perhaps such impotence is an inevitable result of poetry's inability to find convincing collective voices that might make revolutionary sentiments less wistful and less dogged by irony.

Lynn Margulis

on syphilis & Nietzsche's madness: spirochetes awake!

In the foothills of the Italian Alps, in a snow-draped piazza in Turin on January 3, 1889, a driver was flogging his horse when a man flung his arms around the poor beast's neck, his tears soaking its mane. The horse's savior was the German philosopher Friedrich Wilhelm Nietzsche (1844 – 1900). His landlord later found him collapsed in the square and brought him back to his room, where Nietzsche spent the night writing a flurry of bizarre postcards. As soon as his friend and colleague Jacob Burck-

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hardt received a crazed letter, he convinced his close friend Peter Gast to go and accompany Nietzsche on his return to Basel. Much of the rest of the century, the last eleven years of his life, Nietzsche spent in incoherent madness, crouching in corners and drinking his urine. The most productive year of his career had been immediately prior to the psychotic break. After it, he wrote no more philosophy. Deborah Hayden, in her recent book *Pox: Genius, Madness, and the Mysteries of Syphilis* (2003), summed up the famous incident:

> The story of Nietzsche's sudden plummet from the most advanced thought of his time to raving dementia is often told as if there were a razor's edge demarcation between sanity and tertiary syphilis, as if on 3 January armies of spirochetes woke suddenly from decades of slumber and attacked the brain, instead of the biological reality that paresis is a gradual process presaged over many years.

Hayden's case to prove that Nietzsche indeed suffered all his adult life from syphilis is as strong as any posthumous medical history can be. He was diagnosed at a time when clinical familiarity with the disease abounded. Detailed evidence shows that he passed through each of the three stages: the chancre of primary syphilis immediately after infection; the terrible pox, fever, and pain of secondary syphilis that emerges months or years later; and the dreaded third: paresis. 'Paresis,' like the word 'syphilis' itself, refers to a syndrome. An acronym, its mnemonic is: *p*ersonality disturbances; *a*ffect abnormalities; *r*eflex hyperactivity; *e*ye abnormalities; *s*ensorium changes; *i*ntellectual impairment; and *s*lurred speech. Paresis often begins with a dramatic delusional episode, but in the following months and years dementia alternates with periods of such clarity that there seems to have been a cure.

Infection by the spirochete of syphilis – declared eradicated in the mid-twentieth century – still prevails, I believe. The efficacy of early treatment with penicillin, improved hygiene, condom use, and attitudes that lead the afflicted to seek help for venereal disease conspire to bolster the common myth that syphilis has disappeared. We are deceived; many people suffer from syphilis called by other names.

Syphilis symptoms are caused by venereal infection with a spirochete bacterium called *Treponema pallidum*. The treponeme family of spirochetes consists of tiny corkscrew-shaped bacteria, all of which swim and grow in animal tissue. The bacterial flagella are encased within an outer membrane. Spirochetes, like other 'gram negative' bacteria, all have two cell membranes with a space between them. In this periplasmic space between the inner and outer membranes the flagella rotate. Smaller spirochetes such as the syphilis treponeme have only one or two such flagella, whereas some giant spirochetes have more than three hundred. The efficient screw-wise motion into genital and other tissue requires this flagellar arrangement.

Treponema pallidum is one freak among a huge diversity. The vast majority of spirochetes live peacefully in mud, swamps, and waterlogged soils all over the world. Benign, 'free-living' spirochete relatives of *Treponema pallidum* are everywhere. They thrive where food is plentiful: lakeshores rich in decaying vegetation, marine animal carcasses, hot sulfurous springs, intestines of wood-eating termites and cockroaches, and the human mouth. Most kinds are poisoned by oxygen, from which they swim away to avoid. Very few cause illness, yet ticks infected with the *Borrelia*

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burgdorferi spirochete of Lyme disease can induce serious arthritis and other enduring symptoms. Another spirochete nearly indistinguishable from the Lyme disease *Borrelia* is a healthy symbiont in the intestines of termites. A treponeme similar to that of syphilis is associated with the tropical eye disease yaws. Leptospirosis, a systemic and sometimes fatal infection found usually in fishermen, is due to spirochetes that are carried in the kidney tubules of rats that urinate into nearby water. The fishermen acquire *Leptospira* spirochetes from fishhook cuts and other skin lesions. And, of course, there is syphilis.

Nietzsche's letters from 1867 until his breakdown provide a vivid account of the suffering of secondary syphilis. He complains of the pain, skin sores, weakness, and loss of vision that typify the repertoire of the disease. In his last year, his letters give evidence of euphoria. His published works show the grandeur and inspiration that tertiary syphilis sometimes brings to brilliant and disciplined creative minds by removing inhibition as brain tissue is destroyed. When Nietzsche wrote in *Thus Spoke Zarathustra* (1884), "Die Erde, sagte Er, hat eine Haut; und diese Haut hat Krankheiten. Eine diese Krankheit heist zum Beispiel: 'Mensch'" (translated as "The Earth, he says, has a skin, and this skin has a sickness. One of these sicknesses is called 'man,'" or as "The Earth is a beautiful place but it has a pox called man"), what terrible insight Nietzsche must have had into the devastating horror of pox!

Multiple sources indicate that he was treated for syphilis in 1867 at age twenty-three. Seeking medical treatment for eye inflammation, a frequent syphilitic symptom, he consulted Dr. Otto Eiser, who reported not only Nietzsche's penile lesions, but that he had engaged in sexual relations several times on doctor's orders! Years later, in 1889, when Nietzsche broke down and was taken to the clinic of a paresis expert, he was admitted with the diagnosis "1866. *Syphilit. Infect.*"

In 1888 Nietzsche's productivity was, by any standard, extraordinary. He completed his philosophical project: *Twilight of the Idols*, *The Antichrist*, *Ecce Homo*, and *The Case of Wagner*. The style of these works is apocalyptic, prophetic, incendiary, and megalomaniacal, leading many scholars to claim the excesses of these works were due to incipient paresis. Now, after more than half a millennium of the study of syphilis and more than a century after Nietzsche's breakdown, our research suggests that the philosopher really did plummet abruptly into madness; armies of spirochetes *did* awaken suddenly from decades of slumber, and literally began to eat his brain.

Many claim syphilis was known in Europe prior to the return of Columbus; but as Hayden describes and I agree, it is more likely the insidious venereal infection was a new gift of the Americas to the people of Europe. Columbus and his crew returned to Spain with a novel set of symptoms that soon spread to Naples and France. From that year, 1493, the disease was described in detail, first by the physician who treated Columbus and his men, Dr. Ruiz Diaz de Isla. Diaz reported, "And since the Admiral Don Cristobal Colon had relations and congress with the inhabitants . . . and since it is contagious, it spread." Eventually it affected the waterfront prostitutes of Barcelona. Diaz, in work published in 1539, wrote that infected sailors were accepted into the army that Charles of France brought to besiege Naples in 1495 and into the forces that Ferdinand of Spain employed to defend Naples. Ferdinand's army alone is estimated to have had five hundred prostitutes among its camp fol-

lowers. Soon after the victorious entry of Charles's army, the Great Pox of Naples erupted. His multinational mercenaries brought infection back to every European country. Charles himself returned to France infected. By the next year, the disease spread across the continent, puzzling physicians with its novelty.

Within the early decades of the contagion, in cities across Europe physicians reported that between 5 and 20 percent of the population suffered. Variously named at first, it came to be called *morbus gallicus*, the French malady. Charles's army was blamed for its introduction to Naples – perhaps rightly. Physicians who published work on it in the *lingua franca* of Latin soon after the great outbreak of 1495 drew international attention. Girolamo Fracastoro, in 1530, wrote a verse treatise on the disease entitled *Syphilus sive Morbus Gallicus*, in which the eponymous protagonist, a shepherd, is the first to bear the disease, as a punishment for impiety. The name stuck.

Syphilis has been surprisingly well documented since its outbreak in the closing years of the fifteenth century, as microbiologist and sociologist of science Ludwik Fleck (1896 – 1961) wrote in his masterpiece *Genesis and Development of a Scientific Fact*. From the sixteenth through the end of the nineteenth century, the prevalence and peculiarities of syphilis inspired a wide range of literature, from scientific arcana to torrid novels. Meanwhile, the cause of the disease was avidly sought. Then in 1905 Erich Hoffmann sent a genital chancre specimen to German microscopist Fritz Schaudinn, who confirmed the etiology. He aptly called the lively, translucent, thin, corkscrew-shaped bacterium he observed "thin, pale thread": *Treponema pallidum*. In 1913 Udo J. Wile found *Treponema pallidum* spirochetes in the brains of patients that manifested tertiary syphilis symptoms. (The best recent photo I've seen of spirochetes in the frontal cortex of a paresis patient, figure 8-14 in W. E. Farrar's *Atlas of Infections of the Nervous System*, is at too low a magnification to see round-body details. See the inside back cover and page 125 below.)

Syphilis & Nietzsche's madness: spirochetes awake!

Syphilis has gained attention again because of its disputed relationship to AIDS. Today, although physicians rarely record cases of tertiary syphilis, the earlier two stages of the disease seem on the rise. AIDS patients who have a past record of syphilis that was apparently cured by antibiotics succumb again to the disease. "Syphilis in patients infected with HIV is often more malignant with a greater disposition for neurological relapses following treatment," says Dr. Russell Johnson of the University of Minnesota Medical School, a world expert on the Lyme disease spirochete. Dr. Peter Duesberg, discoverer of the retrovirus, rejects exclusive focus on HIV as the cause of AIDS in his excellent book *Inventing the AIDS Virus*. He questions the common assumption that, as a contagious virus, HIV is even the main cause of the lesions, tumors, rashes, arthritis, weakness, pneumonia, and other severities that accompany immunosuppression. Such symptoms, including the presence in tissue of both the HIV antibody and of the virus itself, may, as in other opportunistic infections, be the consequence, not the cause, of AIDS. I suspect that many of the symptoms in the immunosuppressed sufferers correlate both with the tenacity of the syphilis treponeme and the sexual and other behaviors of the patient.

Joan McKenna, a physiologist with a thermodynamic orientation, writes:

> Because spirochetes can be harbored in any tissue for decades and can move from latency to reproductive stages,

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> their survival in any host and despite any known therapy is nearly certain .... [We also] know that unknown factors will activate the microorganism [*Treponema pallidum*] from latency into an aggressive infection ....

She goes on to remark about the relation between syphilis and AIDS: "No symptoms show up in AIDS that have not historically shown up with syphilis and the history of these populations [where AIDS is rampant] includes a high incidence of syphilis."

Clinical confusions (misdiagnoses, anomalous symptoms, conflated multiple infections) have abounded since the early centuries of syphilology. Yet many studies confirm the variety and severity of symptoms attributable to the *Treponema pallidum* spirochete. The malady remains idiosyncratic in its course, with variability in the timing of the stages, and in the absence of any reliable test or single diagnostic. Still, the evidence suggests that the virulence and severity of the disease have diminished dramatically since the initial violent pox outbreak. This behavior is expected of pathogens in first exposure to naive populations. Syphilis in Europe showed the same pattern as measles and smallpox did when Europeans first introduced them to the Americas. As early as the first few decades that followed the Pox of Naples, subsequent generations of Europeans were more resistant. Pathogenic microbes maximize not by rapid lethality, but by transforming into a chronic disease that lasts a lifetime and subtly affects behavior in the stricken animal.

Since the late nineteenth century, the Wassermann blood test has often been touted as the best diagnostic test for syphilis. The fear of syphilis transmission was so common that the Wassermann test was, and often still is, legally mandated in many places, required prior to marriage. However, as shown by Fleck and others, the Wassermann reagent does not measure the presence of *Treponema pallidum*. It indicates, and not even 100 percent of the time, the exposure of a patient to unspecified infectious bacteria: a positive Wassermann test shows only that a person makes antibodies against certain blood-borne bacteria that may include the syphilis treponeme. Furthermore, this test in known syphilitics in advanced stages of the syndrome often converts to negative.

To preclude mother-to-infant transmission of syphilis during parturition, drops of silver nitrate, thought to suppress the syphilitic spirochete, were placed in the eyes of most newborns. This practice occurs in some regions even now, and even when blood tests for syphilis in the mother are negative. These irrational practices measure residual fear of the contagion of syphilis.

In the beginning of the twentieth century, arsphenamine, an arsenic-based remedy, was said to improve the health of syphilitic patients. Often it made people sicker. After 1943 came the 'miracle drug': the claim was that a single or a few massive doses of penicillin cured the body permanently of the dreaded treponeme. After hefty antibiotic treatment in newly detected cases, the insidious corkscrews disappeared. Whereas the apparent remains of 'dead' spirochetes – tiny, shiny round bodies – might sometimes be found in tissue, the moving treponeme was declared gone. J. Pillot, the French researcher after whom the beautiful large spirochete *Pillotina* was named, 'proved' that the round-body remnants of the lively corkscrew are dead. The confusion comes from the fact that – penicillin or not – during the long latent phases of the disease after the primary chancre, moving corkscrew treponemes are not seen anyway. Many

years and studies later we can say that whether or not any treponemes are visible in the patient, penicillin (except when given in an appropriate dose very early in the course of the disease) is not an effective and permanent cure.

Yet some physicians still insist that penicillin and strong immune systems definitively eliminate this disease; others claim that treponemes 'hide' in tissues where antibiotics are inaccessible. Some speculate that tertiary syphilis occurs when the syphilis treponemes finally manage to spread, after decades of invisible stealth, and penetrate the blood-brain barrier. Alas, most physicians and syphilis scholars (and scientists such as I) simply don't know the relationship between *Treponema pallidum*, syphilis symptoms, the immune response, the HIV virus, secondary infection, sexual behavior, and the putative cures.

Finally, in 1998, the description of the entire genome of *Treponema pallidum*, one of the smallest bacterial genomes known, with about nine hundred genes in total, was published. Two other spirochete genomes are known: *Borrelia burgdorferi*, with some eleven hundred genes, and *Leptospira*, with nearly five thousand genes. Spirochetes like *Leptospira*, which are capable of life outside the body of animals, have at least five times as many genes as the syphilis treponeme. The leptospires all by themselves internally produce all their necessary components (proteins, lipids, vitamins, etc.), whereas *Treponema pallidum* does very little by itself; it survives only on the nourishment of rich human tissue. For this reason, it is likely that the syphilis treponeme lost four-fifths of its genes as it became an obligate parasite.

To identify any bacterium, the microbiologist needs to separate it and grow it by itself, that is, in isolation. Despite the specific genome knowledge of the single treponeme strain investigated, however, the routine growth of any *Treponema pallidum* in isolation (outside the warm, nutritious mammalian body) has not been achieved. Whether in organic mud or changing human tissue, these spirochetes depend utterly on their immediate environment. Unfortunately, moreover, no one has ever been able to induce round bodies of *Treponema pallidum* to form in isolation in a test tube, or to test these round bodies in isolation for their ability to resume growth.

My students and colleagues and I are not experts on any disease bacteria, nor on illnesses where symptoms are associated with visible spirochetes. We have been living closely with spirochetes for very different reasons. Our interest is in the possible role these wily bacteria played in the evolution of larger forms of life. Attempts to reconstruct the evolutionary history of the nucleated cell, the kind that divides by mitosis, have led us to study harmless spirochetes.

I suspect that the mitotic cell of animals, plants, and all other nucleated organisms (algae, water molds, ciliates, slime molds, fungi, and some fifty other groups included in the Protoctista kingdom) share a common spirochete ancestor. I believe that with much help from colleagues and students, we will soon be able to show that certain free-swimming spirochetes contributed their lithe, snaky, sneaky bodies to become both the ubiquitous mitotic apparatus and the familiar cilia of all cells that make such 'moving hairs.' Our lab work, coupled with that of other scientists, reveals that certain spirochetes when threatened by death can and do form immobile, shiny round bodies. Furthermore, these round bodies can hide and wait until conditions become favorable enough for growth to resume.

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Since 1977, a group of scientists and students has been traveling to Laguna Figueroa (called Lake Mormona by Anglophones) near San Quintin, Baja California Norte, Mexico, to study microbial mats. These communities of organisms resemble ancient ones that left fossils in rocks. They are the best evidence we have of Earth's oldest life-forms. Many times we have brought microbial mat samples back to our lab and left these bottles of brightly colored mud on the windowsill, where photosynthetic bacteria powered the community. On several occasions the bottles were assiduously ignored through semesters of classes and meetings. From time to time, we took tiny samples and placed them in test tubes under conditions favorable for growth. Various kinds of spirochetes did begin to swim and grow; we suspect they emerged from round bodies after the samples were put into fresh, clean, abundant liquid food. Spirochetes, mostly unidentified, persisted in hiding in these bottles and jars for at least ten years.

Today we study another microbial-community sample, collected by Tom Teal in 1990 at Eel Pond in Woods Hole, Massachusetts. It is in our lab at the University of Massachusetts, Amherst in a forty-liter glass jar. To it we add only 'rain' (distilled water), but with sunlight as the energy source an abundance of life still thrives. Long after no typical spirochetes were seen in the sample, we added bits of either wet or dry mud to food and water known to support the activities of spirochetes, swimming and growing. In a very few samples, within about a week, armies of spirochetes awoke from at least months of slumber.

We have observed and filmed spirochetes in samples from all over the world rounding up to form inactive bodies. Continuation of work on spirochetes led to our collaboration with Spanish colleagues at the delta of the Ebro River. Professors Ricardo Guerrero and Isabel Esteve had begun a strong research project. One stake, a stick in the mud labeled #1 UAB, marks a site on a microbial mat that somehow seems exceptional. Many fascinating organisms were taken from that place, but none as interesting as the large spirochetes we named *Spirosymplokos deltaeiberi*. Whenever these easy-to-see spirochetes are confronted with harsh conditions – such as liquid that does not support their growth, water that is too acidic, sugars that they cannot digest, a temperature that is too high – they make round, dormant bodies much like those that Pillot and nearly all his successors argue are dead.

The spheres of *Spirosymplokos deltaeiberi* we studied look just like the round bodies published by Norwegian microbiologists Oystein and Sverre-Henning Brorson. (They call them cysts.) The Brorsons showed that under unfavorable conditions the *Borrelia burgdorferi* spirochetes of Lyme disease make round bodies. After weeks of dormancy, of no growth and no sensitivity to antibiotics and other chemical insults, these round bodies revive. At high magnification they look just like those of *Spirosymplokos deltaeiberi*, only smaller. The *Borrelia burgdorferi* round bodies convert to form swimming spirochetes all at once and begin to grow easily as soon as they are placed into proper liquid food at the correct temperature and salt concentration.

The Brorsons confirmed what we suspected: spirochete round bodies, like the spheres of *Spirosymplokos deltaeiberi*, are fully alive. Either mixed with other mud organisms or growing by themselves in isolation, just supply them with what they need to grow and within minutes they revert into swimming, active, feeding, corkscrew spirochetes. Armies of

them awake from months of slumber. Our work with Guerrero on *Spirosymplokos deltaeiberi*, coupled with our reading of the literature (especially several studies by the Brorsons), leads us to emphasize an ancient secret of spirochete success: persistence via round bodies.

Nietzsche's brain on January 3, 1889 experienced a transformation like that of the microbial mat sample transferred into new fresh food. Our interpretation is that the spirochetes transformed from dormant round bodies into the swimming corkscrews in a very short time. Deborah Hayden, however, is also correct. Nietzsche was inoculated in his early twenties, and his long-standing condition was confirmed both by the physician's diagnostic on the medical record ("*Syphilit. Infect.*") and, at his autopsy, by pox scars on his private parts. The dormant spirochetes had been hiding out in his tissues for over thirty years. But on January 3, 1889 in Turin, armies of revived spirochetes munched on his brain tissue. The consequence was the descent of Nietzsche the genius into Nietzsche the madman in less than one day.*

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