Rediscovering Ignaz Philipp Semmelweis: some additional thoughts

TO THE EDITORS: I read with genuine enthusiasm the recent comprehensive review of the life and work of Ignaz Philipp Semmelweis—clearly one of the greatest of all obstetricians—and *AJOG* should be commended for realizing the importance of publishing and thus promoting this important work on a monumental chapter in obstetrical history.[1] Over nearly 30 years of practice, I have lectured extensively about Semmelweis and his keen, serendipitous observations, which revolutionized our understanding of obstetrical infection and its prevention and the importance of clinical research. Although conducted in the 19th century, the work of Dr Semmelweis provides contemporary perspective not only on the topic of maternal mortality, but in also serving to remind us that a closed-minded medical community can be a dangerous thing when it comes to the potential benefits of new ideas and innovations. I would only point out that this otherwise excellent paper by Nicholas Kadar concludes with what I felt was an unfortunate tirade of criticism for the late Dr Sherwin Nuland (1930–2014), who wrote and lectured extensively about Dr Semmelweis.[2] By rough count, Dr Kadar saw fit to refer to Dr Nuland by name 33 times, each in a negative light. Sadly, Dr Nuland died from prostate cancer several years ago and is unable to defend his widely sold and, in my opinion, excellent book on Semmelweis. Dr Nuland, who changed his birth name as a young man from Shepsel Nudelman to escape rampant anti-Semitism, received his medical degree from Yale in 1955. He became chief surgical resident at Yale–New Haven Hospital, and from 1962 until 1991 was clinical professor of surgery at Yale, where he also taught bioethics and medical history (despite the authors' statement that "Nuland was a surgeon, not a medical historian"). When he retired he wrote numerous medically related books, including *Doctors: The Biography of Medicine* (1988), *The Wisdom of the Body* (1997), *The Doctors' Plague* (2004), and *The Uncertain Art* (2008). His 1994 book, *How We Die: Reflections on Life's Final Chapter*, was a *New York Times* best seller and won the National Book Award for nonfiction, and was a finalist for the Pulitzer Prize. In 2005, Nuland propelled his interest and expertise in medical history into a highly regarded series of lectures for the Teaching Company's "The Great Courses" on the history of Western medicine, titled "Doctors: The History of Scientific Medicine Revealed Through Biography." I write this not to dismiss Dr Kadar's thoroughly researched and well written review, but simply to note that I doubt strongly that Nuland would simply create a revisionist myth of the life of Semmelweis as the author implies, but more reasonably saw similar information differently; it is history after all. Dr Kadar's review would have been made richer by treating a historical reviewer of Semmelweis with greater deference, and perhaps with a touch of admiration for the early work Nuland did to bring this giant of obstetrics to our modern literature. If it were not for Nuland's book on Semmelweis, I would not have first become enthralled with the wonders and lessons of medical history. ■

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REPLY

I thank Dr Perlow for his interest in my article,[1] and I welcome the opportunity to amplify my statements about what Dr Sherwin Nuland has written about Semmelweis, and to update my account of Semmelweis's prophylaxis with the information I was able to glean from a French article by Friedrich Wieger, an eyewitness to how the prophylaxis was practiced, that Dr Russell Croft has translated for me since my manuscript was submitted.[2] Wieger added the following to the chlorine hand-disinfection, which strikes me as a crucial omission from the Semmelweis historiography:

> "It is above all essential to brush the nails and the skin folds surrounding the nails with the most scrupulous care. This is the whole secret."[2]

I regret that Dr. Nuland has passed away, as I would dearly have wished openly to debate with him the many things he has written about Semmelweis that are not true, as this would be the most effective way to correct them. However, I take

umbrage at Dr Perlow's characterization of my exhaustively referenced rebuttal of what Nuland has written as a "tirade," and his misuse of the number of times I cited to Nuland's work to try to justify his mischaracterization. The norm for citing to sources in the humanities is different from that used in medical journals, in that the exact page(s) of the source document in which the proposition or quotation being cited appears must be provided so that the reader can check the accuracy of the citation. When I prepared my manuscript, each of those 33 references had a page number to ensure the reader that the propositions and quotations in Nuland's work to which I cited were accurate, and not my own characterizations of them, but they could not be retained in the format used by the *Journal*.

Now to substance. My conclusions about what Dr Nuland has written about Semmelweis, based solely on what he has written, and on historical documents I have been able to retrieve on line or on a visit to Vienna and Budapest since I wrote my article, are the following: Nuland traduced Semmelweis, and repeated what he wrote word for word several times in a determined effort to spread his story; none of the defamatory statements Nuland made about Semmelweis has any support in historical documents, and he cited to none; many of Nuland's defamatory statements about Semmelweis are also flatly contradicted by historical documents.

The following is but 1 example, from a memorandum written by Ernst Wilhelm Ritter von Brücke, professor of physiology at the Vienna Medical School, to the Imperial Academy of Sciences when he returned the grant it gave to Semmelweis and Brücke to conduct "further and more varied" animal experiments at Skoda's request.[3] On page 123 of Nuland's book that Dr Perlow cited, Nuland wrote the following about these animal experiments:

> "He [meaning Semmelweis] was not pleased that the academy [of sciences] suggested that he perform more laboratory experiments—even offering him a grant to do them in conjunction with Ernst Brücke, professor of physiology. But he refused as if insulted, stating that there was no point in experiments since the clinical evidence was conclusive."

Nuland simply made this up out of whole cloth. What Brücke actually wrote about how Semmelweis conducted the experiments Nuland claimed Semmelweis refused to do, and a copy of which I am attaching to this reply, is the following:

> "Dr. Semmelweis had already in the spring and summer made these attempts with great zeal and great conscientiousness, and carried out the post-mortems on the animals together with me."[4]

That is my translation, and lest Dr Perlow not accept its accuracy, here is the original:

> "Hr. Dr. Semmelweis hat sich nun im Früling und Sommer diesen Versuchen mit grossem Eifel und grosser Gewissenhaftigkeit unterzogen und die Obductionen der Thiere gemeinschaftlich mit mir vorgenommen."[4]

Another area not covered by my article is Semmelweis's writing. The idea that Semmelweis could not write well is another myth: Semmelweis often expressed himself with extraordinary lyricism, as in this comment on the discussions of childbed fever at the Paris Academy in 1858:

> "but the dry straw, which therein was brought to light, we shall leave unthreshed since there is no grain to be beaten out of it;"

Or in this, on Prague:

> "The sorrowful humanitarian can estimate what a horrible waste of human life took place also in the Prague lying-in hospital."

Nuland was apparently unable to recognize it, but Semmelweis wrote with wit and sophistication, and not as the insecure, diffident man with an inferiority complex Nuland portrayed him to be [page 174]. Here are some brief examples:

> "It would have been good fortune indeed for the birth-giving sex if there were no etiology of childbed fever except that which Scanzoni recognizes…What Scanzoni says about the forms of puerperal fever can certainly be read in many textbooks on obstetrics, but not observed in nature."

> "Braun has reproached me because I depend on the past, and draw therefrom very bold conclusions…Into what barbarity would humanity sink, if the past were lost for the succeeding generations. Can a generation discover navigation and build a great Eastern? How many generations have labored until one contrived the locomotive, which could climb the Semmering [the first mountain railway in Europe]?…Braun may scarcely remember how much he looked about the past as he was compiling his textbook of Obstetrics. For of a surety I am convinced that, if we strike out of this textbook everything which has to do with the past, nothing but the cover will be left which has to do with the present."

I do not understand what point Dr Perlow meant to make by referring to Dr Nuland's background, awards, and other works. Neither his awards nor the unspeakable horrors that Jews suffered at the hands of the Nazis, and from which Dr Nuland's family apparently fled, can alter or excuse the disinformation Dr Nuland seemed determined to spread about Semmelweis, and that continues to spread about him thanks largely to his efforts. ■

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Defining 17OHP-C responsiveness

Check for updates

TO THE EDITORS: We read with interest the Research Letter by Dr Caritis and associates that examined the interval of the gestational age difference at delivery (GADD) between the study pregnancy and prior births for women receiving 17-alpha hydroxyprogesterone caproate (17OHP-C) and placebo.[1] In this analysis, the GADD was analyzed as a surrogate for responsiveness to 17OHP-C by examining a "delta" (ie, difference) in length of gestation between births in a patient's history using data from the 2003 Meis et al report.[2] For example, a 37-week delivery compared to the same woman's prior 34-week delivery would result in a net +3 week GADD. To summarize, 17OHP-C was ineffective when using the GADD analysis to compare study drug—treated births to either an individual woman's earliest prior spontaneous preterm birth or last (ie, proximate) birth. Put another way, placebo and 17OHP-C GADD results were not significantly different for prolongation of pregnancies beyond 3 or 5 weeks when women served as their own controls.

GADDzooks! Are Caritis and colleagues suggesting that GADD failed as a yardstick? Or that 17OHP-C failed? The report by Caritis et al using GADD actually corrects for the known asymmetry in risk of recurrence for preterm birth in the Meis et al trial (41% of the control women in the Meis et al trial had ≥2 prior preterm births compared to 28% in the 17OHP-C-treated group, $P = .004$). By accounting for an individual woman's risk based on her prior preterm birth history, the effectiveness of 17OHP-C in the Meis et al trial appears to be eliminated.[1,2] It seems to us that 17OHP-C is ineffective for prevention of recurrent preterm birth at 35 weeks or less when an individual woman serves as her own control, even in the Meis et al dataset.[2,3] ■

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REPLY

Check for updates

We commend the authors for their clever use of our "GADD" acronym and we thank Nelson and colleagues for the opportunity to present additional data. In our research letter, we demonstrated that 17-alpha hydroxyprogesterone caproate (17-OHPC) responsiveness cannot be defined by the gestational age difference at delivery (GADD) from the earliest prior spontaneous preterm birth (sPTB) to the currently treated pregnancy.[1] The suggestion that GADD intervals could be used to define responsiveness to 17-OHPC stems from the possibility that women may gain a benefit from 17-OHPC even if they do not achieve the typical criterion of 37 weeks to define success.[2] In their letter, Nelson and colleagues ask whether GADD failed as a yardstick or whether 17-OHPC treatment failed. The focus of our analysis was to highlight that the GADD does not appear to be a good measure to define success of treatment with 17-OHPC, but we did not specifically address the efficacy of 17-OHPC.

A common statistical method used to judge success of an intervention is survival analysis, which has been used in many placebo-controlled randomized trials. Since risk at the start of a study should be balanced between subjects in the placebo and treatment group, differences in time to event between 17-OHPC and placebo reflect the efficacy of the intervention. The advantage of randomization is that risk antecedents such