Table S1. Historical Chronology of Milestones - the Gradual Dissection of the "Typhus" Entity.

Year	Important findings	Comments	Ref.
460 BC	Hippocrates defines typhus - as "fever with a confused state of the intellect - a tendency to stupor".		[1]
430 BC	Thucydides and Hippocrates first describe epidemic typhus cases.		[2]
313 BC	First clinical accounts of *Tsutsugamushi disease* in the "*Zhouhofang*", a Chinese clinical manual.	Description of regional vector mites, no linkage to transmission	[3]
15th century	Epidemic typhus and endemic typhus (*Tabardillo*) rages in Europe.	No distinction made between different forms of typhus	[4]
1485–1551	The five epidemics known as the 'English Sweat' occur in the United Kingdom.	Probably relapsing fever (*Borrelia recurrentis*)	[5, 6]
1546	Girolamo Fracastoro–Fracastorius (1478−1553) differentiates typhus from plague in *De contagione et contagiosis morbis.*		[7-9]
Early 1700s	Typhus = Typhoid and Typhus and 'Relapsing Fever'	Era of differential diagnostic confusion!	[10–13]
1750	John Huxham made the first distinction between epidemic typhus and typhoid fever in the United Kingdom.	Typhus = ''slow nervous'' fever Typhoid = ''putrid malignant'' fever	[10]
1760	Boisier de Sauvages in Montpellier creates the clinical term "*Typhus exanthematique*" for epidemic typhus.	Based on clinical appearance of characteristic skin rash	[14]
1762	James Lind (1716−1794) promotes hygienic measures during typhus outbreaks to reduce mortality.	Limes for prevention of scorbut.	[8,9]
1810	Hakuju Hashimoto first described a *tsutsuga* (disease, harm, noxious) resembling typhus, in the Niigata prefecture, Japan.	The basis of the name '*Tsutsugamushi* disease'	[15]
1812–1813	Napoleon suffers the greatest loss of troops in eastern Europe to epidemic typhus (and Trench Fever).		[16,17]
1837	William W. Gerhard (1809−72), first distinguished enteric fevers (i.e. typhoid) from rickettsial fevers (i.e. typhus).	Post-mortem hyperplastic nodules in Peyer's patches	[11, 18]
1843	Craigie and Hendersen differentiate relapsing fevers clinically and pathologically from (epidemic) typhus	Post-mortem observations in autopsies	[12, 19]

1858	Charles Murchison epidemiologically emphasizes the contagious nature of typhus – association of epidemics with poor hygienic standards		[20]
1878	First account of *Tsutsugamushi* disease from Japan to be published in Europe by Theobald Palm.	Reported as Shima-mushi, or Island insect disease	[21]
1898	Brill Disease-an outbreak of atypical typhus, what Brill called abortive-typhoid in New York		[22,23]
1906	Howard T. Ricketts and Russel M. Wilder discover the causative agent and transmission vector (wood tick) of Rocky Mountain spotted fever (RMSF).		[24]
1908	Schüffner describes "Pseudo-typhoid" in Sumatra (later revealed to be *Tsutsugamushi* disease).	Suspected mite transmission	[25]
1909	Charles J.H. Nicolle discovers the transmission of epidemic typhus by the human body louse.	Nobel Prize in 1928	[26,27]
1910	Howard T. Ricketts first discovers rickettsiae in the blood of epidemic typhus patients in Mexico ("*Tabardillo"*), together with Russel M. Wilder.	Ricketts dies of epidemic typhus in Mexico 1910	[28−30]
1916	Rocha Lima who officially first described epidemic typhus rickettsiae as intracellular microorganisms.	*R. prowazekii* - named after Ricketts and Prowazek	[31]
1910	Smithson describes a "sporadic" form of typhus, in Australia.	Later revealed as scrub typhus or *Tsutsugamushi* disease	[32]
1910	Conor and Bruch describe "Fievre Boutonneuse" in Tunis.	Later revealed as Mediterranean Spotted Fever (MSF)	[33]
1911	McNaught describes "Para-typhoid" in South Africa, with suspected tick transmission.	Later revealed to be two forms; MSF and African Tick Typhus	[34,35]
1913	McKenchie describes a typhus-like illness in the Kumaon Region, N-India (Himalayan foothills).	unpublished, reviewed by Megaw 1921–"Megaw's tick bite" in 1916	[36]
1916	Weil and Felix first describe the diagnostic serum agglutination for typhus. Based on *Proteus vulgaris strain* called " *Proteus* X 19."	Diagnostic breakthrough	[37]
1922	Hone describes a new form of typhus in Australia (OX19 positive)	Later revealed as *R. honei*, a spotted fever group rickettsia	[38]

1923	Maxcy and Havens describe murine typhus as an endemic form of sporadic typhus.	Hypothesis that fleas are vectors	[39]
1924	Kingsbury visits Malaya and brings a new strain *Proteus mirabilis* OXK	OXK allows separation of "urban" and "rural" typhus	[40]
1924	Fletcher distinguishes scrub from murine typhus.	Based on the Weil-Felix test using *Proteus* OX19 and OXK	[41]
1926	Fletcher and Lesslar describe co-existance of *Tsutsugamushi* disease and scrub typhus in Malaya.		[42,43]
1926	Fletcher and Lesslar create the term 'tropical typhus'.	Defined as non-contagious or "sporadic" typhus-like fevers.	[40]
1928	Scrub typhus is *Tsutsugamushi* disease.	Based on entomological, cross-immunity and clinical criteria.	[41-45]
1930	Nagayo demonstrates *Rickettsia orientalis* for the first time.	Localization in the Descement's membrane of rabbit eyes.	[46]
1931	Dyer proves Maxcy right–murine typhus is transmitted by rat fleas.	Dyer isolates *Rickettsia* from rat fleas (*Xenopsylla cheopis*)	[47]
1945	"Operation Tyburn"–first mass-production of scrub typhus vaccine.	Based on New Guinea strain (Karp), did not work in Malaya.	[48−51]
1947	Discovery of Chloromycetin, a derivative from Actinomyces bacteria	Cured chick embryos infected with rickettsiae	[52]
1948	Smadel demonstrates chloramphenicol as an effective chemotherapy for scrub typhus.	Volunteer studies with naturally infected chigger inoculation	[52,53]
1959−1975	Vietnam Conflict–Scrub typhus is the leading cause of fevers of unknown origin (FUO).		[54]
1997	Epidemic typhus re-emerged dramatically in Burundi.	Epidemic affects approx. 100,000 refugees of Rwanda.	[55,56]

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