Experiencing West Nile virus

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West Nile virus is entering its fifth summer in North America. This virus has maintained a high profile for public health, medical practitioners, environmental groups and the popular press since the initial recognition of indigenous acquisition of human illness on this continent. The arrival of the virus in North America, in 1999, was unexpected. Through subsequent summers, the range has expanded rapidly, but unpredictably. New modes of transmission continue to be characterized, and the clinical spectrum continues to expand. The illness in humans is untreatable, but human infection is dwarfed by zoonotic impacts.

West Nile virus is certainly a representative poster virus for emerging infections. The warnings that expanding international travel and trade would lead to importation and endemic spread of new infections have been fulfilled (1). West Nile virus arrived at one of the busiest ports and immigrant centres in North America – New York City, New York (2). The initial recognition of the virus highlights the pivotal role of the astute clinician in early identification of a new infectious disease syndrome. An infectious disease practitioner notified public health, on a Friday afternoon of course, of two unusual cases of encephalitis, with illness characterized by marked muscle weakness, at a hospital in Queens, New York. The importance of a responsive public health system was also re-emphasized. Within a week, active surveillance had identified additional cases, an outbreak investigation was initiated, and a flavivirus implicated through initial serological testing at the state laboratory. Recognition that the etiology of the illness was West Nile virus rather than St Louis encephalitis virus, and appreciation of the parallel epizootic in avian species, took a little longer (1). The progress of the virus from these beginnings has been relentless. Despite political will and public funding to sustain high levels of surveillance and diagnostic access, control is not yet achieved nor anticipated.

The 2002 experience was particularly stunning (3). There were over 4000 human cases and 250 deaths in the United States, and hundreds of human cases in Canada (Drebot et al, pages 105-114). Most Canadian cases were in Southern Ontario, but the range of the virus has extended across much of North America. Infected birds have been confirmed in five Canadian provinces and 44 American states. Additional infected animal species – raptors, grouse, mountain sheep and caribou – continue to be described beyond the crows, horses and cows recognized with the first outbreak. Transmission of the virus among humans through blood transfusion, transplanted organs, intrauterine exposure, breast milk and laboratory accidents is also documented.

A positive theme in this story is the low burden of severe human illness relative to total cases of infection. The illness to infection ratio is about 1:140 (4). Severe illness and death are largely restricted to older or immunocompromised people – healthy children and young adults rarely present with symptomatic illness. But the characterization of clinical illness caused by the virus still evolves. Fever alone, respiratory complaints, rash, gastrointestinal symptoms, and a polio-like syndrome are all described, in addition to aseptic meningitis and encephalitis. A second positive theme is the presumed potential life-long immunity following infection. If West Nile virus becomes endemic in North America, early childhood infection associated with little morbidity may be the norm. Elsewhere in the world, epidemics are rare in populations with high background immunity (4). This would also make vaccine development a reasonable expectation (5).

Even at this early stage in our West Nile experience some lessons relevant to response to future disease introductions can be appreciated. Emerging infections occur not only in human populations. The large epizootic in birds, which preceded the first human cases identified in New York City, was not recognized as a potential human health issue (2). A surveillance and response capacity to identify new human illnesses must also evaluate perturbations in animal disease. Effective, timely information sharing between human and animal experts is necessary. A second, sobering observation is that continuing intense surveillance and planning over three summers did not predict the rapid geographic dissemination and large human epidemic of 2002. In the short term, laboratory capacity was overwhelmed, limiting the quantity of tests performed and the timeliness of results. Diagnostic clinical specimens from patients presenting with potential illness but with milder manifestations, such as fever alone, were seldom obtained. This has likely hindered a more complete understanding of the Canadian experience. Delays in laboratory confirmation, while understandable in the context of confirmatory testing, are problematic for public health in providing timely communication for the public, and in addressing other transmission concerns such as blood safety, where component withdrawals or tracebacks may be required. The response plan for the next infection challenge should include options for a laboratory surge capacity for large scale, timely specimen processing, and a diagnostic strategy responsive to clinical and public health needs. This requires continuing review and consultation among laboratories, public health and practitioners both before and during the outbreak.

The American experience of last summer confirmed virus transmission through blood, blood products and transplanted organs (3). While the number of cases is small, recipients of these biological products are more likely to be immunocompromised and at greater risk for more severe illness.

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Progress toward a blood screening test has been rapid. If, as predicted, a test is available by the summer of 2003, it will be an impressive tribute to the current diagnostic technological capability. Understandably, the cost of such a test is of concern. However, the Canadian blood system continues to function under the shadow of Krever, and the balancing of cost and risks in the blood system is another issue.

A secondary theme repeatedly raised in Canadian forums is whether resources invested are justifiable given the limited human disease burden. This argument may have less force after 2002, when hundreds of human cases occurred in Canada (Drebot et al, pages 105-114). In fact, our understanding of the determinants and burden of human disease remains incomplete – we cannot predict the future experience. In addition, long term outcomes following infection are only beginning to be described. Continued monitoring of virus progression in the upcoming years will address these issues. Further characterization of virus dissemination and human disease in the coming years of the epidemic will support the development of future preventive programs. Environmental impacts of infection and, potentially, control measures, are likely greater than adverse consequences directly attributable to human illness, and the continuing description of the nonhuman experience is relevant to human risks. Resources applied to West Nile virus programs also have more general utility when this experience is viewed as a prototype for an emerging infection that appears unexpectedly and disseminates rapidly and widely in an unpredictable manner – as is anticipated with bioterrorist events. From this perspective the West Nile experience allows an opportunity for critical review of responses to such a challenge, including communication strategies, public health and laboratory capacity (6).

The West Nile virus epizootic and human epidemic will likely further expand in North America in 2003. The extent and impact of disease, however, cannot be predicted. Experience with outbreaks of other flaviviruses on this continent, such as Western equine and St Louis encephalitis, describe sporadic outbreaks that are unpredictable in location and severity. Meteorological variables such as temperature and humidity will play a role, but the weather for next summer cannot be reliably predicted, let alone the impact of specific weather conditions at the local level on virus transmission. Meanwhile, a major concern is the direct impact of the virus and indirect impacts of potential control measures on the environment. Advancing our understanding of avian and mosquito populations and their interactions is a necessary element in predicting human health consequences. Adverse outcomes may not be a direct result of human acquisition of infection. For instance, large scale die-off in birds, particularly raptors, may have secondary outcomes such as an increase in the rodent population, with increases in human diseases such as plague, Hantavirus or leptospirosis.

We are now experiencing an episode in the future history of infectious diseases – the West Nile virus outbreak of the early 2000s in North America. This experience has already reminded us that human and animal health are integrated, the blood system remains vulnerable to newly introduced infections, and our models to predict infectious diseases epidemics are imperfect. Continuing to describe the progress and impacts of this virus in North America is worthwhile. Perhaps we will eventually settle into a steady-state endemicity, with sporadic eruptions correlated with climatic factors. Or perhaps the virus will largely disappear, only to reappear in an unpredictable manner like its companion, the North American flaviviruses. By the time stability is reached, there will likely be another infectious disease challenge, and the lessons of West Nile virus will serve us in the future.

REFERENCES

1. Institute of Medicine Emerging Infections. Microbial Threats to Health in the United States. J. Lederberg, RE Shope, SC Oaks Jr, eds. Washington: National Academy Press, 1992.
2. Nash D, Mostashari F, Fine A, et al. Outbreak of West Nile virus infection, New York City area. N Engl J Med 2001;344:1807-14.
3. Centres for Disease Control Provisional surveillance summary of the West Nile virus epidemic – United States, January – November 2002. MMWR Morbid Mortal Wkly Rep 2002;51:1129-33.
4. Martin AA, Gubler DJ. West Nile encephalitis: An emerging disease in the United States. Clin Infect Dis 2001;33:1713-9.
5. Monath TP, Arroyo J, Miller C, Guirakhoo F. West Nile virus vaccine. Curr Drug Targets Infect Disord 2001;1:37-50.
6. Fine A, Layton M. Lessons from the West Nile viral encephalitis outbreak in New York City, 1999; Implications for bioterrorism preparedness. Clin Infect Dis 2001;32:277-82.