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Fungus from the Pharmacy: An Unusual Outbreak of Nosocomial Fungemia

ABSTRACT & COMMENTARY

Synopsis: *An outbreak of fungemia in compromised hosts due to E jeanselmei, a dematiaceous fungus, was traced to deionized water used to compound antiseptic solutions in a hospital pharmacy.*

Source: Nucci M, et al. Nosocomial outbreak of *Exophiala jeanselmei* fungemia associated with contamination of hospital water. *Clin Infect Dis.* 2002;34:1475-1480.

Over a 22-month period, 19 episodes of nosocomial fungemia due to *Exophiala jeanselmei* occurred among patients admitted to a university hospital in Brazil. The majority of patients were immunocompromised due to malignancy, neutropenia, corticosteroid therapy, or HIV infection. Fourteen (74%) had a central venous catheter. In a case-control study, neutropenia, duration of hospitalization, and receipt of corticosteroids were identified as independent risk factors for infection. Nucci and colleagues obtained multiple cultures of blood products, intravenous solutions, and water sources within the hospital. They isolated *E jeanselmei* from 3 sources: a storage tank, a sink in a nonpatient care area, and the deionizer in the pharmacy. Water processed by the latter was used to prepare skin disinfectant solutions, primarily 70% alcohol and alcohol/chlorhexidine. These solutions were routinely used for skin disinfection during venipuncture or vascular catheter care. DNA typing of clinical and environmental isolates by means of random amplification of polymorphic DNA (RAPD) showed that clinical strains and the pharmacy strain were all highly related, and unrelated to *E jeanselmei* isolated from other sites. Once the pharmacy deionizer was taken out of service, no further cases occurred.

COMMENT BY STAN DERESINSKI, MD, FACP

E jeanselmei is a dematiaceous fungus, and members of this group of organisms are common inhabitants of soil and water. They produce melanin, which gives them their characteristic pigmentation

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INSIDE

on culture media. Its nomenclature is the subject of some disagreement; some of the other species reported in human infection include *Alternaria*, *Dactylaria*, *Phialophora*, and *Curvularia.*[1] Disease in immunocompetent patients often manifests as soft tissue, bone, or joint infection after contamination of wounds with soil or water. Susceptibility to antifungal agents is variable, and debridement is a major therapeutic maneuver in these localized infections. More invasive disease occurs in immunosuppressed patients. Fungemia, invasive sinusitis, brain abscess, and pulmonary invasion are among the reported syndromes.[2,3]

The report of Nucci et al is notable in that a nosocomial outbreak was traced to a water source in the hospital pharmacy. Although hospital water is a well-recognized cause of nosocomial infection due to bacterial pathogens, including Legionella and nonfermentative Gram-negative bacilli, there is growing evidence that hospital water may be a source of invasive fungal infection as well. Hospital water has been implicated in nosocomial infection due to *Fusarium solani*[4] and *Aspergillus fumigatus*.[5] The proposed mechanism is inhalation of fungal spores aerosolized from water fixtures.

The population of patients at risk for invasive fungal infection continues to grow due to advances in transplantation, cancer treatment, and care of HIV infection. At present, the magnitude of risk posed by fungal colonization of hospital water systems remains to be elucidated. This is an area deserving serious attention by hospital epidemiologists. ■

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VRSA Has Arrived

ABSTRACTS & COMMENTARY

Synopsis: *The dialysis catheter used to manage a 40-year-old Michigan resident became infected with strains of Staphylococcus aureus resistant to 128 mg/L vancomycin and > 16 µg/mg/L oxacillin.*

Sources: Quirk M. First VRSA isolate identified in USA. *Lancet Infect Dis*. 2002;2:510; *Staphylococcus aureus* resistant to vancomycin—United States, 2002. *MMWR Morb Mortal Wkly Rep*. 2002;51:565-567; Bartley J. First case of VRSA identified in Michigan. *Infect Control Hosp Epidemiol*. 2002;23:480.

A 40-YEAR-OLD RESIDENT OF MICHIGAN, ILL, WITH diabetes and peripheral vascular disease had under-

gone dialysis for chronic renal failure. He had been treated for chronic foot ulcerations with repeated courses of antimicrobial therapy, some of which included vancomycin for over a year. In April of this year he developed bacteremia due to methicillin-resistant *Staphylococcus aureus* associated with amputation of a gangrenous toe. The arteriovenous hemodialysis graft was suspected to be the source and was duly removed and treatment was started with vancomycin and rifampin. In June, a catheter exit-site infection was apparent, the temporary dialysis catheter was removed and cultures of each yielded *S aureus*. The MIC of vancomycin, teicoplaninin, and oxacillin were > 128 mg/L, 32 mg/L, and > 16 mg/L, respectively. The strains contained both the *mecA* gene for methicillin/oxacillin-resistance and the *vanA* gene for vancomycin resistance. The infection responded to outpatient treatment comprising aggressive wound care and systemic antimicrobial therapy with trimethoprim/sulfamethoxazole to which the isolate was susceptible in vitro. The VRSA was also susceptible to chloramphenicol linezolid, minocycline, quinupristin/dalfopristin, and tetracycline.

The *S aureus* was also recovered from a chronic foot ulcer together with vancomycin-resistant *Enterococcus faecalis* (VRE), and *Klebsiella oxytoca* but not from the healed catheter exit site or the anterior nares.

So far, the VRSA has not been isolated from any of the health care workers, dialysis centre patients, familial contacts, or community contacts.

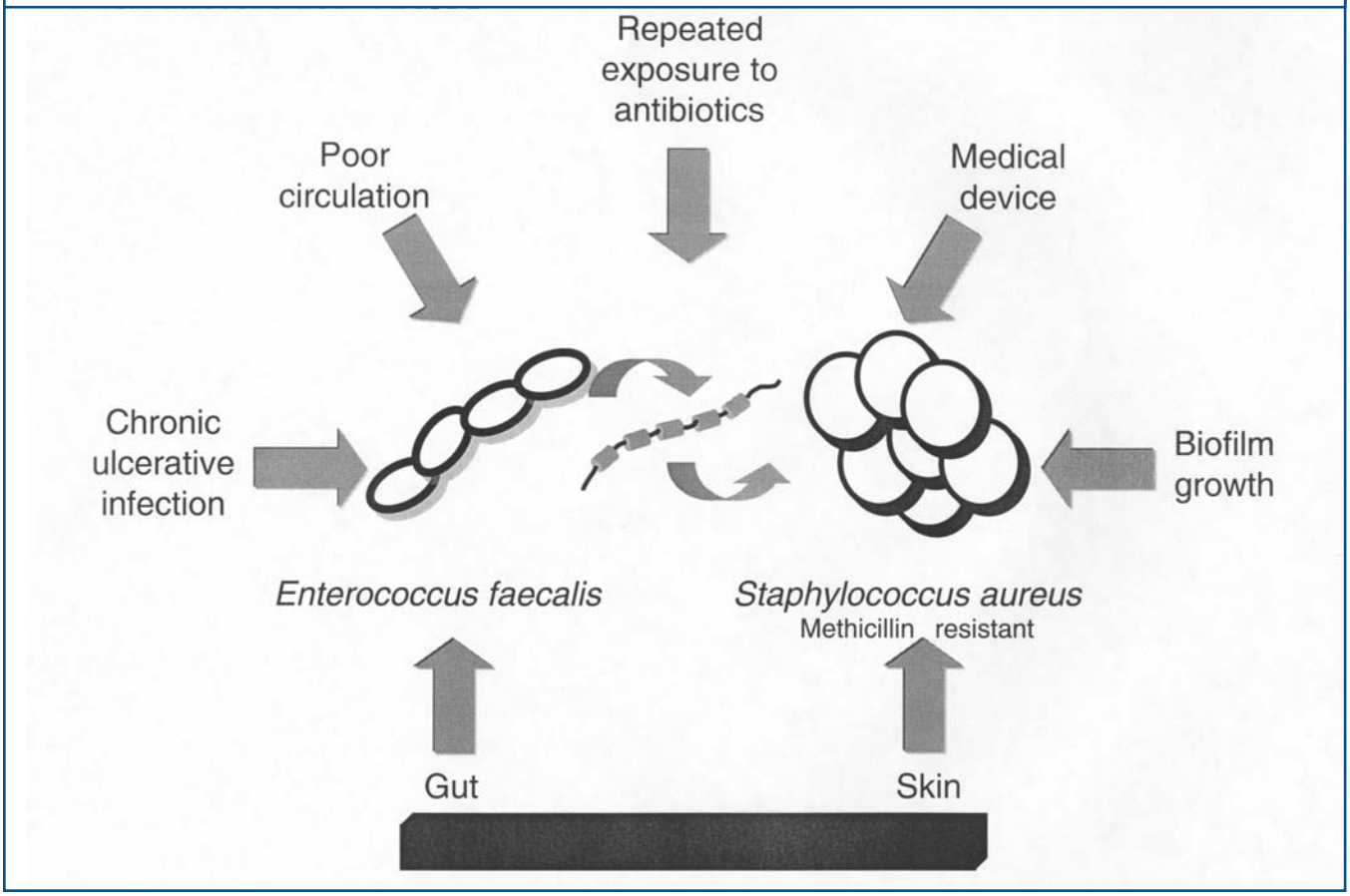
COMMENT BY J. PETER DONNELLY, PhD

It might have taken 8 years since the first vancomycin intermediately susceptible strain of *S aureus* was reported in Japan for the true VRSA to arrive—but it is here, and, likely here to stay. True, there was no evidence of spread and the strain seems to have been effectively eradicated from the patient, but *S aureus* is the emperor of nosocomial infections and knows only too well how to acquire new clothes. In fact, knowing the enemy is actually our best defense. The necessary ingredients for breeding multi-resistant *S aureus* have been known for a long time and were also present in this case (*see Figure*).

S aureus needs to have originated from somewhere and although technically the affected individual was an outpatient, the hospital is the most likely culprit since the patient was in and out for at least a year, had had a

Figure

Risk Factors for VRSA



gangrenous toe amputated, suffered bacteriemia due to the methicillin-resistant *S aureus* emanating from an infected hemodialysis catheter and another clinically defined infection of a temporary dialysis catheter. Although the VRSA was not detected in the foot ulcer and the *Enterococcus* was not found around the catheter exit site, the 2 must have come into close contact with each other for the necessary exchange of DNA to take place. Chronic infection of dead or dying tissue such as the foot ulcer would seem the ideal place. Such lesions are easy prey to other opportunists migrating from their more usual residence and with the help of fingers and fomites, fecal bacteria like *Enterococcus faecalis*, and *Klebsiella oxytoca* could easily have spread from the gut and the MRSA from the catheter exit site. It was unlucky that the particular strain of *E faecalis* bore potentially transmissible genetic material that conferred resistance to vancomycin. Lastly, both enterococci and staphylococci dwell in a biofilm in their natural habitats and cohabitation would provide the intimate contact necessary to allow for the successful exchange of genes. In essence, the Petri dish was recreated. Having known it could happen in-vitro we now know it can also take place in-vivo but can only speculate on where and when it will occur next. My guess is the same places where its cousin MRSA resides and it is likely to happen sometime soon. Seems like a good time to check that the appropriate infection control precautions really are being taken. ■

Outbreak of Mycobacterium Tuberculosis in African Mongooses and Meerkats: What, Me Worry?

ABSTRACT & COMMENTARY

Synopsis: *Mycobacterium tuberculosis caused an outbreak of disease and death in free-ranging wildlife in Botswana and South Africa. Such infections may serve as a reservoir for possible transmission to humans.*

Source: Alexander, KA et al. *Mycobacterium tuberculosis*: An emerging disease in free-ranging wildlife. *Emerg Infect Dis*. 2002;8:598-601.

ALEXANDER AND COLLEAGUES REPORT AN OUTbreak of *Mycobacterium tuberculosis* in free-ranging banded mongooses (*Mungos mungo*) and suricates (*Suricata suricatta*), are small, burrowing mammals more familiarly known as meerkats.

Behavioral ecologists began monitoring 12 troops of meerkats along the dry bed of the Kuruman River in South Africa from October 1998 to December 1999. This epizootic began when an unknown infected male meerkat with enlarged cervical lymph nodes joined the study group of 5 adults and 15 pups. A month later, the lymph nodes of the infected animal ruptured and began draining pus, eventually becoming a persistent nonhealing wound. Progressive cachexia and debilitation occurred until the animal eventually disappeared. Within 2 months, signs of disease such as lymphadenopathy, weakness, and emaciation appeared among other animals in the group. Eventually all members of the troop either died, disappeared (presumed dead), or were euthanized. One human case of tuberculosis (TB) was known to have occurred in the vicinity of the meerkat burrows. The affected animals were seen foraging around roads and "investigating" human sputum.

Another group of scientists identified an epizootic in banded mongooses at the northern extreme of Chobe National Park in Botswana from June to September 1999. Disease spread quickly to 6 different troops. The last case occurred in September 1999. No new cases appeared during monitoring through January 2001. Human garbage pits and a human TB case were near the initial outbreak sites. Banded mongooses were seen feeding regularly at these garbage pits.

Gross postmortem examination of the animals (1 meerkat, 7 mongooses) revealed lymphadenopathy and miliary masses in various organs including liver, spleen, lungs, and kidneys. Histopathologic examination showed granulomas in many organs as well as acid-fast organisms in the cytoplasm of macrophages.

Specimens from 1 mongoose and 1 meerkat grew acid-fast colonies on Lowenstein-Jensen media after 5-6 weeks. The isolates produced niacin and reduced nitrates, characteristics that are typical of *M tuberculosis*. *Mycobacterium bovis* is usually niacin-negative and does not reduce nitrates. In addition, these specimens were PCR amplified using a protocol of de Witt et al to differentiate *M tuberculosis* from *M bovis*.[1] Findings were consistent with *M tuberculosis*.

■ COMMENT BY MARY-LOUISE SCULLY, MD

Humans are the only reservoir for *M tuberculosis* whereas *M bovis* is widespread in domestic, captive and free-ranging wildlife populations.[2] Previous reports have shown possible transmission of *M tuberculosis* in situations of captivity or close, prolonged contact between animals and humans, such as the 4 elephants and their

trainer at an exotic animal farm in Illinois in 1996. The DNA fingerprint comparisons showed that the isolates were the same strain, suggesting transmission of *M tuberculosis* between humans and elephants.[3]

These epizootics reported in mongooses and meerkats occurred in the vicinity of human cases of TB though no further details on the human cases are available. The researchers suspected transmission occurred via an oral route via animal exposure to human excretions and secretions in the surrounding environment. An increase in these exposures seems inevitable. In 1999 alone, more than 89,000 visitors to Chobe National Park were recorded.[4]

Death and disease due to TB continue to increase, especially in developing countries where HIV is prevalent as well. In Botswana, the TB infection rate increased from 202 per 100,000 in 1989 to 537 per 100,000 in 1999. In addition, 36% of women receiving routine antenatal care in Botswana in 1999 were seropositive for HIV.[5] Coexisting HIV and TB can influence the severity of TB infection and shorten the time from initial TB infection to development of overt disease, potentially increasing the amount of TB shed into the environment. Some evidence suggests that concurrent helminthic infections may decrease the host immune response to TB, further increasing the burden of TB in Africa and developing countries.[6]

Transmission of human disease to animals is not new, although public attention is often more focused on the reverse situation. In 1998, evidence strongly linked the death of 6 endangered mountain gorillas in Rwanda to human measles. The epidemic was abruptly stopped by the administration of measles vaccine to the remaining 65 healthy gorillas.[7] As humans and animals share the world's dwindling resources and habitats, more disease overlap will invariably occur. Even more unsettling is whether these infected animals could become new reservoirs for pathogens previously confined to humans. Clearly this would pose a new challenge in the attempt at TB and other disease eradication. ■

Dr. Scully is part of the Group Health Cooperative of Puget Sound, Seattle, Wash.

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Rickettsialpox in North Carolina

ABSTRACTS & COMMENTARY

Synopsis: *This study reports the first case of rickettsialpox in the southern United States caused by infection with R akari. The North American range for rickettsial disease expands even as newer agents are discovered abroad.*

Sources: Krusell A, et al. Rickettsialpox in North Carolina: A case report. *Emerg Infect Dis*. 2002;8(7):727-728; Kelly D, et al. The past and present threat of rickettsial diseases to military medicine and international public health. *Clin Infect Dis*. 2002;34(Suppl 4):S145-S169.

A 48-YEAR-OLD MAN WHO HAD WORKED AT A GOLF course was admitted with fevers, chills, severe headache and a rash. Seven days prior to admission he had felt an insect bite that developed into an ulcerated papule. Two days before admission, red macules appeared over his anterior chest and then became vesicular.

The patient had a pet dog and cat but had not traveled outside North Carolina in the 3 months before admission. He did notice his cat had brought dead mice to his grounds but he never directly touched them. He reported no recent tick exposures or insect bites. On admission the patient appeared ill, was febrile, and had an eschar on his posterior right thigh. A macular vesicular rash was present on his trunk, arms and legs. All lab values were normal except his low platelet count of

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Table

Principal Causative Agents, Modes of Transmission, and Distribution of the Rickettsial Diseases

Group, disease	Causative agent	Mode of transmission	Geographic distribution
Typhus			
Epidemic typhus	*Rickettsia prowazekii*	Infected human body louse feces; flying squirrel flea	Worldwide
Brill-Zinsser disease	*R prowazekii*	Recrudescence of latent *R prowazekii* infection	Worldwide
Murine (endemic) typhus	*Rickettsia typhi (mooseri)*	Infected rat flea feces	Worldwide
Spotted fever			
Rocky Mountain spotted fever, Brazilian spotted fever	*Rickettsia rickettsii*	Tick bite	North and South America
Boutonneuse fever, Mediterranean spotted fever	*Rickettsia conorii*	Tick bite	Mediterranean littoral to India, Africa
Astrakhan spotted fever	*Rickettsia caspii*	Tick bite	Astrakhan, Russia
North Asian (Siberian) tick typhus	*Rickettsia sibirica*	Tick bite	Siberia, Armenia, Pakistan, northern China
Oriental (Japanese) spotted fever	*Rickettsia japonica*	Tick bite	Southwest Japan
Australian (Queensland) tick typhus	*Rickettsia australis*	Tick bite	Queensland, Australia
African tick bite fever	*Rickettsia africae*	Tick bite	Sub-Saharan Africa
Israeli tick typhus	*Rickettsia sharonii*	Tick bite	Israel
Rickettsialpox	*Rickettsia akari*	Mite bite	USA, Korea, Ukraine, Croatia
Flinders Island tick typhus	*Rickettsia honei*	Tick bite	Flinders Island, Tasmania
Asian or thai tick typhus	*TT-118*	Tick bite	Thailand, Malaysia
Cat flea typhus	*Rickettsia felis*	Cat flea bite (?)	Western and southwestern USA
Scrub typhus	*Orientia tsutsugamushi*[a]	Chigger bite	Afghanistan, Pakistan, and India to Siberia, Southwest Pacific Islands, Southeast Asia, northern Australia
Ehrlichioses[b]			
Canine ehrlichiosis; tropical canine pancytopenia	*Ehrlichia canis*	Tick bite	Southeast Asia, southwestern USA, Venezuela
Human monocytic ehrlichiosis	*Ehrlichia chaffeensis*	Tick bite	Americas, Europe, Thailand
Human granulocytic ehrlichiosis	*Anaplasma phagocytophila*	Tick bite	USA, Europe
Sennetsu fever	*Neorickettsia sennetsu*	Unknown	Japan, possibly Malaysia
Q fever	*Coxiella burnetii*	Infectious aerosol, tick bite	Worldwide
Bartonelloses[c]			
Trench fever	*Bartonella quintana*	Infected louse feces into skin; rodent contact (?)	USA, Mexico, Europe, Africa, Middle East, China, Japan, Bolivia
Bartonellosis (Oroya fever, Verruga peruana, Carrion's disease)	*Bartonella bacilliformis*	Infected sand fly	Andes Mountains of Colombia, Ecuador, Peru, 610-2440 m elevation
Cat scratch disease	*Bartonella henselae*	Cat or dog contact	North America, Europe
Bacillary angiomatosis	*Bartonella species*	Unknown	Worldwide
Rodent bartonelloses	*Bartonella elizabethae*, *Bartonella species*	Rattus or other rodent contact	Worldwide

[a] *Rickettsia tsutsugamushi* was renamed *Orientia tsutsugamushi* because of differences > 10% in 16S rRNA and in cell wall structures that lack lipopolysaccharide and peptidoglycan typical of other members of the genus.

[b] Molecular phylogenetic analyses with use of 16S rRNA gene and groESL operon nucleic acid data and serological cross-reactions suggest that current species of genus Ehrlichia should be distributed into genera of the Anaplasmataceae, which are now designated as Ehrlichia, Anaplasma, Neorickettsia, and Wolbachia. *Ehrlichia sennetsu* is now designated *Neorickettsia sennetsu*.

[c] 16S rRNA sequence data, DNA relatedness data, guanine-plus-cytosine content, and other phenotypic characteristics have resulted in unification of genera Bartonella and Rochalimaea, and proposed removal of family Bartonellaceae from order Rickettsiales.

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85,000/µl. A clinical diagnosis of rickettsialpox was made and he was treated with doxycycline and cefazolin. He defervesced within 48 hours.

Two serum samples were submitted to CDC, Atlanta. Samples were tested by a standard IFA for IgG antibodies reactive with *Rickettsia akari* and *R rickettsii* antigens. Because of antibody cross-reactivity among the spotted fever group or organisms, confirmatory cross-adsorption testing was performed and it confirmed *R akari* (rickettsialpox) infection.

COMMENT BY MICHELE BARRY, MD, FACP

This patient had a classic clinical presentation for *R akari* infection with an eschar, vesicular rash, thrombocytopenia, and severe headache. Fever and vesicular rash can sometimes cause confusion with chickenpox or other viral exanthems. However, the presence of an eschar at the site of inoculation and the lack of successive crops of vesicles over time should distinguish the rash from varicella and alert clinicians to the possibility of rickettsialpox.

R akari is transmitted from mice to humans by the house mouse mite. Rickettsialpox was first described in humans in 1946 in a group of residents in apartments clustered within a 3-block area of Queens, NY! Most cases to date have occurred in large metropolitan areas of the northeastern United States. Morbidity and mortality caused by rickettsioses have had a major influence on military activities and public health for > 2000 years. The military experience with epidemic rickettsialpox has been recently described in a *Clinical Infectious Disease* supplement. The diseases caused by these organisms are notoriously difficult to diagnose because they share symptoms with many other febrile diseases with similar epidemiology.

The rickettsioses, historically included the families of Rickettsiaceae, Bartonellaceae and Anaplasmataceae. (*see Table*.) They were originally defined as obligate intracellular parasites that grew only within eukaryotic host cells. Members of the family Bartonellaceae have been removed from this family as they grow fastidiously on enriched culture media and share different DNA/RNA sequences. In the past, human rickettsial diseases caused by members of the genus Rickettsia were collectively called "typhus fever." Later the typhus fevers were differentiated by a characteristic lesion (eg, the eschar of scrub typhus), causative agent or vector (eg, louse, flea, tick, mite). Although all agents caused somewhat similar clinical syndromes, characterization of the causative agents resulted in 3 distinct groupings: spotted fever rickettsiosis; typhus (louse-borne epidemic typhus, murine or endemic typhus); and scrub typhus group.

Diagnosis

Early in the 20th century the nonspecific Weil-Felix serological test using *Proteus* species bacterial antigens was used to diagnose typhus and spotted fever rickettsial disease and modified for diagnosis of the scrub typhus group. Although lacking specificity (66%) and sensitivity (80%), the Weil-Felix test has been inexpensive and commercially available to developing countries. The IFA test was developed in the 1960s and is used as a reference standard for more developed countries. Recently PCR has become available in advanced clinical labs.

Prevention and Bioterrorism Considerations

As rickettsial agents are inexpensively and easily mass produced, they are considered select agents for a potential bioterrorism threat. The US military currently has limited capability to prevent rickettsial diseases. There are no FDA-licensed vaccines for protection although there is evidence that weekly doxycycline prophylaxis can reduce morbidity. DDT used effectively during WWII to control louse-borne typhus is no longer legal to use in the United States, but DEET and permethrin treated uniforms can effectively reduce the risk of chigger, tick and flea-borne transmission of rickettsial diseases. ■

Dr. Barry is Professor of Medicine; Co-Director, Tropical Medicine and International Travelers' Clinic, Yale University School of Medicine, New. Haven Conn.

CME Questions

13. Which of the following is the etiologic agent of Rickettsialpox?

a. *R prowazekii*
b. *R akari*
c. *R deresinski*
d. *C burnetii*

14. Which of the following is correct?

a. *Exophiala jeanselmei* is a dematiaceous fungus.
b. Infection by dematiaceous fungus most commonly occurs by the respiratory route.
c. VRSA are commonly isolated from ICU patients.

Readers are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *Infectious Disease Alert*. Send your questions to: Rob Kimball—Reader Questions, *Infectious Disease Alert*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. ■

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d. Free Distribution by Mail *(Samples, Complimentary and Other Free)*	(1)	Outside-County as Stated on Form 3541	23	26
	(2)	In-County as Stated on Form 3541	2	3
	(3)	Other Classes Mailed Through the USPS	0	0
e. Free Distribution Outside the Mail *(Carriers or Other Means)*			24	0
f. Total Free Distribution *(Sum of 15d and 15e)*			49	29
g. Total Distribution *(Sum of 15c and 15f)*			1120	1135
h. Copies Not Distributed			487	534
i. Total *(Sum of 15g, and h.*			1607	1669
Percent Paid and/or Requested Circulation *(15c divided by 15g times 100)*			96	97

16. Publication of Statement of Ownership — Publication required. Will be printed in the October 1 issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: Publisher — Date: 10/14/02

Donald R. Johnston

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including multiple damages and civil penalties).

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1. Complete and file one copy of this form with your postmaster annually on or before October 1. Keep a copy of the completed form for your records.
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5. If the publication had Periodicals authorization as a general or requester publication, this Statement of Ownership, Management, and Circulation must be published; it must be printed in any issue in October or if the publication is not published during October, the first issue printed after October.
5. In item 16, indicate date of the issue in which this Statement of Ownership will be published.
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In Future Issues:

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