

Salicylates and Pandemic Influenza Mortality, 1918–1919 Pharmacology, Pathology, and Historic Evidence

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“In February 1919...Edward's fever kept getting higher and higher...aspirin...was given to him by the 1/2-handful over and over...Edward sweated through his mattress...Dr....could not save his patient.”

—Clella B. Gregory, Pandemic Influenza Storybook, US Department of Health and Human Services

- 1) The Flu of 1918–1919 had a very high case-fatality rate, especially among young adults. “Early deaths exhibited extremely ‘wet,’ sometimes hemorrhagic lungs.”
- 2) “The hypothesis presented herein is that aspirin contributed to the incidence and severity of viral pathology, bacterial infection, and death, because physicians of the day were unaware that the regimens (8.0–31.2 g per day) produce levels associated with hyperventilation and pulmonary edema.” Aspirin overdose causes pulmonary edema.
- 3) In 1918 there was a spike of official recommendations for toxic regimens of aspirin immediately before the October 1918 death spike. Today, aspirin regimens recommended in 1918 are known to be toxic.
- 4) “In 1918, the US Surgeon General, the US Navy, and the Journal of the American Medical Association recommended use of aspirin just before the October death spike. If these recommendations were followed, and if pulmonary edema occurred in 3% of persons, a significant proportion of the deaths may be attributable to aspirin.”
- 5) The 1918–1919 influenza pandemic showed unprecedented overall mortality. “Deaths in the United States peaked with a sudden spike in October 1918.” The spike in Flu deaths during the fall of 1918 may have been linked to Salicylate.
- 6) “The hypothesis presented herein is that salicylate therapy for influenza during the 1918–1919 pandemic resulted in toxicity and pulmonary edema, which contributed to the incidence and severity of early ARDS-like lungs, subsequent bacterial infection, and overall mortality.” Pharmacokinetic data “indicate that the aspirin regimens recommended for the ‘Spanish influenza’ predispose to severe pulmonary toxicity.”

7) "A confluence of events created a "perfect storm" for widespread salicylate toxicity. The loss of Bayer's patent on aspirin in February 1917 allowed many manufacturers into the lucrative aspirin market. Official recommendations for aspirin therapy at toxic doses were preceded by ignorance of the unusual nonlinear kinetics of salicylate (unknown until the 1960s), which predispose to accumulation and toxicity; tins and bottles that contained no warnings and few instructions; and fear of "Spanish" influenza, an illness that had been spreading like wildfire."

8) "From the 1950s to the 1980s, thousands of deaths among children following influenza and other infections (eg, Reye syndrome) were unexplained until studies identified aspirin as the major contributor."

9) "Salicylates cause immediate lung toxicity and may predispose to bacterial infection by increasing lung fluid and protein levels and impairing mucociliary clearance."

10) "The occurrence of pulmonary edema in humans with salicylate intoxication is well documented."

11) The pathology of the early 1918 Flu deaths is consistent with aspirin toxicity. Autopsy reports by pathologists of the day describe:

- Extremely wet and sometimes hemorrhagic lungs.
- The amount of lung tissue actually "pneumonic" seemed "too little in many cases to explain death by pneumonia."
- A thin, watery, bloody liquid in the lung tissue, "like the lungs of the drowned," as well as pleural exudates with small hemorrhages unlike those seen in "any other form of acute pneumonia."
- The brain was "quite regularly swollen."
- The kidneys were "regularly the seat of cloudy swelling."
- The liver had "superficial fatty change."

These pathology findings are consistent with aspirin toxicity.

12) "Aspirin advertisements in August 1918 and a series of official recommendations for aspirin in September and early October preceded the death spike of October 1918."

13) Bayer's worldwide efforts had left few places lacking aspirin, and in the US Bayer's had a giant aspirin factory.

14) Official recommendations for aspirin were issued as follows:

- September 13, 1918: by the US Surgeon General
- September 26, 1918: by the US Navy
- October 5, 1918: by the Journal of the American Medical Association

15) "Aspirin sales more than doubled between 1918 and 1920. The number of deaths in the United States increased steeply, peaking first in the Navy in late September, then in the Army in early October, and finally in the general population in late October."

16) "Homeopaths, who thought aspirin was a poison, claimed few deaths."

17) "Others may have suspected that aspirin was responsible. On 23 November, 1918, Horder wrote in *The Lancet* that, for 'intensely toxic cases...aspirin and all so-called febrifuge drugs must be rigidly excluded from the treatment'."

18) "In summary, just before the 1918 death spike, aspirin was recommended in regimens now known to be potentially toxic and to cause pulmonary edema and may therefore have contributed to overall pandemic mortality and several of its mysteries."

19) "Prospectively, aspirin should be investigated in countries where aspirin is used for influenza."