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...
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production of West Nile virus into the United
effect on the bird population of the intro-
West Nile virus emergence and large-scale
LaDeau SL, Kilpatrick AM, Marra PP.

This rapid, geographically dispersed
emergence and dominance of this virus,
which universally contains just a single re-
sistance mutation, together with its rapid
emergence in regions with extremely
limited adamantine use, argue strongly
against the selective pressure of use of this
class of agents having a dominant role in
its success. Instead, the investigators pro-
pose that the rapid spread of resistance to
this class of drugs was the result of “hitch-
hiking” 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, elim-
inated 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, restric-
tion of adamantine use will not lead to
reemergence of virus susceptible to these
drugs.

Where Have All
the Birds Gone?

LaDeau SL, Kilpatrick AM, Marra PP. West Nile virus emergence and large-scale
declines of North American bird popu-

LaDeau and colleagues examined the
effect on the bird population of the intro-
duction 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 pop-
ulation lows were reached by 13 of the 20
species in 2002–2003. The most clearly af-
fected species were the crow, blue jay,
American robin, eastern bluebird, chick-
adee, 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 in-
creasing for 2 decades, but which de-
creased 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 pop-
ulations had returned to expected levels
by 2005.

This dramatic ecological effect of an in-
roduced 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 pref-
ences from birds to humans by the mos-
quito vector. Thus, during one season, Cu-
lex 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 some-
what comforting.

Reference


Fluoroquinolone Resistance
in Neisseria gonorrhoeae

Wang SA, Harvey AB, Conner SM, et al. Antimicrobial resistance for Neisseria gon-
orrhoeae in the United States, 1988 to
2003: the spread of fluoroquinolone re-

Despite a ~4-fold decrease in the inci-
dence of gonorrhea in the United States
between 1975 and 2003, the incidence re-
mains as much as 25 times greater than
that in other developed countries. The his-
tory of gonorrhea treatment over the de-
cades has been one of loss of efficacy of
one antibiotic after another, because of
the emergence of resistance. As a conse-
quence of the emergence of penicillin resistance,
fluoroquinolones have replaced penicillins
for treatment of this sexually transmitted
disease. However, fluoroquinolone resist-
ce, first identified in 1991, has now be-
come so problematic that, by 2003, resis-
tance was present in 39% of cities par-
icipating in the Gonococcal Isolate
Surveillance Project, and 4.2% of all iso-
lates were resistant. The highest frequen-
cies were on the West Coast, consistent
with the introduction of antibiotic-resis-
tant strains from Asia. Fortunately, resis-
tance to ceftriaxone, cefixime, azithro-
mycin, and spectinomycin remains rare.
These data are reflected in the Centers for
Disease Control and Prevention’s recently
updated therapy recommendations [1].

Reference

1. Centers for Disease Control and Prevention. Updated recommended treatment regimens for
gonococcal infections and associated conditions
United States, April 2007. 5 June 2007. Available
at: http://www.cdc.gov/std/treatment/
2006/updated-regimens.htm. Accessed 27 Sep-
tember 2007.
DOI: 10.1086/523715