Death and Numbers: Semmelweis the Statistician

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In his efforts to find the etiology of puerperal fever, the nineteenth century Hungarian physician Ignaz Semmelweis was an early user of statistics in medical research. His analyses of statistical evidence led him to identify the major cause of this puerperal fever: the direct transmission of bacteria via physicians from autopsy material to women in labor. For two decades the medical profession widely rejected both his theory of cause and his simple prophylaxis (chlorine handwashes). His response to this rejection was, invariably, another statistical analysis. Eventually his view prevailed. In this paper the statistical aspects of this early research in medicine are discussed as well as the sources of resistance to his theory by medical professionals. PSRQ 1991;1:43–52

The Hungarian physician Ignaz Semmelweis is known today as a troubled fanatic who discovered the cause of the outbreaks of childbed (puerperal) fever that killed tens of thousands of European women in the eighteenth and nineteenth centuries. In his own time, Semmelweis was known as the head of an obstetrical clinic where deaths from puerperal fever were rare. What is not recognized is the extent to which Semmelweis relied on statistical methods to formulate and support his theory about the cause of the spread of puerperal fever.

At a time when most medical theoreticians and practitioners concerned with the problem of puerperal fever espoused many unsupported theories and rejected Semmelweis' arguments, Semmelweis was engaged in work that can be viewed today as a model of the use of statistics in epidemiology. He collected the statistical data bearing on a problem, tabulated it to facilitate analysis, tried to correlate the statistical outcomes with factors in the situation, and experimented to confirm a causal relationship. When challenged with a competing theory, he controlled for the proposed covariate. With these statistical methods, and much perseverance, he proved that the attending obstetricians carried the cause of

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the disease from the dissecting room to the maternity clinic on their hands. These physicians, by failing, even refusing, to cleanse their hands after performing an autopsy, were killing their patients.

The first section of the discussion that follows describes the statistical methods Semmelweis employed and highlights the ways in which his methods conformed to or constituted advances on accepted uses of data in his time. The second section traces the outlines of the contemporary resistance of professionals to his theory, despite the weight of evidence he put forward over the years. The third section speculates about the possible sources of this professional resistance. These sources include 1) the general pattern of scientific opposition to a new theory, 2) the familiar issue of the ethnic outsider challenging the elite establishment, 3) the challenge of the insecure young to the tenured elders, 4) the specific problems created by the manner in which Semmelweis presented his data and the inflammatory nature of his rhetoric, and 5) the psychological barriers to accepting the negative import of his findings.

STATISTICAL METHODS

Initial Observations of Differential Mortality

Throughout the eighteenth century and early part of the nineteenth century the great majority of European women gave birth at home. The estimated maternal mortality rate was less than a few percent [1]. In the late eighteenth century, in an act initially perceived as humanitarian, several cities introduced "lying-in" hospitals to care for women about to undergo difficult births. For example, in 1784, the Allgemeines Krankenhaus (the largest city hospital in Austria), originally built as an alms house for soldiers and other poor, was turned into a "scientific" hospital, with laboratories and clinics for both teaching and healing.

As hospital births became more prevalent, a new risk became apparent: death from puerperal fever, which was virtually unknown to women delivering at home. By the first quarter of the nineteenth century, lying-in hospitals were experiencing monthly mortality rates of 10% due to puerperal fever. In the lying-in department of the hospital in Vienna in which Semmelweis was to serve, the following absolute extreme rates were observed in 1842: 25.5%, (August), 29.3% (October), and 31.4% (December). In London's General Hospital, the 1838 *annual* rate was 26.76% [2]. Then, as now, the mortality rate was the number of maternal deaths divided by the number of live births. (In this paper, we follow Semmelweis in using the absolute percentage rate rather than the current demographic convention of number of deaths per 100,000 live births.)

Compare these maternal mortality rates to the 1915 U.S. rate of 0.6%, before the introduction of antibiotics (but after prophylactic measures were in effect). By 1986, when almost all births occurred in a hospital, the U.S. maternal mortality rate was 0.07% [3]

In 1847, Ignaz Semmelweis joined the lying-in department of the Allgemeines Krankenhaus as an obstetrical assistant. Observing the extremes of puerperal mortality, he began to analyze the data (which went back to 1784). There were two obstetrical clinics in the hospital in which he worked, and he observed for the year 1846 that the mortality rate in one clinic was 11.4% compared to 2.8% in the other clinic. The absolute numbers were large: 459 out of 4,010 women died in the first clinic, but only 105 our of 3,754 died in the second clinic [2]. (The relative risk is 4.1, 95% confidence interval 3.4–4.9; this is strong evidence of a large effect.)

Semmelweis did not need modern statistical tools to see that there was a large practical difference in the mortality rates of the two clinics, nor did the women who were brought to the lying-in hospital. Physical force was often needed to get them into the first clinic because they knew that the first clinic meant fever and death and that the second did not [4].

And what of the longitudinal difference; the performance of this lying-in hospital through time? To make his point that in 1823 there had been a change in the causal system from the prior years, Semmelweis used a simple tabular listing of the total mortality in the two clinics (Table 1). In Figure 1 these data are shown as a time series plot, in which it is easy to see clear evidence of a stable process occasionally going out of control before 1823, then shifting to a higher level with greater variability.

The Search for a Systematic Cause

The medical profession was aware of the excessive mortality from puerperal fever. Over 20 different

Table 1. Statement of the Imperial and Royal Lying-in Hospital from August 16, 1784

Year	Patients	Deaths	%	Year	Patients	Deaths	%
1874*	284	6	2.11	1817	2735	25	0.91
1785	899	13	1.44	1818	2568	56	2.18
1786	1151	5	0.43	1819	3089	154	4.98
1787	1407	5	0.35	1820	2998	75	2.50
1788	1425	5	0.35	1821	3294	55	1.66
1789	1246	7	0.56	1822	3066	26	0.84
1790	1326	10	0.75	1823	2872	214	7.45
1791	1395	8	0.57	1824	2911	144	4.94
1792	1574	14	0.89	1825	2594	229	4.82
1793	1684	44	2.61	1826	2359	192	8.12
1794	1768	7	0.39	1827	2367	51	2.15
1795	1798	38	2.11	1828	2833	101	3.56
1796	1904	22	1.16	1829	3012	140	4.64
1797	2012	5	0.24	1830	2797	111	3.97
1798	2046	5	0.24	1831	3353	222	6.62
1799	2067	20	0.96	1832	3331	105	3.15
1800	2070	41	1.98	1833	3907	205	5.25
1801	2106	17	0.80	1834	4218	355	8.41
1802	2346	9	0.38	1835	4040	227	5.61
1803	2215	16	0.72	1836	4144	331	7.98
1804	2022	8	0.39	1837	4363	375	8.59
1805	2112	9	0.40	1838	4560	179	3.92
1806	1875	13	0.73	1839	4992	248	4.96
1807	925	6	0.64	1840	5166	328	6.44
1808	855	7	0.81	1841	5454	330	6.05
1809	912	13	1.42	1842	6024	730	12.11
1810	744	6	0.80	1843	5914	457	7.72
1811	1050	20	1.90	1844	6244	336	5.38
1812	1419	9	0.63	1845	6756	313	4.63
1813	1945	21	1.08	1846	7027	567	8.06
1814	2062	66	3.20	1847	7039	210	2.98
1815	2591	19	0.73	1848	7095	91	1.28
1816	2410	12	0.49				

English version of Semmelweis' original tabulation of the total mortality rate of the two lying-in clinics in the Allgemeines Krankenhaus, Vienna, Austria, from its founding in 1784 through 1848. The true mortality rate is understated, since some of the women with puerperal fever were transferred to, and died in, other clinics. The first year is shown as 1874, it should read 1784. The close observer may notice minor errors in computation of rates; some are due to Semmelweis' occasional habit of truncating rather than rounding, others are simply errors. None that we have found are significant to the arguments. (Reprinted with permission of publisher from I P. Semmelweis, The etiology, the concept and the prophylaxis of childbed fever. 5(5):398. In: E. Kelly, comp: Medical classics, © by Williams & Wilkins, 1941.)

* Transposition error in original. Should read 1784

theories regarding the cause were current in Semmelweis' time. Unlike most fellow physicians concerned with this disease, he did not begin with a theory, but with a conviction that the data contained the answer. He checked each hypothesis put forward by others against the data or by an experiment that gave new data. He ruled out no hypothesized cause a priori.

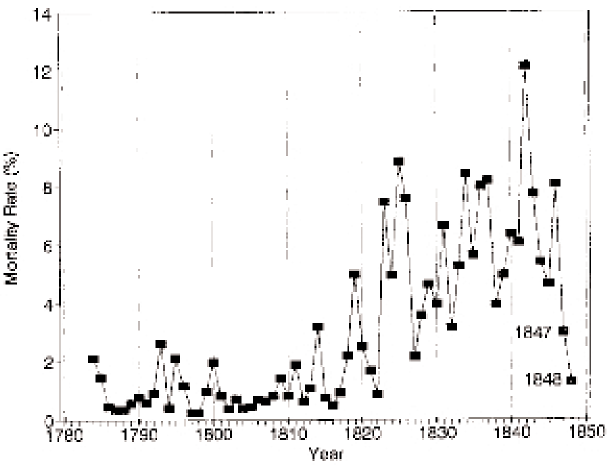

FIGURE 1. Time series plots of the combined total mortality rate of the two lying-in clinics in the Allgemeines Krankenhaus, Vienna, Austria, from its founding in 1784 to 1848 (the data are from Table 1). The rise in mortality starting in 1823 corresponds to the start of anatomical study using cadavers by obstetrical students. The decline in 1847 and 1848 is due to Semmelweis' use of thorough cleansing of the physicians' hands. Errors in computation of rates are corrected in this figure and in Figure 2

He doggedly pursued every suggestion. Was it the women's position on the bed during labor? He tried another recommended position and found no change in mortality. Was it the effect of cold air because of the bed's position in the room? He found no consistent pattern in mortality, and so discarded the hypotheses [2].

The governmental and medical authorities were not oblivious to the problems of excess mortality in the first clinic. A continuing series of commissions, some appointed by "the executive power of the State" (Semmelweis' term) and others by the medical faculties, were formed to investigate this matter. In 1846, one of these commissions came close to finding the true cause. At that time, when the mortality rate was much higher in the first than the second clinic, physicians and medical students delivered babies in the first clinic, but only midwives worked in the second. The medical students were known to be rougher than the midwives. The commission concluded that the disease was caused by the rough handling by students, particularly the foreign students. Students were defined as foreign if they were not native-born or if they completed their studies at a university outside Vienna. The nonforeign category included students who were not native-born, but who studied at University of Vienna institutions for any time. Starting in December 1846, the hospital excluded foreign students. The total number of students decreased from 42 to 20; thus, the number of examinations of patients by medical students also declined [2].

At first, the results were salutary. Prior to this decision, during the first 11 months of 1846, the mean monthly mortality rate in the first clinic was 15% (standard deviation 3%). In the first 4 months after the exclusion of foreign students the mean monthly rate dropped to 3.2%. But in the following 2 months, the rate rose once again to 15% (18% and 12% in April and May of 1847, respectively). At this point, Semmelweis wrote, "Everything was uncertain, everything was doubtful, everything was inexplicable, only the enormous number of deaths is an indubitable fact" [2].

Puerperal fever was considered a disease of females, and 13 of 20 hypothesized causes of puerperal fever listed by Semmelweis were considered specific to the female gender or childbirth, despite the fact that there were documented male deaths from this same disease.

In March 1847, Jakob Kolletschka, a professor of forensic medicine whom Semmelweis admired, died of a disease that was clinically identical to puerperal fever. He became ill after an autopsy during which a medical student accidentally cut the professor's finger. This death led Semmelweis to make the vital connection between the laboratory activities of the medical students and the transmission of puerperal fever to the women in the first clinic.

He framed his fundamental hypothesis with this question: "Did the cadaveric particles make their way into the vascular systems of the individuals, whom I had seen die of an identical disease?" [2]. If the answer was "yes," then the medical students were bringing the disease into the obstetrical clinic because of their contact with "cadaveric particles" acquired during their anatomical studies on cadavers. Since midwives did not engage in autopsies, their absence of exposure would explain the difference in mortality between the two clinics.

Confirmation of the Hypothesis

In a series of experiments Semmelweis and a colleague introduced material from the uteri of diseased women into the uteri of rabbits and produced a disease identical to puerperal fever. Then they showed that blood and other fluids from human cadavers (dead from many causes) also produced the same disease. The statistical association was confirmed through empirical trial. Now, an intervention was required.

Starting in May 1847, Semmelweis had the medical students wash their hands with chloride of lime to remove all traces of "cadaveric particles." The results were striking. In the first 7 months of systematic hand cleansing, the total mortality rate for the first clinic was 3% (for a total of 1,841 births), compared to rates for the preceding 2 months of 18% and 12%. Later Semmelweis could proudly show that the total rate for the first clinic in 1848 was 1.3%.

What was his statistical support for the contention that his chlorinated lime handwashings worked? His evidence was simple: direct comparisons based on time series presented in tables and textual comparisons equivalent to contingency tables. Table 2 presents his three time series tables [2].

Figure 2 shows the time series plots for the two clinics in the period 1833 through 1858. Semmelweis divided the 26-year span from 1833 through 1858 into three distinct periods. In the first period, from 1833 until October 1840, the student obstetricians were not involved in examination of corpses from the clinic, and students and midwives were randomly assigned to both clinics. During this period the mortality rate in the first clinic was 6.56%, and 3.58% in the second clinic, a neither statistically, nor practically, significant difference.

In the second period, from October 1840 through 1846, the students were assigned exclusively in the first clinic and resumed the study of cadavers. Only midwives served in the second clinic. Mortality rose dramatically: 1,989 out of 20,042 women died in the first clinic, but only 691 out of 17,791 died in the second clinic: 9.92% vs. 3.38%.

In 1847, Semmelweis introduced the washing of hands with chlorinated lime; this is the beginning of the third period. From that time until 1858 both clinics had low mortality rates; 3.57% for the first clinic and 3.06% for the second clinic. If we take 1847 to 1858 as a period of no exposure to uncleansed physicians and students in the first clinic, and 1840 to 1847 as a period of exposure, then the relative risk of death associated with exposure to the uncleansed students and physicians is 2.77. Similarly, the relative risk of death due to exposure to midwives in the same two periods is 1.27. The 95%

Table 2.

Year	Births	Deaths	%	Births	Deaths	%
	1st Div.			2d Div.		
1833	3737	197	5.29	353	8	2.26
1834	2657	205	7.71	1744	150	8.60
1835	2573	143	5.55	1682	84	4.99
1836	2677	200	7.47	1670	131	7.84
1837	2765	251	9.09	1784	124	6.99
1838	2987	91	3.04	1779	88	4.94
1839	2781	151	5.04	2010	91	4.05
1840	2889	267	9.05	2073	55	2.06
Total	23,066	1,505	6.56	13,095	73	5.58
	Physician's Division			Midwives' Division		
1841	3036	237	7.7	2442	86	3.5
1842	3287	518	15.8	2659	202	7.5
1843	3060	274	8.9	2739	169	5.9
1844	3157	260	8.2	2956	68	2.3
1845	3492	241	6.8	3241	66	2.03
1846	4010	459	11.4	3754	105	2.7
Total	20,042	1,989	9.92	17,791	691	3.38
First division	Births	Deaths	Percent			
1847	3490	176	5.04			
1848	3556	45	1.27			
1849	3858	103	2.66			
1850	3745	74	1.97			
1851	4194	75	1.78			
1852	4471	181	4.04			
1853	4221	94	2.13			
1854	4393	400	9.10			
1855	3659	198	5.41			
1856	3925	156	3.97			
1857	4220	124	2.96			
1858	4203	86	2.04			
Total	48,938	1,712	3.57			
Second division						
1847	3306	32	0.96			
1848	3219	43	1.33			
1849	3371	87	2.58			
1850	3261	54	1.65			
1851	3395	121	3.56			
1852	3360	192	5.71			
1853	3480	67	1.92			
1854	3396	210	6.18			
1855	2938	174	5.92			
1856	3070	125	4.07			
1857	3795	83	2.18			
1858	4179	60	1.43			
Total	40,760	1,248	3.06			

English version of one of Semmelweis' time series tables in which he illustrated the effect of the initiation and suspension of the chlorinated handwashings. These tables include the period during which the hand-cleansing intervention was in effect (Period 3 in Figure 2). (Adapted from: I.P. Semmelweis. The etiology, the concept and the prophylaxis of childbed fever, 5(5):437-642. In: E. Kelly, comp: Medical classics. © by Williams & Wilkins, 1941.)

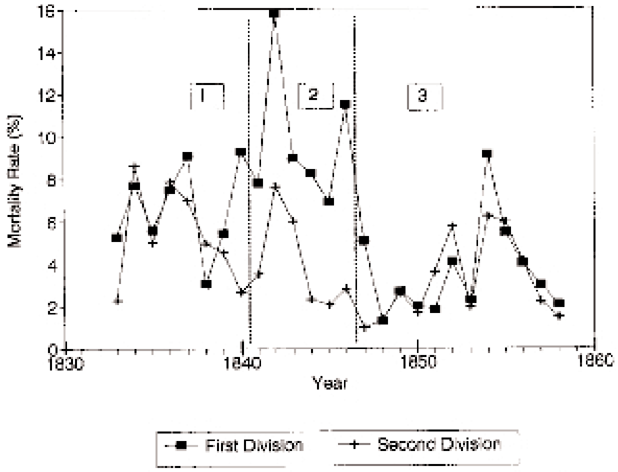

FIGURE 2. Total mortality rate in the two lying-in clinics from 1833 through 1858 (the data are from Table 2). During period 1, there were no anatomical studies and physicians and midwives were randomly assigned to a clinic. Mortality experiences in both clinics were nearly the same. During this period two of the seven resulting contingency tables have Chi-square statistics which are significant at the 1% level. During period 2, physicians resumed anatomical studies and served only in the first clinic and midwives served only in the second clinic. The mortality rate of the midwives' clinic declined and that of the physicians' clinic rose. During this period, *all* contingency tables have Chi-square statistics which are significant at the 1% level. During period 3, the physicians used Semmelweis' hand-cleansing methods and both clinics had lower mortality rates. During this period three of the 12 resulting contingency tables have Chi-square statistics which are significant at the 1% level.

confidence interval for the first clinic (physicians) is 2.65–2.91 and for the second clinic (midwives) is 0.97–1.07. This modern expression of risk not only supports the efficacy of Semmelweis' sanitary precautions, but also is one more verification of Semmelweis' theory that physicians were the carriers of the disease.

Semmelweis now had the theoretical basis to explain the systematic change in the process in 1822. The statistics clearly define the problem. From their founding in 1784 until 1822, *both* clinics experienced a total mortality rate of 1.25%. The total mortality rate for the two clinics was 2.84% in January of 1822, and had risen to 7.45% in December 1822. This was no trivial increase, and the situation grew even worse.

Now, in 1847, Semmelweis deduced what the deadly systematic cause was in the first clinic starting in 1822. This was the year in which Professor Johann Klein, the new director, took charge and introduced regular autopsy practice. The 1822 coincidence of the rise in mortality and the start of regular autopsy practice was an important confirmation of Semmelweis' theory of the mechanism of contamination, for as Ehrenberg observes, "we must always be looking to see whether a generalizable result . . . holds across many sets of data" [5].

But when Semmelweis publicly proposed that the 1822 onset of high levels of mortality was due to Professor Klein's introduction of regular autopsy practice, he was in direct conflict with his immediate supervisor. Professor Klein had tried to get rid of Semmelweis before Semmelweis presented his theories of the causes of puerperal fever, and afterward, not only rejected his theories but also denied Semmelweis his expected promotion in the Vienna clinic [2,4].

OPPOSITION FROM THE MEDICAL PROFESSION

Semmelweis tabulated the data on births and deaths by clinic for 1839 and 1840 to show that the differences in mortality could be attributed to the activities of the attending physicians. He was prevented from publishing these data because "at the time I was compiling them, it was regarded as a denunciation" [2]. The Viennese professors of medicine who had expelled foreign students from practice without basis in fact could not accept the validity of statistical evidence that might have implicated *them*.

In 1849, Semmelweis was denied the expected promotion to Privat-Docent in Midwifery. After a delay of 18 months, he was given the position subject to the condition that he only demonstrate procedures on a dummy. He left Vienna for the St. Rochus Hospital in Pest, Hungary, where he was appointed director of the Obstetric Division. In that position and later as Professor of Theoretical and Practical Midwifery, he achieved a remarkable record in reducing maternal mortality.

Semmelweis, however, was not the first to observe that good hygiene reduced maternal mortality. Charles White, an English obstetrician, argued for cleanliness and the use of antiseptic solutions in a 1773 book available in both French and German by 1775 [6]. In 1793, White's American student, Thomas Kirkland, accurately assigned the cause of puerperal fever to material carried to patients [4]. In 1795, 50 years before Semmelweis, the Scottish physician Alexander Gordon published his observation that if "putrid material" were applied to the uterus, puerperal fever would result and that physicians who scratched themselves while examining cadavers could contract the same disease. Gordon insisted on disinfection and personal cleanliness, but linked this theory to other theories (he also recommended purgation and extensive blood-letting), and his theories did not gain acceptance [4].

In 1829, Robert Collins instituted intensive cleansing measures in the Dublin Lying-In Hospital, and reported total maternal mortality of 0.54% (58 out of 10,785), 0% due to childbed fever. The American physician and author, Oliver Wendell Holmes, summarized this pre-Semmelweis work in an 1843 paper. Holmes' critical points were that the disease was contagious (which, strictly speaking, it is not) and that it was carried by caregivers (which was true at the time). As Carter quotes him as saying, his purpose was to show that "the disease known as puerperal fever is so far contagious as to be frequently carried from patient to patient by physicians and nurses" [7]. Holmes' paper cautioned obstetricians about the danger of infecting women in labor.

In general, the medical community rejected Holmes' 1843 paper, Semmelweis' 1847 paper, and his 1860 book on the etiology of puerperal fever. Ten years after Semmelweis' analyses and experiments, in 1858, the highly influential pathologist Rudolf Virchow, who was noted for his sanitary reforms, attacked Semmelweis' ideas. It is no accident that this was the same year in which Virchow's *Cellular Pathology* was published. Semmelweis' theory that the disease resulted from an infectious cause was in direct contradiction to Virchow's autonomous cell concepts as enunciated in that book. Otto Pertik, the renowned Hungarian pathologist (1852–1913), in his toast at the Semmelweis evening of the Medical Casino in Budapest in 1911 observed:

> Can one wonder that Virchow, who considered the cell to be the seat of all diseases, should have hotly defended the autonomy of his cells, and his doctrine of their functional, nutritive, and formative impulses, in which he believed the causes of illnesses to reside? . . . (Semmelweis') doctrine seemed to him (Virchow) to be an open defiance of his theory of cell-autonomy [4].

In a lecture at the Obstetrical Society of Berlin in

1858, Virchow proposed atmospheric conditions, accompanying diseases, disturbances of lactation, nervous excitement, etc., as causes of puerperal fever. In reply to this statement in his book of 1860, Semmelweis said that his hundreds of Hungarian student midwives would have laughed "in derision" if Virchow were to lecture them on puerperal fever.

In 1861, at a German conference of physicians and others, Virchow called Semmelweis "the churl who speculated," because he allegedly did not follow Virchow's recommended approach of observation and experimentation, and did not consider authority before forming theories [2]. And yet, as Semmelweis himself explicitly noted, he had consistently followed this inductive approach. In 1863, Virchow argued that he had achieved excellent results in treating puerperal fever even though he handled cadavers on a daily basis. Although in 1864, he acknowledged that puerperal fever was an infectious disease [4].

Semmelweis countered professional resistance with further statistics. With time, his data sets increased in number and included data from Pest, London, Dublin, Paris, and elsewhere. Against each opposing argument he would set another time series, another set of tables, controlled in an appropriate way. His final 1860 work contains more than 80 tables, as well as many textual arguments using statistics.

He used different measures to make his point. For example, one widely believed theory was that the atmosphere in some way caused puerperal fever. A consequence of this theory was that the disease prevalence would show a seasonal pattern. To test that hypothesis, Semmelweis tabulated the extreme values for each month, independent of the year. For each month during the years 1841 to 1849, he found the 2 years in which the maximum and minimum rates were observed, and showed that all months had roughly the same pattern of extreme values, as shown in Figure 3. He demonstrated that the maternal mortality rate showed wide variation within months, thus making his point that all months are highly variable and that outbreaks could be observed in every month.

Many influential medical authorities other than Virchow rejected Semmelweis' theories. Karl Braun, Virchow's successor in Vienna, who was considered a great authority, wrote *On the Puerperal Processes,*

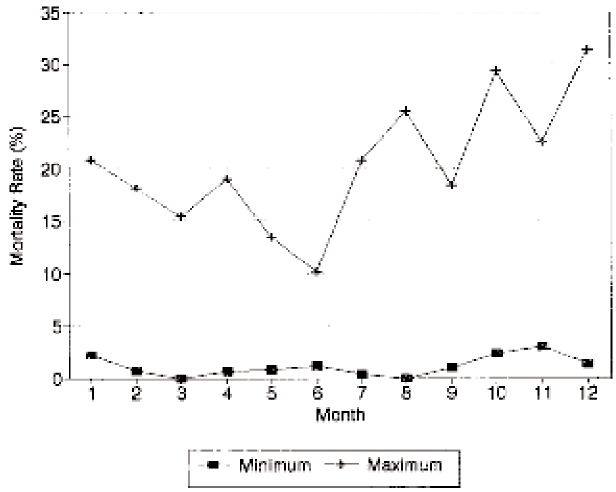

FIGURE 3. Extreme mortality rates by month. Semmelweis used the great difference in the minimum and maximum to show that outbreaks of puerperal fever could occur in any month. The period covered is the years 1841 to 1849.

in which he rejected Semmelweis' infection theory. Braun's statistical analyses of data were incorrect, which Semmelweis easily showed [2]. Dr. Eduard Lumpe, another adversary, wrote a popular textbook on obstetrics in which Semmelweis was never mentioned. Lumpe argued that the famous Dr. Franz Kiwisch's much smaller lying-in hospital was more healthy than the Allgemeines Krankenhaus in Vienna because Kiwisch's hospital had only 27 deaths in 1842 whereas the Viennese hospital had 730. When Semmelweis took into account the number of patients, the mortality rate at Kiwisch's hospital was 26%, compared to 12% at the Viennese hospital.

Semmelweis' doctrine spread quickly in Hungary and was well-received in Britain. It spread slowly elsewhere in Europe, however, despite the October 1860 publication of his book *Die Aetiologie, der Begriff und die Prophylaxis des Kindbettfiebers* with its overwhelming weight of evidence, and in which every opposing theory was countered with a statistical analysis of clinical data. He was losing patience with the physicians who accepted neither his theory of cause nor his prophylactic measures. He met negative receptions to his book with a series of strongly worded open letters to prominent adversaries [8]. In these letters he refers to the first Vienna clinic, the site of excess mortality, as the "physician's clinic," and calls his opponents murderers and hypocrites.

During distribution of the first of the open letters in June 1861, the editor of the *Medical Weekly* (published by the Hungarian Medical Society) wrote:

> The author is delivering a smashing blow to his opponents in the question of puerperal fever, proving by infallible statistics and multiple arguments the truth of his theory. The victory of a good cause may be retarded, especially when delusions have to be defeated, but the final triumph is assured [4].

Our modern understanding of the bacterial cause of puerperal fever confirms the views that Semmelweis fought to advance. Puerperal fever, still a potential threat to women in childbirth, is usually caused by the bacterium Streptococcus hemolyticus, which can invade through any raw or damaged body surface and produce septicemia if it enters the systemic circulation. Some of the competing explanations against which Semmelweis struggled can now be seen as secondary pathways for the same disease process, confounded with, and hidden by, the overwhelming effect of physician transmission from cadavers. Unfortunately for Semmelweis and for the thousands of women who died from unclean practices that he could not change, the medical profession did not adopt his theory of cause or his intervention until late in the nineteenth century, after much discussion of Koch's postulates spurred widespread understanding of the bacterial cause of disease.

SOURCES OF PROFESSIONAL RESISTANCE

In a historical exposition on the subject of epidemiology, the authors A.M. Lilienfeld and D.E. Lilienfeld state, "It is important to emphasize that the use of quantitative reasoning and statistics is an inherent aspect of epidemiologic thought" [9]. They rank Semmelweis along with John Snow (1813–1858), William Budd (1811–1880), and William Farr (1807–1883) as notable early examples of epidemiologic reasoning. The French physician Pierre-Charles Alexander Louis (1787–1872) also had great influence in making quantitative reasoning a part of medical science. Among Louis' students were Holmes (1809–1894), who generally agreed with Semmelweis about the etiology of puerperal fever, and Josef Skoda (1800–1881), who taught Semmelweis (1818–1865).

Semmelweis was one of the first medical scientists to use statistics systematically to establish a cause and confirm a remedy. Today most of us would find his statistical evidence overwhelming. Why did the body of the medical profession reject the evidence, not only of Semmelweis, but of his distinguished predecessors?

Several factors contributed to the rejection of his ideas by the majority of the European medical community.

1. *A new theory always must overthrow the existing theory.* Scientists, like everyone else, are the prisoners of their historical time and its conceptual base. Semmelweis' opponents may have reasoned correctly from their incorrect theoretical premises, and they may have been unable to conceive a different theory that would explain the observed data.

Semmelweis' arguments were based largely on his observations and analyses, but they struck directly at the heart of the contemporary theories of disease. K. Codell Carter, translator of the 1983 edition of the *Aetiologie*, said: "Germ theory, and the new prophylactic measures that were based on it, rested in part on a new strategy for characterizing diseases. Semmelweis was among the first to use this strategy" [7]. Puerperal fever, like other diseases of the period, was characterized by its pathological alterations, as called for by pathological anatomy. This led to great uncertainty in the identification of the disease, and a proliferation of causal theories for the same disease, since many causes could lead to the same pathological results. Semmelweis proposed a necessary cause, which was a dramatic challenge to contemporary thinking.

Another debate raged over whether puerperal fever was contagious. The British and Americans thought it contagious, unlike the European physicians. But none went as far as Semmelweis in proposing a single direct and necessary cause. Holmes believed that cases arising from infection could be distinguished from cases resulting from epidemic or sporadic causes. Epidemic causes were usually identified with atmospheric or terrestrial factors that were hard to pin down, and sporadic causes accounted for cases that were due to neither epidemic influences nor infection. Lumpe, for one, "confidently asserted that the disease was predominantly epidemic" because of the nature of the epidemiological observations [7]. Semmelweis repeatedly used the constant mortality data to refute assertions of epidemic or sporadic causes.

According to Carter, some writers feel that "on the continent, obstetricians simply had no experiences that confirmed the British belief in contagion" [7]. But as Dr. Franz Kiwisch, another opponent of Semmelweis, reveals in a review, he did have experiences reflected in data that would support the British viewpoint. Semmelweis picked up on this revelation and wrote that "only the ability to recognize (the consequences of going directly from the autopsy of a puerperal fever victim to examine patients) was lacking" [7].

The historian, Thomas S. Kuhn, finds it not unusual that "a law which cannot even be demonstrated to one group of scientists may occasionally seem intuitively obvious to another" [10]. This conflict arises because of competing paradigms—models from which come coherent traditions of scientific research. Kuhn quotes the physicist Max Planck as saying, "A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up with it" [10]. Semmelweis' opponents were not fools, but it took almost a full generation (more than two decades) for full acceptance. For as K. Codell Carter observes, "Semmelweis' argument in the *Aetiologie* repudiates the notion that pathological anatomy is the ultimate foundation; in its place he employs a new strategy that was destined to become one of the defining characteristics of scientific medicine" [7].

2. *The challenge of the ethnic outsider.* Could personal animosity or ethnic prejudice have played a role in the rejection of Semmelweis' ideas? The principal opponents of this overtly nationalistic Hungarian were Austrian and German. The Austro-Hungarian Empire was an autocratic and conservative state dominated by the Austrian Hapsburg emperor. Semmelweis wrote his early works in Hungarian, which angered some of his Austrian colleagues and superiors. And he was a Hungarian nationalist who fought in the 1848 revolution against Austria. He made personal enemies among his colleagues who never fully accepted his ideas. Although to a modern reader his early writings may seem to be deferential to authority, as a brash 26-year-old newcomer in Vienna, Semmelweis delivered his first medical challenge to Professor Klein, his direct superior, in an open meeting.

3. *The challenge of the insecure young to the tenured elders.* In 1848, Professor Josef Skoda, then himself a junior faculty member and engaged in his own struggles with the senior faculty, proposed that the Vienna Medical Faculty form a commission to investigate Semmelweis' initial successes in reducing the death rate due to puerperal fever. Semmelweis' superior Professor Klein was not included in the commission (and probably did not participate in the proposal). As chief of the obstetrical clinic, Klein would have had good reason to believe that he was being sidelined by junior faculty, and Semmelweis was the most vocal and threatening of the lot. Klein succeeded in getting "orders from higher up" [2] to stop the commission from going ahead. Others who studied the situation showed that the power struggle between the senior and junior faculty members was a major issue at this time [7]. Two months after the termination of the commission's work, Semmelweis was dismissed from the first clinic and was unable to get his appointment to the Allgemeines Krankenhaus in Vienna extended.

4. *Truth is more persuasive if well-packaged.* W.C. Danforth, an American professor of obstetrics, said that it was mainly because of its bad style and "superfluous" statistical tables that Semmelweis' 1860 book had so little influence [11]. Semmelweis was not a lucid expositor and he relied heavily on his statistical evidence. A modern researcher would use more summary statistics, more comprehensive and revealing tables, graphical presentations, hypothesis tests, and confidence intervals

Some of his contemporaries communicated more gracefully and effectively. One observer noted: "If Semmelweis could have written like Holmes, his *Aetiologie* would have conquered Europe in 12 months" [4]. It was no accident that he communicated so poorly in the medium that was essential to establishing authority, as he freely admits in his August 1860 preface to *Aetiologie*, "To my aversion to all polemics must be added my innate aversion to every form of writing" [7].

Unfortunately, he lacked not only the fluency of Holmes, but also Florence Nightingale's gift for creative presentation of information. In 1860, her graphical analyses of British army mortality in the Crimean War were an essential part of the reports that led Parliament to make radical changes in the health and medical aspects of military administration [12]. Published in the same year, the statistical arguments of Semmelweis' text and tables had little success.

5. *To accept the truth means to accept responsibility.* The resistance of the medical profession seems extreme in view of the weight of the evidence. Yet, to accept the possible validity of a theory that placed responsibility on the obstetricians would undermine the entire structure of the physicians' view of themselves as expressed in the Hippocratic oath, "that into whatsoever house you shall enter, it shall be for the good of the sick."

It made no difference that Semmelweis' primary hygienic demand that physicians thoroughly wash their hands and brush their fingernails with chlorinated lime could be so easily accomplished. This small step aroused resentment and, in many cases, complete dismissal. Even if he were wrong, one could argue, a trial of this proposal would seem a small price to pay for a possible major advance in prophylaxis.

How much easier to denounce the theory as too simple, and the intervention as too mundane than to confront one's own possible complicity! As Semmelweis said, "there can be no defense against childbed fever that is due to atmospheric-cosmic-terrestrial influences. Advocates of the epidemic theory secure themselves behind this indefensibility; they thereby escape all responsibility for the devastations of the disease" [7].

In 1865, the year of Semmelweis' death, antisepsis was introduced into surgery, and 9 years later the Streptococcus hemolyticus bacterium was isolated. By the end of the nineteenth century, obstetrical practice included routine use of antiseptic procedures and puerperal fever became a dread disease of the past. Although his statistical arguments could not overcome the many sources of resistance to his ideas in his time, no one can take away from Semmelweis the fact that he can "be credited with having for the first time constructed a statistically tested system of asepsis (keeping germs away from the patient) before the germ theory had arrived" [13].

AUTHORS' NOTE

No short article can do justice to the complexity of this real-world situation that we have described. K. Codell Carter's introduction to his translation of the *Aetiologie* [7] is a superb summary with an emphasis on medical considerations. Carter abridged the original by removing about 50 pages of tables, cut back on Semmelweis' polemical and repetitious responses to his critics, and greatly improved the syntax, compared to the full English version of 1941. However, it is not Semmelweis. Carter's translation is excellent and easy reading; it is the book that Semmelweis should have written. But you must get close to his original words and construction if you want to know his intensity of feeling, to sense his struggle to understand, and to appreciate his intense moral drive and sense of responsibility for the welfare of those young women—most of whom were poor and single—giving birth and, too often, dying.

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