Tourist Trap

The ease and speed of travel facilitate exposure to conditions not endemic to the area where patients seek treatment. With international travel on the rise, particularly during summer months, emergency physicians must be prepared to evaluate and manage patients who become ill abroad. It is critically important to build a framework for assessing returned travelers who present with fever, as such cases can pose serious threats to patients and public health.

Feeling No Pain

Emergency physicians manage a spectrum of acute medical and traumatic conditions that often require painful treatments. In such cases, aptly administered procedural sedation and analgesia can improve the experience for both the provider and the patient. Because the appropriate regimen varies based on the particulars of each case, clinicians should thoroughly understand the advantages and potential risks of sedatives, dissociative agents, and analgesics.
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The ease and speed of travel facilitate exposure to conditions not endemic to the area where patients seek treatment. With international travel on the rise, especially during summer months, emergency physicians must be prepared to evaluate and manage those who become ill abroad. An estimated 64% of travelers become ill abroad. Fortunately, most of these diseases are mild and self-limiting, evidenced by upper-respiratory and gastrointestinal symptoms.
However, more serious pathogens, including malaria, dengue fever, rickettsial infections, and typhoid fever, are diagnosed with varying frequencies in returned travelers with systemic febrile illness.

Travel-related diseases can pose significant diagnostic challenges for physicians who do not encounter these conditions regularly, but preparation and an organized clinical approach can help mitigate the risks associated with these common disorders.

**CRITICAL DECISION**

What specific details should be obtained when inquiring about a patient’s travel history?

A careful travel history should identify, at minimum, the geographic region visited, reason for travel, timeline of travel, possible exposures, pre-travel immunizations, and chemoprophylaxis.

**Travel Destination**

Disease risk varies significantly by region. For example, a febrile patient who returns from Sub-Saharan Africa may be more likely to have malaria than someone who returns from another region, where dengue fever or other diseases are more prominent. Similarly, rickettsial infections, yellow fever, enteric fever, and many other diseases are endemic to certain areas, so the risk of exposure varies greatly based on the region visited (Table 1).

**Timeline**

It is essential to establish a travel and exposure timeline, including details related to the duration of the trip, timing of exposure, and timing of illness in relation to travel. Some studies suggest that longer trips are correlated with an increased risk and incidence of illness. Furthermore, due to the variation of incubation periods, the timing of symptoms related to travel can help measure a patient’s risk for certain conditions.

**Pre-Travel History**

The emergency physician should also evaluate a patient’s pre-travel preparation. Travelers who visit a clinic prior to departure are less likely to present with fever, acquire malaria, or experience severe disease than those who depart without a pre-trip assessment. When managing a case of suspected malaria, for example, the clinician should ask if the patient received chemoprophylaxis at a travel clinic and assess compliance with the prescribed regimen.

In one case series of US civilians, 6% of patients with malaria reported adherence to appropriate chemoprophylaxis. It is important to remember that a traveler who has taken chemoprophylactic medications can still acquire malaria, although the incidence is less likely.

**Other Historical Details**

To further narrow the differential diagnosis and risk stratify a case, the emergency physician should seek to identify possible exposures, such as a history of freshwater swimming, known ingestions of contaminated food or water, interactions with farm animals, or reported insect bites. Details about a traveler’s accommodations and activities can provide critical information, as business travelers can experience far different exposures than adventure travelers or front-line humanitarian workers. Possible risk factors should be investigated: Did the patient have bed nets or screens? Was the patient in a more rural or urban environment? Was the patient staying in a hotel, camping, or visiting farms? These factors can suggest differing susceptibilities to various infections. Travelers who were visiting friends or family are at increased risk for certain illnesses due to increased exposure to local populations.

In addition, the clinician should inquire as to whether a patient sought medical care overseas. Whether a patient went to a clinic, local hospital, or purchased medications from a local pharmacy can be valuable information. In many countries, antibiotics and other medications can be purchased over-the-counter without a prescription. This information can help to explain a delayed or atypical clinical presentation.

**CRITICAL DECISION**

How should suspected malaria be approached, and what other diseases should be considered?

Several epidemiological studies of fever in returned travelers indicate that, when a specific etiological diagnosis is made, malaria (Figure 1) is the most frequently identified illness. However, differentiating malaria from other travel-
related systemic febrile illnesses can be challenging due to the nonspecific findings that are associated with this condition. Malaria, particularly in uncomplicated infections, is characterized by symptoms similar to those of other minor viral illnesses. Early symptoms of uncomplicated cases include fever, malaise, myalgia, headache, and chills. The classic paroxysms of chills and fever followed by diaphoresis are infrequently observed with falciparum malaria infection. The nonspecific early findings of malaria overlap significantly with other causes of acute febrile illness in returned travelers, such as dengue, chikungunya, and Zika (Figure 2). Although myalgia is common with malarial infections, it is usually less severe than when associated with dengue, and muscle tenderness is less prominent with malaria than with leptospirosis or typhus.

Malaria is also less likely to present with a rash than dengue, chikungunya, Zika, typhus, enteric fever, or meningococcal septicemia. Petechiae are often associated with viral hemorrhagic fevers (VHFs) but are rarely seen with malaria. Petechiae are only found in severe falciparum malaria infections associated with complications such as disseminated intravascular coagulation (DIC). High fevers, splenomegaly, thrombocytopenia, mild jaundice, and abdominal tenderness are commonly found.

Malaria is caused by *Plasmodium* parasites spread via an *Anopheles* mosquito vector. Five *Plasmodium* species cause the disease in humans: *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi*. Other confounding causes of acute febrile illness in the returned traveler are also vector-borne; for example, dengue, Zika, yellow fever, and chikungunya are all arboviruses whose primary vector is the *Aedes aegypti* mosquito.

Details about the travel timeline and geographic area visited can be particularly valuable. Although significant overlap exists in endemic areas of malaria, dengue, chikungunya, Zika, African trypanosomiasis, and leptospirosis, a travel timeline can help differentiate them. Chikungunya, dengue, and Zika have incubation periods of less than 2 weeks, while the incubation period for malaria varies by species. The incubation period for *P. falciparum* is approximately 12 to 14 days, with a range from 7 to 30 days. The overwhelming majority of cases of

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**TABLE 1. Selected Infectious Diseases by Region**

<table>
<thead>
<tr>
<th>Region</th>
<th>Incubation Period of ≤10 Days</th>
<th>Incubation Period of ≤21 Days</th>
<th>Incubation Period of &gt;21 Days</th>
<th>Incubation Period of Months</th>
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<td>Zika</td>
<td>Leptospirosis</td>
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<td>Dengue</td>
<td>Zika</td>
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<td></td>
<td></td>
<td>Leptospirosis</td>
<td>Chagas disease</td>
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<td>Yellow fever</td>
<td>Zika</td>
<td>Leishmaniasis</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Enteric fever</td>
<td>Chagas disease</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Leptospirosis</td>
<td>Leishmaniasis</td>
</tr>
<tr>
<td><strong>South Central Asia</strong></td>
<td>Chikungunya</td>
<td>Dengue</td>
<td>SARS</td>
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<td>Chikungunya</td>
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<td>SARS</td>
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<td>Yellow fever</td>
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<td></td>
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<td>Schistosomiasis</td>
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<td>Filariasis</td>
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<td>Leishmaniasis</td>
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<tr>
<td><strong>Widespread</strong></td>
<td>Malaria</td>
<td>HIV</td>
<td>Malaria</td>
<td>Malaria</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tuberculosis</td>
</tr>
</tbody>
</table>

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**FIGURE 1. Life Cycle of the Malaria Parasite**

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Parasite cannot be visualized, blood
smears should be repeated every 12 to
24 hours for 2 days. In cases of altered
mental status and fever after travel to
endemic areas, cerebrospinal fluid (CSF)
should be evaluated to rule out other
causes of encephalopathies; CSF in
patients with malaria is usually normal
or demonstrates nonspecific, mildly
elevated protein and mild pleocytosis.

Treatment varies based on the
severity of the illness, drug susceptibility,
and species of parasite. Due to
increasing drug resistance in endemic
areas, the World Health Organization
(WHO) recommends artemisinin-based
compounds as the first-line therapy
for falciparum malaria infections. In
addition to initial therapy to treat
erythrocytic forms, patients with
vilax or P. ovale infections require
primaquine to eradicate the dormant
liver hypnozoites and prevent relapse.

The Centers for Disease Control
and Prevention (CDC) maintains a
24-hour malaria hotline, which provides
clinicians with diagnostic and treatment
advice from a Malaria Branch expert at
all times. The CDC Malaria Hotline can
be reached Monday through Friday from
9 AM to 5 PM EST at 855-856-4713; for
after-hours assistance with diagnosis
or management of suspected malaria
cases, health care providers can call the
CDC Emergency Operations Center at
770-488-7100.

While no emergency treatment is
required, the clinical presentation of Zika
can overlap greatly with malaria and is
another important consideration in the
febrile returned traveler, particularly for
females of childbearing age. In cases of
suspected Zika, the emergency provider
should follow state guidelines for testing.
Although dengue, chikungunya, and Zika
have been specifically mentioned, other
diseases can present similarly. Therefore,
a broad differential diagnosis should
be considered in returned travelers who
present with acute febrile illness, including
Acute HIV, enteric fever, leptospirosis,
African trypanosomiasis, yellow fever,
visceral leishmaniasis, hepatitis, influenza,
tick-borne rickettsioses, and many other
illnesses.

**CRITICAL DECISION**

What are the potential causes of
hemorrhagic fever, and how should
they be managed?

The WHO defines acute hemorrhagic
fever syndrome as an acute onset of fever
of less than 3 weeks duration in a severely
ill patient, plus any two of the following:
- Hemorrhagic or purpuric rash
Epistaxis
• Hematemesis
• Hemoptyis
• Blood in stools
• Other hemorrhagic symptoms and no known predisposing host factors for hemorrhagic manifestations.13

Hemorrhagic fevers can be caused by viral, bacterial, or rickettsial diseases. Viral causes can be classified into the following families: filoviruses (Ebola and Marburg), arenaviruses (Lassa fever, Junin, Machupo, Lujo, Sabia, and Chapare), flaviviruses (yellow fever, dengue, Omsk hemorrhagic fever, Kyasanur Forest disease), and bunyaviruses (Crimean-Congo hemorrhagic fever, Rift Valley fever, and Hantaan hemorrhagic fever). Each virus is associated with a specific host species, and human infection is incidental. These host-virus associations generally limit the distribution of each disease to specific geographical areas, although travelers can carry disease to nonendemic areas. Human-to-human spread can cause significant outbreaks, as exemplified by the recent Ebola outbreak in West Africa.

Ebola Virus
Ebola virus disease sets itself apart from other causes of hemorrhagic fever by its virulence and mortality. Mortality rates have reached as high as 70% to 90% in prior epidemics.2 Ebola viruses are found in several African countries. The infamous West African Ebola epidemic of 2014 to 2015 turned the virus into a household name. The Ebola and Marburg viruses, of the filovirus family, are among the most virulent diseases in humans.16 Unlike other causes of VHF, the primary reservoir for Ebola is uncertain, although many believe that fruit bats serve this role.17 Humans can contract the virus through contact with infected bats, primates, or other humans. Once humans are infected, the disease can spread rapidly. Human-to-human transmission occurs through direct contact with bodily fluids from an infected person, by objects that have been contaminated with such bodily fluids, and even through the semen of males who previously recovered from the disease.18,19

The combination of virulence and mortality of both Ebola and other causes of VHF makes transmission prevention a critically important focus. Early symptoms of VHF can be similar to, and therefore difficult to distinguish from, other febrile illnesses. During an outbreak, febrile patients should be routinely screened for travel to endemic areas and symptoms concerning for VHF. Clinicians must maintain a high degree of suspicion in any patient who has recently returned from an endemic area or has had contact with someone with VHF who presents with fever, muscle aches, severe headache, diarrhea, vomiting, abdominal pain, or any unexplained hemorrhage.

If VHF is suspected, extreme caution must be taken to prevent transmission within the health care facility. The patient should immediately be placed in an isolated room with a designated bathroom or bedside commode. Healthcare workers should act in designated roles to minimize the number of workers who manage the patient. All personnel who come into contact with the patient should wear appropriate personal protective equipment, and interactions should be recorded in a log.

For a comprehensive review of appropriate personal protective equipment, see the CDC guidelines at http://www.cdc.gov/vhf/ebola/healthcare-us/ppe/guidance.html. The facility’s infection control program and the local health department should be notified, and a workup should continue, using only dedicated equipment in compliance with local protocols. For further details on the approach to triage, see the algorithm published by the CDC.20

If clinical suspicion remains high after the initial evaluation, testing should proceed in conjunction with the local health department. Various forms of testing are available, including PCR, enzyme-linked immunosorbent assay (ELISA), virus isolation, and IgM and IgG for patients later in the disease course. For most causes of VHF, no specific treatment exists. Management should therefore be supportive with IV fluids, electrolyte replacements, supplemental oxygen, vasopressors, and mechanical ventilation, and combined with the treatment of other infections, as needed.

Dengue Virus
Dengue virus infection is the most common mosquito-borne illness worldwide.11,22 Transmission is ubiquitous throughout the subtropics and tropics, with more than half the world’s population at risk of infection.23 Manifestations of the infection can range from acute febrile illness, commonly referred to as dengue fever, to dengue hemorrhagic fever and dengue shock syndrome.

The Aedes aegypti mosquito is the primary vector for dengue virus transmission. The incubation period ranges from 3 to 14 days, but symptoms usually begin 4 to 7 days after being bitten by an infected mosquito. Dengue fever can present as an acute febrile illness; it is colloquially referred to as “breakbone fever” due to the associated arthralgia. The WHO recommends considering this diagnosis when fever is accompanied by two or more of the following symptoms: severe headache, retro-orbital pain, joint pain, myalgia, nausea, vomiting, swollen glands, or rash.24 Hemorrhagic manifestations, such as epistaxis and scattered petechiae, are seen in cases of uncomplicated dengue infection; however, they can also indicate more severe disease. Patients with dengue fever can also present with abdominal pain, lethargy, restlessness, or elevated liver transaminases, but these should alert the provider to possible severe dengue infection.

Symptoms of severe illness usually manifest 2 to 5 days after the onset of typical dengue fever.25 In addition to fever, patients with hemorrhagic forms of the disease exhibit the following triad of features:

• Evidence of increased vascular permeability
• Marked thrombocytopenia (100,000 cells/mm³ or less)
• Spontaneous bleeding or signs of hemorrhagic tendency26

When dengue is accompanied by signs of circulatory failure (eg, hypotension, narrow pulse pressure, or weak pulses) in addition to features of dengue hemorrhagic fever, the term dengue shock syndrome is often used. Historically, the virus has been classified...
into dengue fever, dengue hemorrhagic fever, and dengue shock syndrome. Although these terms are still frequently used in clinical practice, nomenclature has more recently been simplified to dengue with or without warning signs and severe dengue.26 In the updated classification system, severe dengue fever is defined by severe plasma leakage, severe hemorrhage, and/or severe organ impairment. Understanding both systems can help the provider recognize signs of more serious illness and communicate effectively with consulting services.

Signs of increased vascular permeability include pleural effusion, ascites, or hemoconcentration, which can be diagnosed with bedside ultrasound, chest radiographs, or chest or abdomen CT. These complications usually begin 3 to 7 days after the onset of typical dengue fever, usually coinciding with the time of defervescence. The sequelae of profound vascular leakage can include respiratory distress and overt shock.26

Hemorrhagic manifestations of dengue virus include spontaneous bleeding, generally petechiae or ecchymoses, or evidence of hemorrhagic tendency. Hemorrhagic tendency is demonstrated by a positive “tourniquet test.” The test (Figure 3) is performed by taking the patient’s blood pressure and then inflating the blood pressure cuff on the arm to midway between the systolic and diastolic blood pressures, keeping it inflated for 5 minutes. The pressure is then released for 2 minutes. The skin beneath the cuff is examined for petechiae, and the number of petechiae is recorded. The test is considered positive if there are 10 or more petechiae per 1 square inch of skin. A positive test indicates microvascular fragility and a hemorrhagic tendency.

Although dengue is generally a clinical diagnosis, more advanced confirmatory testing exists. Management is supportive, consisting primarily of volume resuscitation and analgesia. Pain management should be achieved with medications other than nonsteroidal anti-inflammatory agents, as these are contraindicated in cases of dengue fever.26

CRITICAL DECISION
What diseases should be considered in a febrile returned traveler with abdominal pain, respiratory complaints, or neurological symptoms?

For undifferentiated fevers in returned travelers, the involved organ systems can provide additional clues for diagnosis. As with other travel-related illnesses, it is essential to elicit a detailed travel history to identify potentially important exposures. Organ-specific signs and symptoms can assist the clinician. The approach to fever in the returned traveler with abdominal pain, respiratory symptoms, or neurological symptoms should begin with the consideration of nontravel causes, and then be expanded to a differential diagnosis that includes travel-related etiologies.

Abdominal Pain and Fever
Concerning features such as jaundice, organomegaly, or hematochezia should prompt the clinician to pursue an expanded workup. Lab studies and imaging — stool microscopy, stool culture and sensitivity, stool ova and parasites, stool serology, hemoccult testing, blood cultures, or other advanced diagnostic tools — should be ordered as clinically indicated. Empiric treatment can be indicated based on the suspected diagnoses.

Aspects of a patient’s presentation can guide the emergency provider to narrow the differential diagnosis for fever and abdominal pain. For example, a chief complaint of watery diarrhea can suggest enterotoxigenic *Escherichia coli*, cryptosporidiosis, giardiasis, cholera, or a rotavirus. A history of bloody diarrhea can suggest an invasive or inflammatory etiology, including both bacterial and parasitic causes, such as enterohemorrhagic *E. coli*, enteroinvasive *E. coli*, *Salmonella*, *Shigella*, *Campylobacter* enteritis, *Yersinia enterocolitica*, or *Entamoeba histolytica*. However, these patients often present with watery diarrhea as well.

Jaundice can imply etiologies such as hepatitis, severe malaria, leptospirosis, yellow fever, dengue, or other VHFs. Organomegaly can suggest malaria, leishmaniasis, amoebic liver abscesses, enteric fever, brucellosis, schistosomiasis, or hepatitis. Petechiae can be due to leptospirosis, yellow fever, dengue, or other VHFs. Abdominal pain and fever accompanied by a rash should alert the emergency physician to VHFs, brucellosis, or enteric fever, among other illnesses. Shigellosis should be considered in patients with diarrhea, febrile seizures, and a history of travel. In patients with fever, abdominal pain, and eosinophilia associated with pulmonary symptoms, the clinician should consider helminthic sources, such as hookworms or roundworms.

Traveler’s Diarrhea
Diarrhea and gastroenteritis are among the most common travel-related complaints. Although it is important to consider more concerning etiologies, most patients with fever, abdominal
pain, and diarrhea are suffering from traveler’s diarrhea, a mild and self-limited disorder that generally resolves within 3 to 7 days. Primary treatment is targeted at fluid resuscitation, as needed. Antibiotic and antimotility agents can be used to limit the severity and duration of symptoms. When there is suspicion for enterohemorrhagic E. coli (eg, a history of bloody stools), caution should be used, as antibiotic treatment is associated with an increased risk of hemolytic uremic syndrome.

Bacterial and viral pathogens associated with traveler’s diarrhea generally have an incubation period of 6 to 72 hours; the incubation period for protozoal pathogens is considerably longer (typically 1-2 weeks). Markedly elevated fever and blood or pus in the stool are uncommon and should raise suspicion for another etiology.

**Enteric Fever**

Enteric fever, caused by *Salmonella Typhi* or *Salmonella Paratyphi*, can produce fever and abdominal pain in the returned traveler, particularly undifferentiated prolonged fever. The presentation of the disease is somewhat nonspecific. When suspicion exists, malaria should be ruled out, and other diagnoses should be considered, including hepatitis, VHF’s, bacterial enteritis, dengue, brucellosis, rickettsial infections, leptospirosis, amoebic liver abscesses, acute HIV, cholera, amoebic dysentery, and parasitic etiologies, such as *Giardia* and *Cryptosporidium*.

The incidence of enteric fever is highest in South and Southeast Asia, but it should also be considered for travelers returning from Africa, East Asia, West Asia, Central America, and South America. The incubation period for the disease ranges from 5 to 21 days. Humans are the only hosts of *Salmonella Typhi* and *Salmonella Paratyphi*, and both ill and asymptomatic chronic carriers can shed bacteria in stool. Most cases are transmitted via contaminated food or water. However, transmission has been described in health care workers (exposed via both patient and specimen contact) and also between male sexual partners. Risk factors for transmission include the consumption of contaminated water or ice, food washed in contaminated water, raw fruits and vegetables grown in fields fertilized with sewage, food and drinks from street vendors; flooding; and suboptimal hand-washing practices.

Patients should be asked about their immunization history, as many travelers who acquire typhoid fever have not been appropriately immunized, and the vaccine can be less than 75% effective.

The initial presentation of enteric fever is variable, but fever is generally present in the early stages. Vital signs can show relative bradycardia compared to what is expected for fever, sometimes referred to as pulse-temperature dissociation or the Faget sign. The classically described “rose spots” of typhoid fever are groups of faint, salmon-colored, blanching maculopapules, primarily found on the trunk; when present, they are usually evident during the latter part of the first week or during the second week of infection. Abdominal pain, nausea, vomiting, anorexia, hepatosplenomegaly, myalgia, and headache can also be present. Patients with severe infection can present with gastrointestinal bleeding, intestinal perforation with resulting peritonitis, septic shock, or altered mental status.

A definitive diagnosis of *Salmonella Typhi* or *Salmonella Paratyphi* is made by isolation of the organism. The physician should consider ordering stool and blood cultures during the initial evaluation. Stool cultures are often negative during the first week of the disease course, while blood cultures are commonly positive.

An important treatment consideration is the increasing rate of multidrug-resistant strains of *Salmonella Typhi* and strains with decreased ciprofloxacin susceptibility. For severe or complicated disease courses, ceftriaxone is considered the first-line empiric therapy. Antibiotic therapy for uncomplicated disease courses depends on the risk of antibiotic resistance; azithromycin is typically recommended for the empiric treatment of enteric fever acquired in areas with high fluoroquinolone resistance.
Respiratory Complaints

In one study, respiratory complaints associated with fever occurred in about one in seven cases of fever in the returned traveler. Although the vast majority of cases are attributable to common bacterial and viral pathogens, it is important to note that travelers in close contact with the local population, such as those visiting family or staying in relatives’ homes, are at an increased risk for pneumonia and influenza, as compared to tourists and business travelers. Some other considerations include legionellosis, acute schistosomiasis, Q fever, leptospirosis, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS).

Patients with a history of travel that includes farm work, particularly with cattle, goats, or sheep, should be evaluated for acute Q fever caused by Coxiella burnetii, which is typically transmitted in aerosolized animal excrement or contaminated soil (Figure 4). Unpasteurized milk is another source. Incubation is approximately 3 weeks, and patients can present with pulmonary symptoms, headaches, and other nonspecific signs. Emergency physicians should also be aware that Q fever can progress to endocarditis or vascular infections.

Adventures travelers, who participate in boating and swimming activities in Sub-Saharan Africa or Southeast Asia, are at risk for Katayama fever due to acute schistosomiasis. In these patients, an immunological response to the schistosomal worms can cause fever, nonproductive cough, bronchospasm, urticaria, fatigue, and organomegaly. Pulmonary infiltrates on x-ray and eosinophilia typically present 4 to 6 weeks after travel; the diagnosis is primarily clinical.

Recent years have seen outbreaks of rapidly progressive respiratory distress syndromes. Ongoing public health syndromic surveillance and the use of appropriate personal protection and patient isolation can aid in the timely diagnosis and prevention of further disease spread. For the SARS outbreak of 2002 to 2003, risk factors included health care workers, work caring for or slaughtering wildlife for human consumption, male gender, advanced age, and air travel. The coronavirus, transmitted by aerosolized droplets, had an incubation period of approximately 4 to 6 days; patients typically presented with fever greater than 38°C (100.4°F) and pneumonia or acute respiratory distress syndrome (ARDS) on chest radiograph.

Similarly, the CDC currently recommends that patients with fever and pneumonia be assessed for Middle East respiratory syndrome coronavirus (MERS-CoV) if they have returned from travel in the Arabian peninsula within the last 14 days, if they:
- have had close contact with such a traveler,
- are febrile with respiratory complaints after spending time in a health care facility (as a visitor, employee, or patient) in a territory where health care-associated cases of MERS have recently been identified,
- or have had close contact with a MERS patient.

Emergency physicians should follow established guidelines for testing and reporting in such cases.

Neurological Complaints

Altered Mental Status

Altered mental status and fever in travelers returning from malaria-endemic regions requires emergent evaluation for cerebral malaria, bacterial meningitis, and encephalitis. Venezuelan equine encephalitis, Japanese encephalitis, and tick-borne encephalitis should also be considered, depending on the area of travel. Tick-borne encephalopathies are most common in Eastern European outdoor adventurers. Neisseria meningitidis should be considered for those patients who have visited Sub-Saharan Africa’s meningitis belt, which encompasses 26 countries from Senegal to Ethiopia; however, outbreaks are sometimes seen in other parts of the world.

Although a vaccine is now required for Muslim pilgrims who travel to Mecca, the vaccination does not cover all strains; physicians should remain alert for meningococcal meningitis. Cryptococcal meningitis and tuberculous meningitis are further considerations when assessing immunocompromised patients with prolonged travel and those who have lived among local populations in Sub-Saharan Africa.

Seizure

The two most common causes of seizures worldwide, neurocysticercosis and schistosomiasis, can present with fever, but they are uncommon.

### TABLE 2. National Notifiable Travel-Related Diseases (2018)

<table>
<thead>
<tr>
<th>Arboviral diseases</th>
<th>Giardiasis</th>
<th>Typhoid fever</th>
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<tbody>
<tr>
<td>California serogroup virus</td>
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<td>Vibriosis</td>
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<td>Chikungunya virus</td>
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<tr>
<td>Eastern equine encephalitis</td>
<td>Hepatitis E</td>
<td>Crimean-Congo</td>
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<tr>
<td>Powassan virus</td>
<td>HIV</td>
<td>Ebola virus</td>
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<tr>
<td>St. Louis encephalitis</td>
<td>Malaria</td>
<td>Lassa virus</td>
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<tr>
<td>West Nile virus</td>
<td>Meningococcal disease</td>
<td>Lujo virus</td>
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<tr>
<td>Western equine encephalitis</td>
<td>Measles</td>
<td>Marburg virus</td>
</tr>
<tr>
<td>Babesiosis</td>
<td>Plague</td>
<td>Guanaroto virus</td>
</tr>
<tr>
<td>Brucellosis</td>
<td>Q fever</td>
<td>Juvin virus</td>
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<tr>
<td>Campylobacteriosis</td>
<td>Salmonellosis</td>
<td>Mucapuro virus</td>
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<tr>
<td>Cholera</td>
<td>Shigellosis</td>
<td>Salmonella</td>
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<tr>
<td>Cryptosporidiosis</td>
<td>Tuberculosis</td>
<td>Yellow fever</td>
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<tr>
<td>Dengue virus</td>
<td>Tularemia</td>
<td>Zika virus</td>
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</table>

Note: This list is not comprehensive; follow local reporting protocols. Data modified from the Centers for Disease Control and Prevention. https://www.cdc.gov/nndss/conditions/notifiable/2018
in casual travelers.\textsuperscript{38} Seizures with febrile diarrheal illness should raise concern for shigellosis. Patients who present with febrile seizures after travel to endemic areas should also be evaluated for Japanese encephalitis, dengue hemorrhagic fever, and cerebral malaria.\textsuperscript{34} Japanese encephalitis is a mosquito-borne flavivirus that is vaccine preventable. Travelers to rural and periurban areas in Southeast Asia and the Western Pacific are at the highest risk of exposure. Although only 1 in 250 infections causes serious clinical disease, such cases can be heralded by fever, headaches, seizures, parkinsonian features, and even coma. In severe disease courses, the case fatality rate reaches 30%; up to another 30% of patients experience permanent neuropsychological problems.\textsuperscript{39,40}

Diagnosis is based on serologic and CSF confirmatory studies, and treatment is symptomatic. Refer to the previous discussions on dengue shock syndrome and malaria for further information. Remember that pregnant women, children, nonimmune populations, and those taking inadequate chemoprophylaxis are at increased risk for cerebral malaria.

**CRITICAL DECISION**

**Which diseases must be reported to the CDC?**

In the interest of public health, the CDC must be informed of the diagnosis of several infectious diseases. It is the responsibility of the provider, not the patient, to notify the CDC. Such diseases are designated as either reportable or notifiable. It is mandatory to report cases of any disease with a reportable designation; reporting a notifiable disease is voluntary. Each state determines what diseases fall under each category, so reportable diseases are unique to each state. Providers, hospitals, and laboratories should report cases to the local health department, which then shares the information with the CDC. Some laboratories automatically report positive results, but providers should familiarize themselves with the procedures in their individual practice settings.

Reporting cases of certain infectious diseases serves many purposes, most importantly helping to slow the spread of communicable diseases. This information also facilitates surveillance, which can help to identify sources of outbreaks; allows public health organizations to plan preventive measures and control strategies; and expedites the initiation of appropriate treatment options. Specific diseases receive reportable designations based on virulence, communicability, and the potential for morbidity and mortality. Table 2 lists notifiable infectious diseases, as compiled by the CDC, that are unique to the returned traveler.

**Summary**

While travel-related diseases are uncommonly seen in US emergency departments, prompt recognition and appropriate management are essential for the safety of patients and the public. Emergency physicians must be adept at taking a complete travel history, including prophylaxis and immunizations, and should be comfortable forming an appropriate differential diagnosis.

Travel history, incubation period, and organ-system involvement should lead physicians toward specific diagnoses. An increased index of suspicion should be maintained for patients with higher-risk exposures, such as adventure travelers, humanitarian workers, those visiting friends and relatives, and those with fevers lasting longer than 1 week. In addition, physicians must ensure that patients are appropriately isolated, personal protection protocols are followed, and specific diseases of concern are reported to the CDC.

**REFERENCES**

4. Cullen KA, Arguin PM; Centers for Disease Control and Prevention. Malaria surveillance—United States,
CASE RESOLUTIONS

■ CASE ONE

The emergency physician suspected malaria in the woman with generalized malaise, fever, chills, headache, and abdominal pain. Thick and thin blood smears revealed falciparum malaria with a parasite density of 3%. At the time of diagnosis, the patient exhibited no manifestations of severe malaria. She was treated with artesether-lumefantrine twice a day for 3 days and made a complete recovery.

■ CASE TWO

The 40-year-old man with bloody stools was isolated, and mandatory, full-transmission precautions were undertaken. Laboratory tests revealed elevated BUN and creatinine levels, elevated liver enzymes, leukopenia, and thrombocytopenia. PCR confirmed the diagnosis of Ebola virus disease. The patient was treated supportively with IV fluids, electrolyte replacement, blood product transfusions, and eventually mechanical ventilation. Despite these efforts, he died 7 days later.

■ CASE THREE

The 50-year-old man’s respiratory status worsened; he required intubation for mechanical ventilation. His CT scan showed ground-glass opacities. Urine antigens for Legionella pneumophila and Streptococcus pneumoniae were both negative; viral panels for influenza, respiratory syncytial virus, parainfluenza virus, and adenovirus were all negative; and sputum cultures for acid-fast bacilli showed no growth.

The clinician sent a lower respiratory specimen for reverse-transcriptase polymerase chain reaction (rRT-PCR) testing for MERS-CoV, which returned positive. The patient received aggressive supportive care in the ICU, and after a 30-day hospitalization, eventually stabilized for exhuastion.
Dislocation at the temporomandibular joint (TMJ) is caused by dislocation of the mandibular condyle(s). The disorder is commonly precipitated by trauma or excessive opening of the mouth. Spasms of the mastication muscles of the jaw, including the masseter, temporalis, and internal pterygoid, result in trismus and must be overcome for reduction to occur. Anatomically, the mandibular condyle generally becomes fixed in the anterior-superior aspect of the articular eminence.

Benefits and Risks
TMJ reduction in the emergency department is a quick procedure that can alleviate a patient’s discomfort and anxiety. Its primary risks include injury to the person performing the procedure or further injury to the patient. Other risks include adverse effects caused by medications or sedation administered prior to or during the procedure.

Since the clinician’s fingers or hands are often positioned intraorally and the muscles of the jaw are quite strong, a patient’s tooth can puncture the glove or skin. Loose dentition or dental hardware can be damaged during the process. Finally, the possibility of iatrogenic damage to the bone and surrounding tissues during reduction should be considered.

Alternatives
In addition to the intraoral technique previously described, an extraoral method can facilitate TMJ reduction. For the extraoral technique, the clinician massages over the dislocated condyle and muscles to relax the spasm and direct the dislocation back to the joint space. A local anesthetic can be used as an adjunct and injected toward the lateral pterygoid and into the joint space. Surgical repair may be considered if external reduction cannot be achieved.

Reducing Side Effects
Contraindications to the procedure include severe facial trauma and fracture of the mandible. To reduce the risk of clinician injury, some providers wrap their fingers with gauze and/or place a tongue depressor (cut in half) or finger splints between digits and dentition. Alternatively, the mandibular ridge can be used as a resting point, instead of the teeth. Proper positioning and preparation can also improve the odds of success and decrease the risks that can arise from sedation or intraoral manipulation.

Special Considerations
Cases that involve extensive facial trauma, mandibular fractures, or extensive dental hardware should be discussed with a consultant regarding the optimal treatment plan. However, the patient’s pain and anxiety should be considered while defining that plan. After closed reduction, it is important to advise patients to implement a soft diet and avoid extreme opening (eg, yawning) while the jaw heals (approximately 1 week). Additionally, some patients may benefit from a nonsteroidal anti-inflammatory agent and/or a wrap that helps keep the jaw closed.

**TECHNIQUE**

1. Position the patient in the supine/recumbent or sitting position, with the back resting against the bed.
2. Provide sedation and/or an anxiolytic agent; consider adjunctive local anesthesia.
3. Apply gauze (over your glove) to digits that will be positioned intraorally, generally thumb(s). Prior to applying the gauze, consider applying half of a tongue depressor along the palmar surface of the thumb that will be in contact with the patient’s teeth.
4. Apply consistent, downward traction with slight flexion and posterior displacement.
Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is the leading cause of morbidity and mortality in pregnant women in the developed world. Although the absolute incidence of VTE in pregnancy is 1 to 2 per 1,000, this risk is 5 times higher than in nonpregnant patients. Most VTEs during pregnancy occur within the first 20 weeks of gestation, but the overall incidence is greatest during the first 6 weeks postpartum. DVTs in pregnant women are more likely to be in the left leg (85% in the left leg versus 55% in the right leg) and proximal in the iliofemoral region (72% proximal versus 9% distal). The strongest predictive risk factor is previous VTE in pregnancy. Other risk factors include venous stasis, immobilization, elevated BMI, and dehydration from emesis.

Suspected DVT is best assessed with serial compression duplex ultrasonography; one prospective study demonstrated a negative predictive value of 99.5%. If the initial ultrasound examination is negative but clinical suspicion remains high, it is safe to repeat the examination in 3 to 7 days with no interim anticoagulation treatment. Iliocaval venous thrombosis is usually extensive and is often identified with compression ultrasonography; however, MRI or x-ray venography can be considered for evaluation if suspicion is high.

The majority of pregnant patients with PE also have DVT. A PE imaging workup can begin with the same compression ultrasound used for suspected DVT, as these two conditions often arise concurrently. If a patient with PE symptoms has a DVT identified with ultrasound, no further imaging is needed and the diagnosis of PE can be made empirically. As in nonpregnant patients, clinical suspicion for PE should be heightened for those whose ECG shows sinus tachycardia or right heart strain.

Oxygen saturation is an unreliable

**KEY POINTS**

- DVTs in pregnancy are more likely to be proximal and in the left leg. The diagnostic test of choice is serial compression duplex ultrasonography.
- If a DVT is identified in a patient with PE symptoms, no further imaging is needed, and empiric treatment should begin.
- VQ scans and CTPA have similar negative predictive values (100% and 99%, respectively). VQ scans emit a fetal radiation dose of 0.5 mGy, and CTPA emits a fetal radiation dose of 0.1 mGy. Both tests fall below the estimated level for teratogenesis and childhood cancer.
- CTPA can be used in patients with an abnormal chest x-ray or indeterminate VQ scan, or if there is concern for other etiologies.
- LMWH is the first-line treatment for VTE in pregnancy. There is no evidence to support an optimal dosing regimen for pregnant patients.
- Warfarin can be used in the postpartum period but should not be used in pregnant patients. Direct thrombin inhibitors and antifactor Xa inhibitors are contraindicated.
- Thrombolysis is indicated for the management of hemodynamically unstable PEs or for DVTs that threaten leg viability.
diagnostic tool in pregnant or postpartum women. Similarly, D-dimer levels are not sensitive or specific enough to aid in the diagnosis. There is limited clinical data to support the validity of the Modified Wells’ Criteria for Pulmonary Embolism and LEFT clinical prediction tools (left leg >2-cm difference, edema, and first trimester) for diagnosing pregnant patients with VTE.

If further imaging is required to assess for PE, radiation exposure to the fetus must be minimized. It is estimated that 1 mGy of radiation exposure in utero increases the risk of fatal childhood cancer by 0.006%. Chest radiography emits more than 0.1 mGy of radiation; however, x-ray findings can have limited clinical utility in assessing for PE. Ventilation-perfusion (VQ) scans have a high negative predictive value and are commonly performed after a normal chest x-ray. Computed tomographic pulmonary angiography (CTPA) is useful if the VQ scan is indeterminate, or if other diagnoses are suspected.

Both tests minimize radiation to the fetus (CTPA = 0.1 mGy versus VQ scan = 0.5 mGy) and are well below the radiation threshold for teratogenesis. To further decrease radiation exposure, the ventilation portion of the VQ scan can be omitted without decreasing the negative predictive value. CTPA scans emit a maternal dose of 20 mGy to breast tissue, which is 20 to 100 times higher than VQ scan radiation; this risk can be mitigated with breast shields.

The treatment for VTE in pregnancy is low molecular-weight heparin (LMWH), which is more effective and has a better safety profile than unfractionated heparin in this patient population. Warfarin is contraindicated due to teratogenicity. The ideal dosing regimen for LMWH is unknown, and data is insufficient to support specific regimens in pregnant patients. Therefore, enoxaparin (either 1 mg/kg twice daily or 1.5 mg/kg once daily, based on either prepregnancy or current weight) is acceptable. Other appropriate dosing regimens include dalteparin (200 IU/kg once daily or 100 IU/kg twice daily) or tinzaparin (175 units/kg daily). There is no data to support tracking antifactor Xa levels while a patient is taking LMWH.

LMWH should be stopped 24 hours before delivery or neuraxial anesthesia, and when labor starts or is suspected. Anticoagulation can be restarted 4 hours after delivery or after the epidural catheter has been removed. Anticoagulation is continued for at least 6 weeks postpartum (for a minimum total of 3 months). Warfarin may be used in the postpartum period. Oral direct thrombin inhibitors and antifactor Xa inhibitors should be avoided, as they cross the placenta and have adverse effects. Thrombolysis is reserved for life-threatening PEs with hemodynamic compromise or for DVTs that are threatening leg viability. Caval filters can be used for recurrent PEs, despite adequate anticoagulation or if anticoagulation is contraindicated. Elastic compression stockings provide symptomatic relief only in patients with DVT.

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Factors That Increase VTE Risk in Pregnant Patients

<table>
<thead>
<tr>
<th>STASIS</th>
<th>VASCULAR DAMAGE</th>
<th>HYPERCOAGULABLE BLOOD</th>
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<tr>
<td>Compression of iliac veins</td>
<td>Vascular compression at delivery</td>
<td>↑ Procoagulant factors</td>
</tr>
<tr>
<td>Right iliac artery over left iliac vein</td>
<td>Assisted or operative delivery</td>
<td>↑ Fibrogen, factor V, IX, X, and VIII concentrations</td>
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<tr>
<td>Gravid uterus</td>
<td></td>
<td>↓ Anticoagulant activity</td>
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<td>Hormonally mediated vein dilation</td>
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<td>↓ Protein S concentration</td>
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<tr>
<td>Immobilization</td>
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<td>↑ Activated protein C resistance</td>
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<td>↓ Fibrinolytic activity</td>
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<td></td>
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<td>↑ PAI-1 and PAI-2 activity</td>
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<td>↓ tPA activity</td>
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<td></td>
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<td>More thrombin generation</td>
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<td>Less clot dissolution</td>
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</table>
A 30-year-old woman (G2 P2) with a history of ovarian cysts presents with 2 days of left lower-quadrant abdominal pain. The pain was initially sharp, crampy, and intermittent but has now become constant. It is unaffected by eating. The patient reports nausea and vomiting; her last normal bowel movement was 24 hours before her emergency department visit. She denies fever, urinary symptoms, or vaginal bleeding or discharge.

The patient’s vital signs are blood pressure 126/70, heart rate 97, respiratory rate 16, temperature 35.8°C (96.4°F), and oxygen saturation 100% on room air. She appears uncomfortable, and her left abdomen is tender to palpation, without rebound or guarding. Her pelvic examination is normal. Her laboratory tests, including urinalysis, liver function, lipase, and WBC count, are normal. A urine hCG test is negative.

The emergency physician suspects ovarian torsion or a cyst. A pelvic ultrasound is performed, which shows bilaterally normal ovaries with normal blood flow. The patient continues to complain of severe pain, and a CT scan of the abdomen and pelvis with intravenous contrast is performed.

By Joshua S. Broder, MD, FACEP
Dr. Broder is an associate professor and the residency program director in the Division of Emergency Medicine at Duke University Medical Center in Durham, North Carolina.

Case contributor: Brandon Ruderman, MD

A-C. Axial, coronal, and sagittal CT images, soft-tissue window. Enlarged panels are provided for each to highlight the abnormal findings. In the left abdomen, a segment of small bowel is seen telescoped within the surrounding small bowel. The proximal small bowel is not dilated, and therefore does not suggest accompanying obstruction.
CASE RESOLUTION

The patient underwent laparoscopy, which confirmed an intussusced segment of jejunum in the left hemiabdomen. The bowel was reduced and appeared viable, but given the high risk of underlying pathology, a 15-cm segment of bowel, including the previously intussuscepted region, was resected. Pathology tests did not reveal any abnormalities, and the patient recovered uneventfully.

KEY POINTS

- Adult intussusception is rare; the incidence in one study was 37 (0.05%) per 69,040 abdominopelvic CTs performed over 4 years. In another study, 45 cases of adult intussusception (0.08%) were identified in 58,000 surgeries over 12 years.

- Pediatric intussusception is often clinically suspected based on some combination of the classic triad of intermittent pain, bloody stool, and palpable mass; ultrasound is commonly used as a targeted imaging technique. In contrast, adult intussusception is usually identified incidentally during CT performed to evaluate for other potential causes of abdominal pain. Some patients present multiple times and undergo multiple imaging studies before the diagnosis is made, suggesting that adult intussusception is often intermittent.

- Imaging findings in adults are similar to those seen in children with intussusception; in adults, CT images through the short axis of the bowel show a target sign with the intussusceptum visible within the concentric surrounding small or large bowel (intussusceptors). Evidence of proximal obstruction may be present, in which case the diameter of the proximal small bowel will exceed 2.5 to 3 cm. The diagnosis of intussusception does not require the administration of enteric contrast.

- The treatment of adult intussusception differs from that of pediatric cases. In children, ileocolic intussusception is common and typically can be reduced nonsurgically using an air-contrast enema. Although enterocolic intussusception can occur in adults, more proximal enteroenteric intussusceptions frequently make this reduction technique difficult or impossible. Moreover, underlying malignancy reportedly accounts for 16% to 65% of adult cases; as a consequence, surgical reduction with or without resection of the affected bowel segment is frequently performed.

- Other causes of adult intussusception include inflammatory bowel disease, Meckel’s diverticulum, postoperative adhesions, and even devices such as feeding tubes. One retrospective study suggests that intussusceptions shorter than 3.5 cm are likely to be self-limited and more likely to be benign. Other studies suggest that short segment intussusceptions with a narrow diameter and without obstruction are less likely to harbor underlying pathology. However, the rarity of the condition limits study and requires clinical judgment for each case to determine the need for surgery.

A 32-year-old woman with dyspnea.

The Critical ECG

**Sinus rhythm, rate 84, acute pericarditis.** Diffuse ST-segment elevation (STE) is present on this ECG. Although there are many conditions that can induce STE on the ECG, the major diagnostic considerations in patients with diffuse STE are large acute myocardial infarction, acute pericarditis, benign early repolarization, and left ventricular hypertrophy (LVH). LVH can be excluded by lack of voltage criteria. Of the remaining three considerations, acute pericarditis is the only one that causes PR-segment depression/downsloping, which is found in lead I and in the anterior and lateral precordial leads.

By Amal Mattu, MD, FACEP
Dr. Mattu is a professor, vice chair, and director of the Emergency Cardiology Fellowship in the Department of Emergency Medicine at the University of Maryland School of Medicine in Baltimore.

Feeling No Pain

Procedural Sedation

LESSON 16

By Sana Shahbaz, MD; and Sean Kivlehan, MD, MPH

Dr. Shahbaz is an emergency medicine fellow at the South Asia Institute at Harvard University in Cambridge, Massachusetts. Dr. Kivlehan is the director of the International Emergency Medicine Fellowship in the Department of Emergency Medicine at Brigham and Women’s Hospital in Boston, Massachusetts. Reviewed by David J. Pillow, Jr, MD, FACEP

OBJECTIVES

On completion of this lesson, you should be able to:
1. Describe procedural sedation, including its indications and contraindications.
2. Discuss the different levels of sedation achieved through procedural sedation.
3. Evaluate the various drug options available for procedural sedation.
4. Explain whether fasting is necessary prior to procedural sedation.
5. Anticipate, identify, manage, and minimize the complications of procedural sedation.
6. Perform safe procedural sedation in pregnant women.

FROM THE EM MODEL

19.0 Procedures and Skills Integral to the Practice of Emergency Medicine
19.3 Anesthesia and Acute Pain Management
19.3.3 Procedural sedation

Because emergency physicians manage a spectrum of acute medical and traumatic conditions, they often perform painful procedures that require sedation. Procedural sedation and analgesia (previously known as conscious sedation) involves the use of several medications, including sedatives, dissociative agents, and/or analgesics.1 When aptly performed, the process reduces the pain and anxiety caused by invasive and noninvasive procedures, thus improving the experience for both the patient and clinician.2

CRITICAL DECISIONS

- What levels of sedation can be achieved with procedural sedation?
- What are the indications and contraindications for procedural sedation?
- What prerequisites, precautions, and preparations are required for procedural sedation?
- Is fasting a prerequisite for procedural sedation?
- Which procedural sedation medications are safe to use with pregnant patients?
- How can the complications of procedural sedation be managed?
- What are the indications, contraindications, and doses of drugs used for procedural sedation?
CASE PRESENTATIONS

■ CASE ONE
A 26-year-old man presents after slipping and falling onto his shoulder. X-rays confirm a dislocated right shoulder without any fractures. He is given analgesia for pain management, while the emergency physician prepares for a shoulder reduction. On examination, the patient’s neurovascular status is intact in the affected extremity, his vital signs are normal, and his pain score improves from an initial 7 out of 10 to a 5 out of 10.

■ CASE TWO
A 70-year-old man is brought in by paramedics after falling at home. His trauma survey is normal; examination of his right leg shows an internally rotated hip and foot. His neurovascular status is intact. His blood pressure (BP) is 140/100; his vital signs are otherwise normal. His medical history includes hypertension, coronary artery disease, and congestive heart failure. X-rays of the hip show a posterior hip dislocation but no fracture.

Acetaminophen and oxycodone are administered for pain, while informed consent is obtained. The patient is then transferred to the resuscitation room to undergo hip reduction; he receives pretreatment of fentanyl as an analgesic and propofol as a sedative. The hip is successfully reduced, but soon after the procedure, the patient desaturates and becomes hypotensive. His oxygen saturation level falls to 88%, and his BP plummets to 80/60. The physician initiates small boluses of IV normal saline and high-flow oxygen via face mask.

■ CASE THREE
A 22-year-old woman, who is 20 weeks pregnant, presents after twisting her left ankle while walking down the stairs. Her trauma survey is normal, except for the deformed joint that needs reduction. She has no medical history and is hemodynamically stable. No neurovascular compromise is found. After obtaining informed consent, the patient is transferred to the resuscitation room to undergo ankle reduction. Anxious to minimize the side effects in both the mother and fetus, the emergency physician reviews the options for procedural sedation in pregnant patients.

Because the appropriate regimen varies based on the specifics of each case, emergency physicians must thoroughly understand the advantages and disadvantages of these medications and be prepared to choose the most effective agent, administer it safely, and anticipate potential complications.

CRITICAL DECISION
What levels of sedation can be achieved with procedural sedation?

Procedural sedation and analgesia — as defined by the American College of Emergency Physicians (ACEP), American Society of Anesthesiologists (ASA), and Centers for Medicare and Medicaid Services (CMS) — is the technique of administering sedatives or dissociative agents, with or without analgesics, to induce an altered state of consciousness, while preserving cardiorespiratory function. During the process, patients reach different levels of sedation, depending on the dose, type of medication, and response to the drug (Figure 1). Sedation depths are part of a continuum, ranging from minimal sedation to general anesthesia. However, ketamine is unique in that it is the only agent that produces dissociative sedation. Patients respond to medications differently, so levels of sedation vary based on the circumstances. A clear line between these states often does not exist, so clinicians must be prepared to manage patients as they transition between different sedation depths.

Minimal Sedation
Minimal sedation describes a patient with a near-baseline level of alertness, who retains the ability to respond normally to verbal commands. Although cognitive function and coordination may be impaired, ventilatory and cardiovascular functions are unaffected. In the emergency department, minimal sedation is commonly administered to facilitate minor procedures.

Moderate Sedation
With moderate sedation, a patient responds purposefully to verbal commands alone or when accompanied by light touch. Droopy eyelids or slurred speech with delayed verbal responses also can be noted. Protective airway reflexes and adequate ventilation are maintained without intervention, and cardiovascular function remains stable. Patients frequently experience amnesia about the experience.

Dissociative Sedation
Dissociative sedation creates a unique, trance-like state in which a patient experiences profound analgesia and amnesia but retains airway protective reflexes, spontaneous respiration, and cardiopulmonary stability. Ketamine is the pharmacological agent used to produce dissociative sedation.

Deep Sedation
With deep sedation, a patient cannot be easily aroused but responds purposefully to noxious stimulation. Assistance may be needed to ensure that the airway is protected and adequate ventilation is maintained. Cardiovascular function is usually stable; however, the patient must be closely monitored for any changes in ventilatory or cardiovascular function.

General Anesthesia
With general anesthesia, a patient is completely unresponsive to painful stimuli and often requires assistance to protect the airway and maintain ventilation. Cardiovascular function may be impaired.
CRITICAL DECISION
What are the indications and contraindications for procedural sedation?

Procedural sedation can be used in the emergency department for any procedure that causes pain or anxiety in the patient. Common procedures requiring procedural sedation include fracture reduction and dislocation, foreign body removal, laceration repair (particularly in young children), abscess drainage, lumbar puncture, endoscopy, bronchoscopy, and electrical cardioversion. Procedural sedation can also facilitate diagnostic evaluations with CT or MRI, as well as burn dressing changes and the placement of chest tubes and central catheters.5

Contraindications vary according to the type of procedure and the age and comorbidities of the patient. Pulmonary diseases such as chronic obstructive pulmonary disease (COPD), ischemic cardiac disease, heart failure, anemia, and neuromuscular diseases all increase the associated risks of procedural sedation. Emergency physicians should be aware not only of a patient’s chronic conditions, but also of acute presentations that can affect the safety of the sedated patient, including hypovolemia, renal failure, and acute respiratory infections.

Drug allergies can typically be averted by using different medications, but the physician should anticipate and prepare to address a difficult airway. The ASA’s physical status classification system quantifies the risks into a meaningful predictive value (Table 1). For example, ASA class I and II patients have a low risk of complications, but keep in mind that risks rise with deeper levels of sedation.

Anticipating Difficult Airways
Before procedural sedation, all patients should undergo a difficult-airway assessment, and information should be gathered about any previous experience with sedation and analgesia. A history of a difficult or failed airway, or difficult bag-valve-mask ventilation, is a strong risk factor for complications; however, this information is frequently unavailable. One study identified the following five factors as independent predictors of difficult bag-valve-mask ventilation: age greater than 55 years, body mass index (BMI) greater than 26 kg/m2, presence of a beard, absence of teeth, and a history of snoring.7 Additional difficult-airway risk factors include a short neck, micrognathia, a large tongue, trismus, morbid obesity, and anatomical abnormalities of the airway and neck.7

The Mallampati classification system is a simple assessment tool that correlates visualization of anatomical oropharyngeal structures to intubation difficulty (Figure 2). The Mallampati score is one component of a commonly used mnemonic device — LEMON — to predict potential complications (Table 2).8,9 If a difficult airway or difficult mask ventilation is anticipated, anesthesia should be consulted; in such cases, it may be optimal to perform the procedure in the operating room.

Age Considerations
In children, active upper-respiratory infections and asthma significantly increase the risk of laryngospasm, which should factor into the decision to sedate.5 No upper age limit for procedural sedation exists, but the elderly have a higher risk of complications due to several factors, including increased drug sensitivity and interactions with chronic medications. Additionally, the higher prevalence of cardiovascular and pulmonary diseases in geriatric patients increases the likelihood of hemodynamic instability and respiratory difficulty.10 Reducing both the dose and frequency

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TABLE 1. ASA’s Physical Status Classification System

<table>
<thead>
<tr>
<th>Class</th>
<th>Definition</th>
<th>Examples (Including But Not Limited To)</th>
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<tbody>
<tr>
<td>I</td>
<td>A normal healthy patient</td>
<td>Healthy, nonsmoking, and no or minimal alcohol use</td>
</tr>
<tr>
<td>II</td>
<td>A patient with mild systemic disease</td>
<td>Mild diseases only, without substantive functional limitations. Current smoker, social alcohol drinker, pregnant, obese (BMI 30-39.9), well-controlled diabetes mellitus or hypertension, or mild lung disease</td>
</tr>
<tr>
<td>III</td>
<td>A patient with severe systemic disease</td>
<td>Substantive functional limitations, with one or more moderate to severe diseases. Poorly controlled diabetes mellitus or hypertension, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, end-stage renal disease undergoing regularly scheduled dialysis, premature infant with post-conceptional age &lt;60 weeks, history (&gt;3 months) of myocardial infarction, cerebrovascular accident, transient ischemic attack, or coronary artery disease/stents.</td>
</tr>
<tr>
<td>IV</td>
<td>A patient with severe systemic disease that is a constant threat to life</td>
<td>Recent (&lt;3 months) myocardial infarction, cerebrovascular accident, transient ischemic attack, or coronary artery disease/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, disseminated intravascular coagulation, acute respiratory distress syndrome, or end-stage renal disease not undergoing regularly scheduled dialysis</td>
</tr>
<tr>
<td>V</td>
<td>A moribund patient who is not expected to survive without the operation</td>
<td>Ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology, or multiple organ/system dysfunction</td>
</tr>
<tr>
<td>VI</td>
<td>A declared brain-dead patient whose organs are being removed for donor purposes</td>
<td></td>
</tr>
</tbody>
</table>
of medications can help mitigate side effects and avoid oversedation in this vulnerable population.11-14

CRITICAL DECISION
What prerequisites, precautions, and preparations are required for procedural sedation?

Only properly credentialed emergency physicians with privileges at their institution should perform procedural sedation. ACEP recommends that all graduates of an emergency medicine residency program accredited by the Accreditation Council for Graduate Medical Education (ACGME) or the American Osteopathic Association (AOA) be credentialed on the basis of their training.15

The performing clinician is expected to be familiar with the medications used, relevant reversal agents, side effects, and complications. It is also imperative for providers to have the capacity to rescue a patient from a deeper level of sedation and provide emergency airway management, as needed.2 While additional institutional and departmental requirements may apply, ACEP states that “short courses” such as Advanced Cardiac Life Support (ACLS) serve only as focused review and are superseded by board certification.15

The minimum number of providers required to perform procedural sedation is two: the physician who performs the procedure and another trained clinician, such as a nurse, who continuously monitors the patient and vital signs.2 The patient should be informed in detail about the procedure and its potential risks, benefits, and complications. Verbal or written informed consent is acceptable, as long as institutional guidelines are followed.5,11 A history and physical should be completed, including an evaluation of comorbid conditions and allergies to medications.15 Specifically, the patient should be asked about any previous exposure and response to analgesia or anesthesia. Finally, an airway assessment should be performed, as previously discussed.

Procedural sedation should be administered in a spacious room adequately stocked with equipment for airway management and resuscitation. Continuous heart rate and pulse oximetry monitoring should be available, along with interval blood pressure measurements. In addition, oxygen, suction, and airway adjuncts should be immediately accessible. Reversal agents relevant to the agents being used, such as naloxone or flumazenil, should be obtainable. Intravenous (IV) access should be available, as it is needed for most agents; however, the need for access when using agents such as ketamine is controversial.15,16

The ASA has provided detailed guidelines about recommended equipment for nonanesthesiologist-performed sedation and anesthesia.4 All equipment should be checked, and a time-out should be called, with all involved staff present, immediately prior to performing the sedation.

By monitoring end-tidal carbon dioxide (ETCO2) continuously throughout the procedure, clinicians can reduce the risk of hypoxia and other adverse respiratory events. It remains unclear, however, whether continuous capnography monitoring reduces more serious complications.2 The need for automatic supplementary oxygen is debatable; a 2011 ACEP policy statement recommends that its use be left to the physician’s discretion.15

<table>
<thead>
<tr>
<th>TABLE 2. LEMON Mnemonic Device</th>
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<tbody>
<tr>
<td>L</td>
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<tr>
<td>E</td>
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<tr>
<td>M</td>
</tr>
<tr>
<td>O</td>
</tr>
<tr>
<td>N</td>
</tr>
</tbody>
</table>

*Derived from The American Society of Anesthesiologists*
Ketamine, in particular, has been shown to be safe without the use of supplemental oxygen.6 While some physicians argue that supplemental oxygen can prevent hypoxia secondary to hypoventilation, others counterargue that it can delay the recognition of hypoxia and needed interventions.6,5,11,17

CRITICAL DECISION
Is fasting a prerequisite for procedural sedation?

Aspiration is a commonly cited risk of procedural sedation, although evidence of this complication in the emergency department is sparse and documented occurrences are rare. A 2016 meta-analysis found 1 case of aspiration out of 2,370 sedations, an incidence rate of 1.2 per 1,000 sedations.18 ACEP’s Clinical Policy: Procedural Sedation and Analgesia in the Emergency Department states that “Preprocedural fasting for any duration has not demonstrated a reduction in the risk of emesis or aspiration when administering procedural sedation and analgesia.”4 However, guidelines for preprocedural fasting vary by organization and institution.

Based on the current ASA guidelines, many institutions continue to recommend preprocedural fasting states of 2 hours for clear liquids and 6 hours for a meal.19 As noted in ACEP’s policy, the widely used ASA recommendations apply to elective general anesthesia cases in which airway manipulation is expected; neither recommendation applies to emergency situations nor emergency department procedural sedation.

Physicians also debate the need for prophylactic antiemetics with procedural sedation. The ASA does not recommend the routine use of prophylactic antiemetics; however, its guidelines indicate that patients should be fasting.19 While some agents used for procedural sedation (eg, propofol) have antiemetic properties, ketamine stands out as being emetogenic. Ketamine-associated vomiting has been well studied in pediatrics, with reported rates as high as 28%. In one large study, the use of prophylactic atropine and metoclopramide did not decrease this rate.20 Studies show conflicting data on the ability of ondansetron to reduce vomiting.21,22 Thus, the use of prophylactic antiemetics with procedural sedation in the emergency department is best left to the clinician’s discretion.

CRITICAL DECISION
Which procedural sedation medications are safe to use with pregnant patients?

Clinicians must be aware that physiological changes during pregnancy increase certain risk factors during sedation. Decreased functional residual capacity, increased oxygen demand, increased respiratory rate, and relative hypotension are normal in pregnancy and can be exacerbated by procedural sedation agents. Both maternal hypoxemia and hypercapnia have been shown in animal models to be deleterious to the fetus, so the general recommendation is to provide routine supplemental oxygen during the sedation of a pregnant patient.23

Placing the patient in the left lateral recumbent position during sedation is another simple precaution that can reduce medication-related hypotension by shifting the uterus off the vena cava. Another precaution is the administration of IV fluids.11 In addition, pregnant patients have higher rates of reflux esophagitis and heartburn, so prophylactic metoclopramide or an H₂ antagonist is recommended to reduce the risk of vomiting and aspiration.11,21,23

Limited data are available on the safety of procedural medications in pregnancy, so most recommendations are based on animal data. Ketamine is generally safe and has not been found to be teratogenic; however, it increases maternal heart rate and blood pressure and should be avoided when managing a pregnant patient with hypertension.23 Propofol is considered safe, but hypotension should be aggressively prevented and corrected. Furthermore, neonatal depression is a concern when using these agents near the time of delivery.23 Midazolam has a conflicting profile with possible teratogenicity and should be avoided. Short-acting agents, such as remifentanil and nitrous oxide, also can be considered.23

CRITICAL DECISION
How can the complications of procedural sedation be managed?

The major complications of procedural sedation are related to the airway and apnea, although hypotension is common as well. A systematic review and meta-analysis of 9,652 cases found that the most common adverse events are hypoxia (40.2 per 1,000), vomiting (16.4 per 1,000), hypotension (15.2 per 1,000), and apnea (12.4 per 1,000).18 Early recognition of a complication is crucial, which is why close monitoring is a key component of the procedure. Once identified, simple and rapid action can correct most adverse effects (Table 3).

<p>| TABLE 3. Common Complications and First-Step Interventions |
|---------------------|---------------------|</p>
<table>
<thead>
<tr>
<th>Complication</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
<td>Calm patient; benzodiazepine</td>
</tr>
<tr>
<td>Apnea</td>
<td>Oxygen and bag-valve-mask ventilation; evaluate the need for intubation</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Suction; treat hypoxia with oxygen; evaluate for the need for intubation and antibiotics</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Usually self-resolving; atropine if persistent</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>Open airway; stimulate; oxygen</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Usually self-resolving; fluid bolus or push-dose pressor if persistent</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>High-flow oxygen; bag-valve-mask ventilation; consider paralytics and intubation</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Suction; left lateral position; airway management</td>
</tr>
</tbody>
</table>
When performed properly, procedural sedation in the emergency department is safe: In the above cohort, no deaths, one case of aspiration, and two unplanned intubations were reported.

**Hypoxia**
Continuous pulse oximetry should be performed on all patients to immediately detect hypoxia. Many providers also place all patients on continuous oxygen during procedural sedation; however, continuous oxygen can mask early hypoxia and should be performed judiciously. Capnography monitoring can be used with pulse oximetry to provide earlier detection of hypoventilation and apnea, but it has not been shown to reduce serious events.

Propofol and the combined use of midazolam with an opiate result in the highest rates of hypoxia. Once recognized, this complication should be immediately corrected with oxygen and airway management techniques, as required. A basic maneuver (eg, head-tilt/chin-lift or jaw-thrust) is often sufficient to correct hypoxia. However, the physician should be prepared to escalate interventions, as needed, with positive pressure ventilation or advanced airway management.

**Vomiting**
While the highest incidence of vomiting occurs with ketamine, this side effect can be triggered by any of the medications used for sedation. Some providers opt to pretreat nausea with antiemetics such as ondansetron; however, studies conflict on the effectiveness of this approach. Suction should be immediately accessible during sedation so that the airway can be cleared without delay if vomiting occurs. Vomiting patients should receive an antiemetic agent, and airway management should be escalated, as needed. Sedation may need to be aborted, depending on the severity of vomiting; remember that vomiting can continue even after reversal.

**Hypotension**
The clinical definition of hypotension varies, and the significance of mild hypotension during sedation is unclear. Propofol and the combination of midazolam with an opiate most commonly precipitate a decrease in blood pressure. Hypotension caused by propofol is usually self-limiting due to the short duration of action. Mild elevations can be treated with an IV fluid bolus (20 mL/kg) and by putting the patient in the supine position. More severe or persistent hypotension can often be corrected with a push-dose pressor such as phenylephrine.

In rare cases, sedation may need to be aborted if the patient’s hemodynamics cannot tolerate the medication effects. Avoiding hypotension should be a consideration when deciding which drug to use; the decision should be based on the patient’s previous reaction history, comorbidities, and current hemodynamics.

**Apnea**
Midazolam, alone or in combination with an opiate, is the most likely sedative to cause apnea; however, apnea can occur with any sedative at sufficient doses. Early recognition of apnea can be achieved with capnography monitoring and pulse oximetry. While mild symptoms can usually be corrected by stimulating the patient, apnea should always be taken seriously; intermittent apnea can be a warning sign of severe, impending complications. Reversal agents, such as naloxone or flumazenil, can be used, as needed. Newer data show that apnea is frequently preceded by predictable alterations in ventilation (eg, an ETCO2 that rises from <30 mm Hg to >50 mm Hg). Apnea appears to be a common yet easily correctible complication: All apneic events in the study were corrected with stimulation, oxygen, or airway repositioning.

**Laryngospasm**
Laryngospasm is a major concern with the use of ketamine. Large meta-analyses have shown a 0.3% incidence rate in pediatric patients and a 0.4% incidence rate in adults. High doses and pre-existing upper respiratory infections in children are thought to be risk factors, but laryngospasm can occur at any time. Providers must always be prepared...
for the possibility.16 If identified, bag-valve-mask ventilation is generally sufficient, although the provider should be prepared to paralyze and intubate, if needed. Applying inward pressure behind the lobule of the pinna of each ear, while anteriorly dislocating the jaw, at a location known as “Larson’s point” or the “laryngospasm notch” may terminate laryngospasm.29

Clinicians must be vigilant, both during and after every sedation procedure, to watch for warning signs of adverse events that require rapid intervention. The sedated patient should be given special attention directly after the procedure; when the procedure is complete and the painful stimulus is removed, medication-induced apnea or hypotension previously masked by sympathetic stimulation can become more pronounced. To prevent complications, emergency physicians must choose the appropriate medications for each patient in accordance with the procedure, age, comorbidities, and expected difficulty in airway management.

**CRITICAL DECISION**

What are the indications, contraindications, and doses of drugs used for procedural sedation?

No single recommended drug or drug regimen exists for procedural sedation. The process can require a sedative, an analgesic, and/or a dissociative agent, depending on the situation (Table 4). Among the desirable drug qualities are a rapid onset, a short duration, and maintenance of hemodynamic stability—all without causing major side effects.2

**Ketamine**

Ketamine is a dissociative agent that provides analgesia and sedation, while preserving the airway, breathing, and blood pressure.16,20 It can be given intravenously or intramuscularly (IM), the latter being used commonly for pediatric patients. The recommended dose for ketamine is 1 mg/kg to 2 mg/kg IV over 1 to 2 minutes for adults and 1.5 mg/kg to 2 mg/kg IV for pediatric patients. Recommended IM dosing is 4 mg/kg to 5 mg/kg for both populations. The typical duration of action for the drug is 15 to 30 minutes for IV delivery and 30 to 60 minutes for IM delivery.16 Notably, IM delivery produces higher rates of vomiting and a longer recovery time, while IV administration allows for repeat dosing, as needed, to sustain the drug’s action.

Ketamine transiently increases heart rate and blood pressure but does not affect respiration unless rapidly injected. Since rapid injection can cause transient respiratory depression, ketamine should be pushed slowly over 30 to 60 seconds when given by IV.16,29 The agent also has nondissociative analgesic properties at lower doses (<0.3 mg/kg) and can be used for both general pain management and sedation.30

The most commonly reported side effect of ketamine is an emergence reaction (seen in 10%–20% of patients), which can be managed with reassurance in most cases or with benzodiazepines in severe cases.29 Other adverse effects include laryngospasm, vomiting, and hypersalivation.29 Ketamine should not be used for patients younger than 3 months due to an increased risk of adverse airway events, or for any patient with known or suspected schizophrenia.16

**Propofol**

Propofol is a sedative-hypnotic agent without analgesic properties. It has a rapid onset of action (within 30–60 seconds) and a duration of action of 5 to 6 minutes.31 The benefits of the drug include a rapid onset, short duration of action, and rapid recovery of cognitive functions.5,31 Its other benefits include antiemetic and euphoric effects. Since propofol does not have analgesic properties, appropriate analgesia should be provided when using it for painful procedures.32

Propofol in adults and children is slowly injected, with an initial loading dose of 1 mg/kg IV, followed by doses of 0.5 mg/kg IV every 3 minutes, as necessary until the appropriate level of sedation is achieved.24 The agent is contraindicated for patients allergic to egg lecithin and soybeans.24 Major side effects include hypotension and respiratory depression, which usually resolve quickly due to the short duration of action. A short-acting, push-dose pressor can be used if hypotension is severe. Elderly patients often exhibit hypotension, so initial dosing should be reduced by 50%. A small amount of lidocaine can be administered to prevent pain at the injection site.24

**Ketofol**

Ketofol is a combination of ketamine and propofol, coadministered in a 1:1 mixture, which has increased in popularity in recent years. Theoretically, this approach balances the negative inotropic and respiratory effects of propofol with the stimulant effects of ketamine. Furthermore, propofol’s antiemetic properties can balance ketamine’s proemetic effects; propofol’s sedative effects also can negate an emergence reaction.2 Starting doses for this regimen are 0.5 mg/kg of each agent.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose</th>
<th>Route</th>
<th>Peak Effect</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketamine</td>
<td>1 mg/kg</td>
<td>IV</td>
<td>1-3 minutes</td>
<td>15-30 minutes</td>
</tr>
<tr>
<td>2-5 mg/kg</td>
<td>IM</td>
<td>5-20 minutes</td>
<td>30-60 minutes</td>
<td></td>
</tr>
<tr>
<td>Propofol</td>
<td>0.5-1 mg/kg</td>
<td>IV</td>
<td>30-60 seconds</td>
<td>5-6 minutes</td>
</tr>
<tr>
<td>Ketofol</td>
<td>1:1 mixture of 0.5 mg/kg ketamine and 0.5 mg/kg propofol</td>
<td>IV</td>
<td>30-60 seconds</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Etomidate</td>
<td>0.15 mg/kg</td>
<td>IV</td>
<td>15-30 seconds</td>
<td>3-8 minutes</td>
</tr>
<tr>
<td>Midazolam</td>
<td>0.05-0.1 mg/kg</td>
<td>IV</td>
<td>2-3 minutes</td>
<td>20-30 minutes</td>
</tr>
<tr>
<td>0.1 mg/kg</td>
<td>IM</td>
<td>15-30 minutes</td>
<td>60-120 minutes</td>
<td></td>
</tr>
<tr>
<td>0.2-0.5 mg/kg</td>
<td>IN</td>
<td>10-15 minutes</td>
<td>45-60 minutes</td>
<td></td>
</tr>
<tr>
<td>0.5-0.75 mg/kg</td>
<td>PO</td>
<td>15-30 minutes</td>
<td>60-90 minutes</td>
<td></td>
</tr>
</tbody>
</table>

Midazolam is a benzodiazepine with amnestic, hypnotic, and anxiolytic properties, but no analgesic effect. It is frequently used in conjunction with a short-acting opiate like fentanyl. Of all the benzodiazepines, midazolam has the most rapid onset and strongest amnestic effects. The traditional starting dose for midazolam is 0.05 mg/kg IV or IM. When given by IV, onset occurs within 2 to 3 minutes, with a duration of action of 20 to 30 minutes. While repeat doses can be given in 3- to 5-minute increments, as needed, physicians should be cautious to avoid “dose stacking” from the residual effects of previous doses. Midazolam is frequently used in pediatrics and can be given intranasally (IN) at 0.2 mg/kg or orally (PO) at 0.5 mg/kg. While useful for children who fear needles, the IN route can cause irritation, and the PO route produces a variable dosing response.

Midazolam can cause respiratory depression, bradycardia, and hypotension, particularly when combined with an opiate. Paradoxical reactions, in which the patient becomes agitated, occur in 1% to 15% of pediatric patients. Obese patients, the elderly, and those with hepatic dysfunction can experience prolonged sedation. Flumazenil can reverse the effects, but caution should be used for chronic benzodiazepine users, as flumazenil can cause seizures in this population.

The administration of ketofol does not appear to provide a clinical benefit over using either agent alone. Specifically, the drug does not reduce adverse respiratory events. Propofol, on the other hand, causes slightly more hypotension when used alone, which is of unclear clinical significance.

Etomidate

Etomidate is a short-acting, sedative-hypnotic agent that has minimal effects on respiratory and cardiovascular status. It can rapidly produce deep sedation but has no analgesic properties; thus, an analgesic should be provided for painful procedures. Adult dosing of etomidate for sedation is 0.1 mg/kg; onset occurs in less than 1 minute, with a duration of action of 3 to 8 minutes. Repeat doses can be administered every 3 to 5 minutes, as needed. Myoclonus occurs in 20% to 40% of patients; while myoclonus is not dangerous to the patient, it can interfere with the procedure. Adrenal suppression due to an etomidate-induced depression of cortisol levels, particularly in septic or trauma patients, can occur; however, several studies have shown no clinical significance. Additional side effects include respiratory suppression, nausea, and vomiting.

Midazolam

Midazolam is a benzodiazepine with amnestic, hypnotic, and anxiolytic properties, but no analgesic effect. It is frequently used in conjunction with a short-acting opiate like fentanyl. Of all the benzodiazepines, midazolam has the most rapid onset and strongest amnestic effects. The traditional starting dose

**Pearls**

- Prepare all monitoring and airway management equipment prior to sedation, keeping it readily available during the procedure.
- Consider the pros and cons of each medication and then tailor the sedation plan to the specific patient and context, accounting for the patient’s hemodynamic status and the type of procedure.
- Simple maneuvers like stimulation, opening the airway, and providing oxygen can correct most adverse apneic or hypoxic events.
- Ketamine and propofol are safe to use during pregnancy; however, midazolam should be avoided.

**Pitfalls**

- Failing to prepare for hemodynamic and airway complications.
- Disregarding the increased risk of hypotension and apnea when using combinations like propofol and an opiate, or a benzodiazepine and an opiate.
- Overlooking the major risk factors and contraindications of various medications.
- Neglecting the patient immediately following the procedure, while the patient is still sedated.

**Alternative Agents**

Ultrashort-acting opiates, such as alfentanil and remifentanil, have been used for procedural sedation in the emergency department. Early reports describe them as safe and effective, but added benefits remain unclear, when compared to established options. Nitrous oxide is an inhaled gas typically composed of 30% oxygen and 30% to 70% nitrous oxide that provides rapid anesthesia and recovery due to the low solubility of nitrous oxide in the blood. The agent has a rapid onset of less than 1 minute and a recovery time of 5 minutes. Self-administration is recommended for safe titration; cardiovascular side effects are minimal. However, sedation is often not complete for more painful procedures, and overall use has been limited in emergency departments due to the need to use gas scavenger systems.
CASE RESOLUTIONS

CASE ONE

The young man with a dislocated shoulder required procedural sedation to facilitate reduction. A detailed history was gathered, with a special focus on his medical history and details about medication use, allergies, and fasting status. The patient’s airway was assessed for any signs of difficulty, using the LEMON mnemonic device. The patient consented to the procedure after the risks, benefits, and possible complications were explained.

The sedation plan was coordinated with the nurse; monitoring equipment, including pulse oximetry and capnography, were available. An airway and code cart were nearby, and oxygen and suction were checked. A time-out was called immediately prior to administering the medications. After the procedure, the nurse closely observed the patient until he fully regained consciousness and could follow verbal commands.

Since most adverse events occur within 30 minutes after sedation, he was observed for at least 30 minutes prior to discharge. The patient was given written instructions that explained the potential medication-specific side effects and solutions, as well as clear directions on when to return to the emergency department.

CASE TWO

Propofol had several benefits for the elderly man with a dislocated hip and an extensive medical history, including a rapid onset of action and short duration. Fentanyl was appropriately coadministered for its analgesic effects. The downside of using propofol in this situation was its negative inotropic effect.

Although hypotension and respiratory depression frequently occur with propofol alone, they are exacerbated when propofol is combined with an opioid analgesic.

The patient’s blood pressure improved with the 500-mL normal saline bolus, and the hypoxia was corrected with supplemental oxygen and a brief jaw thrust. The patient recovered within 5 minutes and returned to baseline with a newly reduced hip. In retrospect, the provider should have considered a reduced dose of propofol or the use of alternative agents, such as ketamine or etomidate, that are more hemodynamically neutral.

CASE THREE

The young, pregnant woman with a dislocated ankle required sedation and analgesia for reduction. The emergency physician considered the physiological changes that occur during pregnancy, especially the added compression of the inferior vena cava, higher risk of aspiration, and hypoxia secondary to reduced functional residual capacity.

Midazolam was not used because it is categorized as a pregnancy class D drug due to its potential teratogenicity. Instead, the physician used propofol because it is generally considered safe, and then monitored the patient for hypotension. Routine supplemental oxygen was provided, the patient was placed in the left lateral recumbent position, and IV fluids were administered during the procedure. Prophylactic metoclopramide was also given.

REFERENCES


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**CME QUESTIONS**

An individual who visited a clinic prior to travel is likely to experience which of the following?

A. Fever
B. Malaria
C. Self-limited illness
D. Severe disease

Acute hemorrhagic fever syndrome includes a fever of what duration?

A. >1 month
B. <1 month
C. <1 week
D. <3 weeks

By what route is Ebola transmitted?

A. An insect bite
B. Contaminated food
C. Contaminated water
D. Direct contact with infected bodily fluids

A 35-year-old man who recently returned from a trip to East Africa presents with fever and generalized malaise. Other than a temperature of 38.3°C (100.9°F), his vital signs are normal. His physical examination is unremarkable, CBC shows leukocytosis of 14,000 cells/mm³, a basic metabolic panel is unremarkable, and no *Plasmodium* is visualized on peripheral blood smears. What is the most appropriate next step?

A. Continue symptomatic care and repeat blood smears for 12 to 24 hours
B. Inform the patient that he does not have malaria and discharge home
C. Start intravenous treatment with an artemisinin-based compound therapy
D. Start outpatient chloroquine

Travelers from which geographic area are at the highest risk of acquiring enteric fever?

A. South America
B. South Asia
C. Sub-Saharan Africa
D. Western Europe

A 45-year-old health care worker who returns from working in Sierra Leone in West Africa presents with a fever of 38.6°C (101.5°F), abdominal pain, and diarrhea. His physical examination is significant for a purpuric rash. What is the most appropriate next step?

A. Administer IV fluid bolus therapy
B. Contact the local health department
C. Place him in isolation
D. Place him on a cardiac monitor

A 50-year-old man presents with fever and pneumonia after a recent trip to the Arabian peninsula, where he volunteered at a local health clinic. Which of the following pathologies should be suspected?

A. Cryptococcal meningitis
B. Japanese encephalitis
C. MERS-CoV
D. Q fever

Which condition is correctly paired with its usual incubation period?

A. Chikungunya — 3 weeks
B. Hepatitis E — 1 week
C. Malaria — <10 days to months
D. SARS — 2 weeks

When a specific etiological diagnosis can be made, what is the most frequently identified cause of fever in the returned traveler?

A. Dengue fever
B. Ebola virus disease
C. Enteric fever
D. Malaria

Which disease is correctly paired with its typical mode of transmission?

A. Chikungunya — contaminated food or water
B. Ebola virus disease — deer tick
C. Enteric fever — *Anopheles* mosquito
D. Zika — *Aedes aegypti* mosquito

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A 5-year-old boy presents after falling off his bike. He is alert and oriented and has a 5-cm laceration on his chin that requires stitches. He is anxious and crying inconsolably. What medication(s) can be given IM for stitching under procedural sedation?

A. Etomidate  
B. Ketamine  
C. Midazolam and morphine  
D. Propofol  

Under what thyroid cartilage–to-mandible distance would you anticipate a difficult intubation?

A. 2 finger breadths  
B. 3 finger breadths  
C. 4 finger breadths  
D. 5 finger breadths  

A young woman presents with a dislocated ankle that requires reduction. She has no medical history and takes no medications except for oral contraceptives. She is allergic to peanuts and eggs. Acetaminophen and ibuprofen have partially reduced the pain. Which medication is contraindicated for procedural sedation?

A. Etomidate  
B. Midazolam  
C. Morphine  
D. Propofol  

A 65-year-old man requires procedural sedation for a shoulder relocation. He is diabetic and has COPD. Which medication would be most likely to induce hypotension?

A. Etomidate  
B. Ketamine  
C. Morphine  
D. Propofol  

Which side effect is more common with IM ketamine?

A. Agitation  
B. Apnea  
C. Hypotension  
D. Vomiting  

A 20-year-old woman is under procedural sedation for a dental procedure. A few minutes into the procedure she starts shouting that there are bugs all over the ceiling. Which medication can cause this phenomenon?

A. Etomidate  
B. Fentanyl  
C. Ketamine  
D. Midazolam  

What is the most common side effect of etomidate?

A. Hypotension  
B. Myoclonus  
C. Nausea and vomiting  
D. Tachycardia  

Which of the following medications can be administered alone, without an analgesic agent, for procedural sedation?

A. Etomidate  
B. Ketamine  
C. Midazolam  
D. Propofol  

According to ACEP’s clinical policy, how long should a patient fast before undergoing procedural sedation?

A. 2 hours for liquids only  
B. 2 hours for liquids and 6 hours for solids  
C. 6 hours for solids only  
D. No fasting is required  

Which medication should be avoided during procedural sedation to relocate the shoulder of a 25-year-old woman who is 34 weeks pregnant?

A. Flumazenil  
B. Ketamine  
C. Midazolam  
D. Propofol  

**ANSWER KEY FOR JULY 2018, VOLUME 32, NUMBER 7**

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
| D | D | D | B | A | A | D | D | A | B | A | D | A | D | C | D | D | D | B | A |
ANDEXANET ALFA

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Andexanet alfa was recently approved by the FDA for the treatment of life-threatening or uncontrolled bleeding caused by the anticoagulants rivaroxaban and apixaban. It is the first agent approved for the reversal of these two factor Xa inhibitors. Andexanet alfa is available at limited sites throughout the US; wider distribution is expected in early 2019.

Mechanism of Action
The antidote binds to and sequesters the factor Xa inhibitors. In addition, it inhibits the activity of tissue factor pathway inhibitor (TFPI), increasing tissue factor-initiated thrombin generation.

Dosing
If the last dose of medication was taken >8 hours ago, use low dose. If the last dose of medication was taken <8 hours ago or unknown, the dose should be based on the amount of factor Xa taken.
- **Apixaban**: Last dose ≤5 mg, use low dose; last dose >5 mg or unknown, use high dose.
- **Rivaroxaban**: Last dose ≤10 mg, use low dose; last dose >10 mg or unknown, use high dose.

**Low Dose**: 400-mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 4 mg/minute IV infusion for up to 120 minutes

**High Dose**: 800-mg IV bolus administered at a rate of ~30 mg/minute, followed 2 minutes later by 8 mg/minute IV infusion for up to 120 minutes

Adverse Reactions
The most common side effect is a local infusion site reaction (≥10%), followed by deep vein thrombosis (6%), ischemic stroke (5%), urinary tract infections, and pneumonia (both occurring in ≥5% of patients).

**FDA Black Box Warning**: Treatment with andexanet alfa has been associated with life-threatening complications, including arterial and venous thromboembolic events, ischemic events (including myocardial infarction and ischemic stroke), cardiac arrest, and sudden deaths. Monitor for thromboembolic events and initiate anticoagulation when medically appropriate. Monitor for signs and symptoms that precede cardiac arrest and provide treatment as needed.

QUETIAPINE OVERDOSE

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Quetiapine is a second-generation antipsychotic available in immediate- and extended-release formulations. It is FDA approved for schizophrenia, bipolar disorder, and as adjunct treatment for major depressive disorder.

Mechanism of Action
- Weak antagonism at D2, M1, 5HT1A receptors = sedation
- Potent antagonism at α1 adrenergic receptors = hypotension
- Some blockade at fast sodium channels = QRS widening
- Can affect delayed rectifier current = QT prolongation

Clinical Presentation
- Tachycardia from antimuscarinic effects
- Hypotension from peripheral α1 blockade
- Miosis with depressed mental status (opioid mimic)
- Rarely associated with neuroleptic malignant syndrome (NMS)

Diagnostic Evaluation
- ECG nonspecific: tachycardia with prolonged QTc
- Lab testing: nonspecific (may be false positive for TCA)
- Evaluate for coingestants (eg, acetaminophen)

Management and Disposition
- Consider activated charcoal in alert patients who present <1-2 hours after a large overdose, especially with extended release formulations.
- Intubate, if necessary (rare with quetiapine).
- Treat hypotension with IV fluids; if persistent, add norepinephrine or phenylephrine.
- In cases of refractory shock, consider intralipid, given its lipophilicity.
- Treat NMS with benzodiazepines and cooling.
- An asymptomatic patient with a normal ECG 6 hours after an overdose requires no further cardiac monitoring.