Infectious Diseases and Mental Illness: Is There a Link?

To the Editor: The report by Hatalski et al. (1) on Borna virus as a probable human pathogen provides yet another example of an infectious agent being tentatively associated with neuropsychiatric disorders. Earlier this year, researchers at Rockefeller University and the National Institute of Mental Health suggested that after streptococcal infection, some children may be at increased risk for obsessive-compulsive disorders and Tourette syndrome (2). The human B-cell antigen D8/17, believed to be a marker for increased susceptibility to poststreptococcal rheumatic heart disease, has been tentatively linked to this increased risk for psychiatric illness in children. Other reports of patients with complicated Lyme borreliosis, including some whose infections have progressed to encephalopathies, describe persistent verbal and memory deficits among these patients (3). In a few Lyme disease patients, the only overt symptoms of disease at the time of initial diagnosis and treatment were classified as mental confusion (4). Two newly emergent infectious diseases in the United States, leptospirosis and neurocysticercosis, have been found among inner city residents and poor immigrants, respectively. Occasionally leptospirosis has been associated with a variety of postinfectious psychiatric symptoms, including depression, dementia, and psychosis (5). Neurocysticercosis, a tropical parasitic infection, is increasingly associated with emergency room admissions for seizures and epilepsy (6). Still other infectious diseases are being examined for links with cognitive symptoms and emotional disorders.

The primary cause of many common psychiatric disorders, including depression, manic depression, anxiety, and schizophrenia, remains a mystery. The World Health Organization estimates that 1.5 billion people worldwide suffer from a neuropsychiatric disorder. Of the 10 leading causes of disability in 1990, four were psychiatric disorders: unipolar depression, manic depression, schizophrenia, and obsessive-compulsive disorders (7). The National Institute of Mental Health recently estimated that as many as 20% of young Americans ages 7 to 14—approximately 10 million children—have mental health problems severe enough to compromise their ability to function (8). Infectious agents may play a role in some of these diseases to some unknown degree. A better understanding of the role of infection may speed treatment and prevention efforts and reduce the degree of disability and stigma associated with mental illness.

Vaccines and antimicrobial agents might enhance current therapeutic options for mental illnesses. Even if infectious diseases were a primary factor in only 1% of neuropsychiatric illnesses, some 10 million persons might benefit from antimicrobial therapies. Identifying those susceptible to neuropsychiatric illnesses (because of environmental factors or genetic predisposition) may also permit vaccination or antimicrobial prophylaxis and a subsequent lowering of disease incidence.

Physicians and federal agencies addressing the problems of emerging infectious diseases should examine the possibility of infection as a cause of mental illness. Better communication among infectious disease and mental health experts, as well as additional training, will be needed to shed light on the growing phenomenon of infectious diseases manifesting themselves as neuropsychiatric disorders.

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Mycobacterium nonchromogenicum Bacteremia in an AIDS Patient

To the Editor: *Mycobacterium avium* complex is the most common nontuberculous mycobacterium that causes disseminated infection in HIV-positive patients (1). Other less common nontuberculous mycobacteria responsible for disseminated disease in these patients are *M. fortuitum* (2), *M. genavense* (3), *M. gordonae* (4), *M. haemophilum* (5), *M. kansasii* (6), *M. malmoense* (7), *M. marinum* (8), *M. scrofulaceum* (9), *M. simiae* (10), *M. szulgai* (11), *M. terrae* (9), and *M. xenopi* (2,9). Although only *M. genavense*, *M. kansasii*, and *M. xenopi* are significantly more frequent in these patients (2,3,9), HIV infection is likely a predisposing condition for all nontuberculous mycobacterial infections. We report the first case of disseminated infection caused by *M. nonchromogenicum* in an HIV-infected patient.

A 28-year-old man with HIV infection acquired by sharing injection tools was seen in our outpatient clinic because of intermittent fever, drenching nocturnal sweats, and cough with purulent sputum of 4 months' duration. He also reported a weight loss of 10 kg in the previous 2 months. He had been diagnosed with bronchial infection in another hospital and had been treated with an unknown antibiotic. After this treatment, respiratory symptoms had improved somewhat, but fever and constitutional symptoms continued. His only previous opportunistic infection had been recurrent oral and esophageal candidiasis. The last CD4-cell count had been 16/µL 1 year earlier, and he was receiving didanosine and prophylactic therapy with cotrimoxazole and fluconazole. On physical examination the patient appeared ill; he was febrile, cachectic, and had thrush and oral hairy leukoplakia. Neither lymphadenopathy nor abnormal cardiopulmonary symptoms were found. The liver, which had enlarged since the last examination, was palpated 6 cm below the right costal margin. Abnormal laboratory values included aspartate aminotransferase 61 U/L, gamma-glutamyl transferase 209 U/L, lactate dehydrogenase 516 U/L, hemoglobin 12.3 g/dL, leukocyte count 4,300/µL (66% neutrophils, 19% band forms, 1% metamyelocytes, 3% lymphocytes, 11% monocytes), platelet count 130,000/µL, and erythrocyte sedimentation rate 72 mm/h. Chest X-rays were unremarkable, and a set of blood cultures was sterile. A sputum culture yielded *Haemophilus influenzae* sensitive to ampicillin, and smears and cultures for mycobacteria in one stool and three sputum samples were negative.

The patient was treated with oral amoxicillin for 2 weeks without improvement. Empirical therapy against *M. avium* complex with clarithromycin, ciprofloxacin, and ethambutol was started; the patient's condition improved dramatically within the next few days, and the fever and diaphoresis disappeared, although cough and sputum production remained unchanged. Three weeks later, a slow-growing nonphotochromogenic mycobacterium, identified as *M. nonchromogenicum* in a reference laboratory (Centro Nacional de Microbiología, Majadahonda, Madrid, Spain) by biochemical tests and confirmed by polymerase chain reaction-restriction enzyme pattern analysis, was isolated from a blood sample obtained on admission. This microorganism was sensitive to the three drugs administered, and the treatment was continued. Two months later the patient had gained 10 kg, hemoglobin had increased to 13.8 g/dL, the erythrocyte sedimentation rate had decreased to 52 mm/h, and the differential leukocyte count had returned to normal. Antimycobacterial drugs were withheld after 1 year of treatment. Twenty-two months after the diagnosis, the patient is doing well. He is receiving combination antiretroviral therapy, and his CD4-cell count is 128/µL.

M. nonchromogenicum, a slow-growing non-pigmented (Runyon's group III) mycobacterium, belongs to the *M. terrae* complex, together with *M. triviale*; it is traditionally considered nonpathogenic. However, it has been involved in a few cases of pulmonary infection (12) and chronic tenosynovitis secondary to puncture wounds (13), like the related organism *M. terrae*. In fact, some authors think that *M. nonchromogenicum* is the true pathogen in the *M. terrae* complex (13), and it is possible that some reports have misidentified this organism. This complex was first isolated in soil washings from radishes, but it has been found to be ubiquitous in the aquatic environment, including a hospital potable water supply (14).

Unlike osteoarticular infections, which commonly occur in previously healthy people, the scanty reports on pulmonary and disseminated infection by *M. terrae* complex suggest that either immunosuppression or local predisposing conditions (e.g., tuberculous cavities) are necessary pathogenetic cofactors (15). To our knowledge, *M. nonchromogenicum* bacteremia has never been reported before.

No specific DNA probes exist for *M. terrae* complex, but false-positive reactions with *M. tuberculosis* complex DNA probes have been described (16). Isolates are usually resistant to most antituberculosis drugs, with the exception of ethambutol and streptomycin, and susceptible to erythromycin, ciprofloxacin, and sulfonamides.

Only one case of disseminated infection by *M. terrae* has been described in a patient with advanced HIV infection and positive cultures in blood and bronchoalveolar lavage fluid, but no additional data were provided (9). Although the isolate we recovered might represent a laboratory contaminant, several pieces of evidence make this possibility very unlikely: lack of alternative explanation for a persistent and progressive clinical picture of 4 months' duration, absence of response to standard antibiotic therapy, negative results in the search for other pathogens, rapid and sustained clinical and laboratory response to drugs active against this strain, clear improvement despite the lack of treatment for other conditions, and absence of other isolates of this pathogen in our hospital despite the large number of samples examined for mycobacteria.

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Escherichia coli O157:H7 Infection in Colombia

To the Editor: The prevalence of *Escherichia coli* O157:H7 in Colombia is not known; we conducted a study to determine its prevalence in children with infectious diarrhea, in adult cattle, and in ground beef.

Between March 1996 and March 1997, we examined 538 children under 5 years of age with infectious diarrhea who had been admitted to either of the two children's hospitals in Bogotá. Diarrhea was defined as three or more loose stools within the previous 24 hours. One hundred and sixty-one children under 10 years of age admitted to the hospital for a medical reason other than infectious diarrhea served as controls.

Stool samples from children with and without diarrhea were placed in Stuart transport medium and sent to the laboratory within 24 hours; the samples were injected into sorbitol MacConkey agar (Oxoid Basingstoke, United Kingdom). After 24 hours of incubation at 37°C, sorbitol nonfermenting colonies were tested with 4-methylumbelliferyl-ß-glucuronide (MUG); all typical colonies of *E. coli* O157:H7 that were sorbitol-negative were confirmed as *E. coli* by biochemical tests (1,2) and were tested for agglutination with a latex test kit (Oxoid Basingstoke, United Kingdom) for detecting *E. coli* O157 and *E. coli* H antiserum H7 (Difco, Detroit, MI, USA). All human isolates were confirmed as Shiga-toxin producers by latex agglutination (Oxoid Basingstoke, United Kingdom). We used as a control strain *E. coli* O157:H7 provided by M. Karmali.

Rectal swabs from 307 healthy adult cattle from farms in Cundinamarca and Meta Departments were placed in Stuart transport medium, stored at 4°C, and transported to the laboratory within 6 hours. Swabs were injected into sorbitol MacConkey agar, and colonies that did not ferment sorbitol were characterized by standard techniques (3).

One hundred and fifty beef patties (31 cooked, 119 raw), collected in Bogotá, were examined by direct plating and enrichment culturing. Samples (1.0 g each) were serially diluted (1:10) in 0.85% NaCl solution, and 0.1 ml portions were plated in duplicate onto sorbitol MacConkey agar. Serologic and biochemical confirmation was done as mentioned above.

E. coli O157:H7 prevalence among children was 7.2%, with an age range of 0–60 months (average 21 months); diarrheal illness lasted an average of 2.5 days. Of 39 patients, eight were 6 months old or younger, five were 6 to 12 months old, 17 were 12 to 24 months old, and nine were older than 24 months. Renal failure associated with hemolytic uremic syndrome (HUS) developed in three (7.7%). Epidemiologic data were not collected regarding contaminated foods as a possible source of *E. coli* O157:H7 infection in the patients. *E. coli* O157:H7 was isolated from five (3.1%) of the 161 controls; the prevalence of *E. coli* O157:H7 was substantially higher in patients with infantile diarrhea than in controls.

All 39 strains from human cases were sorbitol-negative; five did not display MUG activity. Overall, 39 strains agglutinated strongly with antiserum O157:H7. Antimicrobial susceptibility tests were performed by the Bauer method (4). All *E. coli* O157:H7 isolated were susceptible to ciprofloxacin; 92% were resistant to ampicillin; 76% were resistant to furazolidone; and 76% were resistant to trimethoprim-sulfamethoxazole (TMP-SMZ).

E. coli O157:H7 was isolated from 20 (6.5%) of 307 rectal swabs from cattle. The strains isolated were sorbitol-negative and agglutinated strongly with antisera; five did not present activity. All strains were susceptible to ciprofloxacin; 90% were resistant to ampicillin; and 26% were resistant to TMP-SMZ. *E. coli* O157:H7 was isolated from 13 (87%) of 150 beef patties, six from raw beef, and seven from cooked beef.

*S*tool cultures of all patients with acute bloody diarrhea should be tested for *E. coli* O157:H7 to identify those at risk for HUS (5); however, serotyping, cytotoxicity assays, or DNA probing for *E. coli* O157:H7 are not routinely performed in Colombia.

This preliminary report suggests that *E. coli* O157:H7 is emerging as an important cause of endemic childhood diarrhea in Colombia and that the chain of contamination is present. The incidence is greatly underestimated because of limited surveillance and reporting. Further studies are needed to identify the pathogenic mechanisms of these *E. coli* O157:H7 strains and to determine the fecal carriage rate in healthy children. Data obtained will help elucidate the role of *E. coli* O157:H7 in childhood diarrhea. In addition, molecular analysis should be performed to establish the connection between the strains isolated from different sources in Colombia.

Our findings suggest that the risk for *E. coli* O157:H7 infection in Colombia is high; therefore, more active screening and surveillance would enhance case detection, epidemiologic understanding of *E. coli* O157:H7 infection and HUS, and could lead to more specific therapeutic interventions.

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Autofluorescence and the Detection of Cyclospora Oocysts

To the Editor: From May through July 1997, we searched for the seasonally occurring *Cyclospora cayetanensis,* along with other coccidia and microsporidia, in fecal samples from 385 patients. The samples, in 10% formalin for evaluation of coccidia and microsporidia, were initially processed by a routine formalin-ethyl acetate concentration method; the parasite was detected in 18 patients (1,2). The resulting sediment was examined as follows. A drop of sediment was placed on a slide, cover-slipped, and examined microscopically as a wet mount at 200x and 400x magnification and subsequently at 200x magnification by epifluorescence with a 330 to 380 nm UV filter. Four smears were also prepared and stained by routine trichrome (2), modified trichrome (3), auramine-rhodamine (4), and Kinyoun acid-fast (5) procedures. All wet mount and stained preparations were evaluated by at least two trained persons.

Of the 385 fecal samples examined, 18 were positive for *C. cayetanensis*. The positive samples were from eight states, which encompassed northeastern (Rhode Island, New York, Massachusetts, Pennsylvania), midwestern (Wisconsin), western (Oregon, California), and southern (Florida) sections of the United States.

In 12 of 18 patients, the organisms were detected without much difficulty in wet mounts as round or partially collapsed nonrefractile bodies; however, in the other six, repeated wet preparations were needed to detect the organisms. When the same wet mounts were examined with epifluorescence microscopy, oocysts were easily discerned in all samples, even the six in which repeated wet preparations and stains were needed. While the trichrome procedures were ineffective, the auramine-rhodamine and Kinyoun stains gave varied results. The autofluorescence technique, however, was distinctly superior to the wet mount and staining procedures.

Extensive outbreaks of diarrhea caused by *C. cayetanensis* were reported in 1997 from different parts of the United States (6-8), and several procedures have been used to confirm the diagnosis in clinical samples. While the organisms are large enough to be seen in direct wet mounts, they are frequently caught up in mucus or covered by debris, so they are difficult to detect. Autofluorescence in *C. cayetanensis* oocysts makes them easily visible in clinical samples (1,9) with the use of a 330 to 380 nm UV filter; this feature enhanced their detection at least twofold over the direct wet mount, especially when the wet mount and stained slides contained few oocysts. (The same wet mount preparation can be used for the epifluorescence procedure.)

The 18 patients with cyclosporiasis were ages 2 to 71 years, which indicates that the infection was not specific to any age group. Twelve of the 18 cases were in women. Massachusetts had 11, the largest number of *C. cayetanenis*-positive patients. Of the 18, 16 were adults; the other two were children with a coexisting parasite (*Dientamoeba fragilis*). In one instance, three members of the same family were infected, the parents with only *C. cayetanensis*, the son with *D. fragilis* and *Blastocystis hominis*.

Because *C. cayetanensis* is a seasonal diarrheal agent, fecal samples from persons with persistent unexplained explosive diarrhea during the summer should be carefully evaluated for this infection. Stool specimens should be fixed in 10% formalin and examined with autofluorescence microscopy for enhanced detection.

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Partnerships for Detecting Emerging Infectious Diseases: Nepal and Global Influenza Surveillance

To the Editor: With new influenza strains emerging each year, identification of circulating strains by coordinated global surveillance is crucial to vaccine development for the coming year (1-3). Approximately 110 laboratories in 80 countries voluntarily participate in the World Health Organization (WHO) influenza surveillance network (4). Comprehensive surveillance is especially important in Asia, since new influenza strains often originate there. To participate in influenza global surveillance, countries need not rely on their own laboratory capability. Clinical specimens from patients thought to have influenza can be sent to designated laboratories around the world for analysis. A unique partnership has led to the expansion of the WHO global influenza surveillance network to Nepal.

The U.S. Army Medical Component - Armed Forces Research Institute for Medical Sciences (AFRIMS) (5) in Bangkok, Thailand, is well situated to assist with surveillance in Asia. Scientists at AFRIMS have conducted medical research in collaboration with Nepali colleagues for more than 20 years. Several studies have been conducted in collaboration with the CIWEC Clinic Travel Medicine Center (a travel medicine clinic that serves the diplomatic, aid, and tourist communities in Nepal). The clinic has approximately 5,000 patient visits per year, of which half are drawn from the 2,500 expatriates in Nepal and half from the 200,000 non-Indian tourists who visit Nepal annually.

A protocol was developed for a pilot influenza surveillance program. The staff of the CIWEC Clinic was responsible for volunteer recruitment, clinical evaluation, and specimen collection. Febrile upper respiratory infections were defined as temperature ≥ 100°F (37.8°C, oral or equivalent) and cough or sore throat of ≤ 72 hours duration. Other symptoms, such as streptococcal pharyngitis, were excluded. No age or gender restrictions were included. Volunteers had to have been in Nepal for the 5 days preceding illness. Only the first patient in any single household with similar symptoms within days of other household members was asked to participate.

The AFRIMS field station in Kathmandu (locally known as the Walter Reed/AFRIMS Research Unit - Nepal or WARUN) was responsible for shipping specimens collected by the CIWEC Clinic to AFRIMS, Thailand. Since dry ice was not available in Kathmandu, dry ice and shipping containers were sent by AFRIMS, Thailand for use by WARUN. Shipments from WARUN were then sent back to AFRIMS, where specimens were repacked in dry ice and sent for testing at the central laboratory of the U.S. Air Force's Project Gargle (6) in San Antonio, Texas. Project Gargle has been testing viral respiratory specimens from distant Air Force installations for more than 20 years. Each specimen was tested for influenza A and B; parainfluenza virus 1, 2, and 3; adenovirus; enterovirus; and herpesvirus. Characterization of selected influenza A and B isolates by hemagglutination-inhibition testing was performed by the Centers for Disease Control and Prevention (CDC).

Between December 1996 and February 1997, the CIWEC staff collected specimens from 18 patients. Samples were collected from 11 (61%) residents and seven (39%) tourists, who were evenly distributed by gender and had a median age of 35 years. Influenza B/Beijing/184/93-like viruses were isolated from five (28%) of the 18 specimens. All patients from whom influenza viruses were obtained had mild illnesses with fever and upper respiratory syndromes. Herpes virus type 1 and adenovirus type 6 were each identified in one other specimen. No respiratory viruses were identified in the remaining 11 specimens.

Because of the importance of China in the emergence of new strains of influenza, CDC's WHO Collaborating Center for Surveillance, Epidemiology, and Control of Influenza has worked with colleagues in China to establish a national Chinese network of influenza surveillance sites. Analysis of viruses isolated in China between 1988 and 1997 in comparison with other viruses obtained through WHO's global influenza surveillance network has shown that influenza variants are frequently identified in China before becoming prevalent in other regions of the world. Nepal is another especially valuable surveillance site, given its location between China and India (at the crossroads between northern and southern Asia) and its historic importance as a trans-Himalayan trade route.

Especially relevant are data from China demonstrating that the two antigenically and genetically distinct lineages of influenza B viruses represented by B/Victoria/02/87 and B/Yamagata/16/88 (7) have continued to circulate and evolve in China, while only viruses related to B/Yamagata have been detected elsewhere in the world and are represented in the current trivalent vaccine by the B/Bejing/184/93-like component. Virologic surveillance in surrounding countries (8) such as Nepal is necessary to detect geographic spread of B/Victoria-like virus in the region. Our data suggest that these viruses have not yet spread to Kathmandu.

Our unique international partnership between several civilian and military organizations (e.g., CIWEC Clinic, CDC, U.S. Air Force, and U.S. Army) demonstrates the feasibility of such partnerships as well as the usefulness of influenza surveillance data at both the local and global levels. Despite the small number of isolates obtained during this study, we were able to determine that the influenza B component of the trivalent vaccine prepared for the 1996-1997 influenza season would likely have offered protection for travelers and the local population against the influenza B strains isolated in Kathmandu. Ongoing surveillance data will establish geographic and temporal patterns of circulation of influenza viruses and thus provide valuable information for guiding public health policies for influenza vaccination. On a global level, these data are useful for annual vaccine strain selection.

Advances in communication, laboratory, and specimen transport technologies contributed greatly to the identification of viral pathogens from a new sentinel surveillance site in Nepal. In evaluating future collaborative sites, prior surveillance experience and reliable specimen shipping should be prime considerations. Approaches that use existing resources might foster greater international cooperation toward improved global detection and reporting of infectious diseases.

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HIV-2 Infection and HIV-1/HIV-2 Dual Reactivity in Patients With and Without AIDS-Related Symptoms in Gabon

To the Editor: Between 1996 and 1997, we evaluated the incidence of HIV-2 infection at the Fondation Jeanne Ebori, the second largest hospital in Libreville, capital of Gabon; we found an unexpected high prevalence of HIV-2–infected or HIV-1/HIV-2–dually reactive patients.

During a 10-month period, 147 (14.3%) of 1,029 sera from inpatients and outpatients were found HIV-positive by the type III method recommended by the World Health Organization (two enzyme-linked immunosorbent assays are used to screen anti-HIV antibodies) (1). Further discrimination between HIV-1 and HIV-2 infections was assessed by using synthetic peptides specific for the gp41 and the gp120 of HIV-1 and the gp36 of HIV-2 (ImmunoComb II, PBS Orgenics, Illkirch, France). Of the 147 HIV-positive sera, 141 (96.0%) were exclusively HIV-1–positive; four were exclusively HIV-2–positive; and two were both HIV-1– and HIV-2–positive. Of the six sera with anti-gp36/HIV-2 reactivities, two (from patients A and B) were positive on HIV-2 Western blot, with marked anti-gag HIV-1 cross-reactivity and a discrimination assay positive only for HIV-2; two (from patients D and E) were positive on HIV-2 Western blot, with anti-gag and pol reactivities markedly lower than anti-env reactivities and a discrimination assay positive only for HIV-2; the two remaining sera (from patients C and F) showed typical dual reactivities for HIV-1 and HIV-2 infections, with positive patterns of HIV-1 and HIV-2 Western blots and a discrimination test positive for both viruses. As a whole, six (4.1%) of 147 HIV-positive sera showed either HIV-2 infection alone (n = 4) or dual reactivity. Of those, four were from Gabonese patients B, C, D, and E, and two were from immigrants from West Africa (patient A from Mali and patient F from Nigeria); two were female patients B and E. Among Gabonese patients, only one (patient E) had traveled to West Africa; the remaining three had never visited any neighboring country. However, one Gabonese man (patient C) lived in Port-Gentil, which has many West African immigrants. For all patients, the most likely risk factor for HIV was a heterosexual relationship with an unknown HIV-infected person. In three asymptomatic patients (A, B, and C) the HIV-2–serostatus was unexpected; in contrast, the three other patients had AIDS-related symptoms. Patients D and E had an HIV-2 Western blot pattern showing a marked decrease in anti-gag and pol reactivities compatible with their advanced stage of HIV-2 disease.

The case of a 55-year-old exclusively heterosexual asymptomatic woman (patient B) suggests the possibility of a specific variant of HIV-2 in Central Africa (2). The high frequency in primates in Gabon of natural infection with simian immunodeficiency retroviruses, which show a high degree of genetic relatedness to HIV-2 (3), could support such a hypothesis.

Two patients had typical dual reactivities to HIV-1 and HIV-2 antigens. To our knowledge, such dual reactivities have never been reported in Gabon (4). In the patient from Nigeria (patient F), the serologic pattern was typical of that usually observed in West Africa (5). Dual reactivity can result from genuine mixed infections and from serologic cross-reactivity in HIV-1 and HIV-2 infection alone; theoretically, it could also represent infection with a different, cross-reacting recombinant strain (5).

HIV-2 infection in Gabon is epidemiologically related to West Africa, because of cultural and, above all, economic ties. However, HIV-2 is not limited to immigrant populations from West Africa or to Gabonese citizens traveling in this area; it has also reached the indigenous Gabonese population. The possibility of rare cases of HIV-1 and HIV-2 coinfections, recombinant HIV-1 and HIV-2 strains, and also peculiar HIV-2 variants from Central Africa, should be considered in Gabon. A possible entry of HIV-2 infection into Central Africa from Gabon in the near future could have major public health implications.

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Q Fever in French Guiana: New Trends

To the Editor: Q fever, the endemic disease caused by the rickettsial organism *Coxiella burnetii*, was first described in French Guiana in 1955 (1). Only sporadic cases were reported until 1996 when three patients were hospitalized in the intensive care unit of the Cayenne Hospital for acute respiratory distress syndrome. One of the patients died. Many cases of Q fever were diagnosed in the general population at the same time. A seroepidemiologic study was performed to determine whether the increase in cases was due to an increase in incidence or to an improvement in diagnosis. All paired samples of sera (acute-phase and convalescent-phase) from patients sent to the arbovirus laboratory for diagnosis of dengue infection from January 1, 1992, to December 31, 1996, were tested for antibodies to *C. burnetii* by immunofluorescence. All positive samples were also tested for immunoglobulin (IgM) by the same method; the IgG and IgM titers were determined by using a serial twofold dilution. A diagnosis of Q fever was made when there was a seroconversion from negative to positive or a twofold increase in IgG titer associated with the presence of IgM in the second sample.

One hundred and fifty-one of 426 paired sera collected between 1992 and 1996 were from patients recently infected with dengue fever. Twenty-five (9.1%) of 275 remaining sera were from Q fever patients. Significant differences were observed in the rates of Q fever in different years ($p < 0.01$); one (1.9%) of 53 was positive in 1992, five (9.1%) of 55 in 1993, five (8.6%) of 58 in 1994, three (4.8%) of 63 in 1995; a large increase was observed in 1996 (11 [23.9%] of 46). Differences by residence were also assessed. Rates of infection were higher in Cayenne (21 [13.0%] of 161) than in rural areas (4 [3.5%] of 114) ($p < 0.01$).

This study shows that cases of Q fever have occurred in French Guiana in recent years and that a significant increase in the incidence rate occurred in 1996. The reasons for this increase are unclear, and further studies of the epidemiology of Q fever in French Guiana are necessary. The epidemiology of Q fever is unusual in French Guiana because the rates of infection are much higher in Cayenne, the capital city, than in rural areas. No link with classical sources of infection (cattle, sheep, or goat birth products, or work in a slaughterhouse) was found. Indeed, Cayenne, with 80,000 inhabitants, is located near the Atlantic Ocean, and the prevailing winds blow from the sea. Airborne contamination from rural areas is therefore impossible. Furthermore, no large farm is in the immediate vicinity of the city. For identical reasons, contamination from the abattoirs is not likely; they are located on the west side of the city, near the Cayenne River, and the winds blow from the east. In our study, cases were almost equally distributed throughout the city, although many patients came from the same area.

A seroepidemiologic study to determine possible new sources of infection (e.g., dogs, cats) and estimate rates of seropositivity in cattle and sheep and a case-control study on new cases are being conducted.

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Ixodes dammini: A Junior Synonym for *Ixodes scapularis*

To the Editor: The authors of "A new tick-borne encephalitis-like virus infecting New England deer ticks, *Ixodes dammini*" (1) provide useful information regarding a possibly new tick-borne encephalitis-like virus. However, the use of the name *Ixodes dammini* is not accurate for describing this species. *I. dammini* (Spielman, Clifford, Piesman, and Corwin) was synonymized with *Ixodes scapularis* (Say) in 1993 by Oliver et al. (2) and was redescribed in 1996 (3) to reduce confusion regarding identification. Keirans and colleagues summarize a wide array of rigorous studies involving hybridization, assortative mating, isozymes, and morphometrics, all of which provide evidence supporting the synonymization of the two tick species (3).

The synonymization of *I. dammini* with *I. scapularis* has been widely accepted. "*I. scapularis* (= *I. dammini*)" is still often used, but the use of *I. scapularis* as the sole nomen for this species is becoming more common (4). Oliver et al. (2) have established *I. dammini* as a junior subjective synonym of *I. scapularis.* If scientifically rigorous evidence exists justifying the reestablishment of the species name *I. dammini,* it must be published according to proper procedure. The proper nomenclature of any species, let alone one of such widespread notoriety and public health importance, is too important to be relegated to a footnote. Until such evidence is presented, the continued misuse of *I. dammini* serves only to confuse health-care providers, public health professionals, and lay persons.

On a secondary matter, on page 167 of the dispatch, the authors state that "*I.* (Pholeoixodes) *cookei* is a one-host tick that is only distantly related to *I. dammini* and only rarely feeds on humans or mice" (1). *I. cookei* is a three-host tick (D.E. Sonenshine, pers. comm.), as are all the members of the genus Ixodes.

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The Name *Ixodes dammini* Epidemiologically Justified

To the Editor: Although a large body of evidence has been interpreted as supporting conspecificity of the deer tick (*Ixodes dammini*) and the blacklegged tick (*Ixodes scapularis*), according to Chapter VI, Article 23 L of the International Code of Zoological Nomenclature (1), "A name that has been treated as a junior synonym may be used as the valid name of a taxon by an author who considers the synonymy to be erroneous...."

Current use of *I. scapularis* to refer to the vector of Lyme disease obscures important epidemiologic issues. One of the reasons for "sinking" *I. dammini* was to make it easier to diagnose Lyme disease in areas where the disease was thought to be nonendemic: "The belief that *I. dammini* does not occur south of Maryland and that *I. scapularis* is a separate and distinct species yet unproven as a natural vector of Lyme disease has caused delays in Lyme disease surveillance in the South. The general attitude among physicians and veterinarians has been that Lyme disease is not a problem in that area, although patients present clinical symptoms of it" (2). Recognizing and reporting Lyme disease in southern and southcentral states should not, however, depend on whether the two ticks are conspecific. Only peer-reviewed descriptions of human cases of Lyme disease, with appropriate documentation of the diagnoses, should be accepted as evidence. Few such reports exist, and the evidence does not convincingly support a conclusion that Lyme disease exists as an epidemic zoonosis in southern states (3). This is not to say that residents outside the well-established eastern United States zoonotic sites (the Northeast and upper Midwest) do not have symptoms that fit one or more aspects of the current Centers for Disease Control and Prevention/Council of State and Territorial Epidemiologists/Association of State and Territorial Public Health Laboratory Directors surveillance definition for Lyme disease. Lyme disease-like infections, mainly manifesting as erythema migrans and strongly associated with Lone Star tick (*Amblyomma americanum*) bites are commonly seen in southern and southcentral states, but *Borrelia burgdorferi* does not seem to be the etiologic agent (4).

Enzootic transmission of Lyme disease spirochetes among rodents and ticks had been documented in southern and southcentral states by the late 1980s (5-7). The question, however, is whether there is frequent zoonotic transmission. There are widespread southern U.S. enzootic cycles of *Trypanosoma cruzi*, but few autochthonous human Chagas disease cases seem to occur because the vectors (such as *Triatoma sanguisuga*) have behavioral traits that reduce their capacity to serve as zoonotic vectors (8). Nymphal *I. scapularis* apparently do not frequently bite humans (7,9), although adult ticks do. The major feature of Lyme disease epidemiology in the Northeast and in the upper Midwest, however, is transmission by nymphal *I. dammini* (10).

Whether the predilection of nymphal *I. dammini* to feed on humans is environmentally determined or is a heritable trait with undescribed genetic markers remains unexplored. Particular mitochondrial DNA haplotypes seem to be more characteristic of *I. dammini* (11,12), and the use of such typing methods may enhance future analyses of the vectorial capacity of these ticks. For example, one might test the hypothesis that nymphal ticks removed from residents of sites in coastal North Carolina through Georgia, where both kinds of ticks have been collected, represent only *I. dammini*. But, if it is "widely accepted" that no differences exist between the two ticks, such studies may never be done. Similarly, many may wrongly assume that Lyme disease, human babesiosis, and human granulocytic ehrlichiosis are, or will become, epidemic throughout virtually all of the eastern United States. An equally likely scenario is that these zoonoses may never become public health problems for more southerly states. For the moment, then, distinguishing tick populations that frequently bite humans from those that rarely do seems to be a rational use of nomenclature, particularly for public health officials.

Dr. Sanders is correct in pointing out that all *Ixodes* spp. are "three-host" ticks, although my intent in using the term "one-host" was to indicate that all stages of *I. cookei* tend to feed on the same kind of animal (sometimes a single animal, within burrows), usually woodchucks, skunks, or raccoons. I regret the confusion from my use of the acarologic term in a descriptive context.

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Ebola/Athens Revisited

To the Editor: After our hypothesis that the plague of Athens (430 B.C.–425 B.C.) could have been caused by Ebola virus was published in this journal (1996;2:155-6), it was brought to our attention that this hypothesis had been previously entertained.

Gayle D. Scarrow had published a paper entitled “The Athenian Plague: A Possible Diagnosis” in The Ancient History Bulletin 2.1 (1988). Unfortunately, this had not come to our attention in our literature search, and therefore we assumed that we were the first to recognize the possibility. Clearly, Ms. Scarrow deserves credit for suggesting this first. Her arguments are compelling, even without the support of more recently available information and the observations advanced in our publication.

We believe an evolving knowledge base (e.g., the information about the Côte d'Ivoire outbreak where a protracted epidemic has been meticulously documented) will serve to enhance the credibility of the Ebola/Athens hypothesis.

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Meeting Summaries

The Hot Zone–1997: Conference on Emerging Infectious Diseases

On June 27-28, 1997, the University of Kentucky College of Medicine, University of Cincinnati College of Medicine, and Kentucky AIDS Consortium held a conference for clinicians and researchers in Lexington, Kentucky. Participants presented the latest findings from worldwide epidemiologic studies, basic science, and clinical research on emerging infectious diseases. The findings indicate that the war against infectious diseases is far from over. In the United States, between 1980 and 1992, deaths from infectious diseases increased by 58%, making serious infections the third leading cause of death; HIV infection is the leading cause of death among 25- to 44-year-olds; and antibiotic resistance costs the health-care system an estimated $100 million to $30 billion each year.

With the global population growing from 2.5 to 5.8 billion over the last 25 years, large urban centers throughout the developing world are overcrowded and have inadequate sanitation, ideal for the emergence of infectious diseases. By 2025, the global population will reach 8.6 billion. In developing countries, this represents an 84% increase, which will intensify overcrowding in these areas. In industrialized countries, an aging population base, the advent of immunosuppressive medications, and the emergence of HIV are combining to increase the risk for opportunistic infection. Moreover, with increased travel, clinicians see increasing numbers of patients with exotic diseases acquired abroad. Recent migration of epidemic diphtheria from the former Soviet Union to Europe and the emergence of multidrug-resistant tuberculosis (TB) in the United States and elsewhere are but two examples of infections resulting from international travel; in addition, nearly 70% of the fruits and vegetables consumed in the United States originate in developing countries; disease outbreaks related to imported food frequently go unreported.

Extensive cross-species contact among humans and certain domestic animals can dictate antigenic shifts in influenza viruses. The likelihood of the emergence of a new influenza virus in the near future increases with the growth of the hog population in China. The emergence of new viruses, such as HIV and filoviruses, indicates the virtually unlimited capacity of pathogenic organisms to mutate and rapidly adapt to environmental changes and selective pressures.

HIV/AIDS Research

Recent data from long-term survivors support the concept that HIV replication occurs when the number of CD4+ cells drops below the minimum level required to maintain CD8+ cell control of HIV. CD4+ cell production of IL-2 is needed for strong cell-mediated immunity. Without CD8+ cell responses, a more virulent, highly cytotoxic viral strain emerges, killing greater numbers of CD4+ cells and leading to AIDS. Because CD8+ cell loss appears to be related to a shift from a TH-1- to a TH-2-type cytokine response, therapeutic approaches that maintain TH-1 cell response, or enhance CD8+ cell anti-HIV activity through factors yet to be fully defined, are being actively investigated. Vaccines relying exclusively on antibody responses will almost certainly prove to be of limited value, while those using CD8+ cell antiviral activities hold substantially greater promise.

A basic science research forum described the use of a murine model of immunodeficiency induced by a type C retrovirus. Because models of this type reproduce a number of the clinical pathophysiologic manifestations associated with human AIDS, they can significantly enhance our understanding of retrovirus-induced immunodeficiency.

The results of recent research involving host immune responses to *Pneumocystis carinii* infection indicated that, compared with healthy controls, HIV patients with less than 200 CD4+ cells have similar IL-4 levels but significantly lower peripheral blood mononuclear cell proliferative responses and IFN-γ levels to *P. carinii* major surface class glycoprotein (MSG). Centers for Disease Control and Prevention (CDC) Class 3 patients with previous *P. carinii* pneumonia (PcP) have significantly higher IL-4 (but not IFN-γ) levels than Class 3 patients with no history of PcP. HIV+ patients who have recovered from PcP have sufficient memory cells to recognize MSG, but demonstrate a shift from a TH-1- to a TH-2-type antigen recall response.

HIV Therapy

The current state of CD4 and viral load testing and the 11 drugs available for HIV treatment were reviewed. Although combination drug therapy has consistently proved more effective than monotherapy in maintaining reduced viral load, the results of a recently completed follow-up study confirmed the effectiveness of zidovudine (AZT) in preventing neonatal HIV transmission; in a large cohort of pregnant women, AZT plus high titer immunoglobulin G was no more effective than AZT plus placebo, with both regimens producing results comparable with those achieved with AZT alone. A number of issues in HIV treatment remain unresolved, including when treatment should begin, how to manage inadequate response to therapy, whether to use HIV resistance genotyping to direct therapy, and how to best deal with prophylaxis for opportunistic infections in patients showing dramatic reductions in viral load.

Dengue and Dengue Hemorrhagic Fever (DHF)

Tens of millions of cases of dengue and hundreds of thousands of cases of DHF are reported annually, and more than 2.5 billion people are at risk for infection. Factors contributing to the emergence of dengue include unplanned and uncontrolled population growth associated with urbanization in tropical regions, lack of effective mosquito control, deteriorating water systems that increase densities of *Aedes aegypti*, and viral migration among tropical urban centers due to increasing international air travel. More than 50% of all air travel from the United States is to tropical destinations, and from 1977 to 1994, 2,248 suspected cases of imported dengue were reported in the United States. Because their clinical symptoms are initially nonspecific, dengue and other arboviral infections can be difficult to distinguish from other viral, bacterial, and parasitic infections. Correct diagnosis requires a detailed clinical summary, thorough epidemiologic information (including recent travel history), and a diagnostic laboratory test.

The severe hemorrhagic form, DHF/dengue shock syndrome (DSS), has an average incubation period of 4 to 6 days before sudden onset of fever and nonspecific signs and symptoms. Because the major pathophysiologic abnormality observed in DHF/DSS is increased vascular permeability and leakage of plasma from the vascular compartment, early fluid replacement is effective. The geographic distribution of DHF/DSS has been expanding and now can be found in tropical areas of Asia, the Pacific, and the Americas, including Central America and Mexico. This expansion is associated with increased movement of dengue viruses by airplane travelers and the development of hyperendemicity in the Pacific Region and the Americas. A similar scenario, generated largely from human encroachment into new environments, may also emerge for other *Aedes*-transmitted illnesses such as yellow fever. The most cost-effective approach to control dengue and DHF is larval source reduction in disease-endemic areas. Programs should use both government and community resources to integrate environmental sanitation with the use of insecticides and biologic controls, targeted to breeding grounds such as tire dumps.

Other Viral Diseases

The exponential increase in ecologic change, both environmental and behavioral, was cited as the major driving force for the increasing human risk for viral infection. Microbial variability can play a causal role in disease emergence, but it more often enables viruses to adapt to new circumstances. Travel of infected humans and international transport of microbes and vectors help provide the maximum possible microbial evolutionary opportunities in the minimum amount of time.

Viruses have emerged in the past, with measles providing a good example of the worrisome potential for future emerging RNA viruses. The emergence of cities in the Mesopotamian basin, resulting largely from the advent of irrigated agriculture, provided a populated substrate for interhuman transmission of short-incubation, nonlatent viruses. Domestication of livestock likely brought measles progenitors into close proximity with humans; a precursor of rinderpest/peste de petit ruminants then made an interspecies leap; much later measles spread to Europe, and, in the post-Columbian interchange, to the Americas.

Viral hemorrhagic fevers include those caused by Ebola filovirus and hantaviruses. Ebola hemorrhagic fever is characterized by extensive and disseminated infection and necrosis in major organs, and lymphoid depletion. Aerosol transmission of Ebola virus has occurred between nonhuman primates and guinea pigs, but no evidence exists for interhuman transmission by airborne infection. Barrier nursing precautions generally prevent the spread to humans, but in areas having inadequate medical care facilities, the virus can amplify in humans and cause epidemics. Hantaviruses belong to a single genus in the family Bunyaviridae, and each virus infects a limited or unique rodent species with no apparent disease. Although hemorrhagic fever with renal syndrome has rarely been diagnosed in the Americas, hantaviruses from sigmodontine rodents cause hantavirus pulmonary syndrome, characterized by large bilateral pleural effusions and heavy, edematous lungs, interstitial pneumonitis, and extensive infection of endothelial cells in the pulmonary microvasculature. The first documented interhuman transmission of a hantavirus was an outbreak of 20 cases in Patagonia, with evidence overwhelmingly indicating spread between patients and physicians. The reasons for, and mechanism of, the spread are unknown, but the registry of U.S. cases was revised to ensure that this phenomenon was adequately monitored. Although early diagnosis and supportive care are potentially lifesaving in cases of hantavirus pulmonary syndrome, such efforts are of limited value in Ebola hemorrhagic fever.

Prion Illnesses

In prion illnesses such as Creutzfeldt-Jakob disease (CJD), risk factors (family history of CJD or dementia, history of poliomyelitis, exposure to sheep or cows) and iatrogenic factors (dura or corneal grafts and exposure to pooled human growth hormone) are important. At onset, CJD is commonly misdiagnosed as psychotic illness, Alzheimer's dementia, paraneoplastic syndrome, vascular brain disease, parkinsonism, or even drug-induced delirium. A variant of CJD, caused by a prion with an altered protein configuration, is bovine spongiform encephalopathy (BSE or mad cow disease). Although the precise mechanism of infection originally reported in U.K. cattle is unclear, BSE has been exported to other countries by feeding cattle inadequately processed bone meal. The potential for the emergence of BSE in the United States exists because similar reservoirs of infection are present. Casual handling of beef and beef products in processing plants and uncontrolled disposal of sick cattle may increase that risk. Several cases of CJD have been reported in Kentucky patients who consumed squirrel brains; however, a causal link has not been established. The most recently identified prion illness is a new variant of CJD reported in England that, unlike sporadic CJD, occurs in much younger patients (16 to 50 years of age), can last longer than 1 year, and is characterized by the presence of psychiatric and sensory symptoms and the absence of kuru plaques and electroencephalogram periodic complexes. The illness is thought to be linked to BSE. Mathematical modeling suggests that 75,000 to 80,000 cases will occur in the foreseeable future.

Tick-Borne Diseases

As with many other emerging infectious diseases, concern about tick-borne zoonotic diseases in the United States has increased because of environmental changes brought on by human settlement and socioeconomic factors that place humans at greater risk for tick exposure, such as the development of suburban housing in disturbed natural settings. Current conditions appear favorable for continued increases in vector tick populations and their geographic expansion and for increasing interaction between ticks and humans. In the United States, the prevalence of Rocky Mountain spotted fever may continue to increase as the urbanization of the western and southern regions expands opportunities for human exposure to tick-borne pathogens.

The epidemiology of Lyme disease and tularemia was reviewed, and the concept of a southern (U.S.) tick-associated rash illness (STARI), the epidemiology of which is still being defined, was introduced. STARI is characterized by an expanding erythematous rash resembling that of Lyme disease, mild or absent constitutional symptoms, and no well-described sequelae. The rash responds well to antibiotic treatment. STARI is seen in the range of the human-biting Lone Star tick (*Amblyomma americanum*) and is frequently associated with a Lone Star tick bite. Studies indicate that this infection is not caused by *Borrelia burgdorferi* or other known tick-borne agents. Amplified segments of the genome of this spirochete have recently been described, and some investigators have proposed that it represents a new species, *B. lonestari*. It has been suggested that STARI may be closely related or identical to a commensal spirochete of deer, *B. theileri*.

The need for early diagnosis and treatment of Rocky Mountain spotted fever was stressed by presenting data from 94 infected patients in North Carolina. Death rates were significantly lower (6.5% vs. 22.9%, $p < 0.03$) in patients receiving appropriate treatment within 5 days of onset of illness than in patients who received delayed or no treatment. Predictors of death included renal failure; elevated serum creatinine, aspartate transaminase, and bilirubin; decreased serum sodium; thrombocytopenia; neurologic involvement; and male gender.

Parasitic Diseases

The role of the cell surface glycoconjugate lipophosphoglycan (LPG) in the survival of *Leishmania* parasites whose life cycle alternates between intracellular parasitism and extracellular life in sand fly vectors was explored. Data indicating that LPG is a multifactorial molecule may lead to a biochemical rationale for LPG-targeted chemotherapeutic regimens.

Isolation of a full-length genomic clone of the acid α-mannosidase from an epimastigote genomic library of *Trypanosoma cruzi* was reported. Sequence analysis showed a single open reading frame encoding the α-mannosidase gene. Because the size of this frame is consistent with that of lysosomal mannosidases in humans, these results could lead to the exploration of new chemotherapeutic options in Chagas disease.

A bank of 5,200 insertion mutants has been used to characterize the parasitic mechanisms used by *Legionella pneumophila*. Results from transmission electronmicroscopy indicate that *L. pneumophila* has acquired genetic loci specific for survival and replication within mammalian cells, allowing evolution from a protozoan parasite into its present disease-causing agent. Alternatively, ecologic coevolution of *L. pneumophila* to parasite protozoa has led to the development of multiple redundant mechanisms, some of which do not function within mammalian macrophages.

TB

Poverty, changing immigration patterns, and the emergence of HIV disease were cited as factors contributing to an attenuated rate of decrease of TB incidence in the United States since the late 1980s and its increase as a major global problem. Poorly managed TB control programs, suboptimal access to health care, an inadequate physician knowledge base, and poor patient compliance have combined to increase the incidence of TB and, especially, multidrug-resistant TB; sensitivity testing is critical in the management of resistant TB. Updated CDC guidelines for interpreting the purified protein derivative skin test call for responses to be considered positive if induration is greater than 5 mm in those with HIV or who have recent TB contact, and greater than 10 mm in foreign-born patients, intravenous drug users, the homeless, and immunocompromised patients. Because of the “boosting” phenomenon, two-step purified protein derivative skin testing is now recommended for health-care workers and nursing home patients who are retested periodically. Treatment of active TB should use multiple drugs, avoid adding single agents, and include compliance monitoring, preferably directly observed therapy. Workplace prevention measures should be driven by a consistently high index of suspicion and should include appropriate isolation of suspected cases, work-ups following exposure, rigorous reporting to health departments, and locating recalcitrant patients. Effective control of TB will require social, political, and cultural changes, as well as medical innovation.

Plague

The epidemiology, pathophysiology, and treatment of plague, as well as the improvement of diagnostic techniques for infections caused by *Yersinia pestis,* were reviewed. Such new tests will permit the public health laboratory to quickly identify a plague outbreak and apply the appropriate control measures to limit its spread.

The pathogenesis of plague was explored, and two separate, but essential, iron transport systems were identified in *Y. pestis*. The first, the yersinabactin (Ybt) system, enables the organism to proliferate from the site of an open wound or bite, while the second, identified as Yfe, is used by Ybt mutants to obtain iron during infection of internal organs. The Ybt iron transport system appears to be essential for growth in the early stages of bubonic plague infection, while the Yfe system functions to allow growth during, or after, infection of internal organs. Both systems are required for *Y. pestis* to be fully virulent.

A novel mechanism by which a *Y. pestis* virulence protein is sequestered in, and transported within, host cells was described. When yersiniae contact a eukaryotic cell, a signaling event activates the expression and secretion of a set of four toxins (Yops) and causes their vectorial translocation into the cell cytoplasm. Three of the Yops derange cell signaling and cytoskeletal functions by kinase, tyrosine phosphatase, and actin depolymerization activities. Although no activity or intracellular target has been identified for the fourth known translocated Yop, YopM, immunoblot analysis and laser scanning confocal microscopy demonstrated that most YopM is vectorially translocated into HeLa cells or the macrophagelike cell line J774 by adherent *Y. pestis* and travels to the eukaryotic cell nucleus. Because a growing number of important human pathogens (e.g., *Salmonella, Shigella*, and *Pseudomonas*) have similar, but less well-studied, secretion/translocation mechanisms and putative secreted toxins, these findings will facilitate studies that ultimately could lead to novel therapies for these agents.

Antibiotic Resistance

The current development of staphylococci resistant to methicillin or fluoroquinolones and gram-negative bacilli resistant to extended-spectrum beta-lactams are but the most recently recognized patterns of antibiotic resistance. General approaches for modifying these trends include 1) source control, particularly handwashing, and the need to wear gloves during contacts with all patients, 2) improved antibiotic use and control, 3) improved infection control devices, and 4) better use of pathophysiology and immunologic modulation.

The growing problem of vancomycin-resistant enterococci (VRE), with an incidence of 20% to 40% in some groups of U.S. hospitalized patients, necessitates maximal use of all these approaches. Skin proliferation of VRE produces extensive environmental contamination that may require universal use of gloves to control outbreaks or hyperendemic disease. In addition, vancomycin should be limited to treatment of beta-lactam resistant gram-positive bacteria (such as methicillin-resistant *Staphylococcus aureus* and gram-positive bacteria in beta-lactam allergic patients) and *Clostridium difficile* (only after metronidazole failure) and to endocarditis prophylaxis. Vancomycin should be avoided in routine surgical prophylaxis, empiric treatment of febrile neutropenia with negative cultures, and pneumonia prophylaxis in the intensive care unit. A number of experimental peptides and other agents (such as quinupristin-dalfopristin) under investigation as treatments for VRE infections were identified.

Future trends in resistance may include further spread of vancomycin-resistant staphylococci (already reported in Japan), quinolone- or carbapenem-resistant gram-negative bacilli, and treatment-resistant viruses. Seventeen isolates of methicillin-resistant *S. aureus* with unique genotypes were studied to determine rates of resistance to the fluoroquinolones ciprofloxacin and levofloxacin. The mean single-step resistance to 4 x MIC ciprofloxacin was 1.05×10^{-5} and to levofloxacin was 4.03×10^{-6}. When serially passaged in increasing antibiotic concentrations, the geometric mean MICs for ciprofloxacin and levofloxacin increased 3.0 ± 1.5 times and 1.8 ± 1.4 times, respectively ($p < 0.0005$). Only four strains became resistant to levofloxacin, but eight became resistant to ciprofloxacin, indicating that ciprofloxacin selects methicillin-resistant *S. aureus* more frequently than levofloxacin.

Other Topics

The laboratory evidence supporting the role of *Chlamydia pneumoniae* in the development of atherosclerosis was reviewed. Recent data indicate that infection of vascular endothelial cells with *C. pneumoniae* is associated with the production of chemokines and adhesion molecules that promote transendothelial migration of neutrophils and monocytes. These findings suggest that immunopathogenic responses to *C. pneumoniae* infection may contribute to the development of clogging deposits.

Data were presented demonstrating the proliferation of human CD4+ T cells from unexposed persons in response to in vitro exposure to *Toxoplasma gondii*. Further studies showed that this proliferative response depends on HLA-DR molecules and requires processing of *Tg* antigens. In contrast to typical exogenous superantigens, analysis of TCR Vß expression after stimulation with *Tg* did not show a pattern of preferential increase of a specific TCR Vß-bearing subpopulation. αßT cells secreted significant amounts of IFN-γ after incubation with *Tg*-infected monocytes. This process may play an important role in the early events of the immune response to *T. gondii*.

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International Meeting on Borreliosis, Prague, Czech Republic

Approximately 150 participants from 10 countries gathered in Prague, the Czech Republic, August 27-29, 1997, to discuss research topics related to the theme of the meeting, "Lyme Borreliosis—Basic Science and Clinical Approaches." The meeting was organized by the National Institute of Public Health (Centre of Epidemiology and Microbiology); the World Health Organization Collaborating Center for Reference and Research on Borreliosis; the Second School of Medicine, Charles University (Prague); and the Czech Medical Association J.E. Purkyně. Meeting sessions focused on topics including epidemiology, clinical treatment, dermatology, diagnosis and treatment, neurology, and laboratory diagnosis.

The session on epidemiology presented surveillance data on the incidence of Lyme borreliosis (LB) in the Czech Republic (incidence rates were 61.8/100,000 in 1995 and 41.2/100,000 in 1996) and in Slovakia, Austria, and Slovenia. Data underscored the high risk for transmission of LB in central and eastern Europe. The results of vaccine trials using the recombinant outer surface protein (Osp)A antigen of *Borrelia burgdorferi* were also presented; more detailed studies are needed to examine intraspecies variability of OspA antigens in Europe.

The session on clinical approaches and treatment reviewed research conducted in the United States and discussed the diagnostic importance of organism-specific biologic markers, e.g., Borrelia-specific antigens or DNA, as well as pleocytosis in cerebrospinal or synovial fluid. Experience with the diagnosis and treatment of LB in the hyperendemic-disease regions of west Bohemia underscored the importance of accurate diagnosis in avoiding overtreatment.

The use of nonhuman primates as models for studying neuroborreliosis was examined in the session on neurology. Problems related to the diagnosis and treatment of chronic disease, and their economic consequences, were identified. Several methods to assist clinicians in making a correct diagnosis were presented and discussed. The persistence of *B. burgdorferi* DNA in patients with Lyme arthritis was considered in the rheumatology session. Ultrastructural evidence for the intracellular location of *B. burgdorferi* in synovium also was presented.

The session on laboratory diagnosis focused on the genomic sequence of the linear chromosome of *B. burgdorferi* (B31 strain) and the crystal structure of OspA; both apply to the laboratory diagnosis of LB. Other studies affirmed the importance of standardizing diagnostic methods to ensure reproducibility and uniformity of the results from different laboratories. The influence of certain in vivo–expressed antigens (virulence antigens) on invasiveness and the ability of *B. burgdorferi* to adapt to the host environment were noted. Other topics were the sensitivity and reproducibility of polymerase chain reaction and the importance of the primers selected for the assay.

The studies presented in the poster session addressed a wide array of themes: among them, epidemiology and population awareness, reactivity of *B. burgdorferi* antigens in immunoblot procedures when specimens derived from humans or animals are used, and incidence of ticks and their association with disease in different regions.

The importance of apoptosis in the morphology of LB, the role of Langerhans cells in the skin reactions, and the role of integrin CR3 in the interaction of *B. burgdorferi* with host cells were discussed. The sensitivity and the selection of the primers used for polymerase chain reaction to detect *B. burgdorferi* in ticks were considered. Aspects of vector biology and ecology were investigated (e.g., habitats, the tick as LB's major vector, vector capacity). Other diseases transmitted by *Ixodes ricinus* ticks in Europe (e.g., tick-borne encephalitis, babesiosis, ehrlichiosis) as well as human ehrlichiosis in Europe were reviewed.

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Workshop on Climate Change and Vector-Borne and Other Infectious Diseases

Climate changes may affect human health through a myriad of pathways; of particular interest are pathways affecting the geographic ranges and incidence of vector- and water-borne diseases. As society chooses how to deal with projections of long-term climate change, decisions must be based on scientific knowledge. A 2-day workshop[1] was convened in September 1997 to discuss what is known about the relationship between projected climate changes and the incidence of water-borne diseases (e.g., cholera) and vector-borne diseases, including those typically considered tropical (malaria, dengue fever, yellow fever, and schistosomiasis), plus subtropical or temperate-zone diseases whose vectors are likely to be affected by projected climate changes.

The workshop participants discussed the systems involved in potential climate changes, from the global ocean-atmosphere-landmass system that drives climate to the regional ecologic and human socioeconomic systems where disease dynamics occur. These systems are extremely complex, as are the interactions among them, which underscores the need for more research before accurate projections can be made. Major research gaps were identified, and an agenda was framed for a sound scientific basis for public policy debates and decisions. The proposed agenda included the following items: climate modeling; ecosystem and habitat dynamics; disease surveillance; technologies for disease prevention and mitigation; disease transmission dynamics; data sets for empirical studies; integrated assessments; and detecting, understanding, and responding to unexpected events. Further discussion and implementation of this research agenda is encouraged. A summary of the workshop is available from the Electric Power Research Institute, TR-109516, EPRI Distribution Center, 207 Coggins Drive, P.O. Box 23205, Pleasant Hill, CA 94523; Telephone: 510-934-4212.

[1]The workshop was commissioned by the Electric Power Research Institute, with additional sponsorship from the Department of Energy, the National Institute of Allergy and Infectious Disease, the National Institute of Environmental Health Sciences, and the National Aeronautics and Space Administration. The workshop was organized and conducted by the Washington Advisory Group. The 28 participants included representatives from agencies and institutions that conduct or fund research and experts in the fields of climatology and global climate modeling, public health, and the biology and ecology of vectors, pathogens, and the ecosystems they inhabit.

The Fourth International Conference on HFRS and Hantaviruses

Atlanta, Georgia, USA, March 5–7, 1998

The Centers for Disease Control and Prevention and other cosponsors will host the Fourth International Conference on HFRS and Hantaviruses to facilitate the exchange of scientific information in the following areas: 1) clinical aspects, 2) laboratory diagnostics, 3) pathogenesis and immune response, 4) hantavirus ecology, 5) hantavirus epidemiology, 6) molecular biology and cell interactions, 7) health education and prevention, and 8) antiviral and vaccine development. The meeting will offer plenary sessions with invited speakers, as well as oral and poster sessions based on accepted abstracts.

For further information, contact Amy Corneli, Centers for Disease Control and Prevention, 1600 Clifton Road, MS A26, Atlanta, GA 30333, USA; fax: 404-639-1509; e-mail: akc8@cdc.gov; URL: http://www.cdc.gov/ncidod/diseases/hanta/hantconf.htm.

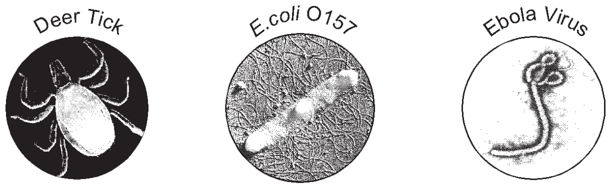
Third International Congress on Tropical Neurology

November 30–December 2, 1998

Organized by the Groupe Francophone d'Etude et de Recherche en Neurologie Tropicale, the Third International Congress on Tropical Neurology will convene in Fort de France, Martinique, from November 30 to December 2, 1998. The four main themes of the congress are central nervous system inflammatory, neurodegenerative, epileptic, and cerebrovascular disorders in tropical environments; however, presentations on other themes are welcome.

A symposium on epilepsy in tropical zones will be held during the congress.

For additional information, contact Professor M. Dumas (phone: 33-5-55-43-58-20, fax: 33-5-55-43-58-21) or Professor J.C. Vernant (phone: 33-5-96-55-22-61, fax: 33-5-96-75-45-90).



International Conference on
Emerging Infectious Diseases

March 8-11, 1998
Atlanta, Georgia

International Conference on Emerging Infectious Diseases
March 8–11, 1998
Atlanta Marriott Marquis Hotel

Late-breaker abstract submission deadline: January 30, 1998

Information on abstract submission, conference registration, and exhibits can be obtained at www.asmusa.org, by sending an e-mail message to meetinginfo@asmusa.org, or by calling 202-942-9248. Proceedings of the conference will be published in the journal Emerging Infectious Diseases.

Registration: limited to 2,500 - register NOW!

Preliminary program information is available at http://www.cdc.gov/ncidod/EID/98conf.htm.