FOREWORD TO E.C. ROSENOW'S 1919-1920 INFLUENZA/PNEUMONIA SERIES

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S. H. Shakman
InstituteOfScience.com

We are nearing the centennial "celebration" of the greatest scourge of the 20th Century. Indeed, the Influenza Pandemic of 1918-1919 rivals only the Bubonic Plague of 1347-1351 as among the greatest global disasters in recorded history. The 1918-9 Pandemic killed an estimated 20-50 million persons world-wide, including some 675,000 Americans. In comparison, three U.S. influenza pandemics experienced since 1919 have caused far fewer deaths, i.e., 68,900 in 1957-8, 33,800 in 1968-9, and 8,870-18,300 in 2009-2010. [flu.gov/pandemic/history/]

Unfortunately this downward trend in deaths can't wholly be attributed to advancements in therapy and vaccines, but rather, at least partly, to luck. The particularly-deadly strain of influenza and influenzal-pneumonia that struck in 1918-19 has not re-emerged since. But it could. Indeed, notwithstanding presumed advances in vaccine technology, e.g., including development of trivalent and quadrivalent vaccines (three or four strains resp.), vaccines have proved to be merely just about 50 to 60 percent effective most years. [cnbc.com/2015/10/19/the-16-billion-business-of-flu.html]

Thus, it is not surprising that the medical community and government(s) approach annual influenza "season(s)" with heightened caution. According to the CDC, while flu activity can occur throughout the year, it tends to start in October and peak between December and March. [cdc.gov/] (The opposite pattern is observed in the Southern Hemisphere, which gives respective hemispheres a "heads-up" as to the possible identities of upcoming flu threats.)

And more than a half-year in advance of each impending flu season, authorities around the world mobilize the necessary resources to attempt to identify the probable or possible strains of the presumed-causative influenza microbe that may be appropriate for inclusion in the ultimate vaccine(s) to be used. Manufacturing and testing vaccines begins, with the ironic hope that these efforts may in the end prove unnecessary if the flu fizzles out on its own.

The costs of these annual exercises are not trivial. For example, the U.S. market for flu vaccine had been estimated at $1.6 billion in 2015, within a worldwide market of $4 billion. In addition there may be special efforts directed at special situations; e.g., in 2009 U.S. had indicated it would spend $1 billion to start the process of making an H1N1 influenza vaccine, beyond amounts being spent on the conventional flu program.

And while the attention in any flu season has been understandably directed to potential victims of influenza itself, special attention is also understandably directed toward those who may be susceptible to associated, potentially deadly, strains of influenzal pneumonia. The 2009 Pandemic turned out to be not the killer that had been feared; however, it had nonetheless fostered discussion of particular concerns regarding pneumonia:

"Preliminary results presented to the CDC vaccine committee in June by Dr. Matthew R. Moore, a CDC medical epidemiologist, indicated that about 40% of swine-flu-related pneumonia had an unknown cause -- and that about 30% were caused by S. pneumoniae. This suggests that at least a third of flu-related pneumonia deaths could be prevented by vaccination." [T.H. Baugh III, *Los Angeles Times*, August 4, 2009]

This suggestion sparked the recollection that E.C. Rosenow, through the Mayo Foundation, had reported a much larger reduction in deaths during the 1918-1919 pandemic with a vaccine he had developed at that time. The mortality rate in a group inoculated three times with Rosenow's vaccine was less than 1/4 (1.00/4.45) that of un-inoculated persons. Thus, Rosenow's vaccine may have prevented more than an *three-fourths of pneumonia deaths* (in persons receiving his vaccine, versus those not)

linked to the 1918-1919 Influenza Pandemic (see last column in Table i, below.) – *much better than the mere one-third* anticipated for the modern pneumonia vaccine!

This was the initial impetus for putting together a book comprised of E. C. Rosenow's comprehensive series of Pandemic articles. Notwithstanding that these 1919-1920 articles are available through most medical libraries, publication in a much more easily accessible combined book form seemed more than appropriate. And as the world keeps a watchful lookout for whatever scourge may strike next, it is clear that Rosenow's work may be as germane as ever.

E.C. Rosenow, MD, had joined the Mayo Foundation at its inception in 1915, after having worked closely for more than a decade with AMA Presidents Frank Billings and Charles Mayo, among a cadre of the finest medical minds of the era. He went on to serve as head of the Division of Experimental Bacteriology at the Mayo Foundation for nearly three decades (1915-1944). Thus he was well established at Mayo when the pandemic of 1918-9 occurred. He was Mayo's primary investigator during the crisis and was uniquely positioned to conduct exhaustive, definitive studies, including extensive vaccine trials.

Rosenow's work on the 1918-1919 pandemic had built on his prior work on pneumonia dating from 1903, including early reports on immunization (JAMA 59:795-796, 1912, and Science Mag., 1908) and treatment with autolysed pneumococci (JAMA 59:2203-2240, 1913, with L. Hektoen.) Prior to 1919, he had already published over 30 articles with titles referring to "pneumonia" and/or "pneumococci".

<u>The state of medicine prior to the pandemic of 1918-9:</u>

There were two particularly-relevant **distinct** medical histories coming into the 1918 pandemic:
(a) The "influenza bacillus" or "Pfeiffer's bacillus" hypothesis, carried over from the Pandemic of 1889-92; and
(b) A separate pneumonia vaccine experience in the early 1900s, following on the prior works of Sir Almroth Wright, Leishmann, Rosenow and others.

"The etiology of influenza was unknown at the time of the 1918 pandemic. Many contemporaneous investigators erroneously believed that bacteria, in particular Bacillus influenzae (Pfeiffer's bacillus, now known as Haemophilus influenzae) was the cause of influenza" [YW Chien, KP Klugman ,DM Morens, *JID* 2010:202, 1639]
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"… the notion that B. influenzae was the true cause of influenza persisted up to the time of the ... pandemic in 1918 ... when Rockefeller scientists Peter Kosciusko Olitsky [of Sabin-polio fame] (1886–1964) and Frederick L Gates (1886–1933) [*J Am Med Assoc* 1920;74:1497–1499] provided strong evidence against a causal association, documenting that the infective influenza agent survived passage through filters that excluded B. influenzae" [JK Taubenberger etal, *Antivir Ther* 2007; 12(4 Pt B): 581–591]
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"Bacterium pneumosintes appeared as a minute bacilloid body of regular morphology, measuring 0.15 to 0.3 micron in the long axis. Usually solitary, the bacteria were often found in diplo form, and occasionally in short chains of three or four members. … When grown on media containing nutrient broth, and especially in the presence of dextrose, Bacterium pneumosintes has developed larger bacillary forms up to 1 micron in length. The identity of these microorganisms with the original strains has been proved by serological reactions and by their reversion to the minute forms on transfer to the original medium." [PK Olitsky, FL Gates, *J Exp Med* 1922 October 31; 36(5): 501–519]

(a) ***The "influenza bacillus", or "Pfeiffer's bacillus", hypothesis***, carried over from the Pandemic of 1889-92, was the widely-considered claim by Pfeiffer to have found the cause of that pandemic in the so called "Influenza Bacillus" (aka *Hemophilus influenzae*). Despite considerable and widespread doubt concerning the role of Pfeiffer's bacillus by the time the 1918-1919 pandemic struck, the lack of a proven alternative kept Pfeiffer's bacillus prominently in consideration. Thus it became somewhat of a requisite for inclusion in seemingly most initially-proposed vaccines by various organizations, such as the New York Department of Public Health and the Public Health Service.

And even a century later, it is nonetheless sadly surprising that some portion of the general medical population is still subject to this apparently persisting wrongful impression, i.e., that *Hemophilus influenzae* caused the 1918 Pandemic. This became shockingly clear through a chance discussion of the subject circa 2011 with a USC internal medicine professor, who asserted in no uncertain terms, that the cause of the pandemic was established – "*Hemophilus influenzae*".

(b) ***The pneumonia vaccine experience***: Meanwhile, a large and distinct other body of work addressing the pandemic at its outset was the pneumonia vaccine experience, following from the prior and coincident works of Sir Almroth Wright, Lister, Leishmann, E.C. Rosenow and others. Pneumonia-directed vaccines

were widely used during the Pandemic, e.g., by U.S. and British armed forces, by Rosenow and the Mayo Foundation and many others. They made a lot of sense: While it was generally agreed that the cause of pandemic influenza had not been established, at least there was indeed a well-documented and successful history of immunization against pneumonia.

Not only do Rosenow's earlier pneumonia articles provide a fitting background for his 1918-1919 work on the Pandemic, and his associated work well beyond, but his continuing impact and importance have been prominently recognized well into the 21st Century. For example, among Rosenow's early pneumonia articles is his 1904 study of pneumonia and pneumococcus, which was reprinted and lavishly praised in a **2004 *J Infect Dis* article by Morton N. Swartz**: "The large body of evidence presented in a logical sequence, the use of appropriate controls, and the clear and thorough explication of results in this article published a century ago in the first issue of the Journal set a suitable standard for future investigators." (Swartz, M.N., *J Infect Dis*, 2004: 189, 1, 128-164, "Commentary: Rosenow EC. Studies in Pneumonia and Pneumococcus Infection". *J Infect Dis 1904; 1:280-312*).

-- Wright, A. E.; Morgan, W. P., et al., Lancet X: 1-10 (Jan. 3) 1914..
-- Lister, F. S.: South African Institute for Medical Research, W. E. Horton and Company, Ltd., 1917, pp. 1-30.
-- Cecil, R. L., and Austin, J. H.: J. Exper. M. 28:19-41 (July 18) 1918.

And a 2010 article by Y.W. Chien, K.P. Klugman & D.M. Morens (herein referred to as "Chien 2010") in this same journal illustrates the continuing importance of Rosenow's pandemic (anti-pneumonia) vaccines, and serves as a comprehensive confirmation of the unassailable body of work by Rosenow on the pandemic. **Most (~80%) of the approximately 230,000 total vaccines listed and assessed by Chien 2010 had been provided by Rosenow –** his own plus ¾ of Cadham's civilian total [see Table i below]. (Y.W. Chien, K.P. Klugman, D.M. Morens, *J Infect Dis* 2010 Vol. 202, 11, "*Efficacy of Whole-Cell Killed Bacterial Vaccines in Preventing Pneumonia and Death during the 1918 Influenza Pandemic"*)

While some of these pandemic pneumonia-directed vaccine efforts included some portion of the so-called Influenza (or Pfeiffer's) Bacillus, this seemingly was in reality a requisite inclusion based on "prevailing wisdom", i.e., insurance of a sort. Indeed, even Rosenow as well as prominent British authorities under Leishmann, who were doubtful about the relevance of Pfeiffer's bacillus, were compelled to include it in their initial mix of vaccine microbes. Some, such as Rosenow, subsequently dropped the Pfeiffer's bacillus out of the mix in the course of improving the vaccine being used.

Table i. Data in Chien 2010 & Incidence Ratios

FIGURES 2 & 3

DATA AS PUBLISHED IN CHIEN TABLES 3 & 4									Incidence Ratios		
	VACCINATED				NON-VACCINATED				per Totals		
Military	Total	Influ	Pneu	Died	Total	Influ	Pneu	Died	Influ	Pneu	Died
Cadham /Mili	4842	282	17	5	2758	238	41	17	1.48	4.23	5.97
Leishman	15624	221	26	2	43520	2059	583	98	3.34	8.05	17.6
Ely-StrepOnly	4212	144		0	8486	1409		96	4.86		96 / 0
Civilian - vaccines with pneumococci											
Watters	1638	89	13	8	1599	471	88	40	5.42	6.93	5.12
Rosenow	143760	13666	745	276	345133	97253	7534	2951	2.96	4.21	4.45
Cadham/Civil	52999	5203	300	85	85941	21285	1869	563	2.52	3.84	4.08
Minaker	6400	111		2	1233782	43671		3716	2.04		9.64
McCoy	390	119	23	10	390	103	17	7	0.87	0.74	0.7

Table i Key:
-- Incidence ratios (IR) are calculated as IR = ARU/ARV. where ARU = unvaccinated attack rate, and ARV = vaccinated attack rate.
-- Thus for Cadham /Military, the Incidence Ratio IR for "Died", "per Total" is: (17/2758) / (5/4842) = 5.97; i.e. the unvaccinated died at a 5.97 times the rate that the vaccinated died.
Chien YW, KP Klugman, DM Morens, *J.Infect.Dis.* 202, Oct. 28, 2010, p. 1639-1648
Cadham FT, *The Lancet,* May 29 1919, p. 885-6
Leishman WB, *The Lancet,* Feb. 14 1920, p. 366-8
Ely CF, BJ Lloyd, CD Hitchcock, DH Nickson, *JAMA,* Jan. 4 1919, p. 24-28
Watters WH, *Bost.Med. & Surg. J,* Dec. 25 1919, p. 727-731
Rosenow EC, BF Sturdivant, *JAMA,* Aug. 9 1919, p. 396-401
Minaker AJ, RS Irvine, *JAMA,* March 22 1919 - 847-850
McCoy GW, VB Murray, AL Teeter, *JAMA,* **71** No 24, Dec. 14, 1918, p. 1997

Table i provides raw data for "VACCINATED" and "NON-VACCINATED" persons, "Military" and "Civilian" categories, for all studies listed in Chien 2010 that provided totals and incidence data. As shown in the last three columns, "Incidence Ratios", vaccinated persons exhibited generally-huge advantages in terms of incidence of influenza, pneumonia and deaths.

At the same time, it would appear that the co-existence of the centenarian- ghost of "Pfeiffer's bacillus" aka *Hemophilus influenzae*, in the presence of the presumed causative influenza virus, might easily cause confusion.

Adding to this confusion is the circumstance that Rosenow's successful anti-pneumonia vaccine was not only remarkably successful against pneumonia, but it also was quite helpful against influenza as well!! Based on results of a half million survey responses to Mayo, those who were not vaccinated suffered influenza three times as often as those who were, and died from pneumonia at a rate four and half times higher!

Leaving aside for the moment consideration of the nature of the frustratingly-variable influenza virus, one might hope that Rosenow's pneumonia vaccine methodology would in any case be given serious consideration as an alternate to the pneumonia vaccines being proffered by contemporary pharmaceutical companies. In summary, its attributes:

-- one vaccine for both influenza and pneumonia;
-- huge quantities produced within 48 hours after isolation, pandemic or not;
-- consequential huge cost savings in research and production;
-- avoiding the complication of allergies to chicken-egg vaccines;
-- availability of an already-developed oral vaccine method;
-- implications for understanding epidemics and seasonality of infections:
-- viability of epidemic vaccine for years, implication for universal vaccine;
-- independence of Rosenow's pandemic work from that on "focal infection".
-- Price's 1923 Emendation – Pandemic Severity Mystery Solved?

<u>One vaccine for both influenza and pneumonia</u>

- Rosenow's vaccine was effective against both the influenza and pneumonia of the pandemic. Rosenow's results are supportive of and in concert with the idea, widely considered at the time, that both pandemic influenza and the associated distinctly-characteristic type of pneumonia may be caused by different phases of the same "pleomorphic" organism.

- But isn't influenza caused by a virus, and pneumonia by bacteria? Yes, but the virus associated with pandemic influenza and bacteria associated with pandemic influenzal-pneumonia are apparently intimately related -- different and reversible phases of the same microbe, depending on environment.

The term "virus" fundamentally denotes a small, filtrable size**.** The ability of some, if not all, microbes to change size and shape under varying environmental influences, or "pleomorphism", has been studied for well over a century (e.g., for early history, see Philip Hadley, *Jour. Infect. Dis.*1927, 1-312; and subsequent related articles, now available through Amazon.com as *Microbic Dissociation I-III*,). Specifically in the case of pandemic influenza, Olitsky [better known for work on polio with Sabin] and Gates (J Exp Med. 10/31/22) were among the first to show how the filtrable (viral) agent can be made to grow larger, to bacterial size, and revert to original smaller form, on appropriate culture media.

Rosenow: Over the years Rosenow conducted extensive tests demonstrating the intimate relation between implicated pneumonia (bacterial/ streptococcal) and influenza (viral) microbes, as described in a 1953 article: *"The Streptococcus appears to be the toxicogenic, antigenic phase, and the virus the relatively non-toxicogenic, non-antigenic, but highly invasive phase."* (from *A.M.A. Arch. Otolaryng. 5*8: 609 622, Nov. 1953 – Appendix B of this compilation)

Huge quantities produced within 48 hours after isolation

- Great quantities of vaccine can be produced quickly, i.e., within 48 hours of isolation of the causative strain. The U.S. Department of Health and Human Services has already committed more than a billion dollars to efforts to speed up the process of producing influenza vaccine, which currently takes months. Rosenow's vaccine, which works against influenza as well as pneumonia, takes a mere couple of days to produce huge batches. Rosenow's methodology is posted at http://instituteofscience.com/Ro-recdi.html, as described in *Am. Practitioner and Digest of Treatment,* 9(5), 1958, 755-761.

Consequential huge cost savings in research and production

- HUGE cost savings, annually -- BILLIONS.

Avoiding the complication of allergies to chicken-egg vaccines

- ***The Rosenow vaccine methodology does not involve chicken eggs***, thus avoiding the problem of egg allergies that afflicts many persons, as well as the time-consuming process of shipping hundreds of thousands of eggs to vaccine manufacturing plants, growing the virus in the eggs, extracting and killing the virus and distributing the vaccines.

Availability of an already-developed oral vaccine method

- ***An oral version of Rosenow's vaccine yielded "striking results"*** in preliminary tests in laboratory animals. "With its high concentration of hygroscopic sugars, bacteria are dehydrated, contaminants cannot grow, it does not require refrigeration, and dosage can be adjusted." (*Am. J. Clin. Path.* 8: 17-27, Jan. 1938, with FR Heilman)

Implications for understanding epidemics and seasonality of infections

- Rosenow addressed the cause of epidemics and seasonality of respiratory infections including influenza, as well as encephalitis and polio; he demonstrated how variations in the implicated causative organisms, directly attributable to variations in radiant energy, are the probable cause of seasonality. (*Postgrad. Med.* 7: 117-123, Feb. 1950; 8: 290-292, Oct. 1950.)

Viability of epidemic vaccine for years, implication for universal vaccine

- Rosenow's pandemic vaccine was successfully used against influenza for several years afterwards, having been preserved in glycerine-salt solution.

The late C.F. Williamson, Bacteriologist and Dean of the College of Arts and Sciences, U. of Miami, Oxford Ohio, had worked directly with Rosenow and was the last to have produced Rosenow's vaccines. According to Dean Williamson, "for many years I supplied those to physicians who would give those prior to the season arriving, and with very good results." (Quote at 7:00 in a 1999 telephone interview with this writer; audio is posted at: https://www.youtube.com/watch?v=zqesi_Q88ok)

"The holy grail for flu, researchers say, is to find a universal vaccine that would render remaking the vaccine every year unnecessary. … NIH's Dr. Anthony Fauci said he's optimistic a universal vaccine is five to 10 years away." [cnbc.com/2015/10/19/the-16-billion-business-of-flu.html]

Perhaps Rosenow's methodology might help accelerate this schedule.

Independence from Rosenow's work linking oral and systemic infections.

Further impetus for putting together this book was the apparent independence of Rosenow's Pandemic work vis-à-vis his seemingly-separate legendary work with Frank Billings and Charles Mayo et al. that had already thoroughly documented the relationship between oral infections and systemic disease – the so-called doctrine of "focal infection". Frank Billings, former AMA President and generally-acknowledged father of American medical education, had considered his focal infection work to be the landmark achievement of his incredible career. His 1916 book *Focal Infection* had featured Rosenow's 1915 JAMA article on the subject. But notwithstanding Rosenow's unimpeachable 3-decade-long career at the Mayo Foundation (1915-1944) and beyond, opposition by some dental and as well as some medical interests have continued to push back on the arguably-physiologically-sound science behind the focal infection concept. [For further discussion of historical opposition to Rosenow's focal infection legacy, see *Medicine's Grandest PhD*, available through Amazon.com.]

In any case, Rosenow's work on the 1918-9 pandemic seemingly opened a new vista for exposure – a chance to show his genius through a prism un-fettered by the continuing controversy over the role of oral foci in causing or contributing to systemic diseases. That said, a hospital study conducted by Weston Price DDS during the Pandemic but published later provides evidence that pre-existing oral infections may indeed have contributed to the severity of pandemic pneumonia and associated deaths.

Price's 1923 Emendation – Pandemic Severity Mystery Solved?

- So why did some suffer severe consequences in the 1918-9 pandemic, and others did not? This was the big take-away surprise of this research effort.

As indicated above, Rosenow's foundational work on pneumonia and pneumonia vaccines preceded, and was seemingly independent of, his well-known body of works implicating oral foci in a range of disease conditions. Thus it was hoped that the success of his pneumonia-related works, and his Pandemic contributions, could help shed fresh light on his monumental works overall.

Nonetheless, it was of great interest that, as the research progressed, "circumstantial" evidence seemed to be pointed to a virulent phase of a streptococcus (streptococcus viridans) commonly found in the mouth, albeit usually in a relatively non-virulent form, as the underlying organism responsible. The role of this organism in pandemic influenza-pneumonia seems to have been implicated first by Mathers (*JAMA* 1917 March 3, **68** (9):678-680, who was also an early victim) and confirmed in depth by Rosenow and others. The distinctive age of victims, i.e., adults in their prime, versus the age of victims of common forms of influenza (generally the very young or very old) is further suggestive that pre-existing oral infections may have contributed to the severity of the pandemic in some persons.

- Weston Price's documentation of the correlation between oral infections and severity of pandemic complications: Adding evidence to the hypothesis of an oral infection/ pandemic correlation is a study published by Weston Price in his 1923 book, "Oral Infections and Systemic Disease" (Volume I, Chapter xxi, p. 266-7), which reported:

" … I made a careful study of influenza patients in five hospitals, three in city [Cleveland] and two in Columbus, in the epidemic of 1918. This was a exceedingly difficult study to make for several reasons: First, the patients involved were frequently too ill to be questioned with sufficient care to bring out all the data; and second, it was not possible to make roentgenographic studies, and many cases of dental infections were undoubtedly overlooked, since only those were included which were sufficiently gross to be determined definitely by oral examination, palpation, etc. A study of **two hundred sixty influenza patients in five different hospitals, Figure 137**, disclosed that that when the patients were divided into two groups – those with, and those without clearly demonstrable dental infections – the **percentage of individuals developing serious complications** (in which we included pneumonia, empyema, carditis, severe neuritis and severe rheumatism) was found to be **in the group without dental infections 32 per cent, and in the group with serious dental infections 72 per cent.** Several factors should be carefully noted: In the pneumonias, the tendency to strangulation following coughing spasms, as a result of the bronchial exudates, produced violent inspirations which draw into the lung, fluids and infections from the mouth. This makes gingival infections a very marked contributing factor to the development of pneumonia. In general, however, the so-called locked infections (by which we mean those at root apices without opportunity for drainage in to the oral cavity, which therefore must drain into the system, into the lymphatic and hematogenous circulations) are more to be feared since the system much of necessity become invaded from this source, with a breaking down of the local defense which has tended to wall off and defend the patients in times of their normal defense."

[Weston Price, *Dental Infections, Oral and Systemic,* 1923, Vol. I, 265-6]

Not proof positive, but certainly suggestive! This study by Weston Price, Rosenow's close associate for decades, was not available until 1923, thus not incorporated nor cited within Rosenow's 1919-1920 Pandemic series.

Table ii – from Weston Price, Oral Infections and Systemic Disease I, p. 267

ORAL INFECTIONS AND INFLUENZA COMPLICATIONS

Hospital	Date	No. of Flu Cases Studied	Flu Only	Flu with Various Complications	Flu with Pneumonia	With Oral Infection			Without Oral Infection		
						Total	Flu Only	Flu with Complications	Total	Flu Only	Flu with Complications
1 Lakeside, Cleveland Men's Ward	Nov. 30	20	13–65%	7–35%	7–35%	8–40%	2–25%	6–75%	12–60%	10–83%	2–17%
2 Lakeside, Cleveland Women's Ward	Dec. 1	6	1–17%	5–83%	5–83%	5–83%	1–20%	4–80%	1–17%	0	1–17%
3 St. Francis Columbus	Dec. 4-5	23	5–21%	18–78%	9–48%	18–22%	3–17%	15–83%	5–78%	2–40%	3–60%
4 Grant, Columbus Nurses	Dec. 5	50	41–82%	9–18%	2– 4%	0	Held certificates from dentists		50–100%	41–82%	9–18%
5 Grant, Columbus Private Patients	Dec. 5	51	38–74%	13–26%	8–16%	0	None known		51–100%	38–74%	13–26%
6 City Hospital Cleveland	Dec. 7	26	8–31%	18–69%	15–51%	23–88%	7–30%	16–70%	3–12%	1–33%	2–67%
7 Mt. Sinai Cleveland	Dec. 19	31	14–45%	17–54%	10–32%	21–68%	8–38%	13–62%	10–32%	6–60%	4–40%
8 Mt. Sinai Cleveland Nurses	Dec. 16	53	38–72%	15–28%	13–24%	0	Clean mouths		53–100%	38–72%	15–28%
Eight Sources		260	158–61%	102–39%	69–26%	75–29%	21–28%	54–72%	185–71%	136–68%	49–32%
Private Practice Patients		37	14–38%	23–62%	14–23%	37–100%	14–38%	23–62%	0		

But even without the Price emendation, the success of Rosenow's and the other Pandemic vaccines argues forcibly for renewed consideration in modern times. Swartz's 2004 endorsement of Rosenow's earlier pneumonia work, as well as Chien 2010's support for further investigation and reconsideration, are certainly welcome steps in this direction.

E.C. Rosenow's multi-faceted perspective on the pandemic was published as an eleven-part series, parts 1-4 in 1919 in the *Journal of the American Medical Association*, and parts 5-11 in 1920 in the *Journal of Infectious Diseases*. This series comprises the essential body of this present publication, as augmented by:

– Appendix A: Rosenow's summary 1929 article (*Minnesota Med.* **12**, 1929);

– Appendix B: His last dedicated influenza/pneumonia article, 1953, which discussed his substantial associated body of work on this subject over five decades (*A.M.A. Arch. Otolaryng.* **58,** Nov. 1953); and

– Afterword: A supplemental overview of the intimate relation of Rosenow's Pandemic work to the subsequent Post-Influenzal (Von Economo's) Encephalitis Lethargica ("sleepy sickness") epidemic, and this to the issue of the infectious etiology of various neurological conditions.

S. H. Shakman
Institute Of Science
InstituteOfScience.com / I-o-S.org
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