

# INFECTIOUS DISEASE ALERT<sup>®</sup>

*A twice-monthly update of developments in infectious disease, hospital epidemiology, microbiology, infection control, emporiatrics, and HIV treatment*

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## Is it Anthrax or the Flu?

### ABSTRACTS & COMMENTARY

**Synopsis:** *The initial symptoms of inhalational anthrax are similar to those of influenza and other viral respiratory tract infections. Since no rapid diagnostic test is available for early anthrax, the use of rapid viral diagnostics assumes great importance.*

**Sources:** CDC. *MMWR Morb Mortal Wkly Rep.* 2001;50:941-948;  
Jernigan JA, et al. Posted Nov. 8, 2001.  
<http://www.cdc.gov/ncidod/EID/index.htm>

The cdc has reviewed the first 16 confirmed (see Table) and 5 suspected cases of bioterrorism-related anthrax occurring in the United States since October 3, 2001, and has made suggestions for the clinical evaluation and diagnostic testing of individuals who may have this disease.

#### Table

#### Anthrax: Operational Definitions

**CDC defines a confirmed case of anthrax as:** 1) a clinically compatible case of cutaneous, inhalational, or gastrointestinal illness that is laboratory confirmed by isolation of *B anthracis* from an affected tissue or site or 2) other laboratory evidence of *B anthracis* infection based on at least 2 supportive laboratory tests.

**CDC defines a suspect case as:** 1) a clinically compatible case of illness without isolation of *B anthracis* and no alternative diagnosis, but with laboratory evidence of *B anthracis* by 1 supportive laboratory test or 2) a clinically compatible case of anthrax epidemiologically linked to a confirmed environmental exposure, but without corroborative laboratory evidence of *B anthracis* infection.

For more information see: <http://www.bt.cdc.gov/Agent/Anthrax/Anthrax.asp>

The 10 patients with inhalational anthrax, 7 of whom were men, ranged in age from 43 to 73 years. The incubation period in the 7 patients for whom the date of exposure was known ranged from 5 to 11 days (median, 7 days). The onset of illness was associated with fever in 9 and/or sweats with or without chills in 6. Nine had nonproductive cough and 1 of these had blood-tinged sputum. Eight had chest discomfort or pleuritic pain while 5 reported "chest heaviness;" 7 had shortness of breath. Five had abdominal pain, nausea, or vomit-

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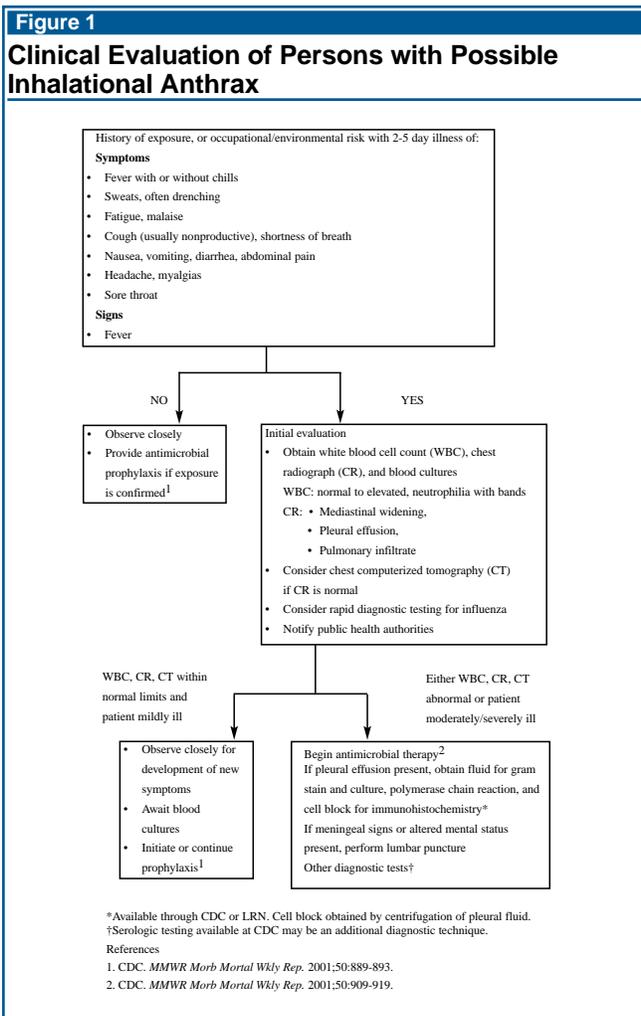
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ing. Other symptoms included severe fatigue or malaise, headache, myalgias and, in 2 patients, sore throat. One patient had rhinorrhea.

The initial white blood cell (WBC) count in these 10 patients with inhalational disease ranged from 7500/mm<sup>3</sup> to 13,300/mm<sup>3</sup>, often with a "left shift." Abnormalities were present on the chest x-ray of all 10; 7 of 8 who had a chest CT had mediastinal widening and/or hilar enlargement, although evidence of mediastinal widening on plain radiograph was absent or had been subtle in some. Seven patients had pleural effusions that were often large and hemorrhagic; in 2 of these 7, no mediastinal widening was seen on chest x-ray. Four of the 10 had pulmonary infiltrates and these involved more than 1 lobe in 3 of the 4. One patient had meningitis.

*Bacillus anthracis* grew from blood cultures of 7 patients, including all who had not received antibiotics prior to obtaining the specimen. The diagnosis in



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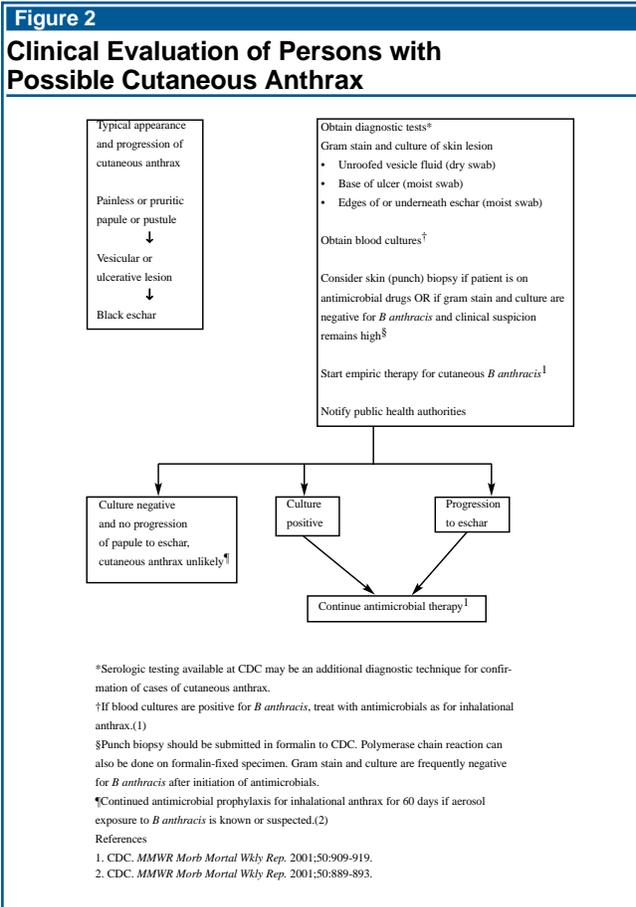
patients with negative blood or pleural fluid cultures was made by immunohistochemical staining of bronchial or pleural biopsy specimens, by PCR of fluids, or by a 4-fold increase in IgG antibody to protective antigen (PA). Six of the 10 patients, including all who received antibiotics during the initial prodromal phase of the illness, survived.

The estimated incubation period in the 11 patients with cutaneous anthrax ranged from 1 day to 10 days (mean, 5 days). The patients complained of tingling sensation or pruritus, but not pain, at the site of the lesion. The diagnosis was made in some cases when only an erythematous papule was present.

No cases of anthrax have occurred in individuals who had started prescribed antibiotic prophylaxis prior to the onset of symptoms.

**COMMENT BY STAN DERESINSKI, MD, FACP**

As we approach the winter season, we are likely to be faced with increasing numbers of patients with influenza-like illnesses who are fearful that they may have inhalational anthrax. This will present a difficult problem in



clinical management. The algorithms from the CDC publication provide some help in this regard (see Figures 1,2). As can be seen, however, the initial symptoms of inhalational anthrax are extremely similar to those of influenza and many other respiratory tract infections. Thus, a recent analysis of a large number of patients with laboratory-documented influenza found that the most frequently reported symptoms, occurring in at least 90%, were weakness, myalgia, cough, and nasal congestion, feverishness, anorexia, and headache.<sup>1</sup> Sore throat was reported by 84%. These symptoms were as common or almost as common in patients in the study who were not found to have influenza virus infection. A comparison of symptom lists suggests to me that the only potential differentiating feature may be the absence of nasal congestion as a common complaint in inhalational anthrax.

The similarity of symptoms in inhalational anthrax and viral respiratory tract infection, especially influenza, together with the absence of a rapid diagnostic test for early inhalational anthrax (although 1 from Roche Labs and the Mayo Clinic may be available soon), makes the task for the clinician exceedingly difficult. A useful approach may be the use of rapid diagnostic tests for viral respiratory tract infection in patients presenting with compatible symptoms.

A number of rapid tests are available for the diagnosis of influenza virus infection. In a direct comparison, with influenza culture and DFA testing as the comparison, 3 rapid diagnostic tests—Flu OIA<sup>TM</sup>, Quickvue Influenza Test<sup>TM</sup>, and Directigen Flu<sup>TM</sup>—were essentially equivalent, with sensitivities of 82-88% and specificities of 93-96%. A fourth test, Z Stat Flu<sup>TM</sup>, had comparable sensitivity, but its specificity was only 73%.<sup>2</sup> These immunoassays require 10 to 20 minutes for completion and have similar costs. A number of tests are also available for rapid diagnosis of other viral infections, including RSV and parainfluenza virus infections. A multiplex PCR assay, Hexaplex<sup>TM</sup>, under review by the FDA, detects RSV A and B, influenza A and B, and parainfluenza 1-3, but requires approximately 8 hours to perform. The test is under FDA review. ❖

## References

1. Monto AS, et al. *Arch Intern Med*. 2000;160:3242-3247.
2. Infectious Diseases Society of America Annual Meeting. San Francisco, Calif., Oct. 25-28, 2001. Abstract #604.

## Itraconazole— Life in the Old Drug Yet

ABSTRACT & COMMENTARY

**Synopsis:** *It is now possible to treat pulmonary aspergillosis safely and effectively by giving itraconazole parenterally for 14 days, then continuing therapy orally.*

**Source:** Caillot D, et al. *Clin Infect Dis*. 2001;33:E83-90.

A series of 31 immunocompromised patients were given itraconazole intravenously (2 days at 400 mg/d, then 200 mg/d thereafter) for a median duration of 14 days followed by oral capsules (400 mg/d) for a median duration of 11 weeks to treat invasive pulmonary aspergillosis. A satisfactory response (complete or partial response) was achieved in 15 (48%), with another 6 (19%) showing stable disease. Itraconazole was well tolerated and there were no unexpected side effects. Trough plasma concentrations of at least 250 µg/L (considered the therapeutic level) were attained by day 7 of intravenous therapy in all 22 patients for which data were evaluable and in all patients and therapeutic levels were maintained after switching to oral capsules. The average duration of treatment was 45 days (ie, 6

weeks) and only 2 patients had a definite adverse drug reaction (a rash and the other rigors during infusion). Caillot and colleagues considered this regimen to be safe, well tolerated, and effective for treating invasive pulmonary aspergillosis.

#### ■ COMMENT BY J. PETER DONNELLY, PhD

Itraconazole was first brought to the market in 1992 in capsule form but quickly failed to meet some expectations. Like its predecessor, ketoconazole, absorption was erratic but there was no parenteral form available nor did one seem likely to become available because a suitable solvent for this hydrophobic drug had yet to be found. Neither did the notion of attempting to treat a life-threatening disease among allogeneic haematopoietic stem cell transplant recipients, and those given intensive chemotherapy for leukemia exclusively with a capsule appeal, especially as these patients tend to refuse taking anything by mouth because of nausea and mucositis. This dampened enthusiasm for an otherwise promising drug that just couldn't be given to the patient at the desired dose in the most efficient way. Five years later in 1997 the absorption problem was solved by the introduction of an oral solution and then, finally, 2 years later, in 1999, a parenteral form of the drug finally made it in the nick of time, 7 years after the initial launch of itraconazole and just 2 years before its patent expired. IV-oral switch antifungal therapy had arrived.

It was a long time coming but there now seems to be a real alternative to amphotericin B in one or another of its formulations for treating the devastating disease of invasive pulmonary aspergillosis. True, there is no large trial comparing this IV-oral switch regimen for treating probable invasive pulmonary aspergillosis and none is planned. The evidence for judging efficacy is based on small series such as that of Caillot et al. Yet, while numerically small, such studies do represent a year or more of experience since few centers see more than 10 probable cases of invasive pulmonary aspergillosis per year. Clearly, the evidence that itraconazole is effective in treating probable or proven invasive pulmonary aspergillosis is not of the highest level because of the lack of a proper randomised, controlled, trial comparing the drug with the gold standard amphotericin B. Nonetheless, an examination of the literature available shows efficacy rates for itraconazole of 40-70%, in the same range as reported for amphotericin B. However, unlike the polyene, and earlier versions of itself, itraconazole can now be given parenterally and orally offering the physician the one and only flexible regimen to date. The optimum duration of parenteral treatment is not known, but is probably closer to 14 than 7 days, and

the duration of follow-up oral therapy has yet to be determined. Those physicians that have hitherto relied on starting amphotericin B treatment while the patient is in the hospital and then discharging him or her on oral itraconazole now have a simpler alternative. Just as important, this approach to managing invasive pulmonary aspergillosis has a good chance of becoming the standard of care, if not with itraconazole, then with another azole antifungal agent such as voriconazole. ❖

## Vitamins and Flu Vaccine a No-No?

ABSTRACT & COMMENTARY

**Synopsis:** *Taking a multivitamin was associated, in a randomized trial, with diminished antibody response to influenza vaccine.*

**Source:** Ender PT, et al. *Infect Dis Clin Pract.* 2001;10:81-85.

In this study, a group of military physicians studied the effect of multivitamin use on the immunologic response to influenza vaccinations. Seventy-nine adults, age 65 and older, were randomized in a double-blinded manner to receive either a multivitamin or placebo for 100 days prior to flu vaccination. The study drug was continued for an additional 30 days after vaccination. Blood was collected just prior to flu vaccination and 30 days after vaccination. Of those completing the study, there were 32 in the placebo group and 34 in the multivitamin group. Both groups were demographically similar and patient compliance was assessed via telephone interviews twice during the study period.

Sera were tested with a hemagglutination antibody inhibition assay using the A/Beijing/262/95 (A-H1N1), A/Sydney/5/97 (A-H3N2), and B/Beijing/184/93 antigens found in the 1998-1999 vaccine. End points that were analyzed included the development of 2- or 4-fold increase in antibody titer at 4 weeks postvaccination, the postvaccination geometric mean titer (GMT), and the increase in the GMT. Subjects were considered to have 2- or 4-fold increase in titer if they had a 2- or 4-fold increase in titer to any of the antigens tested.

Twelve of the 34 subjects (35%) in the multivitamin group had a 4-fold titer increase, vs. 18 of 32 (56%) in the placebo group ( $P = .072$ ). Nineteen of 34 (56%) in the multivitamin group had a 2-fold increase in titer, vs. 25 of 32 (78%) in the placebo group ( $P = .048$ ).

Ender and colleagues cited various articles that

have reported the deleterious effects of specific vitamins on the immunologic response and further noted that higher dosages of vitamins may be required to exhibit this response.

■ **COMMENT BY THOMAS G. SCHLEIS, MS, RPh**

This study is interesting in that it is in contrast to previous studies that suggested an improved response to the influenza vaccine in the elderly. In a 1992 study, Chandra demonstrated that healthy elderly patients, without chronic disease, had improved postvaccination influenza titers if multivitamins were taken.<sup>1</sup> This study differs from the one described above in that it had a healthier patient population, baseline titers were not obtained, and that the multivitamin used included minerals. Another study performed in 1999 by Girodon and associates, involving institutionalized elderly patients, showed an improved immunologic response with vitamin use,<sup>2</sup> but, again, a multivitamin with minerals was administered.

While the information presented here is insufficient to make a definitive recommendation, it would be prudent to either avoid multivitamin supplements prior to and after flu vaccination, or to only use a multivitamin supplement that includes minerals. Obviously, a larger study that looks at other variables such as prior vaccination responses, serum levels of vitamins and minerals, and clinical outcomes is needed. ❖

**References**

1. Chandra RK. *Lancet*. 1992;340:1124-1127.
2. Girodon F, et al. *Arch Intern Med*. 1999;159:748-754.

## Practice Parameter: Bell's Palsy

ABSTRACT & COMMENTARY

**Source:** Grogan PM, Gronseth GS. *Neurology*. 2001;56:830-836.

Various treatment options exist for bell's palsy, some undeniably useful, some unequivocally pointless. Artificial tears, lubricating ophthalmic ointment, and eyelid taping prevent corneal drying. Massage and facial nerve electrical stimulation provide psychological support, but little else. Within this spectrum, wither steroids, acyclovir, and facial nerve surgical decompression?

A special article by the Quality Standards Subcom-

mittee of the American Academy of Neurology addresses this question. A MEDLINE search of the National Library of Medicine's database from 1966 to June 2000, and review of the references of these articles to identify other relevant reports on Bell's palsy, uncovered 230 articles examining steroids (only 9 were prospective), 92 addressing acyclovir (3 prospective), and 104 discussing surgical decompression (4 prospective). None were adequately powered class I studies, defined as a randomized, controlled trial with 1) clearly defined primary outcomes and exclusion and inclusion criteria; 2) equivalent baseline characteristics among treatment arms; and 3) satisfactory accounting of dropouts and crossovers. Results of class I and II (3 of 4 above criteria) were pooled where possible.

No definite benefit could be established for steroids, acyclovir, or surgical decompression. Probable benefit from steroids, with acyclovir possibly effective when combined with prednisone, was suggested by the available evidence. No recommendation could be made regarding surgical decompression. Bell's palsy remains a disease in search of a proven effective therapy.

■ **COMMENT BY MICHAEL RUBIN, MD**

Herpes simplex virus (HSV) type 1 is reportedly the major cause of Bell's palsy,<sup>1</sup> but HSV type 6 may also be a common culprit. Using polymerase chain reaction (PCR), type 6 HSV DNA was detected in the tear fluid of 35% of patients (7 of 20) with Bell's palsy.<sup>2</sup> Varicella zoster virus (VZV) reactivation (Ramsay Hunt syndrome), which may appear without skin lesions and mimic Bell's palsy, was found in 10% (2 of 20). VZV is more resistant to acyclovir, and may be responsible for some treatment failures. If suspected, higher doses of acyclovir are recommended.

Transmastoid decompression may benefit severe Bell's palsy. Among 101 adults with significant denervation following prednisone therapy for Bell's palsy, defined as > 95% amplitude drop in compound muscle action potential on facial motor nerve stimulation, 58 underwent decompression and 43 were followed conservatively. Two months following surgery, the operated group demonstrated a significantly better House-Brackmann grade than the nonsurgical group.<sup>3</sup> Further studies are warranted, however, before recommendation of this procedure is justified. ❖

*Dr. Rubin is Associate Professor of Clinical Neurology, New York Presbyterian Hospital-Cornell Campus, New York, NY.*

## References

1. Morrow MJ. *Curr Treat Options Neurol*. 2000;2: 407-416.
2. Pitkaranta A, et al. *J Clin Microbiol*. 2000;38: 2753-2755.
3. Yanagihara N, et al. *Otolaryngol Head Neck Surg*. 2001;124:282-286.

# Culture-Negative Endocarditis

## ABSTRACT & COMMENTARY

**Synopsis:** Use of modified Duke criteria were reasonably accurate in the diagnosis of culture-negative endocarditis—but expert clinical judgment was almost as good.

**Source:** Kupferwasser LI, et al. *Am Heart J*. 2001;142: 146-152.

Kupferwasser and colleagues reviewed their database of patients who had undergone echocardiography in order to evaluate the relative accuracy of diagnosis of culture-negative native valve endocarditis by use of the Duke criteria, the von Reyn criteria, and expert clinical judgment.

The records of 49 patients with fever, heart murmur, elevated acute phase reactants, and at least 1 cardiac abnormality considered to be a risk factor for endocarditis, but who had at least 3 negative blood cultures, were examined. In each case, examination of specimens of valve tissue obtained at autopsy (6 patients) or surgery (43 patients) served as the “gold standard” for diagnosis of culture-negative endocarditis (CNE). Clinical judgment was rendered by 2 masked “clinically experienced investigators” who reviewed abstracted patient records (the manner in which investigator disagreement was managed is not indicated).

Thirty-two of the 49 patients proved to have endocarditis; valve culture was positive in only 6 of the 32 (18.8%)—4 with nutritionally variant streptococci and 1 each with *Haemophilus spp* and *Aspergillus spp*. Of the 32 with proven endocarditis, 23 (71.9%) were classified as definite and 9 as possible by the Duke criteria. In 5 of the Duke “possibles” who proved to have endocarditis, 0.2-0.3 mm length vegetations had not been detected by transthoracic or transesophageal echocardiography. Each of these 5 had also been classified as possible by clinical judg-

ment. The other 4 patients with proven endocarditis classified as possible by the Duke criteria were classified as definite by clinical judgment. The performance of the von Reyn criteria was inferior.

In 14 of the 17 patients who proved to not have CNE, the diagnosis of endocarditis had been rejected by the Duke criteria as the consequence of the presence of an alternative diagnosis or resolution of the clinical syndrome in fewer than 5 days. The other 3 without endocarditis had been classified as possible by the Duke criteria and as definite by clinical judgment; in each case, echocardiography had been interpreted as revealing a mobile vegetation that proved to be absent at valve examination; all 3, however, were believed to have non-bacterial thrombotic endocarditis.

Overall, the von Reyn criteria were inferior to the other 2 methods of classification. On the other hand, the Duke criteria and clinical judgment yielded identical classifications in 78% of the 49 patients. The sensitivity and negative predictive value of the latter 2 methods for the diagnosis of CNE were each 100% when both possible and definite classifications were considered “CNE-positive” and when only cases in which transesophageal echocardiography (TEE) results were available in application of the Duke criteria. However, the Duke criteria (with TEE data) appeared to be somewhat superior to clinical judgment with regard to both specificity (82% vs 53%) and positive predictive value (91% vs 80%).

### ■ COMMENT BY STAN DERESINSKI, MD, FACP

Previous studies have validated the accuracy of the

Criteria	Definite Dx.	Possible	No Endocarditis
<b>Pathologic</b>			
Histologic	Vegetation/abscess; active histologically	Can't tell	No pathologic evidence w/ ≤ 4 days prior antibiotic Rx.
<b>OR</b>			
Microbiologic	+ culture or histology of vegetation or cardiac abscess	Can't tell	No pathologic evidence w/ ≤ 4 days prior antibiotic Rx.
<b>Clinical</b> (any one of the following)			Doesn't meet criteria resolution of manifestations w/ ≤ 4 days antibiotic Rx <b>or</b> firm alternate diagnosis
Major	2	Does not apply	
Minor	5	3	
Major & Minor	1 major + 3 minor	1 major + 1 minor	

Table 2

**Modified Duke Criteria Continued\*****Major Criteria**a. Supportive Laboratory Evidence:

- Typical microorganism for infective endocarditis from 2 separate blood cultures (viridans streptococcus, *S aureus*, *S bovis*, HACEK group, **or** community-acquired enterococcus in the absence of a primary focus).
- Persistently positive blood cultures, drawn more than 12 hours apart, yielding one of the above organisms.
- Single positive blood culture for *Coxiella burnetti* or phase I antibody > 1:800.

b. Evidence of Endocardial Involvement:

- Echocardiogram supportive of infective endocarditis: oscillating intracardiac mass on valve or supporting structures, or in the path of regurgitant jets, or on implanted material in the absence of an alternative explanation **or** myocardial abscess or new partial dehiscence of prosthetic valve.

c. New Valvular Regurgitation (change in pre-existing murmur insufficient)**Minor Criteria**

- Predisposing cardiac condition or intravenous drug use
- Fever  $\geq 38.0^{\circ}$  C ( $100.4^{\circ}$  F)
- Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesion.
- Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor.
- Positive blood culture not meeting criteria above (excluding coagulase-negative staphylococci and organisms unlikely to cause endocarditis) or serological evidence of active infection with an organism consistent with infective endocarditis.

\*Modified from Li SJ, et al. *Clin Infect Dis*. 2000;30:633-638. ([http://www.med.upenn.edu/bugdrug/antibiotic\\_manual/duke.html](http://www.med.upenn.edu/bugdrug/antibiotic_manual/duke.html))

Duke criteria in the overall endocarditis population, as well as their superiority to the von Reyn criteria, largely as a consequence of the inclusion of echocardiographic data in the former. Studies have also previously demonstrated general agreement between clinical judgment and the Duke criteria in mostly culture-positive patients. In this study of CNE, clinical judgment was more likely to yield false-positive diagnoses of endocarditis than the Duke criteria, but neither method produced false-negatives.

The Duke classification produced somewhat more frequent equivocal results, classifying cases as possible in 24.5% compared to 18.4% when clinical judgment was used. These cases are, as stated by Kupferwasser et al, problematic in that there is no agreement on how such patients should be managed. However, in most instances, such patients will be managed as if they have endocarditis because of the potential consequences of failure to treat if the infection is, in fact, present.

This study, while demonstrating the potential value of the Duke criteria in the diagnosis of CNE, also demonstrates that clinical judgment is almost as effective. Given the small sample size, the performance of the study at a referral center, and possible selected nature of the cohort, it is not possible to say that one method is preferred over the other in the clinical setting, provided that the clinician making the judgment is experienced and sagacious. ❖

**CME Questions****29. Which one of the following statements is correct?**

- The von Reyn criteria are superior to the modified Duke criteria in the diagnosis of culture-negative endocarditis.
- The von Reyn criteria are superior to expert clinical judgment in the diagnosis of culture-negative endocarditis.
- The sensitivity and negative predictive value of the modified Duke criteria and expert clinical judgment in the diagnosis of culture-negative endocarditis were each 100%.
- The modified Duke criteria were associated with more false-positive results in the diagnosis of culture-negative endocarditis than was expert clinical judgment.

**30. Which one of the following is correct with regard to the first 10 cases of inhalational anthrax in the United States since Oct. 3, 2001?**

- None of the patients complained of sore throat.
- The mean incubation period was 3 weeks.
- None of the patients complained of abdominal symptoms.
- Mediastinal widening and/or hilar enlargement was present in at least 8 patients.

**31. Which one of the following statements is correct?**

- The initial symptoms of inhalational anthrax can be readily distinguished from those of influenza.
- The mean incubation period in the first 11 patients with cutaneous anthrax in the United States since Oct. 3 was 3 weeks.
- The skin lesion was painless in the first 11 patients with cutaneous anthrax in the United States since Oct. 3.
- The absence of mediastinal widening on plain chest x-ray eliminates the possibility of inhalational anthrax.

**In Future Issues:**Does *Lactobacillus* Prevent Antibiotic-Associated Diarrhea?

## What's Up Tiger Lily?

**Source:** ProMED-mail posts July 2, July 4, August 8, and August 13, 2001; [promed@promedmail.org](mailto:promed@promedmail.org).

**A***edes albopictus*—the notorious Asian Tiger mosquito—was recently found hitching a ride in maritime cargo entering Los Angeles' busy port. Port authorities in Los Angeles contacted the CDC on July 14 after opening a container of "lucky bamboo" and out flew several of the mosquitoes. Similar shipments of lucky bamboo were bound for ports in San Francisco, Seattle, New York, and New Jersey. The bamboo typically originates from China, Thailand, and Malaysia, and is shipped in 2 inches of standing water. The CDC subsequently issued an embargo on the importation of lucky bamboo in standing water, but the bug appeared again at an import facility in Portland, Ore, on August 7 in another shipment of lucky bamboo. Only 10 or so mosquitoes were found (let's hope they swatted them all). The mosquito has not been previously seen on the West Coast, although it has been found in other parts of the United States, including Ohio, Texas, Pennsylvania, and Florida, where it was possibly introduced in standing water in imported tires.

The Asian Tiger, so-called because of the stripes on its legs, is of particular concern because it is an aggressive day time biter and an efficient vector of a number of viral infections, including Dengue. In the United States, it could feasibly become a vector for a number of viruses, including St. Louis, Eastern Equine, Western Equine, and La Crosse Encephalitis viruses. In addition, West Nile Virus was isolated from an *A. albopictus* mosquito found in

Pennsylvania last year. ■

## Sporotrichosis— Another Zoonosis?

**Source:** Barros MB, et al. *Mem Inst Oswaldo Cruz*. 2001;96:777-779.

**M**edical experts at the Research Center Evandro Chagas Hospital in Rio de Janeiro have been surprised by an apparent outbreak of sporotrichosis in humans that they believe may be associated with cat bites or cat scratches. Sporotrichosis, which is a saphrophytic fungus associated with decaying plant material and moss, is typically thought of as a disease of gardeners and rose handlers. The infection is introduced into the skin via thorns or splinters. It is not generally thought of as a zoonosis, although isolated cases have been reportedly due to the bites of various animals, such as badgers, rodents, squirrels, and iguanas, and has been associated with handling of armadillos (in Uruguay).

Barros and colleagues identified 66 human cases of sporotrichosis between 1998 and 2000, 79% of which were associated with cat contact and 47% of which occurred in persons reporting cat scratches or cat bites. They also saw 117 cats and 7 dogs diagnosed with sporotrichosis during this 2-year period. In apparent contrast, only 13 human cases of sporotrichosis were diagnosed at the same research center during a 9-year period from 1987 to 1998, 2 of which were associated with cat scratches. This difference could be accounted for based on the increased awareness or recognition of infection and not an actual increase in disease incidence.

While it is entirely plausible that sporotrichosis could be introduced through the skin via a cat scratch, as opposed to a thorn, Barros et al should consider a case-control study to examine the relationship between the risk of sporotrichosis and cat scratches or other high-risk activities in their patients. ■

## Q Fever from British Animal Carcasses

**Source:** ProMED-mail post July 1, 2001; [promed@promedmail.org](mailto:promed@promedmail.org).

**T**hree british soldiers assigned to the worst imaginable duty of slaughtering and disposing animal carcasses in Northumberland have been diagnosed with Q fever. All 3 developed flu-like symptoms and shortness of breath, possibly associated with the development of pneumonia in 2 of the men. Six others have tested negative for the infection.

Q fever is apparently not uncommon in certain parts of Great Britain and Ireland, where it may infect up to 1 in 4 farmers. Based on this information—and the slaughter to date of more than 530,000 cattle and 2.7 million sheep (including many pregnant ewes and baby lambs)—it is remarkable that other cases of Q fever have not been recognized in workers disposing of carcasses. Nonfarm workers used to clearing carcasses, such as soldiers, may be especially vulnerable, as they lack any pre-existent immunity. Because *Coxiella burnetii* can be spread by dust and debris and can reside in soil for years, mass burial sites of animals possibly infected with the organism may present a risk for years to come. ■