

# Milestones... in Investigative Pathology

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## Semmelweis and Puerperal Fever

**The Etiology, Concept, and Prophylaxis of Childbed Fever**  
Hartleben's Verlags-Expedition, Pest, Vienna, and Leipzig, 1861.

(Translated into English in) *Medical Classics* 5:339-773, 1940,  
Williams and Wilkins, Baltimore, USA



Dr. Ignaz Semmelweis

While you read the published results of clinical trials, and while you discuss experimental design and data sample comparisons with your biostatistician, you should tip your hat to Dr. Ignaz Semmelweis, who crafted and documented an unintentional 1847 clinical trial that defined the etiology and prevention of puerperal (peripartum) fever of women and their newborns.

As an obstetrician in Vienna in the mid-19th century, Dr. Semmelweis was confronted by annual puerperal fever mortality rates of up to 16%. Current thought leaders speculated that the etiology of puerperal fever was different for different patients,

and that it was some combination of climate, ventilation, diet, overcrowding, patient fear/injured modesty/social status, or national differences in quality of obstetrics practice. If this multivariable explanation failed to convince the uninitiated, thought leaders assigned the etiology to "atmospheric – cosmic – telluric (terrestrial) influences," which would seem to trump all other possibilities.

After graduating from medical school at the University of Vienna in 1844, Dr. Semmelweis trained as an obstetrician at the Vienna General Hospital. By government edict in 1840, the obstetrical service consisted of two Divisions, differing only by who staffed the clinics and wards. The 1st Division was staffed by medical students, and the 2nd Division was staffed by midwife students. The services were otherwise identical with respect to physical plant, temperature control, demographics/social status of the women admitted to the service, bed density, quality of obstetrical care and procedures, hygiene of bed linens, patient diets, etc. This created a clinical experiment that controlled for all variables except staff and staff duties. Semmelweis made a series of critical observations. He noted that puerperal fever was associated with prolonged (>24h) dilation phase of labor of women on the 1st Division service, but not on the 2nd Division service. He noted that death from puerperal fever was more common in both women and their newborns on the 1st Division service. He noted that autopsy findings in affected women and their affected newborns were similar, arguing for a common etiology. He noted that puerperal fever was sporadic rather than generalized in crowded wards, arguing against patient-to-patient contagious transmission. He noted that puerperal fever incidence was independent of season, bed location, ventilation, room temperature, diet, frequency of religious rites, and patient social status. Although he did not document the data for comparison, he noted that women who delivered in transit to the hospital ("street births") had lower rates of puerperal fever than women attended to by medical students in the 1st

Division. He formalized his observations by documenting annual mortality rates for the two Divisions during the period 1841-46, showing that 1st Division (staffed by medical students) had an average mortality rate due to puerperal fever of 9.9%, while the 2nd Division (staffed by midwife students) had an average mortality rate due to puerperal fever of 3.4% (see Table 1). Semmelweis recognized that the only difference between the two Divisions was the staff, and he recognized that the only difference in staff duties was the involvement by medical students in autopsy examination. He noted that (gentlemen) medical students saw no need to wash their hands between patients. His hypothesis was that puerperal fever was due to "conveyance of decomposed animal-organic matter from without," meaning from autopsy patient via medical student to obstetric patient.

Semmelweis should have thanked the Habsburg Empire for their imperial edict of 1840 that stratified staffing of the 1st and 2nd Obstetrical Divisions. From 1833 to 1840, these two Obstetrical Divisions had been staffed by a mixture of medical students and midwife students. This allowed Semmelweis to compare his 1841-46 puerperal fever mortality data to earlier 1833-40 puerperal fever mortality data. He noted that puerperal fever mortality rates 1833-40 (during a time when each Division was staffed by both medical students and midwife students) were comparable (average 6.6% in 1st Division, and average 5.6% in 2nd Division). He concluded from these sample comparisons that puerperal fever was due to "conveyance (by medical students) of decomposed animal-organic matter from without." The only improvement in trial design that we could offer 160 years later would be to document and compare puerperal fever mortality rates in the control group of women who delivered before reaching the hospital. Semmelweis practiced before the isolation of bacteria (van Leeuwenhoek's 'animalcules' from ca. 1673) and the evolution of germ theory, so it was left to Koch in ca. 1870 to isolate the particular streptococcus in women with puerperal fever, and to Pasteur in 1879 to culture the particular streptococcus from the blood of women with puerperal fever.

Semmelweis anticipated Koch's postulates (1890) by 40 years, in the sense that his presumed etiologic agent could be proven if puerperal fever mortality dropped following elimination of the putative etiologic agent. Semmelweis did this experiment starting in 1847 by interrupting the transmission of the "decomposed animal-organic matter" by requiring handwashing in calcium hypochlorite (chlorine bleach) between cases. He collected and documented puerperal fever mortality data for the period 1847-58 (Table 1). He found that puerperal fever mortality rates in the 1st Division fell to an average of 3.6%, comparable to the 3.1% seen in the 2nd Division. He concluded that puerperal fever mortality could be reduced by interrupting the "conveyance of this decomposed animal-based organic matter" from autopsy suite via medical student to obstetrics ward. We don't know why he chose calcium hypochlorite as a proto-antiseptic, although he commented that "it eliminated the smell on the hands." Here's to the archencephalon as a trigger for empirical science.

Semmelweis published his initial observations in a Viennese medical society journal (*Zeitschrift d. k. k. Gesellschaft d. Ärzte in Wien* 4, pt 2: 242, 1847-48), but his conclusions were not widely disseminated, not understood, not confirmed, and/or not embraced, because practice habits did not change. He published 'open letters' to other obstetricians to promote his perspective, but practice habits did not

change. He died in an asylum in 1865 (his wife had him committed, so be careful out there), possibly following inoculation at his last autopsy. His erstwhile reputation was rebuilt only after Koch's isolation of streptococcus from a woman with puerperal fever ca. 1870 and Pasteur's culture of streptococcus from the blood of a woman with puerperal fever in 1879.

This history of Semmelweis and puerperal fever contains several practical teaching points. Semmelweis capitalized on an opportunity to gather data in a government-regulated practice environment that controlled for all variables except staff and their duties. He measured and trended mortality data to show by sample comparison that increased risk for puerperal fever was correlated with manual examinations of peripartum women by medical students with contaminated hands. He postulated a single etiology for all peripartum women and their newborns, postulated the mechanism of exposure to this etiologic agent, and interrupted this process of manual inoculation of peripartum women by use of a proto-antiseptic hand wash. Although not accepted at the time, his work presaged the work of Koch, Pasteur, and Lister with regards to microbial infection, prophylaxis, and Koch's postulates for defining etiologic micro-organisms. Semmelweis's persistent defense of his data-driven conclusions, in the face of an unaccepting medical community, is laudable. However, like the rest of us, Semmelweis was not perfect. Although a careful student of data, he didn't like to write, delaying by 14 years the full publication of his critical work. Had he published in the peer-reviewed, widely-read literature of his era, antiseptic approaches would probably have been adopted well before Lister, saving the lives of thousands of peripartum women. Semmelweis's letters to practicing obstetricians, full of ad hominem arguments and thinly veiled accusations of murder, did not strengthen his argument. Finally, his book would have benefited from careful editing – it runs for several hundred pages, is frequently redundant, and could have been collapsed into a five-page paper in a modern journal. Ignore your editor at your peril.

<b>Table 1:</b>	<b>Mortality from Puerperal Fever (Mean Range)</b>	
	<b>Vienna General Hospital</b>	
	<b>1st Division</b>	<b>2nd Division</b>
1833-40	6.56% (3.04, 9.09)	5.58% (2.26, 8.60)
1841-46	9.92% (7.80, 15.75)	3.38% (2.03, 7.59)
1847-58	3.57% (1.27, 9.10)	3.06% (1.33, 6.18)