Influenza - The Last 100 Years, 1918 to 2018
By Paul A. Granato, Ph.D., Director of Microbiology

Introduction
Influenza is a seasonal viral respiratory disease that has likely caused human infections since antiquity. The first major documented outbreak of influenza was in 1918 and caused pandemic disease resulting in an estimated 50 million deaths worldwide. Since that time, there have been periodic epidemics, the most recent being the outbreak of the “swine” flu in 2009. Given the severity of disease and the high incidence of influenza that the United States recently experienced, the purpose of this article is to provide a brief overview of the last century of influenza disease, the viruses responsible for infection, and public health measures to prevent or at least minimize the severity of the disease.

The Spanish Flu - 1918
A century ago, a third of the world’s population, or around 500 million people, came down with a disease that was dubbed the Spanish flu. The disease got its name when the king of Spain, Alfonso XIII, his prime minister, and several cabinet members came down with the disease. Worldwide, at least 50 million and perhaps as many as 100 million people died from the disease with more than two thirds of them dying in a single 10-week period in the autumn of 1918. In the United States, 675,000 people died in about a year, which is the same number of individuals who died from AIDS over the last four decades.

The first confirmed case of flu in the 1918 outbreak occurred in a mess cook stationed at an Army training facility in Kansas. The military camp, with its crowded conditions and over 100,000 troops in transit, served as a “perfect storm” for the transmission of disease. These soldiers were then shipped to Europe to fight WWI where the infection was transmitted throughout Europe and subsequently around the world, producing the resultant global pandemic. By the end of 1918, flu had killed at least 57,000 American soldiers – 4,000 more than those killed in combat.

It is of interest that influenza was first mistakenly thought to be caused by a bacterium, *Haemophilus influenzae*, an opportunistic organism that commonly accompanies influenza infections. It was not until 1931 that Dr. Ernest Goodpasture, an American pathologist, discovered that influenza was actually caused by a virus. From that initial Spanish flu outbreak of mistaken identity, the influenza virus got its name.

Other Flu Epidemics
Since the 1918 flu pandemic, periodic outbreaks of influenza A disease have been documented throughout the world. Some of the notable U.S. outbreaks occurred in 1976 and 1988 and, most recently, the swine flu outbreak in 2009. All of these outbreaks were caused by influenza A H1N1. Worldwide influenza A outbreaks have also been documented. Some of the more notable outbreaks have originated in Hong Kong (1968, influenza A H3N2), in the Philippines (2007, influenza A H1N1), in Northern Ireland (2009, influenza A H1N1), in Nepal (2015, influenza A H1N1), and in India (2015 and 2017, influenza A H1N1). During the current 2017 to 2018 flu outbreak, most of the infections occurring in the U.S. are caused by influenza A H3N2.

Influenza Virus
There are four types of influenza viruses: type A, type B, type C, and type D. Influenza D viruses primarily infect cattle and are not known to cause infections in humans while influenza C can cause infections in both humans and pigs. However, infections in humans are generally mild and rarely diagnosed or documented.

Influenza A viruses are of the greatest significance to public health because of their potential to cause epidemic and pandemic outbreaks. The influenza A viruses are classified into subtypes according to the combinations of two major virus surface glycoproteins, called hemagglutinin (HA) and neuraminidase (NA). To date, there are at least 18 different...
Your cooperation in providing diagnostic information is essential to the efficient operation of our lab. Without appropriate diagnostic documentation, we cannot get paid for our services.

Additionally, diagnostic information can determine whether or not an ABN should be signed. You can either provide an ICD-10 code or a written diagnosis in the space provided on the requisition.

Providing diagnostic information when ordering a test not only helps us operate efficiently and get paid for our services, it can also eliminate the time and expense the physician office may incur when reviewing files and responding to our requests.

**NCDs and LCDs**

National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs) tests and information concerning appropriate diagnosis codes can be found on Laboratory Alliance’s website at [laboratoryalliance.com](http://laboratoryalliance.com) under the **Healthcare Providers** tab. There, you will find:

- Specific test CPT codes for which medical necessity rules have been defined.

- The ICD-10 or diagnosis codes that Medicare will accept as documentation that the listed test is reasonable and necessary for diagnosis or treatment. ICD-10 codes supporting medical necessity must be included on the requisition form. The diagnosis must be present for the procedure to be paid and there must be documentation within the patient’s medical record. **Medicare and Medicare Managed Care plans do not pay for laboratory testing that is ordered using screening diagnosis codes.** Codes such as Z00.00 through Z13.9 will not be paid by Medicare. The non-covered ICD-10 codes are listed on our website at [laboratoryalliance.com](http://laboratoryalliance.com) under the **Healthcare Providers** tab. If a non-covered ICD-10 code is used, the test may be billed to the Medicare beneficiary without billing Medicare first.

**Note:** When ordering a test that does not meet NCD or LCD guidelines, an Advanced Beneficiary Notice (ABN) should be signed by the patient. The purpose of the ABN is to give the patient advance notice that Medicare may not pay for the test ordered. When payment is denied as not medically necessary, Laboratory Alliance can only bill the patient if we have received a valid (i.e., signed) ABN.

**Reflex Testing**

Reflex testing is testing that is performed as a result of initial test results which are used to further identify significant diagnostic information required for appropriate patient care. A list of the reflex tests that are performed when appropriate is on our website at [laboratoryalliance.com](http://laboratoryalliance.com) under the **Healthcare Providers** tab, and on the back of our requisitions.

**Panels**

Organ or disease panels will only be billed and reimbursed when all test components are medically necessary. If only some components are medically necessary, or if the physician wishes to order other tests not included in the panel, those tests should be ordered individually. A list of tests included in the American Medical Association acceptable panels is included on our requisition and on our website at [laboratoryalliance.com](http://laboratoryalliance.com) under the **Healthcare Providers** tab. Medicare reimbursement amounts for these tests can be found at: [www.cms.hhs.gov/ClinicalLabFeeSched/](http://www.cms.hhs.gov/ClinicalLabFeeSched/). Medicaid reimbursement will usually be equal to or less than the Medicare reimbursement.

**Clinical Consultation Services**

Appropriate test use and ordering may be discussed with Laboratory Alliance’s Medical Director, Michael Graber, M.D., available by contacting our Customer Service Department at 315-461-3008.
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Brenda Alkins Advocates for Cancer Patients in our Nation’s Capitol

Lead Device Trial Specialist Brenda Alkins, MT(ASCP), M.S., was selected by Hematology-Oncology Associates of CNY as their patient advocate representative to attend the Community Oncology Alliance Conference from April 10 to 13 in Washington, D.C.

Brenda, who works in our Microbiology Department at the Operations Center, participated in the Patient Advocacy track at the conference, attending meetings and sessions for two of the days. On the remaining day, she served as a representative advocating for all cancer patients and survivors to members on Capitol Hill. Brenda was one of 90 cancer patient advocates representing 12 states who met with congressional representatives and senators to discuss issues relating to cancer, survivorship, community-oncology centers, healthcare, pharmacy and insurance coverages. Each patient advocate had an opportunity to share their life stories and personal experiences of their cancer journeys by putting a human face to these sessions.

“I was honored for the opportunity to represent Central New York cancer survivors as a patient advocate at this important congressional conference,” Brenda said. “We appreciated meeting with Congressman Katko and the time he spent listening to our concerns.”
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hemagglutinin subtypes and 11 different neuraminidase subtypes. Depending on the host origin, influenza A viruses can be classified as avian influenza, swine influenza, or other types of animal influenza viruses. Some examples include avian influenza or “bird flu” virus subtypes A H5N1 and A H9N2, or swine influenza or “swine flu” virus subtypes A H1N1 and A H3N2.

Influenza B viruses circulate among humans and can cause seasonal epidemics. Some studies have shown that seals can also be infected by influenza B virus.

Epidemiology and Transmission

Influenza causes seasonal epidemics in geographical areas with temperate climates but, in tropical climates, seasonality is less apparent with influenza infections occurring throughout the year. In temperate regions of the United States, epidemics generally occur between December and April. The year 2017 was unusual for influenza because, according to Laboratory Alliance's Microbiology Department, which began documenting influenza infections in September, the numbers significantly increased with each succeeding month. As of April 7, 2018, a total of 168 influenza-associated pediatric deaths alone have been documented already in the U.S. for the 2017 to 2018 season. Sadly, this number will likely increase with each passing day until the flu season “runs its course” and finally ends.

According to the World Health Organization, in a typical year, seasonal influenza epidemics cause three to five million severe cases and 300,000 to 500,000 deaths globally each year. In the U.S., influenza accounts for 140,000 to 710,000 influenza-related hospitalizations and 12,000 to 56,000 deaths each year with the highest burden of disease occurring in the very young, the very old, and individuals with coexisting underlying medical conditions.

Influenza viruses are transmitted from person to person primarily via droplets generated by sneezing, coughing, and speaking. Direct and indirect contact with inanimate objects contaminated with secretions and small particle aerosols are other potential routes of transmission. Following exposure to influenza, the typical incubation period before the development of symptomatic disease is one to four days, but may be as long as two weeks. Influenza A and B virus infections spread rapidly through the community with clinical attack rates as high as 70% following a common source exposure in an enclosed space.

Symptoms of Disease

Influenza A and B virus infections typically cause a febrile respiratory illness characterized by fever, cough, upper respiratory tract symptoms including sore throat, runny nose, and nasal congestion. Systemic symptoms of headache, muscle aches, and malaise may also be present. The fever generally lasts three to five days, but the symptoms of dry cough and malaise may persist for several or more weeks. Complications may include otitis media in children, sinusitis, lower respiratory infection with secondary bacterial pneumonia, exacerbation of underlying cardiac or pulmonary disease, myositis, and neurologic complications of seizures, acute encephalitis, and death. In contrast, influenza C viruses cause very mild respiratory illnesses that are indistinguishable from the common cold, which is one reason they are rarely diagnosed.

Diagnosis

Early diagnosis of infection is important for the prompt administration of an appropriate antiviral agent. Many clinical microbiology laboratories, such as Laboratory Alliance, offer a molecular gene amplification (PCR) assay that can establish the laboratory diagnosis of influenza infection within 60 minutes of specimen receipt. This laboratory service is offered by Laboratory Alliance's three hospital Rapid Response Laboratories, as well as Laboratory Alliance's Operations Center. The service is available 24 hours per day, seven days per week.

Treatment

A few antiviral agents, such as Tamiflu (Oseltamivir) and Relenza (Zanamivir), are available for the treatment of influenza. These antiviral agents, however, do not cure the disease but minimize the severity of symptoms and reduce the period of viral shedding.

Prevention

Vaccination is the most effective way to prevent influenza infection. Even though vaccines are not always effective in preventing disease, the immunity that develops following vaccination can minimize the symptoms of infection and the serious life-threatening complications that can result.

A factor that can alter vaccine effectiveness is the manner in which they are manufactured. In the United States, most influenza-vaccine viruses are propagated in eggs. During this egg-based production process, the vaccine virus may undergo changes in the HA glycoprotein that facilitates replication in eggs. Since the influenza HA glycoprotein is the primary target for the neutralizing humoral antibodies that are produced following vaccination and are necessary to prevent infection, small modifications in the HA glycoprotein can cause minor changes in the virus which may decrease vaccine effectiveness. Because of this, efforts are currently underway to develop a universal vaccine which will offer protection against the majority of influenza viruses by inactivating the virus by influenza-specific T-cells instead of humoral antibodies. The universal influenza vaccine is not yet commercially available.

Other useful personal protective measures include: frequent washing of hands with soap and water or with alcohol-based hand sanitizers; good respiratory hygiene (covering one’s mouth and nose when coughing or sneezing); and wearing a mask.

Vaccination is the best way to prevent influenza infection.
Syracuse City School District P-TECH Program

P-TECH Freshmen Present at Laboratory Alliance
By Mark Jordan, Ed.D., Education Coordinator

The Pathways in Technology Early College High School (P-TECH) program is a progressive educational model designed to provide academically at-risk students with the opportunities to graduate high school, complete a two-year degree, and secure employment in high-demand STEM careers (Science, Technology, Engineering and Mathematics). P-TECH is a collaborative model incorporating a K-12 school district, an institution of higher education, and a business partner. Each of these participants contribute to the development of students’ academic, technical, and career readiness skills and prepare them to hit the ground running as they enter the workforce.

Laboratory Alliance is a proud business partner in the Syracuse City School District’s P-TECH program in Clinical Laboratory Technology. As a business partner, our employees volunteer to serve as career coaches and work with P-TECH students, preparing them for a career as medical laboratory technicians. On a regular basis, our career coaches participate in mentoring events where they work with students, either one-on-one or in small groups, to complete challenges that target certain professional, technical or academic skills.

On April 17, Laboratory Alliance hosted 23 freshmen from the district’s Clinical Laboratory Technology and Health Information Technology programs. At this culminating event, students highlighted their research on Laboratory Alliance and the clinical laboratory science profession. Synthesizing the information they collected from multiple resources (including structured interviews they conducted with career coaches from prior mentoring events), the students summarized their findings in PowerPoint presentations. While some students presented as a team, other students presented independently.

The audience was diverse, comprising the students’ peers, teachers, career coaches and parents. Fifteen career coaches — representing Laboratory Alliance, Upstate Medical University, and Crouse Health — attended this event and praised the students for their accomplishment as well as provided constructive feedback for further development. The most noted praises awarded by several of the career coaches included the students’ professional appearance, demonstration of teamwork and courage to speak confidently in front of a group of professionals. Following the presentations, career coaches provided scaffolding to students as they completed mock job applications and interviews, as students prepare for future volunteering or part-time work opportunities.

Engaging with adult professionals during mentoring events, such as this one, provides a unique and highly effective mechanism for the P-TECH students to develop professional, academic and technical skills. The process of the student-career coach interaction ultimately strengthens the P-TECH students’ employability post-graduation, providing them with a competitive advantage over their peers. The success of this mentoring event is a testament to the commitment from all the partners and the integrity of the students. I would like to offer a special “thank you” to the career coaches who dedicated time to participate in this event: Michael Adetu, Maria Dillon, Brenda Henry, Dan Ho, Susan Maloney, Lazaro Martinez, Katie Raimondo, Rita Romano, Debra Shannon, Angela Smith and Jennifer Walczyk.

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Sneezing); imposing self-isolation by staying home when feeling unwell, feverish, and having symptoms of the flu; avoiding close contact with influenza infected people; and, avoiding touching one’s eyes, nose or mouth as such contact may facilitate virus entry into the body resulting in infection.

Summary

Despite the best efforts of public health officials to combat influenza and to develop effective vaccines, it is likely that the influenza viruses will continue to cause disease each year for the foreseeable future. In some years, the vaccines available may be less effective because the influenza A virus has the unique ability to undergo spontaneous re-assortment of its H and N surface glycoproteins. When this happens, as has been the case this year, the vaccines may offer only partial immunity against infection. Despite this, individuals must be encouraged to receive the vaccine because partial immunity is better than none at all.

Perhaps our yearly battle with influenza can best be summarized by the words spoken by Nobel Laureate, Dr. Joshua Lederberg, as he was discussing the AIDS epidemic in the early 1990s, “The 1990s have been marked by a renewed recognition that our human species is still locked in a Darwinian struggle with our microbial and viral predators.”
Announcing

Dr. Steve Landas Joins St. Joseph’s Pathology, PC

Laboratory Alliance welcomes Steve Landas, M.D. to our affiliated pathology practice at St. Joseph’s Health. Dr. Landas brings with him more than 30 years of experience as a practicing anatomic and clinical pathologist. He earned his medical degree in 1983 at the University of Iowa Carver College of Medicine, where he also completed his residency in 1987. This was followed by a fellowship in surgical pathology at Ohio State University College of Medicine.

Kristina Mennig Named RRL Manager at St. Joseph’s Health

Kristina Mennig was named laboratory manager of Laboratory Alliance’s Rapid Response Laboratory (RRL) at St. Joseph’s Health. Previously, Kris was manager of our RRL at Upstate University Hospital Community Campus and she served as technical supervisor of chemistry at the RRL at St. Joseph’s Health (from 2011-2013.)

Kris’s medical technology experience includes director of clinical lab services at Crystal Run Healthcare in Middletown and Rock Hill N.Y., and medical technologist positions at Polymedco Inc. in Cortlandt Manor, N.Y., and at Vassar Hospital in Poughkeepsie, N.Y.

She earned her Bachelor of Science in Medical Technology from Marist College and her Master of Science in Health Management and Policy from New School University in New York City. She is licensed as a clinical laboratory technologist in the state of New York.

Publications and Presentations

Dr. Granato co-authored the following scientific articles:


Workshops:

Lead Device Trial Specialist Brenda Alkins MT(ASCP) and Director of Microbiology Paul Granato, Ph.D., were invited guests to attend a users’ group workshop in Limerick, Ireland, sponsored by Serosep. Serosep is a manufacturer and distributor of laboratory diagnostic solutions based in Limerick.

Presentations:

Dr. Granato was an invited presenter at the Association of Molecular Pathology annual meeting held in November in Salt Lake City. His talk was titled “Applications of Molecular Diagnostics for the Early Detection of Septicemia.”

Dr. Granato and Device Trial Specialist Melissa Unz were co-authors on the scientific abstract “Evaluation of clinical performance of PanNat nucleic acid STEC test for detection and differentiation of Shiga-toxin expressing E. coli in diarrheal stool specimens,” submitted in 2018 at the ASM Microbe 2018 conference, sponsored by the American Society for Microbiology in Atlanta, Ga.

Abstracts:


Dr. Granato, Medical Technologist Nancy Tucci and former Laboratory Alliance Device Trial Specialist Jennifer Lillie were co-authors on a scientific publication titled “Multicenter evaluation of the Bruker MALDI Biotyper CA system for the identification of clinically-important bacteria and yeasts.” It was published in 2017 in the American Journal of Clinical Pathology.

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www.hospicecny.org/golf2018

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LA Newsmakers

New Employees
Please welcome our new employees

At our Operations Center
Sandra Barone - Shift Supervisor
David Bugnacki - Courier
Jannati Chowdhury - Technical Assistant
Deneen Cole - Technical Processing Assistant
Daniel Dennis - Laboratory Office Assistant
Nicola Giles - Phlebotomist
Joelle Kerr - Laboratory Office Assistant
David Korycinski - Courier
Marina Lupu - Technical Processing Assistant
Gregory Moore - Phlebotomist
Megan Phelan - Technical Processing Assistant
Roxanna Randall - Referral Testing Specialist
Teresa Rumble - Histotechnician
Trinisha Sanjurjo - Phlebotomist
Thomas Tracy - Courier

At our Rapid Response Laboratory
at Crouse Hospital
Khadijah Kabba - Medical Technologist
Janelle McBride - Laboratory Office Assistant
Hannah Reilly - Technical Processing Assistant

At our Rapid Response Laboratory
at St. Joseph’s Hospital
Minda Flores - Technical Processing Assistant
Colleen Jackson - Point of Care Technician
Tiffani Meglino - Laboratory Office Assistant
Kristina Mennig - Manager, RRL
Dylan Washburn - Medical Laboratory Technician

At our Rapid Response Laboratory
at Upstate University Hospital-Community Campus
Corrinne Spaulding - Medical Technologist

Laboratory Alliance employees contributed $560 to The American Heart Association® Go Red For Women and participated in the National Wear Red Day® on Feb. 2.

Employee Anniversaries

January, 10 years
Donald Stone

January, 20 years
Maureen Conklin
Mary Ellen Milczarski
Russell Rawling
Rebecca Reynolds
Debra Shannon
Margaret Thompson

February, 5 years
Jaclyn Hughes

February, 10 years
Jeffrey Baker

February, 20 years
Mary K Clancy
Nancy Crossett
Cheryl Haskins
Janet Miller

March, 10 years
Kathleen Hass

March, 15 years
Malinda Desjardins
Carol Freitas

March, 20 years
Eric Henry
Kathleen Laubenstein
Michele Scott

Thanks, Laboratory Alliance

Laboratory Alliance employees filled 10 boxes with non-parishable food and household items during Laboratory Professionals Week ‘Wear Jeans to Work Day,’ which were delivered to the Food Bank of CNY.

“Opportunity is missed by most people because it is dressed in overalls and looks like work.” - Thomas Edison

Lab Crew Wins League
Rachel Elder, M.D., (bottom row, left), the director of our Rapid Response Laboratory at Crouse Hospital and head of Pathology Associates of Syracuse, is also a soccer star in her free time. Her team, the “Lab Crew,” has been playing for several years and this year the team was number one in their women’s soccer league.
laboratory medicine helped save lives. The professionals in the medical laboratory save lives every day.

In 2014, I authored an Elsevier article about our profession entitled “The Hidden Profession that Saves Lives.” [6] Yet, when I ask almost anyone in the public who we are (medical laboratorians) and what we do, they typically do not know the answer. Since we are often doing your important and critical medical laboratory work, you do not see us in the immediate healthcare environment (bedside, family physician office, etc.). You see the physician, the nurse, the respiratory therapist, the physical therapist, and others. These healthcare professionals may even take blood from you or other types of specimens for analysis. However, most people do not know what happens to their specimens (blood, sputum, urine, etc.) once they arrive in the laboratory. They do not know that medical laboratory professionals will conduct some of the most complex and important work on those specimens, and that knowing the results of that work may very well save your life. [6,7] Did you know that medical laboratory professionals provide up to 70% of the medical lab results/data for physicians and others to make informed decisions about one’s diagnosis and treatment plan? [6,7]

In a recent TEDx talk at Texas State University, I used the metaphor of the airline industry to help explain this issue. [8] Most people know who the doctor (airline pilot), nurse, respiratory therapist, etc. (flight attendant), or medical staff at the front desk of an emergency department (ticket taker) are when they go to the hospital or their family care office; however, they have no idea who the medical laboratory professionals (airline ground crew) are that are taking care of everything else. [7] The medical laboratory professionals are the healthcare ground crew! In addition, just as you may not think about the critical role that the airline ground crew plays in your safe flight, you probably do not think about the lifesaving role that your healthcare ground crew – the medical laboratory professional – plays in your healthcare! Nevertheless, I bet you want them doing their job well every day!

Ask your physician, nurse, pharmacist, or biology graduate about vitamin C acting as interference in glucose and triglyceride testing, or causes of false positives in pregnancy testing, or World Health Organization classifications for Hodgkin disease and diagnostic criteria, or ways to test for swine flu (H1N1) and avian flu (H5N1), or genetic testing modalities for cystic fibrosis, or who is most likely to show antibodies to Kell during a STAT emergency test for life-saving blood in surgery, or any other critical laboratory test and its interpretation. These aspects of laboratory testing are generally not in the body of knowledge of any of these medical professionals, and yet it is completely in ours. Formal coursework training in medical laboratory testing comprises a small portion of the curriculum for physicians, nurses, pharmacists, physical therapists, occupational therapists, and biology graduates. However, for MLS and MLT students, medical laboratory theory for all 1,000+ available laboratory tests, sources of interference, and connections between test results and diagnoses is the primary focus of their studies. [6,7]

We must share lessons learned, short-term remediation, and future opportunities so other medical laboratories and their personnel can be better prepared for future mass casualty incidents. I, and many of my medical lab colleagues, hope to reveal this profession to the masses that do not know about this college major and amazing career path and journey.

Learn more about this lifesaving profession today and share it with everyone. We just might end up saving your life one day!

References

7. Rohde RE. Medical Laboratory Professionals Save Lives every day, but do you know who we are? April 20, 2016. https://infectioncontrol.tips/2016/04/20/medical-laboratory-professionals/

Calendar of Events

Friday, June 1
St. Joseph’s Hospital Health Center Foundation’s Gala at Turning Stone. Laboratory Alliance is a sponsor.

Monday, June 11
Upstate Foundation Towsley Pro-Am Golf Tournament at Shenendoah at Turning Stone Resort and Casino. Laboratory Alliance is a participant and sponsor.

Friday, June 15
Hospice Golf Open, The Links at Erie Village. Laboratory Alliance is a sponsor.

Monday, July 16
Crouse Health Foundation Classic Golf Tournament at Bellevue Country Club. Laboratory Alliance is a sponsor.