



BY JEFF MORTIMER

TEAM FLU

ANSWERS THE CALL

To learn from history, and avoid a repeat, government turns to the U-M

Howard Markel is used to all sorts of telephone calls from the media, government officials, public health professionals, doctors and scientists. As someone who has spent two decades studying epidemics and American society, he has been particularly in demand in our age of HIV, tuberculosis and malaria, not to mention the recent concerns over SARS and influenza. But one call late on a Friday afternoon before the July 4 weekend in 2005 surprised even Markel — it was from the Pentagon.

At the other end of the line was Cleto DiGiovanni Jr., M.D., of the Department of Defense's Defense Threat Reduction Agency (DTRA).

DiGiovanni needed medical historians who understood the social, scientific, as well as epidemiological contexts of pandemics. The staff of the U-M Center for the History of Medicine fit the bill precisely.

The agency was looking for evidence of the effectiveness of so-called non-pharmaceutical interventions (NPI) in slowing the spread and mitigating the damage of a devastating outbreak of



The Princeton Student Naval Training Corps in 1918. Princeton was one of the sites studied by Team Flu.
From the *The Princeton Bric-a-Brac*, Vol. XLIV, June 1, 1919. Courtesy of the Princeton University Library.

infectious disease. These interventions included quarantine of those exposed to the illness; isolation of the infected; social distancing (i.e. closing schools and prohibiting public gatherings); wearing masks in public; frequent hand washing; and educating the public. Until adequate supplies of vaccine and antivirals became available, they would be the only arrows in the public health quiver.

In an age of avian flu and bioterrorism, when no place on Earth is more than a day's flight from any other place, it was hardly a far-fetched scenario, yet such evidence would be impossible to come by experimentally. DiGiovanni had studied the containment strategies used in Toronto during the 2003 SARS epidemic, but that was a small, localized data set.



“In looking at potential interventions, the only source of actual experience that we had was historical, not scientific,” he says. “Once I came to that fairly obvious conclusion, it became equally obvious that we needed to get a historian on board.”

It also was obvious that the richest vein of such data was the influenza pandemic that swept the world in four deadly waves between 1918 and 1920. Fueled by troop concentrations in trenches and military installations in the waning months of World War I, the disease eventually claimed an estimated 50 million lives worldwide, including 675,000 in the United States. A comparable mortality rate today would mean more than two million American fatalities.

Although the agency primarily was interested in protecting military personnel, a disaster of such magnitude, whether occurring naturally or as an act of war, clearly would be a “defense threat.” Virology was in its infancy in 1918, and the most widely administered anti-flu vaccine at the time was useless. Any community that escaped the scourge had to have relied on non-pharmaceutical interventions.

Most of the popular accounts of the pandemic have provided some anecdotal evidence of communities that experienced unusually low morbidity and mortality. Yet they are scant on specifics, and, with avian flu on everyone’s radar, specifics are urgently needed by federal government officials. Indeed, with effective vaccine only on the horizon, non-pharmaceutical interventions have become a major part of the national containment strategies announced by the federal government in early February.

DiGiovanni consulted with senior public health officials around the country who would ultimately use this kind of information, as well as key people in the disease containment areas at the U.S.

Centers for Disease Control and Prevention (CDC). U-M physician and historian Markel’s name kept coming up. He is the George E. Wantz Distinguished Professor of the History of Medicine, professor of pediatrics and communicable diseases, and director of the Center for the History of Medicine.

As it turned out, the study DiGiovanni had in mind — to define and identify provisional escape communities and document what they did — required a *team* of historians. A massive amount of newspapers, posters, diaries, letters, and public health records, tucked away in archives from California to Vermont, had to be located, accessed, evaluated and analyzed, and a report produced, in little more than six months.

Thus, Team Flu was born. In addition to Markel as principal investigator, it comprised Alexandra Stern, M.D., associate director of the center and the Zina Pitcher Collegiate Professor of the History of Medicine, as co-PI; Joseph Michalsen, a recent U-M honors history graduate, and Alexander Navarro, Ph.D., a lecturer in the Program in American Culture, joined as research associates.

The team defined a provisional escape community as a municipality or institution reporting relatively few cases of influenza and one death or fewer while non-pharmaceutical interventions were employed during the second, and worst, wave of the pandemic, from September to December 1918. They found seven that fit that description: Gunnison, Colorado; Fletcher, Vermont; Princeton University, Princeton, New Jersey; Bryn Mawr College, Bryn Mawr, Pennsylvania; Western Pennsylvania Institution for the Blind, Pittsburgh, Pennsylvania; Trudeau Tuberculosis Sanatorium, Saranac Lake, New York; and the San Francisco Naval Training Base, Yerba Buena Island, California.

Gunnison, Fletcher and Yerba Buena all benefited from their geographic isolation. Although Yerba Buena Island is in San Francisco Bay, for example, there was no bridge from the mainland at the time, and the naval station was supplied via ferry from San Francisco. The tale that it had been secured at gunpoint was one of the myths shattered by the study — sailors unloading the ferries at the Yerba Buena docks were required to maintain a distance of at least 20 feet from ferry operators, according to Markel.

Constructing accurate narratives was one of the team’s major achievements. “Along the way, we made an important discovery. Specifically, we identified a concept we called protective sequestration, which, unlike a quarantine that isolates those suspected of being ill, describes those communities that shut themselves off from the outside world before an epidemic even reaches their border,” says Markel.

The study concluded that protective sequestration, if enacted early enough in the pandemic, crafted so as to encourage the compliance of the population involved, and continued for the lengthy period of time in which the area is at risk, stands the best chance of protection against infection.

“Such conclusions are easier to describe than to implement,” Markel says. “If you are a small town nestled in the Rockies, or an island in the middle of San Francisco harbor, where you could protectively sequester yourself before the advent of the flu in 1918, you had a fighting chance. Unfortunately, that’s not necessarily a useful strategy for most people living in today’s world.”

Nevertheless, the concept of protective sequestration has caught on among many policy makers as a possible tool in the containment of a worst-case scenario pandemic of 1918-like proportions until ➤



Alexandra Sloan, Alexandra Stern, Howard Markel, Alexander Navarro and Joseph Michalsen

enough vaccine could be produced and distributed to immunize a susceptible population.

The report, published in abbreviated form in *Emerging Infectious Diseases*, the journal of the CDC, can be accessed at www.med.umich.edu/medschool/chm/influenza/assets/dtra_final_influenza_report.pdf.

The project's fruits included a boon to future researchers — the digitization of all the archives that were analyzed, available at www.med.umich.edu/medschool/chm/influenza/.

Understanding the full limits of historical inquiry, DiGiovanni insists the U-M study opened up a dialogue on how to use a variety of research tools, from historical research to evidence-based studies, in evaluating the efficacy of non-pharmaceutical interventions in mitigating influenza pandemics.

"This study is not hard evidence that you would present to a grand jury," he notes, "but it certainly tells an intriguing story, one we ought at least to consider when we look at measures that might be employed during a future influenza pandemic."

The story of Team Flu hardly ends here. In June 2006, Markel received a call from Atlanta. This time it was Martin Cetron, M.D., director of the CDC Quarantine and Global Migration Division. Cetron and his colleagues at CDC, the U.S. Department of Health and Human Services, and the White House Homeland

Security Council are playing a principal role in developing public health guidelines in the event of a 1918-like worst-case-scenario pandemic.

Cetron was in the audience when the results of the first study were presented in April 2006 to a gathering of scholars and government officials concerned with pandemic control. The report included a recommendation for further study — the analysis of major American cities, some of which did better than others in terms of mitigation of the 1918 pandemic. Cetron had been thinking the same thing.

"I find that I can learn a lot to apply to current practice and future strategy by understanding the historical context in which our work has arisen," Cetron says. "It became very important for me to understand what lessons we could glean from non-pharmaceutical interventions that may have been taken by cities in 1918, because the first wave of a pandemic in the 21st century might be fought with a similar toolbox until a vaccine is developed or an adequate supply of antiviral is around."

As a result, CDC hired Team Flu for a far more comprehensive project. "They said, in effect, 'We really liked your methods, we really liked your results and conclusions, let's do an even bigger study,'" says Stern, whose specialty is the development of local public health agencies. "They wanted us to look at 45 of the most populous U.S. cities for which the data exist, in order to see what public health meas-

ures they implemented, the timing of those measures, who implemented them, and what compliance was."

It was a good thing Team Flu already had a steep learning curve behind it — the CDC wanted a preliminary report by December 2006 and a final report by July 2007.

"In my career, this is the project that has entailed detailed analysis of the largest amount of paper, with the most manpower and the shortest turnaround time," Markel says.

Typically, historians work alone, but this project is so mammoth that the center has become "almost like a history laboratory," says Stern.

"It's collaboration in the truest sense of the word," says Navarro, who is the project manager for the CDC study. "We each have certain areas that we've become mini-experts on, so it's doubly important that we're able to pop into each other's offices here at the center or discuss issues with our partners at the CDC."

The team was bolstered for the CDC study by the addition of Alexandra Sloan, a student of Markel for four years who had just completed her undergraduate degree in history. By December 2006, Team Flu had collected and processed data on all the communities in the study in consultation with a team of statisticians and epidemiologists at the CDC.

"The conventional wisdom of the sweeping history of flu in America in 1918, is

that every American city was decimated by the pandemic. Indeed, nearly three-quarters of a million Americans died during the event and millions more became critically ill. The conclusion of such a story might be that none of the NPI measures taken back then had any impact at all on the containment or mitigation of influenza,” Markel says. “But if you look at them individually with very fine-grained statistical and qualitative analysis,” he quickly adds, “you find that every city had a very different experience and not a few did surprisingly better than most of the others.”


Although data analysis is ongoing, the preliminary conclusions Team Flu is making on the utility of non-pharmaceutical interventions are striking. To begin, cities that applied NPIs earlier in the pandemic wave appeared to have lowered and delayed peak excess death

rates; moreover, earlier non-pharmaceutical interventions implementation was associated with proportionately lower death rates than expected.

That this research is of such pressing interest to policy makers lends what Stern calls a *frisson* to the enterprise. It could have ramifications for how communities think about the implementation of public health strategies. “There really is a sense of urgency that something needs to be generated so that Americans can be prepared,” she says. “That’s what makes it exciting and that’s what makes it daunting. We can come to a variety of understandings of what happened in 1918, but to draw conclusions that might have potential policy ramifications for today is a very tricky thing to do.”

How their work will pay off in that regard is an open question. Nevertheless,

the center already has garnered international accolades for its work.

Says Markel, “Here you have the confluence of a group of scholars who are adept in studying the history of epidemics, the potential threat of a devastating flu pandemic, an extraordinary archive of NPI data from the last, most serious influenza pandemic (1918), and the need to come up with a policy of how to comfort such contagious challenges. This marriage of federal governmental agencies, policymakers, and the U-M Center for the History of Medicine has catapulted us to places we never expected to go. Perhaps this has become the greatest adventure of my career at Michigan because our work has proven to be of such critical importance to the nation’s health.” 

TEAM FLU — WEST COAST STYLE

*Archive helps students experience
medical research*

One of the outcomes of Team Flu’s project for the Defense Threat Reduction Agency is a complete digital archive of all historical materials consulted for the study. Accessible since fall, the site allows researchers and the general public access to records to better understand how some communities responded to the devastating pandemic of 1918-20.

Among the first to use it were four juniors at Valley High School in Sacramento, California. The team of Nazeela Sabir, Ashleen Kishore, Khanh Nguyen and Deepika Vijay is competing in National History Day, an annual contest in which middle and high school students conduct extensive primary research and present their findings. Their project is an exhibit on the 1918-20 influenza pandemic.

At the Sacramento Archives Museum Collection Center, the students found a master’s thesis written by Linda Johnson on the flu’s effects in Sacramento. They located and interviewed Johnson, an archivist at the California State Archives, who had helped Team Flu members research the use of face masks in California.

Johnson directed the students to the Team Flu Web site, www.med.umich.edu/medschool/chm/influenza, and put them in touch with Alexandra Stern, Ph.D., co-principal investigator of the study.



Photo: Scott Lorenzo

Clockwise from top left: Khanh Nguyen, Deepika Vijay, Nazeela Sabir and Ashleen Kishore

“I talked to them for over an hour, answering their questions about the project and discussing the content and scope of the digital archive,” Stern says. “I think it’s great that they’re using the archive to do their project. That is precisely why we put it on the Web.”

The Sacramento group found the death records especially helpful because it allowed them to see how influenza affected many areas in California. “They did what they could during that time, which was the non-pharmaceutical interventions,” Vijay says.

“This connects to how we can face an epidemic today if we’re not able to create an effective vaccine,” Sabir says. And investigating the effects of one bug seems to have infected them with another. Sounding a little surprised, she adds, “We’ve actually become more interested in the history of medicine, and in doing research.”

—Jeff Mortimer