinary research to our greatest advantage. Medical anthropology, paleopathology, epidemiology, virology, and DNA research each offer unique insights into the nature of disease and how they have affected humans for thousands of years. We must continue to work together in order to finally solve the puzzle of syphilis: when it began to affect our ancestors, where it migrated to and how it mutated on its journey, and how it has changed our lives. When we understand all of these factors, perhaps we will be able to finally eradicate this and other infectious diseases as well.

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