

Health Network Watches for Epidemics, Bioterror

BY MARK BLOOM
Contributing writer

Every 15 minutes, every day, every tidbit of medical and health news from thousands of the world's newspapers streams by computer into a small room at the Canadian Centre for Emergency Preparedness and Response.

There, seven analysts sift the most relevant of the fresh articles in a ceaseless hunt for hints of a newly emerging disease epidemic or the subtle signs of a spreading bioterror attack.

The worldwide computer network that brings articles from 10,000 public news sources into the nerve center of the Global Public Health Intelligence Network (GPHIN) is ever alert, seeking suggestions of an outbreak of SARS or avian influenza in Asia, a sign of Ebola in Africa or anthrax in Florida, or an indication of excessive radiation anywhere. It looks for the barest hints of an illness no one has seen before. It looks for a known disease to pop up for the first time in a continent where it is unknown—much like the West Nile virus's appearance in North America.

Most of the reports are trashed by the

computer out of hand, but a few stay on the system for human analysis. Once or twice a day, the computer spots something so ominous or so important, in the view of the automated program, that it e-mails an alert to the World Health Organization and other GPHIN users, Peter Uthoff, M.D., said in an interview. He is chief of counterterrorism coordination and health information networks for the Public Health Agency of Canada. GPHIN is one of his networks.

The automatic alerts have usually involved infectious disease but have also focused on chemical spills and radionuclear accidents. As for bioterrorism, Dr. Uthoff added, "our purpose is to give an advance notice, as early as possible, and get the information as soon as possible to our users. The sooner they know, the better. Whether it is bioterrorism or an accidental nuclear event, it makes little difference, because the initial stages of reaction are the same."

The GPHIN II network scans 10,000 Web sites, and articles not discarded immediately are reviewed by a language analyst for public health implications.

GPHIN was inaugurated in 1998 to screen the English-language newspaper literature. Last November, GPHIN was relaunched as GPHIN II, and it now sifts reports in Arabic, French, Russian, Spanish, and both simplified and traditional Chinese. Each language has an analyst fluent in the language and familiar with public health issues.

The GPHIN II upgrade was funded with \$560,000 Canadian by the Nuclear Threat Initiative, a Washington-based group founded by Sam Nunn, the former U.S. senator, and Ted Turner. It is dedicated to reducing the worldwide threat of nuclear, biological, and chemical weapons.

The articles that are not trashed immediately or that don't merit an automatic e-mail are the ones that need to be reviewed by a language analyst for public health implications. The analyst also edits the computer's translation to English, going back to the source language if necessary; each sees about 200 articles a day, Dr. Uthoff said.

Articles that pass muster are retained after editing on the GPHIN system and passed on to the GPHIN subscribers, such as the WHO and the U.S. Centers for Disease Control and Prevention.

Some reports might be of local interest with national implications; the arrival of West Nile virus in New York City would have been such a story. Others could have global implications, such as a worsening or spread of the avian flu outbreak in Asia.

U.S. reports with immediate patient implications are relayed to primary care physicians in the standard way, by state public health authorities. Yet with its active surveillance, GPHIN II allows authorities to rapidly connect the dots of isolated incidents in an outbreak.

Mark Smolinski, M.D., senior program officer of biological programs at the Nuclear Threat Initiative, cited the hantavirus outbreak a few years ago in the southwestern United States as a regional but isolated pattern. "Doctors are going to benefit by better, earlier detection of epidemic disease throughout the world and subsequently getting [the information] to the physician much earlier than if we didn't have such a system in place," he said. ■

Telithromycin Offers a Path to Tailored Treatment in Respiratory Infections

BY BRUCE JANCIN
Denver Bureau

ORLANDO, FLA. — Telithromycin is an excellent first-line choice for empiric outpatient treatment of mild-to-moderate respiratory tract infections, Carman A. Ciervo, D.O., declared at a satellite symposium held in conjunction with Wonca 2004, the conference of the World Organization of Family Doctors.

The drug, first in the novel ketolide class of antibiotics, has well-established efficacy against the full spectrum of respiratory tract pathogens: the typical and atypical ones, as well as resistant strains. Most importantly, it provides a tailored spectrum of coverage, sparing the primarily enteric gram-negative pathogens such as *Escherichia coli* and *Proteus mirabilis*. This will minimize emergence of resistance among gram-negatives that cause important GI and urinary tract infections, explained Dr. Ciervo, chairman of the department of family medicine at the University of Medicine and Dentistry of New Jersey School of Osteopathic Medicine, Stratford.

"I think the advantage that the ketolides have, similar to what the macrolides had in the early '90s, is that they really are a judicious way to prescribe to treat a respiratory tract infection. They cover the bugs that you need to cover for a respiratory tract infection, including the resistant organisms. I wouldn't be prescribing drugs in this class if I was concerned about diverticulitis or a urinary tract infection, but for the respiratory tract telithromycin is certainly a good choice," added Dr. Ciervo, who is on the speakers' bureau for Aventis, which sponsored the symposium.

Collateral damage to gram-negative pathogens is a significant problem with the fluoroquinolones, with their broad spectrum. It's for this reason that the Centers for Disease Control and Prevention recommends the newer fluoroquinolones not be used as first-line therapy in community-acquired pneumonia.



The ketolides 'really are a judicious way to prescribe to treat a respiratory tract infection.'

DR. CIERVO

"Better that we reserve them for when we really need them to cover the gram-negatives. When you're treating a respiratory tract infection, why not prescribe an antibiotic that's tailored for patients with respiratory tract infections? That way we can impact future resistance rates of GI tract and urinary pathogens," he continued.

The fluoroquinolones and ketolides share a property that imparts a low propensity to develop resistance: dual binding to the bacterial ribosome. Alteration of the ribosomal binding site is an important mechanism by which bacteria become resistant to antibiotics. This is less likely to occur when a drug has two binding sites.

Unlike the fluoroquinolones, the macrolides, another often-prescribed class of drugs in outpatient respiratory tract infections, don't cause collateral damage to gram-negative pathogens. But they don't cover the full spectrum of respiratory tract pathogens. Macrolide-resistant *S. pneumoniae* is also an emerging problem. It appears to be promoted by use of macrolides having a very long half-life. Azithromycin, for example, has a 72-hour half-life and, consequently, a high potential to select for resistance due to prolonged exposure to subtherapeutic drug concentrations. Telithromycin, in contrast, has a 10-hour half-life.

Telithromycin features once-daily dosing and a 5-day treatment course. This is the direction in which state-of-the-art antimicrobial therapy is headed. There is a growing appreciation that patient compliance falls off dramatically with dosing more than once daily or for more than 5 days, he said.

In response to an audience question, he described doxycycline as "an important and underutilized option" for respiratory tract infections in younger patients—say, those aged 15-50—without comorbid conditions or other significant risk factors for resistant infection, such as having kids in day care, chronic renal insufficiency, asplenia, or a recent history of β -lactam therapy. "I think doxycycline is still a good agent," he stressed. ■

FluMist Found Safe And Effective in Children, Teens

The live, attenuated, cold-adapted influenza vaccine, also known as CAIV-T (FluMist) was safe and effective in children aged 60 months to 17 years in the second year of its use for prevention of flu.

The CAIV-T vaccine was first available for use during the 2003-2004 season and was designed to contain three flu strains that matched those recommended by the FDA for the annual trivalent inactivated vaccine. Robert B. Belshe, M.D., of St. Louis University and colleagues reviewed a safety trial that included 6,657 children aged 5-17 years and an efficacy trial including 312 children aged 60-71 months. (*Clin. Infect. Dis.* 2004;39:920-7).

The safety trial evaluated medically attended events within 42 days of vaccine administration. Overall, the frequency of events in four categories—acute respiratory events, acute gastrointestinal events, systemic bacterial infections, and rare events possibly associated with wild-type influenza—was not significantly different between the 4,452 children in the vaccine group and the 2,205 children in a placebo group.

Results from the efficacy study showed an efficacy rate of 87% for children aged 60 months and older and no significant increase in the frequency of fevers greater than 37.8° C. In addition, no significant increase in frequencies of runny nose, nasal congestion, vomiting, or muscle aches was noted among the vaccine recipients compared with the placebo group.

The data confirm that the efficacy of CAIV-T extends to the youngest children in the age range for which it is currently recommended, Peter F. Wright, M.D., of Vanderbilt University, Nashville, Tenn., said in an editorial (*Clin. Infect. Dis.* 2004;39:928-9).

—Heidi Splete