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Dengue Fever in Paradise

RECENT OUTBREAK

Synopsis: *Dengue fever has returned to Hawaii after an absence of more than a half-century.*

Sources: ProMed Mail. Hawaii Department of Health Dengue Fever Information Center. http://www.state.hi.us/health/dengue.

We are now experiencing a global pandemic of dengue, with activity in more than 100 countries, including virtually every country in the tropical zone. Dengue fever has now reared its ugly head on the island paradise of Hawaii.

On November 2, 2001, the Hawaii Department of Health reported that 74 cases of dengue fever had been confirmed in their state since early September, when the first cases appeared in Hahiku in eastern Maui. Of the 74 cases, 56 (75.7%) of the confirmed cases have occurred in Maui with a large proportion in and around Hana (*see map*). Cases have also been reported from Oahu, Kauai, and, most recently, the island of Hawaii. In addition to these confirmed cases, 300 cases of febrile illness in the state are under investigation.

These cases represent the first autochthonous instances of dengue in Hawaii since World War II, a time when *Aedes aegypti* was being eliminated from Maui. Currently, *A albopictus* is the predominant mosquito present in eastern Maui. Dengue is widely present in the South Pacific, having been reintroduced in the 1970s after an absence of 25 years. The Hawaiian cases are believed to have been introduced by travelers from Tahiti or American Samoa. They were first recognized in a rain forest community oriented to native medicine and where mosquitoes abound.

Aedes mosquitoes are generally found in or near human habitats, often resting in dark rooms and breeding in collections of water in small receptacles. Thus, in response to these cases, the Hawaii Department of Health has introduced a statewide mosquito control program with spraying of pesticides and larvicides. Residents were asked to cover or discard items that collect or store rainwater, empty and clean pet and animal watering containers at least weekly, use air conditioning or screened windows and doors, wear long-sleeved shirts and pants, and use mosquito repellent when exposure

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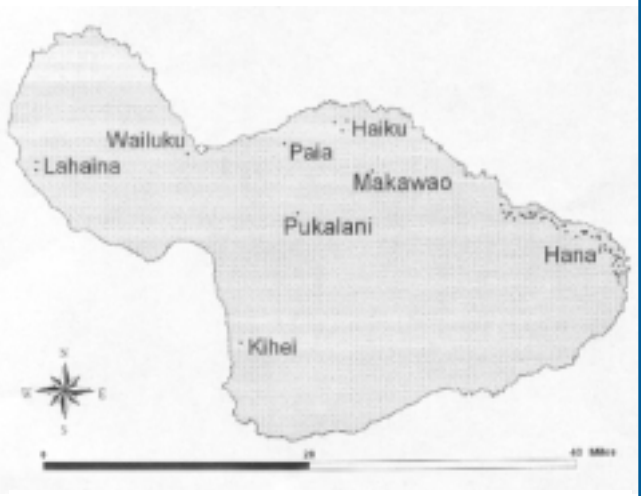
is unavoidable. Television spots announce that every Sunday is "Clean-Up Day." What the long-term effect will be is unclear. The prospect of totally eliminating mosquitoes is likely not tenable. Travel to and from endemic areas will likely not diminish. Plans for a response also include a new dengue laboratory, as the only one in the United States has been in Puerto Rico.

COMMENT BY STAN DERESINSKI, MD, FACP, & ALAN D. TICE, MD, FACP

So far, there have been no dengue hemorrhagic fever cases. This may be because all the endemic cases being serotype 1. It appears the hemorrhagic fever manifestations occur when a person has immunity to one serotype then becomes infected with another. In Thailand, for example, there are 4 different serotypes. The risk for the Hawaiians who had dengue before WWII and for travelers from other endemic areas is unclear.

Figure

Maui: Distribution of 56 Confirmed Cases of Dengue Fever



• *CDC confirmed dengue cases (n = 56)*

The differential diagnosis of dengue includes a wide variety of febrile illnesses. Among these are 2 uncommon treatable infectious diseases that are present in Hawaii—leptospirosis and murine typhus.[1,2] A total of 61 confirmed cases of leptospirosis were identified in Hawaii from June 1998 through February 1999. Twenty-two were from Hawaii, 19 were from Oahu, 18 were from Kauai, and 2 were from Maui.

From 1994 to 1998, there were 27 reported cases of murine typhus in Hawaii—20 from Maui (where there is a persistent hyperendemic focus in the Kihei area), 2 from Oahu, and 5 from southwestern Kauai. ❖

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Prions Beget Prions?

ABSTRACT & COMMENTARY

Synopsis: *The generation of disease-producing prions requires less stringent conditions than previously thought.*

Source: Derkatch IL, et al. Prions affect the appearance of other prions: The story of [PIN(+)]. *Cell.* 2001;106:171-182.

While studying the yeast model, derkatch and colleagues at the University of Illinois in

Chicago discovered that the existence of 1 type of prion could enhance the spontaneous appearance of other types of prions. Derkatch et al had previously established that the yeast non-Mendelian trait [PIN(+)] is required for the de novo appearance of the [PSI(+)] prion. In this study, they showed that the presence of prions formed by Rnq1 or Ure2 is sufficient to make cells [PIN(+)]. This, combined with other work they performed, suggests the existence of a general mechanism by which the appearance of prions is enhanced by heterologous prion aggregates. Since most cases of Creutzfeldt-Jakob disease (CJD) have no known origin, Derkatch et al feel that this may be how prions first appear in humans.

COMMENT BY THOMAS G. SCHLEIS, MS, RPh

The prion diseases constitute an unusual group of neurodegenerative disorders. Similar in many ways to diseases such as Alzheimer's disease and amyotrophic lateral sclerosis (ALS), they differ in their transmissible natures. The prion diseases also demonstrate that the expression of diverse disease phenotypes is possible from a common etiologic factor. Prion diseases are of concern because there are no definitive tests available for detecting the infectious agent, they have relatively long incubation periods, and the inevitable result is death.

The human prion diseases include kuru, sporadic Creutzfeldt-Jakob disease (sCJD), familial CJD (fCJD), iatrogenic CJD (iCJD), Gerstmann-Straussler-Scheinker (GSS) disease, fatal insomnia (FI), and more recently, new variant CJD (nvCJD or vCJD). Animal prion disease includes transmissible mink encephalopathy (TME), chronic wasting disease (CWD) of deer and elk, feline spongiform encephalopathy (FSE), and bovine spongiform encephalopathy (BSE), among others. While most of these animal diseases are presumed to result from ingestion of animal byproducts contaminated with sheep scrapie, CWD appears to be a naturally occurring disease of North America.

The transmissible nature of prion disease was first demonstrated experimentally in 1936 when Cuille and Chelle transmitted scrapie to a healthy goat by the intraocular administration of scrapie-infected spinal cord.[1] Thirty years later, kuru, a disease transmitted among the Fore people of New Guinea through cannibalism, was experimentally transmitted to chimpanzees.[2] While the etiologic agent was first thought to be viral, the current predominant theory is that a small protein is responsible.[3,4]

How a small protein may be a transmissible pathogen has also been extensively studied. It appears that the prion protein (PrP) exists in 2 major isoforms or stuctures: the nonpathogenic or cellular form, designated PrP^{c}, and the pathogenic form, designated PrP^{Sc}. Both have the same amino acid sequence, but PrP^{c} is predominantly helical whereas PrP^{Sc} contains at least 40% of a pleated sheet structure. PrP^{Sc} has different solubility characteristics than PrP^{c} and is more resistant to proteases.[5] The potential mechanism as to how the conversion from PrP^{c} to PrP^{Sc} is initiated, involves a germ line mutation of the human prion protein gene (PRNP), a somatic mutation within a particular neuron, and the resultant conversion of PrP^{c} to PrP^{Sc}. Once this event takes place, the PrP^{Sc} appears to act as a template by which more PrP^{c} is converted to PrP^{Sc}, hence the "infectious" process. In the article reviewed here, it would appear that there is not a complete specificity for one type of prion over another and that spontaneous mutations can occur.

CJD has been the most common human prion disease that has appeared in recent literature. Confirmed transmission of CJD in humans has only been shown to occur with corneal and dura mater transplants or human pituitary growth hormone injections. Nevertheless, blood and blood products that are administered intravenously are immediately recalled if a donor is determined to have vCJD, but not sCJD, fCJD, or iCJD. This is done as a precautionary measure because of its more rapid onset of vCJD vs. other CJDs and the possible association of vCJD to BSE, or Mad Cow disease. Because of the resistance of prions to normal antiviral inactivation steps that are used with such blood products as intravenous immunoglobulins (IVIG) and albumin, manufacturers are attempting to develop methods for the testing and removal of prions from these preparations. So far this has proven to be quite difficult.

Prion disease is an area that requires a great deal of additional research in order to identify the mechanism of transmission and develop methods of prevention and treatment. While the greatest press have been given to the epidemic of mad cow disease in the United Kingdom and CJD disease in the United States, the presence of prion disease is worldwide and will continue to be an area of active research. ❖

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Does Lactobacillus Prevent Antibiotic-Associated Diarrhea?

ABSTRACT & COMMENTARY

Synopsis: *Lactobacillus GG failed to prevent diarrhea in a large group of adults treated with intravenous and oral antibiotics.*

Source: Thomas MR, et al. Lack of effect of Lactobacillus GG on antibiotic-associated diarrhea: A randomized, placebo-controlled trial. *Mayo Clin Proc*. 2001;76:883-889.

Diarrhea associated with administration of antibiotics is an all-too-common phenomenon. Although the importance of *Clostridium difficile* toxin as a mediator of diarrhea has been recognized for a quarter-century, most cases of antibiotic-associated diarrhea (AAD) occur without a clear understanding of etiology and pathogenesis. Current hypotheses presume that alteration of gut bacterial flora leads to diarrhea, perhaps as a result of perturbation of fatty acid metabolism or an effect on *C difficile* or other toxin receptors in the intestinal mucosa.

In this prospective, randomized, double-blind, placebo-controlled study performed at the Mayo Clinic, patients with presumed or proven infections were treated with intravenous and oral antibacterial medication. They were randomized to receive either Lactobacillus GG (LGG, a *L casei* subspecies *rhamnosus* strain, available in a capsule containing 10^{10} cfu) or an identical-appearing placebo twice daily for a 2-week period, commencing within 24 hours of institution of antibiotic therapy. Diarrhea was defined as 2 or more watery or liquid stools for 2 or more consecutive days during a 3-week observation period, or 3 or more bowel movements in excess of the patient's normal daily number of bowel movements. Patients recorded data on bowel movement number and consistency using a standardized grading scale. Other symptoms, including nausea, cramping, gas, and bloating, were also recorded. Thomas and associates monitored laboratory tests, such as stool cultures, fecal leukocyte counts, and stool osmolality, that patients' physicians obtained, and whether a diagnosis of *C difficile* disease was made.

Of nearly 3000 adults who were considered eligible for the study, 349 met the inclusion criteria. The remainder were excluded because they received antibiotics for ≥ 24 hours before being considered for the study, they had pre-existing gastrointestinal tract disease with diarrhea, or for a variety of other reasons. Because of failure of some individuals to consent to the study or others to complete the study, a total of 267 patients completed the trial and provided outcome data.

What were the results? Diarrhea occurred with equal frequency (about 30%) in both placebo and LGG groups. Detailed subset analysis uncovered no significant differences among the groups with respect to receipt of either β-lactam antibiotics or non-β-lactam antibiotics, whether results were assessed solely on stool consistency or stool frequency, or whether only severe diarrhea was selected as an end point.

Documented *C difficile* colitis (as defined by a positive toxin assay) occurred in only 1.5% and 2.2% of LGG and placebo patients, respectively, a difference that was not statistically significant. Likewise, there was no difference in incidence of nausea, abdominal cramping, or bloating between the 2 groups.

COMMENT BY JERRY D. SMILACK, MD, FACP

The term, probiotic, refers to live microbial supplements that have a positive effect on health. Many microorganisms have been touted to possess probiotic properties. Much research has centered on lactobacilli, bifidobacteria, and *Saccharomyces*.[1] How lactobacilli might exert a beneficial effect in treatment of gastrointestinal disorders remains conjectural, but they are known to produce a number of antimicrobial substances, including free fatty acids, hydrogen peroxide, and bacteriocins, and also to inhibit in vitro binding of *E coli* O157:H7 to cells. Evidence suggests that LGG shortens duration of diarrhea and decreases viral shedding in children with rotaviral infection and may lessen incidence of travelers' diarrhea in adults.[2]

There are few studies of LGG as prophylaxis or treatment of *C difficile*-mediated colitis or AAD.[2] However, a recent report by Vanderhoof et al demonstrated benefit, albeit modest, in children treated with a variety of oral antibiotics for respiratory and other

infections.[3] In the present study, the Mayo Clinic investigators speculated as to why their patients failed to receive benefit from LGG. Among the possibilities: Could the fact that most patients initially received intravenous antibiotics—and presumably had high intraluminal concentrations of antibiotic in their gastrointestinal tracts, perhaps killing the ingested LGG bacilli—have negated any effect of LGG? Thomas et al suggest that future studies might demonstrate that higher doses of LGG might overcome an inhibitory effect of large doses of antibiotic, and result in demonstrable benefit. ❖

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Antifungal Susceptibility Testing—Getting the Answer you Want

ABSTRACT & COMMENTARY

Synopsis: *Any of the process variables such as inoculum, medium, incubation conditions involved in antifungal susceptibility testing can affect the results dramatically even those thought to be too trivial to mention, such as sealing the plates.*

Source: Rambali B, et al. Susceptibility testing of pathogenic fungi with itraconazole: A process analysis of test variables. *J Antimicrob Chemother*. 2001;48:163-177.

Several sources of variation, such as inoculum size and incubation conditions, are already known to influence the results of antimicrobial susceptibility tests including those involving antifungal drugs. However, virtually all investigations into the sources of variation have examined only 1 or 2 factors at a time. This approach does not allow the relative importance of each source of variation to be determined nor does it identify possible interactions between factors that may be greater than the individual factors. Like other activities, antifungal susceptibility testing is a process and, as such, is amenable to systematic analysis of each of the elements simultaneously. To this end, Rambali and colleagues set up a factorial design in order to identify which of 10 elements exerted the most influence on determining the susceptibility of 8 *Candida* yeast isolates and 8 molds of different genera including a strain of *Aspergillus fumigatus* to itraconazole.

Statistical analysis indicated that while the source of the medium, the cultivation of the inoculum, and the nature of the solvent used to dissolve the drug did not seem important, incubation time and atmosphere, the shape of the microtitration well, and whether the well was sealed all influenced yeasts and mold in both media. However, other factors, such as glucose concentration, initial inoculum, and incubation temperature, affected yeasts and molds differently (*see Table 1*).

The range of MICs was also impressive averaging 0.06 to 8.41 mg/L for RPMI and 0.02 to 2.69 mg/L for CYG—a 419- to 539-fold difference. This means that alterations in the process in one direction can result in a low MIC but in a very high MIC in the other direction. For instance, 9 of the 30 combinations in RPMI resulted in an MIC > 4 mg/L for *C glabrata* J940839 compared with only 2 of the combinations tested in CYG (*see Table 2*).

COMMENT BY J. PETER DONNELLY, PhD

Finally, a group of scientists has risen to the challenge of systematically testing each of the processes involved in determining the MIC of yeasts and molds to an antifungal agent, and the results are a revelation. They clearly show that antifungal susceptibility tests are affected markedly by even trivial things such as the shape of the microtitration well and whether the opening is sealed. Moreover, different strains are

Table 1

Factors that Affected Yeasts Differently from Molds

	Growth of yeasts	Growth of molds
Glucose concentration (0.2 *or* 2.0 %)	Improved at 2 %	No influence
Sticker seal (yes *or* no)	No influence	Decreased when sealed
Initial cell concentration (1,000 *or* 40,000 cfu/mL)	Improved when high	No influence
Incubation time (24 h *or* 48 h)	Optimal by 24 h	Optimal by 48 h
Incubation temperature (30°C *or* 35°C)	Improved at 35°C	Improved at 30°C

Table 2

Range of MICs obtained

	RPMI			CYG		
	Lowest	Highest		Lowest	Highest	
Isolate	MIC	MIC	range	MIC	MIC	range
Candida albicans B2630	0.016	4	256	0.016	32	2048
Candida albicans B59630	0.5	32	64	0.125	32	256
Candida glabrata B63155	0.125	32	256	0.016	2	128
Candida glabrata J931545	1	32	32	0.016	2	128
Candida glabrata J940839	1	32	32	0.016	32	2048
Candida krusei ATCC 6258	0.016	0.5	32	0.016	0.25	16
Candida parapsilosis ATCC 22019	0.016	0.25	16	0.016	0.016	1
Candida tropicalis CDC 44	0.016	32	2048	0.016	32	2048
Aspergillus fumigatus NCPF7099	0.016	32	2048	0.016	2	128
Aspergillus fumigatus J980617	0.016	1	64	0.016	0.5	32
Fusarium oxysporum J990081	0.125	32	256	0.5	32	64
Paecilomyces lilacinus J980407	0.125	32	256	0.016	8	512
Scedosporium apiospermum J961338	0.016	4	256	0.016	2	128
Trichophyton rubrum B68183	0.016	4	256	0.016	0.125	8
Average	0.06	8.41	419	0.02	2.69	539

affected differently and molds clearly require different conditions than yeasts. This is bad news for those striving to achieve a unified approach to antifungal susceptibility testing based on the conditions and materials. It also bodes ill for standardization since one method clearly doesn't fit all and even minor variations in technique can lead to widely divergent results. The results also vindicate the notion that one cannot refer to *the* MIC but only to *an* MIC and also provide a plausible explanation for the marked interlaboratory variation often seen in quality control programs in which participants purport to adopting the same technique but probably have only adhered to the main aspects while ignoring the apparently minor details. Last but not least, the consumers of such tests must now be aware that it is possible to obtain the result that best suits. Given the increasing number of available antifungal agents, it is important that appropriate tests are used to define susceptibility and detect resistance in vitro since these data are crucial for epidemiological purposes, patient management, and research. The results of this study are challenging to say the least as they report the influence of process variable for only one antifungal agent, itraconazole, but show clearly the need to explore much more thoroughly the influence of each element in the process of testing the susceptibility to the rest including fluconazole, amphotericin B, caspofungin, and those close to reaching the marketplace, such as voriconazole. ❖

Statins and Infection

ABSTRACT & COMMENTARY

Synopsis: *Statin administration was associated with a reduced mortality in bacteremic patients.*

Source: Liappis AP, et al. The effect of statins on mortality in patients with bacteremia. *Clin Infect Dis.* 2001;33: 1352-1357.

Liappis and colleagues analyzed 243 episodes of aerobic Gram-negative bacteremia and 145 cases of *Staphylococcus aureus* bacteremia occurring in Veterans Administration patients to evaluate the effect of statin therapy on mortality. Thirty-five (9%) of patients were receiving a statin at the time of admission and continued it during hospitalization—20 had gram-negative bacteremia and 15 had *S aureus* bacteremia. Most statin recipients were receiving simvastatin. All but 2 of the total patients were male.

While 100 of 353 (28%) bacteremic patients not receiving statins died, only 2 of 35 (6%) bacteremic statin recipients did so (P = 0.002). Mortality rates attributable to infection were, respectively, 70 of 353 (20%) and 1 of 35 (3%) (P = 0.10). Multivariate analysis found that, while use of ACE was associated with an increased risk of mortality, only statin use was associat-

ed with improved survival (OR. 7.63; 95% CI, 1.01-57.5). Also noted was that skin and soft tissue infections were more commonly identified as sources of bacteremia in the statin recipients ($P = 0.008$).

COMMENT BY STAN DERESINSKI, MD, FACP

A subsequent retrospective analysis of 9651 diabetic patients by the same investigative group confirmed a reduced mortality as well as an increased incidence of lower extremity infections among those receiving statin (HMG-CoA reductase inhibitor) therapy.[1] Thus, 596 of 1932 (30.8%; $P < 0.00001$) statin recipients had lower extremity infection compared to only 1287 of 7719 (11.6%; $P < 0.00001$).

Liappis and colleagues reviewed some experimental work that might provide a potential explanation for these remarkable findings. Studies have suggested that statins reduce the inflammatory reactions within atherosclerotic plaques by a mechanism that does not involve lowering of serum lipid levels.[2] Statin administration reduces neutrophil migration into lung after intranasal instillation of endotoxin and diminishes TNF production in a murine model.[3] Pravastatin has been demonstrated to inhibit neutrophil and monocyte chemotaxis in vitro.[4,5] In addition, cerivastatin reduces in vitro monocyte adhesion to vascular endothelium by down regulation of adhesion molecules and by inhibition of actin polymerization by inactivation of the G protein, RhoA.[6] Fluvastatin increases nitric oxide synthase activity in endothelial cell cultures while reducing expression of the adhesion molecules, E-selectin, and ICAM-1.[7] Statins improve endothelial function by stimulation of endothelial constitutive nitric oxide synthase activity.[8]

Thus, a variety of studies provide evidence that statins, in a manner independent of their lipid-lowering activity, significantly modify the inflammatory response. Liappis et al speculate that these effects may result from the statin-induced depletion of isoprenoids. These non-sterol cholesterol precursors are required for covalent binding of farnesyl and geranyl groups to membrane G proteins involved in signal transduction pathways. These critical pathways regulate cell signaling, migration, and proliferation.

Thus, it is possible that the observed reduced mortality in bacteremic males may be the consequence of the anti-inflammatory effects of the statins. In addition, the statin-induced reduction in chemotactic activity may provide an explanation for the observed increased incidence of skin and soft tissue infections and of infections of the lower extremities in diabetic patients since defects in neutrophil chemotactic activity are generally associated with an increased risk of skin and soft tissue infection.

It will be interesting to see where these novel observations ultimately lead. ❖

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CME Questions

32. The probiotic agent, *Lactobacillus rhamnosus* strain GG, has been shown to lessen the incidence of antibiotic-associated diarrhea in both children and adults.

a. True
b. False

33. Which of the following is true?

a. Creutzfeldt-Jakob disease is caused by a virus.
b. Variants of Creutzfeldt-Jakob disease are identical to BSE or mad cow disease.
c. Prions are able to replicate by expressing a gene that results in the manufacture of more prion.
d. Prions are easily removed from blood and blood products due to their instability and ability to complex.
e. None of the above

34. Which of the following is true?

a. There is currently no vaccine or treatment for prion diseases.
b. All versions of Creutzfeldt-Jakob disease have similar incubation periods and manifestations.
c. Transmission of Creutzfeldt-Jakob disease can result from dura matter and ocular transplants, human growth hormone injections or infusion of blood products.
d. Prions of identical composition may exist in either pathogenic or nonpathogenic forms.

In Future Issues:

Meanwhile, Back at the Farm. . .

UPDATES

By Carol A. Kemper, MD, FACP

Can HAART Worsen PCP?

Source: Wislez M, et al. *Am J Respir Crit Care Med.* 2001;164:847-851.

Wislez and colleagues describe 3 HIV-infected patients being treated for *Pneumocystis carinii* pneumonia (PCP) who developed respiratory function following initiation of highly active antiretroviral therapy (HAART). All 3 patients had severe PCP that had initially improved with antiPCP treatment and adjunctive corticosteroids (the latter was administered for 2 weeks). HAART was begun within 1 to 16 days of diagnosis and initiation of treatment. Within 7 to 17 days after intitiation of HAART, all 3 patients developed respiratory failure with recurrent fever and patchy alveolar infiltrates. Following discontinuation of HAART and reintroduction of steroids, all 3 eventually improved.

This report is interesting for all kinds of reasons. Based on reports that initiation of HAART during acute OI may speed recovery, it has been recommended that HAART be administered as soon as possible to all such patients. On the other hand, there are increasing reports that the initiation of antiretroviral therapy can trigger a variety of inflammatory responses, presumably because of enhancement of the immune response, with worsening, for example, of underlying hepatitis, mycobacterial infection, and CMV.

It is known that about 10% of patients with PCP experience deterioration in respiratory function within 3-7 days of initiation of antiPCP treatment, an effect that is mitigated by the administration of adjuvant corticosteroids. Hence the widespread use of corticosteroids in the treatment of moderately-severe-to-severe PCP (A-a gradient ≥ 30). The original California Collaborative Treatment Group protocol from the early 1990s specified 21 days of adjuvant corticosteroids, which has been shortened to 2 weeks by some clinicians because of concerns of immune suppression. Anecdotal reports have, however, described patients with premature "flares" of PCP when corticosteroids were stopped prematurely at 10 or 14 days. Whether the deterioration in respiratory function in these patients with severe PCP occurred because of the normal course of disease, the administration of HAART, or the premature discontinuation of steroids is not known, but a controlled trial to answer this question is probably no longer possible. ■

An Ephemeral Virus?

Sources: ProMED mail post, October 16, 2001; Kliatchko IR. *The Manila Times*. October 12, 2001.

This unusual report describes a lesser known virus, bovine ephemeral fever (BEF) virus, which causes significant morbidity in cattle and buffaloes in Asia, Africa, and Australia. A member of the family Rhabdoviridae, which also includes vesiculoviruses such as vesicular stomatitis virus, this ephemerovirus is transmitted by mosquitos, and is widespread in certain areas. Infection is associated with acute pharyngoesophageal paralysis, muscular weakness and twitching, and acute paresis, possibly from hypocalcemia. Eventually the animal weakens and develops permanent paresis from cervical myelopathy. While the mortality is ~4-13%, the morbidity is significant (~50%); administration of anti-inflammatories and calcium may diminish symptoms. Detection of infection is complicated by cross-reactivity with other similar rhabdoviridae. A vaccine is available but must be administered annually. ■

Hotel Histo!

Source: ProMED-mail post. October 16, 2001. www.promedmail.org.

An earlier report this year described a series of 229 students from 44 colleges throughout the United States who had developed histoplasmosis after traveling to Acupulco for spring break during the first 2 weeks of March (Kemper CA. *Infectious Disease Alert.* 2001;20:144). The possible source of infection had not been identified but the Calinda Beach hotel was a suspect. In total, more than 400 guests of the hotel reported developing symptoms of histoplasmosis last spring. However, when guests who had stayed at the hotel in September began complaining of symptoms of histoplasmosis, authorities finally acted in October to close the hotel. The specific focus of infection in the hotel or the grounds still had not been identified. ■

Anthrax—Northern California

Source: ProMED-mail post. November 1, 2001. www.promedmail.org.

By some amazing coincidence, between October 20 and 26, 21 cattle in the southern part of Santa Clara County, California (where I work) developed acute anthrax infection and died. All of the cattle, which belonged to a single ranch about 5 miles south of Morgan Hill, have been buried, and another 120 have been vaccinated. At least 15 people, including the veterinarian who performed the necropsies in the field, several ranch hands, and 10 laboratory workers who handled the samples have received prophylactic antibiotics.

Anthrax in cattle is not unheard of—just uncommon in these parts. Before this report, there were only 10 reported cases of anthrax in cattle in California during the past 10 years! Because the spores can lay dormant in soil for many years, cattle, elk and other ruminants are more vulnerable to infection, especially when the soil is dry or overgrazed. Interestingly, the veterinarian who initially examined the cattle in the field found no overt signs of anthrax; specifically, there were no signs of hemorrhage, which may be a clue but is not invariably present. Since the events of early October on the East Coast, authorities have alerted large animal vets to be alert for similar outbreaks. ■