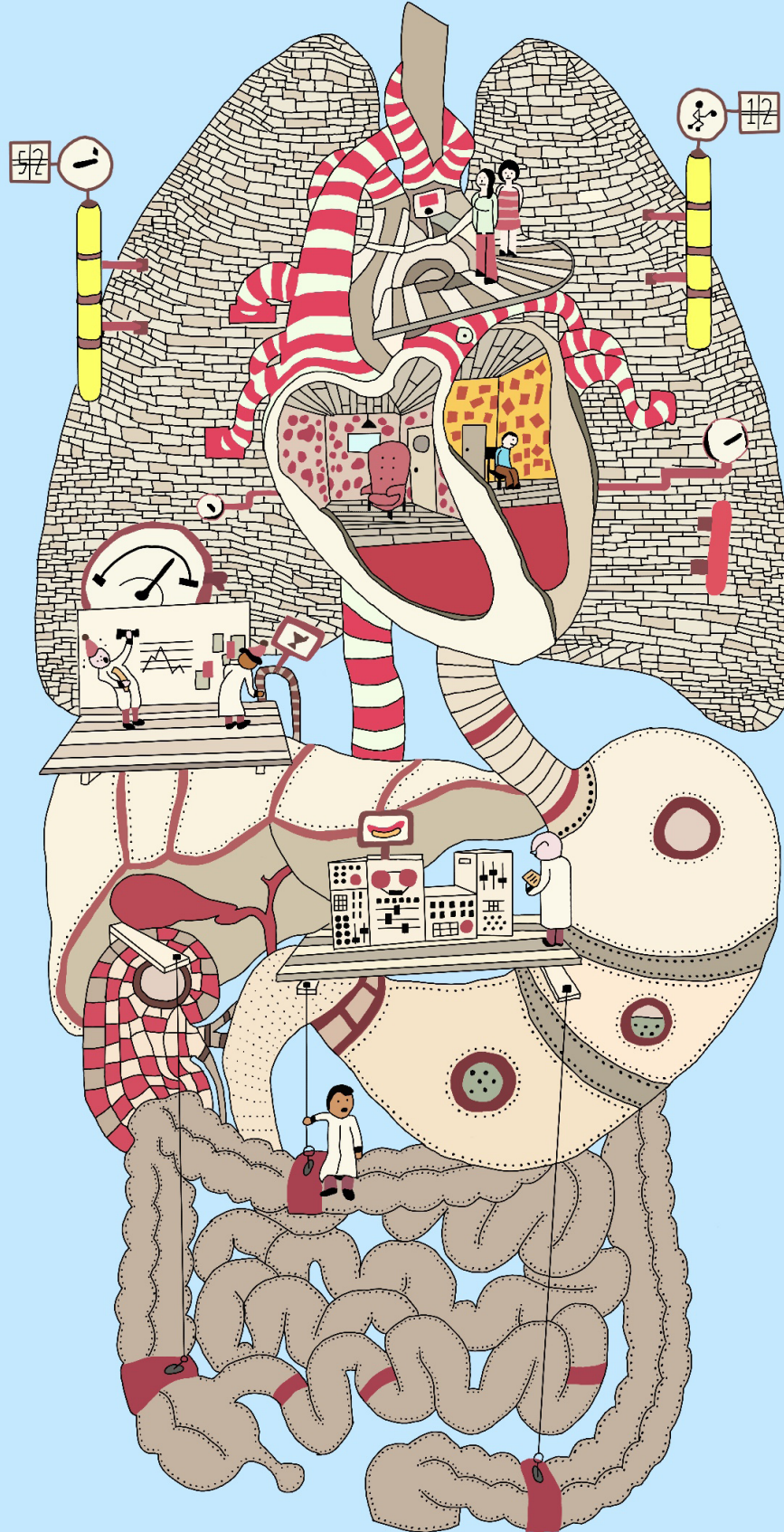


# ANNALS OF B POD

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- 2 **Hypokalemia** *Gottula*
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- Back **EKG Focus: Hypokalemia** *Scanlon*
- Cover

# AIR CARE: HYPOKALEMIA

Adam Gottula, MD  
*University of Cincinnati R3*

## History of Present Illness

Air Care was dispatched to a referring hospital for a middle aged female who presented with lower extremity weakness. Upon presentation to the hospital, the patient was somnolent with weakness in the bilateral lower extremities and full strength in her upper extremities. Providers were concerned for stroke. The patient underwent a non-contrast CT scan and prior to any therapeutic interventions suffered a pulseless electrical activity (PEA) arrest. The patient received chest compressions and two rounds of epinephrine with return of spontaneous circulation (ROSC) after 6 minutes. The patient was intubated and started on an amiodarone drip following a brief episode of wide complex tachycardia. Following ROSC the patient's labs resulted with a potassium of 1.5 mEq/L. 10 mEq of potassium chloride was started via a peripheral line.

### Past Medical History

Bipolar disorder, morbid obesity,  
hypertension, hyperlipidemia,  
COPD

### Medications

Unknown

### Past Surgical History

Unknown

### Allergies

Unknown

### Physical Exam

HR	BP	RR	SpO2
88	90/60	24	84% ventilator

Volume Assist Control: RR 16, TV 550cc, PEEP 8, FiO2 100%

The patient was pale, obese, and ill appearing on the ventilator. Breath sounds were symmetric. Patient was in normal sinus rhythm on the monitor, with occasional premature ventricular complexes (PVCs). The patient's pupils were equal, round and reactive to light (4-->2mm). She opened her eyes and moved all four extremities to command.

## Pre-Hospital Interventions

Upon HEMS arrival, the first 10 mEq of potassium had completed administration. An additional 10 mEq of potassium was ordered and administered prior to departure. Immediately after takeoff, the patient became bradycardic to the 20s and pulseless. The patient underwent resuscitation via ACLS guidelines, and ROSC was achieved after 8 minutes.

The patient remained hypotensive with a normal sinus rhythm and frequent PVCs. The remaining potassium was rapidly administered intravenous push with resolution of the patient's PVCs. 20 ug of epinephrine was administered with improvement in blood pressure to 100/60. The patient remained stable throughout the rest of the flight. At the receiving tertiary care center the patient's initial blood gas was significant for a normal pH and potassium of 1.7 mEq/L.

## Discussion

Potassium was first isolated from potash by Sir Humphrey Davy in 1807, but the biologic significance of potassium was not recognized until over one hundred years later. Potassium is primarily an intracellular cation, with concentrations 30- 40-fold greater intracellularly than extracellularly. This differential is achieved by the sodium-potassium ATPase enzyme found in the plasma membrane of cells. ATPase hydrolyzes ATP to pump three sodium ions out of the cell in exchange for two extracellular potassium ions into the cell. This gradient facilitates an outward current of potassium through potassium-selective ion channels

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in the plasma membrane resulting in a negative resting membrane potential (RMP) in the cardiac myocyte. The negative RMP works to stabilize excitable tissue, such as atrial and ventricular myocytes, thus preventing spontaneous action potentials. With hypokalemia, the repolarization reserve is reduced. This leads to intracellular sodium and calcium accumulation leading to early afterdepolarization arrhythmias such as polymorphic ventricular tachycardia (VT), which can degenerate to ventricular fibrillation (VF) causing sudden cardiac death.

on EKG. Initial changes include T wave flattening/inversion, PR prolongation, prominent U waves, and ST depression. The U wave is a small (0.5 mm) deflection immediately following and in the same direction as the T wave, best seen in V2 and V3.<sup>6</sup> The later cardiac effects of hypokalemia include fatal arrhythmias such as bradycardia, ventricular tachycardia, ventricular fibrillation, and Torsades de Pointes. “Classic” ECG findings have poor sensitivity for diagnosing hypokalemia, as many patients with low potassium have a normal ECG.

Causes of Hypokalemia	
<b>Abnormal Losses</b> 1) Medications - Diuretics - Laxative/Enemas - Corticosteroids 2) Gastrointestinal losses 3) Renal losses - Osmotic diuresis - Mineralocorticoid excess - Type 1&2 renal tubular acidosis - Polydipsia 4) Hypomagnesemia 5) Dialysis	<b>Transcellular Shift</b> 1) Medications - Insulin - Beta-2 sympathomimetics - Decongestants - Xanthines - Amphotericin B - Verapamil 2) Alkalosis 3) Refeeding Syndrome 4) Increased beta-2 adrenergic stimulation - Delirium tremens - Head injury - Myocardial ischemia 5) Thyrotoxicosis
<b>Inadequate intake</b> 1) Anorexia 2) Dementia 3) Starvation 4) Total parenteral nutrition	<b>Pseudohypokalemia</b> 1) Extreme leukocytosis 2) Delayed sample analysis

Table 1 Causes of hypokalemia.

Hypokalemia is defined as potassium less than 3.6 mEq/L (3.6 mmol/L) and is present in up to 21% of hospitalized patients and 2-3% of outpatients.<sup>1,2,3</sup> The most frequent causes of hypokalemia are diuretic use and gastrointestinal (GI) illness. Diuretic-induced hypokalemia occurs through direct renal loss, is dose-dependent, and tends to be mild (3 - 3.5 mEq/L).<sup>4</sup> The mechanism by which upper GI loss induces hypokalemia is indirect and is thought to result from a maladaptive renal response to the vomiting induced alkalosis. Lower GI losses in the form of diarrhea can also result in hypokalemia, as a portion of daily potassium is excreted in the colon. Hypokalemia secondary to lower GI losses may be accompanied by hyperchloremic acidosis.<sup>5</sup> Less common causes of hypokalemia include renal tubular acidosis, transcellular shift, and inadequate intake.

It is important to evaluate for possible GI losses, review medications (diuretics, laxatives etc.), and assess for underlying cardiac comorbidities. Neurologic manifestations can range from generalized weakness to ascending paralysis, though the latter is uncommonly seen. Early cardiac effects of hypokalemia can be demonstrated

Prior to initiation of treatment for hypokalemia it is first important to assess whether the patient has pseudohypokalemia. Pseudohypokalemia is an aberrant laboratory phenomena where a sample from a patient with a normal potassium is reported as hypokalemic. This is a laboratory phenomenon caused by both delayed sample analysis and leukocytosis. When rechecked the potassium will usually be normal provided sample analysis is not again delayed. It is however important not to delay potassium administration in a patient with a classic history and EKG changes while awaiting confirmation. Once the diagnosis of hypokalemia is certain further laboratory work-up must be pursued if a cause is not known. When there is concern for renal losses of potassium, urine potassium and potassium-to-creatinine ratios should be checked.

Initial treatment is focused on preventing cardiac conduction disturbances and neuromuscular dysfunction by repleting potassium. Goal potassium levels are > 3.6 mEq/L for the general population and > 4.0 mEq/L for patients with a history of heart failure or myocardial infarction.<sup>6</sup> Empiric administration of magnesium should be considered as patients will be unable to absorb potassium in a hypomagnesemic state. This is a consequence of the effects of magnesium on the luminal potassium (ROMK) channels within the connecting tubule and cortical collecting tubules of the kidney. Low levels of intracellular magnesium decrease the magnesium-mediated inhibition of the ROMK channels leading to increased renal potassium secretions, ultimately decreasing the efficacy of potassium replacement.<sup>7</sup>

Laboratory Analysis in Hypokalemia
<ul style="list-style-type: none"> <li>- Repeat serum potassium measurement</li> <li>- Obtain serum glucose and magnesium levels</li> <li>- Obtain urine electrolyte (24 hour timed urine potassium collection is the most accurate) and creatinine levels</li> <li>- Assess acid-base balance</li> <li>- Consider thyroid and adrenal work-up if initial work-up is unrevealing</li> </ul>
Normal urine potassium excretion: 15 - 30 mEq/L Spot Potassium-to-Creatinine ratio: < 1.5 mEq/mmol (> than 1.5 mEq/mmol is indicative of renal potassium wasting)

Table 2 Laboratory analyses to consider in hypokalemia.

Replacement of potassium is simple and formulaic. Serum potassium concentration decreases approximately 0.3 mEq/L (0.3 mmol/L) for every 100-mEq (100-mmol) reduction in total body potassium.<sup>8</sup> Using the patient’s measured potassium

Hypokalemia  
*continued on page 12*



# MALARIA

Colleen Laurence, MD MPH  
University of Cincinnati R2

## History of Present Illness

A male in his 30s first presents to the Emergency Department (ED) with a chief complaint of headache three times over a five-day period. Onset of the headache was one week prior to presentation and has been intermittent since then. The patient describes the headache as throbbing and diffuse in nature, localizing it to his sinuses and temporal area. Ibuprofen and combined acetaminophen-acetylsalicylic acid-caffeine tablets have provided some intermittent relief. The patient denies a history of chronic headaches and known sick contacts. The patient does, however, note that he had recently received the influenza vaccination. On review of systems, the patient endorses recent subjective fevers and chills as well as dark urine. He denies neck stiffness or pain, dizziness, gait disturbance, cough, congestion, sinus pain, photophobia, or preceding fall or trauma. The patient was born in western Africa but had not traveled outside of the United States in the past three years. He reports working at a “desk job” as he termed it, as a systems analyst with no environmental or chemical exposures.

Past Medical History: Typhoid fever

Past Surgical History: Tooth extraction

Medications: None

Allergies: Ampicillin

## Physical Exam

The patient was well appearing. He was alert and oriented, moved all four extremities, and had intact cranial nerves, sensation, and motor function throughout. He demonstrated no signs of ataxia on finger-to-nose testing or in his gait. He was able to range his neck fully and demonstrated no meningismus with a negative Brudzinski sign. His head was atraumatic. There were no signs of scleral icterus. Conjunctiva were normal. There was no tenderness on palpation of his sinuses. His tympanic membranes and oropharynx were clear without erythema or exudate. His lungs were clear to auscultation bilaterally and the patient did not appear in any distress. He had a regular rate and rhythm with no murmurs, rubs, or gallops and 2+ radial pulses bilaterally. His abdomen was soft, non-distended with no rebound or guarding. He had no signs of organomegaly with deep palpation. There was no obvious peripheral edema or rash.

## Visit 1

T 39.6 °C / HR 94 / BP 135/84 / RR 17 / SpO2 98%  
WBC 4.9 / Hgb 13.5 / Hct 40.9 / Plt 203  
BMP / Influenza / Mononucleosis / UA negative  
CXR negative

---  
He was treated symptomatically with acetaminophen, ketorolac, metoclopramide, diphenhydramine, and one liter of normal saline with significant improvement in his headache. He was advised to

follow-up with a primary care provider regarding his thrombocytopenia.

## Visit 2

T 37.1 °C / HR 71 / BP 125/74 / RR: 18 / SpO2: 98%  
WBC 5.9 / Hgb 12.1 / Hct 35.9 / Plt 84  
BMP / LDH / Haptoglobin / Fibrinogen / PTT / PT / INR / LFTs / ADAMST13 negative  
D-Dimer 2.82  
CT head non-con / CTA head negative  
LP opening pressure 31cm H2O / CSF studies negative

---  
The patient received symptomatic treatment with morphine, prochlorperazine, diphenhydramine, and two liters of intravenous fluids with subsequent resolution of his headache. He was discharged with recommendations for oral hydration and a prescription for oxycodone-acetaminophen.

## Visit 3

T 39.3 °C / HR 87 / BP 123/66 / RR 18 / SpO2 97%  
WBC 6.0 / Hgb 11.5 / Hct 34.6 / Plt 75  
BMP / Respiratory viral panel / HIV / LFTs / Acute hepatitis panel negative

Thick and thin blood smears: Present, suggestive of Plasmodium ovale or Plasmodium vivax, 0.6% parasitemia

---  
The patient was admitted to medicine. Two

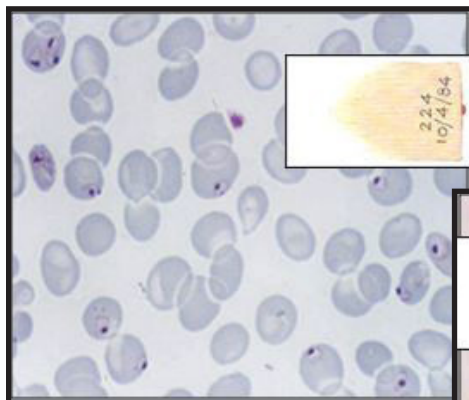


Image 1: Thin smear. Courtesy of <https://microbeonline.com/microscopic-diagnosis-of-malaria/>

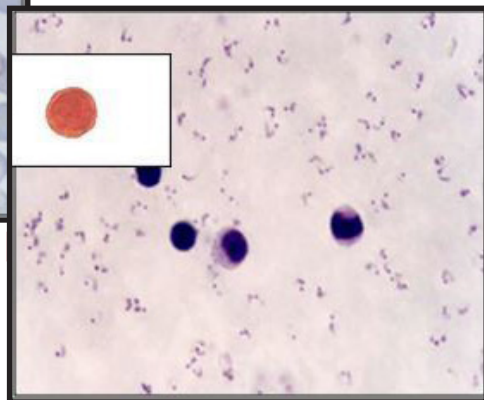


Image 2: Thick smear. Courtesy of <https://microbeonline.com/microscopic-diagnosis-of-malaria/>

peripheral blood cultures as well as labs to assess for metabolic, autoimmune, and other

infectious etiologies were ordered. The Infectious Diseases (ID) service was consulted. On hospital day two, his thick and thin peripheral blood smears returned positive for malarial organisms – thought likely to be Plasmodium ovale or Plasmodium vivax given their morphology and the patient’s history. The patient had a relatively low parasitemia burden at 0.6%. Treatment with atovaquone-proguanil 1000-400 mg was initiated and subsequently completed on hospital day four. Patient discharged with ID follow up on hospital day five.

## Discussion

Febrile illness in patients who have lived or traveled abroad are often attributable not to tropical disease but rather typical viral illnesses.

Nonetheless, malaria and other tropical diseases should be considered in patients who have spent time in endemic regions.

### Epidemiology

Malaria is caused by protozoal parasites of the genus *Plasmodium*. There are five *Plasmodium* species that are known to cause disease in humans: *falciparum*, *vivax*, *malariae*, *ovale*, and *knowlesi*. While global efforts to prevent the spread of malaria have reduced mortality from malaria by an estimated 25% between 2010 and 2016, *Plasmodium* species remain a major cause of morbidity within the global community.<sup>1</sup> In 2017, the World Health Organization (WHO) estimated 219 million cases of malaria in 90 countries and recorded 435,000 deaths due to malaria. Sub-Saharan Africa (SSA) carried a disproportionate share of the global malaria burden, with 92% of malaria cases and 93% of deaths attributable to malaria in 2017. However, India, along with Nigeria, the Democratic Republic of the Congo, Mozambique, and Uganda, accounted for nearly half of all malaria cases worldwide that year.<sup>2</sup>

The majority of malaria infections in the United States occur in individuals who have traveled to areas with ongoing malaria transmission. In 2015, 1,517 confirmed cases of malaria in the U.S. were reported to the CDC. *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae* were identified in 67.4%, 11.7%, 4.1%, and 3.1% of cases respectively, and the species was not reported or was indeterminate in 12.9% of cases. 17.1% of the cases were classified as severe illness, and 11 persons died as a result of infection in 2015.<sup>3</sup>

The persistence of malaria in certain regions of the world stems from a complex interplay of multiple factors, including limited resources and socio-economic instability which complicate malaria control. These issues are further compounded by the tropical and subtropical geography and climate that facilitates year-round transmission by malaria's vector, the female *Anopheles* mosquito. Certain *Plasmodium* species variably predominate in different regions: *P. falciparum* has the broadest reach, accounting for the majority of cases in SSA, southeast Asia, the Eastern Mediterranean, and the Western Pacific.<sup>4</sup> Conversely, *P. vivax* is more common in the Americas, representing 74.1% of the cases.<sup>5</sup> *P. malariae* and *P. ovale* are both rarer in general and occur most often in SSA, though *P. malariae* is found in all endemic areas.<sup>6</sup> Finally, *P. knowlesi* has been identified in southeast Asia and, as yet, is still considered a zoonotic species, as it has not been known to pass from human to human without an intermediate host, the macaque monkey.<sup>7</sup> The species of malaria is important to consider as the species have slightly different life cycles, incubation

periods, and illness severities, which influence clinical presentation and antimalarial options.

### Lifecycle of Malaria

Once the female *Anopheles* mosquito bites a human, thus transmitting the *Plasmodium*, the sporozoite form of the parasite travels first to the liver where they infect liver cells and undergo asexual reproduction. They produce merozoites that rupture from the infected cells and are released into the blood stream. This process is termed the exoerythrocytic stage. Importantly and as we saw in our patient, the *P. vivax* and *P. ovale* may also enter a dormant stage at this time with a form of the parasite called a hypnozoite persisting in the liver until weeks, months, or even years later, when they are released into the blood stream. More often, however, merozoites then invade erythrocytes, asexually multiply to produce more daughter merozoites, and release them into the blood stream to perpetuate reproduction, destroying the erythrocyte and causing hemolysis in the process. This

occurs during the erythrocytic stage and is when most patients develop symptoms of malaria.

At this time, some of the parasites may also differentiate into sexual reproduction to produce male (microgametocyte) and female (macrogametocyte) gametocytes, which are released into the blood stream and taken up by the mosquito during their next blood meal. In the mosquito, the sporogonic cycle commences. The microgametocyte penetrates the macrogametocyte to produce a zygote, which develops into a motile ookinete that invades the gut wall and develops into

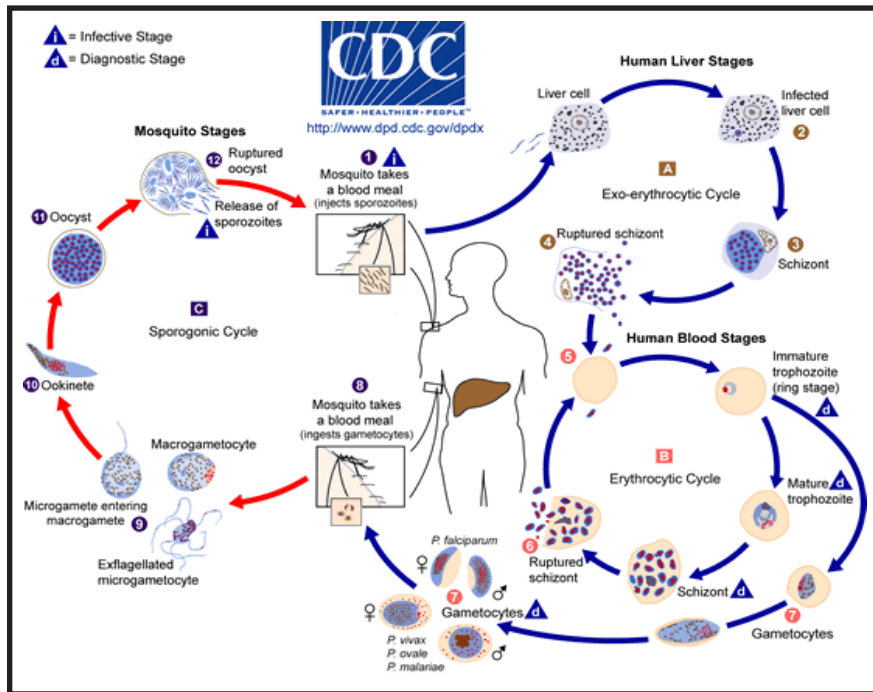


Figure 1: Life cycle of malarial parasite. Courtesy of [https://commons.wikimedia.org/wiki/File:Malaria\\_lifecycle-CDC.gif](https://commons.wikimedia.org/wiki/File:Malaria_lifecycle-CDC.gif)

an ookinete. Eventually, these ookinets rupture, releasing sporozoites, which travel to the mosquito's salivary glands and perpetuate malaria's life cycle when they, in turn, invade their next human host.<sup>8</sup> Notably, malaria may also be transmitted by blood transfusion or passed transplacentally from mother to fetus, though this is rare.

### Clinical Presentation

The clinical manifestations of malaria vary with species, immune status, and age of the human host, among other factors. Individuals are generally asymptomatic until the parasites reach the erythrocytic stage. The incubation period following the bite of an infected *Anopheles* mosquito ranges from one to four weeks. Longer incubation periods are more common in semi-immune individuals and in those on chemoprophylaxis. Infection with *P. falciparum* typically becomes clinically apparent within seven to fourteen days, with virtually all infected hosts demonstrating symptoms within one month following inoculation. By contrast, *vivax*, *malariae*, and *ovale* infections commonly have longer incubation periods, ranging anywhere from fourteen

Malaria  
*continued on page 14*

# TRAUMATIC DIAPHRAGMATIC RUPTURE

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University of Cincinnati R2

## History of Present Illness

The patient is an otherwise healthy middle aged female who presents following a motor vehicle collision. She is the restrained driver of a vehicle with significant front end damage, air bag deployment, and prolonged extrication. On arrival of helicopter emergency services (HEMS), the patient was hypotensive to 40/30s, tachycardic to 140, had an oxygen saturation in the 80s, and a GCS of 4 (1/1/2). She was intubated via rapid sequence induction with ketamine and succinylcholine, and she received 2 units of fresh frozen plasma (FFP), 1 unit of packed red blood cells (pRBCs), and 1 gram of tranexamic acid (TXA). HEMS providers also noted decreased breath sounds in the left lung field and performed needle decompression on the left in the midaxillary line with reported improvement of her hypoxia.

## Physical Exam

HR	BP	RR	SpO2
128	159/126	27	100% ventilator

General: Intubated. Immobilized on backboard with a cervical collar.

HEENT: Left forehead laceration, pupils 4-5 mm bilaterally.

Neck: Trachea midline

Pulmonary: Clear to auscultation bilaterally with no wheezes or crackles. No chest wall crepitus. Needle decompression catheter present in the mid-axillary line.

Abdomen: Soft, non-distended. No tenderness to palpation. No masses appreciated. No external evidence of trauma. Pelvis stable to compression with T-pod in place.

Musculoskeletal: Lacerations to bilateral lower extremities distal to the knees. Left foot externally rotated and shortened with open left ankle fracture. No step-offs or deformities of the cervical, thoracic, or lumbar spine. Normal rectal tone.

Skin: Cool, pale

Neurologic: Intubated. GCS 1,T,4

## Diagnostic Work Up

<del>10.7</del>	143	108	13	<del>213</del>
<del>24.8</del>	3.5	25	1.37	
<del>31.7</del>				

Lactate: 4.0

pH 7.2 / pCO2 57 / base deficit: 6.3

TEG ACT: 128 / R time: 50 / Time: 75 / Angle: 76.2 / Max Amplitude 66.1 / Lysis 30: 1.1

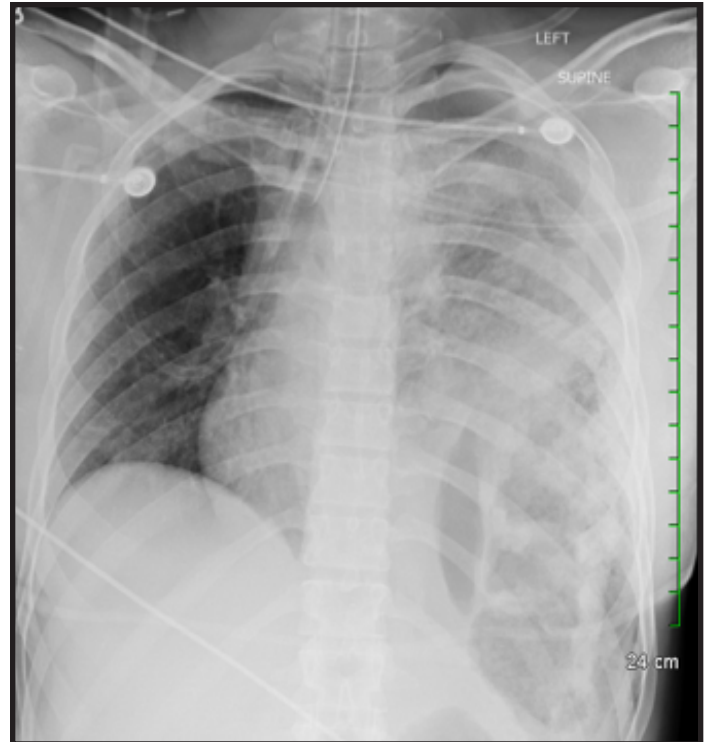


Image 3: Representative chest X-ray depicting left-sided diaphragmatic rupture with herniation of abdominal contents

Pelvis: Left pubic fracture

CT Head – left frontal and temporal contusions/shear

CT Chest: Left diaphragmatic rupture, traumatic aortic injury with pseudoaneurysm, multiple pulmonary lacerations, bilateral pneumothoraces left greater than right, right 1st rib fracture, left 2-4, 6-9 rib fractures

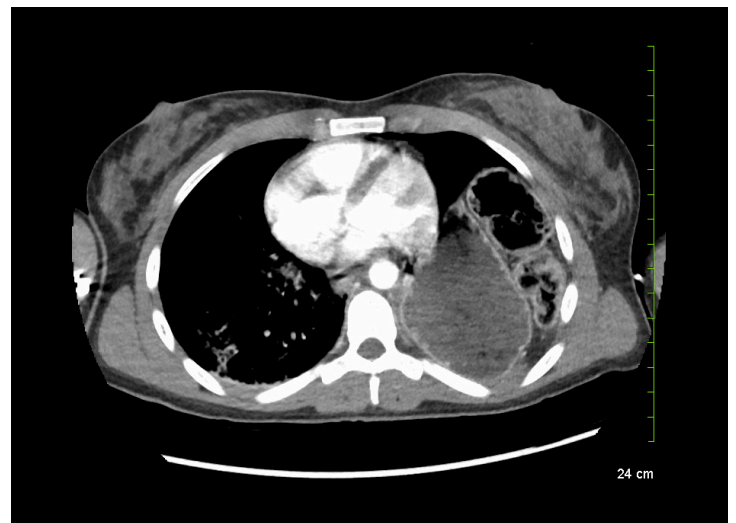


Image 4: Representative CT chest depicting left-sided diaphragmatic rupture with herniation of abdominal contents



## Hospital Course

The patient is assessed and managed in collaboration with the trauma team. The patient has a GCS of 5T (1-T-4) on arrival. She ultimately receives an additional 2 units of packed red blood cells (pRBC) and 1 unit of fresh frozen plasma (FFP) for a total of 4 units of pRBCs and 3 units of FFP. Once stabilized, she undergoes additional imaging. She is then taken to the operating room where she undergoes an exploratory laparotomy, splenectomy, simple hepatorrhaphy, and reduction of her stomach, spleen, and colon from the thoracic cavity and repair of the diaphragmatic defect. The left chest is irrigated, and a left chest tube is placed. She is discharged on hospital day 26 and continues to improve with rehabilitation and follow up with specialists for her multiple injuries.

## Discussion

Diaphragmatic injury is relatively uncommon, comprising less than 1% of all traumatic injuries.<sup>1,2</sup> Diaphragmatic rupture typically occurs in association with other thoracic and abdominal organ injuries. It may result from both penetrating trauma and blunt trauma, though there is a higher incidence of traumatic penetrating diaphragmatic injury (67%) compared to traumatic blunt diaphragmatic injury (33%).<sup>3</sup>

In blunt trauma, rupture is thought to occur due to an abrupt increase in the intraabdominal pressure. At baseline, there is a positive pressure gradient of 7-20 cm H<sub>2</sub>O between intraperitoneal and intrapleural pressures, which can increase ten fold with severe abdominal trauma. This pressure overcomes the strength of the diaphragmatic tissue, avulsing or shearing the diaphragm from its various attachments.<sup>4,5,6</sup> Blunt trauma most often causes large radial tears in the diaphragm; by comparison, penetrating trauma typically causes smaller defects in the diaphragm, primarily where the intrusive object has directly damaged this structure. Thus, penetrating diaphragmatic injuries are more likely to be missed because of their smaller size.<sup>3</sup>

The left posterolateral hemidiaphragm is most commonly injured due to the relative weakness of the left hemidiaphragm, whereas the right hemidiaphragm is protected by the liver. In one review of 1589 patients, left-sided injury was noted in 75% of the cases, right-sided injury in 23%, and bilateral injuries in 2%.<sup>7</sup> In addition to laterality, the severity of the defect should also be considered. The American Association for the Surgery of Trauma (AAST) classifies diaphragm injuries using the organ injury scale (Table 3). If bilateral diaphragmatic injuries are present, the injury grade is automatically a Grade III. It is important to note, however, that this scale has yet to be studied for its correlation with morbidity and mortality and does not determine specific management.<sup>8</sup>

## Diagnosis

The diagnosis can be challenging to make, so a high index of suspicion is paramount. Evaluation for diaphragmatic injury begins with the patient history and identification of the injury mechanism, physical exam, and assessment of associated injuries. Motor vehicle collisions are responsible for up to 90% of blunt diaphragm ruptures, but a high level of suspicion should be maintained in patients presenting with fall or crush injuries

Diaphragm Injury Scale	
Grade	Description of Injury
I	Contusion
II	Laceration <2cm
III	Laceration 2-10cm
IV	Laceration >10cm with tissue loss ≤25cm <sup>2</sup>
V	Laceration with tissue loss > 25cm <sup>2</sup>
Advance one grade for bilateral injuries up to grade III	

Table 3: Diaphragm Injury Scale depicting grades of diaphragmatic injury

as well.<sup>2</sup>

Given the higher-impact mechanisms that are associated with traumatic diaphragmatic rupture, it is not surprising that approximately 50% of patients with diaphragmatic injury suffer concomitant injuries.<sup>9,10</sup> Among patients found to have traumatic diaphragmatic rupture,

48% have liver injuries, 47% have a hemothorax and/or pneumothorax, 35% have splenic injuries, 28% have rib fractures, 23% have bowel injury, 16% have kidney injuries, 14% have pelvic fractures, 11% have closed head injuries, 4% have thoracic aorta injuries, and 4% have spinal cord injuries.<sup>2</sup>

The difficulty in diagnosing diaphragmatic trauma is twofold: the first being that patients often present with polytrauma, and more apparent injuries at the time of initial evaluation tend to take precedence. In conjunction with this, there is no particular physical exam finding that is pathognomonic for a diaphragmatic rupture. Patients are often asymptomatic initially and may only become significantly symptomatic in later stages of the injury course.

Complications from diaphragm rupture include not only the herniation of bowel contents into the limited space of the chest wall leading to displacement of lung tissue and other intrathoracic contents, but also elimination of one of the primary respiratory muscles that assists with oxygenation and ventilation. Diaphragmatic injury affects respiratory status significantly, and if the injury is severe enough or goes undetected for long periods of time, patients may develop tachypnea, hypoxia, tachycardia, and hypotension. The other consideration in this injury is to the bowel itself, which can progress quickly to bowel strangulation, ischemic gut, and multiorgan failure. Thus, without early detection and intervention, diaphragmatic defects tend to grow over time with escalating consequences on patient morbidity and mortality.

The second difficulty in diagnosing diaphragmatic injury is that the most common imaging modalities used in the initial evaluation of trauma patients do not have the desired level of accuracy in detecting early trauma. Chest radiography is a common initial imaging modality for most trauma patients and may reveal elevation or blurring of the hemidiaphragm, hemothorax, or abnormal gas patterns obscuring the hemidiaphragm that may indicate underlying trauma. However, chest radiography is not sensitive and can appear normal 50% of the time when a true diaphragm injury exists. One study attributed a sensitivity of 46% to chest radiographs in detecting left-sided rup-

Traumatic Rupture  
*continued on page 13*

# ACUTE PANCREATITIS

Meaghan Frederick, MD  
University of Cincinnati R2

## History of Present Illness

A middle aged male with a past medical history of hypertension, cholecystectomy, and a previous episode of pancreatitis presents to the ED with one day of constant epigastric abdominal pain radiating to the back with associated bloating. He denies any fevers, nausea, vomiting, or diarrhea. The patient denies prior abdominal surgeries or instrumentation with the exception of a prior cholecystectomy. He endorses alcohol and marijuana use. The patient is mildly hypertensive and tachycardic with a taut, diffusely tender abdomen and voluntary guarding. His blood work is notable for a mild leukocytosis of 12.9 with otherwise unremarkable renal panel, hepatic function testing, and lipase. A CT abdomen/pelvis demonstrates a 10 cm x 9 cm peripancreatic fluid collection suggestive of pseudocyst formation, with narrowing of the portal vein and splenic vein occlusion. The patient's pain improves with symptomatic treatment. Gastroenterology is consulted and the patient is planned for outpatient esophagogastroduodenoscopy and discharged home.

The patient returns to the ED the next day with significant worsening of epigastric abdominal pain unmitigated by his home oral pain medication.

**Past Medical History**  
Pancreatitis in 11/2018  
Hypertension

**Past Surgical History**  
Cholecystectomy

**Social History**  
Alcohol, marijuana

**Medications**  
Amlodipine, lisinopril,  
pantoprazole, oxycodone

**Allergies**  
Ciprofloxacin

## Physical Exam

Temp	HR	BP	RR	SpO2
36.4	117	185/102	19	97% on RA

Lying in bed, uncomfortable and diaphoretic. He is tachycardic with a regular rhythm. Normal respiratory effort with relatively shallow breaths secondary to abdominal pain. His abdomen is diffusely tender, distended, with guarding and rebound as well as moderate rigidity.

## Diagnostic Work Up

<del>15.1</del>	<del>250</del>	134	94	12	<del>162</del>
<del>20.8</del>	<del>46.1</del>	3.7	29	0.98	

AST 15 / ALT 10 / ALP 64 / TBili 0.8 / DBili 0.3 / Lipase 75



Image 4: Representative ultrasound depicting FAST exam

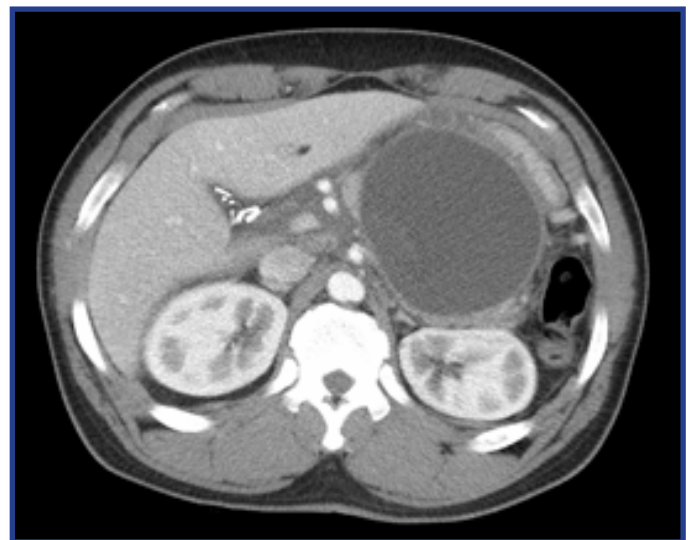


Image 5: Representative CT abdomen/pelvis depicting unchanged walled-off peripancreatic fluid collection compared to the prior study. Stable portal vein thrombosis with significant interval worsening of ascites concerning for significant flow impedance. There is also mild wall thickening and fat stranding about the transverse and proximal descending colon which is likely due to portal vein thrombus resulting in increased venous pressure.

## Hospital Course

The patient was admitted to acute care surgery. He was placed on a heparin drip to treat his portal vein thrombosis and was gradually transitioned to enoxaparin. The patient began to have nausea, vomiting, and constipation with concern for secondary small bowel obstruction for which a nasogastric tube was placed. Gastroenterology was consulted and, after reviewing the patient's images, suggested that the peripancreatic fluid collection was more consistent with walled-off necrosis than a pancreatic pseudocyst. The patient subsequently underwent cystogastrostomy with drainage of 500 mL of fluid and debris. The nasogastric tube was removed, his constipation resolved, and the patient was able to tolerate oral intake. He was discharged home on enoxaparin with plans for repeat imaging in the following weeks.



## Discussion

### Etiology and Disease Severity

Acute pancreatitis is defined as a serum lipase at least three times the upper limit normal, abdominal pain consistent with acute pancreatitis (acute, severe, epigastric pain often radiating to the back), and findings consistent with acute pancreatitis on CT, MRI, or US imaging. The presence of two out of the three criteria is considered diagnostic. Acute pancreatitis can further be classified by morphology and severity.

Morphologically, there are two categories of pancreatitis: acute edematous interstitial pancreatitis and acute necrotizing pancreatitis. Interstitial edematous pancreatitis is the most common presentation, defined by diffuse inflammatory edema of the pancreas on imaging. Necrotizing pancreatitis, by comparison, is relatively rare, occurring in <10% of patients with acute pancreatitis. It most commonly manifests as necrosis of both the pancreas and peripancreatic tissues, rarely damaging either structure in isolation. Radiographic findings typically develop on CT imaging over several days. This necrotic tissue is at high risk of superimposed infection, potentially leading to additional complications discussed in greater detail below. Prognostication and identification of high-risk patients are confounded by the lack of correlation between the extent of necrosis and likelihood of it becoming infected in addition to the delayed nature of infections, with most occurring greater than one week following the insult. A necrotizing infection is defined radiographically by extra-luminal gas in the pancreas or peripancreatic tissues on CT. It is important to recognize pancreatic necrosis as it often necessitates the use of antibiotics in addition to traditional therapies.

The severity of acute pancreatitis is divided into mild, moderate, and severe. Mild acute pancreatitis is defined by features of pancreatitis

without objective evidence of organ dysfunction. These patients are most often managed conservatively and may be discharged safely with overall low morbidity and mortality. Moderately severe pancreatitis is characterized by either transient organ failure or local or systemic complications in the absence of persistent organ failure (>48 hours). Outcomes of moderately severe acute pancreatitis vary drastically, ranging from complete recovery to death, though the associated mortality remains significantly lower than that of severe acute pancreatitis. Severe pancreatitis is defined as persistent organ failure lasting beyond 48 hours and is thought to affect 20-30% of all patients suffering from acute pancreatitis.<sup>9</sup> Severe pancreatitis carries a mortality rate as high as 50%, and potentially be even higher when complicated by pancreatic necrosis.<sup>14</sup>

### Epidemiology

Acute pancreatitis has an estimated incidence of 13 to 45 cases per 100,000 individuals and carries a mortality of approximately 5% for all patients. Gallstones are the most common cause of acute pancreatitis, accounting for approximately 35-40% of all causes. In the United States, alcohol use is implicated in roughly 30% of cases of acute pancreatitis, making it the second most prevalent etiology of pancreatic injury. Beyond gallstones and alcohol use, episodes of pancreatitis may stem from pathologic anatomic variants such as pancreatic divisum, infectious agents, toxicologic exposures, hypercalcemia, hypertriglyceridemia, hypothermia, mumps, cock-sackie A virus, HIV, tuberculosis, and the rare but memorable scorpion sting.<sup>26</sup>

### Treatment

#### Fluid Resuscitation

Patients with acute pancreatitis are prone to hypovolemia due to decreased oral intake and third spacing. This hypovolemia can worsen outcomes by predisposing patients to renal injury and cardiovascular collapse, as well as increasing the risk of perfusion defects to the already damaged pancreas. There are numerous guidelines with varying recommendations regarding the appropriate volume for intravascular repletion, rate of resuscitation, and choice of crystalloid agent. Of the available crystalloid products, Lactated Ringers (LR) confers the theoretical benefits of decreasing pancreatic acidosis and reducing trypsin activity, although current evidence suggests a modest morbidity/mortality benefit at most.<sup>21</sup> Conversely, patients with acute pancreatitis due to hypercalcemia should not undergo fluid resuscitation with calcium-containing LR given concerns of further exacerbating the underlying pancreatic injury and saponification of peripancreatic tissues.

With regards to the rate, Gardner et. al demonstrated that those who received more than one third of their cumulative 72-hour IV fluids within the first 24 hours experienced a reduction in persistent organ failure (35% vs 43%) and overall mortality (0% vs 18%) when compared to those who did not receive sufficient early fluid resuscitation.<sup>19</sup> This reduction in morbidity afforded by early fluid resuscitation has been continually demonstrated in subsequent studies.<sup>20</sup> Many experts advocate for goal directed therapy, targeted at addressing hypotension, tachycardia, elevated hematocrit (suggestive of hemoconcentration), elevated blood urea nitrogen (BUN), and ensuring adequate urine output. Trends in BUN measured at admission, 24 hours, and 48 hours has been demonstrated to predict Acute Pancreatitis mortality in acute pancreatitis, with those

*continued on page 10*

Acute Pancreatitis	
<b>Definition (2 out of 3 criteria):</b> Lipase $\geq$ 3X upper limit of normal Abdominal pain Diagnostic imaging consistent with acute pancreatitis	
Morphology	
<b>Acute edematous interstitial pancreatitis</b> - Common - Diffuse inflammatory edema	<b>Acute necrotizing pancreatitis</b> - Rare - Necrosis of pancreas and peripancreatic tissues
Severity	
<b>Mild</b>	- No evidence of organ dysfunction - Conservative management - Low morbidity and mortality
<b>Moderate</b>	- Local or systemic complications - Transient organ failure <48 hours - Varying morbidity and mortality
<b>Severe</b>	- Persistent organ failure >48 hours - High morbidity and mortality

Table 4: Table outlining acute pancreatitis definition, morphology and severity characteristics

## Acute Pancreatitis

*continued from page 9*

having a BUN of 20 mg/dL or higher on admission having a mortality OR of 4.6; furthermore, any increase in BUN 24 hours from admission confers an OR of 4.3 for mortality.<sup>22</sup> As such, many experts recommend fluid therapy be directed at decreasing the BUN within the first 24 hours of admission.<sup>13,23</sup> Currently, guidelines from the American College of Gastroenterology recommend an infusion of 2.5 to 4 liters in the first 24 hours, with an initial infusion rate of 250-500 mL/hr. While adequate fluid resuscitation is a pillar of acute pancreatitis management, it is important to remember that overly aggressive fluid resuscitation can increase the risk for developing abdominal compartment syndrome.

In summary, fluid resuscitation is paramount in acute pancreatitis, early resuscitation is better than late resuscitation, therapy should be targeted at decreasing BUN within the first 24 hours, and lactated ringers may be a superior fluid choice.

### Antibiotics

As our understanding of acute pancreatitis has evolved, the role of prophylactic antibiotics has been hotly contested, in no small part secondary to the mixed and frequently contradictory evidence published in recent literature. A 2001 meta-analysis by Sharma and Howden evaluating prophylactic antibiotics in patients with acute necrotizing pancreatitis demonstrated a greater than 20% reduction in the incidence of sepsis and a 12% reduction in mortality when compared to patients not receiving prophylactic antibiotics.<sup>16</sup> Curiously, despite the robust reduction in mortality, the same study showed no decrease in the incidence of developing a pancreatic infection. Subsequent meta-analyses published in 2008 and 2011 failed to demonstrate a benefit of prophylactic antibiotic administration in reducing infection rates, incidence of multiorgan failure, need for surgical intervention, or mortality.<sup>17,18</sup> Compilations of more recent literature seem to support this lack of demonstrable benefit.<sup>15</sup> Current guidelines recommend against the routine use of prophylactic antibiotics for acute pancreatitis, regardless of morphology or severity, and suggest that they should not be utilized as part of management unless infection is objectively demonstrated.

### Pain

Acute pancreatitis is associated with significant pain, and adequate analgesia is an important consideration as patients may be unwilling or unable to tolerate oral nutrition/hydration without satisfactory pain control. Opioid agents are frequently employed to this effect. Traditionally, providers were encouraged to avoid the use of morphine in acute pancreatitis due to the theoretical 'risk' of increased tone in the sphincter of Oddi, obstructing passage of biliary contents into the duodenal lumen. The use of meperidine was encouraged as it was considered a non-contracting alternative. This practice has been thoroughly refuted by recent literature, however, with one study actually demonstrating a greater effect on increasing common bile duct pressure with use of meperidine in comparison to morphine.<sup>24</sup> Given its numerous side-effects and black box warnings, the routine use of meperidine for analgesia has fallen from clinical practice. Instead, providers are encouraged to optimize analgesia using appropriate doses of agents individually selected and titrated to the unique physiologic characteristics of their patient.

## Local Complications

### Peri-pancreatic Fluid Collections

As discussed previously, there are two morphological classifications of acute pancreatitis, each of which is associated with a unique pancreatic fluid collection. Acute edematous pancreatitis may result in an acute peripancreatic fluid collection (APFC) and pseudocyst formation, while patients with acute necrotizing pancreatitis may develop acute necrotic collection (ANC) and walled-off pancreatic necrosis (WOPN).

An acute peripancreatic fluid collection typically develops early in acute pancreatitis (within four weeks of symptom onset) and refers to peripancreatic fluid without a well-defined wall and without solid or necrotic contents. APFCs are at low risk of superimposed infection, with the majority spontaneously involuting within 7-10 days.<sup>25</sup> As such, APFCs do not typically require additional treatment. When APFCs do persist beyond four weeks, however, they frequently develop a defined wall and coalesce into a pancreatic pseudocyst.

Similarly, for necrotizing pancreatitis, an acute necrotic collection typically occurs within the first four weeks of insult and is defined as a collection of fluid and necrotic tissue which lacks a well-defined wall. Despite superficial similarities to an APFC, an ANC is differentiated in that it develops following necrotizing pancreatitis and contains necrotic tissue. Ultrasonography, both transcutaneous and endoscopic, may be used to confirm the presence of solid material within the collection, distinguishing ANC from APFC. Persistent necrotizing collections lasting greater than four weeks may organize into a cystic structure similar to a pancreatic pseudocyst, termed walled-off necrosis.

Both pseudocysts and areas of walled-off necrosis present with varying symptoms such as pain, fevers, chills, jaundice, or early satiety. In asymptomatic patients, pseudocysts are typically managed conservatively with routine imaging every 3-6 months until resolution or significant decrease in size. In one study by Cui, more than 80% of patients saw reduction or complete resolution of their pseudocyst at one year.<sup>1</sup> Supportive care for both pseudocysts and WOPNs also includes enteric feeding for nutritional support with concomitant use of proton pump inhibitors and somatostatin analogues to decrease pancreatic secretions. When secreted, the pancreatic enzyme trypsinogen is activated into trypsin by enterokinase in intestinal mucosa. Activated trypsin is then able to activate additional trypsinogen into more trypsin. Acute pancreatitis results in widespread activation of pancreatic enzymes, triggering a vicious cycle which leads to autodigestion and pancreatic damage. Under this premise, inhibition of pancreatic secretions should minimize the occurrence of autodigestion and forestall subsequent damage. Furthermore, somatostatin analogues may hasten pseudocyst resolution by minimizing pancreatic secretions into the fluid collection.

In patients with clear symptoms, rapidly enlarging cysts, or dysregulated systemic responses to infected cysts, providers may consider drainage of pseudocystic structures to alleviate symptoms. Infected pancreatic necrosis or symptomatic sterile necrosis should also undergo drainage. There are several options for drainage including endoscopic, percutaneous, or surgical. With recent advances in fiberoptic technology, endoscopic management has superseded both

surgery and percutaneous techniques as the preferred option. A recent study has shown >90% success rate of endoscopic drainage with lower associated morbidity compared to other modalities; another study that compared various approaches to drainage demonstrated a 70% success rate with endoscopic techniques in contrast to a 31% success rate with percutaneous treatment.<sup>3,4,5</sup> Additionally, percutaneous approaches were three times as likely to progress to surgery as compared to endoscopic management.<sup>5</sup> Unfortunately, successful endoscopic management is predicated on several assumptions: first, the fluid collection must be mature (completely walled-off); in addition, the collection wall must be adherent to the bowel lumen to facilitate transluminal puncture into the pseudocyst; and finally, the collection must be >6 cm to increase the likelihood of successful to the cystic contents.<sup>2</sup> The development of a pseudoaneurysm (discussed later) is an absolute contraindication for endoscopic drainage due to the risk of accidental vascular injury and potential large-volume hemorrhage. For these reasons, endoscopic drainage is not always a viable choice. It is also worth noting that, due to the nature of the contents of WOPN, they frequently require multiple or combined means for drainage, as endoscopic drainage alone has lower success rates in WOPN when compared to its pseudocyst counterpart.<sup>4,6</sup>

#### Infection

Both ANC and WOPN are sterile on initial formation but have the potential to become infected. The rate of infection in ANC and WOPN is notably higher than their edematous non-necrotic counterparts, with approximately 1/3 of patients with pancreatic necrosis developing infection.<sup>7</sup> Despite this increased risk, prophylactic antibiotics are not routinely indicated given the potential adverse effects of broad-spectrum antibiotics and difficulty in predicting infections due in part to the lack of correlation between extent of necrosis and risk of developing a subsequent infection. When they occur, infections are most frequently monomicrobial secondary to an enteric organism, such as Escherichia, Pseudomonas, Klebsiella, or Enterococcus species. Signs of developing or fulminant pancreatic infections are consistent with those of traditional systemic infectious response, typified by leukocytosis, fevers, and hemodynamic decompensation. The mainstay of treatment for infected pancreatic necrosis is IV antibiotics with or without debridement, with surgical interventions tailored to the patient's individual clinical course. In patients who do not improve promptly with intravenous antibiotics, necrosectomy (i.e., surgical debridement) is performed. In clinically stable patients, however, delaying debridement with a prolonged course of antibiotics may reduce the extent of necrotic tissue or potentially even completely resolve the infection, thereby eliminating the need for surgical management entirely.

#### Vascular Complications

##### Splanchnic Venous Thrombosis

Thrombosis of the splanchnic venous system, including the portal, splenic, and superior mesenteric veins, has been identified in up to as many as 24% of patients with acute pancreatitis.<sup>8</sup> Though

the exact etiology of thrombosis is unclear, it is theorized that clot formation may stem from local inflammation or mass effect from nearby peri-pancreatic fluid collections. A 2011 prospective study by Gonzelez et al following 127 consecutive patients with acute pancreatitis found that 20 patients had splanchnic venous thrombosis and all were associated with severe, acute pancreatitis.<sup>12</sup> In affected patients, the splenic vein was most commonly implicated, followed by the portal vein and the superior mesenteric vein, respectively.<sup>12</sup> Of note, 19 of the 20 patients with splanchnic venous thrombosis also had adjacent peri-pancreatic fluid collections. The sequelae of splenic vein thromboses include liver dysfunction, portal hypertension, and variceal formation. Supportive therapy of the underlying pancreatitis is the mainstay of treatment; however, extension of the clot into the portal vein or mesenteric veins with resultant liver or bowel compromise may warrant anticoagulation.

#### Pseudoaneurysm

Approximately 10% of patients with pancreatic fluid collections may develop pseudoaneurysms. These can form independently as a primary pseudoaneurysm due to direct vascular injury or by arterial rupture into a pseudocyst, ultimately forming a pseudoaneurysm. Risk factors for pseudoaneurysm formation include peri-pancreatic fluid collections, sepsis, multi-organ failure, long term anticoagulation, underlying vasculitis, necrotizing pancreatitis, and previous pancreatic necrosectomy.<sup>10</sup> Pseudoaneurysms may expand rapidly and rupture into the peritoneal cavity, retroperitoneum, or adjacent bowel with potentially catastrophic consequences. Therefore, patients with rapidly expanding pancreatic fluid collections, a sudden drop in hemoglobin, or evidence of gastrointestinal hemorrhage should raise suspicion of possible pseudoaneurysm formation. Computed tomography with arterial phase contrast can be useful in detecting and evaluating pseudoaneurysms, though digital subtraction angiography remains the gold standard for diagnosis. Pseudoaneurysms most commonly develop in the splenic artery, though they may also occur within the hepatic and gastroduodenal arteries.<sup>11</sup> Intervention should occur rapidly once identified, as the mortality from complications is exceedingly high. There are numerous techniques for management including endovascular management (coiling or foam), ultrasound-guided percutaneous thrombin injections, or open surgical management. Angiographic management is preferred as it is less invasive and allows easier access and more concise identification of the bleeding vessels, which are frequently deep within the friable pancreatic parenchyma. However, angiography is reserved for relatively stable patients, and those who are unstable or who have failed angiography often require surgical management.<sup>11</sup>

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#### Abdominal Compartment Syndrome

Abdominal compartment syndrome is defined as a sustained intra-abdominal pressure above 20 mmHg with new onset organ failure. Patients with severe pancreatitis, those who underwent substantial fluid volume replacement, with ascites, or

<b>Pancreatitis Treatment</b>
Fluid Resuscitation Pain Management
<b>Pancreatitis Complications</b>
<b>Local Complications</b> - Pseudocyst - Necrosis - Infection
<b>Vascular Complications</b> - Splanchnic venous thrombosis - Pseudoaneurysm
<b>Abdominal Compartment Syndrome</b>

Table 5: Table outlining acute pancreatitis management and complications to consider

Acute Pancreatitis  
*continued on page 12*



## Acute Pancreatitis

continued from page 11

those with significant peri-pancreatic edema are at higher risk of developing abdominal compartment syndrome.<sup>13</sup> For this reason, patients with severe pancreatitis or in the ICU should have regular bladder pressure monitoring. Management is the same as that for abdominal compartment syndrome due to other causes.

### Summary

Acute pancreatitis is a disease process frequently encountered in the emergency room and, when severe, can carry a high mortality. It is diagnosed by two of the following: lipase greater than three times the upper limit of normal; signs and symptoms of acute pancreatitis; or imaging findings. It can be characterized by morphology and severity. Gallstones are the most common cause of acute pancreatitis in the United States, followed by alcohol and various other etiologies. Management focuses on adequate fluid resuscitation, pain control, and oral nutrition as tolerated. Notably, antibiotics are not standard of care in acute pancreatitis without proven infection. Complications of acute pancreatitis include peripancreatic fluid collections, infection, abdominal compartment syndrome, and local vascular complications.

1. Cui, M. L., Kim, K. H., Kim, H. G., Han, J., Kim, H., Cho, K. B., ... & Kim, T. N. (2014). Incidence, risk factors and clinical course of pancreatic fluid collections in acute pancreatitis. *Digestive diseases and sciences*, 59(5), 1055-1062.
2. Binmoeller, K. F. (2013). EUS-guided drainage of pancreatic fluid collections using fully covered self-expandable metal stents. *Gastroenterology & hepatology*, 9(7), 442.
3. Antillon, M. R., Shah, R. J., Stiegmann, G., & Chen, Y. K. (2006). Single-step EUS-guided transmural drainage of simple and complicated pancreatic pseudocysts. *Gastrointestinal endoscopy*, 63(6), 797-803.
4. Hookey, L. C., Debroux, S., Delhaye, M., Arvanitakis, M., Le Moine, O., & Deviere, J. (2006). Endoscopic drainage of pancreatic fluid collections in 116 patients: a comparison of etiologies, drainage techniques, and outcomes. *Gastrointestinal endoscopy*, 63(4), 635-643.
5. Keane, M. G., Sze, S. F., Cieplik, N., Murray, S., Johnson, G. J., Webster, G. J., ... & Pereira, S. P. (2016). Endoscopic versus percutaneous drainage of symptomatic pancreatic fluid collections: a 14-year experience from a tertiary hepatobiliary centre. *Surgical endoscopy*, 30(9), 3730-3740.
6. Baron, T. H., Harewood, G. C., Morgan, D. E., & Yates, M. R. (2002). Outcome differences after endoscopic drainage of pancreatic necrosis, acute pancreatic pseudocysts, and chronic pancreatic pseudocysts. *Gastrointestinal endoscopy*, 56(1), 7-17.
7. Banks, P. A., & Freeman, M. L. (2006). Practice guidelines in acute pancreatitis. *The American journal of gastroenterology*, 101(10), 2379.
8. Nadkarni, N. A., Khanna, S., & Vege, S. S. (2013). Splanchnic venous thrombosis and pancreatitis. *Pancreas*, 42(6), 924-931.
9. Balthazar, E. J. (2002). Acute pancreatitis: assessment of severity with clinical and CT evaluation. *Radiology*, 223(3), 603-613.
10. Sharma, P. K., Madan, K., & Garg, P. K. (2008). Hemorrhage in acute pancreatitis: should gastrointestinal bleeding be considered an organ failure? *Pancreas*, 36(2), 141-145.
11. Barge, J. U., & Lopera, J. E. (2012). Vascular complications of pancreatitis: role of interventional therapy. *Korean journal of radiology*, 13(Suppl 1), S45-S55.
12. Gonzalez, H. J., Sahay, S. J., Samadi, B., Davidson, B. R., & Rahman, S. H. (2011). Splanchnic vein thrombosis in severe acute pancreatitis: a 2-year, single-institution experience. *HPB*, 13(12), 860-864.
13. Working, G. I., & APA, A. P. G. (2013). IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology: official journal of the International Association of Pancreatology (IAP)*...[et al.], 13(4 Suppl 2), e1.
14. Banks, P. A., Bollen, T. L., Dervenis, C., Goosszen, H. G., Johnson, C. D., Sarr, M. G., ... & Vege, S. S. (2013). Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. *Gut*, 62(1), 102-111.
15. Crockett, S. D., Wani, S., Gardner, T. B., Falck-Ytter, Y., Barkun, A. N., Crockett, S., ... & Gupta, S. (2018). American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. *Gastroenterology*, 154(4), 1096-1101.
16. Sharma, V. K., & Howden, C. W. (2001). Prophylactic antibiotic administration reduces sepsis and mortality in acute necrotizing pancreatitis: a meta-analysis. *Pancreas*, 22(1), 28-31.
17. Wittau, M., Mayer, B., Scheele, J., Henne-Bruns, D., Dellinger, E. P., & Isenmann, R. (2011). Systematic review and meta-analysis of antibiotic prophylaxis in severe acute pancreatitis. *Scandinavian journal of gastroenterology*, 46(3), 261-270.
18. Bai, Y., Gao, J., Zou, D. W., & Li, Z. S. (2008). Prophylactic antibiotics cannot reduce infected pancreatic necrosis and mortality in acute necrotizing pancreatitis: evidence from a meta-analysis of randomized controlled trials. *The American journal of gastroenterology*, 103(1), 104.
19. Gardner, T. B., Vege, S. S., Chari, S. T., Petersen, B. T., Topazian, M. D., Clain, J. E., ... & Sarr, M. G. (2009). Faster rate of initial fluid resuscitation in severe acute pancreatitis diminishes in-hospital mortality. *Pancreatology*, 9(6), 770-776.
20. Wardorf, M. G., Kurtzman, J. T., Bartel, M. J., Cox, M., Mackenzie, T., Robinson, S., ... & Gardner, T. B. (2011). Early fluid resuscitation reduces morbidity among patients with acute pancreatitis. *Clinical gastroenterology and hepatology*, 9(8), 705-709.
21. Wu, B. U., Hwang, J. Q., Gardner, T. H., Repas, K., Delee, R., Yu, S., ... & Conwell, D. L. (2011). Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. *Clinical Gastroenterology and Hepatology*, 9(8), 710-717.
22. Wu, B. U., Bakker, O. J., Papachristou, G. I., Besselink, M. G., Repas, K., van Santvoort, H. C., ... & Banks, P. A. (2011). Blood urea nitrogen in the early assessment of acute pancreatitis: an international validation study. *Archives of internal medicine*, 171(7), 669-676.
23. Janisch, N. H., & Gardner, T. B. (2016). Advances in management of acute pancreatitis. *Gastroenterology Clinics*, 45(1), 1-8.
24. Radnay, P. A., Brodman, E., Mankikar, D., & Duncaif, D. (1980). The effect of equi-analgesic doses of fentanyl, morphine, meperidine and pentazocine on common bile duct pressure. *Survey of Anesthesiology*, 24(6), 382.
25. Lenhart, D. K., & Balthazar, E. J. (2008). MDCT of acute mild (nonnecrotizing) pancreatitis: abdominal complications and fate of fluid collections. *American Journal of Roentgenology*, 190(3), 643-649.
26. Forsmark, C. E., & Baillie, J. (2007). AGA Institute technical review on acute pancreatitis. *Revista de gastroenterologia de Mexico*, 72(3), 257-281.

## Hypokalemia

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level, this can be used to estimate the amount of potassium needed to correct the patient's hypokalemia. Oral potassium is the preferred route of administration with intravenous potassium reserved for patients with ECG changes, physical signs or symptoms of hypokalemia, inability to tolerate potassium by mouth or severe hypokalemia (<2.5 mEq/L). Intra-

venous potassium correction should not exceed 20 mmol/hour except for emergent situations where central venous access is available.<sup>9</sup> Administration of potassium at rates exceeding 20 mmol/hour may cause cardiac toxicity, including arrhythmias and cardiac arrest. Patients should be monitored on a continuous cardiac monitor and the serum potassium level should be measured hourly when intravenous potassium is administered at rates exceeding 20 mmol/hour. Additionally, infusion site checks should be conducted regularly as high concentrations administered via a peripheral line can cause phlebitis and pain.<sup>10</sup> Identification and treatment of concurrent hypomagnesemia are also important because magnesium depletion impedes potassium repletion and can exacerbate hypokalemia-induced rhythm disturbances.<sup>11,12</sup> Dextrose containing solutions can worsen hypokalemia and should not be used as the replacement fluid. All patients should have cardiac monitoring while potassium is being replaced intravenously.

### Potassium Administration

- Administer potassium at 10-20 mEq/h IV, 40mEq orally if able
- Can administer potassium at 40 mEq/h with life-threatening hypokalemia
- Consider giving empiric 2g magnesium as patient will be unable to absorb potassium effectively if hypomagnesimic

Table 6: Recommendations on treating hypokalemia

### Summary

While hyperkalemia is the more commonly encountered and feared complication of abnormal potassium homeostasis, hypokalemia too can be devastating. When concerned for hypokalemia always assess the cardiac and neurologic status, confirm the diagnosis with repeat labs if time/acuity permits, and initiate treatment early once the diagnosis is made. Oral and intravenous potassium are the initial treatment. Simultaneous magnesium administration should be considered particularly if magnesium levels are unknown. All patients should have EKGs performed to assess for cardiac abnormalities. Initial efforts should be focused on replacement and resuscitation but exploring the potential etiology of the patient's hypokalemia can serve to guide inpatient management.

1. Paice BJ, Paterson KR, Onyanga-Omara F, Donnelly T, Gray JM, Lawson DH. Record linkage study of hypokalaemia in hospitalized patients. *Postgrad Med J*. 1986;62(725):187-191.
2. Lippi G, Favaloro EJ, Montagnana M, Guidi GC. Prevalence of hypokalaemia: the experience of a large academic hospital. *Intern Med J*. 2010;40(4):315-316.
3. Liamis G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ. Electrolyte disorders in community subjects: prevalence and risk factors. *Am J Med*. 2013;126(3):256-263.
4. Morgan DB, Davidson C. Hypokalaemia and diuretics: an analysis of publications. *Br Med J*. 1980;280(6218):905-908.
5. Gennari FJ. Hypokalemia. *N Engl J Med*. 1998;339(7):451-458.
6. Girish MP, Gupta MD, Mukhopadhyay S, Yusuf J, Sunil Roy TN, Trehan V. U wave: an important noninvasive electrocardiographic diagnostic marker. *Indian Pacing Electrophysiol J*. 2005 Jan 1;5(1):63-5.
7. Huang, Chou-Long, and Elizabeth Kuo. "Mechanism of Hypokalemia in Magnesium Deficiency." *Journal of the American Society of Nephrology*, vol. 18, no. 10, 2007, pp. 2649-2652. doi:10.1681/asn.200707092.
8. Macdonald JE, Struthers AD. What is the optimal serum potassium level in cardiovascular patients? *J Am Coll Cardiol*. 2004;43(2):155-161.
9. Kim GH, Han JS. Therapeutic approach to hypokalemia. *Nephron*. 2002;92(suppl 1):28-32.
10. Gray A, Wright J, Goodey V, Bruce L. *Injectable Drugs Guide*. London: Pharmaceutical Press; 2011: p699-702
11. Whang R, Whang DD, Ryan MP. Refractory potassium repletion. A consequence of magnesium deficiency. *Arch Intern Med*. 1992;152(1):40-45.
12. Millane TA, Ward DE, Camm AJ. Is hypomagnesemia arrhythmogenic? *Clin Cardiol*. 1992;15(2):103-108.
13. Weiner ID, Wingo CS. Hypokalemia—consequences, causes, and correction. *J Am Soc Nephrol*. 1997;8(7):1179-1188.
14. Gennari FJ. Disorders of potassium homeostasis. Hypokalemia and hyperkalemia. *Crit Care Clin*. 2002;18(2):273-288.

To Learn more on Hypokalemia EKGs - turn to  
**EKG Corner** on the Back Cover

## Traumatic Rupture

*continued from page 7*

tures and 17% for right-sided ruptures.<sup>11,12</sup> Ultrasound can also be used to evaluate the diaphragm, looking for discontinuity of the structure and herniation of the liv

er or bowel loops; however, its use is not standardized and thus cannot be used to exclude the diagnosis.<sup>13,14</sup> Furthermore, plain radiographs and ultrasound will largely depend on bowel content herniation as an obvious sign of diaphragm rupture, but several studies have postulated that positive pressure ventilation in intubated patients will obscure this finding by inhibiting the degree of herniation into the thoracic cavity. As such, providers must be cautious when using these imaging modalities to rule out diaphragmatic injury in intubated and mechanically ventilated patients.

In general, CT imaging is more useful in detecting these injuries, though studies attribute a variable sensitivity and specificity to the modality of 61-87% and 72-100%, respectively. There are several radiographic findings that can assist with making the diagnosis. The discontinuity sign, or obvious discontinuation of the normal curvature of the diaphragm on imaging, and diaphragmatic thickening sign are the most common radiologic findings. The collar sign (hour-glass constriction at the level of the injured diaphragm as herniated hollow viscus is forced into the thoracic cavity) and dependent viscera signs (found in supine patients where herniated hollow viscous are found dependent along the posterior ribs) were almost exclusively found in blunt trauma patients, and the dangling diaphragm sign (free edge of the torn diaphragm curves in on itself) and organ herniation signs were seen more commonly in patients with blunt trauma. Unfortunately, CT imaging still has a wide range of sensitivity, especially if the injury is on the right where homogeneity between the liver and diaphragm can obscure potential findings.<sup>15</sup> The gold standards for diagnosing diaphragmatic injuries remain more invasive techniques such as diagnostic laparoscopy, thoroscopy, or open surgical exploration.<sup>16</sup>

## Management

Management of patients with diaphragm injury depends largely on timing of diagnosis, laterality and extent of injury. According to the Eastern Association for the Surgery of Trauma (EAST) guidelines, right-sided injuries may require repair, but if small and asymptomatic with a hemodynamically stable patient, supportive care and nonoperative observation may be a feasible treatment option. Conversely, the majority of left-sided diaphragmatic injuries will require repair, though it may be delayed depending on extent and severity of associated injuries.<sup>16</sup> Regardless of degree of injury, if diaphragm injury is diagnosed in the ED, the first steps include decompressing the stomach with a gastric tube and providing supportive care.

Mortality rates from diaphragmatic injury depend on the mechanisms and presence of associated injuries. In addition to the aforementioned complications of bowel herniation and possible strangulation of abdominal organs, other possible complications include diaphragmatic paralysis, pulmonary complications, and biliary fistulas which can evolve with combined injury to the

liver, diaphragm, and lung.<sup>17</sup> Diaphragmatic paralysis may develop as a result of phrenic nerve injury, which occurs most often with high cervical spine or penetrating neck trauma, but can also occur as a result of diaphragmatic tears. The contraction of the diaphragm is responsible for 75-80 % of a healthy individual's tidal volume, so if patient sustains an injury resulting in a paralyzed hemidiaphragm, then lung capacity may decrease as much as 20-30%. These patients may be eventual candidates for diaphragmatic plication.

The National Trauma Data Bank (NTDB) reports an overall mortality for patients with diaphragmatic injury of 25%.<sup>2</sup> In a study using data from NTDB, patients with blunt diaphragmatic injury had both a significantly higher mortality rate (19.8% v 8.8%) and higher rate of pulmonary complications (14.8% v 6.6%) compared to those with penetrating trauma.<sup>3</sup> If patient presentation is delayed such that abdominal contents become incarcerated, then mortality increases to 20%, and mortality further increases to 40-57% if bowel strangulation develops.<sup>18</sup>

## Summary

Traumatic diaphragmatic rupture is a relatively rare injury that may be present in both blunt and penetrating trauma patients and frequently occurs in conjunction with other thoracic and abdominal injuries. It is a challenging diagnosis to make, necessitating a high index of suspicion based on injury mechanism, exam, and associated injuries. Chest radiography has poor sensitivity in detecting injuries, so CT is the primary imaging modality used to diagnose diaphragmatic injury. Without intervention, the size of the diaphragmatic defects generally increases over time. Herniation of abdominal viscera with subsequent ischemia and infarction is the most common complication of traumatic diaphragmatic ruptures; however, the injury can also precipitate important pulmonary complications, diaphragmatic paralysis, and fistulas.

1. Trauma, 6, Feliciano, DV, Mattox, KL, Moore, EF (Eds), McGraw-Hill, 2008.

2. National Trauma Data Base. American College of Surgeons 2000-2004. <https://ntdbdatacenter.com/> (Accessed on January 01, 2005).

3. Fair KA, Gordon NT, Barbosa RR, Rowell SE, Watters JM, Schreiber MA. Traumatic diaphragmatic injury in the American College of Surgeons National Trauma Data Bank: a new examination of a rare diagnosis. *Am J Surg.* 2015;209(5):864.

4. Lochum S, Ludwig T, Walter F. Imaging of diaphragmatic injury: a diagnostic challenge? *Radiographics.* 2002; 22:103-108

5. Waldhausen JA, Kilman JW, Helman CH, et al. The diagnosis and management of traumatic diaphragmatic injuries of the diaphragm including the use of marlex prostheses. *J Trauma* 1966;6:332-43.

6. de la Rocha AG, Creel RJ, Mulligan GW, et al. Diaphragmatic rupture due to blunt abdominal trauma. *Surg Gynecol Obstet* 1982;154:175-80.

7. Asensio JA, Petrone P. Diaphragmatic injury. *Current Surgical Therapy.* 2004; :946-955

8. Moore EE, Malangoni MA, Cogbill TH, Shackford SR, Champion HR, Jurkovich G, McAninch JW, Trafton PG. Organ injury scaling IV: Thoracic vascular, lung, cardiac, and diaphragm. *J Trauma - Injury, Infection, and Critical Care.* 1994; 36 (3): 299-300

9. Williams M, Carlin AM, Tyburski JG, Blocksom JM, Harvey EH, Steffes CP, Wilson RE. Predictors of mortality in patients with traumatic diaphragmatic rupture and associated thoracic and/or abdominal injuries. *Am Surg.* 2004;70(2):157.

10. Shanmuganathan K, Killeen K, Mirvis SE, White CS. Imaging of diaphragmatic injuries. *J Thorac Imaging.* 2000;15(2):104.

11. Gelman R, Mirvis SE, Gens D. Diaphragmatic rupture due to blunt trauma: sensitivity of plain chest radiographs. *AJR Am J Roentgenol.* 1991; 156: 51-57.

12. Killeen KL, Mirvis SE, Shanmuganathan K. Helical CT of diaphragmatic rupture caused by blunt trauma. *AJR Am J Roentgenol.* 1999;173 (6): 1611-6.

13. Blaivas M, Brannam L, Hawkins M, Lyon M, Sriram K. Bedside emergency ultrasonographic diagnosis of diaphragmatic rupture in blunt abdominal trauma. *Am J Emerg Med.* 2004;22(7):601.

14. Gangahar R, Doshi D. FAST scan in the diagnosis of acute diaphragmatic rupture. *Am J Emerg Med.* 2010;28(3):387.e1.

15. Panda A, Kumar A, Gamanagatti S, Patil A, Kumar S, Gupta A. Traumatic diaphragmatic injury: a review of CT signs and the difference between blunt and penetrating injury. *Diagn Interv Radiol.* 2014;20(2):121.

16. McDonald AA, Robinson BRH, Alarcon L, Bosarge PL, Dorion H, Haut ER, Juern J, Madbak F, Reddy S, Weiss P, Como JJ. Evaluation and management of traumatic diaphragmatic injuries: A Practice Management Guideline from the Eastern Association for the Surgery of Trauma. *J Trauma Acute Care Surg.* 2018;85(1):198.

17. Petrone P, Leppaniemi A, Inaba K, Soreid e K, Asensio JA. Diaphragmatic injuries: challenges in the diagnosis and management. *Trauma.* 2007;9:227-36

18. Sullivan RE. Strangulation and obstruction in diaphragmatic hernia due to direct trauma. Report of two cases and review of the English literature. *J Thorac Cardiovasc Surg.* 1966; 52 (5): 725.

## Malaria

*continued from page 5*

and ovale infection can present even years later due to activation of residual hypnozoites.

Fever and headache are two of the most common symptoms in patients with malaria. Otherwise, initial symptoms of uncomplicated malaria are non-specific and may include malaise, lightheadedness, chills, myalgias, arthralgias, cough, abdominal pain, anorexia, and nausea. On examination, providers may find evidence of anemia, splenomegaly, hepatomegaly, jaundice, in addition to vital sign abnormalities such as fever, tachycardia, and tachypnea. Given the breadth and variability of presentation, it is unsurprising that uncomplicated malaria is often misdiagnosed as influenza, hepatitis, gastroenteritis, or meningitis.<sup>9,10</sup>

All patients who are suspected of having malaria should be assessed for features of severe malaria, which differs between adults and children and necessitates a different treatment regimen. *P. falciparum* and *P. knowlesi* are the most likely to progress to severe malaria. Severe malaria is thought to develop in part from the sequestration and cytoadherence of infected red blood cells in smaller caliber vasculature. Essentially, red blood cells become adherent to the walls of capillaries, precipitating peripheral and cerebral hypoxia, capillary leakage, cytokine-driven inflammatory response, and multisystem organ dysfunction.

Clinical findings of severe malaria include altered consciousness with or without seizures, acute respiratory distress syndrome, hypotension, metabolic acidosis, acute kidney injury, hemoglobinuria (“blackwater fever” from high parasitemia), hepatic failure with or without jaundice, coagulopathy or disseminated intravascular coagulation, severe anemia (hemoglobin < 7 g/dL) or massive intravascular hemolysis, and hypoglycemia. The presence of any one of these features constitutes severe malaria.<sup>8,11,12</sup> In children with severe malaria, respiratory distress, anemia, convulsions and hypoglycemia are more common. Conversely, pulmonary edema, acute respiratory distress syndrome, and renal failure rarely occur in children, but are present in over half of all adult cases of severe malaria. In patients with severe malaria, case fatality rates range between 5-30%.<sup>9</sup>

Patients with cerebral malaria will present with impaired consciousness, delirium, and/or seizures. Focal neurologic signs and symptoms are unusual.<sup>8,13</sup> Cerebral malaria is a medical emergency because of its propensity to rapidly progress to coma and death. Even with treatment, mortality in patients with cerebral malaria is estimated at 15-20%.<sup>8</sup>

### Evaluation and Diagnosis

In light of malaria’s non-specific clinical presentation, patients should undergo a broad work-up, including blood cultures, CBC, BMP, LFTs, PT/INR, VBG, thick and thin peripheral blood smears, as well as non-contrast computed tomography of the head and a lumbar puncture to evaluate for meningitis or overt intracranial pathology. Malaria should be confirmed by either microscopy, which is the gold standard, or by rapid diagnostic testing. A thick blood smear assesses presence of the parasite whereas the thin smear facilitates identification of the species and percent parasitemia. A parasite load >4% parasitized red blood cells indicates severe malaria. If index of

days to months after the initial exposure. As demonstrated in this case, signs and symptoms of vivax

suspicion is high after an initial negative smear, it is recommended that peripheral blood smears be repeated every 12 hours until there are three negative smears, as the first smear is negative in up to 10% of patients.<sup>8,9,14</sup> Frequent finger stick blood glucose may be helpful as well given the frequency of hypoglycemia in malaria. Regardless, in highly suspicious cases, absence of parasitemia should not delay initiation of antimalarial therapy.<sup>9</sup> The CDC Yellow Book is also a useful resource for both patients and clinicians, as it contains the most up-to-date travel health guidelines, including disease-specific guidance regarding vaccination, chemoprophylaxis, and preventive measures.<sup>15</sup>

### Management and Treatment

Once the diagnosis of malaria is confirmed, even without identifying a specific species, initiation of prompt, appropriate antimalarial therapy and supportive care are of paramount importance. Treatment is determined by the severity of presentation, species of malaria, and region-specific incidence of antimalarial resistance stemming from where the patient was likely exposed. If the species is not yet known, it is reasonable to treat the patient for suspected *P. falciparum* infection and deescalate as appropriate.

For uncomplicated falciparum malaria, almost all patients should be initiated on monotherapy with either atovaquone-proguanil (Malarone) or artemether-lumefantrine (Coartem), as both agents remain effective in spite of the increasing prevalence of chloroquine-resistant *P. falciparum*. Alternative, and less commonly used, agents include artesunate-mefloquine, artesunate-amodiaquine, and dihydroartemisinin-piperaquine. Given the potential teratogenicity of the aforementioned agents during organogenesis, uncomplicated *P. falciparum* malaria occurring during the first trimester is treated with quinine and clindamycin. In the second and third trimesters, however, women can be treated with the same medication regimens used for non-pregnant patients. *P. knowlesi* should be treated in the same

Antibiotics for Malarial Infections	
<b><i>P. falciparum</i></b> <b><i>P. knowlesi</i></b>	
Most common: Atovaquone-proguanil (Malarone) Artemether-lumefantrine (Coartem)	Less common: Artesunate-mefloquine Artesunate-amodiaquine Dihydroartemisinin-piperaquine
Pregnancy: First trimester: quinine and clindamycin Second trimester: treat with non-pregnant regimen	
<b><i>P. malariae</i></b>	<b><i>P. vivax</i></b> <b><i>vP. ovale</i></b>
Chloroquine	Chloroquine + Primaquine* or Tafenoquine*
	*prevent relapsing malaria due to dormant hypnozoite activation *can precipitate hemolytic anemia in G6PD deficiency

Table 7: Treatment regimens for malaria depending on speciation and population



manner as falciparum given its propensity to cause severe infection. Patients with uncomplicated, confirmed *P. vivax*, *P. malariae*, or *P. ovale* infection can be treated with chloroquine unless the patient has suspected exposure to chloroquine-resistant *P. vivax*. Patients with *P. vivax* or *P. ovale* should also receive primaquine or the newly FDA-approved tafenoquine to prevent relapsing malaria that occurs due to dormant hypnozoite activation. Of note, both primaquine and tafenoquine can precipitate hemolytic anemia in patients with G6PD deficiency, so admission and testing are recommended prior to initiation of this drug.

Patients with severe malaria, including women in all trimesters of pregnancy, require parenteral artesunate. Though artesunate, quinine, and quinidine may all be administered parenterally, artesunate has proven superior in reducing mortality in endemic populations. Furthermore, quinine therapy can exacerbate the hypoglycemia that often accompanies severe malaria, especially in pregnancy women. Quinidine is associated with substantial cardiotoxicity, ventricular arrhythmias, QT prolongation, and hypotension. Patients with hypotension or acidosis should receive cautious fluid resuscitation at the risk of volume overload and pulmonary edema. Benzodiazepines are an appropriate first line treatment for seizures. Given the association of severe malaria with concomitant bacterial sepsis, most often with nontyphoidal *Salmonella*, patients with cerebral malaria should receive concomitant broad-spectrum antibiotics pending negative blood culture results and clinical improvement.<sup>16</sup> Information on appropriate dosing and susceptibility of infecting parasites is available through the CDC and should be referenced as treatment is initiated.

The need to admit all patients with *P. falciparum* or unidentified *Plasmodium* species has been a point of controversy. There have been attempts to define triage criteria for patients requiring admission versus those appropriate for outpatient therapy; however, given American providers' relative inexperience with malaria and the potential for patients with *P. falciparum* to rapidly deteriorate, the CDC advises admission for these patients. This allows providers to tailor species-specific therapy, ensure that the medication is tolerated by the patient, and observe for clinical improvement or deterioration.<sup>17</sup> Regardless of severity, all cases of malaria and treatment thereof should be discussed in consultation with Infectious Disease clinicians to ensure appropriate dosing, follow-up, and surveillance reporting.

### Global Perspective

For health care providers who work with patients in endemic regions, it is useful to be aware of the variances in presentation, evaluation, and treatment of malaria. Rapid diagnostic tests (RDTs) are increasingly available in endemic countries and may be employed in patients with suspected malarial exposures. These tests can detect the presence of malaria parasite using a finger-prick blood sample and, depending on design, may variably detect one or multiple species. Malaria RDTs provide a useful and relatively reliable alternative to diagnosis if microscopy is not readily available, though they do not always provide information about species or degree of parasitemia.

Patients may present at a later, more severe stage of their disease course, which can present another challenge for providers operating in endemic regions. Patients may experience significant barriers to accessing care secondary to local conflict, displacement, logistical and economic barriers, poor infrastructure, and sociocultural reti-

cence in seeking care. Thwing et al. estimated that fewer than half of those who suffer severe malaria are able to reach a health facility and, assuming a case-fatality rate of 90% at home and 20% in hospital, estimate the global annual incidence of severe malaria to be approximately 2 million.<sup>19</sup> As such, it is important to carefully screen patients for signs and symptoms consistent with severe malaria in these settings and to escalate treatment to parenteral antimalarials as appropriate and if available.

Finally, the prevalence of antimalarial resistance varies significantly geographically. *P. falciparum* is almost entirely resistant to chloroquine and antifols, so the aforementioned artemisinin-based combination treatments are recommended as first-line treatment for uncomplicated malaria. An unfortunate and evolving challenge in malaria treatment is the increasing prevalence of substandard and falsified antimalarials. A 2017 World Health Organization report estimated that at least 69,000 individuals die as a result of reduced effectiveness, substandard or falsified antimalarials each year.<sup>20</sup> Global surveillance programs are working to address the issue, starting with greater scrutiny of the medication supply chain.

Ultimately, malaria remains one of the foremost global health problems, causing tremendous morbidity, mortality, and socioeconomic distress in endemic regions. However, the global community continues to levy incredible resources and attention not only to the treatment of malaria, but also to innovative means of preventing its transmission – from malaria hot spot targeting to impregnated bed nets that target the parasite rather than the vector.

### Summary

Malaria is a devastating disease that exacts a tremendous toll on human health and productivity worldwide. Cases in the U.S. are observed among those who have lived or traveled in endemic regions, but diagnosis requires a high index of suspicion as the symptoms can be non-specific. A thorough travel history – including places visited, malaria prophylaxis taken, and previous infection – is important. Peripheral blood smears detailing presence of malaria, percent parasitemia, and speciation, are key to both diagnosis and appropriate treatment. In patients diagnosed with *P. falciparum* or *P. knowlesi* malaria or suspected of having severe malaria, prompt initiation of antimalarial therapy is critical as these patients can decompensate rapidly.

1 Malaria's Impact Worldwide. [https://www.cdc.gov/malaria/malaria\\_worldwide/impact.html](https://www.cdc.gov/malaria/malaria_worldwide/impact.html). Accessed on 3/12/2019.  
2 Malaria. <https://www.who.int/news-room/fact-sheets/detail/malaria>. Accessed on 3/12/2019.  
3 Mace, KE, Arguin PM, Tan KF. Malaria Surveillance – United States, 2015. *MMWR Surveillance Summary*. 2018; 67 (7): 1-28.  
4 Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature*. 2005; 434 (7030): 214.  
5 Price RN, Tjitra E, Guerra CA, Yeung S, White NJ, Anstey NM. *Vivax* malaria: neglected and not benign. *American Journal of Tropical Medicine and Hygiene*. 2007; 77 (6 Supplementary): 79.  
6 Mueller I, Zimmerman PA, Reeder JC. *Plasmodium malariae* and *Plasmodium ovale* – the “bashful” malaria parasites. *Trends in Parasitology*. 2007; 23 (6): 278.  
7 White NJ. *Plasmodium knowlesi*: the fifth human malaria parasite. *Clinical Infectious Disease*. 2008; 46 (2): 172.  
8 Malaria: Biology. <https://www.cdc.gov/malaria/about/biology/index.html>. Accessed on 3/13/2019.  
9 Walker NF, Nadim B, Whitty CJ. Special Situations: Malaria. *Medicine*. 2014; 42 (2): 100-106.  
10 Molyneux, Malcolm. Malaria. In *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*, 8e. Eds. Judith E. Tintinalli et al. New York, NY: McGraw-Hill, 2016. <http://accessmedicine.mhmedical.com/content.aspx?bookid=16588&sectionid=109413077>.  
11 Treatment of Malaria: Guidelines for Clinicians (United States). [https://www.cdc.gov/malaria/diagnosis\\_treatment/clinicians2.html](https://www.cdc.gov/malaria/diagnosis_treatment/clinicians2.html). Accessed on 3/15/2019.  
12 Mung'ala-Odera V, Snow RW, Newton CR. The burden of neurocognitive impairment associated with *Plasmodium falciparum* malaria in sub-Saharan Africa. *American Journal of Tropical Medicine and Hygiene*. 2004; 71 (2 Supplementary): 63.  
13 Severe Malaria. *Tropical Medicine & International Health*. 2014; 19 Supplementary: 7-131.  
14 Helman, A, Meshkat, N, Muller, M. Fever in the Returning Traveler. *Emergency Medicine Cases*. March, 2016. <https://emergencymedicinescases.com/fever-returning-traveler/>. Accessed on 3/14/2019.  
15 Centers for Disease Control and Prevention. *CDC Yellow Book 2018: Health Information for International Travel*. New York: Oxford University Press; 2017.  
16 Ashley EA, Aung PP, Woodrow CJ. Malaria. *The Lancet*. 2018; 391: 1608-1621.  
17 Griffith KS, Lewis LS, Mali S. Treatment of Malaria in the United States: A Systematic Review. *JAMA*. 2007; 297 (20): 2264-2277.  
18 How malaria RDTs work. World Health Organization. <https://www.who.int/malaria/areas/diagnosis/rapid-diagnostic-tests/about-rdt/en/>. Accessed on 3/29/2019.  
19 Thwing J, Eisele TP, Steketee RW. Protective efficacy of malaria case management and intermittent preventive treatment for preventing malaria mortality in children: a systematic review for the Lives Saved Tool. *BMC Public Health*. 2011; 11 (Suppl 3): S14.  
20 A study on the public health and socioeconomic impact of substandard and falsified medical products. Geneva: World Health Organization; 2017.

# EKG focus

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An elderly male presents to the emergency department with complaints of dehydration after several days of profuse, watery diarrhea and emesis. The patient complains of persistent nausea even after treated with a 5-HT3 antagonist and is written for 1.25 mg of intravenous droperidol. Minutes after receiving the medications, the patient becomes diaphoretic and complains of severe chest pain before becoming unresponsive. Cardiac monitoring reveals polymorphic, wide-complex tachycardia. The patient is defibrillated once with return of spontaneous circulation. A subsequent 12-lead EKG reveals pronounced U-waves and a QTc of 640 ms. The patient's bloodwork returns with a serum potassium of 2.4 mEq/L.

Hypokalemia is a metabolic derangement marked by abnormally low serum concentrations of the potassium ion, typically defined as <3.5 mEq/L. Numerous pathologic processes may precipitate hypokalemia, but common causes include gastrointestinal volume losses (e.g., emesis, diarrhea, short gut syndrome), prolonged or high-dose diuretic use, malnutrition, and iatrogenic causes (such as the use of beta-adrenoreceptor agonists and insulin). Found primarily within the cytosol of both cardiomyocytes and somatic cells, potassium plays an important role in re-establishing the transmembrane potential necessary for normal conduction of electromechanical impulses through the heart (as well as neurons and myocytes). Consequently, severe reductions in potassium stores may lead to problems with cellular repolarization.

Electrocardiographically, hypokalemia first manifests as flattening or inversion of T-waves. With more severe losses (typically <3.0 mEq/L), patients may evince QT-prolongation, the evolution of U-waves (most notably in the precordial leads), and even ventricular extrasystoles. Hypokalemia below 2.3 mEq/L is associated with increased risk of polymorphic ventricular tachydysrhythmias (e.g., torsades de pointes, ventricular fibrillation)

On identifying patients with electrocardiographic stigmata of

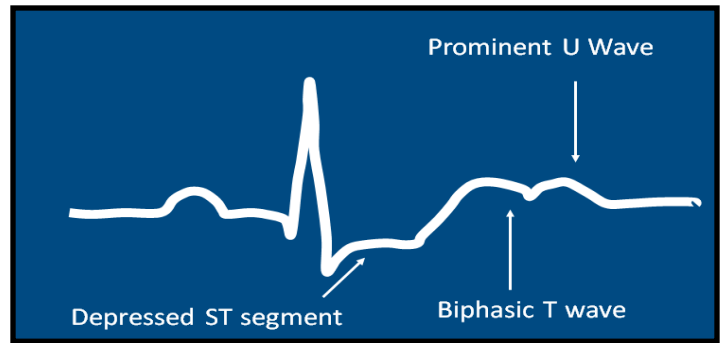


Figure 2: EKG depicting biphasic T wave and U wave that can be found as early changes in hypokalemia.

hypokalemia, emergency providers should act promptly to replete the patient's potassium stores. Magnesium supplementation is often administered concomitantly with potassium given the high concurrence of hypomagnesemia with hypokalemia. Furthermore, patients' hypokalemia may prove refractory to repletion without magnesium, possibly secondary to magnesium-mediated resorption of potassium from the distal renal tubule. QT-prolonging agents and medications that reduce extracellular potassium stores should be used judiciously and with caution. Tachydysrhythmias should be ablated with electrical cardioversion/defibrillation; patients with persistent or recurrent episodes of polymorphic ventricular tachycardia may benefit from overdrive pacing, given the rate-dependent shortening of the QT-interval. Antiarrhythmic medications should be used with extreme caution as many also prolong the QT-interval and decrease heart rate, paradoxically increasing the risk of early afterdepolarization (the so-called "R on T phenomenon").



Figure 3: EKG depicting ventricular dysrhythmias that can be found in severe hypokalemia. EKG courtesy of Creative Commons SA-4.0 via LlifeinTheFastLane

1. Widimsky, P. (2008). Hypokalemia and the heart. *e- Journal of Cardiology Practices*, 7(9).
2. Kjeldsen K. (2010). Hypokalemia and sudden cardiac death. *Experimental and clinical cardiology*, 15(4), e96-e99.
3. Chua, C. E., Choi, E., & Khoo, E. Y. H. (2018). ECG changes of severe hypokalemia. *QJM: An International Journal of Medicine*, 111(8), 581-582.
4. Lewis, J. (2012). ECG Diagnosis: Hypokalemia. *The Permanente Journal*, 16(2).
5. Huang, C.-L., & Kuo, E. (2007). Mechanism of Hypokalemia in Magnesium Deficiency. *Journal of the American Society of Nephrology*, 18(10), 2649-2652.

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