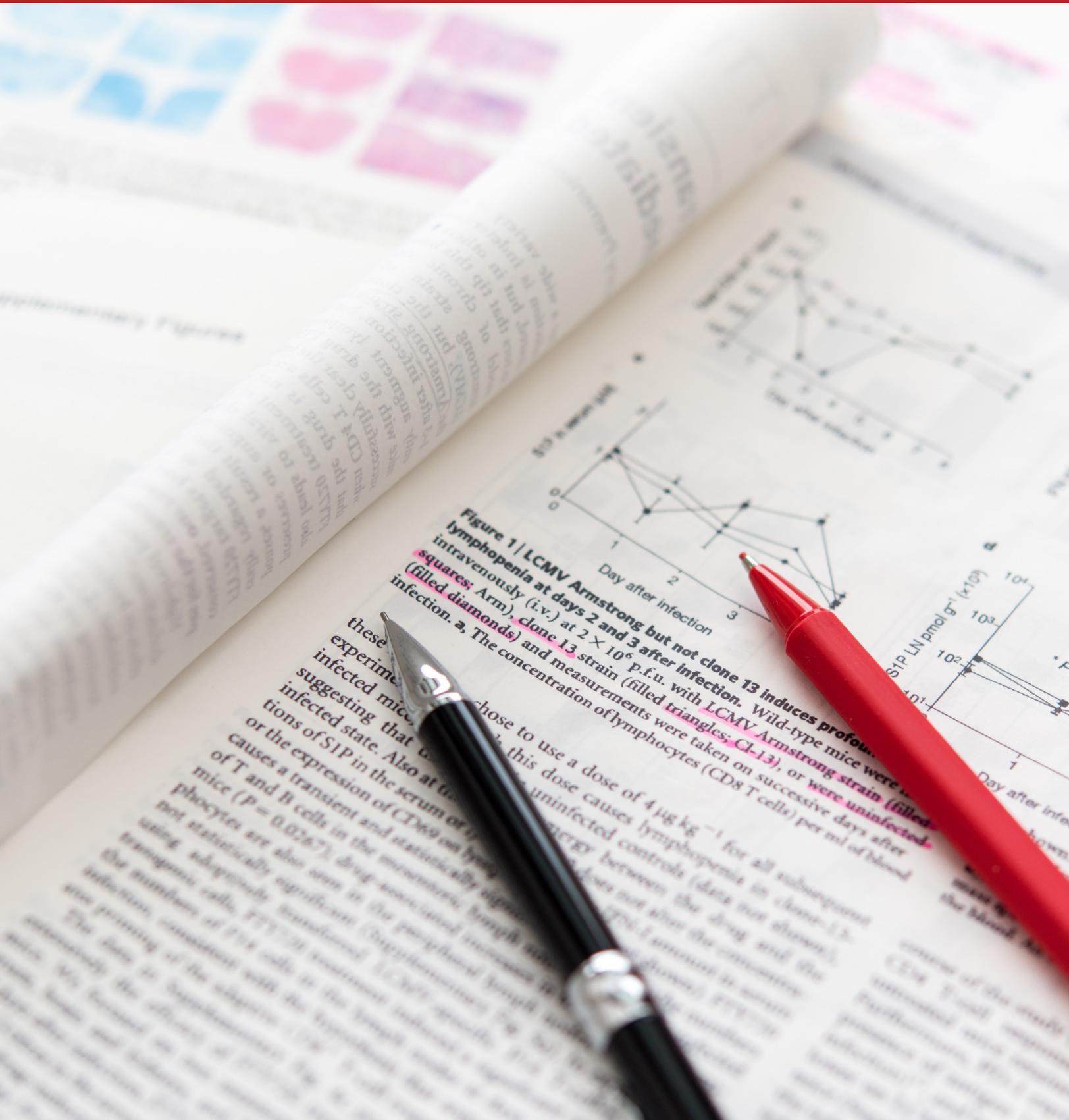


# Critical decisions

in emergency medicine

## THE 2025 LLSA LITERATURE REVIEW



**Figure 1 | LCMV Armstrong but not clone 13 induces profound lymphopenia at days 2 and 3 after infection.** Wild-type mice were intravenously (i.v.) at  $2 \times 10^6$  p.f.u. with LCMV Armstrong strain (filled squares; Arm), clone 13 strain (filled diamonds) and measurements were taken on successive days after infection. a, The concentration of lymphocytes (CD8 T cells) per ml of blood



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# The LLSA Literature Review

## Synopses of articles from ABEM's 2025 Lifelong Learning and Self-Assessment Reading List

### FROM THE EDITORS

Since April 2003, Critical Decisions in Emergency Medicine, ACEP's monthly CME publication, has included the feature "The LLSA Literature Review." The impetus for this section was our desire to provide ACEP members with yet another tool to use when preparing for the continuous certification initiative of the American Board of Emergency Medicine (ABEM), specifically the Lifelong Learning and Self-Assessment (LLSA) tests. Each year, as part of this program, ABEM has published a list of articles focused on selected portions of the emergency medicine core content. These articles become the LLSA reading list for that year, and the questions for the tests are drawn from these articles.

The EM 2025 LLSA reading list is the last ABEM will publish as they transition from the former 10-year certification cycle to a 5-year cycle. ABEM now offers Key Advances, and Critical Decisions in Emergency Medicine will continue to publish a "Literature Review" in each issue, covering current literature relevant to emergency physicians.

This online supplemental issue is, therefore, the last compilation of Critical Decisions in Emergency Medicine LLSA articles, it includes the 12 summaries of the EM 2025 LLSA reading list, which are intended to highlight the important concepts of each article. We are pleased to offer this benefit free to ACEP members and hope you find it useful. ACEP members can also download full versions of the articles by logging in at [acep.org/education/moccenter/llsa](https://www.acep.org/education/moccenter/llsa).

If you would like to see what else Critical Decisions has to offer (clinical lessons, ECG and imaging reviews, clinical cases in orthopedics and trauma, clinical pediatrics, drug reviews, and more), we invite you to explore ACEP Anytime, the online platform that houses Critical Decisions ([acep.org/acepanytime](https://www.acep.org/acepanytime)).

Best wishes,

**Andrew J. Eyre, MD, MS-HPEd, FACEP**, Section Editor

Brigham and Women's Hospital

Harvard Medical School, Boston, MA

**Danya Khoujah, MBBS, MEHP, FACEP**, Editor-in-Chief

University of Maryland, Baltimore, MD

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*Critical Decisions in Emergency Medicine* is the official CME publication of the American College of Emergency Physicians. Additional volumes are available.

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# Bystander CPR in Black and Hispanic Communities

By Anjali Misra, MD, MPH; and  
Andrew J. Eyre, MD, MS-HPed

Harvard Affiliated Emergency  
Medicine Residency Program, Boston,  
Massachusetts

### Objective

*On completion of this article, you should be able to:*

- Discuss the featured study's findings and its recommendations for increasing rates of bystander CPR in Black and Hispanic communities.

Garcia RA, Spertus JA, Girotra S, et al. Racial and ethnic differences in bystander CPR for witnessed cardiac arrest. *N Engl J Med*. 2022 Oct 27;387(17):1569-1578.

### KEY POINTS

- Bystander CPR is a time-critical, lifesaving intervention that can reduce the risk of anoxic brain injury and improve survival after OHCA.
- Regardless of whether OHCA occurred at home or in public, Black and Hispanic patients were less likely to receive bystander CPR than White patients. This disparity was observed across different neighborhood compositions and income strata.
- Potential strategies to address these disparities include improving access to bystander CPR training, dispatcher-assisted bystander CPR, and the overall 911 response system in Black and Hispanic communities.

For patients who experience out-of-hospital cardiac arrest (OHCA), bystander CPR is a time-critical, lifesaving intervention that can reduce the risk of anoxic brain injury and improve survival. Communities that are predominantly Black or Hispanic have been shown to have lower rates of CPR training and a lower incidence of bystander CPR. However, prior studies have not examined whether this difference varies between OHCA that occurs at home versus in public locations, where more bystanders trained in CPR would be expected. Better understanding of racial and ethnic differences in the incidence of bystander CPR is an important prerequisite for future policy interventions aimed at decreasing disparities and improving survival after OHCA.

The featured study was retrospective and contained deidentified data from 110,054 witnessed OHCA cases between 2013 and 2019 from the Cardiac Arrest Registry to Enhance Survival (CARES). CARES is a large prospective registry of nontraumatic OHCA cases in the United States. The study's main outcome of interest was initiation of bystander CPR. Secondary analyses were conducted on rates of survival to hospital discharge and favorable neurologic survival. The main exposure of interest was patient race or ethnicity (as reported by the patient, a family member, or EMS personnel), classified as Black or Hispanic versus non-Hispanic White. Analysis was stratified by (1) location of OHCA, classified as home versus public location and (2) income composition, classified as low income (median annual household income <\$40,000), middle income (\$40,000-\$80,000), and high-income (>\$80,000). Multivariate hierarchical logistic regression models were created and adjusted for patient and location characteristics, cause of arrest, and clustering of outcomes by EMS agency. Secondary analyses for survival to hospital discharge and favorable neurologic survival were adjusted for these same characteristics, as well as arrest rhythm.

Overall, 35,469 (32.2%) patients who experienced OHCA were Black or Hispanic. OHCA occurred at home in 84,296 (76.6%) cases and in public in 25,758 (23.4%) cases. Regardless of location, Black and Hispanic patients were less likely to receive bystander CPR compared with White patients: Rates were 38.5% versus 47.4% at home (adjusted odds ratio [OR], 0.74; 95% confidence interval [CI], 0.72-0.76) and 45.6% versus 60% in public (OR, 0.63; 95% CI, 0.60-0.66). This difference was observed across different neighborhood compositions (ie, predominantly White, predominantly Black or Hispanic, and integrated neighborhoods) and income strata (ie, low income, middle income, and high income). In every subcategory of public location (ie, workplace settings, recreational facilities, and public transportation centers), Black and Hispanic patients were less likely to receive bystander CPR compared with White

patients. Both after OHCA at home and in public, Black and Hispanic patients also had a lower incidence of survival to discharge and favorable neurologic discharge compared with White patients.

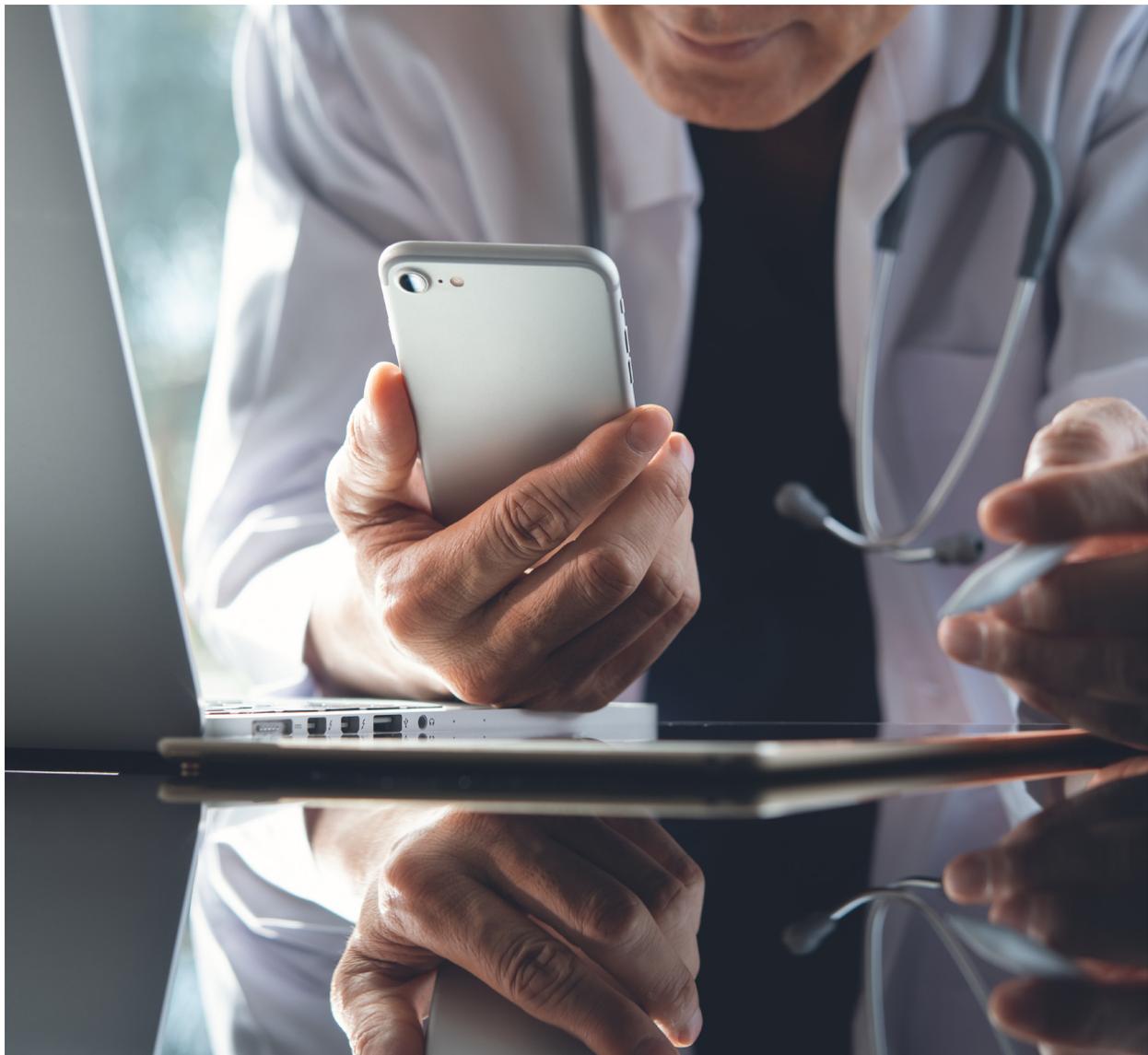
This study demonstrates large disparities in the incidence of bystander CPR for OHCA. After OHCA, Black and Hispanic patients have a 26% lower relative likelihood of receiving bystander CPR at home and a 37% lower relative likelihood of receiving it in public. These differences persisted across different neighborhood compositions and income strata. Possible etiologies include structural racism that contributes to lower rates of CPR training and less access to dispatcher-assisted bystander CPR in Black and Hispanic communities, and explicit and implicit biases that affect bystander willingness to respond.

Limitations of this study include constraints related to the dataset, such as potential misclassification of race and ethnicity (which is not always self-reported) and a lack of generalizability to rural areas that did not participate in the registry used in this study. Additionally, bystander characteristics may be unmeasured confounders because the study did not adjust for the number of bystanders, their reason for not responding, or their race for a given OHCA.

The authors emphasize that addressing disparities in the incidence of bystander CPR for OHCA requires a multimodal approach that includes expanded access to bystander CPR training in Black and Hispanic communities and cultural sensitivity in training materials. Allocating funding for dispatcher-assisted CPR in a diverse range of languages in these areas and improving trust and efficacy of the 911 system are other potential strategies to increase access to lifesaving CPR intervention for patients who experience OHCA.

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*Critical Decisions in Emergency Medicine's* LLSA literature reviews feature articles from ABEM's 2025 Lifelong Learning and Self-Assessment Reading List. Available online at [acep.org/moc/llsa](http://acep.org/moc/llsa) and on the ABEM website.



# Balloon Tamponade for Unstable GI Bleeds

By Daniel Ruiz-Betancourt, MD; and  
Laura Welsh, MD

Harvard Affiliated Emergency Medicine  
Residency Program, Boston, Massachusetts

Reviewed by Andrew J. Eyre, MD, MS-HPEd, FACEP

## Objective

On completion of this article, you should be able to:

- Explain when and how to use balloon tamponade for upper GI bleeds.

Bridwell RE, Long B, Ramzy M, et al. Balloon tamponade for the management of gastrointestinal bleeding. *J Emerg Med.* 2022 Apr;62(4):545-548.

## KEY POINTS

- Balloon tamponade devices have demonstrated a success rate of upward of 90% in securing hemostasis in patients with hemodynamically unstable GI bleeding.
- Balloon tamponade is indicated in hemodynamically unstable upper GI bleeding when there is a delay in endoscopy, an inability to perform endoscopy, a failed endoscopy, or a need for stabilization prior to facility transfer.
- Intubation and resuscitation should be performed *prior* to the use of balloon tamponade devices.

GI varices are among the most severe complications of liver cirrhosis. The prevalence of esophageal varices in patients with cirrhosis ranges from 40% to 95%, and approximately one-third of these patients experience a variceal bleed. Variceal bleeding is a life-threatening emergency that can rapidly result in hemodynamically unstable hemorrhage and airway compromise. Each episode of bleeding can have a mortality rate up to 30%. As such, it is critical that emergency physicians learn how to optimally manage patients who present with variceal bleeding. In general, the medical management of variceal bleeding includes airway protection, blood product transfusion, and administration of antibiotics and vasoactive medications. Balloon tamponade is reserved for unstable patients with refractory bleeding despite maximal medical therapy, and it functions as a bridge to definitive management, such as variceal band ligation, sclerotherapy, or a transjugular intrahepatic portosystemic shunt procedure.

### Balloon Tamponade Devices

Balloon tamponade devices function by exerting direct pressure to stop varices from bleeding. These devices have demonstrated variable efficacy, ranging from 30% to 90% in controlling severe upper GI bleeding. The three major balloon tamponade devices are the Linton-Nachlas tube (LNT), Sengstaken-Blakemore tube (SBT), and Minnesota tube (MT). The LNT has a single 600-mL gastric balloon and three ports, including a balloon inflation port and two separate gastric and esophageal suction ports. The SBT and MT have two balloons, one gastric and one esophageal. The SBT differs from the MT in that it has a 250-mL gastric balloon and only three ports, including a single gastric suction port and two separate gastric and esophageal balloon inflation ports. The MT has a 500-mL gastric balloon and four ports: two separate gastric and esophageal balloon inflation ports and two separate gastric and esophageal suction ports. Data are insufficient to suggest head-to-head superiority between any of the balloon tamponade devices.

### Indications, Contraindications, and Complications

Balloon tamponade devices should not be used in all patients with upper GI bleeding. Balloon tamponade is indicated for *hemodynamically unstable* upper GI bleeding when there is a delay in endoscopy, an inability to perform endoscopy, a failed endoscopy, or a need for stabilization prior to facility transfer. The two major contraindications are placement in hemodynamically stable patients and placement in patients who are not intubated. Relative contraindications include esophageal strictures and prior esophageal or gastric surgeries. Twenty percent of patients may experience complications

from balloon tamponade. Complications include aspiration, airway obstruction, esophageal perforation, and mucosal ulceration. Furthermore, variceal rebleeding is seen in approximately 50% of patients after balloon tamponade devices are removed.

### **Tube Placement**

Prior to placing the tube, ensure that the patient is intubated and resuscitated. Next, ensure that all equipment is available, present at the bedside, and checked for leaks. Place the patient in supine at 45°. The estimated length of the tube is measured from the bridge of the nose to the xiphoid process. The balloon is then lubricated and inserted through the oral cavity and, subsequently, into the esophageal cavity using Magill forceps, being careful not to damage the balloons. The manometer or syringe is attached to the gastric balloon port, and the gastric balloon is partially inflated with 50 mL of air; a chest x-ray is performed to ensure intragastric balloon positioning. Once its position is confirmed, the gastric balloon should be fully inflated. While inflating the gastric balloon, ensure that pressure does not exceed 15 mm Hg (pressure that exceeds 15 mm Hg suggests esophageal placement).

Once the gastric balloon is fully inflated, tie one end of rolled gauze to the external end of the device and tie the other end of the rolled gauze to a 1-L bag of intravenous fluids. Hang the bag of fluids over an IV pole to generate 1 to 2 lb of constant traction. Aspiration and irrigation of the gastric and esophageal aspiration ports should be performed. If hemostasis is not achieved and an SBT or MT is being used, the manometer should be placed on the esophageal balloon port, and the esophageal balloon should be inflated to reach 30 to 40 mm Hg. A repeat chest x-ray should be obtained to ensure final placement. After successful placement, continuous suction can be used through the aspiration ports for the first 12 hours. If a balloon tamponade device is needed for longer than 24 hours, the esophageal portion of the device, if present, should be deflated every 6 hours for a few minutes to limit mucosal ulceration.

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# Intranasal Topical Application of Tranexamic Acid for Atraumatic Anterior Epistaxis

By Alexa Curt, MD; and Laura Welsh, MD

Harvard Affiliated Emergency Medicine Residency Program, Boston, Massachusetts

Reviewed by Andrew J. Eyre, MD, MS-HPed, FACEP

## Objective

On completion of this article, you should be able to:

- Discuss results from a study on TXA for atraumatic anterior epistaxis.

Hosseinalhashemi M, Jahangiri R, Faramarzi A, et al. Intranasal topical application of tranexamic acid in atraumatic anterior epistaxis: a double-blind randomized clinical trial. *Ann Emerg Med.* 2022 Sep;80(3):182-188.

## KEY POINTS

- Intranasal application of TXA for atraumatic anterior epistaxis is associated with a shorter emergency department stay, a lower rate of anterior nasal packing, and a lower rate of rebleeding within 24 hours.
- No difference was noted between TXA and control groups in the need for electrical cauterization and the rate of rebleeding within 1 to 7 days.
- Topical TXA is low cost and simple to use. This treatment can be performed quickly before more invasive steps are taken.

Epistaxis is common, accounting for 1 in 200 emergency department visits in the United States. Although many cases of epistaxis are self-limited, some require intervention. Anterior nasal packing effectively controls epistaxis in up to 85% of cases, but it is associated with complications such as mucosal irritation, infection, necrosis, and rebleeding on removal. Topical tranexamic acid (TXA) has been proposed as a definitive treatment for atraumatic anterior epistaxis. However, the efficacy of TXA and its ability to reduce the need for anterior packing are unclear.

A single-center, double-blind, randomized controlled trial was performed to examine this issue. Participants included patients who were 18 years or older and had active atraumatic anterior epistaxis that had failed conservative measures of hemostasis. Patients were excluded for hemodynamic instability, allergy to TXA, pregnancy, nasopharyngeal malignancy, known bleeding disorders, recent use of anticoagulation drugs, or posterior or traumatic epistaxis. A total of 240 patients were enrolled. Half were randomly assigned to the control group and received cotton pledgets soaked in phenylephrine and lidocaine. The other half in the intervention group received TXA with phenylephrine and lidocaine. Both groups were treated for 15 minutes. The primary outcome was the need for anterior nasal packing. Secondary outcomes were length of stay, the need for electrical cauterization, and rebleeding within 24 hours and 1 to 7 days after the initial emergency department visit.

The study's results demonstrated significant benefits for the TXA group. Compared to the control group, patients who received TXA were less likely to require anterior nasal packing (50% vs 64.2%), were less likely to stay in the emergency department for more than 2 hours (9.2% vs 20.8%), and had lower rates of rebleeding within 24 hours (15% vs 30%). The two groups had no significant differences in the need for electrical cauterization and the rebleeding rate within 1 to 7 days.

The study had several limitations. It was conducted at a specialty ear, nose, and throat emergency department rather than at a general emergency department, and the patient population was younger and had lower rates of anticoagulant use compared with patients in similar studies. Despite these limitations, the study's findings suggest that topical TXA is a safe and effective treatment option for anterior epistaxis and could, potentially, reduce the need for more invasive interventions like nasal packing. TXA treatment is cost-effective and simple to administer, making it an attractive option for initial management of atraumatic anterior epistaxis in the emergency department.

# High-Dose Nitroglycerin for SCAPE

By Divya Krishna, MD; and Michael E. Abboud, MD, MEd  
University of Pennsylvania, Philadelphia

Reviewed by Andrew J. Eyre, MD, MS-HPed, FACEP

### Objective

On completion of this article, you should be able to:

- Explain the results of the HI-DOSE SCAPE study for managing patients with SCAPE.

Houseman BS, Martinelli AN, Oliver WD, et al. High-dose nitroglycerin infusion description of safety and efficacy in sympathetic crashing acute pulmonary edema: the HI-DOSE SCAPE study. *Am J Emerg Med.* 2023 Jan;63:74-78.

### KEY POINTS

- In SCAPE, rapidly increasing blood pressure manifests as acute heart failure and pulmonary edema, often necessitating treatment with nitroglycerin and positive-pressure ventilation.
- HDN infusions can be started at 100 µg/min (or higher) and rapidly up-titrated to safely lower blood pressure.
- No statistically significant difference in outcomes (eg, intubation, ICU admission, hypotension) occurred between patients who were immediately started on HDN infusions without adjuncts and patients who were given HDN infusions with adjuncts.
- HDN infusions may be a safe and effective alternative to intermittent bolus HDN for the management of SCAPE.

Sympathetic crashing acute pulmonary edema (SCAPE) occurs when patients who have acute blood pressure elevation develop sudden heart failure and pulmonary edema. If patients with SCAPE do not receive intervention, they can develop respiratory distress that quickly progresses to respiratory failure, and they may require invasive positive-pressure ventilation and ICU admission. Both noninvasive positive-pressure ventilation (NIPPV) and antihypertensives like nitroglycerin are usually required to prevent these patients' respiratory status from declining. In these scenarios, nitroglycerin is typically given as boluses, low-dose infusions (<60 µg/min), high-dose infusions (>100 µg/min), or a combination of these options. Previously, only limited case reports on the use of high-dose nitroglycerin (HDN) infusions for SCAPE were available in the literature. The featured HI-DOSE SCAPE study sought to describe the characteristics and outcomes of patients who received an HDN infusion for SCAPE with or without adjunctive therapies. The authors of the study also analyzed the safety of these adjunctive therapies, which included diuretics, angiotensin-converting-enzyme (ACE) inhibitors, and angiotensin receptor blockers.

The study involved a retrospective chart review of patients with SCAPE who arrived at the emergency department of a large academic medical center in 2018. These patients were started on an HDN infusion. The measured key adverse outcomes were hypotension, intubation, acute kidney injury, ICU admission, and length of hospital stay. The study population was mostly men (63%), Black people (84%), and people with known heart failure (51%).

Approximately half of the patients (48%) received either a sublingual dose (0.4 mg) or an intravenous bolus (typically 100 µg or 200 µg) of nitroglycerin before HDN infusions were started. HDN infusions were initially started at a median rate of 100 µg/min in the first hour and were rapidly up-titrated to 200 µg/min on average. Most patients (73%) also received NIPPV in the form of bilevel positive airway pressure (BiPAP). Many patients (58%) also received loop diuretics, on average the equivalent of 120 mg of oral furosemide. Some patients (34%) also received an ACE inhibitor or angiotensin receptor blockers. HDN infusions alone, without adjunctive medications, were given to patients with lower initial systolic blood pressures, although there was no statistically significant difference in systolic blood pressure across the groups in the study. The degree of blood pressure reduction in all patients, regardless of whether they received HDN infusions alone or HDN infusions with adjuncts, was similar, between 32% and 37%. Rates of unfavorable outcomes were relatively low: Intubation occurred in 21% of patients, acute kidney injury in 13%, and hypotension in 4%. Patients who received higher rates of intravenous nitroglycerin (>200 µg/min) were more likely to be intubated and admitted to the ICU than those who received lower doses; the authors suggested that this finding occurred because patients who received higher rates of nitroglycerin were sicker at presentation. In summary, the HI-DOSE SCAPE study suggests that a continuous infusion of HDN may be a safe alternative to intermittent boluses for managing SCAPE.

# Digital Nerve Blocks

By Maximilian J. Pany, MD, PhD; and Laura Welsh, MD

Harvard Affiliated Emergency Medicine Residency Program, Boston, Massachusetts

Reviewed by Andrew J. Eyre, MD, MS-HPed, FACEP

### Objective

On completion of this article, you should be able to:

- Summarize how to select appropriate digital nerve blocks for emergency department patients.

Gottlieb M, Penington A, Schraft E. Digital nerve blocks: a comprehensive review of techniques. *J Emerg Med.* 2022 Oct;63(4):533-540.

### KEY POINTS

- Digital nerve blocks provide effective anesthesia for fingers and toes without distorting local anatomy.
- Commonly used digital nerve block techniques include the dorsal web space block (ring block), transthecal block (tendon sheath block), volar subcutaneous block, and circumferential ring blocks.
- Each approach has unique advantages and limitations, allowing tailored application based on location of the injury and patient factors.

Injuries of the digits are a common complaint in the emergency department. Digital nerve blocks provide effective anesthesia for a variety of finger and toe injuries — including fractures, dislocations, infections, lacerations, and nail bed injuries — without distorting local anatomy or manipulating painful and potentially infected tissue. Multiple nerve block techniques exist. Each technique has distinct advantages and limitations, allowing emergency physicians to tailor their approach to the specific patient and injury. In the featured article, Gottlieb et al reviewed four major digital nerve block techniques: the dorsal web space, transthecal, volar subcutaneous, and circumferential ring blocks.

#### Dorsal Web Space Block

The dorsal web space block is a traditional technique and is often referred to as the *ring block* or the *two-injection method*. It involves injecting anesthetic into the web spaces on both sides of the affected digit to target both palmar and dorsal branches of the common digital nerve. This technique can also be used for the toes by injecting just distal to the metatarsophalangeal joint. These injections provide effective dorsal anesthesia, but distal coverage can be incomplete. Therefore, some authors recommend a third dorsal injection to ensure complete anesthesia, particularly for nail bed injuries, which may otherwise be incompletely covered. A major disadvantage is the need for multiple injections with dorsal web space blocks.

#### Transthecal Block

The transthecal block, also known as the *flexor tendon sheath block*, is a single-injection technique in which the anesthetic is injected into the flexor tendon sheath along the proximal palmar digital crease. By targeting both palmar and dorsal nerves, the transthecal block minimizes the number of injections needed, making it particularly valuable for children and other patients who are highly sensitive to pain. However, the transthecal block has a slower onset of anesthesia compared to the dorsal web space block and can cause post-procedure tendon sheath pain.

#### Volar Subcutaneous Block

The volar subcutaneous block, also known as the *tumescent block*, provides another single-injection alternative. This approach delivers anesthetic into the subcutaneous space of the palmar surface, allowing for rapid distribution to the dorsal and palmar nerves. It is simple to perform and is associated with reduced procedure-related pain. However, it may provide less effective dorsal anesthesia compared with other techniques.

#### Circumferential Ring Block

For thumb or great-toe injuries, three-sided or four-sided ring blocks are often employed. These techniques involve additional injections along the dorsal or palmar digit surfaces to ensure

comprehensive anesthesia. Although the four-sided ring block can provide superior coverage, its associated discomfort and (small but increased) risk of elevated compartment pressures can make the three-sided technique the preferred choice.

### Summary

In practice, selecting the appropriate digital nerve block technique depends on the location and type of injury. The volar subcutaneous block is recommended for palmar injuries due to its simplicity and rapid onset. For injuries with dorsal involvement, the dorsal web space or transthecal block (supplemented with dorsal injection if needed) is ideal. For the thumb and great toe, a three-sided ring block offers reliable coverage. By understanding the nuances of these techniques, emergency physicians can maximize patient comfort and procedural success, ensuring effective management of digit injuries.

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# Outpatient Treatment for Pulmonary Embolism

By Spencer J. Carbone, MD; and  
Andrew J. Eyre, MD, MS-HPEd, FACEP

Brigham and Women's Hospital and Harvard  
Medical School, Boston, Massachusetts

## Objective

*On completion of this article, you should be able to:*

- Discuss how to risk stratify patients with pulmonary embolism and decide when they can be treated as outpatients.

Outpatient treatment for pulmonary embolism. Key advances clinical policy alert. American Board of Emergency Medicine Key Advances Panel. Published June 2023.

## KEY POINTS

- Patients with low-risk pulmonary embolism can effectively be treated in the outpatient setting with direct oral anticoagulants if they have reliable access to medications, the ability to follow up, and adequate home support.
- Patients who meet intermediate- or high-risk criteria, such as clinical instability or evidence of right heart strain on imaging or laboratory tests, should be hospitalized for treatment and monitoring.
- Clinical decision-making tools are supported by data as being effective for stratifying patients with pulmonary embolism into those needing to be hospitalized versus those who are safe for home treatment.

### Why is outpatient treatment for low-risk pulmonary embolism preferable to hospitalization?

If patients have ample access to medication, access to outpatient follow-up care, and adequate home circumstances, then treatment at home for pulmonary embolism is more convenient, less expensive, and preferred by most patients. Outpatient treatment has become easier with modern direct oral anticoagulants like rivaroxaban and apixaban.

### Do outcomes differ for patients with low-risk pulmonary embolism who are hospitalized versus those who are treated at home?

In short, no. Patients with deep vein thrombosis and pulmonary embolism in various locations (ie, subsegmental, segmental, lobar, and main pulmonary artery) who received outpatient treatment were all treated successfully. Additionally, no deaths occurred in these patients, and they had a low 30-day recurrence rate of pulmonary embolism and deep vein thrombosis (1%) and a low rate of bleeding complications that required hospitalization (0.8%).

### How can patients with pulmonary embolism be stratified into low-, intermediate-, and high-risk categories?

Patients in the low-risk category are clinically and hemodynamically stable, without evidence of end-organ damage. They satisfy low-risk criteria for clinical decision-making tools and are suitable for outpatient treatment.

Patients in intermediate- and high-risk categories have evidence of right heart strain on imaging (ECG, CT, echocardiogram) or elevated troponin and BNP levels. If they also have signs of shock, end-organ damage or hypoperfusion, hypotension, or cardiac arrest, then they are stratified into the high-risk group. Both intermediate- and high-risk patients are suitable for hospitalization.

### Can clinical decision-making tools help physicians decide whether a patient has a low-risk pulmonary embolism and is stable enough for outpatient management?

Yes, physicians can use the Hestia criteria, or clinical judgment in concert with the simplified Pulmonary Embolism Severity Index (sPESI) score (*Table 1*). Studies have shown that treatment at

Modified Hestia Criteria	sPESI Score
<ul style="list-style-type: none"> <li>• Systolic blood pressure &gt;100 mm Hg</li> <li>• No thrombolysis needed</li> <li>• No active bleeding</li> <li>• SaO<sub>2</sub> &gt;94% while breathing room air</li> <li>• Not already anticoagulated</li> <li>• No more than 2 doses of IV narcotics in the emergency department</li> <li>• No other medical or social reasons to admit</li> <li>• Creatinine clearance &gt;30 mL/min</li> <li>• Not pregnant, no severe liver disease, and no heparin-induced thrombocytopenia</li> </ul>	<ul style="list-style-type: none"> <li>• Age 18-81 yr</li> <li>• No history of cancer</li> <li>• No history of heart failure or chronic lung disease</li> <li>• Pulse &lt;110 bpm</li> <li>• Systolic blood pressure &gt;99 mm Hg</li> <li>• O<sub>2</sub> saturation &gt;89%</li> </ul> <p>Used in concert with an assessment that shows the patient's medical and social situations are favorable for outpatient management</p>

**TABLE 1. Criteria used to decide if low-risk pulmonary embolism patients can be managed as outpatients**

home is noninferior to hospitalization if all of either set of criteria are met, and that this treatment significantly reduces costs while increasing patient satisfaction. Importantly, however, clinical judgment should overrule these criteria in favor of hospitalization if there are doubts about the patient's clinical or social status.

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# Phenobarbital for Alcohol Withdrawal Syndrome

By Lydia Buzzard, MD; and Laura Welsh, MD  
Harvard Affiliated Emergency Medicine Residency  
Program, Boston, Massachusetts

Reviewed by Andrew J. Eyre, MD, MS-HPed, FACEP

## Objective

On completion of this article, you should be able to:

- Summarize findings from the featured study on phenobarbital versus benzodiazepine treatment for AWS.

Pistore A, Penney S, Bryce R, et al. A retrospective evaluation of phenobarbital versus benzodiazepines for treatment of alcohol withdrawal in a regional Canadian emergency department. *Alcohol*. 2022 Aug;102:59-65.

## KEY POINTS

- Phenobarbital's advantages for treating AWS include its longer half-life and its dual mechanism for targeting both GABA and glutamate receptors.
- Phenobarbital treatment compared to diazepam treatment resulted in fewer hospitalizations for AWS.
- There was no difference in the emergency department length of stay between patients treated with phenobarbital and patients treated with diazepam.

Alcohol withdrawal syndrome (AWS) affects almost half of alcohol-dependent patients and can be lethal, with mortality rates ranging from 5% to 15%. Symptoms range from mild agitation to severe complications, including seizures, coma, and death. Although benzodiazepines are standard for AWS in North America, phenobarbital offers advantages of a longer half-life and a dual mechanism for targeting both GABA and glutamate receptors. Although phenobarbital is a promising adjunctive treatment option — with some research suggesting it is beneficial in reducing admissions and improving outcomes — its use as monotherapy in emergency departments remains unclear.

The retrospective, observational study by Pistore et al set out to explore outcomes of phenobarbital monotherapy versus benzodiazepine monotherapy for AWS in a Canadian emergency department. The study included 83 patients who presented to the emergency department between June 2019 and January 2021. The primary outcomes were emergency department length of stay and rate of admission.

The study authors created two potential pathways for AWS treatment. The phenobarbital pathway included a loading intravenous dose of 10 mg/kg ideal body weight, followed 1 hour later by 120 to 240 mg intravenously; additional doses were titrated to symptoms every 30 minutes thereafter. The benzodiazepine pathway included administration of diazepam if the patient's score on the Clinical Institute Withdrawal Assessment Alcohol Scale Revised (CIWA-Ar) was  $\geq 8$ . Initial dosing for diazepam was 10 mg orally or intravenously, followed by additional doses every 15 minutes as needed based on symptoms. These two pathways were made available as order sets for the study, without additional guidance for triaging patients to a pathway or criteria for admission.

Results demonstrated no significant difference in emergency department length of stay between the two pathways. However, after adjustments were made for confounders, the patients treated with phenobarbital were found to be 71.3% less likely to be hospitalized than the patients treated with benzodiazepines. Compared with other studies that have examined phenobarbital versus benzodiazepine treatment for AWS, this study used more aggressive phenobarbital therapy and controlled for more confounders (such as comorbid illness) than some studies with negative findings for phenobarbital treatment for AWS.

Limitations of this study include its small sample size (especially the number of hospitalizations for AWS [n = 26]), individual physician preference for one pathway rather than randomization, and potential confounding due to unmonitored metrics such as bed availability, emergency department volume, and staff limitations. Despite its limitations, this study's observation that phenobarbital may reduce hospitalizations in patients with AWS suggests value in comparing the two pathways in a randomized trial.

# Updates on Sexually Transmitted Infections

By Jack G. Johnston, MD; and  
Nicholas G. Maldonado MD, FACEP  
University of Florida College of Medicine, Gainesville

Reviewed by Andrew J. Eyre, MD, MS-HPed

## Objective

On completion of this article, you should be able to:

- List current recommendations for diagnosing and treating STIs.

Niforatos JD, Rothman RE. Update on emerging infections from the Centers for Disease Control and Prevention. *Ann Emerg Med.* 2022 Jul;80(1):68-70.

## KEY POINTS

- Chlamydia is the first and gonorrhea is the second most frequently reported bacterial infection in the United States.
- NAAT is the preferred testing modality for chlamydia and gonorrhea infections. Patient-collected specimens are an acceptable method of collection.
- Doxycycline is the current first-line treatment for uncomplicated chlamydia infection.
- Ceftriaxone is the current first-line treatment for uncomplicated gonorrhea infection.

Sexually transmitted infections (STIs) are frequently encountered in the emergency department, where many patients seek screening, diagnosis, and treatment for these infections. In the featured article, Niforatos and Rothman provided important updates on the diagnosis and treatment of *uncomplicated* chlamydia and gonorrhea infections according to the CDC's 2021 STI treatment guidelines.

Updates focus on recommendations for chlamydia infections — the most frequently reported bacterial communicable disease in the United States — and gonorrhea infections — the second most commonly reported bacterial communicable disease. Table 1 summarizes the diagnosis, first-line treatment, alternative treatments, and important considerations for emergency department patients with *uncomplicated* chlamydia or gonorrhea infections.

Changes from previous guidelines involve diagnostic and treatment recommendations. Nucleic acid amplification testing (NAAT) is now the preferred testing modality for both chlamydia and gonorrhea infections. Patient-collected specimens are an acceptable method of collection if patients are given adequate instruction.

For chlamydia infections, azithromycin is no longer a first-line treatment option (except for in pregnant patients) and is considered an alternative for special circumstances. Instead, doxycycline is the antimicrobial of choice. Erythromycin is also no longer a recommended treatment. These changes are based on results from comparative trials, rates of anorectal detection, and limited efficacy of azithromycin with concomitant anorectal infection.

For gonorrhea infections, ceftriaxone remains the antimicrobial of choice. However, to maintain optimal mean inhibitory concentrations, the dose for uncomplicated gonorrhea infections has increased from 250 mg IM to 500 mg IM for patients who weigh less than 150 kg (330 lb) and to 1 g for patients who weigh  $\geq 150$  kg (330 lb). Cefixime remains an alternative treatment, but its dose has also increased, from 400 mg PO to 800 mg PO. Cefixime should be limited to special circumstances because indiscriminate use could accelerate ceftriaxone resistance. For patients allergic to cephalosporin, a regimen of gentamicin combined with high-dose azithromycin is now an option. Because of antimicrobial resistance patterns, fluoroquinolones and macrolides are no longer recommended. Cephalosporin-resistant and multidrug-resistant *Neisseria gonorrhoeae* have also been emerging. Specialists should be involved in treating patients who have failed standard treatments.

2021 Updated CDC STI Treatment Guidelines for Uncomplicated Chlamydia and Gonorrhea Infections				
STI	Diagnosis	First-line Treatment	Alternative Treatments	Pregnancy Considerations
<i>Chlamydia trachomatis</i>	<p><b>Urogenital infections:</b></p> <ul style="list-style-type: none"> <li>• NAAT</li> <li>• First-void urine or vaginal or cervical swabs as specimen for female patients</li> <li>• First-void urine or urethral swab as specimen for male patients</li> </ul> <p><b>Chlamydia screening:</b></p> <ul style="list-style-type: none"> <li>• NAAT</li> <li>• Vaginal swabs for female patients</li> <li>• First-void urine for male patients</li> </ul> <p>Note: Patient-collected vaginal swab specimens have comparable diagnostic accuracy to clinician-collected specimens for NAATs.</p>	<p>Doxycycline 100 mg PO twice daily for 7 d</p>	<p>Single dose of azithromycin 1 g PO</p> <p>Note: Consider azithromycin when high concern for nonadherence; may require post-treatment evaluation and testing</p> <p><b>OR</b></p> <p>Levofloxacin 500 mg PO daily for 7 d</p> <p>Note: Levofloxacin is more expensive.</p>	<p>First-line treatment is single dose of azithromycin 1 g PO</p> <p><b>Alternative:</b></p> <p>Amoxicillin 500 mg PO 3 times daily for 7 d</p> <p>Note: Doxycycline is contraindicated in the second and third trimesters due to risk of tooth discoloration; erythromycin is no longer recommended.</p>
<i>N. gonorrhoeae</i>	<p><b>Urogenital infections:</b></p> <ul style="list-style-type: none"> <li>• NAAT</li> <li>• Vaginal swabs as specimen for female patients</li> <li>• First-void urine as specimen for male patients</li> </ul> <p><b>Other methods of detection:</b></p> <ul style="list-style-type: none"> <li>• Point-of-care NAAT; culture (requires endocervical or urethral swab)</li> </ul> <p>Note: Patient-collected urine samples, vaginal swabs, rectal swabs, or oropharyngeal swabs can be used for specific sites of testing after patients are instructed on collection methods.</p>	<p><b>Weight &lt;150 kg (330 lb):</b></p> <p>Single dose ceftriaxone 500 mg IM</p> <p><b>Weight ≥150 kg (330 lb):</b></p> <p>Single dose ceftriaxone 1 g IM</p> <p>Note: For patients in whom chlamydia infection has not been excluded, concomitantly treat for chlamydia as described above.</p>	<p><b>For patients with cephalosporin allergy:</b></p> <p>Single dose of gentamicin 240 mg IM</p> <p><b>PLUS</b></p> <p>Single dose of azithromycin 2 g PO</p> <p><b>If ceftriaxone is unavailable or infeasible:</b></p> <p>Single dose of cefixime 800 mg PO</p> <p>Note: Cefixime has limited efficacy for pharyngeal gonorrhea; indiscriminate use could hasten ceftriaxone resistance.</p>	<p>Single dose of ceftriaxone 500 mg IM</p> <p>Note: If a cephalosporin allergy or other factor precludes this treatment for pregnant patients, consult an infectious disease or STI treatment specialist. Risks of gentamicin during pregnancy include birth defects, nephrotoxicity, and ototoxicity.</p>

**TABLE 1. Testing and treatment updates for uncomplicated chlamydia and gonorrhea infections.**  
*Adapted from:* Niforatos JD, Rothman RE. Update on emerging infections from the Centers for Disease Control and Prevention. *Ann Emerg Med.* 2022 Jul;80(1):68-70.

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# ISPAD 2022 Guidelines Summary

By Jon McGill, DO, LT, MC, USN; and  
 Daphne P. Morrison Ponce, MD, CDR, MC, USN  
 Naval Medical Center, Portsmouth, Virginia  
 Reviewed by Andrew J. Eyre, MD, MS-HPed

## Objective

On completion of this article, you should be able to:

- Summarize updated ISPAD recommendations for managing DKA and HHS.

ISPAD clinical practice consensus guidelines 2022: diabetic ketoacidosis and hyperglycemic hyperosmolar state. *Pediatr Diabetes*. 2022 Nov;23(7):835-856.

## KEY POINTS

- Fluid resuscitation remains a mainstay of therapy for both DKA and HHS, but care must be taken to avoid complications.
- Both DKA and HHS require insulin therapy but at different doses.
- Management of hyperglycemic conditions requires a multifaceted and multidisciplinary approach to address different causes and triggers.

The 2022 International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines introduced several important updates in the management of diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS). Notable changes include the addition of a serum bicarbonate threshold of <18 mmol/L to the diagnostic criteria for DKA, the recommendation that fluid boluses be infused over 20 to 30 minutes, and removal of the requirement that the serum sodium concentration be increased during DKA treatment (*Table 1*).

### DKA Treatment

Management of DKA focuses on correcting dehydration, acidosis, and ketosis while restoring glucose and osmolality to near-normal levels and preventing complications like cerebral injury. Any precipitating factors for DKA must also be identified.

Initial treatment includes administering a 0.9% saline bolus at 10 to 20 mL/kg over 20 to 30 minutes. The total fluid deficit should be replaced gradually over 24 to 48 hours using 0.45% to 0.9% saline, based on clinical factors. Intravenous insulin therapy should begin at a rate of 0.05 to 0.1 units/kg/hr, only after at least 1 hour of fluid resuscitation has been completed. Insulin boluses increase the risk of complications and are not recommended.

Electrolyte monitoring is critical throughout treatment. Potassium replacement should begin when the serum potassium level is below 5.5 mmol/L and after adequate urine output has been confirmed. Bicarbonate administration is generally not recommended unless patients have a life-threatening acidosis (pH <6.9) and compromised cardiac function or severe hyperkalemia. Frequent monitoring of vital signs, neurologic status, blood glucose levels, and laboratory markers (such as serum electrolyte, bicarbonate, and ketone levels) is essential. Treatment can transition to subcutaneous insulin once patients can tolerate oral intake and their ketoacidosis has resolved. Before intravenous insulin is stopped, a basal insulin dose should be given in addition to rapid-acting insulin.

Several complications may arise during DKA treatment. The most serious is cerebral injury, which affects a small percentage of patients but carries significant morbidity and mortality. Other potential issues include hypoglycemia, hypokalemia, acute kidney injury, thrombosis, and pulmonary complications. DKA-related cerebral injury is most likely to occur within the first 12 hours of treatment and is more common in younger children and patients with severe acidosis, hypocapnia, or elevated BUN levels. The

DKA Diagnostic Criteria	HHS Diagnostic Criteria
<ul style="list-style-type: none"> <li>• Hyperglycemia (blood glucose &gt;11 mmol/L or ≈200 mg/dL)</li> <li>• Venous pH &lt;7.3 or serum bicarbonate &lt;18 mmol/L</li> <li>• Evidence of ketonemia (β-hydroxybutyrate ≥3 mmol/L) or moderate to large ketonuria</li> </ul>	<ul style="list-style-type: none"> <li>• Hyperglycemia (blood glucose &gt;33.3 mmol/L or ≈600 mg/dL)</li> <li>• Venous pH &gt;7.25 or serum bicarbonate &gt;15 mmol/L</li> <li>• Minimal or no ketonuria or ketonemia</li> <li>• Effective serum osmolality &gt;320 mOsm/kg</li> </ul>

**TABLE 1. DKA and HHS diagnostic criteria**

diagnostic criteria for cerebral injury include abnormal motor or verbal responses to pain, decorticate or decerebrate posturing, cranial nerve palsy, or abnormal neurogenic respiratory patterns (Cheyne-Stokes respiration). Treatment includes mannitol 0.5 to 1 g/kg IV over 10 to 15 minutes, repeated after 30 minutes if necessary. Hypertonic saline (3%) at a suggested dose of 2.5 to 5 mL/kg over 10 to 15 minutes can be used as an adjunct or alternative therapy to mannitol.

Prevention of DKA is an essential component of long-term diabetes care. For patients with newly diagnosed diabetes, education on symptoms can reduce delays in DKA diagnosis. For diabetic patients who are not newly diagnosed, DKA often results from missed insulin doses or malfunctioning insulin pumps. Regular follow-up visits with a diabetes care team and education on sick day management are critical to preventing recurrent DKA episodes. A multidisciplinary approach that includes social workers and psychological support is recommended when nonadherence to diabetes treatment is suspected.

### **HHS Treatment**

Management of HHS requires more aggressive and rapid fluid replacement because of profound dehydration and the risk of circulatory collapse. Initial therapy includes a  $\geq 20$  mL/kg bolus of 0.9% saline, followed by replacement of an assumed 12% to 15% fluid deficit over 24 to 48 hours. Insulin administration should be delayed until the glucose level declines by less than 3 mmol/L/hr with fluids alone. Insulin is then started at a lower rate of 0.025 to 0.05 units/kg/hr. Electrolyte deficits, particularly in potassium and phosphate, are often more severe in HHS than DKA and require vigilant replacement and monitoring. Unique complications such as rhabdomyolysis, hyperthermia-like syndromes, and venous thrombosis can occur and must be anticipated in patients with HHS.

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### **Disclosure**

The views expressed in this article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government. This work was prepared as part of our official duties as military service members. Title 17 USC §105 provides that "copyright protection under this title is not available for any work of the United States Government." A United States Government work is defined in 17 USC §101 as a work prepared by a military service member or employee of the United States Government as part of that person's official duties.

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# Albuterol-Budesonide Rescue Inhalation for Asthma

By Elise Prehoda, MD; and  
Andrew J. Eyre, MD, MS-HPEd, FACEP  
Harvard Affiliated Emergency Medicine  
Residency Program, Boston, Massachusetts

## Objective

On completion of this article, you should be able to:

- Discuss the featured study's recommendations on asthma treatment with albuterol-budesonide.

Papi A, Chipps BE, Beasley R, et al. Albuterol-budesonide fixed-dose combination rescue inhaler for asthma. *N Engl J Med*. 2022 Jun 2;386(22):2071-2083.

## KEY POINTS

- Asthma exacerbations involve both bronchoconstriction and airway inflammation.
- SABAs do not address the inflammatory changes associated with asthma.
- The MANDALA study demonstrated a decrease in the risk of recurrent asthma exacerbations in patients treated with a combination of 180 µg albuterol and 160 µg budesonide compared with patients treated with albuterol alone.

Patients frequently present to the emergency department with acute asthma exacerbations. These patients often obtain symptomatic relief from short-acting  $\beta_2$ -agonist (SABA) therapy in the form of a rescue inhaler or nebulizer. This treatment, however, does little to address the underlying inflammatory physiology of asthma or to prevent future severe asthma exacerbations. The MANDALA trial was developed to evaluate the efficacy and safety of a combination treatment as an asthma rescue medication. This combination treatment included a glucocorticoid (budesonide) and a fast-acting bronchodilator (albuterol) in the form of a fixed-dose rescue inhaler. The treatment was intended for acute asthma symptoms in patients with moderate to severe asthma who were receiving inhaled glucocorticoid maintenance therapy.

This multinational, double-blind, randomized, event-driven phase 3 clinical trial was conducted at 295 sites throughout North America, South America, Europe, and South Africa. The study enrolled patients aged  $\geq 4$  years with a primary diagnosis of asthma who had experienced a severe asthma exacerbation within the past 12 months. The study excluded patients with chronic obstructive pulmonary disease or other lung disease and patients who had used systemic glucocorticoid or biologic treatments within the 3 months prior to screening. Adolescent and adult patients were randomized in a 1:1:1 ratio to a high-dose combination group (two actuations of 90 µg albuterol and 80 µg budesonide for a total of 180 µg and 160 µg, respectively), a low-dose combination group (two actuations of 90 µg albuterol and 40 µg budesonide for a total of 180 µg and 80 µg, respectively), or an albuterol-alone group (two actuations of 90 µg albuterol for a total of 180 µg). Patients who were between 4 and 11 years old were randomized to the low-dose combination group or the albuterol-alone group. Patients were instructed to use their assigned rescue medication when they felt symptomatic.

The primary end point was the first event of severe asthma exacerbation. Secondary end points included the annualized rate of severe asthma exacerbations, total systemic glucocorticoid exposure during the study period, and response at week 24 on the Asthma Control Questionnaire-5 (ACQ-5) and Asthma Quality of Life Questionnaire (AQLQ 12+). Patients aged 4 to 6 years completed the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) rather than the AQLQ 12+. The incidence of adverse events was tracked as safety end points.

The study included 5,620 patients, 3,132 of which were randomized to parallel treatment groups with treatment periods of 24 weeks. Of the randomized patients, 241 discontinued treatment prior to the end of the trial; however, all 3,132 patients were assessed on efficacy end points, and 3,127 were assessed on safety end points. Results were analyzed by both intention-to-treat and preplanned on-treatment efficacies.

A 26% decrease in the risk of severe asthma exacerbation occurred in the higher-dose combination group compared to the albuterol-alone group (hazard ratio, 0.74; 95% confidence interval [CI], 0.62-0.89;  $P = 0.001$ ) in the intention-to-treat analysis. The hazard ratio for the lower-dose combination group compared to the albuterol-alone group was 0.84, which was not statistically significant (95% CI, 0.71-1.00;  $P = 0.052$ ). No statistically significant difference was found in adverse outcomes between the groups. Based on these results, the authors suggest replacing SABA-alone therapy with a fixed-dose combination therapy as a rescue treatment for patients with moderate to severe asthma.

# The LLSA Literature Review

## Managing Patients With Acute Visual Loss

By Nicholas G. Maldonado, MD, FACEP  
University of Florida College of Medicine, Gainesville  
Reviewed by Andrew J. Eyre, MD, MS-HPed, FACEP

### Objective

On completion of this article, you should be able to:

- Discuss recommendations for emergency management of AVL according to the featured study.

Edlow JA, Hoffmann B. Managing patients with acute visual loss. *Ann Emerg Med.* 2022 May;79(5):474-484.

### KEY POINTS

- AVL can be categorized into four major etiologic groups: ocular or orbital pathology, ocular neurovascular dysfunction, brain-related pathology, and functional neurologic disease.
- A focused history and thorough ocular or neurologic examination — including assessment for the persistence of symptoms, monocular or binocular involvement, and presence of pain or redness — are critical for localization and diagnosis.
- Ocular POCUS is a valuable bedside tool for diagnosing conditions such as vitreous or retinal detachment, vitreous hemorrhage, and papilledema, especially when direct visualization is limited.
- Emergency management should prioritize vision-saving interventions, such as corticosteroids for suspected giant cell arteritis and thrombolytics for central retinal artery occlusion, and early consultation for critical diagnoses.

Acute visual loss (AVL) is a distressing symptom that requires prompt evaluation in the emergency department, appropriate consultation, and disease-specific treatments to prevent permanent vision impairment. In the featured LLSA article, Edlow and Hoffman provide a comprehensive framework for the emergency management of adult patients who present with spontaneous and isolated AVL. Key clinical pearls and management strategies can guide emergency physicians in the evaluation and treatment of AVL.

### Diagnostic Framework

The authors categorize AVL etiologies into four major groups: ocular or orbital pathology, ocular neurovascular dysfunction, brain-related pathology (optic chiasm or retrochiasm pathways), and functional neurologic disease. Mechanisms for optic nerve dysfunction are framed as ischemic, inflammatory, infectious, toxic, or compressive. An algorithmic approach to AVL is presented that focuses on three key considerations during history gathering: whether AVL is persistent or transient, monocular or binocular, or associated with ocular pain or redness. The history is supplemented by a detailed ophthalmologic and neurologic examination and targeted diagnostic testing (*Table 1*).

### History and Physical Examination

In addition to the three key considerations previously mentioned, a focused history for AVL should include the timing of symptom onset. Information gathered from the patient's history can help narrow the differential diagnosis and guide the next steps of the evaluation. For example, persistent monocular AVL that is associated with ocular pain and redness suggests an ocular pathology, such as corneal abrasion, keratitis, acute narrow-angle glaucoma, iritis or uveitis, or endophthalmitis. By contrast, persistent binocular AVL without associated ocular pain and redness suggests brain pathology, such as pituitary apoplexy, stroke, posterior reversible encephalopathy syndrome, or specific ocular neurovascular conditions like idiopathic intracranial hypertension or neuromyelitis optica. Transient AVL should increase suspicion for giant cell arteritis, transient ischemic attack, or idiopathic intracranial hypertension. The presence of cardiovascular risk factors may heighten suspicion for ischemic mechanisms, the presence of associated inflammatory symptoms (eg, joint pain, jaw claudication, scalp tenderness) may increase suspicion for inflammatory mechanisms like giant cell arteritis, and the presence of other neurologic symptoms may increase suspicion for brain pathology. This approach to history gathering can establish an initial clinical impression that can then inform and be supplemented by a detailed ophthalmologic and neurologic examination.

Persistent AVL Etiologies			
Monocular Visual Loss		Binocular Visual Loss	
Ocular Pain or Redness Present	Ocular Pain or Redness Absent	Ocular Pain or Redness Present	Ocular Pain or Redness Absent
<b>Ocular pathology:</b> <ul style="list-style-type: none"> <li>• Corneal abrasion</li> <li>• Corneal edema</li> <li>• Keratitis</li> <li>• Acute narrow-angle glaucoma</li> <li>• Iritis or uveitis</li> <li>• Endophthalmitis</li> <li>• Other ocular infection</li> </ul>	<b>Ocular pathology:</b> <ul style="list-style-type: none"> <li>• Vitreous hemorrhage</li> <li>• Vitreous detachment</li> <li>• Retinal Detachment</li> </ul>	<b>Ocular pathology:</b> <ul style="list-style-type: none"> <li>• Photokeratitis</li> </ul>	<b>Brain pathology:</b> <ul style="list-style-type: none"> <li>• Pituitary apoplexy</li> <li>• Stroke (occipital or visual pathways)</li> <li>• Posterior reversible encephalopathy syndrome</li> <li>• Retinal migraine</li> </ul>
	<b>Ocular neurovascular dysfunction:</b> <ul style="list-style-type: none"> <li>• Optic neuritis (nonischemic)</li> <li>• Retrobulbar optic neuritis</li> <li>• Anterior ischemic optic neuropathy (nonarteritic)</li> <li>• Anterior ischemic optic neuropathy (arteritic [giant cell arteritis])</li> <li>• Central retinal artery occlusion</li> <li>• Central retinal vein occlusion</li> </ul>	<b>Ocular neurovascular dysfunction:</b> <ul style="list-style-type: none"> <li>• Methanol toxicity</li> </ul>	<b>Ocular neurovascular dysfunction:</b> <ul style="list-style-type: none"> <li>• Increased intraocular pressure</li> <li>• Idiopathic intracranial hypertension</li> <li>• Neuromyelitis optica</li> </ul>

Transient AVL Etiologies
<b>Critical diagnoses to consider:</b> <ul style="list-style-type: none"> <li>• Giant cell arteritis</li> <li>• Transient ischemic attack</li> <li>• Idiopathic intracranial hypertension</li> </ul>

**TABLE 1. Differential diagnosis of spontaneous, isolated AVL by category and key historical features (nonexhaustive).** Of note, functional neurologic disease that causes functional AVL should be a diagnosis of exclusion in the emergency department after careful consideration, extensive evaluation, and consultation. *Adapted from:* Edlow JA, Hoffmann B. Managing patients with acute visual loss. *Ann Emerg Med.* 2022 May;79(5):474-484.

Edlow and Hoffman emphasize that the ophthalmologic examination should include an external examination to note ocular position and extraocular movements (including whether pain is elicited), a pupillary examination that includes the swinging light test, visual acuity testing, visual field testing, measurement of intraocular pressure, ophthalmoscopy, and slit-lamp evaluation with fluorescein staining. Characteristic findings of specific causes of AVL may be present during one or more components of the ophthalmologic examination. Notable examples include findings of a midposition pupil, shallow anterior chamber, and increased intraocular pressure in acute narrow-angle glaucoma; retinal pallor, a “cherry red spot,” and optic disc swelling on ophthalmoscopy in central retinal artery occlusion; retinal hemorrhages and “cotton wool spots” on ophthalmoscopy in central retinal vein occlusion; and a relative afferent pupillary defect on the swinging light test in unilateral optic nerve dysfunction, as seen in arteritic and nonarteritic anterior ischemic optic neuropathy and other conditions of ocular neurovascular dysfunction. If giant cell arteritis is suspected, the temporal artery should be assessed for swelling, erythema, tenderness, and nodularity.

### Targeted Diagnostic Testing

Laboratory testing has limited diagnostic utility in the evaluation of AVL. Edlow and Hoffman recommend testing glucose levels to evaluate for hyper- or hypoglycemia causes, lactate levels when methanol toxicity is suspected, and inflammatory markers (ie, erythrocyte sedimentation rate and C-reactive protein levels) to assess the probability of giant cell arteritis.

With respect to imaging, orbital CT can assist with evaluating orbital compression, and MRI can assist with evaluating for stroke and neuromyelitis optica. Static and dynamic ocular point-of-care ultrasonography (POCUS) performed by appropriately trained emergency physicians can be diagnostic in some cases, especially for persistent, monocular, painless AVL caused by vitreous hemorrhage, vitreous detachment, or retinal detachment. Additionally, evaluation of the optic nerve sheath’s diameter via POCUS may suggest papilledema from various causes, such as space-occupying lesions or idiopathic intracranial hypertension.

### Disease-Specific Treatments

The authors note that most AVL presentations require consultation based on the likely cause. For instance, ophthalmology should be consulted for ocular-related pathology, neurology for brain-related

pathology, and either or both specialties for specific neurovascular conditions. The authors also highlight several disease-specific treatments for emergency physicians to consider.

Acute narrow-angle glaucoma should be treated emergently with eye drops (eg, timolol, apraclonidine, pilocarpine) and carbonic anhydrase inhibitors (eg, acetazolamide), pending consultation. Patients with suspected central retinal artery occlusion who present within 4.5 hours of symptom onset can be treated like stroke patients, including with activation of the institution's stroke notification and with administration of a fibrinolytic agent (when contraindications do not exist). For these patients, Edlow and Hoffman recommend against other previously described historical treatments like ocular massage, noting their potential harm.

Because giant cell arteritis can progress, the threshold should be low for empirically treating suspected cases with high-dose glucocorticoids. Glucocorticoids have a limited effect on the results of a temporal artery biopsy (used to diagnose the condition) when the biopsy is performed within 2 weeks of medication initiation. Other disease-specific treatments include fomepizole for methanol toxicity, acetazolamide and lumbar puncture for idiopathic intracranial hypertension, and hormone replacement and possible surgical decompression (after emergent neurosurgical consultation) for pituitary apoplexy.

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# Noninvasive Respiratory Support for Acute Respiratory Failure

By Andrew J. Eyre, MD, MS-HPEd, FACEP

Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts

## Objective

On completion of this article, you should be able to:

- Discuss noninvasive respiratory support strategies for adults with acute respiratory failure.

Munshi L, Mancebo J, Brochard LJ. Noninvasive respiratory support for adults with acute respiratory failure. *N Engl J Med*. 2022 Nov 3;387(18):1688-1698.

## KEY POINTS

- Noninvasive respiratory support strategies — including HFNC, CPAP, and NIPPV — are increasingly popular interventions for patients with respiratory failure.
- Noninvasive respiratory support strategies are commonly used for patients with noncardiogenic pulmonary edema and COPD.
- Although HFNC, CPAP, and NIPPV have some similarities, each has unique features that must be considered before their selection and application.

Patients frequently present with respiratory failure that requires rapid, thoughtful, and targeted intervention to avoid morbidity and mortality. Although a wide range of conditions can cause respiratory failure, all patients with respiratory failure will exhibit significant hypoxemia, an inability to effectively ventilate, or in some cases, both. Invasive mechanical ventilation, typically via endotracheal intubation or a tracheostomy tube, is often necessary to treat respiratory failure; however, a variety of noninvasive interventions exist and have gained popularity in recent years. The featured 2022 *New England Journal of Medicine* review article focuses on the use of high-flow nasal cannula (HFNC), continuous positive airway pressure (CPAP), and noninvasive positive-pressure ventilation (NIPPV) (sometimes referred to as bilevel positive airway pressure [BiPAP]).

### HFNC

HFNC systems use a specially designed nasal cannula to provide gas at high flow rates ( $\geq 30$  L/min, up to 80 L/min), with an  $\text{FiO}_2$  that can be titrated from 0.21 to 1. HFNC likely provides a small amount of positive end-expiratory pressure (PEEP), although it cannot be specifically titrated like other modalities. Additionally, through a mechanism of dead-space washout, HFNC provides a very small amount of ventilatory support. As such, HFNC is particularly useful when hypoxemia, rather than ventilation, is the primary issue in respiratory failure. Although HFNC may improve oxygenation and, in some cases, prevent the need for intubation, Munshi et al highlight the importance of caution and careful monitoring when using HFNC because questions remain about which patients will decompensate and about the physiologic effects of prolonged increased work of breathing.

### CPAP

CPAP provides patients with a preselected, continuous, and consistent amount of positive airway pressure during both inhalation and exhalation. The patient must generate breaths spontaneously, but the additional pressure provided with CPAP can ease the work of breathing, keep the airways open, and help recruit poorly aerated alveoli. Additionally, in some cases of left ventricular dysfunction, CPAP can decrease both preload and afterload. CPAP can be provided through a wide range of devices, each with variable settings and functions. Some CPAP setups use room air, while others are oxygen powered or allow for titration of oxygen levels. These latter models can improve hypoxemia by directly delivering supplementary oxygen. Although CPAP does not directly improve or drive ventilation, it may improve ventilation by indirect mechanisms such as opening the airway, decreasing atelectasis, and easing overall respiratory effort. CPAP circuits can be connected to a patient with a range of interfacing devices,

including nasal pillows, nasal masks, oronasal masks, and helmets. For CPAP to be effective, physicians must work to maximize patient compliance by addressing a variety of variables such as the type of interface and the interface's size, seal, and overall comfort. Although CPAP can be used to improve work of breathing and temporize a variety of respiratory conditions, it is most often used in the acute setting, alongside supplemental oxygen, to treat hypoxemic respiratory failure, especially when the respiratory failure is caused by cardiogenic pulmonary edema and chronic obstructive pulmonary disease (COPD).

### **NIPPV**

CPAP and NIPPV have many similarities, but they also have critical differences. Unlike the single, consistent pressure provided by CPAP, the pressure provided by NIPPV is higher for the inspiratory phase and lower for the expiratory phase (ie, PEEP). When a patient triggers a breath, the increased pressure level directly augments inhalation, reducing the effort required by the patient and the overall work of breathing. In the acute setting, most NIPPV devices can be augmented with varying levels of oxygen to address hypoxemia. Compared to CPAP, the differing inspiratory and expiratory pressures of NIPPV augment ventilation more. Like CPAP, NIPPV can be applied to patients through a variety of masks or alternative interfaces. Also, like CPAP, NIPPV is effective for a variety of causes of hypoxemic respiratory failure. NIPPV, however, is likely more beneficial for cases of hypercarbic respiratory failure.

### **Additional Uses of Noninvasive Respiratory Support Strategies, and Patient Monitoring**

The use of noninvasive respiratory support strategies has grown dramatically in recent decades. Evidence suggests that when these strategies are selected and implemented appropriately, they help support patients with respiratory failure, temporize respiratory conditions while other therapies are initiated, and potentially avoid some intubations. Additionally, interest and evidence are growing for using noninvasive respiratory strategies to help wean patients from mechanical ventilators and to support patients in the postoperative setting. In the acute setting, the patients who receive noninvasive respiratory support are typically critically ill and extremely tenuous. Emergency physicians must carefully consider if a noninvasive approach is appropriate for their patient and, if so, which method is best. Further, these patients must be carefully monitored for signs of decompensation so that the medical team can rapidly intervene and prepare for more invasive support. The authors describe a number of physiologic parameters that should be monitored, along with a variety of scores that may be effective in identifying patients at risk of failing noninvasive strategies.

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