**APPENDIX FIGURE. Timeline in the history of therapeutics for infectious diseases**

Depicted is a historical timeline of therapies for various infectious diseases that harmed or were of no benefit to the disease-afflicted patient. Errors of commission are indicated by plus symbol and errors of omission are indicated by minus symbol. (A) Prior to the discovery of penicillin, syphilis was treated by mercury, potassium iodide, and/or Salvarsan (ie, arsphenamine, an arsenic derivative). Mercury (also known as quicksilver) poisoning is characterized by hyper salivation, mucosal ulceration, tooth loss, chronic kidney disease, and polyneuropathy. Potassium iodide therapy for syphilis was introduced in the 1800s and caused side effects of gastrointestinal disturbance, potassium toxicity (confusion, arrhythmia, hand numbness), iodism (hypersalivation, metallic taste, gingivitis, and headache), and hypo or hyperthyroidism. Salvarsan, an arsenic-based therapy derived by Paul Ehrlich, was associated with rash and hepatotoxicity and was ineffective for the treatment of secondary and tertiary syphilis. (B) Koch proposed the use of tuberculin for treatment of pulmonary tuberculosis, yet it promoted the disease. (C) Treatment of African sleeping sickness with atoxyl, a name bestowed by its nontoxicity in animal models, was found to promote optic nerve atrophy and blindness in humans. (D) Development of bacteriophage as therapy for bacterial infection has sorely lagged behind its initial discovery by Twort (1915) and d’Herelle (1917). (E) Historical accounts of treatment prior to and during the Spanish Flu of 1918 note the frequent use of opium derivatives. (F) Hideyo Noguchi’s yellow fever vaccine prevented nothing of the sort given it targeted *Leptospira icteroides*, the agent he mistook as the cause of yellow fever. (G) Yellow fever vaccine contaminated with hepatitis B from serum donors was inadvertently administered to United States serviceman during World War II causing an outbreak of 330,000 infections. (H) Incomplete formaldehyde-inactivation of polio vaccine from Cutter laboratories was mistakenly administered to 120,000 children causing 40,000 cases of abortive poliomyelitis, 51 with permanent paralysis, and five deaths. (I) An outbreak of H1N1 influenza, a strain of swine flu, among military recruits at Fort Dix, New Jersey, motivated the design, mass distribution, and vaccination of the US population using a vaccine targeting this strain. Five hundred forty-three cases of H1N1 vaccine–associated Guillain-Barré syndrome ensued in the weeks following these efforts. (J) Despite early fanfare from the PROWESS trial (2001), administration of recombinant human activated protein C (Drotrecogin alfa; Xigris) was found to have no impact on mortality in severe sepsis and septic shock. K) Question remains if hydroxychloroquine, interleukin-6 receptor inhibitors, and remdesivir provide a mortality benefit to those with COVID-19–induced respiratory failure and acute respiratory distress syndrome.