Emergence of Epidemic O'nyong-nyong Fever in Southwestern Uganda, After an Absence of 35 Years

To the Editor: In July 1996, an uncommon disease suspected to be O'nyong-nyong fever was recognized in the Rakai district of southwestern Uganda. It was reported to have started in June 1996. The disease spread into the neighboring Mbarara and Masaka districts of Uganda and in the bordering Bukoba district of northern Tanzania.

The initial symptoms of O'nyong-nyong fever are high fever and generalized maculopapular skin rash with crippling arthritis, primarily in the big joints, in the absence of joint effusion. Other features are lymphadenitis, eye pain and reddening with no discharge, chest pain, and general malaise. The disease is self-limiting. All age groups and both sexes are equally affected. In areas where the disease is epidemic, 60% to 80% of the people are infected, and familial clustering is found in affected households. No deaths have been reported, but two miscarriages have been associated with infection.

The Ministry of Health (Uganda), in collaboration with the Uganda Virus Research Institute, began epidemiologic and clinical investigations of the epidemic in August 1996. Acute-phase serum samples were collected from patients, and adult mosquitoes were collected from within and around patients' homes. Virus isolates were made from acute-phase serum samples from several patients by intracranial inoculation and passage in baby mice. Attempted virus isolations from mosquito specimens are in progress. Serum samples and aliquots of the virus isolates were sent to the Centers for Disease Control and Prevention, Fort Collins, Colorado, USA, for reisolation and identification. A portion of the capside and NS4 genes of the virus isolates was sequenced and identified as O'nyong-nyong virus; the virus was isolated and sequenced directly from another serum sample. Two serum samples were positive for IgM antibody to O'nyong-nyong antigen.

O'nyong-nyong virus was responsible for a similar epidemic in 1959 to 1961, which started in northern Uganda and spread south and eastward into Kenya, Tanzania, and Zambia, and then northward from Tanzania into southwestern Uganda, where it subsided. The disease has reemerged in this area after 35 years of absence.

E.B. Rwaguma,* J.J. Lutwama,* S.D.K. Sempala,* N. Kiwanuka,† J. Kamugisha,‡ S. Okware,‡ G. Bagambisa,§ R. Lanciotti,¶ J. T. Roehrig,¶ and D.J. Gubler¶

*Uganda Virus Research Institute, Entebbe, Uganda; †Rakai Project Uganda Virus Research Institute; ‡Communicable Disease Control, Ministry of Health, Uganda; §Ministry of Health, Rakai, Uganda; ¶Centers for Disease Control and Prevention, Fort Collins, Colorado, USA

Prostatitis and Benign Prostatic Hyperplasia: Emerging Infectious Diseases?

To the Editor: In their excellent article, Molecular Approaches to the Identification of Unculturable Infectious Agents, Gao and Moore (1) point out that molecular approaches should be unleashed on diseases such as sarcoidosis, Kawasaki disease, and type I diabetes mellitus, which are thought but not proven to be infectious. The authors, however, are overlooking the more common and most likely infectious disease of unknown etiology today—prostatitis.

According to the pathologist McNeal, the prostate gland is the most commonly diseased internal organ of the human body (2). Prostatitis is the most common prostate disease, resulting in more physician visits than either benign prostatic hyperplasia or prostate cancer, according to the National Institutes of Health (3). Despite its frequency, prostatitis as a disease and as a histologic lesion is understudied (4).

By the Meares and Stamey culture localization procedure, in which the first voided urine, a midstream urine, the expressed prostatic secretions, and a final voided urine are compared, more than 90% of cases in patients with chronic pelvic symptoms are labeled as "nonbacterial" prostatitis or prostatodynia, both of which are thought to be incurable diseases (5).

The University of Washington has documented white blood cell counts as high as 38,000 per mm^3, in "nonbacterial" prostatitis patients (6). According to urologist Thomas Stamey, up to 50% of all men experience symptoms of prostatitis during

their lifetimes (7). The prostatitis lesion was found in 40 (44%) of 91 men at random autopsy (8). In another study of 100 consecutive autopsies on men who died suddenly in automobile accidents and from other causes, the prevalence of histologic signs of prostatitis increased with age and was highest when benign prostatic hyperplasia was also present. Prostatitis was present in 22% of men under 40 years of age and in 60% of those over 40 years of age (9).

In fact, the line between benign prostatic hyperplasia and prostatitis is blurred. Prostatitis as a histologic lesion has been found in 98% of patients with benign prostatic hypertrophy (10). Microbial tests on benign prostatic hyperplasia tissue have found significant rates of infectivity. In another study, more than 70% of transurethral resection of the prostate specimens showed clinical or laboratory signs of infection (11). Benign prostatic hyperplasia and prostatitis cannot be distinguished by symptoms, and some believe that they may be the same disease.

In these days of prostate specific antigen testing, more than 50% of men who undergo biopsies for prostate cancer have a prostatitis lesion whether they have cancer or not (Gottesman et al., unpublished data; McNeal, personal communication, 1995). Prostatitis occurs at an early age, and prostate cancer decades later, in the same part of the prostate gland, the peripheral zone.

Why aren't DNA techniques being unleashed on what is apparently the most common and most purulent unknown inflammatory disease in men—an inflammatory lesion that is associated with benign prostatic hyperplasia and prostate cancer? Surely, DNA microbial testing has important implications for all three major prostate diseases—prostatitis, benign prostatic hyperplasia, and prostate cancer.

Brad Hennenfent
Director, The Prostatitis Foundation
Chicago, Illinois, USA

References

1. Gao S-J, Moore PS. Molecular approaches to the identification of unculturable infectious agents DNA vaccines for emerging infectious diseases: what if? Emerg Infect Dis 1996;2:159-67.
2. McNeal JE. The prostate gland: morphology and pathobiology. Monographs in Urology 1988;9:3.
3. National Institutes of Health. The National Kidney and Urologic Diseases Advisory Board 1990 long-range plan. Bethesda (MD): U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, 1990.
4. Hennenfent BR. The economics of urological care in the 21st century [letter]. Urology 1996;47:285-6.
5. Weidner W, Schiefer HG, Krauss H, Jantos CH, Freidrich HJ, Altmannsberger M. "Chronic prostatitis" a thorough search for etilogically involved microorganisms in 1,461 patients. Infection 1991;19:S119-25.
6. Krieger JN, Egan KJ, Ross SO, Jacobs R, Berger RE. Chronic pelvic pains represent the most prominent urogenital symptoms of "chronic prostatitis." Urology 1996;48:715-22.
7. Stamey TA. Pathogenesis and treatment of urinary tract infections. Baltimore: Williams and Wilkins, 1980.
8. McNeal J. Regional morphology and pathology of the prostate. Am J Clin Pathol 1968;49:347-57.
9. Bostrom K. Chronic inflammation of the male accessory sex glands and its affect on the morphology of the spermatozoa. Scand J Urol Nephrol 1971;5:133.
10. Kohnen PW, Drach GW. Patterns of inflammation in prostatic hyperplasia: a histologic and bacteriologic study. J Urol 1979;121:755-60.
11. Riedash G, Morhing K, Brkovic D. Concentration of ofloxacin in prostatic tissue during TURP. Drugs 1993;45 (Suppl. Preprint).

Risk Factors for Severe Leptospirosis in the Parish of St. Andrew, Barbados

To the Editor: Leptospirosis, an important zoonosis in most warm-climate areas, is endemic in most Caribbean countries (1). The disease was first reported in Barbados 60 years ago (2), and since 1979 has been the subject of continual study as the result of the establishment of the Leptospira Laboratory by the governments of Barbados and the United Kingdom. The annual incidence of severe leptospirosis in Barbados over the past 17 years has been approximately 11.5 cases per 100,000 population with a death rate of 13%. However, the incidence rate varies in the parishes of Barbados. For the 12-year period from 1979 to 1991, the lowest incidence rates were in St. Peter (9.5 cases per 100,000 population) and St. Michael (9.9 cases per 100,000 population), while the highest was in St. Andrew (40 cases per 100,000 population). This greater than fourfold difference in incidence rates has been attributed to differences in rainfall (3). We performed a retrospective case-control study to determine what other factors were important.

We identified cases of leptospirosis from the records of the Leptospira Laboratory and included them in the study if they occurred from January 1980 to December 1993, if the home address was in the Parish of St. Andrew, and if laboratory evidence of leptospirosis was confirmed by one or more of the following: an IgM ELISA titer ≥160 in a single sample, a titer in the microscopic agglutination test (MAT) of ≥800 in a single sample, a fourfold or greater rise in antibody titer between two samples tested by the same method, or isolation of leptospires from blood or urine cultures (3).

Of the 36 cases of laboratory-confirmed leptospirosis and 41 controls (selected for residence close to the case-patient), 22 patients and 38 controls were included in the study. For case-patients, the mean age at onset of symptoms was 30.8 years (range 8 to 73 years); 28 (78%) of 36 cases occurred in males. The mean age of controls was 31.3 years (range 13 to 78 years); 15 (39.5%) of 38 controls were male. Controls were matched for age, but because St. Andrew is a sparsely populated parish, and because the survey was conducted during the day, it was difficult to recruit sufficient male controls. The participants were administered a questionnaire, and blood samples were taken and tested for leptospiral antibodies. Serologic results were compared with the results obtained for each of the patients during their acute illness and with the results of previous follow-up studies conducted over several years.

Gardening was a significant risk factor (odds ratio [OR] 4.57, 95% confidence level [CL] 1.09-20.36) and appeared to remain so whether gloves were worn or not, as was the presence of dogs around the home (OR 7.82, 95% CL 1.79-46.55). With few exceptions, the respondents kept dogs, and these animals are an important risk factor for leptospirosis in Barbados (6). A positive association was observed between illness and wearing boots in the garden or yard (OR 8.5, 95% CL 1.93-42.55), but this may be because case patients had changed their behavior since recovery, because they were working in wetter areas than the controls, or because the male/female ratio was lower among controls. We were unable to define the odds ratios for walking barefoot some or all of the time because none of the controls admitted to going barefoot. The most important risk factor we identified was walking through ponds or stagnant water (OR 25.62, 95% CL 2.89-1151.84). Flooding is common during the rainy season in Barbados, and people living in rural areas such as St. Andrew are often exposed in this way. These risk factors bear a striking resemblance to those identified in the outbreak in Nicaragua a few months after our study (7).

We conclude that almost all of the patients had multiple risk factors for leptospiral infection. Few indicated a change in lifestyle since recovering from leptospirosis. Serologic evidence of recent re-exposure to leptospirosis was detected in two (17%) of 12 case-patients.

The relatively high rainfall in St. Andrew may have contributed to their risk for leptospirosis by enhancing the survival of leptospires in the soil and water. The incidence of leptospirosis in St. Andrew shows a close association with mean monthly rainfall, the highest incidence during the period studied being October and November. However, when individual cases were examined, a less strong correlation was observed between onset of symptoms and rainfall in the preceding month and with rainfall in the preceding 3-month period. No evidence was observed of clustering of cases in months or years with rainfall above the mean. Similar findings have been reported for the island as a whole (4,5). The incidence of leptospirosis appeared to lag behind the rainfall, since rainfall tended to increase from June to a peak in November, while leptospirosis incidence increased from August to November. There was a marked decrease in rainfall in December each year, with the dry season continuing until May. However, continuing low incidence of leptospirosis was seen throughout the less wet months, until during the months of May to July only one case occurred during the study period.

On the basis of these findings, we conclude that the ground remains sufficiently damp during the period from December through the early months of the year for leptospires to survive. As the middle months of the year are reached, the ground may become too dry for leptospires to survive. This would also account for the apparent lag between the onset of the rainy season and the rise in leptospirosis incidence, as the ground may take some weeks of consistent rainfall to become saturated.

No clustering of cases in time was observed, which confirms that leptospirosis in Barbados is endemic and that increases in incidence result from multiple sporadic cases rather than microepidemics (5). Cases were clustered geographically, but this may have been an artifact resulting from

variation in population density. Moreover, the place of residence is not necessarily the place of exposure to leptospirosis.

We emphasize the importance of public education regarding the relative risks, as a means of preventing exposure, and of continuing education of physicians and primary health-care workers to raise their awareness of the seasonal distribution and early symptoms of leptospirosis.

Acknowledgments

We thank Mr. J. Charlery (Meteorological Department) for supplying the rainfall data and Ms. C. Whittington and Ms. S. Branch (Leptospira Laboratory) for their technical assistance.

C. P. Douglin,* C. Jordan,† R. Rock,†
A. Hurley,* P.N. Levett*‡
*Leptospira Laboratory, St. Michael, Barbados;
†Maurice Byer Polyclinic, St. Peter, Barbados;
‡University of the West Indies, School of Clinical Medicine and Research, Barbados

References

1. Everard JD, Everard COR. Leptospirosis in the Caribbean. Reviews in Medical Microbiology 1993;4:114-22.
2. Bayley HH. An investigation of the infectious jaundice of Barbados. Caribbean Medical Journal 1939;1:135-42.
3. Everard COR, Edwards CN, Everard JD, Carrington DG. A twelve-year study of leptospirosis on Barbados. Eur J Epidemiol 1995;11:311-20.
4. Everard COR, Bennett S, Edwards CN, Nicholson GD, Hassell TA, Carrington DG, et al. An investigation of some risk factors for severe leptospirosis on Barbados. Journal of Tropical Medicine and Hygiene 1992;95:13-22.
5. Bennett S, Everard COR. Absence of epidemicity of severe leptospirosis in Barbados. Epidemiol Infect 1991;106:151-6.
6. Everard COR, Jones CJ, Innis VA, Carrington DG, Vaughan AW. Leptospirosis in dogs on Barbados. Israel Journal of Veterinary Medicine 1987;43:288-95.
7. Spiegel RA, Ashford DA, Trevejo RT, Rigau-Perez JG, McClure EM, Amador JJ, et al. Leptospirosis outbreak associated with pulmonary hemorrhage--Nicaragua, 1996. Abstracts of the First Meeting of the International Leptospirosis Society; 1996 Sept; Nantes, France. Nance, France: International Leptospirosis Society, 1996.

Electronic Communication and the Rapid Dissemination of Public Health Information

To the Editor: In the United States, communicable disease surveillance, investigation, and control are the responsibility of the states. The Centers for Disease Control and Prevention (CDC) provides epidemiologic and laboratory support to the state and territorial epidemiologists (state epidemiologists) and state public health laboratory directors (state laboratory directors), who are located in each of the 50 states, Washington, D.C., the Virgin Islands, the Federated States of Micronesia, American Samoa, the Marianas Islands, and Puerto Rico. Historically, communication between CDC and these state representatives has been conducted by telephone, facsimile, or letter, and more recently by the WONDER (1) electronic mail (e-mail) system. We examined the timeliness and coverage of the WONDER system when used to contact state epidemiologists and laboratory directors during two recent foodborne outbreaks.

The first outbreak was reported to CDC on February 10, 1995, by the Communicable Disease Surveillance Centre (CDSC) in the United Kingdom. CDSC had linked an outbreak of salmonellosis in the United Kingdom to a snack food distributed to many countries including the United States (2). CDC decided to notify all state epidemiologists about the outbreak immediately so that they could take appropriate action to protect consumers and report suspected cases. This e-mail message was ready to be accessed by all state epidemiologists from 4:27 p.m. Eastern Standard Time (E.S.T.) on Friday, February 10, 1995.

The second outbreak involved *Salmonella* serotype Stanley infections associated with the consumption of alfalfa sprouts. In the United States, the outbreak was recognized when a larger than expected number of isolates of *Salmonella* Stanley for the first week of June 1995 was reported (3). CDC notified state epidemiologists and laboratory directors about the outbreak and requested that cases of *Salmonella* Stanley infection be reported and *Salmonella* Stanley isolates be sent to CDC. This e-mail message was ready to access from 9:41 a.m. E.S.T. on Friday, June 9, 1995.

These two e-mail messages were sent to two group codes maintained by the Council for State and Territorial Epidemiologists and the Association of State and Territorial Public Health Laboratory Directors on the CDC WONDER e-mail system. The subject heading for these messages indicated that they were urgent and from CDC. The messages were available for 22 days from the day of posting, at which time unaccessed messages were automatically returned to sender. Each message was sent with an automatic receipt acknowledgment function.

Because many of the territories are not regularly connected to WONDER, only the 50 states, the District of Columbia, and Puerto Rico were included in the study. The time to receipt was calculated on the basis of working days (Monday through Friday) only. E-mails accessed during a weekend were attributed to the following Monday.

In February, 48 of 50 states were on the state epidemiologists WONDER e-mail distribution list; 47 states, Puerto Rico, and the District of Columbia accessed the e-mail message within 22 days; one state did not access it within that period; 8 (16%) accessed the message the day it was sent; 28 (57%) accessed it within 1 working day—three of these accessed the message during the weekend; and 43 (88%) of 49 recipients accessed the message within 1 week. While no additional cases were reported, e-mail communication may have hastened product recall, thereby preventing further cases.

In June, 49 states were on the state epidemiologists WONDER e-mail distribution list; 48 states and Puerto Rico accessed the e-mail message within 22 days; two did not access the message within that period; 25 (51%) accessed the message the day it was sent; and 40 (82%) accessed the message by the second working day—two of these accessed the message on a weekend.

Thirty-eight states and Washington, D.C., were on the state laboratory directors WONDER distribution list in June; 25 (64%) accessed the message the day it was sent, and 32 (84%) of 38 accessed the message by the second working day—one of these accessed the message on a weekend. All 38 states and Washington D.C. accessed the e-mail message within the systems' 22-day limit. The pattern for state laboratory directors was almost identical to that for state epidemiologists.

Within 3 weeks of transmission of the June message (by June 30, 1995), state health department laboratories had forwarded 55 *Salmonella* Stanley isolates to CDC: 44 (80%) of these were the outbreak strain. These reports contributed to a traceback that implicated a single alfalfa seed distributor.

The use of e-mail to communicate health related messages to epidemiologists and laboratory directors was timely and highly successful in these incidents. By the second working day, more than half of the intended recipients had accessed the February message, and more than 80% had accessed the June message. However, not all state epidemiologists and laboratory directors access WONDER e-mail daily, and so other means of communication would be necessary if contact were required within 1 working day.

Because epidemiologists and laboratory directors have to dial into the WONDER mainframe by modem to find out if they have new messages and to receive them, retrieving WONDER e-mail messages can be less than timely; there is no mechanism to alert users to incoming WONDER e-mail messages. This delay is likely to be overcome as more epidemiologists and laboratory directors become connected to the Internet by local area networks that automatically check for incoming messages several times per hour. Some epidemiologists and laboratory directors have been slower to access their WONDER e-mail address because they also had an Internet address and thus accessed the WONDER system less often.

Perhaps more than one person in each state office should be on the distribution list to ensure message delivery when one representative is absent. We confirmed only that the message had been accessed by someone using the state epidemiologists' password; however, it is possible that someone other than the state epidemiologists accessed the message on their behalf adding to the delays.

Electronic communication by public health groups (e.g., Epi-net links public health agencies in the United Kingdom, Salm-net links agencies involved in foodborne disease surveillance and control in Europe) is rapidly increasing (4). However, there is a need for a global network that allows public health agencies of every country to rapidly communicate real or potential emergent disease threats.

Craig B. Dalton, Patricia M. Griffin, and Laurence Slutsker
Centers for Disease Control and Prevention, Atlanta, Georgia, USA

References

1. Fried A, Roser DH, Reid JA. CDC WONDER: A cooperative processing architecture for public health. J Am Med Inform Assoc 1994;1:303-12.
2. An outbreak of *Salmonella agona* due to contaminated snacks. Commun Dis Rep CDR Wkly 1995 Feb 17;5:29,32.
3. Martin SM, Bean NH. Data management issues for emerging diseases and new tools for better methods. Emerging Infectious Diseases 1995;1:124-8.
4. Vacalis DT, Bartlett CL, Shapiro CG. Electronic communication and the future of international public health surveillance. Emerging Infectious Diseases 1995;1:34-5.