In the Literature

**Social Distancing and Pandemic Influenza**


The attack rates and associated mortality during the 1918 influenza pandemic varied greatly among cities in the United States. The fact that cities, at a time when there was no effective vaccine or antiviral therapy, took greatly different social approaches in their attempts to control the outbreak has provided an opportunity for 2 groups of investigators to make correlations between those measures and outbreak severity in an attempt to estimate the potential efficacy of individual measures.

These analyses concluded that among the most effective measures were those that created “social distancing,” such as closure of schools, churches, theaters, and other places of gathering. Simultaneous implementation of multiple measures was more effective than less aggressive approaches. As might be expected, efficacy was greater when multiple measures were instituted earlier in the pandemic than later and when they were continued for longer periods of time. Maintenance of restrictive measures for prolonged periods becomes difficult as the population begins to resist them after the initial shock of the effects of the pandemic. This proved to be problematic, because the 1918 epidemic tended to sweep through cities in waves, so that a new wave would hit the city after the initial large-scale social distancing measures had been lifted.

Modern day urban populations in the United States are, by some estimates, less likely to be compliant with restrictions on lifestyle than were populations 90 years ago, making prolonged maintenance of similar measures likely to be more difficult. Furthermore, there have been vast social changes, including greater urbanization, as well as greater local and international mobility. On the other hand, antiviral drugs will be available for some individuals, and a vaccine may become available during a pandemic, although after a considerable delay.

The Centers for Disease Control and Prevention’s recent Community Strategy for Pandemic Influenza Mitigation [1] indicates the need for a variety of protective measures. These include the isolation and treatment of all individuals with confirmed or probable pandemic influenza; the voluntary home quarantine of other household members; the dismissal of students from child care, schools, and school activities at all levels together; and maintenance of social distancing outside of those settings. Measures should also be taken to reduce contact between adults in both the community and the workplace with such tactics as cancellation of large public gatherings and alteration of workplace environments and schedules to decrease social density.

**Reference**


**Hitchhiking Adamantine Resistance in Influenza A**


The incidence of resistance to the adamantines, amantadine and rimantadine, among clinical isolates of influenza A virus in the United States increased from ~1%–3% before the 2004–2005 season to >90% during the 2005–2006 influenza season; a similar pattern also occurred in China and Japan. It was generally assumed that the rapid emergence of resistance to this class of antivirals was the result of selective pressure exerted by widespread use of adamantines. Simonsen and colleagues have now examined publicly available influenza virus sequences and have concluded that an alternative evolutionary mechanism was at play.

Every recently examined adamantine-resistant isolate from the United States has the same amino acid substitution (S31N) in the M2 protein, which is the target of this class of antiviral agents. S31N, however, is only 1 of 5 amino acid replacements in M2 known to be associated with amantadine resistance. If selective pressure exerted by these agents was the single cause of emergence of resistance, substitutions in addition to S31N would also have been expected in individual isolates. Furthermore, despite the widespread emergence of this virus in Japan, there had been little use of adamantines in the previous 6 years.

Phylogenetic analysis indicated that the recent S31N viruses, which are altered in an additional 17 amino acids, comprised a single lineage, which is called the “N-lineage” by the investigators. This lineage apparently emerged, possibly in China, in early 2005 and then spread to other regions. Evidence suggested that this lineage arose as the result of an extensive reassortment event.

The increase in the prevalence of this virus from <5% to >90% over a very short period of time strongly indicates the effects of powerful natural selection. Such a rapid event, in fact, is common with influenza A virus, because it escapes immune pressure by alteration of surface antigens by reassortment events. The mutations associated with N-lineage virus do not, however, measurably alter results...
in a standard hemagglutinin inhibition assay. At least 1 of the amino acid substitutions (D225N) is located adjacent to a key receptor-binding site, and its presence may result in enhanced fitness under the pressure exerted by the immune system.

The rapid, geographically dispersed emergence and dominance of this virus, which universally contains just a single resistance mutation, together with its rapid emergence in regions with extremely limited adamantane use, argue strongly against the selective pressure of use of this class of agents having a dominant role in its success. Instead, the investigators propose that the rapid spread of resistance to this class of drugs was the result of “hitchhiking” of resistance mutations along with other mutations that provided a selective advantage to the virus. This linkage to beneficial mutations allowed S31N to go along for the ride and, in the process, eliminated the usefulness of amantadine and rimantadine for the treatment of human influenza virus infections. Furthermore, as Simonsen and colleagues point out, if this accurately describes the evolutionary events that have occurred to date, restriction of adamantane use will not lead to reemergence of virus susceptible to these drugs.

Where Have All the Birds Gone?


LaDeau and colleagues examined the effect on the bird population of the introduction of West Nile virus into the United States. They examined 20 species from 11 families, including species spanning a range of expected impacts. Ten-year population lows were reached by 13 of the 20 species in 2002–2003. The most clearly affected species were the crow, blue jay, American robin, eastern bluebird, chickadee, tufted titmouse, and the house wren. These 7 species are all peridomestic and associated with suburban environments.

The effect was most dramatic in American crows, whose population had been increasing for 2 decades, but which decreased by almost one-half between 1998 and 2005. This decline was correlated with the intensity of the human epidemic within each region studied. In contrast, however, blue jays and house wren populations had returned to expected levels by 2005.

This dramatic ecological effect of an introduced virus has implications not yet fully understood. One short-term result, which initially seems paradoxical, may be an increase in human cases of infection as a consequence of a shift in feeding preferences from birds to humans by the mosquito vector. Thus, during one season, Culex pipiens, which bites both birds and humans, demonstrated a 7-fold increase in feeding preference from the former to the latter coincident with a reduction in the local population of its preferred host, the American robin [1]. The longer-term effects remain to be seen, but the rapid recovery of at least some species is somewhat comforting.

Reference


Fluoroquinolone Resistance in Neisseria gonorrhoea


Despite a ∼4-fold decrease in the incidence of gonorrhea in the United States between 1975 and 2003, the incidence remains as much as 25 times greater than that in other developed countries. The history of gonorrhea treatment over the decades has been one of loss of efficacy of one antibiotic after another, because of the emergence of resistance. As a consequence of the emergence of penicillin resistance, fluoroquinolones have replaced penicillins for treatment of this sexually transmitted disease. However, fluoroquinolone resistance, first identified in 1991, has now become so problematic that, by 2003, resistance was present in 39% of cities participating in the Gonococcal Isolate Surveillance Project, and 4.2% of all isolates were resistant. The highest frequencies were on the West Coast, consistent with the introduction of antibiotic-resistant strains from Asia. Fortunately, resistance to ceftriaxone, cefixime, azithromycin, and spectinomycin remains rare. These data are reflected in the Centers for Disease Control and Prevention’s recently updated therapy recommendations [1].

Reference