Mumps Virus–associated Hemophagocytic Syndrome

To the Editor: Virus-associated hemophagocytic syndrome (VAHS) is a fulminant disorder associated with systemic viral infection and is characterized pathologically by the proliferation of hemophagocytic histiocytes in the lymphoreticular tissues. Here we report a case of mumps VAHS following parotitis and pancreatitis.

A 39-year-old, previously healthy woman sought treatment for abdominal pain on June 14, 2002. On physical examination, her bilateral parotid glands were swollen, and her left upper quadrant was tender. Laboratory studies showed a leukocyte count of 4,640/mm^3, a hemoglobin concentration of 13.9 g/dL, and a platelet count of 19.1×10^4/mm^3. The level of amylase was elevated in her blood (1,613 IU/L; normal 50–160 IU/L) and urine (12,940 IU/L; normal 200–1,100 IU/L). Her level of pancreatic enzymes was also elevated: lipase level was 194 IU/L (normal 7–60 IU/L) and phospholipase A2 level was 1,340 ng/dL (normal 130–400 ng/dL). Parotitis and acute pancreatitis due to a mumps virus infection were diagnosed. After supportive therapy, the laboratory abnormalities improved.

On July 1, the patient's temperature suddenly rose to 39°C. At that time, pancytopenia was evident, with a leukocyte count of 2,350/mm^3, a hemoglobin concentration of 10.9 g/dL, and a platelet count of 9.1×10^4/mm^3. Laboratory studies showed an elevation of lactic dehydrogenase (1,403 IU/L; normal 180–460 IU/L), ferritin (12,727.0 ng/mL; normal 4.0–64.2 ng/mL), and soluble interleukin-2 receptors (1,660 U/mL; normal 145–519 U/mL). Hypercytokinemia was also shown, with an interleukin-6 of 12.7 pg/mL (normal <3.1 pg/mL). Her bone marrow was normocellular, and an increased number of histiocytes with hemophagocytosis was found. Extensive cultures and serologic studies for microbial and viral infections were all negative, whereas tests for immunoglobulin G and immunoglobulin M antibodies against the mumps virus were both positive. Mumps VAHS was diagnosed. Treatment with corticosteroids led to a complete remission of symptoms.

VAHS was initially reported by Risdall et al. in 1979 (1). Although the precise pathogenesis of VAHS remains unknown, current hypotheses focus on the roles played by activating cytokines. VAHS has been reported in connection with a variety of viruses: adenovirus, cytomegalovirus, dengue, Epstein-Barr, hepatitis A, hepatitis B, hepatitis C, herpes simplex, HIV, human herpesvirus 6, human herpesvirus 8, influenza A (antigenic type H1N1), measles, parainfluenza type III, parvovirus B 19, rubella, and varicella-zoster (2). This report is the first of a VAHS case associated with a mumps virus infection. The clinical course of VAHS is highly variable, and in some cases, especially in Epstein-Barr virus infection, VAHS is a dramatic illness with a potentially fatal outcome (2). This case implies that mumps VAHS may have a positive prognosis.

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Imported Cutaneous Diphtheria, Germany, 1997–2003

To the Editor: The March 2004 report by de Benoist et al. on the incidence of imported cutaneous diphtheria in the United Kingdom (1) prompted us to describe the situation of cutaneous diphtheria in Germany and to analyze the cases reported to the German Consiliary Laboratory on Diphtheria since its establishment at our institute in 1997. The laboratory provides advisory and diagnostic services mainly to microbiologic laboratories throughout Germany.

From 1997 to 2003, 6 cases of cutaneous infections caused by toxigenic *Corynebacterium diphtheriae* were documented (Table). None of these was accompanied by secondary diphtheria infection. Toxigenicity was determined by both *dtx* polymerase chain reaction and Elek test (2). As in the United Kingdom, all cases for which clinical information was available (N = 5) were imported. Three were found in tourists who had traveled to tropical countries: a 20-year-old diver had injured her heel after stepping on coral in Thailand; a 60-year-old tourist had a chronic ulcer develop in the thigh after a trip to Indonesia (no history of an insect bite); and a 39-year-old traveler to Kenya returned with a purulent ear infection with no memory of trauma or insect bite. The remaining imported *C. diphtheriae* skin infections were reported in 2 Angolan children,

5 and 10 years of age, who were brought to Germany by a humanitarian organization for surgery on severe gun wounds to their lower extremities (foot and thigh with chronic osteomyelitis, respectively). To our knowledge, these reports are the first of cutaneous diphtheria in gunshot wounds in recent years. Moreover, in the patient with the thigh wound, *C. diphtheriae* was also isolated from a deep fistula, which suggests involvement of *C. diphtheriae* in the chronic osteomyelitis.

As in the United Kingdom, all cases of diphtheria reported since 1997 were caused by *C. diphtheriae mitis*. In 4 of 5 cutaneous diphtheria patients who had an available medical history, mixed infections with *Staphylococcus aureus* and *Streptococcus pyogenes* were found; 3 of 5 patients were not sufficiently vaccinated against diphtheria as recommended. Systemic symptoms, such as malaise and general weakness, developed in the 20-year-old Thailand tourist, although she had received a booster dose just before her travel. Cutaneous diphtheria must be expected even in vaccinated patients; for instance, among serum samples of 287 healthy German adults with a complete record of basic immunization against diphtheria, only 42.2% showed full serologic protection as indicated by antitoxin levels $\geq$ 0.1 IU/mL (3).

As de Benoist et al. outline, cutaneous diphtheria might be difficult to diagnose because of its unspecific clinical appearance and the presence of mixed infections in chronic nonhealing skin lesions. Because of the nearly complete disappearance of cutaneous diphtheria in many parts of the western world, microbiologists lack experience in identifying *C. diphtheriae* grown from specimens. From 1997 to 2003, approximately one fifth of the strains sent to our Consiliary Laboratory on Diphtheria for species identification and toxin testing were either nondiphtheria *Corynebacterium* spp. or noncoryneform bacteria of different genera (including lactobacilli, *Dermabacter hominis*, and *Propionibacterium acnes*).

Clinicians (4) and microbiologists (5) should be aware of the possibility of cutaneous diphtheria in chronically infected skin lesions in patients returning from disease-endemic regions. Medical personnel should include this in civilian as well as military health services, since our cases indicate that toxigenic *C. diphtheriae* might affect not only travel-related skin injuries caused by leisure or tourist activities but also wounds in patients from war regions in diphtheria-endemic areas.

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Antimicrobial Drug Consumption in Companion Animals

To the Editor: During the last decade, use of antimicrobial drugs for growth promotion and therapeutic treatment in food animals has received much attention. The reservoir of resistant bacteria in food animals implies a potential risk for transfer of resistant bacteria, or resistance genes, from food animals to humans. Subsequent emergence of infections in humans, caused by resistant bacteria originating from the animal reservoir, is of great concern. These unintended consequences of antimicrobial drug use in animals led to termination of antimicrobial growth promoters in food animals in countries in the European Union, including Denmark, where the consumption of antimicrobial drugs by production animals was reduced by 50% from 1994 to 2003 (1).

In Denmark, the VetStat program monitors all veterinary use of medicines for animals. VetStat is based on reporting from the pharmacies and from veterinary practitioners and contains detailed information, such as animal species, reason for prescription, and dosage on each prescription. In Denmark, antimicrobial drugs can be obtained only by prescription and only at pharmacies.

So far, use of antimicrobial drugs in companion animals has received little attention; monitoring programs have focused on antimicrobial drug consumption in food animals. According to data generated by the VetStat program in 2003, consumption of fluoroquinolones and cephalosporins in companion animals was substantial when compared to consumption in food animals (1). Fluoroquinolones and cephalosporins are antimicrobial drugs ranked by the U.S. Food and Drug Administration as critically important in human medicine, and for which emergence of