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Nosocomial Transmission of Parvovirus B19 Infection in Transplant Patients

ABSTRACT & COMMENTARY

Synopsis: *This report shows that chronically infected transplant patients can be the source of a nosocomial outbreak among immunocompromised patients.*

Source: Lui SL, et al. Nosocomial outbreak of parvovirus B19 infection in a renal transplantation unit. *Transplantation.* 2001;71:59-64.

A 52-year-old woman undergoing intensive immunosuppressive treatment for renal allograft rejection developed severe anemia (hemoglobin 6 g) with < 0.1% reticulocytes. Bone marrow biopsy showed decreased erythropoiesis with giant pronomoblasts, consistent with parvovirus B19 infection. This was confirmed by detection of viral DNA in serum by PCR. She was given 2 courses of IVIG without response, and she subsequently died of Gram-negative sepsis. Two renal transplant patients who had been hospitalized on the unit during the first patient's hospitalization developed parvovirus B19 infection characterized by severe anemia and presence of viral DNA in serum. One of these patients was being treated for graft rejection. A 5-day course of IVIG led to transient hematologic and virologic improvement; a second course was followed by recovery of serum hemoglobin levels to normal and clearance of viremia. The third patient was receiving maintenance immunosuppression only and recovered spontaneously.

Although all 3 patients were hospitalized simultaneously on the same unit, they were never roommates. Viral DNA sequences obtained from the sera of the 3 patients were identical, and were distinct from those found in 7 community acquired cases. None of the unit staff had clinical or virologic evidence of acute infection.

COMMENT BY ROBERT MUDER, MD

Parvovirus B19 is a DNA virus that causes Fifth disease, a common childhood exanthem characterized by fever and rash. Person-to-person transmission most likely occurs via respiratory droplets

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during the prodromal or early symptomatic phase of the illness. Adults acquiring the infection (typically after contact with infected children) may develop acute polyarthritis, often without typical rash.

The virus specifically infects red-cell precursors in the marrow and profoundly depresses red cell production during acute infection. In a healthy child or adult, interruption of hematopoiesis for several days is without significant consequences. However, patients with chronic hemolytic anemias may have dramatic drops in circulating red cells. Parvovirus B19 is the most frequently identified cause of aplastic crisis in patients with sickle-cell disease. As patients with sickle-cell disease are immunologically normal, the infection is self limited. Transfusion to maintain adequate hemoglobin levels until spontaneous recovery occurs is usually sufficient.

Patients who are immunosuppressed, including those with HIV infection or organ transplantation, may have chronic infection with severe, refractory anemia and prolonged viremia. IVIG may be effective in reducing viremia and permitting resumption of hematopoiesis. The therapeutic effect may be temporary, and repeat courses of treatment may be required. The cases reported by Lui and colleagues demonstrate the spectrum of disease in the immunocompromised. This may include refractory infection, infection responsive to 1 or more courses of IVIG, or spontaneous recovery.

Nosocomial outbreaks of parvovirus B19 have been reported among immunocompetent patients and hospital staff. The current report illustrated that chronically infected transplant patients can be the source of a nosocomial outbreak among immunocompromised patients. The index patient had been infected for approximately 2 months before the second-case patient was admitted to the unit. There was no documentation of direct contact among the involved patients, and the mode of transmission is not certain. However, parvovirus B19 is excreted in respiratory secretions and urine of infected patients. It is a particularly hardy virus. It is fairly resistant to killing by heat and physical agents, and it can persist in the environment for prolonged periods. Indirect contact transmission therefore seems likely. It would seem prudent to isolate hospitalized patients with acute or chronic parvovirus B19 infection, particularly if they are housed on a unit with immunocompromised patients. ❖

Additional Reading

1. John JF. Parvovirus and leukopenia. *Infectious Disease Alert.* 2000;19:179-180.

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A Simple Blood Test for Diagnosing Invasive Aspergillosis?

ABSTRACT & COMMENTARY

Synopsis: *An ELISA test for Aspergillus galactomannan may prove to be a sensitive, noninvasive tool to assist in the early diagnosis of invasive aspergillosis.*

Source: Maertens J, et al. Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients and stem cell transplantation recipients: A prospective validation. *Blood.* 2001;97:1604-1610.

A sandwich elisa method is commercially available for detecting galactomannan (GM), which is a component of the cell wall of the *Aspergillus*

species found in serum plasma and other sterile body fluids. The test involves using the rat monoclonal antibody EB-A2, which recognizes the 1->5-ß-D-galactofuranoside side chains of the GM molecule to both capture and detect as little as 1 ng/mL GM.

This study set out to validate this GM-ELISA test prospectively by surveying 362 treatment episodes in 191 neutropenic patients and recipients of a hematopoietic stem cell transplant (HSCT) for the presence of sinus and pulmonary signs and subjecting them to a standard diagnostic work-up for invasive fungal infective disease. Serum was collected at least twice weekly from admission to discharge or death or, in the case of HSCT recipients, once weekly as outpatients until immunosuppressive therapy was stopped altogether. The results were not used to diagnose disease prospectively or to decide therapy. Instead, aspergillosis was defined according to the criteria proposed by the EORTC/MSG in which aspergillosis is considered as being proven only when there was histological evidence of tissue invasion and recovery of *Aspergillus* species from culture. This is probable when there is both clinical and mycological evidence (*see Table*) or possible if there is either clinical or mycological evidence.

Use of these criteria allowed cases to be classified on the basis of premortem data. Autopsy was also vigorously pursued and performed unless explicitly refused by the patient or his family. This allowed a more accurate estimate of the incidence of proven cases than would otherwise have been possible since invasive procedures were avoided in thrombocytopenic patients. The GM-ELISA was conducted according to the manufacturers instructions, and GM was considered present when detected in 2 consecutive serum samples.

The diagnostic use of the GM-ELISA test was assessed using both premortem data and after incorporating all the data available. True positives were defined by the presence of proven aspergillosis and GM and true negatives by the absence of both.

None of the 30 proven cases was missed and GM was detected in at least 2 consecutive serum samples. However, GM was also detected in 5 (55.5%) of the 9 probable cases, 4 (7.4%) of the 54 possible cases, as well as in 5 (2%) of the 264 cases without aspergillosis. Hence, while the sensitivity and negative-predictive value with regard to proven aspergillosis were both 100%, the specificity was 96% and the positive-predictive value only 68%.

COMMENT BY J. PETER DONNELLY, PhD

If these results are correct, the diagnosis of invasive aspergillosis will have made a quantum leap into the 21st century. Diagnosing this disease in neutropenic patients

Table

Evidence Required for Defining Cases of Invasive Aspergillosis

Site	Clinical Evidence	Mycological Evidence
Pulmonary	**a) Any 1 of the following:** CT scan 1) halo sign 2) air-crescent sign 3) cavity within an area of consolidation **or** **b) Any 2 of the following:** 1) symptoms of lower respiratory tract infection (cough, pleuritic chest pain, dyspnoea, or haemoptysis) 2) pleural rub 3) a new infiltrate other than those considered as evidence of aspergillosis but for which there is no alternative diagnosis	**Any 1 of the following:** 1) Microscopic demonstration of septate, acutely branching hyaline hyphae 2) culture of *Aspergillus* species from sputum or bronchoalveolar lavage
Sinuses	**a) Radiographic evidence of invasion** **or** **b) Any 2 of the following:** 1) upper respiratory symptoms 2) nose ulceration, eschar, epistaxis 3) periorbital swelling 4) maxillary tenderness 5) necrotic lesions or perforation of hard palate	None

and HSCT recipients has been notoriously contrary and frustrating, driving clinicians to start antifungal therapy empirically to shift the odds in favor of survival. In this study, empirical antifungal therapy was used in 43% of episodes with all that that entails whereas reliance on the GM-ELISA test would have reduced the use of empirical therapy to a more moderate 12%. True, serum needs to be tested regularly (Maertens and associates screened their patients at least twice weekly and collected on average 12 samples per patient), since a single test is not sufficiently informative, but the additional costs would be partially offset by savings on the drug budget.

The GM-ELISA test cannot be used in isolation as it is complementary to other techniques, particularly CT imaging, used in the work-up of persistently unexplained fever in neutropenic patients and the exploration of invasive fungal infective disease among all hematology patients at high risk. Just as important, the test has to form an integral part of a strategy that also includes the adoption of explicit commonly agreed on criteria for classification. Maertens et al opted to use the criteria proposed by the EORTC/MSG for case definition, which has yet to be published in full. Briefly, these criteria rely on 3 elements, namely: 1) the presence of a host risk factor (eg, neutropenia or HSCT recipient receiving immunosuppressive therapy); 2) clinical evidence (radiographic or clinical signs and symptoms); and 3) mycological evidence (demonstration by culture or microscopy and, importantly, by an indirect test such as the GM-ELISA test). Besides the real possibility of making a diagnosis, the clinician also has the opportunity to explore other avenues for managing invasive aspergillosis including pre-emptive treatment. Furthermore, having decided to begin treatment empirically anyway, a repeatedly negative GM test should encourage a search for an alternative diagnosis as well as stopping antifungal therapy. As Maertens et al state, "The real value of any non-invasive test will largely depend on its potential to discriminate "unproven" IA from alternative aetiologies with similar clinical presentations ie, cases normally classified as probable or possible."

This is not the first study to demonstrate the use of GM-ELISA, but it is the largest so far to attempt to formally evaluate its use in a large prospective series of patients at risk. The current study is not perfect because a credible alternative explanation was not found for the cases that resembled invasive aspergillosis but that nonetheless did not fit the case definition. But Maertens et al should be congratulated for their efforts, and their approach deserves to be adopted as a temporary or tentative standard of best-practice until a better one comes along.

There are some quirks associated with the GM-ELISA test. GM is frequently detected for the first and only time during mucositis, and certain foods and drugs have also tested positive.[1] The test has also been around for some 6 years in Europe, but it has yet to gain formal approval for use in North America. This paper should at least help dispel lingering doubts about the potential diagnostic use of GM-ELISA. The body of evidence may not yet be sufficient to meet the demanding standards of the FDA, but its weight should certainly tilt the balance and shift the odds in favor of expediting the process so that the GM-ELISA becomes available to all. ❖

References

1. Ansorg R, et al. Detection of *Aspergillus* galactomannan antigen in foods and antibiotics. *Mycoses.* 1997; 40:353-357.
2. Deresinski SC. Conference summaries: ICAAC 2000, IDSA 2000, and ASTMH 2000: Part III. *Infectious Disease Alert.* 2000;20:41-44.

Isolation Guidelines for Nipah Virus

ABSTRACT & COMMENTARY

Synopsis: *Nosocomial transmission of Nipah virus was not observed in this 3-hospital study.*

Source: Mounts AW, et al. A cohort study of health care workers to assess nosocomial transmissibility of Nipah virus, Malaysia, 1999. *J Infect Dis.* 2001;183:810-813.

The emergence of 2 new viral illnesses in the South Pacific has been carefully followed. Hot on the heels of Hendra virus infection, first identified in Australia in 1995, came a more devastating infection of pigs in Malaysia in 1999.[1] Thousands of pigs were infected and millions were sacrificed. Furthermore, secondary cases of Nipah virus infection occurred among humans manifested primarily as encephalitis, thereby necessitating hospitalization.

This study was performed to ascertain if health care workers (HCWs) attendant to patients sick with Nipah contracted the virus. There was an attempt to identify an equal number of nurses and doctors at the 3 hospitals in the study—one group exposed to Nipah patients and the other group not exposed. Infection with Nipah (or Hendra) virus was documented by an EIA for anti-Nipah IgM and IgG.

At the 3 study hospitals, there was a total of 211 patients admitted with Nipah virus infection. There were 388 HCWs exposed to these patients. More than half of the HCWs had contact with Nipah patients before isolation practices were in place.

None of the HCWs exposed became sick with Nipah virus illness. There were 3 exposed HCWs who developed IgG antibodies on the second serum tested, likely a false-positive result since none was positive for IgM.

COMMENT BY JOSEPH F. JOHN, MD

It is probably much easier to contract Nipah infection from infected pigs than from infected humans. The reason for this is that pigs probably harbor much more virus in the upper respiratory tract. Nevertheless, because the pathogenesis of Nipah in humans is not well understood and since Nipah and Hendra are *Paramyxoviruses*, a group that includes the measles virus, caution is needed to protect HCWs.

This small study cannot exclude the possibility of nosocomial transmission. Thus, for the time being, HCWs caring for Nipah patients should observe standard and droplet precautions: good handwashing, and use of a mask and gloves when coming in contact with "secretions, excretions, and body fluids" of patients suspected or proven to have these 2 emerging viruses. ❖

Reference

1. Deresinski SC. Another new human pathogen: The Nipah virus. *Infectious Disease Alert.* 1999;18: 113-114.

Blood Cultures Taken During the First 72 Hours of Antibiotic Therapy Are a Waste of Time and Money

ABSTRACT & COMMENTARY

Synopsis: *There appears to be no diagnostic value of blood cultures obtained in the first 72 hours after institution of antibiotic therapy.*

Source: Grace CJ, et al. Usefulness of blood culture for hospitalized patients who are receiving antibiotic therapy. *Clin Infect Dis.* 2001;32:1651-1655.

Grace and colleagues reviewed the notes of 1446 patients to identify 139 who had been admitted to the hospital for suspected infection, who had had 2 sets of blood cultures taken before antibiotic therapy (preantibiotic blood cultures), who had been given antibiotic therapy within 24 hours, and who had had a further 2 sets of blood cultures taken during the first 72 hours of therapy (antibiotic blood cultures). Most of the 785 patients were excluded from the study because of an inadequate number of blood cultures—133 because of antibiotic use before admission, 72 because no therapy was given, 187 because of admission to the ICU, and the remaining 130 because they were neutropenic. Of the 598 blood culture sets obtained, 272 (45%) were taken before antibiotic therapy was started. Blood cultures were negative or contaminated in 83 cases and remained so during the first 72 hours of antibiotic therapy. Staphylococci were isolated from the preantibiotic blood cultures of 25 patients and the same isolate from the antibiotic blood cultures of 19 (76%) patients (*Staphylococcus aureus* was involved in 18 cases), streptococci from 14 preantibiotic blood cultures with the same isolate from the antibiotic blood cultures of 5 (36%) patients, and Gram-negative bacilli from the preantibiotic blood cultures of 17 patients and the same isolate from the antibiotic blood cultures of 2 (12%) patients. The antibiotic blood cultures of only 1 patient yielded a new bacterium, *Bacteroides fragilis* in addition to the *Escherichia coli* identified before therapy. Having been admitted initially for the evaluation of fever, this patient underwent a CT scan of the abdomen on day 3 anyway, which revealed sigmoid diverticulitis. The rates of positive blood cultures on day 1, 2, and 3 of therapy were 16% (26/162 sets), 15% (15/99 sets), and 20% (13/65 sets), respectively. Grace et al conclude that the results of blood cultures taken during the first 72 hours of antibiotic therapy can be predicted from the preantibiotic blood cultures, and they advise physicians to wait for the results of the preantibiotic blood cultures before deciding to order more.

COMMENT BY J. PETER DONNELLY, PhD

This is a straightforward study with a simple message: taking blood cultures during the first 72 hours of antibiotic therapy is not going to reveal any new information, so why not simply wait for the preantibiotic culture results before deciding on ordering more? Are they justified in their conclusion? The answer is yes if the purpose of taking blood cultures during therapy is to uncover the cause of persisting fever. Grace et al clearly show that no useful new information is to be gained. They remind us that it is

not uncommon anyway for fever to persist for 72 hours when a patient has an infection, and they can find no justification for taking blood cultures as a reflex action to persisting fever. However, if one is trying to assess the efficacy of therapy in eradicating the cause of bacteremia, the question then becomes "when is the appropriate time for taking follow-up cultures to assess microbiological efficacy?" In the current study, *S aureus* and, to a lesser extent, the streptococci, seemed to have persisted despite 72 hours of therapy. This would make any physician uncomfortable and want to modify treatment if he or she was aware of this. However, this information wouldn't usually be known until 48 hours after the blood cultures were taken simply because of the turnaround time. So, by day 4 of therapy (ie, after a full 72 hours of therapy) only the results of the pre-antibiotic cultures and any taken on day 1 and perhaps day 2 would be known making it impossible to judge the microbiological efficacy of treatment in eradicating the pathogen simply because this would be considered too short for treatment to have worked. The question of eradication is usually only posed after 72 hours of therapy so the blood cultures taken on day 3 would be taken too soon although they would become known on day 5. Hence, the question of microbiological efficacy is also not addressed by taking cultures during the first 72 hours of therapy. Therefore, the 55% of blood cultures taken during therapy were of no clinical value and hence were a waste of time and resources. If these results were echoed throughout the hospital including the ICU and neutropenic patient, there would be considerable savings because the number of blood cultures taken could be reduced by half.

I doubt if anyone really knows why taking blood cultures on a daily basis ever became commonplace. The arguments advanced in favor of this practice are not evidence-based but seem appealing and plausible. For instance, the more often one takes blood cultures, the less likely a causative agent will be missed. This would only be true if antibiotic therapy was not being given since the presence of antibiotics in blood cultures reduces their yield. Another argument is that persistent fever might represent constant bacteremia or repeated bouts of bacteremia. This may be true in endocarditis, or perhaps catheter-related infections, but little else. Instead, like many of the customary practices in medicine, what seems reasonable may turn out to be little more than a ritual that should actually be considered a relic of the past and abandoned altogether. ❖

Pneumococcal Conjugate Vaccine and Otitis Media: Reality and Perspective

ABSTRACT & COMMENTARY

Synopsis: *An efficacy study of the heptavalent pneumococcal conjugate vaccine showed a 57% reduction in cases of otitis media caused by vaccine serotypes, which resulted in a 6% overall decrease in the incidence of otitis media. The conjugate pneumococcal vaccine has a small additional benefit against otitis media, but the vaccine should not be promoted as a vaccine for otitis media.*

Source: Eskola J, et al. Efficacy of a pneumococcal conjugate vaccine against otitis media. *N Engl J Med*. 2001;344: 403-409.

Eskola and colleagues conducting a prospective, randomized, double-blind, efficacy trial in Finland of the heptavalent pneumococcal conjugate vaccine, using hepatitis B vaccine as the control, found 2596 cases of otitis media (OM) among 1662 infants between 6.5-24 months of age. The efficacy of the vaccine was 6% (95% confidence interval, -4-16%) against acute OM from any cause, 34% (95% CI, 21-45%) against culture-confirmed pneumococcal OM, and 57% (95% CI, 44-67%) against pneumococcal OM caused by vaccine serotypes. The number of episodes attributed to serotypes that are cross-reactive with those in the vaccine was reduced by 51%, and the number of episodes caused by all other serotypes increased by 33%. Compared to the hepatitis B vaccine, the pneumococcal was more commonly associated with local reactions and with temperature > 39ºC.

COMMENT BY HAL B. JENSON, MD, FAAP

The heptavalent pneumococcal vaccine (PCV7) was licensed by the FDA in February 2000 and is recommended for routine administration to all children at 2, 4, 6, and 12-15 months of age, and children 24-59 months of age at high risk of pneumococcal disease. The pneumococcal conjugate vaccine is recommended to prevent pneumococcal bacteremia, pneumonia, and meningitis.

Among children younger than 5 years of age, *Streptococcus pneumoniae* causes 17,000 cases of meningitis and 200 deaths annually in the United States. *S pneumoniae* is also the most common bacterial cause of OM, accounting for 28-55% of cases. The most common

pneumococcal serotypes causing OM are 3, 6B, 9V, 14, 19F, and 23F; the vaccine serotypes are 4, 6B, 9V, 14, 18C, 19F, and 23F. The 7 million cases of acute OM each year in the United States account for 20 million office visits and 18% of ambulatory care visits among preschool children. Thus, even the modest 6% reduction in incidence of OM would theoretically prevent 1.2 million office visits annually. But it is important not to misrepresent the benefits of the vaccine as being a "vaccine for otitis media." This underemphasizes the greatest benefit of the vaccine in preventing invasive pneumococcal disease, and it overstates the modest 6% benefit on reducing the incidence of OM.

The 7 serotypes in the vaccine cause 80-90% of invasive pneumococcal disease. This study showed a 51% reduction in the number of episodes of OM caused by vaccine serotypes, with a relative increase of 33% in the number of episodes of pneumococcal OM caused by other serotypes. Whether the use of this heptavalent pneumococcal conjugate vaccine, or other conjugate vaccines currently in trials that contain up to 11 pneumococcal antigens, alters the epidemiology of the pneumococcal serotypes causing invasive disease or otitis media remains to be seen. ❖

CME Questions

37. What virus that causes infection in humans most closely resembles Nipah virus?
a. Hepatitis A
b. Respiratory syncytial virus
c. Measles
d. Ebstein Barr Virus

38. Which one of the following is correct regarding the GM-ELISA assay?
a. Invasive aspergillosis was considered probable if cultures yielded *Aspergillus* irrespective of the presence of clinical features.
b. The GM-ELISA test could detect as little as 1 ng/L of GM.
c. The test had too high a false-negative rate because the specificity was 96%.

39. Which of the following is correct?
a. Parvovirus B19 is an RNA virus.
b. Parvovirus B19 preferentially infects megakaryocytes.
c. Parvovirus B19 is transmitted to humans from dogs.
d. Parvovirus B19 causes Fifth disease.

40. The heptavalent pneumococcal conjugate vaccine:
a. has been demonstrated to reduce the incidence of otitis media in children.
b. is recommended for administration to children beginning at age 14 months.
c. includes all the pneumococcal serotypes most commonly associated with childhood otitis media.
d. includes 7 serotypes that cause 80-90% of cases of invasive pneumococcal disease.

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In Future Issues:

Guidelines for CAP—Are They Really Worth It?

UPDATES

By Carol A. Kemper, MD, FACP

E coli 0157 as a Zoonosis

Source: *MMWR Morb Mortal Wkly Rep.* 2001;50:293-297.

Outbreaks of *Escherichia coli* 0157:h7 have been previously reported in visitors of a petting zoo and a farm in the United Kingdom. Two similar outbreaks have now been reported in Pennsylvania and Washington, leading to 56 episodes of illness and 19 hospitalizations. During the first outbreak, which occurred in May 2000 in Washington, 5 people (aged 2-14 years) developed enteritis due to *E coli* 0157. The isolates had identical PFGE patterns. Further investigation revealed that 4 of the patients, as part of a class field trip, had visited a dairy farm. The fifth patient was a sibling of one of the case patients. The children were allowed to handle young poultry, rabbits, goats, and a calf. They then had lunch in a nearby field. Stool samples from 5 animals at the farm were negative for *E coli* 0157.

The second outbreak in November 2000 in Pennsylvania involved many more people: 51 people, ranging in age from 1 to 52 years (most were preschool and school-aged children) developed a diarrheal illness within 10 days of visiting a dairy farm. Fifteen patients had either positive stool cultures or developed hemolytic-uremic syndrome. Visitors could eat and drink while petting various farm animals, including cattle, llamas, and a pig. A case-control study of visitors to the farm showed that direct contact with cattle, nail biting, and purchasing food from an outdoor concession stand were significant risk factors for the development of disease.

The CDC has since published guidelines for prevention of transmission of enteric pathogens at petting zoos and farms. Institution of good hand washing facilities with soap and water and distribution of instructional leaflets to visitors were effective at halting the outbreak at the first facility. Visitors to zoos and farms need to be counseled that various human pathogens, including *Salmonella*, *Campylobacter*, and *E coli* can be readily transmitted from animals to people. Activities with hand-to-mouth contact, such as eating, drinking, smoking, and using pacifiers should be discouraged while having contact with animals, and good hand washing should be reinforced. (How long is 15 seconds?). ■

Bad Business Deals Attributed to Mefloquine

Source: Torassa U. *San Francisco Chronicle*. April 8, 2001:T10.

Former us representative edward Mezvinsky (Iowa), who has been indicted on charges of fraud, is suing Hoffman-LaRoche, makers of mefloquine. Mezvinsky claims that his use of mefloquine exacerbated his underlying bipolar disorder, resulting in a series of bad business decisions that ultimately cost his investors millions of dollars and landed him in court. Mezvinsky is apparently only one of a number of people who have attempted to sue the manufacturer of mefloquine, claiming various untoward and unexpected neurologic and psychiatric effects (including suicide). This is the first time, however, that a criminal defendant has used the "Larium defense." ■

Magic Mushrooms and Mefloquine

Source: ISTM Physicians (TRAVEL-MED@YorkU.CA); March 19-20, 2001.

Physicians on the international Travel Medicine (ISTM) chat line reviewed a case of an 18-year-old student traveling in Southeast Asia and India as part of a class "project" who developed an acute reaction following an ingestion of raw "magic mushrooms" in Thailand. He presented several days later to a physician in Calcutta complaining of nausea, sweats, palpitations, and intermittent attacks of confusion, anxiety, and, according to friends, possible paranoia. He was also experiencing bad dreams.

He was also receiving mefloquine for malaria prophylaxis.

He consumed the mushrooms—also known as LSG/ecstasy mushrooms—and some possible marijuana, along with several friends, none of whom had a similar reaction. Such mushrooms have been popular with certain travelers looking for a "natural" (someone said the word—organic?) high since the 1960s and are apparently available at clubs and resorts in Southeast Asia.

Whether this young man's symptoms were secondary to the mushrooms, the mefloquine, or both is uncertain. However, retrospective data suggest that up to 11.3% of travelers, none with previously identified psychiatric problems, report some kind of neuropsychiatric symptoms while receiving mefloquine, including sleep disturbances, vivid dreams, and fatigue in about one-half to frank depression in 0.5% (see Kemper CA. *Infectious Disease Alert* 2000;19:112). About 1.2% report prolonged symptoms lasting longer than 2 months.

Critics of these data argue that good prospective data identifying a significant risk of neuropsychiatric problems in persons receiving mefloquine is lacking. Mefloquine remains an important prophylactic antimalarial agent for many travelers. Since a major complaint of some patients appears to be a perception of a lack of adequate warning regarding potential side effects, travel medicine clinics may find a simple handout outlining potential problems helpful. It seems reasonable to add that patients should probably not take psychoactive substances with their mefloquine. ■