PALLIATIVE CARE NETWORK OF WISCONSIN

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FAST FACTS AND CONCEPTS #33
VENTILATOR WITHDRAWAL PROTOCOL

Charles von Gunten MD, PhD and David E Weissman MD

Introduction This is the first part of a three-part series on withdrawing ventilators in patients expected to die. *Fast Fact* #34 will review use of sedating medication for ventilator withdrawal and *Fast Fact* #35 will review information for families.

Once it is decided that further aggressive medical care is incapable of meeting the desired goals of care for a ventilator-dependent patient, discussing ventilator withdrawal to allow death is appropriate (see *Fast Fact* #16). Such a decision is never easy for family members, doctors, nurses, and other critical care staff. All members of the care team should be involved and apprised of the decision-making process and have the opportunity to discuss the plan of care.

Options for Ventilator Withdrawal Two methods have been described: immediate extubation and 'terminal weaning.' The clinician's and patient's comfort, and the family's perceptions, should influence the choice. In immediate extubation, the endotracheal (ET) tube is removed after appropriate suctioning. Humidified air or oxygen is given to prevent the airway from drying; comfort medications are administered. This is the preferred approach to relieve discomfort if the patient is conscious, the volume of secretions is low, and the airway is unlikely to be compromised after extubation. In terminal weaning, the ventilator rate, positive end-expiratory pressure (PEEP), and oxygen levels are decreased while the endotracheal tube is left in place. Terminal weaning may be carried out over a period of as little as 30 to 60 minutes (see reference 3 for a protocol). If the patient survives they can be extubated with ongoing symptomatic care. If it is decided to leave the endotracheal tube in place (to, for instance, ensure the patency of the upper airway) a Briggs T-piece can be placed.

Prior to Immediate Ventilator Withdrawal

1. Encourage family to make arrangements for special music or rituals or support during and following the procedure. (See *Fast Fact* #35).
2. Counsel families on potential outcomes following withdrawal.
3. Document clinical findings, discussion with families/surrogates, and goals of care.

4. Ensure that all monitors and alarms are turned off. Ensure that respiratory therapy or nursing staff is assigned to override alarms that cannot be turned off.
5. Remove restraints and unnecessary medical paraphernalia.
6. Turn off blood pressure support and paralytic medications; discontinue other life-sustaining treatments (e.g. artificial nutrition/hydration, antibiotics, dialysis).
7. Maintain intravenous access for administration of sedating medications.
8. Clear a space for family access to the bedside. Invite family into the room if they wish to be present. If the patient is an infant or young child, offer to have the parent hold the child.
9. Establish adequate symptom control prior to extubation (See *Fast Fact* #34).
10. Have a syringe of an additional sedating medication at the bedside (midazolam, morphine, or lorazepam) to use in case distressing tachypnea or other symptoms.

At the time of ventilator withdrawal

1. Once you are sure the patient is comfortable, set the FiO_2 to 21% (room air); observe for signs of respiratory distress; adjust medication as needed to relieve distress before proceeding further.
2. If the patient appears comfortable, prepare to remove the ET tube; try a few minutes of "no assist" ventilation before the ET tube is removed.
3. A nurse or respiratory therapist should be stationed at the opposite side of the bed with a washcloth and oral suction catheter.
4. When ready to proceed, deflate the ET tube cuff. If possible, someone should be assigned to silence, turn off the ventilator, and move it out of the way. Once the cuff is deflated, remove the ET tube under a clean towel which collects most of the secretions and keep the ET tube covered with the towel. If oropharyngeal secretions are excessive, suction them away.
5. The family and the nurse should have tissues for extra secretions, and for tears. The family should be encouraged to hold the patient's hand and provide assurances to their loved one.
6. Be prepared to spend additional time with the family discussing questions concerns. After death occurs, encourage the family to spend as much time at the bedside as they require; provide acute grief support and follow-up bereavement support

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #34
SYMPTOM CONTROL FOR VENTILATOR WITHDRAWAL IN THE DYING PATIENT

Charles von Gunten MD, PhD and David E Weissman MD

Introduction This is the second of a three-part series. *Fast Fact* #33 reviewed a protocol for removing the ventilator, and *Fast Fact* #35 will review information for families.

The most common symptoms related to ventilator withdrawal are breathlessness and anxiety. Opioids and benzodiazepines are the primary medications used; concerns about unintended hastened death are exaggerated, particularly if established dosing guidelines are followed (see *Fast Fact* #8). There is no medical or ethical justification for withholding sedating medication when death following ventilator withdrawal is the expected outcome. However, increasing doses beyond the levels needed to achieve comfort/sedation, *with the intention of hastening death*, is euthanasia and is not acceptable/legal medical practice.

A 2004 study suggests that opioids and benzodiazepines do not shorten survival but do help minimize respiratory distress in terminal extubations. Therefore, pre-bolus doses should be strongly considered even for those who are comatose, in order to control labored breathing. The doses needed to control symptoms depend on the neurological status of the patient and presence of drug tolerance (these same drugs are commonly used in routine ICU care). In all cases, a senior-level physician should remain at the bedside prior to and immediately following extubation until adequate symptom control is assured.

Medication Protocol

1. Discontinue paralytics; do not use paralytic agents for ventilator withdrawal. Besides ensuring a patient cannot breathe, they do not prevent or treat any discomfort in patients off ventilators, and prevent patients from communicating or demonstrating distress. When patients have multi-organ failure, some paralytics may not be cleared for 2-18 hours. Therefore, if there is doubt as to whether the paralytics have worn off, utilize a peripheral nerve stimulator. It is ok to extubate when you see muscle twitches with 4 consecutive nerve stimulations.
2. Administer glycopyrrolate (Robinul®) 0.2 to 0.4 mg IV 20-30 minutes prior to the extubation to minimize secretions.
3. Administer an IV bolus dose of an opioid (i.e. morphine 2-10 mg IV) and a benzodiazepine (lorazepam 1-2 mg IV) if anxiety is anticipated. Consider an IV continuous infusion of sedating medication (see below). Do not rely on subcutaneous or enteral drug administration as these take longer to work. *For children, obtain dosing advice from a pharmacist or pediatric intensivist.*
4. Titrate medications to control labored respirations and achieve the desired state of sedation prior to extubation. Testing the eyelid reflex is a common method of quickly assessing level of consciousness.
5. Have additional medication drawn up and ready to administer at the bedside if needed.
6. After ventilator withdrawal: Most respiratory distress ensues in the first few hours after the extubation. If distress is noted, utilize additional bolus doses of opioids and benzodiazepines (e.g. morphine 5-10 mg IV push q 10 min, and/or midazolam, 2-4 mg IV push q 10 min, until distress is relieved). You can adjust infusion rates to maintain relief, but remember infusion rates have a delayed effect. Therefore, avoid relying on infusion rates to control distress seen after the extubation.
7. Specific dosages are less important than the goal of symptom relief. A goal should be to keep the respiratory rate < 30 and eliminate grimacing, agitation, and labored respirations.
8. Orders such as "*morphine drip 1-20 mg/hr, titrate as needed*" are inappropriate as they will likely mismanage the acute symptom distress and place undue burden on the bedside nurse to make clinical management decisions.

NOTE: The following regimens are commonly used; all require a bolus dose commonly followed by a continuous infusion. Dose ranges are approximations and depend in part on patients' prior

exposure to opioids and benzodiazepines. Clinicians should use clinical judgment when deciding on what specific drugs and doses to use. Many institutions have policy and clinical guidelines about the use of opioids and sedatives in these circumstances. *Clinicians unfamiliar with the use of these agents in the setting of ventilator withdrawal are urged to consult with an anesthesiologist, critical care specialist, or pain/palliative specialist prior to use.*

Regimen A: Morphine plus Midazolam (Adult doses)

Good for comatose patients or patients with limited consciousness and/or patients with little prior exposure to these drugs (and thus less risk of tolerance).

Bolus: Morphine 2-10 mg; Midazolam 1-2 mg
Infusion: Morphine 50% of the bolus dose in mg/hr; Midazolam 1 mg/hr

Regimen B: Pentobarbital (Adult doses)

Good for the awake patient who can be expected to have respiratory distress following ventilator withdrawal.

Bolus: 1-2 mg/kg (at rate of 50 mg/min)
Infusion: 1-2 mg/kg/hr

Regimen C: Propofol (Adult doses)

Good for the awake patient who can be expected to have demonstrable respiratory distress following ventilator withdrawal.

Bolus: 20-50 mg
Infusion: 10-100 mg/hr

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #35
INFORMATION FOR PATIENTS AND FAMILIES ABOUT VENTILATOR WITHDRAWAL

Charles von Gunten MD, PhD and David E Weissman MD

Introduction This is Part 3 of a three-part series on ventilator withdrawal. *Fast Fact* #33 reviewed a protocol for removing the ventilator; *Fast Fact* #34 reviewed medications for symptom control. Physician-counseling of families is a critical aspect of care for the dying patient who is to be removed from a ventilator. Ideally the family will be involved in the decision to withdraw the ventilator and thus apprised of the goals of care. Before withdrawal, the following issues should be discussed.

Potential outcome of ventilator withdrawal
Assuming all other life-sustaining treatments have been stopped, including artificial hydration and nutrition, there are several potential outcomes: rapid death within minutes (typically patients with sepsis on maximal blood pressure support), death within hours to days, or stable cardiopulmonary function leading to a different set of care plans, including potential hospital discharge. If the latter possibility is realistic, future management plans should be discussed prior to ventilator removal, since some families may desire to resume certain treatments, notably artificial hydration/nutrition. Generally, by the nature of the underlying illness and the established goals, it is fairly easy to predict which category will be operative, but all families should be prepared for some degree of prognostic uncertainty (see *Fast Fact* #30).

The procedure of ventilator withdrawal
Never make assumptions about what the family understands; describe the procedure in clear, simple terms and answer any questions. Families should be told before-hand the steps of withdrawal and whether or not it is planned/desired to remove the endotracheal tube. In addition, they should be counseled about the use of oxygen and medications for symptom control. Assure them that the patient's comfort is of primary concern. Explain that labored breathing and signs of breathlessness may occur shortly after the extubation, but that they can be managed. Confirm that you will have medication available to manage any discomfort. Ensure they know that the patient will likely be asleep and that involuntary moving, noisy or irregular breathing, or gasping do not reflect suffering if the patient is properly sedated or in a coma. Some families may wonder if leaving their loved one intubated and on the ventilator may be more comfortable. Explain that ET tubes are a source of discomfort and anxiety for most patients and therefore are not recommended at the end of life when comfort is the primary goal.

Explain how the family, clergy and others can be at the bedside before, during and after withdrawal. If asked, explain that they can show love and support through touch, wiping of the patient's forehead, holding a hand and talking to him or her.

Support the decision
Even though a family is able to make a definite decision for ventilator withdrawal, such a decision is always emotionally charged. Families may constantly second-guess themselves, especially if the patient appears to linger following ventilator withdrawal. Physician support, guidance and leadership are crucial, as the family will be looking to the physician to ensure them that they are "doing the right thing." Furthermore, it is common for families to have concerns that their decision constitutes euthanasia or assisted suicide—explicit counseling from a physician will be needed. Finally, support needs to continue following death during the bereavement period (see *Fast Fact* #22).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #122
PALLIATIVE CARE AND ICU CARE: PRE-ADMISSION ASSESSMENT

Richard A Mularski MD and Molly L Osborne MD

Background What are the indications for Intensive Care Unit (ICU) admission in the chronically and/or terminally ill and how can one integrate palliative care into the daily interdisciplinary agenda? A good approach is to determine the patient-centered goals of care and then decide if ICU care will help promote or detract from these goals. The use of a pre-admission checklist can be helpful to determine the appropriateness of ICU therapy and to initiate communication about goals and preferences **before** a trial of ICU care. With use of a complementary strategy after admission, the patient can benefit from a care plan that integrates palliation into the daily agenda and anticipates needs. This *Fast Fact* will discuss the pre-ICU-admission assessment of patients with advanced illnesses; *Fast Fact* #123 will discuss ongoing ICU assessment of these patients to ensure appropriate symptom management and medical decision-making.

Pre-Admission ICU Checklist

A. Clarify the underlying medical condition and possibilities with ICU treatment:
1. What is/are the underlying chronic fatal illness disease(s)?
2. What has been the clinical course of the chronic illness over the past few months/ year?
3. What was the patient's functional status and quality of life in the weeks preceding admission?
4. What are the acute illnesses and conditions that the ICU might improve?
5. What interventions do you expect will be required in the first 48 hours?
6. What do you foresee as the best possible outcome from treatment in ICU:
    a. Cure the acute process with return to baseline function (e.g. pneumonia).
    b. Cure or improve the acute process but the patient will likely have a reduced functional capacity permanently (e.g. large stroke).
7. Is there prognostic information to guide you/patient/family in decision making?

B. Address and document decision-making with patient/family/surrogate:
1. Does the patient have decision-making capacity (see *Fast Fact* #55)?
2. Does the patient have an advance care planning document or a legally designated agent?
3. Who are the important people that assist the patient in decision making?
4. With or without an advance care planning document, has the patient or surrogate expressed clear goals of care with their physician in the recent past or during the current illness?

C. Discuss and document ICU-based and patient-focused goals and preferences:
1. Review what therapeutic trials and palliative care issues can be addressed by an interdisciplinary ICU team; consider whether needs can be met in alternative care settings.
2. Document advance care planning and do not resuscitate orders (see *Fast Facts* #23, #24, #292).
3. Agree upon specific, time-limited, ICU goals (e.g. three days trial of mechanical ventilation).
4. Identify physical symptoms and develop a treatment plan for palliation.

D. Coordinate interdisciplinary communication & time reappraisal of therapy and goals:
1. Meet with ICU team members to review goals of care, symptoms, family needs, etc.

2. Document goals of care and details of decision making in medical record.
3. Schedule a time to assess clinical response and whether goals need to be changed.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPT #123
PALLIATIVE CARE AND ICU CARE: DAILY ICU CARE PLAN CHECKLIST

Richard A Mularski MD and Molly L Osborne MD

Background A pre-admission checklist (see *Fast Fact* #122) can be used before intensive care unit (ICU) admission to initiate communication about goals and preferences for an ICU trial. An ICU daily care plan checklist can be used to promote palliative care, simultaneously with curative or life-prolonging therapies. The checklist can help clarify the goals of care for the ICU team, consultants, patients, and significant others and serve as a vehicle for quality improvement.

Palliative ICU Daily Care Plan Checklist

A. Address short-term medical progress and goals:
1. Assess whether specific criteria toward progress has been met (e.g. mental status or ventilator needs). Has there been improvement, stability, or worsening in the past 24 hours?
2. Have there been clinical changes that will impact the patient's ability to meet desired clinical goals (e.g. new GI bleeding)?
3. Review interventions that may be needed in the next 48 hours and set overt criteria to measure progress (e.g. objective indicators of progress towards ventilator weaning).
4. Use this information to review goals and determine if there are changes in prognosis that can guide you/patient/family in decision making.

B. Address patient symptoms and psychosocial needs:
1. Review progress in managing current symptoms and psychosocial needs (patient and family).
2. Identify existing or new physical symptoms and psychosocial needs; discuss among team members (e.g. patient depression, family stress).
3. Develop a treatment plan for each symptom/need for the next 24 hours.
4. Identify both ICU and non-ICU resources to assist in care plan (e.g. palliative care nurse, clinical psychologist, etc.) and clarify roles for members of the interdisciplinary team.

C. Clarify understanding and coordinate patient/family communication:
1. Review patient/family understanding and concerns about diagnosis, prognosis, possible outcomes, and details of above items.
    a. Inquire if the patient or significant others have new information or new perspectives that can help clarify the understanding of the patient's goals and preferences.
    b. Decide if goals of care need refinement or change.
    c. Agree on specific criteria for reassessment of clinical responses and goals.
2. Determine what new information needs to be communicated within next 24 hours.
3. Agree on who and how the team will communicate with family/patient today (e.g. attending will meet with family at 3 PM; resident will attend then call out-of-town relative after meeting).

D. Document care plan and coordinate follow-up and next day's assessment:
1. Document clinical status, symptoms, daily goals of care, and details of decision making.
2. Change orders as necessary (e.g. new do-not-resuscitate order).
3. Schedule next meeting for interdisciplinary team that includes patient (if able) and family to update goals, medical evaluation, responses to current therapy, and future plans.

Suggestion for Faculty - Improving the Process of Care

Establish a written checklist containing the above elements that can be completed during daily rounds and entered into the medical record.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #141
PROGNOSIS IN END-STAGE COPD

Julie Wilson Childers MD, Robert Arnold MD, and J Randall Curtis MD

Background Prognostic variables in COPD patients are not well described, thus decision making regarding when to move away from aggressive life-sustaining treatments is challenging. This *Fast Fact* will review prognostication in patients with advanced COPD.

Ambulatory COPD Patients The forced expiratory volume in one second (FEV_1) has traditionally been used to assess COPD severity. A FEV_1 of less than 35% of the predicted value represents severe disease; 25% of these patients will die within two years and 55% by four years. A number of other studies have shown that age, low body mass index (BMI), serum inflammatory biomarkers (such as C-reactive protein, IL-6, and fibrinogen) and low PaO_2 were independent predictors that correlated to reduced survival time. The BODE scale, consisting of BMI, exercise capacity, and subjective estimates of dyspnea, has been shown to help predict survival over 1-3 years (2).

Variable	**Points on BODE Index**			
	0	**1**	**2**	**3**
FEV1 (% predicted)	≥65	50-64	36-49	≤35
Distance walked in 6 min (meters)	>350	250-349	150-249	≤149
MMRC dyspnea scale*	0-1	2	3	4
Body-mass index (BMI)	>21	≤21		

***MMRC dyspnea scale range from 0 (none) to 4 (4 dyspnea when dressing or undressing).**

BODE Index Score	**One year mortality**	**Two year mortality**	**52 month mortality**
0-2	2%	6%	19%
3-4	2%	8%	32%
4-6	2%	14%	40%
7-10	5%	31%	80%

Note: these variables do not appear to help predict prognosis within six months of death.

Hospitalized COPD Patients Mortality statistics vary for patients admitted with COPD exacerbations depending on age, functional status, co-morbidities, and physiological variables such as hypoxia and hypercarbia. Roughly 10% of patients admitted with a $PaCO_2$ >50 mmHg will die during the index hospitalization, 33% will die within six months, and 43% die within one-year (3). Patients with less severe COPD have lower in-hospital mortality rates (4). COPD patients who require mechanical ventilation have an-hospital mortality of ~25% (5,6). Poor prognostic factors include: co-morbid illnesses, severity of illness (APACHE II score), low serum albumin, and/or low hemoglobin. Previous mechanical ventilation, failed extubation, or intubation for greater than 72 hours all increase mortality (5). In one study, patients ventilated more than 48 hours had a 50% one year survival; functional status and severity of illness were associated with short term mortality while age and co-morbidities were associated with one year mortality (2).

National Hospice and Palliative Care Organization Criteria NHPCO guidelines for hospice admission in COPD include factors such as cor pulmonale and pO2 <55 mmHg while on oxygen,

albumin < 2.5 gm/dl, weight loss of > 10%, progression of disease, and poor functional status. However, a study showed when using these factors, 50% of the patients were still alive at six months, implying that the NHPCO criteria have a limited role in predicting six month mortality and thus should be used with caution in determining hospice eligibility under the Medicare Hospice Benefit (7).

Summary COPD is a heterogeneous disease without a simple prognostic trajectory. For ambulatory patients, age, degree of dyspnea, weight loss (BMI), functional status, and FEV_1 are relevant prognostic factors for predicting 1-3 year survival. For hospitalized patients, the same factors are relevant. In addition, the need for prolonged or recurrent mechanical ventilation is predictive of a shorter prognosis.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #160
SCREENING FOR ICU DELIRIUM

Richard Altman MD, Eric Milbrandt MD, MPH, and Robert Arnold MD

Background Delirium is an acute, fluctuating change in mental status, accompanied by sleep/wake cycle disruption, inattention, and altered perceptions (hallucinations/delusions) (see *Fast Facts* #1, 60). Delirium can be hypoactive or hyperactive and is often multifactorial (1). Patients with hypoactive delirium are calm, but inattentive and manifest decreased mobility. Patients with hyperactive delirium are agitated and combative, and also lack the ability to maintain attention to complete tasks. Delirium can be considered a marker of acute brain dysfunction, much like shock is evidence for dysfunction of the cardiovascular system (2). When recognized early, it is potentially modifiable depending on the patient's circumstances.

ICU Delirium Delirium occurring in the ICU is associated with an increased length of hospitalization, increased need for institutionalization, and higher short and long-term mortality (3). In the ICU, delirium occurs in as many as 80% of patients, but is often overlooked or misdiagnosed because of the difficulty of assessing mental states in intubated patients. Three assessment tools have been described in the literature to aid in delirium diagnosis.

1) The Confusion Assessment Method-Intensive Care Unit (CAM-ICU) Assessment Tool is the best documented method of diagnosing delirium in the ICU (4). This tool was specifically designed for use in non-verbal (i.e. mechanically ventilated) patients. With the CAM-ICU, delirium is diagnosed when patients demonstrate 1) an acute change in mental status or fluctuating changes in mental status, 2) inattention measured using either an auditory or visual test, and either 3) disorganized thinking, or 4) an altered level of consciousness. Importantly, the CAM-ICU can only be administered if the patient is arousable to voice without the need for physical stimulation. The CAM-ICU includes very specific assessment questions/tools, found online at http://www.icudelirium.org/delirium.html.

When administered by a nurse, the CAM-ICU takes only 1 to 2 minutes to conduct (3,5). A systematic review of nine studies evaluating the CAM-ICU showed a pooled sensitivity of 80% and a pooled specificity of 95.9% for detecting delirium as compared to full DSM-IV assessment by a geriatric psychiatrist (6). National guidelines recommend routine use of the CAM-ICU for delirium assessment in all critically ill patients and treatment with haloperidol when delirium is present (7). However, these recommendations are based on expert opinion and limited case series. It remains unknown whether diagnosis and/or treatment of delirium will lead to better patient outcomes. While there are some early observational cohort data suggesting that patients treated with haloperidol have lower hospital mortality, this finding needs confirmation in a randomized, controlled trial before being applied to routine patient care.

2) The Intensive Care Delirium Screening Checklist assesses eight features of delirium: altered level of consciousness, inattention, disorientation, hallucinations, psychomotor agitation/retardation, inappropriate mood/speech, sleep/wake cycle disturbance, and symptom fluctuation. The pooled sensitivity and specificity of this tool were 74% and 81.9% respectively per a systematic review (6).

3) The Delirium Screening Checklist is another recent tool that uses a checklist similar to the Intensive Care Delirium Screening Checklist (8).

Recommendation It is believed that prompt recognition and treatment of ICU delirium is important for patient safety. Use of rapid tools such as CAM-ICU can help identify ICU delirium and are recommended when assessing mental status changes. A key to effective implementation of ICU delirium screening includes addressing attitudinal barriers that delirium is an inevitable part of critical illness via multi-faceted training such as lectures, case-based scenarios, one-on-one teaching, and bedside teaching to provide real time feedback (1).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #199
OPIOIDS FOR COUGH

Sean Marks MD and Drew A Rosielle MD

Background Cough is a common, and at times distressing, symptom. Up to 40% of advanced cancer patients report cough, and while a smaller percentage find their cough distressing, severe cough can lead to dyspnea, nausea/vomiting, sleep impairment, chest and throat pain, and impaired communication. This *Fast Fact* will focus on the use of opioids for the symptomatic treatment of cough. *Fast Fact* #200 will address other agents for cough.

Etiologies & Evaluation Common etiologies of cough include infections of the upper and lower airway, asthma and COPD, lung cancer or lung metastases, interstitial pulmonary processes (such as lymphangitic tumor spread or pulmonary edema), gastroesophageal reflux, aspiration, and drugs. Common drug causes include ACE inhibitors, NSAIDs, and inhalant medications. Evaluating for reversible causes is appropriate if consistent with the goals of care and prognosis. If feasible, treatment should be directed at the underlying cause. Many patients however will benefit from symptomatic therapy for a distressing cough while waiting for acute therapy to work or have a chronic cough not amenable to treatment (e.g. cough due to advanced lung cancer).

Opioids are the only clearly effective centrally-acting anti-tussive drugs and are thought to work by suppressing the brainstem cough center through mu and kappa opioid receptor agonism. They are the first-line symptomatic treatment for severe, distressing cough. All opioids used to treat cough have typical opioid side effects such as sedation, constipation, and nausea.

- *Codeine:* Duration of action is 4 hours; usual adult dose is 10-20 mg every 4-6 hours. It has shown to be effective for acute and chronic cough in several placebo-controlled trials. It is available alone or as an elixir with guaifenesin.

- *Dextromethorphan:* Duration of action 3-6 hours; usual adult dose is 10-20 mg every 4-6 hours. It is the most commonly used anti-tussive. Confirmed to be as effective as codeine for cough in multiple studies. It is available alone or as an elixir with guaifenesin. Note: dextromethorphan inhibits the cytochrome P450 system and thereby affects the metabolism of many drugs. Dextromethorphan can also cause a serotonin syndrome if used with serotonergic drugs such as antidepressants.

- *Hydrocodone:* Duration of action 4-6 hours; usual dose 5-10 mg every 4 hours. Hydrocodone is only available as a combination product in the US: as a short-acting elixir with the anticholinergic drug homatropine or as an extended release elixir with the antihistamine chlorpheniramine (dosed at 10 mg every 12 hours). These other agents magnify hydrocodone's sedative effects, and limit the maximum dose a patient can take. Hydrocodone has been shown to be as effective as codeine in head to head studies but with fewer gastrointestinal side-effects. For this reason it is considered by many experts as the anti-tussive of choice (Homsi 2001).

- *All opioid* analgesics have anti-tussive activity and their use has been mostly based on convention; there is no strong evidence that any one opioid has superior efficacy for cough. For patients already taking opioids for pain, it is unclear whether adding a second opioid such as codeine for cough is effective. One uncontrolled, open-label study showed hydrocodone to be helpful in this setting; it has not been repeated (Homsi 2001).

Fast Fact #200 will discuss non-opioid agents for cough, as well as address some general treatment strategies.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #200
NON-OPIOID ANTI-TUSSIVES

Sean Marks MD and Drew A Rosielle MD

Background Cough is a common and at times distressing symptom. *Fast Fact* #199 discussed opioids for the symptomatic treatment of cough. This *Fast Fact* will address non-opioid anti-tussives.

Controversies Commonly used prescription and over-the-counter anti-tussive formulations which contain some combination of antihistamines (e.g. diphenhydramine), a mucolytic (e.g. guaifenesin), and/or dextromethorphan are often used for acute cough due to upper respiratory infections and acute bronchitis. Evidence for these agents in the acute setting is poor (either no better than placebo or sweet syrup) and cannot be recommended. Due to concerns about inadvertent overdose and lack of efficacy, these products are now being *actively* discouraged for use in the pediatric setting.

Centrally-acting non-opioid anti-tussives

- *Gabapentin:* the pathophysiology of refractory chronic cough is thought to resemble central sensitization as seen in neuropathic pain. A randomized, double-blind placebo controlled trial demonstrated that gabapentin can meaningfully improve cough-specific quality of life and reduce cough frequency and severity compared with placebo. Doses up to 1800 mg a day were studied.
- *Other neuromodulating agents*: paroxetine, amitriptyline, and benzodiazepines have been anecdotally reported to have efficacy in chronic, refractory cough but lack published controlled evidence.

Peripherally-acting anti-tussives

- *Sweet syrups* are commonly used as cough suppressants, whether as bases for prescription elixirs (such as codeine with guaifenesin) or home remedies (honey, simple syrup). The mechanism of action is unknown; some authors hypothesize it acts as a protective barrier to sensory receptors in the throat that heighten the cough reflex. A few controlled trials have shown sweet syrups reduce coughing in upper respiratory infections.
- *Benzonatate* inhibits cough by anesthetizing stretch receptors in the respiratory tract. Its duration of action is 3-8 hours; dosed at 100-200 mg three times a day. No published controlled studies confirm its effectiveness but multiple uncontrolled studies support its use. Side effects are uncommon but include sedation, headache, bronchospasm, and nausea. Empirically many experts recommend adding it to an opioid.
- *Antihistamines and anticholinergics* are often part of combination anti-tussive elixirs with or without an opioid. Anticholinergics such as hyoscyamine and scopolamine are most helpful in the setting of copious upper respiratory secretions leading to cough. See *Fast Fact* #109 for dosing information.
- *Expectorants* thin bronchial secretions and ease expectoration. Examples include guaifenesin (200-400 mg every 4 hours) and nebulized acetylcysteine or hypertonic saline. Empirically they have been recommended for severe, chronic, wet coughs. Because they may increase fluid in the respiratory tract, they are not recommended if the cough reflex is diminished.
- *Nebulized local anesthetics* are thought to work by anesthetizing afferent receptors in the respiratory tract. There have been no trials evaluating their effectiveness; anecdotally they have been reported to be effective for refractory cough. Published regimens include lidocaine 2% solution, 5 mL nebulized every 6 hours; and bupivacaine 0.25%, 5 mL nebulized every 8 hours. Bronchospasm is a potential side effect.
- *Other agents* such as bronchodilators and corticosteroids have not been shown to be effective apart from specific indications (e.g. for COPD or asthma exacerbations).

Recommendations Treatment for cough should be directed at the underlying cause if feasible and consistent with a patient's prognosis and goals of care. When symptomatic treatment for a distressing cough is necessary, it is reasonable to start with an opioid product, adding benzonatate if needed. A trial of anticholinergics and expectorants for the indications described above is reasonable, but they should be stopped after a couple days if they have no effect. Sweet syrups appear to be helpful in upper respiratory infections; their role otherwise is uncertain. If these strategies fail to control distressing symptoms, gabapentin should be tried for chronic cough.

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Background Non-invasive positive pressure ventilation (NPPV, often called 'BiPAP') is commonly used in patients with respiratory failure from COPD, CHF, and other disorders. NPPV decreases the work of breathing and allows respiratory muscle rest during inspiration. This *Fast Fact* discusses medical decision making around its use at the end of life. *Fast Fact* #231 discusses practical aspects of applying NPPV in dying patients, as well as how to discontinue it safely.

Goals of NPPV at the end of life NPPV is used in 3 general circumstances in patients close to death, all of which are likely to be encountered by palliative specialists (1):

1. *Patients who desire full, life-prolonging interventions, regardless of prognosis*. If the patient's respiratory status deteriorates, intubation and ventilation are initiated.
2. *Patients who want life-prolonging therapy but with limitations* (e.g., patients with a 'Do Not Intubate' order but otherwise want all attempts at life prolongation). Ideally, NPPV is used only if the etiology for the respiratory failure is thought to be reversible and is stopped if it is not producing the desired response or the patient is not tolerating NPPV. In practice, this may not be the case.
3. *Dying patients with respiratory failure or dyspnea for palliative purposes.* This category includes dying patients who have decided to forego life-prolonging therapies and wish to focus on comfort measures. NPPV can be used with the intention to reduce the work of breathing, to ease dyspnea, and to help maintain wakefulness by reducing the amount of opioids a patient needs to be comfortable. NPPV can also be used to prolong life for a short period to meet a patient's goals while otherwise providing a comfortable death (e.g., to allow time for family to visit). Unlike #2, the goal is not to bridge a patient through a reversible illness, but to forestall death to meet a specific goal.

Research Findings

- In several trials NPPV has been shown to reduce mortality, intubation rates, and hospital length of stay in patients with COPD, as well as reduce intubation rates in patients with respiratory failure from heart failure and in immunocompromised patients (2-4).
- For the second category of patients, there are no high-quality trials. Some observational studies suggest that NPPV can reverse acute respiratory failure and decrease hospital mortality in patients with COPD or CHF who have 'Do Not Intubate' orders (5,6). Apart from ALS (see *Fast Fact* #73, #300) there are no data to affirm its use in other patient populations.
- There is a small body of research about the use of NPPV to alleviate dyspnea in dying patients. In a survey, a majority of pulmonologists endorsed a belief that NPPV relieves dyspnea in dying patients in addition to anxiolytics and analgesics (7). In multiple controlled studies of hospitalized cancer patients with acute respiratory failure and life expectancy less than 6 months, NPPV was shown to improve dyspnea much faster and have an opioid sparing effect in the first 48 hours compared with passive oxygen therapy (8,9). However, it is unclear what effect NPPV had on the overall quality of dying and death, a much more complex and subjective dimension, seeing that the use of NPPV in these studies was restricted to intensive care settings.
- With wider availability of new interfaces and ventilators (e.g. nasal NPPV), the rate of discontinuation due to poor tolerance is estimated to be <15% when used for acute respiratory failure (10).

Drawbacks of NPPV NPPV is noisy and can be uncomfortable and frightening. It may interfere with sleep and family intimacy and could confuse care goals if not discussed carefully. Initiating NPPV outside of acute care environments (e.g. at home, nursing home, or hospice facility – see *Fast Fact* #231) may be challenging if not impossible. Some experts have published concerned that NPPV may complicate end of life decision-making for the bereaved and by consequence increase the risk of associated anxiety (11).

Medical Decision Making and Counseling

- Patients in categories #1 & 2, as with all patients nearing the end of life, need ongoing discussions about their realistic prognosis, goals, and options (see *Fast Facts* # 164, 165, 222-7).

- For dying patients with distressing dyspnea and comfort-only goals of care, opioids are first line agents (see *Fast Fact* #27). For patients who need sedating doses of opioids to be comfortable, and who articulate a strong preference to be as awake as possible, it is reasonable to offer NPPV if the patient is in an environment which can accommodate it and the risks are acceptable to the patient, *including the possibility that the dying process will be prolonged.* Reassure patients that you can alleviate their symptoms even if NPPV is unhelpful or intolerable.
- For dying patients who wish to forestall death briefly for a specific goal, it is reasonable to start a trial of NPPV. Before initiating NPPV, it is important to discuss withdrawal of NPPV after the above goal has been achieved, and to caution the patient/family that NPPV might not be able to forestall death long enough as hoped.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #231
PRACTICAL ASPECTS OF USING NPPV AT THE END OF LIFE

Mei-Ean Yeow MD and Eytan Szmuilowicz MD

Background Non-Invasive Positive Pressure Ventilation (NPPV) can be used to palliate dyspnea in dying patients. *Fast Fact* #230 discusses medical decision making around using NPPV. This *Fast Fact* discusses practical aspects of using NPPV in dying patients. Little research has occurred on this topic; unless otherwise noted the following discussion is based on clinician opinion and common practice.

Location The cost and experience needed to initiate NPPV limit its use to the hospital setting, with some exceptions (see below). Most NPPV use occurs in ICUs or transitional care ('step-down') units, and at some institutions continuous NPPV is not allowed outside of these settings. While the use of NPPV for palliation can occur at home or a hospice facility, it requires adequate nursing, respiratory therapy, and physician support to employ it safely. This can be a practical barrier to its use, and NPPV should not be offered unless one is sure it can be provided appropriately. Ensuring adequate respiratory therapist support is particularly crucial, as they have unique expertise at initiating and trouble-shooting the machines. *Continuing* NPPV for palliation in patients and families who are already comfortable managing home NPPV (e.g. for COPD or ALS) can be practical in the home or hospice facility setting, as long as it is consistent with care goals. *Initiating* NPPV in the home setting for dying patients is impractical and, given how uncertain its real benefits are (see *Fast Fact* #230), is not advised.

Starting NPPV

- **Masks**: While full facemasks are commonly used in the in-patient setting, some patients find these claustrophobic. Nasal masks tend to be better-tolerated, but they do not work as well in patients who are mouth breathers. Patient preference and clinician familiarity should guide this decision.
- **Settings**: Two parameters need to be set: the inspiratory positive airway pressure (IPAP) and end-expiratory positive pressure (EPAP). The breaths are usually triggered by the patient. On many devices it is possible to set a back-up rate if the patient does not trigger a breath spontaneously– this is inappropriate in dying patients receiving NPPV for symptom relief.
- **Strategies**: There are two general approaches to initiating NPPV settings: a 'high to low' approach and a 'low to high' approach, referring to the initial IPAP settings. The EPAP is usually set at 3-5 cmH2O. In order to maximize the tolerability of NPPV for symptom relief in dying patients, a 'low-high' approach is recommended. Start with a lower IPAP (8-10 cmH2O), and gradually increase as tolerated to achieve alleviation of dyspnea, decreased respiratory rate, increased tidal volume, and patient-machine synchrony.

Monitoring Pulse oximetry and arterial blood gas monitoring are not needed for patients using NPPV only for symptom control. Rather, its effect should be based on subjective improvement of dyspnea and decrease in respiratory rate. It is important to reassess patients frequently (looking specifically for respiratory rate, use of accessory muscles, signs of anxiety, and facial skin integrity), and to inquire if they are comfortable with the NPPV and deriving any benefit from it. Breaks from NPPV to eat, drink, communicate, and alleviate skin shearing specifically on the nasal bridge should be encouraged. Transparent films or thin foams over the bridge of the nose are recommended to prevent facial pressure ulcers, as well as periodic repositioning of the mask and alternating between mask types as tolerated.

Contraindications Contra-indications are facial surgery/trauma/deformities that limit placement of the NPPV mask and patients with active nausea and vomiting. Decreased mental status is also considered a contraindication it increases the risk of aspiration from NPPV.

Discontinuing NPPV NPPV should be discontinued if it does not provide relief from dyspnea within an hour of the maximally tolerated setting, once a patient is no longer alert, or at any point when it is no longer meeting a patient's goals. If the patient does not tolerate the mask, or feels claustrophobic, a small dose of a benzodiazepine can be administered to alleviate anxiety. If the patient is still uncomfortable, then NPPV should be stopped as it is then not adding to patient comfort. Opioids and benzodiazepines should be used to decrease dyspnea once NPPV is stopped. Remember that NPPV provides ventilatory support to patients and the work of breathing can dramatically increase without it. Be prepared to rapidly control any distressing symptoms, *just as you would with discontinuing invasive mechanical ventilation* (see *Fast Facts* #27, 33, 34).

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #235
PROGNOSTIC MODELS IN CRITICALLY ILL ADULTS

René Claxton MD, Derek Angus MD, and Robert Arnold MD

Background Prognostication for ICU patients is challenging. Grieving families, trying to make informed decisions about their loved ones care, often ask *What are the chances he or she will get through this?* Several prognostic models have been developed to predict survival for groups of patients stratified by severity of illness. These are used in outcomes research to compare patient groups, assess and compare ICU performance and help guide resource allocation. Anecdotally, data from these models is sometimes used in discussing prognosis with family members of critically ill patients. This *Fast Fact* discusses common ICU prognostic models and their role in guiding patient care and communication.

Widely used ICU prognostic models Common models for predicting mortality in medical-surgical ICU patients include the Acute Physiologic and Chronic Health Evaluation (APACHE) score, the Mortality Probability Model (MPM), the Simplified Acute Physiology Score (SAPS) and the Sequential Organ Failure Assessment (SOFA) score (1-4). The SOFA score can be calculated at the bedside based on laboratory and physiologic data; however, this model has not been widely used in either clinical or research practice by the critical care community to predict mortality. The APACHE, MPM, and SAPS models are more widely used and require computer software to calculate a score based on multiple variables including type of admission, the patient's underlying diseases, physiologic data, and – in the case of APACHE – laboratory data. The APACHE score is based on the worst values available during ICU Day 1 whereas MPM and SAPS scores are calculated based on data obtained within one hour of ICU admission. The models require re-validation over time as ICU interventions and outcomes change. The APACHE score is currently in its fourth version. MPM and SAPS are in their third versions. Although APACHE IV and MPM III require proprietary software to calculate a score, the SAPS3 score can be computed using a downloadable calculator (5). Individual institutions may use a model for all ICU admissions for purposes of quality monitoring, outcome reporting, or research, and so some clinicians may have these scores readily available to them.

Accuracy of the prognostic models The discrimination and calibration ability of ICU prognostic models determine their predictive accuracy (6). Discrimination is the ability of a model to predict a mortality rate similar to the observed rate; calibration reflects a model's ability to predict an outcome at multiple levels (mortality rates). The most recent versions of APACHE, MPM, AND SOFA show both high discrimination and calibration. All three models report a score based on the above variables that correlates with a predicted in-hospital mortality rate. For example, a SAPS3 score of 73 correlates with a hospital mortality rate of 62%. The other two models work similarly.

Clinical use of ICU prognostic models All of these models accurately predict *rates of in-hospital mortality in a population* of critically ill patients. This is different than predicting survival for an individual patient (7), let alone using them to guide individual treatment decisions. None of the models alone can, for instance, predict 100% mortality, a standard that some families and clinicians may require in order to limit life-sustaining treatments. Also, as these models focus solely on in-hospital mortality as the outcome measure, a patient's functional status, quality of life, and long-term prognosis are not predicted. These considerations can be equally as important as short-term survival for families and clinicians in determining appropriate treatment goals. Practically, then, the clinical use of the models is best limited to three uses:

1. *As a single 'data point' among many to guide patient-centered decision-making.* Clinicians can use outcome data from the tools, along with patient co-morbidity, long-term prognosis, baseline and anticipated functional status and quality of life, etc., to guide discussions (see *Fast Facts* 222-227). *Chances are your loved one is not going to survive this illness. She might, and currently we are doing everything we can to get her through this. However, even if she does, her emphysema is severe enough that we will*

not be able to improve her breathing or ability to take care of herself any more than before she became this ill, and it is very likely another event like this will happen again in the near future.

2. As a screening tool to identify those ICU patients uniquely 'in need' of palliative care evaluation.
3. As a research tool to look at the impact of interventions on mortality, morbidity and quality of life.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #250
TRACHEOSTOMY CARE

Elliott Kozin MD, Joseph Straton MD, and Jennifer Kapo MD

Background Many patients with advanced illness have tracheostomies, which require careful observation and specialized management. Common indications for tracheostomies in patients being seen in palliative care and hospice settings include chronic long-term ventilation, aid with ventilation weaning, and upper airway obstruction (from, for instance, head and neck cancer). A working knowledge of tracheostomy equipment and the basic handling procedures can avoid complications and improve a patient's comfort.

Tracheostomy Equipment 101 At its most basic level, a tracheostomy appliance consists of a cannula (or tube), cuff, obturator, and ties. The cannula maintains the patency of the stoma and airway, and it facilitates movement of air into the trachea. Tracheostomy cannulas can be cuffed or uncuffed. The inflatable cuff, typically filled with air by a syringe, surrounds a portion of the cannula inside the trachea. The inflated cuff occludes the trachea around the cannula, which allows for increased protection against aspiration and also for greater degrees of positive pressure ventilation. Cuffs require monitoring to maintain a pressure of 20-25 mmHg. Higher pressures can produce tracheal ischemia, mucosal injury, and difficulty swallowing; lower pressures can potentially aggravate aspiration around the cannula (1,2,3). Obturators, usually packaged with new tracheostomy tubes, are inserted into the lumen of the cannula and provide for increased rigidity during placement of the tracheostomy tube. Tracheostomy ties secure the tracheostomy tube to the patient and typically wrap around the back of the patient's neck.

Complications of Tracheostomy Placement S*hort-term complications* include bleeding from surgical site (~5%), wound infection, subcutaneous emphysema, pneumothorax, tracheostomy tube obstruction, recurrent laryngeal nerve damage, and posterior tracheal wall injury (4, 5). *Long-term complications* include dysphagia, airway obstruction from secretions, infection, rupture of the innominate artery, tracheo-innominate artery fistula (<0.7%), tracheosophageal fistula, tracheal dilation, tracheal stenosis (1-2%), granuloma formation, and tracheal ischemia and necrosis (4, 5).

Approach to Complications and Emergencies

- *Acute Dyspnea.* If a patient with a tracheostomy becomes acutely dyspneic, it may be due to partial or complete blockage by retained secretions. Ask the patient to cough and then attempt to suction the tracheostomy in place with a flexible suction catheter. If the tracheostomy stoma and tract is not fully matured, do not attempt to remove the cannula as it may be difficult to re-insert. (3)
- *Bleeding.* Bleeding from the surgical site is among the most common early complications. Treatments include packing around the edges of the stoma with gauze, correction of coagulopathies, and cautery or suturing of site of bleeding (3,5). Massive pulsatile bleeding may indicate erosion of the innominate artery, which can occur days to weeks after a tracheostomy procedure. This can rapidly lead to airway compromise and/or exsanguination. To minimize bleeding, place a gloved finger in the stoma, feel for a pulsatile mass, and apply forward motion on the backside of the upper border of the sternum thereby compressing the pulsatile artery against the posterior surface of the sternum (6). Other techniques include overinflating the cuff. If the patient's goals of care allow this, the patient should be transported emergently to the operating room for management (3). See *Fast Fact* #251for further details about caring for hemorrhaging patients who do not want further invasive treatments.
- *Accidental Decannulation.* Don't panic. Reassure the patient. If the tube has been in place less than 5 days, consider endotracheal intubation if a tracheostomy tract cannot be immediately re-established (5). If the tube has been in place for 5-10 days, the tract should be well formed and should not suddenly close (2). To reinsert the tracheostomy tube, insert the obturator (if applicable) into the cannula. Slowly insert the cannula with obturator into the tracheostomy, following the path of the airway. When reinserting, be mindful of any

resistance. If met with resistance, it is possible to create a false passage, and one should reevaluate the entry approach. After insertion, remove the obturator while keeping the cannula in place. Listen for and feel for air movement through the tracheostomy tube and ensure that there is no subcutaneous emphysema, which may indicate improper placement.

If you cannot insert a new cannula and the patient cannot breathe comfortably on their own through the stoma, use a bag-valve mask to ventilate the patient through the upper airway. Ventilate gently to prevent air from escaping through the stoma or carefully occlude the stoma with a gloved hand to maximize oxygenation. Next steps depend on the patient's current indication for a tracheostomy (airway patency vs. ventilation vs. secretion management) and goals of care. If the patient has a patent airway and is not on a ventilator there may be time to have the patient evaluated by a specialist to replace the cannula. If the patient is ventilator dependent or has an upper airway obstruction, endotracheal intubation and/or emergency transport is indicated.

- *Resuscitation via Tracheostomy Tube*. Treat the patient like patients without tracheostomy, with the following exceptions. Do not remove the tracheostomy. Check that the cannula is patent. Ventilate by using a manual resuscitation bag attached directly to tracheostomy tube. If unable to ventilate, try suctioning. If still unable to ventilate, try to change tracheostomy tube. The last resort is oral intubation.

Conclusion Careful discussions with dying patients and their families about options and preferences if there are tracheostomy complications can help prevent chaotic, emergency decisions about urgent transportation, surgeries, or oral intubation.

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Margaret L Campbell PhD, RN, David E Weissman MD, and Judy E Nelson MD, JD

Background The Intensive Care Unit (ICU) is the setting for high-intensity health care designed to resolve life-threatening illnesses and extend life. However, risks of mortality and severe morbidity remain high and virtually all ICU patients have palliative care needs. Integration of palliative care services into ICU care is increasingly seen as a method to improve clinical care (1,10). This *Fast Fact* reviews the role of palliative care consultations in the ICU along with options for more generalist palliative care services provided by ICU clinicians.

What occurs in an ICU Palliative Care Consultation

- Assess/treat distressing physical, psychological, and spiritual symptoms/problems.
- Communicate information about prognosis and treatment options to patient/family in concert with ICU, primary care and subspecialty colleagues.
- Establish/clarify goals of care that are realistic and appropriate in relation to the patient's condition, values and preferences, and help match treatments to these goals.
- Formulate a transition care plan that accounts for prognosis, goals of care and patient/family needs.
- Provide support for the families.
- Support the ICU medical team in making clinically, ethically, and emotionally challenging decisions.

Research Data on Benefits of Palliative Care ICU Consultation

- Early identification of a dying trajectory leading to decreased time to institution of patient- and family-centered, comfort-focused treatment goals (2-3).
- Movement of appropriate patients to lower intensity care sites (ward, palliative care unit, home hospice) (5-6).
- Reduction in ICU length of stay for adult patients (2-4, 7).
- Reduction in the cost of care, without an increase in mortality, due to early establishment of realistic treatment goals leading to reduction in use of high-cost ICU resources/interventions (2-4, 7-8).
- Support for staff in challenging and emotionally draining/morally distressing patient/family care situations.
- Palliative Care consultation for hospitalized patients can reduce the need for ICU admission through establishment of treatment goals that preclude future ICU admission (7-8).
- Continuity of care when the patient transitions from the ICU to ward or palliative care unit as the Palliative Care team follows the patient.

ICU/Palliative Care Collaboration A range of options exist for integrating palliative care services into the ICU. At one extreme, ICU staff consult a palliative care specialist team for problems the ICU staff deems appropriate for consultative advice on an ad hoc basis. At the other extreme, the ICU embeds systems in place to provide ICU-led generalist palliative care services to all ICU patients, utilizing palliative care specialists for complex problems. Embedding systems that ensure the needs of all patients are met includes screening all patients on admission and daily for unmet palliative care needs, early identification of a surrogate, timely symptom management, and routinely-scheduled family meetings to discuss goals of care (1,9,10). Quality outcomes related to patient and family experience and to health care utilization should be tracked within the framework of available resources (1,11).

When to use Specialist Palliative Care Services Consultations can either be initiated on a case-by-case basis by ICU or other primary clinicians, or triggered proactively using a system to identify patients at high-risk for unmet needs (2-4). Key indications for consultation include:

- Difficult-to-control physical symptoms despite usual treatment approaches.
- Patients/surrogates wish to explore non-ICU supportive care options such as hospice services.
- Staff have questions about the appropriateness of life-sustaining therapies in the setting of advanced complex illnesses.
- There are complex family dynamics impacting decisions about use of life-sustaining treatments.

- There are disagreements among staff or between staff and patients/surrogates about prognosis and/or use of life-sustaining treatments.
- Patients are being readmitted to the ICU more frequently within a given time frame.

Summary Specialist palliative care consultations, together with integration of palliative care principles into the care of all ICU patients, can improve the patient/family experience, reduce length of stay and improve ICU throughput without increasing mortality, and lower health care costs.

Additional resources: *Fast Facts* # 122-123.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #264
PROSTACYCLIN WITHDRAWAL IN PULMONARY HYPERTENSION

Christi Bartlett MD and Lindy Landzaat DO in cooperation with the COPE Collaborative*

Background Pulmonary artery hypertension (PAH) is a disease of the pulmonary vascular system characterized by elevated pulmonary vascular resistance. Patients with advanced PAH are often treated with prostacyclins. This *Fast Fact* reviews suggested guidelines for withdrawal of prostacyclin therapy in dying patients with PAH.

Physiology/Symptoms PAH is defined as a mean pulmonary arterial pressure greater than 25 mmHg and may lead to right ventricular failure (1). Symptoms include dyspnea, cough, syncope, fatigue, angina, and peripheral edema, often progressing to respiratory failure and cardiovascular collapse.

Prostacyclin Treatment Prostacyclin medications, epoprostenol and treprostinil, are effective in extending life in PAH (2). These drugs are administered via continuous parenteral infusion (IV; treprostinil can be given subcutaneously). Epoprostenol's half life is six minutes (3); abrupt withdrawal can lead to significant symptom burden (dyspnea, anxiety, nausea, light-headedness, chest and abdominal pain) and rapid death.

Discontinuation of Prostacyclin Therapy Despite the use of prostacyclins and other life-prolonging treatments, PAH is usually progressive and fatal without lung transplantation. When the goals of care include discontinuation of prostacyclins, this process can create anxiety among patients and caregivers due to concerns about the rapid development of distressing symptoms. Because of this, it is felt best to taper prostacylins in a planned, controlled manner. There are no guidelines regarding how to taper off IV prostacyclins, let alone any research data to guide clinicians. The following recommendations, however, have been developed by the COPE Collaborative * and are based on clinical experience and rational pharmacology.

- A benzodiazepine and/or opioid should be given as premedication and be readily available for rapid administration following initiation of withdrawal of prostacyclin therapy. Actual doses however need to be closely tailored to an individual patient's prior exposure to opioids and benzodiazepines and acceptable level of consciousness. See *Fast Fact* #34 (regimen A) for some general guidelines.
- The rate of medication taper should account for the medication's half-life. Because epoprostenol has a short half life, we recommend waiting 4-6 half lives (generally 25-30 minutes) and monitoring for symptoms prior to further titration. Treprostinil, with a half life of approximately 4 hours, can be titrated downward every 4-6 hours.
- Reduce the prostacyclin in 20-25% increments, with close monitoring for symptoms as a new steady state is achieved.
- With each dose reduction, the patient should be closely monitored for increasing symptoms. If symptoms are minimal or otherwise well controlled with opioids or benzodiazepines, the prostacyclin taper may continue. If the patient experiences distressing symptoms (dyspnea, anxiety, chest pain), the taper should be held until symptoms are managed and the taper resumed at a slower rate, with smaller interval dose reductions. Conversely, if the patient is unresponsive and is tolerating the titration well with minimal symptom burden, the rate of titration can be cautiously increased.
- Similar to the planned discontinuation of mechanical ventilation in a dying patient (see *Fast Facts* #33-35), it is recommended that the de-escalation of IV prostacyclins occur in the inpatient setting under close physician supervision. In the home setting, a physician should be present at the bedside along with the support of a knowledgeable hospice team, with ample medications readily available in-home, as symptoms can develop quickly and patients often need rapid medication adjustments to maintain comfort.

*Care Of Pulmonary hypertension patients at End-of-life (COPE) Collaborative members: Christi Bartlett MD, Lindy Landzaat DO, Karin Porter-Williamson MD, Lewis Satterwhite MD, Leslie Spikes MD, Ryan Westhoff MD, Tim Williamson MD; University of Kansas, Kansas City, KS.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #265
PALLIATIVE CARE FOR PATIENTS WITH CYSTIC FIBROSIS

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Background Cystic fibrosis (CF) is an autosomal recessive disorder of the cystic fibrosis transmembrane regulator (CFTR) that affects the respiratory tract, pancreas, intestines, male genital tract, hepatobiliary system, and exocrine sweat glands resulting in multisystem disease. This *Fast Fact* discusses the natural history of CF and issues related to palliative care for patients with CF.

Morbidity and Death in CF The life expectancy of patients with CF has improved over the last 50 years. In 1959, the median age at death was 6 months and in 2008 it increased to 27 years. For those born in the year 2010, the median age of survival is predicted to be greater than 50 years (1). This improved survival is attributed to advances in the supportive care of patients including early diagnosis, family support, attention to nutrition, infection control, and the use of nebulized mucolytics and antimicrobials (3).

- Chronic progressive pulmonary disease and respiratory failure remain the major cause of morbidity and mortality. End-stage lung disease is characterized by cysts, abscesses, and fibrosis of lungs and airways. Patients frequently die from overwhelming lung infections.
- Factors associated with earlier death in CF include the deltaF508 mutation, pancreatic insufficiency, low body mass index, certain infections (*Pseudomonas aeruginosa*, *Staphylococcus aureus,* and *Burkholderia cepacia*), low socioeconomic status, tobacco smoke exposure and female sex (2,3).
- For select candidates, lung transplantation improves survival and quality-of-life. The 5-year survival post-transplant is about 50%.
- Other important causes of morbidity include CF-related diabetes mellitus, pancreatic insufficiency (manifesting as fat malabsorption, poor growth, and hemolytic anemia), hepatobiliary disease (including portal hypertension and varices), male infertility, and meconium ileus in newborns.
- CF patients commonly suffer from cough, fatigue, and dyspnea; these symptoms tend to worsen as lung disease progresses. Chest wall and back pain from cough, pleurisy, rib fractures, and chest physiotherapy is common (4). Fears of addiction, respiratory depression, and concern that chronic opioid use complicates lung transplant success can create barriers to appropriate opioid administration (3,5,6).
- With multiple medications, therapies, and nutritional supplements required each day, routine care can be physically and emotionally exhausting for CF patients and family members.
- Adolescents with CF report a high quality-of-life and they abuse substances less frequently than their healthy counterparts (7). Nonetheless, in this age group, chronic anxiety and depressive disorders are common and treatment adherence routinely declines (7).

Common Issues Near the End-of-Life

- Prediction of short-term mortality is difficult and largely subjective. Most predictive models focus on clinical severity of pulmonary disease using age, FEV1%, BMI, the presence of pancreatic insufficiency, and opportunistic infections as parameters. These models however are designed to stratify lung transplant candidates rather than assist with end-of-life care planning (3,9).
- The dynamic, chronic, progressive course of CF creates challenges for timing goals-of-care discussions. Periodic planned meetings amongst patient, family, and care team are advised. Single-center studies reinforce that, despite documented need, palliative care consultation is rarely offered until days before death or when lung transplantation becomes contraindicated (8).
- Do-not-resuscitate (DNR) orders are often not written until the final few days of life. Many patients continue to receive disease-modifying therapies up until the last 24 hours of life (9). Although many disease-specific therapies can be administered in the home setting, most CF

patients die in the hospital setting (5). This likely reflects a combination of prognostication challenges, reluctance to abandon aggressive therapies, patient/family preference, and caregiving burdens. CF patients may be uniquely suited to Medicaid 'concurrent care' waiver programs in which patients can receive hospice and routine medical care simultaneously (10).

- Although guidelines are lacking, progressive hypoxic respiratory failure may benefit from long-term oxygen therapy (6). Non-invasive positive pressure ventilation (NIPPV) has a role for hypercapneic respiratory failure, dyspnea management, and, in select candidates, as a bridge to lung transplant. Use of invasive positive pressure ventilation (IPPV) should always involve clear discussions around therapeutic options and goals-of-care (8).
- In the past, intensive care for CF patients was generally considered futile. More recently, ICU outcomes have improved, particularly for patients requiring NIPPV (as opposed to IPPV), and for patients who are candidates for lung transplantation (6,8). Long-term outcomes for respiratory failure requiring IPPV remain dismal however, and intensive care management may commit many patients to eventual end-of-life care in the ICU setting.
- Common symptoms at the end of life include dyspnea, fatigue, anxiety, anorexia, pain, and cough (see *Fast Facts* #27, 199, 200). Care providers must balance benefit vs. burden of disease-specific treatments such as nebulized medications, NIPPV, and chest physiotherapy (6,8).
- Patients who survive multiple episodes of acute respiratory failure may come to overestimate their resilience, making appropriate goals-of-care discussions or end-of-life care planning more challenging (6,7).

Key teaching points

- Pulmonary involvement in CF is the most common cause of morbidity and mortality in people affected by this disease. Symptoms such as dyspnea, anxiety, cough, and pain commonly interfere with CF patients' quality-of-life. For some patients, lung transplantation offers hope of improved survival and quality-of-life. However, most will die of their disease in the hospital setting.
- Accurate temporal prognostication in CF is challenging. However, the natural history of CF without transplantation is well-established and patients and families should be prepared for the physical and emotional challenges of end-stage CF, including end-of-life decision-making, even without a precise estimation of survival time.

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PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #310
THE ONCOLOGY-ICU-PALLIATIVE CARE INTERFACE
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Background: Cancer patients may be admitted to an intensive care unit (ICU) at any point in the disease trajectory (1). When these patients have an advanced malignancy, and/or when their disease has progressed despite standard anti-cancer treatments, it is common for conflicts to arise between oncologists and the critical care team regarding appropriate management. This *Fast Fact* discusses an approach to conflict management for cancer patients in the ICU.

Same Patient-Different Opinions: Every specialty has a unique culture based on the type of diseases it treats and the attitudes learned from peers and teachers during training years. Having a general awareness of these cultural tendencies among various specialty groups could better enable Palliative Care (PC) clinicians to manage inter-specialty conflicts.

Oncologists …
- See a wide range of patients, some who are cured and others who die.
- Are trained to examine all potential anti-cancer treatments to extend life.
- May view ICU care as nothing more than a "bump in the road," noting that the prognosis of cancer patients in the ICU is similar to non-cancer patients. This point of view may be especially apparent in patients who have recently undergone a bone marrow transplant, but have not yet shown signs of bone marrow recovery – *re-engraftment* (1,5).
- Often have long-term outpatient relationships with patients creating strong emotional connections.

Intensivists …
- Are likely to see many cancer patients near the time of death when ICU care may represents a 'last-ditch' effort to sustain life.
- Often have brief relationships with patients/families during a time of crisis.
- Like many non-oncology specialties, they may have a more negative view of the potential benefits of anti-cancer treatments than oncologists.
- May worry about prolonging suffering through ICU interventions when death appears imminent (1).

How can palliative care help? By performing careful independent evaluations of the medical situation and exploring the points of view of the various specialty teams, the PC team members can serve as mediators who assist in creating a shared message for the family (2).
- Neutral Caring: An important trait of a PC consultant is the mindset of neutral caring. **Neutral** in that he or she should avoid taking sides between the different clinical teams but instead work to find a common story that they can agree on. PC consultants should be aware of their own potential biases or conflicts of interest, which could influence the direction of the patient's care. For example, PC teams may be more likely to assume that a focus on comfort with a shortened hospital stay is preferred (3). **Caring** because the PC consultant needs to remember that all the clinicians are doing their best to care for the patient. Thus even if the PC clinician is sure that their view is "right", they need to respectfully negotiate with other clinicians who also may be sure their view is correct.
- Pre-meeting of clinicians: Regardless of who initiates the consult, PC teams should reach out to both the oncologist and the intensivist to understand their points of view regarding disease, treatment options and prognosis. In many such circumstances, attending-to-attending level conversations are necessary. Given that prognosis is often uncertain, it may help to reach agreement on the best, worst, and most likely prognosis (4). This may identify areas of agreement among the specialist teams involved and clarify what medical data are needed to better forecast prognosis.

Managing Conflict: Multi-disciplinary goals of care meetings are often the most effective and efficient way to bring all specialty care teams together along with the patient and/or family and negotiate the best way forward (see *Fast Facts* #16, 65, 183-184, 222-227). If there is disagreement between specialty teams, it is critical that such attending clinicians talk directly before meeting with the family. Often reports of what one clinician said is from the family or another indirect source. Consequently, these descriptions may be incomplete or filtered by the family's hopes. In cases in which medical agreement cannot be reached, the PC team can assist by presenting the differing opinions to the family as part of a cohesive medical reality on which the family can base their decisions or pursue a time-limited trial.

Summary: The goal of the PC consultant is to perform an independent evaluation in order to help the medical care team develop a unified medical narrative that is agreeable with all clinicians involved. As such, PC teams can be vital in conveying an accurate and understandable medical narrative to the families of critically ill cancer patients. By fostering an environment that allows regular clinician meetings to occur throughout a patient's hospital stay, PC teams can better ensure that medical teams talk directly to each other about the patient's prognosis and present a unified approach to the family and patient.

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FAST FACTS AND CONCEPTS #343
CHRONIC CRITICAL ILLNESS IN ADULTS
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Background Chronic critical illness (CCI) was first coined in 1985 (1). Although it does not have a single accepted definition, most authors apply CCI to patients who survived an initial critical illness with mechanical ventilation or other intensive care therapies, but remain dependent on these technologies beyond 14 days neither improving nor imminently declining (2). The usual CCI patient does not have respiratory failure in isolation. Instead, many have protracted comorbidities such as neuromuscular weakness, debility, delirium, skin breakdown, and edema. Palliative care clinicians may be asked to help in complex medical decision-making for CCI

patients in various care settings. These decision points include whether to consider a tracheostomy for long-term ventilation or whether to withdraw long-term ventilator support in a patient at a long-term acute care hospital (LTACH) or ventilator weaning facility. This *Fast Fact* reviews the long-term outcomes and palliative care challenges for CCI patients.

Prevalence Approximately 5-10% of patients who require mechanical ventilation develop CCI (3,4). It can emerge from a critical illness of any reason, including medical (e.g., pneumonia), surgical (complications after an operation), a stroke, or a trauma. Risk factors for developing CCI have not been clearly established (5). Of note: CCI does not apply to all patients on long-term mechanical ventilation as some were never critically ill. For example, a patient with amyotrophic lateral sclerosis who electively pursued a tracheostomy and mechanical ventilation.

Outcomes For many CCI patients, proceeding to tracheostomy and long-term ventilation represents a fundamental decision point, often 14-21 days after critical illness presentation. Uncertainty in identifying which CCI patients will eventually functionally recover makes this decision challenging. When leading these discussions, clinicians should be aware of the following outcomes data:

- Mortality in CCI is high. A meta-analysis of patients requiring mechanical ventilation for > 14 days, who were either admitted to a ventilator weaning unit or had a tracheostomy found that the pooled mortality at 1 year was 73% in the US (7). Patients >65 years of age; patients who continue to require dialysis or vasopressor support at 14-21 days; and patients with thrombocytopenia and acute kidney injury are at even greater 1-year mortality risk (8).
- Long-term functional outcomes in CCI are poor. In the US, < 50% of patients ventilated for >14 days are ever weaned from the ventilator (7). A single-institution, US-based prospective study found that only 15% of the 203 patients studied at a respiratory care unit for ventilator weaning were functionally independent after 6 months. At 6 months ~2/3 patients had died, and most of the survivors had profound physical, cognitive, or communication deficits (9).
- Symptom burden in CCI is high. In a prospective cohort study of 36 participatory patients requiring tracheostomy and admission to a respiratory care unit for ventilator weaning, 44% experienced high intensity pain, 80% reported unsatisfied thirst, > 60% reported dyspnea, and > 60% reported worry or sadness frequently or almost constantly (6).

Communication Most CCI patients are unable to engage in medical decision making, and family members or friends are used as surrogates. Unfortunately, current research indicates neither patients nor surrogates are well-informed about realistic long-term outcomes of CCI.

- In one study, a majority of patients reported receiving no information about choices other than continuing mechanical ventilation, financial burdens for the family, and expected functional and cognitive status after hospitalization, even though >90% or participants rated these topics as important (10). About 93% of patients reported that they did not receive information about 1-year mortality risk, even though 74% rated this as important (10).
- In another prospective study, only 26% of CCI surrogates reported that physicians discussed prognosis, functional limitations, quality of life, or expected caregiving needs (11). Among these surrogates, 93% expected their loved ones to survive 1 year and 71% expected their loved one to have no major functional limitations; the physicians expected similar outcomes only 44% and 6% of the time, respectively (11).

Recommendations Considering the poor outcomes and the communication deficiencies involved with CCI patients, we empirically recommend the following:

- Hospitals should implement policies and practices to improve patient and surrogate knowledge about CCI outcomes, as well as alternatives prior to tracheostomy placement such as the discontinuation of life-prolonging technologies and the allowance of a comfortable death (9,10) so that these goals of care discussions are not needlessly deferred to LTACH or ventilator weaning facilities.
- Ideally, inter-disciplinary palliative care teams should be available to support clinicians in leading these discussions not just at hospitals and ICUs, but LTACHs and ventilator weaning facilities as well.

- Patient preferences, values, and meaning should be ascertained and utilized in CCI decision-making.
- Despite pressure to hurry the decision-making process, palliative care consultants should avoid acting as agents of the primary team's agenda, especially during the initial encounter. Rather, a pause to complete an independent clinical and prognostic assessment is essential.
- Palliative care clinicians may help certain CCI patients and surrogates by offering to make a medical recommendation. If there is still difficulty deciding on an acceptable care plan, a time limited trial of continued endotracheal mechanical ventilation may be reasonable, as long as there are clearly defined targets when tracheostomy placement or comfort care would be pursued.

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