THE HISTORICAL IMPACT OF EPIDEMIC TYPHUS

by

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INTRODUCTION

Louse-borne Typhus Fever is undoubtedly one of the oldest pestilential diseases of mankind. Called by many names and confused with other fevers, it is not until the late fifteenth century that it can be recognized with certainty as causing devastating epidemics. With Plague, Typhoid, and Dysentery, it was the scourge of armies and civilian populations throughout the Middle Ages and frequently played a decisive role in wars conducted in Europe from the 15th through the 20th centuries. The manner in which the course of European history has been affected by Typhus epidemics has been graphically portrayed by a number of authors. This paper will attempt a further analysis of the historical impact of Louse-borne Typhus and how its epidemic propagation has led many to regard Pediculus humanus corporis as having a more profound effect on human history than any other animal.

EPIDEMIC TYPHUS FEVER
(TABARILLO, CLASSIC OR EUROPEAN TYPHUS, JAIL FEVER, WAR FEVER)

Causative Agent. Typhus fever is an acute specific infection caused by Rickettsia prowazeki as isolated and identified by DaRocha-Lima in 1916. Named in honor of H. T. Ricketts and L. von Prowazek, both of whom contracted typhus in the course of their investigations and died, R. prowazeki was originally believed to be a virus because of its minute size and difficulty of cultivation. R. prowazeki is now recognized as being morphologically and biochemically a type of bacterium. A rod-shaped microorganism, R. prowazeki is an obligate intracellular parasite whose cell wall contains muramic acid, diaminopimelic acid, and other components similar to those of the gram-negative bacteria. The cell wall is exceedingly permeable to many large metabolites. This feature may account for the microorganism's requirement for a living host.

Metabolically, R. prowazeki has a tricarboxylic acid (TCA) cycle, electron transport system, and many of the enzymes required for the biosynthesis of macromolecules. The host is believed to supply ATP, NAD, and CoA, components that have been experimentally shown to leak through the cell wall and membrane (Brezina et al., 1973).

Clinical Diagnosis and Pathogenicity. The appellation "typhus" originated with Aquavees in 1760 and was derived from the Greek, typhos, literally meaning "smoke". Hippocrates used this word to describe a "confused state of the intellect; a tendency to stupor". Originally, "typhus" designated any of the self-limiting fevers characterized by stupor. In 1829, the French clinician Louis clearly differentiated Typhus Fever from Typhoid Fever (Wolback et al., 1922). At present, the disease is recognized as having an incubation period of 6 to 16 days, commonly about 12 days. The onset is more or less sudden, with chills, fever, and severe headache. Between the fourth and seventh days a macropapular rash appears and becomes generally distributed on the chest and abdomen, later spreading to the hands, feet, and rarely, to the face. At first the spots are erythematous in character, disappearing on pressure. After the second day they become persistent and are often converted into true petechia. This mottling led to the belief that the Tabarillo of Mexico was identical with the Spotted Fever of Montana, a supposition proven erroneous by Ricketts and Wilder (1910) in which investigation Ricketts contracted Typhus and died. There is early and profound prostration, backache, and bronchial disturbances. A heavy flushed face "besotted expression" and injected conjunctivae are present in classic cases. Nervousness, mental dullness, and insomnia may be followed at the end of the first week by delirium. In severe cases, this develops into stupor and coma, accompanied by secondary infections and renal failure. Duration of the fever is from 10 to 21 days, usually 14 days, with termination by rapid lysis. Convalescence may be characterized by weakness and depression. Mortality varies; it is low in children under 15 years of age but usually ranges from 10 to 100 percent in adults, increasing with age. Today, with good supportive care and early judicious use of antibiotics such as the tetracyclines, quinilones, chloramphenicol, and para-aminobenzoic acid, the risk of a fatal issue is greatly reduced. Because of the toxic effects of chloramphenicol, tetracycline is the preferred drug.

The clinical manifestations are due to the ability of the Rickettsiae to multiply inside the endothelial cells lining the small blood vessels. The infected endothelial cells detach from the blood vessels and bring about vascular obstruction, eventually leading to tissue necrosis. Vascular lesions

having distinct histological appearance, sometimes referred to as Fraenkel's Nodules, are most numerous in the skin, central nervous system, and myocardium.

Laboratory Diagnosis and Vaccine. Serological confirmation of a clinical diagnosis of Epidemic Typhus is sought through employment of complement-fixation reactions, serum-agglutination techniques, and the Weil-Felix test.

The investigations of Weil and Felix (1916) and of Felix (1944) established the fact that patients sick with Typhus Fever develop agglutinins for certain strains of Proteus, namely X19 and X2. X19 was found to be the most sensitive indicator and suspensions made from the nonmotile O variant the most specific. Agglutinins for OX19 appear in the sera of most Typhus patients between the fifth and eighth day of illness, sometimes reaching a titer of 1:2,560 or more. Diagnostic significance is attached to a rise to 1: 160 or greater. However, nonspecific reactions to Proteus OX19 are often found in patients not suffering from Typhus Fever. Hence, the Weil-Felix test is used primarily in establishing a presumptive diagnosis of rickettsial disease, rather than distinct serological proof.

The discovery by Cox (1938) that R. prowazeki could be grown in the yolk sac of developing chick embryos made it possible to prepare large amounts of antigen for serological tests. Compliment-fixing antibodies appear in the sera of patients as early as the fifth to seventh day of illness. Plotz and others (1943) described a method for the preparation of purified compliment-fixing antigens from infected yolk sacs which would permit differentiation between Epidemic Typhus and Murine Typhus. This differentiation, however, depends upon carefully standardized antigens and is not routinely available in diagnostic laboratories. Therefore, microagglutination techniques and immunofluorescence using fluorescein isothiocyanate (FTIC) to detect R. prowazeki in tissue cytoplasm have been devised. These supplement guinea pig inoculation tests to provide specific diagnostic evidence.

In 1940 Cox and Bell prepared an Epidemic Typhus vaccine based upon the use of tissue culture. This vaccine consisted of a killed suspension of R. prowazeki grown on the yolk sac membrane of a chick and purified by centrifugation. Concentration of the effective antigenic materials led to a vaccine which is satisfactory not only from the point of view of potency, but also with respect to commercial production. Epidemic Typhus vaccine used by the U. S. Army during World War II consisted of 10 percent yolk sac suspension of R. prowazeki extracted by ether. The protection afforded lasted from 6 months to one year.

Critical evaluation of protection afforded by this vaccine under conditions of natural exposure leads to the conclusion that the risk of attack is reduced, the course of the disease is modified, and the probability of a fatal issue is decreased. In addition, there is the important observation that lice infected with R. prowazeki transmit it with difficulty, if at all, when permitted to feed upon a patient with typhus who has been previously vaccinated (Gilliam 1946; Sadusk, 1947; Wheeler, 1946).

Transmission By Lice. Transmission of Epidemic Typhus by the body louse (Pediculus humanus corporis) was first demonstrated experimentally by Nicolle and others (1909). Their observations were confirmed by Ricketts and Wilder (1910) and Anderson and Goldberger in 1912.

Transmission by the head louse (P. humanus capitis) cannot be overlooked, however, as was shown by Anderson and Goldberger in successfully transmitting typhus by means of a crushed head louse to a rhesus monkey. Furthermore, Weyer (1960) has shown that the rickettsial pathogen will multiply in the gut of the crab louse (Pthirus pubis). Nevertheless, sound epidemiological evidence incriminates the body louse as the primary vector with the head louse and crab louse of little importance in the chain of transmission. Nicolle's findings were the starting point of a series of investigations during World War I by von Prowazek, da Rocha-Lima, Nicolle, and by Wolbach and associates, which revealed the essential biologic relationship of lice to human typhus and the causative agent, R. prowazeki.

Pediculus humanus corporis is the common clothing louse, known during World War I as the "cootie", or "grayback". During World War II it was popularly termed "mechanized dandruff". They are most commonly found where clothing comes in close contact with the body; for example the waistline, neck, groin, and armpits. The eggs, so-called "nits", are usually cemented to the fibers of body clothing and/or body hairs. The female body louse begins to oviposit a day or two after maturation and insemination, the average number of eggs laid per day being about 10 for twenty or thirty days. According to Leeson (1941), hatching does not occur when the temperature goes below 23 C or above 38 C. The incubation period at 35-38 C (approximately human body temperature) varies from five to seven days. As the surrounding temperature is lowered, the incubation period lengthens so that at 24 C it is from seventeen to twenty-one days. Hopkins (1949) found that essentially the same temperature parameters also apply to the well-being of adult lice. The optimum for the adult body louse is approximately the temperature of the normal human body. Body temperatures outside the 23 - 38 C parameters, due to host fever or death, are extremely detrimental to the adult louse and are important in propagation of host diseases through migrations of the louse to a more temperature-suitable (healthy) human host.

After hatching, the young lice begin to suck blood at once. Throughout their development they feed frequently both day and night, particularly when the host is quiet. There are three molts, with the egg-to-egg cycle averaging about three weeks. Adult lice live about 30 days, engorging at frequent intervals, discharging relatively large pellets of dark red excrement as they feed.

When lice are fed upon a typhus patient during the febrile period of the illness, and possibly for a few days afterward as well, a large proportion become infected with R. prowazeki. The organisms enter the cell lining of the intestinal tract of the louse, where they multiply. The parasitized cells rupture and the organism may them be passed in the feces of the louse or may enter other cells lining the intestinal tract. Rickettsiae appear in the feces of typhus-infected lice about three to five days after the first infective meal. Rickettsiae have not been demonstrated in louse tissues, such as the salivary glands. The louse usually succumbs to the infection after 7 to 10 days; those that survive are infective for life.

The situation is humorously depicted by Zinsser:

> The louse shares with us the misfortune of being prey to the typhus virus. If lice can dread, the nightmare of their lives is the fear that some day of inhabiting an infected....human being. For the host may survive; but the ill-starred louse that sticks

> his haustellum through infected skin, and imbibes the loathsome virus with his nourishment, is doomed beyond succor. In eight days he sickens, in ten days, he is in extremis, on the eleventh or twelfth his tiny body turns red with blood extravasated from his bowel, and he gives up his little ghost. Man is too prone to look on all nature through egocentric eyes. To the louse, **we** are the dreaded emissaries of death. He leads a relatively harmless life - the result of centuries of adaptations; then,
>
> out of the blue, an epidemic occurs; his host sickens, and the only world he has ever known becomes pestilential and deadly; and, if as a result of circumstances not under his control, his stricken body is transferred to another host whom, he, in turn, infects, he does so without guile from the uncontrollable need for nourishment, with death already in his own entrails. If only for his fellowship with us in suffering, he should command a degree of sympathetic consideration.

The course of typhus infection in Pediculus humanus capitis is the same as that in the body louse. However, the latter is far more important in epidemic transmission.

Apparently the infection is transmitted to humans by fecal contamination of the wound made by the louse in feeding, or made by the host in scratching. However, Wolback (1922) has shown that crushing of the louse itself into the feeding wound can result in passage of the rickettsiae to the human host prior to extrusion of the organisms in the louse feces. In louse feces, rickettsiae may survive for years under experimental conditions if temperature and humidity are kept low. Since the clothes of patients are frequently heavily contaminated with louse feces, it has been suggested that infections are occasionally transmitted by the air-borne route to the respiratory tract of a susceptible person. While air-borne infection is theoretically possible, it is relatively unimportant under conditions of natural exposure (David, 1947). The common mode of transmission without a doubt is the inoculation of a louse bite with louse feces containing rickettsiae.

Epidemic Propagation. Nicolle's elucidation of the role of the human body louse in transmission helped to explain the epidemiology of typhus. Propagation is maintained in human populations by the circulation of lice from person to person. The louse is a relatively inefficient vector, since it has a very short range of movement; it crawls and does not fly. Furthermore, active stages will only survive a week or ten days without a suitable host upon which to feed. The fact that they are exclusively human parasites makes this an important consideration. In addition, transovarian transmission of rickettsiae in lice has not been demonstrated. It would follow, then, that epidemic spread is favored by the existence of a large louse population on humans who are crowded together in their living or sleeping quarters. Scratching and restlessness on the part of heavily infested individuals will cause lice to wander about and reach the outer surface of clothing, from which they may be readily transferred to other persons. Thus, in crowded tenements, prisons, refugee camps, or under conditions or times of war or disaster, when prisoners, refugees, or troops are unable to change clothes or bath regularly, lice may spread rapidly through the entire population. This is particularly true during the winter, when bathing is made more difficult by the cold weather. Thus, as typhus is more or less continuously propagated among primitive peoples in the colder climates - in Russia, Poland, Southeastern Europe, North Africa, Mexico and the Andean regions of South America - its epidemic propagation depends upon temporary conditions favorable to the dissemination of lice and their attendant rickettsiae. Lice are sensitive to temperature, and will readily leave a febrile host or a

cadaver in search of a temperature-suitable host. Hence, spread of lice in army field hospitals or in places where sickness and death abound provides a rapid means of dispersal for typhus as well, and may account for grave complications in those already weakened by malnutrition.

Inter-Epidemic Propagation. In 1910 Dr. Nathan Brill called attention to a typhus-like disease occurring in New York City. It was similar to typhus in its clinical course but relatively mild in that the case fatality rate was less than 1 percent. He noted that it seemed to appear especially among Jewish immigrants from southeastern Europe. As it showed no tendency for familial spread and occurred more frequently in the summer months than in the winter, Brill was inclined to believe that he was dealing with a new clinical entity of unknown origin. In 1912 Anderson and Goldberger were successful in the inoculation of a rhesus monkey with the blood from a case of Brill's disease in New York and found that infection rendered monkeys immune to subsequent inoculation with Mexican typhus (Tabarillo) and vice versa. From these observations, they concluded that Brill's disease was in fact identical with louse-borne typhus fever, albeit milder, and they assumed that the cases of Brill's disease in the United States originated either from infected lice or clothing contaminated by louse feces brought into this country by immigrants from European areas in which Epidemic Typhus existed.

Although Maxcy (1926) in his studies of Murine Typhus concluded that it and Brill's disease were one and the same, Zinsser (1924) isolated from cases of Brill's disease strains of typhus that proved by guinea pig inoculation to correspond to the louse-borne type in every respect, effectively discounting Maxcy's conclusions. Furthermore, Zinsser reviewed the epidemiologic distribution of Brill's disease in New York and Boston and advanced the hypothesis that the cases observed represented recrudescences of infections originally acquired many years previously when the individual had been living in a European country where typhus had been epidemic. He suggested further that recrudescent cases might serve to maintain continuity of prevalence by bridging breaks in the chain of man-louse-man propagation. He further proposed that this was the manner in which the European rickettsia had survived in continental foci for centuries. Zinsser's hypothesis that patients with recrudescent attacks residing in louse-infested communities could initiate epidemics of typhus was confirmed by Murray and Snyder (1951) using cross-immunity and serologic tests. They established the fact that Brill's disease was indeed caused by Rickettsia prowazeki.

THE HISTORICAL IMPACT OF EPIDEMIC TYPHUS

In a society where public health sanitation and personal hygiene have attained some measure of importance and are generally taken for granted as a natural outgrowth of "civilized" man, it is difficult to imagine previous societies where the imperatives of cleanliness went largely unheeded, or in some instances, were even looked upon as contrary to a "moral" way of life. Our romanticized, and largely unrealistic, view of history as a product of great men and great deeds ignores, for the most part, the fact that natural disaster and pestilence have dictated the lives of men far more then kings and queens. Man's egocentric view of himself as the progenitor of his own destiny and that of the world around him fails to recognize that many of the events that have come to shape our lives were subject to environments in which Homo sapiens, despite all his grandiose machinations, played but a small part. In this context we should view our historical antecedents as constrained to a great degree by environmental and medical parameters. It is true that warfare has been employed as a

means of shaping political and economic history, and is responsible for a great deal of European history in particular. Yet, diseases, in turn, bear a large responsibility for European history as well; with epidemic typhus, and its close association with warfare and economic hardships, taking a sometimes commanding role.

Early History. Due to the difficulty of making a precise clinical diagnosis of Epidemic Typhus and the similarity of its symptomatology to other fevers prevalent in times of historical duress, its origins remain obscure. The first pestilence that might be attributed to louse-borne typhus was the Athenian Plague of 430 B.C. Thucydides, in his accounts of the Pelopponesian Wars between Athens and Sparta, describes a typhus-like disease that ravaged the Greek populace and Athenian navy, contributing ultimately to the downfall of Athens (Hare 1955). Zinsser (1934), however, disputes the fact that this plague was due to typhus, concluding that Thucydides description is too vague to establish louse-borne typhus as the cause. Epidemiological considerations would seem to support Zinsser's conclusions. The deleterious effects of R. prowazeki on both its arthropod vector and human host would suggest a recent origin in the pathogen-vector relationship. In point of fact, R. prowazeki may be a genetic variant of R. rickettsii, the causative agent of Murine Typhus (Zinsser 1963). While this is highly speculative, the fact that R. prowazeki is highly pathogenic to its primary means of spread would indicate that a mutual survival scheme has not evolved yet for the vector or the pathogen. It is this relationship that leads us to believe that R. prowazeki came to parasitize P. humanus corporis sometime later than 430 B.C..

The Dark Ages. While there is no definite record of typhus in its epidemic form prior to the late fifteenth century, it is necessary to understand the sociological conditions present prior to that time to fully appreciate how and why louse-borne typhus finally made its appearance and began its historical influence. In this light, Michelet, in his classic treatise on medieval superstition, "Satanism and Witchcraft" states:

> It (typhus) was supposed due to the crusades, to be an importation from Asia; but as a matter of fact Europe had only herself to thank for the scourge. The war persistently waged by the Middle Ages against the flesh and cleanliness was bound to bear fruit. More than one female saint is commended for having never washed even the hands - how much less the rest of the body! An instants nakedness would have been a mortal sin. The society of those days, so subtle and refined, which makes sacrifice of marriage and appears animated only by the poetry of adultery, retains singular scruples on this simple point of personal ablutions, dreading every form of purification as a defilement. Never a bath known for a thousand years! We may be quite certain that not one of those gallant knights, those fair ladies and damsels, ever washed.

It is quite evident, then, that the stage was set for any of a number of filth-borne diseases to wreak havoc among even the most erudite and refined of the Middle Ages. Indeed, unsanitary

conditions were positively encouraged and practiced by those seeking favor with the all-powerful Church. It's little wonder that louse-borne typhus should be among the myriad plagues that ravaged the European continent during those thousand years and hence. Constant warfare, lack of any sanitation whatsoever, social values - all contributed to the role played by louse-borne typhus in that period of history and its contemporary ramifications.

The Fifteen Century. The earliest definite record of the role played by typhus in history is the epidemic that ravaged the army of Ferdinand and Isabella in their futile attempt to oust the Moors from Spain. In 1489, a Spanish army of 25,000 had finally managed to blockade the Moors inside their stronghold at Granada and laid siege to the city, hoping that a successful campaign would end, once and for all, the presence of Moslem influence on the European continent. An epidemic of louse-borne typhus struck the besieging army of Spanish, however, and within a month had killed 17,000 of the original 25,000 soldiers. Only 3,000 men had died in actual combat. The remnants of the Spanish army fled, and in so doing, introduced typhus to many other parts of Europe. Indeed, these established endemic foci of typhus that were later to arise in epidemics. As a result of the devastation that typhus wrought upon the Spaniards in their siege, Granada held and the Moors were driven out of Spain only after another hundred years of ceaseless fighting. As this is the earliest time that typhus can be recognized on the European continent, it is surmised (Zinsser 1934) that typhus was initially introduced by soldiers returning from Cyprus during the Crusades, in which Spanish troops played a large role.

The Sixteen Century. Typhus had finally made it to the war-torn European continent, and it was only a matter of time before the foci established by the returning crusaders and fleeing Spanish army would use prevailing conditions to provide epidemic fodder. It must be remembered that the conditions necessary for the spread of epidemic typhus are also conducive to concomitant prevalence of such diseases as cholera, dysentery and Plague. Therefore, in the proceeding scourges of typhus, other diseases were also present.

In the early part of the Sixteenth Century both the French and Spanish were locked in a struggle to determine which was to be the major power and controlling force in Europe. Both countries were of comparable military strength, with the power balance greatly in favor of whomever could incur the favor of Pope Clement VII and his Catholic constituency. Clement VII secretly sided with Francis I of France, although protocol demanded that he show no outward preference. However, in 1525, as Francis I was marching into Italy to establish hegemony over the papal states (as Clement VII secretly desired), he was ambushed by a large army of Charles V of Spain and taken prisoner by the Spanish. Charles V's forces immediately invaded Italy and forced the Pope to flee the Vatican. With the signing of the Peace of Madrid in 1526 Francis I was freed and delivered to his French subjects; whereupon war immediately broke out anew and Rome was sacked by the Spanish in reprisal of Clements now vocal preference for the French. At the sacking of Rome, all of Europe turned on the Spanish and Charles V found himself confronted on a dozen different fronts by enemies intent on vengeance for what was considered an affront to European religion itself. Moreover, the Ottoman Turks were threatening to invade Italy from the east. Charles V was in an exceedingly desperate position. The Spanish were in danger of being destroyed as a European power lest a miracle occur. As of 1527 the Spanish Imperial Navy had been destroyed and Francis I was again marching into Italy to free the papal states. The Prince of Orange, in charge of the Spanish army in Italy, upon receiving the news of the triumphal march into Italy by the French,

marched his entire army out of Rome south to make a final desperate stand against the French at Naples. When the Spaniards reached Naples they found the port blockaded by ten French ships. Nevertheless, the Spanish occupied the city and awaited the arrival of the French army. At this time, an epidemic of Plague struck the Spanish within the city and reduced their army to a force of 11,000 - malnourished and diseased. The French finally arrived and laid siege to the city with an army of approximately 35,000. The situation for the Spanish grew steadily worse to the point that the Prince of Orange escaped through the French lines one night and sent a servant to Charles V with the message that the Spanish garrison was going to surrender to the French and give up all of Italy. At this point, the "miracle" that Charles V needed occurred in the form of Epidemic Typhus. Within one month 25,000 French soldiers perished of the disease. The remainder fled from the area, with the Prince of Orange's newly inspired troops overtaking them and destroying their remnants. All of Europe looked upon the deadly pestilence that obliterated the French army as an act of God. Their capitulation shortly thereafter resulted in Charles V being crowned Holy Roman Emperor in 1530. In this light it must be remembered that Western civilizations at that time regarded their God as a somewhat capricious tyrant, who either gave life or took it, and whose will was manifest in disastrous epidemics such as this. Having no recourse to medicine as a means of explaining their devastations, medieval man turned to spiritual and metaphysical sources. This not only obfuscated the real causes of the epidemics, but gave the stamp of divine intervention to the entire process. This, in turn, gave it ramifications far in excess of the purely physical damage caused. This is of the utmost importance toward a full realization of the profound effect of Epidemic Typhus in its personal as well as political dimensions.

But Epidemic Typhus knows no loyalties, and Charles V had to break off the siege of Metz, Germany in his war to subject the Teutonic Protestants when 10,000 of his men died from typhus in the first month of siege. As a result, he was never able to subdue Protestantism in Germany and Northern Europe. This provided a sound backdrop for the 30 Years War to be fought a century later.

Upon the rise of the Hapsburg monarchy in Austria-Hungary in the mid-16th century, the rule of Charles V as Holy Emperor ended in favor of Maxmillian II, a Hapsburg. As such, Maxmillian assumed the protectorate of Christian Europe in its constant campaigns against the Ottoman Turks, who were still threatening to invade Europe from the East. The threatened invasion of Italy during Charles V's reign had failed to materialize due to infighting among the ruling sheiks of the time. Nonetheless, in 1560 a consolidation of leadership in the Ottoman Empire provided the impetus formerly lacking and the Turks invaded Hungary - long the eastern-most bastion of Christendom - in that year. The Austrian army in Hungary fought valiantly but was forced to retreat when typhus struck down 30,000 troops in a three-month period, leaving Hungary in Turkish hands. Maxmillian II responded by mobilizing a great army and marching on the invaders, meeting with huge success.

The victories of the Christian armies were of such magnitude that the complete route of the Turks in Hungary was inevitable. In fact, in view of his overwhelming success, Maxmillian fully planned to invade Turkey itself and put a final end to the Saracen threat. Furthermore, the reclamation of the Holy Land, in which the Crusades had been such a miserable failure, was a distinct possibility and provided further motivation to the Holy Roman Emperor and his well-equipped army. But it was not to be so. When the Christian army reached the Danube, with the Turks in full flight before them, typhus struck once again in such devastating force that Maxmillian's

entire army scattered in all directions to escape the sickness. As a result, Maxmillian's imperialistic aims were never fulfilled and he was forced to make peace with the Turks at the previous boundaries.

By this time Epidemic Typhus had established itself in numerous foci throughout mainland Europe and Great Britain as well. A number of so-called "Assize Epidemics" occurred in England at this time, most notably at Oxford in 1577 and Exeter in 1589. The Assize Epidemics were so named because of their connection with criminals being brought from prisons, whose sanitary conditions were beyond description, to the courts where, in the midst of the trial proceedings, typhus would break out. The Oxford epidemic was of such import that the University there was closed for 30 years afterward. It is interesting to note that, at this time, fevers such as "London sweat", "Picardy Sweat", typhus, and the like, were attributed to bad smells. The sanitation of the times was at best horrid. This resulted in a preponderance of foul odors which could be designated as the causative agents of epidemic sickness if only on a coincidental basis. At any rate, the foul odors emitted by prisoners being brought up from the dungeons were incriminated as the source of the epidemics. In order to avoid inhaling the stench inevitably emanating from those to be tried, British magistrates wore nosegays of highly-scented flowers - a tradition still practiced today. The last of the Assize Epidemics at the Old Bailey in 1750 prompted the sweeping sanitation and prison reform carried out by John Howard in that year; although the real cause, body lice, was never suspected.

The Seventeenth Century. The Thirty Years War of 1618-1648 was not without its share of typhus either. Along with Plague and starvation, typhus was responsible for the loss of 10,000,000 people during the course of the war in which only 350,000 men died in combat (Hare 1955). Although Plague was responsible for the great majority of deaths in the latter half of the war, Epidemic Typhus caused the most damage in the first 15 years. In fact, in 1632, typhus was responsible in preventing a battle from actually occurring. Gustavos Adolphus, the Swedish king, and Baron Von Wallenstein, the Catholic commander, prepared to engage in a major battle at Nuremburg, Germany. Typhus broke out amongst both armies, killing 18,000, and both commanders withdrew their forces.

The first real challenge to "Divine Right" monarchy in Europe was abetted by typhus in England in 1643. The Earl of Exeter had mobilized an army, with the aid of parliament, in order to depose Charles I, considered unfit to rule. Charles I, with his far superior loyalist army, was unable to march on London from his palace at Hampstead to crush Exeter's uprising due to an outbreak of typhus in his army. Although the uprising was quelled sometime later, typhus had given it time to gather what momentum it could muster. The concept of absolute inviolate monarchy in Europe since then has never been the same.

The Eighteenth Century. The 18th century was marred by many small epidemics of typhus whose analysis is beyond the scope of this paper. The War of the Austrian Succession in 1741, however, provided a scenario for typhus which was to have far-reaching impact for the Prussian forces involved. Typhus made its major contribution in killing 30,000 Prussians during the siege of Prague by the French. The Prague epidemic, resulting in the fall of the city and loss of the war made a deep impression on the German military commanders involved as to the necessity of military preventive medicine. Thereafter, German military tactics in large part recognized the overwhelming impact of disease-induced morbidity. Avoidance of situations and conditions responsible for diseases such as typhus thereafter became an integral part of German military strategy.

The Nineteenth Century. Epidemic Typhus had long been a scourge of armies prior to the nineteenth century. Yet, the devastation it had wrought in terms of military mortality was far overshadowed by that encountered by the huge armies fielded by commanders the world over in the 1800's.

Napoleon Bonaparte's campaign against the Russians in 1812 remains the classic example of the utter destructiveness of environmental agents encountered in wartime. At that time, Napoleon had organized his "Grande Armee", numbering 600,000 well-seasoned troops - by far the most powerful land force ever assembled. With it Napoleon aspired to conquer Europe, invade Russia, and swing south to India to restore France's former glory - and deprive England of her only significant possession. Mainland Europe offered little resistance as Napoleon marched eastward toward Russia to attain his pivotal objective. As of Autumn 1812 he had partially crossed Germany and was gathering momentum for his drive through Poland to the Russian border. It should be pointed out that Napoleon had assembled a fine medical corps, well-versed in the nuances of military preventive medicine. Napoleon himself was well aware of the importance of sanitation in maintaining combat effectiveness and had issued strict orders regarding such that were stringently enforced throughout his chain of command. He also established many large field hospitals in Germany to care for the sick and wounded that were to come in the campaigns ahead. However, while issuing orders regarding his troops personal hygiene and providing for medical exigencies by the establishment of military hospitals, Napoleon disregarded his chief surgeons advice to make special preparations for the Russian winter to be encountered. Napoleon argued that the Russian winters could not be that much worse than the French winters to which his troops were accustomed - a fatal fallacy. Furthermore, his major commanders recommended that the invasion of Russia be conducted in late spring, to obviate the need for special preparations due to weather altogether. Again Napoleon refused, ostensibly on the grounds that the "Grande Armee" was invincible, and the restoration of France's glory could not wait.

While not encountering any problems in Germany, the "Grande Armee" began to experience logistical difficulties upon reaching Poland. The Polish roads were not built to withstand the heavy guns and, most importantly, the heavy supply wagons used to support an army of 600,000. As a result, Napoleon's supply trains ground to a halt upon crossing the Nieman river and were unable to advance any further. Contrary to some rather strongly-worded advice from both his Chief Surgeon and Support Commanders, Napoleon decided to advance the main body of his army with as much haste as possible into Russia, leaving his supply trains to catch up on their own. Napoleon had been repeatedly warned by the Surgeon that Poland had large endemic foci of typhus throughout the country and that the peasantry therein were rife with disease. As a consequence, orders were issued forbidding the soldiers to fraternize with the Polish citizenry under pain of death. His orders went largely unheeded, however, as his army, which rapidly ran out of food and supplies, began raiding nearby villages in search of food for its starving personnel. These forays inevitably brought the soldiers into contact with the Polish peasantry. This resulted in Epidemic Typhus being brought into the camps along with the returning troops. The consequences were disastrous. More than 80,000 French soldiers died the first month of the epidemic. An abnormally hot summer had produced nearly drought conditions in Poland prior to Napoleon's arrival. What scarce water was available was used for drinking, with bathing and clothes washing nearly impossible. In such an environment heavy infestations of body lice were inevitable. To make matters worse, Poland was suffering from

an abnormally cold winter in 1812, forcing the ill-prepared French soldiers to huddle together for warmth at night, facilitating the spread of typhus amongst themselves. Still, the beleaguered army marched forward and crossed the Russian border in December of 1812, with the objective of capturing Moscow still its final goal.

The Russian commanders, knowing full well the might of the French army despite the breakdown of morale and military efficiency due to typhus and starvation, decided that the supply difficulties encountered by Napoleon in Poland would be augmented a thousand-fold while in Russia. The Russian army, therefore, made no great effort to engage the French in major battles but was content to draw the French farther and farther into Russian territory, away from what few supplies could reach them. With luck, the infamous Russian winter could complete what the typhus epidemic had started. To this end, several Russian raiding parties were dispatched nightly to harass the French flanks and add to the general fear amongst the army in the midst of its frostbitten, starving, typhus-ridden regiments. The losses these raids helped engender were enormous - not in terms of killed-in-combat, but in terms of slowing the French advance. The morale of the individual soldiers sank to the point where there was not the least vestige of hygiene to be found anywhere in the ranks, with the possible exception of the elite Imperial Guard. Despite the inconceivable hardships faced by the "Grande Armee" throughout its long trek across Eastern Europe, Moscow was captured in January of 1813. Only 90,000 French soldiers reached Moscow out of the original army of 600,000. The great majority, possibly as high as 300,000, had died of Epidemic Typhus and dysentery. Actual combat losses amounted to less than 100,000. As the "Grande Armee" entered Moscow, they found that all the food stores had been burned by the Russians in order make the critical food shortage of the French even worse.

Realizing that, although his goal had been reached, the war had been lost, Napoleon called for a full-scale retreat back to France. The Russian army, which had used evasive maneuvers up to this time, took the offensive and repeatedly attacked the remnants of the retreating "Grande Armee". Only a gallant rear-guard action by Napoleons 3000-man Imperial Guard saved the retreating force from total annihilation by General Kutusov's army of 200,000. Epidemic Typhus and frostbite continued to take their toll - the portion of Napoleon's Grand Armee of 600,000 that finally reached France numbered only 20,000. Of these, only 3,000 remained alive by June of 1813. Never before had disease and the elements exacted such a price in human life in one army in so short a time. Many historians and military tacticians assert that, had Napoleon waited till spring of 1813 to enter Russia; and, had he waited for his supply trains to regroup and follow him through Poland, the "Grande Armee" would undoubtedly have conquered Russia and the entire scenario of 19th century Europe would have changed. Napoleon's megalomania proved his downfall - with cold, starvation, and Epidemic Typhus playing major parts.

Yet, it is a tribute to Napoleon's genius as a leader that, in early 1813, he was able to organize another army of 500,000 to accomplish what his first campaign failed. This army was made up of enthusiastic, but rather poorly trained soldiers, mostly teenagers, who were no match for the combined European forces thrown against them. In the campaign of that year over 219,000 of the ill-kept French were to die of Epidemic Typhus. Disease and battle were to account for 330,000 French casualties. By the time Napoleon engaged his enemies at "The Battle of Nations" in October of 1813 at Leipzig, Germany, he had only 170,000 men left to face an army of over 200,000. It is little wonder that Napoleon finally came to meet his demise at Waterloo. Epidemic Typhus had

helped defeat Napoleon and end his dreams of a French-ruled world. For an excellent account of the Napoleonic Wars and the major part that environmental factors played in them, the reader is referred to Cartwright (1972).

The Crimean War was the first time in history that accurate statistics were kept regarding casualties and the precise causes of morbidity rates. For this reason, it is included in this text more to illustrate the devastating impact of disease-produced casualties as compared to combat losses. Prior to the development of sophisticated anti-personnel weapons, it was usually a matter of the relative numbers of men in the opposing forces which determined the winner. It is well to remember that, in a field commanders view, the amount of men available for battle is determined by the number of casualties suffered - whether from disease or combat. The fluctuation in numbers thereof is of the utmost importance in any military strategy, for they in a large part determine what the army can, and cannot do on the battlefield. Although the outcome of the Crimean War was influenced very little by the comparative losses suffered by both sides due to typhus, cholera, and dysentery, the statistics presented below show that soldiers were far more likely to be out of action due to sickness, than to wounds suffered in combat (Hare, 1955).

	Wounded	Sick	Died of Wounds	Died of Sickness
French/English	58,000	350,000	25,000	65,000
Russian	92,000	322,000	38,000	38,000

During the entire nineteenth century Ireland was the scene of many devastating typhus epidemics resulting from relatively low socio-economic conditions (compared to Western norms), and a standard of living almost wholly dependent upon the vicissitudes of the chief agricultural commodity - the potato. Typhus had been recognized in Ireland as early as 1652, but it was not until 1816 that a major epidemic of the disease produced 700,000 cases out of a population of 6,000,000. Three more major epidemics thereafter, in 1821 and 1836, accompanied harvest failures. In terms of sheer mortality, the Potato Famine of 1846 was by far the worst. The complete failure of the potato crop in that year brought about a total collapse in the tenuous economic sphere to which almost the entire rural population was subject. The starving population was forced to turn to the British for economic assistance. The British, feeling that welfare payments and the like were beneath the dignity of all British subjects, established workhouses to provide lodging for the Irish families. Their meager subsistence was "earned" by helping to drain peat bogs, building roads that led nowhere, and other useless work. It was the workhouse itself, however, that was to become the bane of the Irish people. Over-crowded and lacking sanitary facilities of any type, they provided a perfect environment for the spread of any number of diseases - most notably Epidemic Typhus. Approximately 190,000 Irish citizens died from typhus contracted in the louse-infested workhouses they were forced to inhabit. Another 120,000 died of starvation and typhoid fever. The conditions were such that over 1,000,000 Irish citizens chose to emigrate elsewhere rather than subject themselves further to the intolerable hardships of the workhouses. In all, over one quarter of Ireland's population was lost in that year due to typhus, starvation, and the threat of such. Hare (1955) goes so far as to say, "There can be little doubt that typhus had much to do with the

Anglophobia which still affects many of the citizens of the United States of America."

The Twentieth Century. Nicolle's proof of the transmission of typhus by body lice in 1910 finally provided a means by which Man could reduce the scourge of Epidemic Typhus during times of duress. No longer would typhus' sudden epidemic spread be a mystery to the medical profession charged with the responsibility of preventive medicine. But, alas, research and control techniques did not advance rapidly enough to prevent major typhus outbreaks in the eastern theater of World War I which were to change the course of the entire war.

Austria's declaration of war on Serbia (Yugoslavia) following the Archduke Ferdinand's assassination was immediately followed by an all-out invasion of Serbian soil by Austrian forces. The population of Northern Serbia was forced to flee south, along with the government, when the capital city of Belgrade was overrun early in the campaign. The provisional capitol of Nis, deep in the southern portion of Serbia, became a haven for the destitute populace fleeing before the Austrian juggernaut. Over-crowding, a dearth of sanitary facilities and hospitals, and the general panic caused by the Austrian invasion provided an ideal milieu for the spread of disease, in particular Epidemic Typhus. And so it began, with a Serbian counter-attack, the fury of which threw the Austrian army back across the border.

The typhus which had been incubating in the crowded southern portion of Serbia suddenly struck the Serbian army. The Austrians, who in the meantime had regrouped and elicited massive reinforcements from the Germans, watched in disbelief. In the month of November, 1914, typhus killed 200,000 Serbian soldiers on the front, almost one-quarter of their entire armed forces, and spread to the rest of the population in the south. Out of 400 physicians in the country, 126 succumbed to typhus while caring for the patients in the few poorly-equipped hospitals available. The entire country lay helpless amidst one of the worst epidemics in history. The Serbian army was in a shambles. Almost 30,000 of the 60,000 Austrian prisoners captured in the counterattack died as a result of typhus, unable to obtain adequate treatment from what few medical personnel were available.

Yet, the combined German-Austrian army made no attempt to move into Serbia, which, by this time, could have offered no resistance whatsoever. Typhus was effective in holding battle lines the Serbian Army could not. The Germans had been taught a rather severe lesson in the War of the Austrian Succession and knew that marching an army through a typhus-ridden country could have disastrous consequences. As a result, the Prussian forces held their position for six months till the typhus epidemic in Serbia had subsided due to summertime conditions.

The six-month hiatus in the fighting was to have dire ramifications for the Prussian war effort. Original strategy called for a combined German-Austrian drive down through Serbia, across the Balkan's to secure the Rumanian oilfields at Ploesti, and upward through the Russian Ukraine to obtain much-needed food supplies and/or keep them from the Russians. Most importantly, this would force the Russians into a two-front war. The six-month wait allowed the western powers to establish a stationary front in France while the Russians poured millions of men into a futile effort to stave off the Germans northern push. The Germans finally succeeded in forcing the Russians to sue for peace, but much later than had originally been hoped.

To make matters worse from the German viewpoint, were scattered outbreaks of typhus among the Russian forces with whom they were engaged. The withdrawal of German forces from the eastern front after the Russian capitulation became a tedious process with delousing procedures, which at that time were only temporary corrective measures, providing much of the delay. As a result, German reinforcements from the eastern front were unable to bolster the western lines against the rapidly growing U.S. and British involvement in time to keep Europe in German hands. Had it not been for louse-borne typhus and its effect on military operations, the entire complexion of the First World War, and quite possibly its final outcome, might have changed in favor of the Germans.

For the Russian people the upheaval following their suit for peace was to change their entire way of life - but, not without a tremendous cost in human life. The conditions following the overthrow of Tsar Nicholas were indescribable. Socioeconomic, military, and political chaos - all were made much worse by mass starvation, murder, and disease. The appearance of Epidemic Typhus in such circumstances was inevitable and its epidemic propagation amongst the innumerable starving, lousy transients was to add incredible misery to an already intolerable period of Russian history. Peasants in huge numbers descended upon the cities in search of food that was all too often non-existent or hoarded by the military. Their flight to the cities was usually accompanied by outbreaks of typhus, which was spread even further by the infamously louse-infested Russian railways. No social group, regardless of patronage, was spared typhus' ravages. Tarassevitch, a Russian physician and epidemiologist, is quoted by the Statistical Bulletin of the Metropolitan Life Insurance Company as saying that as many as twenty-five million cases of typhus occurred during the years 1918-1922 with upwards of three million deaths. What effect this had in the political and economic spheres is purely a matter of conjecture, but it can reasonably be assumed that typhus played an important role in creating the frenzied quest by the Russian people for an end to their miseries that culminated in a new system of government.

The historical role played by Epidemic Typhus in World War II, due to the mass of research on its prevention and control by Cox, Durand, and others, became largely a matter of introducing and refining methods for its control in military and civilian populations so as to minimize its overall effects. This is not to say that typhus did not play a role in determining courses of action taken by the powers involved - indeed it did. Rather, typhus did not affect the outcome of the war because Mankind did not let it. The perfection and use of Cox's chick-embryo vaccine, along with the mass issue of lousicides such as DDT and MYL, were of great import in reducing the risk of typhus in those using them and bringing an end to the threat of typhus outbreaks in wars and disasters of the future.

The history of the typhus control program instituted and employed by the U.S. Army in WWII is provided in excellent reviews by Gordon (1948) and Stanhope Bayne-Jones (1948). The threat of encountering typhus in both the European and Mediterranean theaters was obviated by the compulsory immunization of all Allied personnel entering the area with the Cox vaccine. However, epidemics among the civilian populations in North Africa were of such magnitude that the United States of America Typhus Commission was formed by executive order in June 1942 to further research ways to minimize typhus in the military forces soon to be sent there. Epidemics of 19,000 typhus cases in Iran and 90,000 cases in Egypt, both in 1943, were studied extensively by the Commission, resulting in new ways to control the body louse. In addition, the epidemics provided an opportunity for health officials to work in close association with all levels of the governments

involved in a cooperative effort to eradicate the disease which was to serve as a model for public health campaigns thereafter.

In addition to the research done by the U.S.A. Typhus commission, Wheeler and Soper, of the Rockefeller Foundation Health Commission, invented and employed the use of power-dusters for the mass delousing of populations with DDT. Ironically, the development of the power-duster was prompted by the refusal of Moslem women to disrobe for the application of DDT to their clothing. A device was needed to permit the lousicide to come in contact with the inside of clothing while it was being worn and the power-duster provided the answer. More importantly, the power-duster provided a means of rapid mass-delousing which were to help curb the typhus epidemic in Naples a year later. Due to the power-duster, the widespread availability of DDT and typhus vaccine, and the efforts of military and civilian preventive medicine officials, typhus was held in check in all U.S. -occupied lands in North Africa and the Middle East and caused no great hindrance to the supply operations headquartered there.

The winter of 1943 found the city of Naples, Italy in the grip of a rapidly growing typhus epidemic that, had it gone unchecked, threatened to wipe out the entire city. The German army of occupation had fled the city the preceding autumn, destroying buildings, water and sewer systems, and food supplies prior to their departure lest the Allies use them for their own purpose. The entire population of Naples was forced to live in bomb-shelters to avoid the incessant bombings by the Allies which, along with the German scorched-earth retreat, reduced the city to smoking ruins. These overcrowded bomb shelters served as perfect foci for typhus spread among their louse-infested occupants. As the winter progressed, conditions grew steadily worse and the typhus mortality rose to 700 cases in the first week of January, 1944. Fortunately, the Allies had by now occupied the city and immediately mobilized a massive immunization, delousing, and medical care program using the techniques developed by both the U.S.A. and Rockefeller Foundation commissions. The results were dramatic and represented the first time in history that a typhus epidemic was halted in mid-winter. The means to prevent and control typhus had proven to be successful. It was a remarkable accomplishment and is widely acknowledged as one of the greatest achievements in modern preventive medicine (Wheeler, 1946).

The conditions in Germany at this time were especially conducive to typhus outbreak. Repeated Allied bombings of German cities and the general chaos abounding in conjunction with the crumbling of the Third Reich helped to provide typhus and other diseases a means of survival and spread. Major typhus outbreaks occurred throughout Germany during the course of the war with statistics available in 1945 revealing 16,000 cases of typhus in that year. The U.S. Army, which had been vaccinated for typhus and had good supplies of DDT available, set up many delousing stations throughout occupied areas in order to keep the disease within Germany from spreading westward via repatriated POW's and the number of civilians meandering back and forth to their homelands through German and Allied lines. These typhus-control procedures were largely successful, although undoubtedly large numbers of military as well as civilian personnel were missed in the confusion. The situation might have been far worse had not the Battle of the Bulge postponed the Allies confrontation with the German typhus problems until Spring, 1945, when the epidemics were receding. To be sure, typhus was a major scourge of the concentration camps and it will never be known how many inmates succumbed to the disease. Upon the liberation of Buchenwald, it was found that over 8,000 inmates were suffering from typhus.

Japan also was afflicted by the scourge of typhus during World War II. An outbreak among Korean workers imported by the Japanese to work in the coalmines of Hokkaido, disseminated through the entire population, causing 45,000 cases. Scoville (1948) reports that no prefecture within the country escaped the pestilence. Again, prompt and pervasive control programs instituted by the U.S. occupational forces brought the epidemic under control.

Typhus has been of little historical import in the United States. Although the nineteenth century saw typhus being frequently imported with the arrival of shiploads of infested immigrants, typhus was never able to establish large endemic foci in the continental U.S. Localized epidemics were precipitated, but after the middle of the century conditions were evidently not favorable to its continuous propagation. During the Civil War, it was an unimportant cause of morbidity. The last epidemic in the eastern United States was caused by the importation of immigrants into New York City, in 1883. Since then, except for the occasional case imported from Europe or Mexico, and small outbreaks among the Navajo Indians in 1915 and 1921, the United States has been free of louse-borne typhus. Evidently, there are not enough lousy people in this country to support the passage of R. prowazeki.

CONCLUSION

It is evident, then, that a truly astounding amount of Western History has evolved out of Man's contact with the body louse and the pathogens it harbors. The untold misery that has been part and parcel of this association can never be calculated in its truest sense, for historical facts and statistical data are rather pale shadows of the human experience of typhus. Indeed, the spectacular advances of Western science have all but relegated typhus to a pestilence of yesteryear. Nevertheless, the World Health Organization still classifies it as a "disease under surveillance". Should typhus ever rise again to its previous epidemic heights, Man has only himself to blame, for the wherewithal for its complete control are within Mankind's grasp. The eradication of poverty, famine, and warfare are not only political ideals, but medical and historical ideals as well. Yet one cannot help but wonder if the truly salient feature of Man's encounter with louse-borne typhus is not its effects on Man's continual struggle to overcome his enemies, but rather the opportunity afforded to those in retrospect to feel the humility necessary for the survival of our species in a world of which we are, of necessity, but a small part.

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