ID CONSULT

Flu Season Throws Some Clinical Curveballs

This year's influenza season, while mild so far, comes with a few of Mother Nature's curveballs that will impact our approach to prevention and treatment.

Normally, peak influenza activity hits by mid-January, and as of mid-January this year, the Centers for Disease Control and Prevention (CDC) had reported influenza in 49 of the 50 states. However, only one state (Virginia) has had widespread influenza activity, 5 have had regional activity, and 10 have had local disease activity. Sporadic activity has been reported in 33 states, the District of Columbia, and Puerto Rico. But at this writing in early February, we're just now seeing a notable increase in influenza-like illnesses and culture documentation that both influenza A and B have arrived here in Kansas City.

BY CHRISTOPHER J. HARRISON, M.D.

This late start sends a clear message about prevention: It's not too late to vaccinate. All children aged 6 months and older now are recommended to receive influenza vaccination. But because infants younger than 6 months are not eligible for influenza vaccine and antiviral medications are not indicated for those younger than 1 year, a "cocoon" strategy is best for infants. This approach works by immunizing the persons most in contact with infants—mostly family members, but ideally also the day care personnel, babysitters, etc., thereby creating a "zone of protection" around the child.

The CDC's Advisory Committee on Immunization Practices (ACIP) is moving toward a universal recommendation for *all* persons over age 6 months to receive the influenza vaccine. Expect that recommendation to be made within the next year. In the meantime, recent data suggest that cross-protection and protection in general is likely to be superior with intranasal vaccine, compared with injected vaccine. Unfortunately, the intranasal vaccine (FluMist) is not approved for use in children under 2 years old or adults older than 50 years. I'd like all health care staff to be able to receive it, and I wish the ACIP would recommend its use in the 50-plus age group, despite current labeling.

To date it appears that this season's influenza vaccines match the circulating A strains, while the influenza B match may not be quite as good. However, it's still too early to predict for certain because the number of isolates is small and so far mostly from only three states.

With regard to influenza treatment, the circulating strains thus far are presenting us with a clinical conundrum: For the last 2 years, we've been told to stop using rimantadine and amantadine because they don't work on influenza A (they were never effective for influenza B), and to restrict antiviral therapy to two available products, oseltamivir and zanamivir. Now we find that we need to partially reverse course. This year, two-thirds of typed circulating strains are H1N1 strains that are resistant to oseltamivir but surprisingly susceptible to rimantadine/amantadine.

Of the strains currently circulating, one-quarter is influenza B and is still susceptible to oseltamivir and zanamivir. Less than 10% of all circulating strains have been H3N2, and these also are still susceptible to oseltamivir and zanamivir, but resistant to rimantadine/amantadine, similar to last year. So far, the proportions of types A vs. B in Kansas City have been the same as the proportions reported nationally by the CDC.

So here's how it could work clinically: If the patient presents within 48 hours of fever onset and a rapid antigen test shows influenza B, you can proceed as in the last 2 years and treat with oseltamivir or zanamivir.

But if it's influenza A, it gets tricky: About 90% of the influenza As—the H1N1s—will be susceptible to rimantadine and resistant to oseltamivir, but the reverse is true for the 10% or so that are H3N2s. So for influenza A, it seems reasonable to offer rimantadine but explain that there's a 10% chance it won't work. Amantadine also is an option, although it has more frequent and often more severe side effects.

If the patient desires 100% certainty, the CDC says to consider both antivirals—rimantadine plus oseltamivir. We don't have prospective controlled data for using these two together, because this particular problem previously was not on our radar screen. Doing so also doubles the cost of treatment.

And here's another odd twist: Zanamivir, the neuraminidase-inhibitor cousin of oseltamivir, is still active against all circulating strains we've seen so far, including those that are resistant to oseltamivir. The problem with zanamivir, though, is that it's not approved in children under 7 years of age. Also, it is administered via rotahaler (also called a diskhaler), which can be tricky to manipulate. But if your patient is skilled in or capable of using this device, zanamivir is another option.

Remember, though, that these antiviral drugs are likely to reduce the duration of illness in otherwise normal influenza patients only if started within 2 days of fever onset, so the earlier we can intervene, the better. One study showed that starting oseltamivir within the first 12 hours of fever reduced illness by 3 days (41%) more than starting it at 48 hours of fever.

To be able to distinguish among the H1 and H3 influenza A strains, the most widely available tool is multiplex polymerase chain reaction. However, this can be expensive, ranging from $600 to $1,200 depending on the lab. Despite the conundrum posed by this year's A-strain divergent resistance, I don't think that these tests are worth the cost in outpatients. Consider such testing, however, in hospitalized patients or those at high risk for influenza complications, such as immunocompromised patients.

You can keep track of changes in influenza activity or resistance at www.cdc.gov/flu. Also, interim guidelines for treatment of confirmed or suspected influenza infection can be found at www2a.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00279. ■

DR. HARRISON *is a professor of pediatrics and pediatric infectious diseases at Children's Mercy Hospitals and Clinics, Kansas City, Mo. He has no financial conflicts of interest pertaining to any of the products discussed in this column. Write to Dr. Harrison at pdnews@elsevier.com.*

Behavioral Screening Helps Catch HSV-2 in Young Women

BY HEIDI SPLETE
Senior Writer

WASHINGTON — Herpes simplex virus type 2 infected approximately one-third of the young women in a study of 127 adolescents, but behavioral and demographic factors were more predictive of disease than were clinical symptoms.

Data from population-based studies have shown that herpes simplex virus type 2 (HSV-2) most often is acquired by women between the ages of 20 and 29 years, but many of them have no clinical symptoms, said Dr. Kenneth Fife of Indiana University in Indianapolis.

To determine the demographic and behavioral factors associated with HSV-2 infection in young women, Dr. Fife and his colleagues collected data for 4-6 years from 127 adolescents aged 14-18 years at baseline. The researchers presented their results in a poster at the jointly held annual meeting of the Interscience Conference on Antimicrobial Agents and Chemotherapy and the Infectious Diseases Society of America.

Of the study population, 92% were black and 7% were white; 33% were antibody positive for HSV-2 at baseline. Only three participants had a history of clinically diagnosed herpes when they entered the study, and the participants underwent quarterly screening for incident STDs.

Each participant kept a detailed behavioral diary for two 12-week periods each year and collected weekly vaginal swab samples during these 12-week periods. At the conclusion of the study, the average age of the participants was 21 years.

"Only increasing age, increased time since sexual debut, and an increased number of lifetime sexual partners were significantly correlated with a positive HSV-2 test," Dr. Fife noted. The odds ratios for these factors were 1.36, 1.17, and 1.09, respectively.

The researchers found no significant association between a positive test result and recorded clinical symptoms of genital pain or discharge.

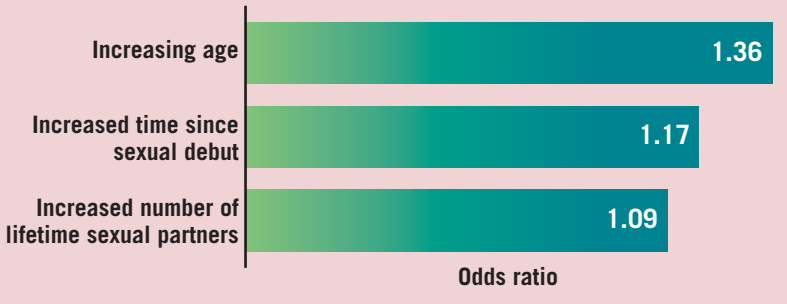
Of 121 participants for whom complete behavioral data were available, 67 had previous sera available for HSV-2 antibody testing, and 17 (25%) of these women seroconverted from negative to positive during the course of the study.

The DNA testing for HSV-2 in the study population is ongoing, but preliminary results from 13 women with positive results on polymerase chain reaction tests showed that most of the participants shed virus from the genital tract and most had several positive DNA tests over a single 12-week period.

The study was limited by the use of self-reports, but the results suggest that HSV-2 control programs should include young women because they shed virus frequently despite a lack of clinical symptoms, and early signs of infection may go unrecognized, Dr. Fife said.

The study was supported by a grant to Dr. Fife from GlaxoSmithKline and funding from the National Institutes of Health. ■

Factors Significantly Associated With HSV-2 Positivity



Note: Based on a study of 127 adolescents aged 14-18 at baseline.
Source: Dr. Fife