The Fifty Essential *Fast Facts*

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FAST FACTS AND CONCEPTS

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FAST FACTS AND CONCEPTS #18
SHORT-ACTING ORAL OPIOID DOSING INTERVALS
David E Weissman MD

Background Oral opioids are among the most commonly prescribed drugs in palliative care. Despite national analgesic guidelines, the use of excessive intervals for short-acting oral opioids continues to pose a significant barrier to good analgesic care. Understanding the pharmacological rational for dosing intervals is key to proper prescribing and patient counseling.

Short-Acting Oral Opioids Short-acting products are administered as either single agents (oral morphine, hydromorphone, oxycodone and codeine) or as combination products containing acetaminophen, aspirin or ibuprofen. For all these products, the peak analgesic effect occurs in 60-90 minutes with an expected total duration of analgesia of 2-4 hours. Standard reference sources generally cite a 4 hour dosing interval for the single-agent opioids, but 4-6 or 6 hour intervals for combination products (PDR, Micromedex). However, the Agency for Health Care Policy and Research (AHCPR) Clinical Practice Guideline (1994) recommends dosing intervals for all short-acting opioids at an interval or every 3-4 hours, an interval more consistent with patient reports of pain relief and the half-life of oral opioids.

Is there a danger to more frequent drug administration? There is no danger of dosing intervals as often as every 2 hours for single agent products (e.g. morphine), *in patients with normal renal function and who are currently tolerating the opioid without sedation*, as the peak effect will be reached in 60-90 minutes and there is rapid renal excretion. For combination products, the concern is excessive acetaminophen. Thus, if patients need opioids on an every four hour basis, it is appropriate to change to single agents without acetaminophen and/or add a long-acting opioid product so as to keep the total daily acetaminophen dose at less than 4 grams.

Note: Transmucosal fentanyl citrate and oral oxymorphone have different pharmacokinetics than the agents mentioned above and are dosed differently – see *Fast Facts* #103 and #181.

Summary

- Prescribe the products listed above at intervals *no greater* than every 4 hours.
- Closely monitor daily acetaminophen intake when combination products are used.
- Provide explicit patient/family counseling regarding safe and allowable dosing intervals.
- Review your institutional opioid policies – ask if there is a hospital policy or guidelines for oral opioid doing intervals; if not, such guidelines should be developed to help guide practice.

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FAST FACTS AND CONCEPTS #20
OPIOID DOSE ESCALATION
David E Weissman MD

Background A common question from trainees is how fast, and by how much, can opioids be safely dose escalated? I like to use the analogy of furosemide (Lasix) when discussing this topic. I have never seen a resident order an increase in Lasix from 10 mg to 11 mg, yet that is precisely what often happens with opioids, especially parenteral infusions. Like furosemide, dose escalation of opioids should be done on the basis of a *percentage* increase. In fact, this is reflexively done when opioid-non-opioid fixed combination products are prescribed; going from one to two tablets of codeine/acetaminophen represents a 100% dose increase. The problem arises when oral single agents (e.g. oral morphine) or parenteral infusions are prescribed. Increasing a morphine infusion from 1 to 2 mg/hr is a 100% does increase; while going from 5 to 6 mg/hr is only a 20% increase, and yet many orders are written, "increase drip by 1 mg/hr, titrate to comfort." Some hospitals and nursing units even have this as a standing pre-printed order or nursing policy.

Key Points: In general, patients do not notice a change in analgesia when dose increases are less than 25% above baseline. There is a paucity of clinical trial data on this subject. A common formula used by many practitioners is:

- For ongoing *moderate to severe* pain increase opioids doses by 50-100%, *irrespective of starting dose.*
- For ongoing *mild to moderate* pain increase by 25-50%, *irrespective of starting dose*.
- These guidelines assume the patient is tolerating the opioid well (with no or minimal sedation); clinicians will need to be more cautious and should consider expert help for patients with ongoing uncontrolled pain despite sedation from opioids or another cause.

When dose escalating long-acting opioids or opioid infusions, *do not increase the long-acting drug or infusion basal rate more than 100% at any one time*, irrespective of how many bolus/breakthrough doses have been used. These guidelines apply to patients with normal renal and hepatic function. For elderly patients, or those with renal/liver disease, dose escalation percentages should be reduced (see *Fast Facts* # 161 for Opioid use in renal failure and # 260 for Opioid use in liver failure).

The recommended frequency of dose escalation depends on the half-life of the drug.

- Short-acting oral single-agent opioids (e.g. morphine, oxycodone, hydromorphone), can be safely dose escalated every 2 hours.
- Sustained release oral opioids can be escalated every 24 hours.
- For methadone, levorphanol, or transdermal fentanyl no more frequently than every 72 hours is recommended.
- **Note:** transbuccal fentanyl products have specific guidelines for dose escalation. See the manufacturers' prescribing information and *Fast Fact* #103

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FAST FACTS AND CONCEPTS #36
CALCULATING OPIOID DOSE CONVERSIONS
Robert Arnold MD and David E Weissman MD

Introduction A variety of published conversion tables exist to provide clinicians a rough guide for making calculations when switching between different opioid routes or preparations. Listed below are methods for common conversions using standard published conversion ratios. The examples assume a change in drug or route at a time of stable pain control using equianalgesic doses. See *Fast Fact* #2 about conversions involving transdermal fentanyl; #75 and #86 about methadone; and #181 about oxymorphone. **Caution:** Published values in equianalgesic tables should be considered a rough clinical guide when making dose conversions; substantial inter-individual variation exists. The final prescribed dose needs to take into account a patients' age, renal, pulmonary and hepatic function; their current pain level and opioid side effects such as sedation; as well as prior and current opioid use.

Opioid Equianalgesic Conversion Ratios for use with the following examples:

Morphine 10 mg parenteral = Morphine 30 mg oral = Hydromorphone 1.5 mg parenteral = Hydromorphone 7.5 mg oral = Hydrocodone 30 mg oral = Oxycodone 20-30 mg oral (see Reference 1).

A. Change route, keeping drug the same (e.g. oral to IV morphine)
Example: Change 90 mg q12 Extended Release Morphine to Morphine by IV continuous infusion

1. Calculate the 24 hour current dose: 90mg q 12 = 180 mg Morphine/24 hours
2. Use the oral to parenteral equianalgesic ratio: 30 mg PO Morphine = 10 mg IV Morphine
3. Calculate new dose using ratios: 180/30 x 10 = 60 mg IV Morphine/24 hours or 2.5 mg/hour infusion
4. Some experts recommend starting the new opioid at 75% of the calculated dose to account for inter-individual variation in first pass clearance.

B. Change drug, keep the same route (e.g. po morphine to po hydromorphone)
There is *incomplete cross-tolerance* between different opioids, but the exact amount will differ. Thus, equianalgesic tables are only approximations. Depending on age and prior side effects, *most experts recommend starting a new opioid at 50% of the calculated equianalgesic dose*, in the setting of well-controlled pain.
Example: Change 90 mg q 12 Extended Release Morphine to oral Hydromorphone.

1. Calculate the 24 hour current dose: 90 Q12 x 2 = 180 mg PO Morphine/24 hrs
2. Use the equianalgesic ratio: 30 mg PO Morphine = 7.5 mg PO Hydromorphone
3. Calculate new dose using ratios: 180/30 X 7.5 = 45 mg oral Hydromorphone/24 hours.
4. Reduce dose 50% for cross-tolerance: 45 x 0.5 = 22 mg/24 hours = 4 mg q4h

C. CHANGING DRUG AND ROUTE (E.G. ORAL MORPHINE TO IV HYDROMORPHONE)
Example: Change from 90 mg q12 Extended Release Morphine to IV Hydromorphone as a continuous infusion.

1. Calculate the 24 hour current dose: 90 Q12 x 2 = 180 mg PO Morphine/24 hrs
2. Use the equianalgesic ratio of PO to IV morphine: 30 mg po Morphine = 10 mg IV Morphine
3. Calculate new dose using ratios: 180/30 x 10 = 60 mg IV Morphine/24 hours
4. Use the equianalgesic ratio of IV Morphine to IV Hydromorphone: 10 mg Morphine = 1.5 mg Hydromorphone
5. Calculate new dose using ratios: 60/10 x 1.5 = 9 mg IV Hydromorphone/24 hours
6. Reduce dose 50% for cross-tolerance: 9 x 0.5 = 4.5 mg/24 hours = 0.2 mg IV continuous infusion
7. Note: one would also get the same amount of hydromorphone if you directly converted from oral morphine to IV hydromorphone using the 30 mg :1.5 mg ratio

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FAST FACTS AND CONCEPTS #54
OPIOID INFUSIONS IN THE IMMINENTLY DYING PATIENT
Elizabeth Weinstein MD, Robert Arnold MD, and David E Weissman MD

Introduction Opioid infusions, either intravenous (IV) or subcutaneous (SQ – see *Fast Fact* #28), can provide smooth and efficient control of distressing pain or dyspnea in the imminently dying patient. Opioids correctly titrated to provide symptom relief will not cause respiratory depression (see *Fast Fact* #8). It is common for physicians to order an opioid infusion in the dying patient as follows: *Start morphine infusion at 1 mg/hr, titrate to effect*. This type of order is pharmacologically unsound and unsafe; hospitals should adopt clinical practice guidelines that meet current national standards. The following is a step by step approach to rational opioid infusion prescribing in the dying patient, and is most appropriate for morphine or hydromorphone infusions; a future *Fast Fact* will discuss the use of methadone.

First, before starting an opioid infusion, calculate an equianalgesic dose of currently used opioids; then convert this to an equianalgesic basal rate.

Example: a patient on oral extended release morphine 60 mg q12, now unable to swallow. 60 mg q 12 = 120 mg/24 hours PO morphine = 40 mg IV morphine/24 hours = approximately 2 mg/hr IV infusion basal rate).

Second, if the current opioid dose is not effective, dose escalate the basal dose by 25-100% (see *Fast Fact* #20).

Third, if the patient is opioid naïve or when increasing the basal rate above the current equianalgesic rate, give a loading dose when starting the infusion.

Example: for a 1 mg/hr basal rate, give 2-5 mg loading dose (see reference 4 for additional dosing guidelines).

Fourth, choose a bolus dose (i.e. 'rescue' or 'PCA' dose if a patient controlled analgesia system is being used). This can be a nurse initiated bolus dose when using a standard IV infuser, or a patient, nurse or family initiative bolus using a PCA device. Even though the dying patient may be unable to press the button, the nurse or family members can use the PCA device, depending on local hospital policy. Based on patterns of breakthrough pain, a bolus dose of 50% - 150% of the hourly rate is a place to start. For example, for a morphine infusion of 2 mg/hr, choose a starting bolus dose of 1-3 mg.

Fifth, choose a dosing interval. The peak analgesic effect from an IV bolus dose is 10-20 minutes. Thus, the dosing interval (i.e. 'lockout interval' for a PCA device) should be in the range of 10-20 minutes.

Sixth, reassess for desired effect vs. side effects every 10-15 minutes until stable. Adjust bolus dose size every 30-60 minutes until desired effect is achieved. The 'right' bolus dose is one which controls undesirable symptoms with acceptable toxicities.

Seventh, reassess the need for a change in the basal rate no more frequently than every 6-8 hours. Use the number of administered bolus doses as a rough guide when calculating a new basal rate; never, however, increase the basal rate by more than 100% at any one time. When increasing the basal rate, always administer a loading dose so as to more rapidly achieve steady-state blood levels.

Common sense caution: The above guidelines should be thought of as a rough guide; differences in age, renal and pulmonary function and past responses to opioids must be considered when developing an appropriate analgesic treatment plan. When patients become anuric close to death, continuous dosing may be discontinued in favor of bolus dosing to prevent metabolite accumulation and agitated delirium.

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FAST FACTS AND CONCEPTS #72
OPIOID INFUSION TITRATION ORDERS
David E Weissman MD

Introduction This *Fast Fact* will discuss appropriate ways to write opioid infusion titration orders. See *Fast Fact* # 34 for further information on the appropriate symptom management during a ventilator withdrawal.

A bad example: '*Morphine 2-10mg/hour, titrate to pain relief.'* This order is commonly written for terminally ill patients and in the context of terminal ventilator withdrawals.

What is wrong with this order?

1. It places full responsibility for dose titration upon the nurse.
2. It provides no guidance regarding how fast to titrate (e.g. every hour, every shift?) or dose titration intervals (e.g. for poorly treated pain, should the dose be raised from 2 to 3 mg, 2 to 10 mg, other?).
3. It poses the potential for over-dosage by too zealous dose escalation and provides only one option for poorly controlled pain – increasing the continuous infusion rate.
4. Given that it takes at least 8 hours to achieve steady-state blood levels after a basal dose change, it makes no pharmacological sense to dose escalate the basal dose more frequently than q 8 hours.

A better way to write this order: *'Morphine 2 mg/hour and morphine 2 mg q 15 minutes for breakthrough pain (or 2 mg via PCA dose). RN may dose escalate the PRN dose to a maximum of 4 mg within 30 minutes for poorly controlled pain.'*

Why is this better?

1. This order is preferred as it provides a basal rate and a breakthrough dose. The breakthrough dose has a peak effect within 5-10 minutes. Thus, if the breakthrough dose is inadequate it can be safely increased, as often as every 15-30 minutes, to achieve analgesia – without a need for rapid upward titration of the basal rate.
2. Reassess the need for a change in the basal rate no more frequently than every 8 hours; use the number of administered bolus doses as a rough guide when calculating a new basal rate. However, never increase the basal rate by more than 100% at any one time. When increasing the basal rate, always administer a loading dose so as to more rapidly achieve steady-state blood levels.

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FAST FACTS AND CONCEPTS #68
IS IT PAIN OR ADDICTION?
David E Weissman MD

Background A very commonly requested educational pain topic by clinicians, surrounds differentiating the patient in pain from the patient with a substance abuse disorder. The key to proper assessment lies in understanding 1) the definitions of tolerance, physical and psychological dependence, 2) the components of an addiction assessment, and 3) the differential diagnosis of the symptom of "pain."

Definitions

- *Tolerance*: the need to increase a drug to achieve the same effect. In clinical practice, significant opioid tolerance is uncommon. Tolerance may be present in the pain patient or the addict; by itself it is not diagnostic of addiction.
- *Physical Dependence*: development of a withdrawal syndrome when a drug is suddenly discontinued or an antagonist is administered. Most patients on chronic opioids will develop physical dependence; its presence cannot be used to differentiate the pain patient from the addict.
- *Psychological Dependence* (Addiction): overwhelming involvement with the acquisition and use of a drug, characterized by: *loss of control, compulsive drug use, and use despite harm.* Research suggests that opioids used to treat pain rarely leads to psychological dependence.

Addiction (Substance Abuse) Assessment Assess for addiction in the domains presented in the list below (see Reference 1). Note: one positive item from the list does not establish a substance abuse disorder. Rather, the diagnosis rests on a pattern of behavior that includes several positive findings (see Reference 4).

- Loss of control of drug use (has no partially filled med bottles; will not bring in bottles for verification).
- Adverse life consequences – use despite harm (legal, work, social, family).
- Indications of drug seeking behavior (reports lost/stolen meds, requests for high-street value meds).
- Drug taking reliability (frequently takes extra doses, does not use meds as prescribed).
- Abuse of other drugs (current/past abuse of prescription or street drugs).
- Contact with drug culture (family or friends with substance abuse disorders).
- Cooperation with treatment plan (does not follow-up with referrals or use of non-drug treatments).

Differential Diagnosis The differential diagnosis for a patient reporting "pain" includes physical causes (broken leg, sciatica, pseudoaddiction – see Fast Fact #69); psychological causes (depression, anxiety, hypochondriasis, somatization disorder, etc.); spiritual causes (impending death, grief); substance abuse; and secondary gain/malingering/criminal intent (desire for attention, disability benefit, or financial gain from pain medications).

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FAST FACTS AND CONCEPTS #69
PSEUDOADDICTION
David E Weissman MD

Introduction The term *pseudoaddiction* was first used in 1989 to describe an iatrogenic syndrome resulting from poorly treated cancer pain. The index case was a 17 year old man with leukemia, pneumonia, and chest wall pain. The patient displayed behaviors (moaning, grimacing, increasing requests for analgesics) wrongly interpreted by the physicians and nurses as indicators of addiction, rather than of inadequately treated pain. The term pseudoaddiction is not a diagnosis, but rather a way to describe a phenomenon about the attitudes and motivation of clinicians in managing pain through our fears and mis-understanding of pain, pain treatment, and addiction.

a. Features

- Behaviors that suggest to the health care provider the possibility of psychological dependence (addiction):
  - Moaning or other physical behaviors in which the patient is trying to demonstrate to the provider that they are in pain.
  - Clock-watching or repeated requests for medication prior to the prescribed interval.
  - Pain complaints that seem "excessive" to the given pain stimulus.
- Inadequately prescribed and titrated opioids analgesics; typically the use of an opioid of inadequate potency and/or at an excessive dosing interval (e.g. oral morphine q6 hours PRN – see *Fast Fact* #18).

Assessment Perform a complete pain and substance abuse assessment:

- Is this a pain syndrome that typically responds to opioids?
- Is the current opioid dose, route and schedule pharmacologically appropriate?
- Does the patient have a history of a substance abuse disorder? (FF #311-312)

b. Management *If you believe the current problem is under-treated pain leading to pain seeking behaviors (pseudoaddiction):*

1) Establish trust. A primary issue in most cases is the loss of trust between the patient and the health care providers. The physician and nursing staff should meet to discuss how they will restore a trusting therapeutic relationship; outside assistance from a pain or palliative care service can be helpful. Plan to meet with the patient and openly discuss the events leading up to the current problem. Engage the patient in the decision-making process about the current and future use of analgesics.
2) Prescribe opioids at pharmacologically appropriate doses and schedules. Aggressively dose escalate until analgesia is achieved or toxicities develop (see *Fast Facts* #18, 20, 36). Frequently re-evaluate progress in pain management and ask for consultation assistance.
3) Pain behaviors due to pseudoaddiction can improve with the provision of adequate analgesia, including opioids. In contrast, behaviors associated with a substance abuse disorder will not change or worsen.

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FAST FACTS AND CONCEPTS #86
METHADONE: STARTING DOSING INFORMATION
Charles F von Gunten MD

Background Methadone is an effective opioid analgesic for severe pain. Because of low cost (a month's supply may be US $5-10) and apparent efficacy in complex pain syndromes, it is increasingly used as a first-line opioid. Retrospective analyses of consecutive patients initiated on methadone in an outpatient palliative care clinic confirm its effectiveness and safety (1). It is, in effect, a combination drug – part opioid and part NMDA receptor antagonist – although there is yet to be any evidence from controlled trials that it is a superior first-line analgesic to other opioids. Methods of dose conversion to methadone from other opioid analgesics that account for its dual action were discussed in *Fast Fact* # 75. This *Fast Fact* will describe strategies for beginning methadone when the patient has not been taking a strong opioid. **Note**: due to its complex pharmacology, clinicians are advised to seek consultation prior to initiating therapy (see *Fast Fact* #171).

Pharmacology Methadone is lipophilic, thus it takes time to develop tissue stores that maintain serum levels. There is enormous inter-individual variation in how long this takes. After a single dose there is a short distribution phase (associated with acute pain relief) with a half-life of 2-3 hours and a slow elimination phase (half-life 15-60 hours). Dosing must account for the accumulation of drug over days. It is this accumulation that accounts for most therapeutic misadventures. Liver metabolites are inactive; therefore no dose reduction is required with renal failure. After steady-state is reached, about two-thirds of patients will get adequate pain relief with twice a day dosing. **Note:** a number of drugs will alter methadone metabolism, **so** there needs to be close follow-up to drug interactions.

There are several approaches to starting methadone for the treatment of pain. All take into account the long-half life of the drug that leads to drug accumulation over days.

I. Conservative Approach

a) Begin fixed dose methadone 5 or 10 mg orally bid or tid for 4-7 days.
b) If incomplete pain relief, increase the dose by 50% and continue for 4-7 days.
c) Continue increasing dose every 4-7 days until stable pain relief achieved.
d) Breakthrough pain: use an alternative short acting oral opioid with short half-life (e.g. morphine 10 mg) every 1 h PRN for breakthrough pain and to provide pain relief during titration phase. This dose too may need to be titrated based on efficacy.

II. Loading Dose Approach

a) Load: Start methadone at fixed oral dose (e.g. 5 or 10 mg) q 4h **PRN only**.
b) Calculate Maintenance: On day 8, calculate the total methadone dosage taken over the last 24 hour period and give that in scheduled, divided doses bid or tid. Give 10% of total daily methadone as PRN drug q1h for breakthrough pain. Instruct the patient to call you if they need to use more than 5 breakthrough doses per day. *Example:* if someone took a total of 45 mg methadone on day 7 they would be converted to 15 mg tid scheduled with 5 mg as the prn dose.

Cardiac Safety Due to methadone's potential to prolong the QTc interval, an independent expert panel developed five cardiac safety recommendations for clinicians (4):

1. Clinicians should inform patients for the potential risk for arrhythmia before initiating methadone
2. Clinicians should ask about any history of structural heart disease, arrhythmia or syncope
3. Clinicians should obtain a pretreatment ECG to measure the QTc interval as well as a follow up ECG within 30 days, annually, and/or if the dosage exceeds 100 mg/day or an unexplained syncopal event occurs
4. If the QTc > 500 ms, consider discontinuing methadone, reducing the dose, or eliminating cofactors which may raise the QTc unless prognosis is short (i.e. weeks to months).

   If the QTc is between 450 ms to 500 ms, the clinician should discuss the risks and benefits with the patient

5. Clinicians should be aware of drug interactions with methadone which could slow its metabolism or prolong the QTc even more.

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FAST FACTS AND CONCEPT #126
PAIN ASSESSMENT IN THE COGNITIVELY IMPAIRED
L Scott Wilner MD and Robert Arnold MD

Background The inability of cognitively impaired patients to communicate information about pain places them at high risk for inadequate pain control. Two common risk groups in palliative care include:

- Patients with underlying brain pathology such as dementia, Parkinson's disease, stroke, or developmental abnormalities (see *Fast Fact* #192).
- Patients receiving sedating medications such as ICU patients receiving sedative/hypnotics to control anxiety/agitation from mechanical ventilation.

General Strategies Recommended strategies to assess pain in these patients include the following:

- Ask the patient: many patients who appear cognitively impaired may still be able to provide useful information concerning pain.
- Interview the caregivers and family: patterns of particular behaviors may have developed that indicate pain (e.g. placing a hand on the forehead for headache).
- Review the medical record for known pain-inducing pathology: for instance a diabetic patient with painful neuropathy that was manifest when the patient was cognitively intact.
- Complete a physical examination and directed laboratory studies to assess for common pain-inducing problems (e.g. fracture, urinary tract infection).

Pain Scales In addition to these measures, clinicians should use a validated pain rating system for the cognitively impaired. Such rating systems focus on the following observational items:

- Facial expression
- Body posture
- Vocalizations
- Appetite
- Interactivity

Representative examples of pain rating scales for the cognitively impaired, along with background information concerning validation studies and clinical experience can be found at: http://www.healthcare.uiowa.edu/igec/tools/categoryMenu.asp?categoryID=7.

- Doloplus-2 scale www.doloplus.com (1997)
- Assessment of Discomfort in Dementia Protocol (1999)
- Pain Assessment in Advanced Dementia (PAINAD) (2003)
- Checklist of Nonverbal Pain Indicators (2000)
- Pain Assessment for the Demented Elderly (2003)
- Pain Assessment for Seniors with Limited Ability to Communicate (2004)
- Abbey Pain Scale (2004)

To date, there are no trials showing clear superiority of one of these scales. Thus, clinicians should choose one tool and use it consistently to ensure uniformity among health care providers and across shifts.

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FAST FACTS AND CONCEPTS #161
OPIOID USE IN RENAL FAILURE
Robert Arnold MD, Peg Verrico RPh, Sara N Davison MD

Background Chronic pain is common in chronic kidney disease impacting 50% of hemodialysis patients, 82% of whom experience moderate to severe pain. The absorption, metabolism, and renal clearance of opioids are complex in renal failure. However, with the appropriate selection and titration of opioids, patients with renal failure can achieve analgesia with minimal risk of adverse effects. This *Fast Fact* reviews recommendations for opioid use in the setting of renal failure and in patients receiving chronic dialysis.

Not Recommended for Use:

- **Meperidine** is not recommended in renal failure due to accumulation of normeperidine, which may cause seizures.
- **Codeine** has been reported to cause profound toxicity which can be delayed and may occur after trivial doses. We recommend that codeine be avoided in patients with a Glomerular Filtration Rate (GFR) <30 mL/min.
- **Dextropropoxyphene** is associated with central nervous system (CNS) and cardiac toxicity and is not recommended for use in patients with renal failure.
- **Morphine** is not recommended for chronic use in renal insufficiency (GFR <30 mL/min) due to the rapid accumulation of active, non-dialyzable metabolites that are neurotoxic. If morphine must be used, avoid long-acting preparations and monitor closely for toxicity (see *Fast Facts* #57, 58).

Use with Caution:

- **Oxycodone** is metabolized in the liver with 19% excreted unchanged in the urine. There are reports of accumulation of both the parent compound and metabolites in renal failure resulting in CNS toxicity and sedation.
- **Hydromorphone**, as the parent drug, does not substantially accumulate in hemodialysis patients. Conversely, an active metabolite, hydromorphone-3-glucuronide, quickly accumulates between dialysis treatments but appears to be effectively removed during hemodialysis. With careful monitoring, hydromorphone may be used safely in dialysis patients. However, it should be used with caution in patients with a GFR < 30mL/min who have yet to start dialysis or who have withdrawn from dialysis.

Safest in Renal Insufficiency:

- **Fentanyl** is considered relatively safe in renal failure as it has no active metabolites. However, very little pharmacokinetic data exist regarding fentanyl in end stage renal disease. While some studies have shown decreased clearance in renal failure, most studies do not show drug accumulation. Fentanyl is not dialyzable due to high protein binding and a high volume of distribution.
- **Methadone** is considered relatively safe in renal failure. It has no active metabolites and limited plasma accumulation in renal failure due to enhanced elimination in the feces. However, precautions regarding the use of methadone exist (See *Fast Facts* # 75, 86). It does not appear to be removed by dialysis.

Opioid Dosing Given the lack of pharmacokinetic and pharmacodynamic data of opioids in renal failure, it is difficult to advocate for specific analgesic treatment algorithms. However, the following guide has been proposed (Broadbent 2003) for the *initial* dosing of the safer opioids in renal impairment and renal failure.

- Creatinine Clearance > 50 mL/min: normal dosing.
- Creatinine Clearance of 10-50 mL/min: 75% of normal.
- Creatinine Clearance < 10 mL/min: 50% of normal.

The “normal opioid dose” for any given patient is the dose that adequately relieves pain without unacceptable adverse effects (see *Fast Fact* #20). Rarely, do opioids need to be adjusted when GFR is > 50 mL/min. While opioids can be used when GFR is <50, they require closer monitoring and constant

reassessment to ensure that accumulation of active metabolites does not result in toxicity. This should not preclude the effective use of opioids in these patients.

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FAST FACTS AND CONCEPTS #175
OPIOID ALLERGIC REACTIONS
Hunter E Woodall MD, Asriani Chiu MD, and David E Weissman MD

Background Patient reports of opioid "allergies" are common, most often due to symptoms of nausea, vomiting, itching, hypotension, or constipation. This *Fast Fact* will review signs, symptoms, and management options of opioid allergies and pseudo-allergies.

Pathophysiology Allergies can be defined as an *exaggerated immune reaction to an antigen*. There are different types of allergic, or hypersensitivity, reactions (immediate, cytotoxic, immune complex, or delayed), but the common feature is that all such reactions are *mediated by the immune system*. In contrast, the vast majority of opioid side effects are not immune related. Opioid side effects can be divided into three categories: those that have no element of an immune reaction, those that mimic an immune reaction, and those that are immune mediated.

Side effects with no immune mechanism: these include nausea/vomiting, constipation sedation, delirium, respiratory depression, and urinary retention.

Side effects that mimic immune reactions: common signs/symptoms include mild itching, uticaria, brochospasm, or hypotension. **Note:** if all these occur soon after an opioid dose, and the patient appears acutely ill, this may represent an anaphylactoid reaction (see below). For most patients, these symptoms are mild and self-limited. The etiology most commonly involves direct mast cell degranulation with histamine release, unrelated to a true immune-mediated reaction. Such reactions to opioids are usually idiosyncratic and may or may not recur with re-challenge of the same opioid; they are not a contraindication to continued opioid use, since an alternative opioid may be well tolerated. Hypotension can also occur due to arterial and venous vasodilation, thus, hypotension is more common in a volume depleted patient. Opioids can also have negative inotropic effects and induce a vagally-mediated bradycardia leading to hypotension – again, not a true allergic reaction.

Immune mediated reactions:

- **Allergic dermatitis** in response to opioids has been described. It is characterized as erythroderma, scarlatina, eczema, or exudative vesicular eruptions; these may represent a Type IV (delayed) hypersensitivity reaction. Patients can undergo diagnostic patch testing for confirmation.
- **Anaphylaxis/Anaphylactoid Reactions.** Anaphylaxis is a systemic IgE mediated reaction resulting in the immediate release of potent mediators; anaphylactoid reactions are clinically the same, but not IgE mediated. Early symptoms include nasal congestion, flushing, pruritus, angioedema; if the process worsens, patients can develop nausea, diarrhea, urinary urgency, brochospasm, hypotension, and death. Opioids can lead to an anaphylactoid reaction, but such events are very rare.

Management True allergic reactions appear to be rare. If you suspect an immune-mediated skin rash you should consult a dermatologist or allergist to establish a definitive diagnosis and determine the need for desensitization or appropriate alternatives. Anaphylactoid reactions require emergent management with epinephrine and histamine blockers. For milder histamine-related symptoms, common practice is to rotate to an opioid in a different pharmacologic class (see below) along with use of anti-histamines or steroids. Anecdotal reports suggest that methadone and fentanyl cause fewer instances of itching.

Opioid Class	Drugs
Phenanthrenes	morphine; codeine; hydrocodone; oxycodone; oxymorphone; hydromorphone; levorphanol.
Phenylpiperadines	fentanyl; meperidine; sufentanil; remifentanyl
Diphenylheptanes	methadone; propoxyphene

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FAST FACTS AND CONCEPTS #215
OPIOID POORLY-RESPONSIVE CANCER PAIN
Tamara Sacks MD, David E Weissman MD, and Robert Arnold MD

Background Relief of cancer pain from opioids is rarely all or nothing; most patients experience some degree of analgesia alongside opioid toxicities. When the balance of analgesia versus toxicity tips away from analgesia, the term 'opioid poorly-responsive pain' is invoked. While opioid poorly-responsive pain is not a discreet syndrome, it is a commonly encountered clinical scenario. This *Fast Fact* reviews key points in its assessment and management.

Differential Diagnosis of Opioid Poorly-Responsive Pain

1. *Cancer-related pain*
    a. Cancer progression (new fracture at site of known bone metastases).
    b. Causes of pain (e.g. neuropathic pain, skin ulceration, rectal tenesmus, muscle pain) that are known to be less responsive to systemic opioids or opioid monotherapy.
    c. Psychological/spiritual pain related to the cancer experience (existential pain of impending death).
2. *Opioid pharmacology/technical problems*
    a. Opioid tolerance (rapid dose escalation with no analgesic effect).
    b. Dose-limiting opioid toxicity (sedation, delirium, hyperalgesia, nausea – see *Fast Facts* #25, 142).
    c. Poor oral absorption (for PO meds) or skin absorption (e.g. transdermal patch adhesive failure).
    d. Pump, needle, or catheter problems (IV, subcutaneous, or spinal opioids).
3. *Non-cancer pain*
    a. Worsening of a known non-cancer pain syndrome (diabetic neuropathy).
    b. New non-cancer pain syndrome (dental abscess).
4. *Other psychological problems*
    a. Depression, anxiety, somatization, hypochondria, factitious disorders.
    b. Dementia and delirium both can effect a patient's report of and experience of pain.
    c. Opioid substance use disorders or opioid diversion.

Management Strategy

1. *Initial Steps*
    a. Complete a thorough pain assessment including questions exploring psychological and spiritual concerns. If substance abuse or diversion is suspected, complete a substance abuse history (see *Fast Facts* #68, 69).
    b. Complete a physical examination and order diagnostic studies as indicated.
    c. Escalate a single opioid until acceptable analgesia or unacceptable toxicity develop, or it is clear that additional analgesic benefit is not being derived from dose escalation. If this fails, consider:
        i. Rotating to a different opioid (e.g. morphine to methadone).
        ii. Changing the route of administration (e.g. oral to subcutaneous).
    d. Treat opioid toxicities aggressively.
    e. Use (start or up-titrate) adjuvant analgesics, especially for neuropathic pain syndromes.
    f. Integrate non-pharmacological treatments such as behavioral therapies, physical modalities like heat and cold, and music and other relaxation-based therapies – see *Fast Fact* #211.

2. *Additional steps* – Pain refractory to the initial steps requires multi-disciplinary input and care coordination.
    a. Hospice/Palliative Medicine consultation to optimize pain assessment, drug management, and assessment of overall care goals.
    b. Mental health consultation for help in diagnosis and management of suspected psychological factors contributing to pain.
    c. Chaplain/Clergy assistance for suspected spiritual factors contributing to pain.
    d. Interventional Pain and/or Radiation Oncology consultation.

e. Rehabilitation consultations (Physiatry, Physical and Occupational Therapy) to maximize physical analgesic modalities.
f. Pharmacist assistance with drug/route information.

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FAST FACTS AND CONCEPTS #244
SCREENING FOR OPIOID MISUSE AND ABUSE
Rene Claxton MD and Robert Arnold MD

Background Opioid analgesics are often effective in relieving both cancer and chronic non-malignant pain but can be misused and abused by patients and others (1, 2). Clinicians need to identify patients at risk of misusing prescribed opioids in order to prescribe and monitor opioid therapy safely. This *Fast Fact* discusses how clinicians can screen for risk of misuse. See *Fast Facts* #68, 69, 110, and 127 for further discussions about differentiating pain complaints from abuse, urine drug testing, and substance use disorders in palliative care patients.

Definitions Medication *misuse* is the intentional or unintentional use of a prescribed medication other than as directed. Misuse can include a patient taking more pain medicine than prescribed to control otherwise inadequately controlled pain as well as abusive and addictive behaviors. *Abuse* refers to the intentional self-administration of a medication for non-medical purpose or the use of an illegal drug. *Addiction* is a primary, chronic disease defined by one or more of the following behaviors: impaired control over drug use, compulsive use, continued use despite harm, and craving (4). *Aberrant behavior* is a research term defined differently by various investigators which typically includes activities of misuse and abuse.

Benefits of Screening Opioid therapy is a safe and effective treatment for pain in many patients. However, opioid misuse carries the risk of development of addiction, overdose, and death which require providers to balance individual patient's pain and risk levels. Patients with high risk for opioid misuse should not necessarily be denied opioid therapy but should be followed under closer supervision than those patients with lower risk estimates. In patients with short life expectancies, clinicians may be willing to accept greater risk in prescribing opioids than in patients with chronic non-malignant pain. However, providers should remember that opioids do not improve quality of life for patients who misuse them as a remedy for other symptoms such as anxiety or existential suffering, and that active substance abuse is as devastating to terminally ill patients and families as it is to others (5).

Risk Factors Risk factors for misuse can be grouped into three categories: biological, social and psychological. Biological risk factors include family history of drug abuse and male gender. Social risk factors include poor social support and history of convictions related to drugs or driving while impaired by substances. Psychological risk factors include a personal history of substance abuse (including alcohol or tobacco), pre-adolescent history of sexual abuse, and co-morbid psychiatric illness (i.e. major depression, bipolar disorder, personality disorder) (6).

Screening for Misuse No screening tests have been developed to screen for opioid misuse specifically in cancer patients. However, several screening tests predict the potential for opioid misuse in patients with chronic non-malignant pain. Common instruments include the Screener and Opioid Assessment for Pain Patients (SOAPP) and the Opioid Risk Tool (ORT). While these tools can be applied to patients seen in palliative care settings (such as cancer patients or patients with advanced illnesses), clinicians should be aware they have not been validated in these patient populations. *Clinicians should always keep in mind that these are screening tools used to identify high-risk patients appropriate for close monitoring and further assessment, but are not diagnostic tools to diagnose substance use disorders or to definitively identify patients who should not be prescribed opioids for pain. In addition, they do not assess the risk of diversion of drugs by family or community members.*

- The SOAPP predicts risk potential for aberrant drug behavior via a 14-item self-report. Items included in the SOAPP cluster into categories of: antisocial behavior, substance abuse history, doctor/patient relationship, medication-related behaviors, and psychiatric and neurobiologic need for medicine. Responses are based on a 5 point Likert scale (possible score range 0-56). Using 7 as cut off, this test had a sensitivity of 91%, specificity of 69%, positive predictive value (PPV) of 71% and negative predictive value (NPV) of 90% (7) to predict aberrant drug behavior. It is important to note that while a score of 7 maximizes this test's sensitivity, i.e. identifies most patients with a risk of opioid misuse, it will also result in a large number of false positive tests given the lower specificity at this cut-off.

- The ORT is a 5-item yes/no tool which predicts the probability of opioid misuse or abuse among patients being considered for opioid therapy for chronic pain. This measure is based on several risk factors including: family history of substance abuse, personal history of substance abuse, age (16-45 years is a risk factor), history of pre-adolescent sexual abuse, and psychological disease. This tool categorizes patients as low, medium or high risk for aberrant behavior. The sensitivity and specificity for the test for patients who score at least 'medium risk' is 99% and 16%, respectively. For those with 'high risk' scores, the test sensitivity is 53% and specificity 96% (8). Because clinicians administering the ORT could be misled by patients with a history of opioid use who downplay past behavior, it is best to apply the tool in lower-risk clinical settings such as primary care rather than in higher risk settings.

Which method is the best way to predict opioid misuse or abuse? In a study of 48 chronic pain patients, the sensitivity of predicting aberrant behavior was compared using three different methods: a trained psychologist's clinical interview, SOAPP and ORT. The clinical interview showed highest sensitivity (77%). SOAPP showed a sensitivity of 73% (score ≥6 as cut-off). ORT showed sensitivity of 45% (score ≥4 as cut-off) (9).

Bottom Line Given the limited number of studies comparing and validating these instruments, it is reasonable to choose a measure based on practicality such as familiarity, ease and time of completion or patient versus provider administration (both the SOAPP and ORT can be completed by patients in less than 10 minutes). Regardless of whether one uses a tool, a thorough history including personal and family history of psychiatric conditions, substance abuse, and sexual abuse is key to identifying patients who need closer assessment and monitoring.

Additional Resources
For an electronic version of the SOAPP, click here: http://www.painedu.org/soapp.asp.
For an electronic version of the ORT, click here: http://www.opioidrisk.com/node/884.

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FAST FACTS AND CONCEPTS #271
ANTI-EPILEPTIC DRUGS FOR PAIN
Seth Hepner and René Claxton MD

Introduction Tri-cyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and anti-epileptic drugs (AEDs) are the mainstays of adjuvant therapy for neuropathic pain. This *Fast Fact* reviews the evidence for the use of AEDs in the treatment of neuropathic pain. For a more in-depth look at gabapentin, pregabalin, and antidepressants for neuropathic pain see *Fast Facts* #49, 187, 288, and 299. Due to lack of head-to-head data, evidence is presented as numbers needed to treat (NNT) and numbers needed to harm (NNH). For instance, an NNT of 5 for 50% pain reduction means for every 5 patients treated with a drug, only 1 of them would achieve a 50% reduction in pain. All data presented and doses mentioned are for adults and based on investigations of patients with chronic pain. Given the paucity of research about the use of adjuvants for pain management in patients with life-limiting illnesses, many clinicians empirically extrapolate available data to palliative care patients.

Gabapentin is effective in treating central and peripheral neuropathic pain. According to a 2011 Cochrane review of the effect of gabapentin on chronic neuropathic conditions (including post-herpetic neuralgia, painful diabetic neuropathy, mixed neuropathic pain), the NNT is 5.8 (4.8-7.2) to achieve at least moderate benefit. Adverse effects are frequent, usually tolerable and include drowsiness, dizziness and edema (1). Gabapentin should be dose adjusted for renal dysfunction. It should be withdrawn gradually to avoid precipitating seizures. Maximum dose is 3,600 mg/day (2).

Pregabalin is effective in treating peripheral and central neuropathic pain. Its effectiveness increases as the dose approaches 600 mg/day. At a dose of 600 mg/day, the NNT to decrease pain by 50% for the following conditions is: 3.9 (range 3.1-5.1) for post-herpetic neuralgia; 5.0 (range 4.0-6.6) for diabetic neuropathy; and 5.6 (range 3.5-14) for central neuropathic pain. There was no difference in incidence of side effects among participants taking pregabalin vs placebo and no indication of a dose response to side-effects (3). Dosing starts at 150 mg/day in divided doses either twice or three times daily (2).

Carbamazepine is effective for neuropathic pain, specifically trigeminal neuralgia, but is not considered first-line therapy due to its adverse effects. A meta-analysis reported that carbamazepine reduced chronic neuropathic pain compared to placebo with NNT of 1.7. However, adverse events occur frequently: NNH = 2.6 (4). Common side effects include leukocytosis, thrombocytopenia, dizziness, drowsiness, ataxia, nausea/vomiting and blurred vision. Additionally, there is a risk of agranulocytosis, aplastic anemia, and Stevens Johnson syndrome. Laboratory tests (BUN, complete blood count, sodium, liver function tests, urinalysis) and serum drug levels should be checked at baseline and during treatment. Dosing starts at 100-200 mg twice a day and is titrated by 200 mg/day every 3 – 5 days until pain relief is achieved. Maximum dose is 1,200 mg/day (2).
Oxcarbazepine is an analogue of carbemazepine which is equally effective at treating trigeminal neuralgia (5) but with fewer side effects (6). Oxcarbazepine can be started at 300 mg twice a day and titrated up by 300 mg/day every 3 days to therapeutic effect. Maximum dose is 2,400 mg/day (2).

Valproic acid was evaluated in a 2011 meta-analysis for the treatment of neuropathic pain. There were insufficient data for reliable pooled analysis, and the authors recommend against its use as first line therapy (7). Several small studies (n<60) showed benefit (maximum of 1200 mg/day in divided doses) over placebo in the treatment of diabetic neuropathy (8). However, studies of valproic acid have failed to find an effect (9). Adverse effects include liver function test abnormalities, dizziness, drowsiness and nausea. Maximum dose is 60 mg/kg/day (2).

Topiramate has not demonstrated convincing efficacy for painful diabetic neuropathy. In three studies totaling more than 1200 participants, topiramate did not show a statistically significant effect (9). A subsequent randomized controlled trial of 317 patients with diabetic neuropathy showed a benefit over placebo with a NNT of 6.9. Serious adverse events include convulsion, bradycardia, and syncope (10). Additional adverse effects include sedation, nausea, diarrhea and metabolic acidosis (2). Dosing starts at 50 mg/day and can be titrated up to 400 mg/day (10).

Lacosamide has weak evidence supporting its use. In a randomized, placebo controlled study, patients treated with lacosamide (100-400 mg/day) for diabetic neuropathy showed a decrease in baseline pain by 2 or more points on an 11-point scale compared to controls, NNT 10.9. Side effects were similar (12). Subsequent trials have failed to show similar effects except for a subgroup analysis of 400 mg/day (9). Dosing starts at 50 mg twice daily. Abrupt discontinuation can precipitate seizures (2).

Using other AEDs including phenytoin and levetiracetam is not supported by clinical research. Although, a single small study (n=92) demonstrated benefit for lamotrigine in treating painful HIV-related neuropathy at doses of 200-400 mg daily (12, 9, 13).

Summary TCAs, SNRIs, and the AEDs gabapentin and pregabalin are the best adjuvant analgesics for neuropathic pain. For patients who are intolerant to or who have pain refractory to the above medications, one can consider therapy with carbamazepine, oxcarbazepine, valproic acid, topiramate or lacosamide, keeping in mind they are associated with more side effects and lower rates of efficacy.

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FAST FACTS AND CONCEPTS #294
OPIOID INDUCED CONSTIPATION PART 1: ESTABLISHED MANAGEMENT STRATEGIES
Andrew Badke MD and Drew A Rosielle MD

Background Opioid induced constipation (OIC) affects 45-90% of patients (1, 2) and can cause significant morbidity. It is the most common reason patients avoid and/or discontinue opioids (3, 4) and can often result in an increase in hospital length of stay (5) and overall healthcare costs (6). This *Fast Fact* will describe the physiology of OIC and describe established treatment strategies. *Fast Fact # 295* will discuss newer management strategies.

Physiology OIC is mediated through several different mechanisms including ineffective GI motility, inhibition of mucosal transport of electrolytes and fluids, and interference with the defecation reflex (7). The greatest risk factor for developing OIC is duration of opioid therapy. Route of delivery or increased opioid dosing does not appear to affect the risk of developing OIC (2). While patients usually develop tolerance to most other side effects from opioids, they do not develop tolerance to OIC (1).

Non-pharmacologic Therapies Physical activity, scheduled toileting, fiber, and adequate fluid intake have been traditional non-pharmacologic mainstays for preserving GI regularity in constipation (8). However, there is no specific evidence in favor for any of these interventions to treat OIC and adherence may be challenging for chronically ill patients.

Pharmacologic Therapies In general, patients with regular opioid exposure will require pharmacologic therapy to appropriately manage OIC. Both stimulant and osmotic laxatives have shown to be effective in treating OIC and are considered the cornerstone of treatment. Failure of oral pharmacologic therapy usually requires more invasive rectal based interventions or one of the newer treatment modalities (see *Fast Fact #295).*

- **Stimulant Laxatives:** Senna and bisacodyl are the main stimulant laxatives available in the US and work by increasing enteric muscle contraction and GI motility. The onset of action for oral senna and bisacodyl is around 6-12 hours. Starting dose for senna is two 8.6 mg tabs; bisacodyl is one 10mg tab. However, higher doses are usually needed for OIC. Senna can be safely dosed up to 12 tabs daily and bisacodyl up to 30 mg (9). Both medications are relatively inexpensive. Because stimulant laxatives cause intestinal contractions their use can be limited by abdominal cramps and pain. This can sometimes be avoided by dividing the total dose into smaller more frequent doses (9).
- **Osmotic Laxatives:** These include non-absorbable sugar molecules such as polyethelyne glycol (PEG), lactulose, and sorbitol, as well as poorly absorbed salt-based molecules like milk of magnesia and magnesium citrate. Osmotic laxatives have limited intestinal absorption leading to an increase in colonic intraluminal water through oncotic pressure. With increased intraluminal volume and distension, reflex peristalsis subsequently occurs. Additionally, the increase in intraluminal water also leads to softer stool and allows for easier intestinal transit. The starting daily dose for PEG is 17 g, for lactulose is 15 ml, and 30 ml for 70% sorbitol solution. Osmotic laxatives will have a linear effect on bowel function with dose increases; the maximum effective daily dose of PEG is 68 g (10), lactulose is 60 ml, and for sorbitol is 150 ml. The onset of action for osmotic laxatives tends to be variable ranging from 12 to 48 hours, but when used regularly patients will have a more consistent effect. Osmotic laxatives generally do not lead to a loss of fluids or electrolytes as they only bind to orally taken fluid. With this, PEG requires 125 ml of fluid per 17 g dose (11) and similarly ~200 ml is recommended with every 30 ml of lactulose (12). Major side effects from osmotic laxatives include abdominal cramping, pain, and flatulence. Lactulose and sorbitol tend to have more of these side effects than PEG (11). While sorbitol and lactulose have shown similar efficacy, sorbitol tends to be more cost effective (13). Magnesium based compounds (milk of magnesia and magnesium citrate) are also effective, but the magnesium load can be dangerous for patients with renal insufficiency.
- **Rectal Based Laxatives:** Unfortunately, there is a lack of clinical research to support rectal based laxatives, but anecdotally they are often used for refractory constipation. Stimulant suppositories such as bisacodyl and rectal vault lubricants such as glycerin are inexpensive. Their onset is usually within 10-15 minutes and can be dosed daily (9). Warm tap water and milk of molasses enemas (12) can be dosed more frequently (up to every two hours). They work by causing rectal distension and reflex

defecation. Other enema formulations, such as phosphate or saline enemas, should be used with caution in renal insufficiency due to concern for electrolyte shifts.

- **Manual Evacuation:** Digital stimulation and manual disimpaction may be necessary if fecal impaction is suspected. Due to the discomfort associated with manual evacuations, these are often interventions of last resort and may require pre-medication with pain medications and/or anxiolytics.
- **Ineffective Therapies:** Docusate sodium not demonstrated efficacy in randomized controlled studies for OIC compared with placebo (14). Bulk forming laxatives (psyllium or fiber) require at least 1.5 L of water to be effective and can actually lead to worsened constipation with inadequate fluid intake. Consequently, most guidelines do not routinely recommend their use (11,15,16).

Practical Advice A consistent bowel regimen is essential in preventing constipation in patients on chronic opioid therapy. Providers should educate their patients about the signs and symptoms of OIC and seek appropriate consultation in a timely manner. A scheduled stimulant laxative regimen such as Senna 2 tabs twice daily should be prescribed at the onset of regular opioid use regardless of opioid dosing. The goal for the bowel regimen should be an unforced bowel movement at least every other day. If a patient has not had a bowel movement in 48 hours, increasing stimulant laxative dose and/or adding an osmotic laxative is appropriate. Failure of oral laxative therapy usually requires rectal based interventions and/or one of the newer treatment modalities (see *Fast Fact #295).*

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FAST FACTS AND CONCEPTS #295
OPIOID INDUCED CONSTIPATION PART II: NEWER THERAPIES
Andrew Badke MD and Drew A Rosielle MD

Background *Fast Fact #294* introduces OIC and discusses well-established treatments. This *Fast Fact* discusses emerging management approaches. In general, these agents are used for refractory OIC, which implies persistent and distressing symptoms despite exposure to typically effective doses of stimulant and osmotic laxatives. When exactly to use these emerging therapies remains largely empiric.

Opioid Antagonists Since the majority of symptoms associated with OIC are secondary to stimulation of μ-opioid receptors in the gut, opioid antagonists offer an attractive pharmacologic rationale for OIC (1).

Naloxone: Until recently, naloxone was the only available opioid antagonist for OIC treatment. Typically, patients orally ingest the contents of IV ampules. Naloxone has a high first pass metabolism, so it is possible for patients who take it orally to have peripheral μ-opioid receptor antagonism *without* significant impact on central receptors which could lead to opioid withdrawal and loss of analgesia (2). In a small, non-controlled study, 80% of chronic opioid users had bowel evacuation in 1-4 hours after naloxone administration. Unfortunately, over two-thirds reported a 10-15% loss of analgesia and nearly one-third had withdrawal symptoms (3). Therefore, if used, it is recommended to start at a low dose of 0.8 mg twice daily. Effective doses typically need to be at least 10% of equivalent daily morphine dose, so naloxone usually requires slow up-titration with max dosing of 12 mg daily (2).

Methylnaltrexone bromide: Methylnaltrexone is a peripherally-acting μ-opioid receptor antagonist. It is a methylated form of naltrexone and formulated as a subcutaneous injection. It is less able to cross the blood brain barrier, reducing the risk of altering analgesia or inducing central opioid withdrawal. An industry-funded randomized controlled trial of chronic opioid users showed that weight based methylnatrexone dosing led to laxation in nearly half of subjects within 4 hours as opposed to 15% of placebo (4). A subsequent meta-analysis of 6 separate trials with methylnaltrexone demonstrated the number needed to treat (NNT) is 3 for OIC patients that have failed to respond to standard laxative therapy (5). Its use is limited by cost which averages $55 per dose, and it is also contraindicated when bowel obstruction is suspected or for patients with compromised bowel integrity. The most common side effects are nausea, diarrhea, and cramping – which can be severely painful.

Naloxegol: Two oral peripheral acting μ-opioid receptor antagonists are available in the US: alvimopam, which is only approved for post-operative ileus, and naloxegol (pegylated naloxone), which has recently been approved for OIC in non-cancer patients. Two separate phase-three clinical trials showed an increase from 1 to >3 bowel movements per week in non-cancer patients on chronic opioids with daily dosed naloxegol compared to placebo. There was also a significant improvement in a subset of patients who had failed traditional laxative therapy as well (7). Both 12.5 mg and 25 mg have been studied; the 25 mg dose has a higher success rate but is associated with more abdominal pain, nausea, vomiting and diarrhea (7). Its current price is approximately $300 for 30 pills.

Other Agents
Lubiprostone: Lubiprostone is a selective chloride channel-2 activator that acts locally on the small intestine to increase fluid secretion and GI motility. It is FDA approved for OIC. Two randomized controlled trials in non-cancer chronic opioid users demonstrated an increase in frequency of spontaneous bowel movements by week 8. Moreover, approximately 40% of subjects had a bowel movement at 24 hours, 60% within 48 hours, and 27% of subjects had > 3 bowel movements per week (8,9). The most studied dose is 24 mcg orally twice per day. Common side effects included nausea, diarrhea and abdominal distension. Curiously, lubiprostone does not appear to be effective for methadone induced constipation (10).
Linactolide has a different mechanism than lubiprostone, but is also a small intestinal secretogogue. It currently is approved for irritable bowel syndrome. Though there is interest in its efficacy in OIC, it has yet to be specifically studied in this population.

Prucalopride is a serotonin receptor type-4 agonist which is available in Canada and parts of Europe and Asia to treat chronic constipation. It is a prokinetic agent which has shown promise for treating OIC in a phase 2 study (5). It is unclear if or when it will be released in the US.

Practical Advice Traditional oral and rectal laxatives have been the mainstay of treatment in OIC for many years. However, recent development of novel approaches to treat OIC show promise for the future. Of the pharmacologic interventions described above, methylnatrexone has been the best studied and shown to be the most efficacious. It is reasonable to give methylnaltrexone after failure of oral laxatives (see *Fast Facts* #294) in OIC, and potentially can be used prior to using more invasive rectal based interventions. With time and more clinical trials, other oral formulations targeting OIC may become more standard of care. Patient and caregiver education about the importance of adherence to recommended therapy and guidance about signs and symptoms of OIC is essential to ensure effective treatment.

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FAST FACTS AND CONCEPTS #1
DIAGNOSIS AND TREATMENT OF TERMINAL DELIRIUM
David E Weissman MD and Drew A Rosielle MD

Background Some degree of loss of cognitive function occurs in most patients in the week or two before death. The typical scenario presented to housestaff is a late-night call from a ward nurse saying, "*Mr. Jones is confused, what should we do*?" This *Fast Fact* reviews assessment and management issues in terminal delirium. See *Fast Fact* #60 for a discussion of newer pharmacological treatments.

Key teaching points:

1. The term "confusion" is not an accurate descriptive term—it can mean anything from delirium, dementia, psychosis, obtundation, etc. Patients need a focused assessment, including a brief mini-mental examination. Clinicians should use one of several validated delirium assessment tools to help quantify and document cognitive function.
2. "Terminal delirium" is not a distinct diagnosis, although it is a commonly used phrase. It implies delirium in a patient in the final days/weeks of life, where treatment of the underlying cause is impossible, impractical, or not consistent with the goals of care.
3. Delirium can be either a *hyperactive /agitated delirium* or a *hypoactive delirium*. The hallmark of delirium is an acute change in the level of arousal; supporting features include altered sleep/wake cycle, mumbling speech, disturbance of memory and attention, and perceptual disturbances with delusions and hallucinations.
4. The most common identifiable cause of delirium in the hospital setting is drugs: anti-cholinergics (e.g. anti-secretion drugs, anti-emetics, anti-histamines, tricyclic anti-depressants, etc.), sedative-hypnotics (e.g. benzodiazepines), and opioids. Other common causes include metabolic derangements (elevated sodium or calcium, low glucose or oxygen); infections; CNS pathology; or drug/alcohol withdrawal.
5. The degree of work-up to seek the cause of delirium is determined by understanding the disease trajectory and overall *goals of care* (see *Fast Fact* #65).
6. The drug of choice for most patients is a neuroleptic. There is one controlled clinical trial of haloperidol versus lorazepam in HIV patients; haloperidol was the superior agent. Haloperidol is administered in a dose escalation process similar to treating pain. Start haloperidol 0.5-2 mg PO or IV q1hour PRN. Atypical antipsychotics have also been studied for delirium are probably as efficacious as haloperidol. There are insufficient data to make a strong recommendation about the best drug or dosing of antipsychotics for delirium.
7. It is best to think of benzodiazepines as *sedatives* and *anxiolytics* but not as therapy for underlying delirium. On the rare occasion one wants to actually *sedate* a delirious patient a benzodiazepine may be indicated. If anxiety is a prominent part of a patient's delirium, a benzodiazepine may help. Generally, however, benzodiazepines should be avoided as they can cause paradoxical worsening of the delirium and agitation.
8. Non-pharmacological treatments should always be used in delirium management: reduce or increase the sensory stimulation in the environment as needed; ask relatives/friends to stay by the patient; frequent reminders of time/place.

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FAST FACTS AND CONCEPTS #5

THE CAUSES OF NAUSEA AND VOMITING (V.O.M.I.T.)

James Hallenbeck MD

Background By understanding the pathophysiology of nausea and targeting antiemetics to specific receptors, therapy can be optimized and side effects minimized. An easy way to remember the causes of vomiting is the **VOMIT** acronym. In the table below receptors involved in different types of nausea are highlighted using this acronym. Blockade of these receptors allows rational, focused therapy.

Cause - Vestibular
- Receptors Involved - Cholinergic, Histaminic
- Drug Class Useful - Anticholinergic, Antihistaminic
- Drug Examples - Scopolamine patch, Promethazine

Cause - Obstruction of Bowel by Constipation (See FF #294 and #295)
- Receptors Involved - Cholinergic, Histaminic, likely 5HT3
- Drug Class Useful - Stimulate myenteric plexus
- Drug Examples - Senna products

Cause - Dys**M**otility of upper gut
- Receptors Involved - Cholinergic, Histaminic, 5HT3, 5HT4
- Drug Class Useful - Prokinetics which stimulate 5HT4 receptors
- Drug Examples - Metoclopramide

Cause - Infection, **I**nflammation
- Receptors Involved - Cholinergic, Histaminic, 5HT3, Neurokinin 1
- Drug Class Useful - Anticholinergic, Antihistaminic, 5HT3 antagonists, Neurokinin 1 antagonists
- Drug Examples – Promethazine (e.g. for labyrinthitis), Prochlorperazine

Cause - Toxins stimulating the chemoreceptor trigger-zone in the brain such as opioids (see FF 25) or chemotherapy (see FF #285)
- Receptors Involved - Dopamine 2, 5HT3
- Drug Class Useful - Antidopaminergic, 5HT3 Antagonists
- Drug Examples - Prochlorperazine, Haloperidol, Ondansetron

Notes
- 5HT3, 5HT4 refer to the serotonin receptors, subtypes 3 & 4.
- Promethazine and prochlorperazine are very different drugs. Promethazine is most useful for vertigo and gastroenteritis due to infections and inflammation. Prochlorperazine is preferred for opioid related nausea.
- There is no evidence supporting the use of lorazepam as a sole agent for nausea. Sedated patients are more prone to aspiration.
- 'O' here relates to 'obstruction' of bowels *by constipation*, not mechanical blockage (see *Fast Facts* #45, 119 for management of mechanical obstructions).
- See FF #93 & #279 for information on cannibinoids and cannabis for nausea and vomiting

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FAST FACTS AND CONCEPTS #27
DYSPNEA AT END-OF-LIFE
David E Weissman MD

Introduction Dyspnea is defined as a subjective sensation of difficulty breathing. This *Fast Fact* reviews key elements in the assessment and treatment of dyspnea near the end-of-life.

Etiology The causes of dyspnea include a wide spectrum of serious lung or heart conditions, anemia, anxiety, chest wall pathology, electrolyte disturbances or even urinary retention or constipation.

Assessment Looking for simple problems is always warranted: is the Oxygen turned on? Is the tubing kinked? Is there fluid overload from IV fluids or TPN? Is dyspnea part of an acute anxiety episode, severe pain, constipation or urinary retention? Is there a new pneumothorax or worsening pleural effusion? Understanding 1) where patients are at in the dying trajectory, and 2) their identified goals of care, is essential to guide the extent of workup to discover reversible causes. If the patient is clearly dying (see *Fast Fact* #3), and the goals of care are comfort, then pulse oximetry, arterial blood gases, EKG, or imaging are not indicated.

Treatment

- **General measures** Positioning (sitting up), increasing air movement via a fan or open window, and use of bedside relaxation techniques are all helpful. In the imminently dying patient, discontinuing parenteral fluids is appropriate.

- **Treatment with opioids** Opioids are the drugs of choice for dyspnea at the end-of-life as well as dyspnea refractory to the treatment of the underlying cause. In the opioid naïve patient, low doses of oral (5-10 mg) or parenteral morphine (2-4 mg) will provide relief for most patients; higher doses will be needed for patients on chronic opioids. When dyspnea is acute and severe, parenteral is the route of choice: 1-3 mg IV every 1-2 hours, or more aggressively if needed, until relief in the opioid naïve patient. In the inpatient setting, a continuous opioid infusion, with a PCA dose that patients, nurses or families can administer, will provide the timeliest relief (see *Fast Facts* #28, 54). Nebulized morphine has been reported to provide benefit in uncontrolled case reports, however a controlled trial demonstrated no greater efficacy or lower rate of side effects compared to subcutaneous morphine.

- **Treatment with oxygen** Oxygen is often, but not universally, helpful. When in doubt, a therapeutic trial, based on symptom relief, not pulse oximetry, is indicated in dying patients. A well-designed randomized, controlled trial of oxygen vs. ambient air, delivered by nasal cannula, in normoxic patients with advanced illness and dyspnea showed no benefit of oxygen over ambient air delivered by nasal cannula. Patients generally prefer nasal cannula administration than a mask, especially in setting of imminent death when agitation from the mask is commonly seen. There is little reason to go beyond 4-6 L/min of oxygen via nasal cannula in the actively dying patient. Request a face-tent for patients who are claustrophobic from a mask.

- **Treatment with other drugs** Anti-tussives can help with cough (see *Fast Fact* #200), anti-cholinergics (e.g. scopolamine) will help reduce secretions, anxiolytics (e.g. lorazepam) can reduce the anxiety component of dyspnea. Other agents that may have specific disease modifying effects include diuretics, bronchodilators, and corticosteroids.

Family/Team Discussions While there is no evidence that proper symptom management for terminal dyspnea hastens death, the course and management of terminal dyspnea, especially when opioids are used, should be fully discussed with family members, nurses and others participating in care to avoid confusion about symptom relief vs. fears of euthanasia or assisted suicide (see *Fast Fact* #8).

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FAST FACTS AND CONCEPTS #309
PHARMACOLOGIC MANAGEMENT OF DEPRESSION IN ADVANCED ILLNESS
Leah Rosenberg, MD; Jane deLima Thomas, MD

Adults with serious illness have a higher incidence of major depressive disorders than healthy adults, with an estimated incidence of 15% (1). In this *Fast Fact*, we will provide a clinical framework for selecting pharmacologic agents for seriously ill patients with depression. See *Fast Facts* # 7, 43 and 146 for assistance in diagnosing and screening for depression in palliative care patients.

Determine the patient's prognosis Because most traditional antidepressants take more than 4 weeks to become effective, they should only be considered in patients expected to live at least that long (2). Use is also limited to patients who are able to swallow oral medications or place them in a feeding tube. For patients with a prognosis < 4 weeks, a psychostimulant such as methylphenidate or dextroamphetamine may act within 1-2 days and be safe in patients without significant cardiovascular disease or delirium. Although the data on psychostimulants are somewhat mixed, controlled trials have shown benefit as both a monotherapy or to augment the effects of another anti-depressant (3-5). See *Fast Fact* #61.

Consider co-morbid symptoms When choosing an antidepressant, consider the patient's other co-morbid symptoms such as insomnia, neuropathic pain, or poor appetite (6). Other considerations include the patient's past responses to specific agents and possible drug interactions. Common classes of antidepressants include serotonin-selective reuptake inhibitors (SSRIs), serotonin-selective norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), and others.

SSRIs Also called "second generation antidepressants", these are the most commonly prescribed antidepressants. SSRIs should be started at a low dose and then titrated to the minimum effective dose to minimize adverse effects such as QTc prolongation, sexual dysfunction, headaches, nausea and diarrhea. Fluoxetine is associated with emotional activation and may worsen anxiety. Paroxetine can be sedating and lead to withdrawal phenomena with missed doses. Because sertraline, citalopram, and escitalopram have lower side effect profiles and are neither activating nor sedating, they may be better choices for palliative care patients (7). The starting dose of sertraline is 25-50 mg/day with a usual effective dose of 50-200 mg/day; it is available in a concentrated liquid formulation for patients with dysphagia related issues. Both citalopram and escitalopram have been shown to have few drug interactions. The starting dose of citalopram is 20 mg/day with a maximum daily dose of 40 mg. The starting dose of escitalopram is 10 mg/day with a usual effective dose of 10-20 mg/day (8-10).

SNRIs inhibit serotonin and norepinephrine reuptake, two neurotransmitters important in endogenous pain pathways (11). This class may be helpful for neuropathic pain, vasomotor instability, and anxiety-predominant depression. In particular, venlafaxine has shown effectiveness for the amelioration of hot flushes and the prevention of chemotherapy-induced polyneuropathy (CIPN); duloxetine has shown efficacy for the treatment of CIPN (12). SNRIs may prolong bleeding times and therefore may not be safe in patients with active bleeding or intracranial metastases. The starting dose for venlafaxine is 37.5 mg with a usual effective dose of 75-225 mg/day. It requires close monitoring for missed-dose withdrawal and hypertension. The starting dose for duloxetine is 30 mg with a usual effective dose of 60-120 mg/day. It has been associated with hepatic insufficiency and a worsening of acute-angle glaucoma.

TCAs are an older class of anti-depressants that can be cost-effective when used at lower doses. They also are proven adjuvant analgesics for neuropathic and chronic low back pain. Unfortunately, their anticholinergic properties can induce delirium, prolong the QTc interval, and be dangerous in overdose. Therefore, their use is limited to heart-healthy patients under the age of 65 with comorbid neuropathic pain and insomnia. Although the preponderance of supporting data for the analgesic effects is for amitriptyline (usual starting dose 10-25 mg/day; usual effective dose is 150 mg/day), nortriptyline is felt to be less sedating (usual starting dose 25 mg/day; usual effective dose is 50-100 mg/day).

Other Medications **Mirtazapine** has histaminergic side effects that can be helpful especially for cancer patients who often experience insomnia, poor appetite, and nausea (13). It has few drug interactions but can be associated with orthostatic hypotension. Its usual starting dose is 7.5-15 mg/nightly; usual

effective doses are 15-30 mg/day. **Buproprion** is thought to be less sedating and have a lower incidence of sexual side effects, but it may lower the seizure threshold. The usual starting dose for buproprion is 150 mg/day; the usual effective dose is 150-300 mg/day (14). Single-dose treatment with NMDA antagonist **ketamine** has shown promise in early investigational studies (15). **Aripiprazole** may augment the antidepressant effects of SSRIs and SNRIs as early as a week after initiation (16).

Summary Recommendations:

- For patients with prognoses of weeks, consider the use of a psychostimulant like methylphenidate.
- Consider duloxetine or venlafaxine when neuropathic pain is present.
- When polypharmacy is present, consider citalopram, escitalopram or mirtazapine.
- If the patient has insomnia, nausea, or anorexia, consider the use of mirtazapine.
- Closely monitor patients initiated on an antidepressant for adverse effects and dose titration.
- Refer to a mental health clinician for pre-existing major depression, the presence of comorbid psychiatric illness, suicidal ideation, refractory symptoms, or psychiatric polypharmacy.
- Refer to social work and/or spiritual support services if the depression appears to be escalating in relation to social or spiritual factors.

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FAST FACTS AND CONCEPTS #23
DISCUSSING DNR ORDERS – PART 1
Charles F von Gunten MD, PhD and David E Weissman MD

Background 'Code status' discussions with seriously ill patients should always take place in the context of the larger goals of care, using a step-wise approach. This *Fast Fact* introduces an approach to having these discussions; *Fast Fact* #24 discusses disagreements about 'code status.' Prior to any discussion of a do-not-resuscitate (DNR) order, physicians must know the data defining outcomes and morbidity of cardiopulmonary resuscitation in different patient populations (see *Fast Fact* #179) and care settings (see *Fast Fact* #292 regarding DNR orders in the Operating Room).

1. Establish the setting. Ensure comfort and privacy; sit down next to the patient. Ask if family members or others should be present. Introduce the subject with a phrase such as: I'd like to talk with you about possible health care decisions in the future.

2. What does the patient understand? An informed decision about DNR status is only possible if the patient has a clear understanding of their illness and prognosis. Ask an open-ended question to elicit patient understanding about their current health situation. It is important to get the patient talking – if the doctor is doing all the talking, it is unlikely that the rest of the conversation will go well. Consider starting with phrases such as: *What do you understand about your current health situation? What have the doctors told you about your condition?* If the patient does not know/appreciate their current status this is time to review that information.

3. What does the patient expect? Ask the patient to consider the future. Examples of ways to start this discussion are*: What do you expect in the future? or What goals do you have for the time you have left—what is important to you?* This step allows you to listen while the patient describes a real or imagined future. Many patients with advanced disease use this opening to voice their thoughts about dying—typically mentioning comfort, family, and home, as their goals of care. If there is a sharp discontinuity between what you expect and what the patient expects, this is the time to clarify.

Listen carefully to the patient's responses; most patients have thought a lot about dying, and only need permission to talk about what they have been thinking. Setting up the conversation in this way permits the physician to respond with clarifying and confirming comments such as:

So what you're saying is – you want to be as comfortable as possible when the time comes? Or – What you've said is – you want us to do everything we can to fight, but when the time comes, you want to die peacefully? Whenever possible, ask patients to explain the values that underlie their decisions: Can you explain why you feel that way?

4. Discuss a DNR order. Use language that the patient will understand; give information in small pieces. Don't introduce CPR in mechanistic terms (e.g. "starting the heart" or "putting on a breathing machine"). Never say: *Do you want us to do everything?* "Everything" is euphemistic and easily misinterpreted. Using the word "die" helps to clarify that CPR is a treatment that tries to reverse death. To most lay-people, when the heart and/or lungs stop, the patient dies.

If the patient and doctor mutually recognize that death is approaching and the goals of care are comfort, then CPR is not an appropriate medical intervention and a clear recommendation against CPR should be made. You can say: *We have agreed that the goals of care are to keep you comfortable and get you home. With this in mind, I do not recommend the use of artificial or heroic means to keep you alive. If you agree with this, I will write an order in the chart that if you die, no attempt to resuscitate you will be made.*

If the clinical situation is more ambiguous in terms of prognosis and goals of care, and you have no clear recommendation, the issue of DNR can be raised by asking: *If you should die in spite of all of our efforts, do you want us to use heroic measures to attempt to bring you back?* Or, *How do you want things to be when you die*? If you are asked to explain "heroic measures", then describe the purpose, risks and

benefits of CPR in greater detail. The clinical pearl here is to start general and become specific later in the conversation.

5. Respond to emotions. *Strong emotions are common when discussing death. Typically the emotional response is brief. The most profound initial response a physician can make may be silence, providing a reassuring touch, and offering facial tissues (see* Fast Fact #29*).*

6. Establish a plan. *Clarify the orders and plans that will accomplish the overall goals you have discussed, not just the DNR order. A DNR order does not address any aspect of care other than preventing the use of CPR. It is unwise and poor practice to use DNR status as a proxy for other life-sustaining therapies. Consider using words:* We will continue maximal medical therapy to meet your goals. However, if you die, we won't use CPR to bring you back. *Or,* It sounds like we should move to a plan that maximizes your comfort. Therefore, in addition to a DNR order, I'd like to talk further with you how we can best do that.

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FAST FACTS AND CONCEPTS #24
DISCUSSING DNR ORDERS – PART 2
Charles F von Gunten MD, PhD and David E Weissman MD

Introduction The basic steps in the DNR discussion for seriously ill hospitalized patients were described In *Fast Fact* # 23. If you have followed those steps, what do you do if the patient or family/surrogate continues to want CPR and you think it is not in the patient's best interest? The seemingly unreasonable request for CPR typically stems from one of several themes:

1. Inaccurate information about CPR. The general public has an inflated perception of CPR success. While most people believe that CPR works 60-85% of the time, in fact the actual survival to hospital discharge is more like 10-15% for all patients, and less than 5% for the elderly and those with serious illnesses. This is a time to review/clarify the indications, contraindications, potential outcomes and morbidity of CPR. Start the discussion by asking, "*What do you know about CPR?"*

2. Hopes, fears, and guilt. Be aware that guilt (*I haven't lived nearby to care for my dying mother*) and fear (*I am afraid to make a decision that could lead to my wife's death*) are common motivating emotions for a persistent CPR request. Some patients or families need to be given an explicit recommendation, or permission from the physician, to stop all efforts to prolong life, to be told that that death is coming and that they no longer have to continue "fighting". Whenever possible, try to identify the underlying emotions and offer empathic comments that open the door to further conversation. *This decision seems very hard for you. I want to give you the best medical care possible; I know you still want CPR, can you tell me more about your decision?*

Agreeing to a DNR order for many patients feels equivalent to them "choosing" to die. Acceptance of impending death occurs over a vastly different time course for different patients/families; for some, it never occurs. Some patients see CPR as a "last chance" for continued life. Probe with open-ended questions: *What do you expect to happen? What do you think would be done differently, after the resuscitation, that wasn't being done before?* Many patients describe hope for a new treatment. Use the opportunity to respond by describing that you are doing everything in your power to prolong their life before a cardiopulmonary arrest – you wouldn't be "saving something" to do after they had died. If patients are not ready for a DNR order, don't let it distract you from other important end-of-life care needs; emphasize the goals that you are trying to achieve; save a repeat discussion for a future time; good care, relationship building and time will help resolve most conflicts.

3. Distrust of the medical care system. Patients or families may give you a clue that there is a fundamental distrust of doctors or the medical system; this should be addressed openly. *What you said makes me wonder if you may not have full trust in the doctors and nurses to do what is best for you? Can you tell me about your concerns?*

4. Managing persistent requests for CPR. Decide if you believe that CPR represents a futile medical treatment—that is, CPR cannot be expected to either restore cardiopulmonary function or to achieve the expressed goals of the patient (see *Fast Fact* #136). Physicians are not legally or ethically obligated to participate in a futile medical treatment, and some facilities have a policy that a physician may enter a DNR order in the chart against patient wishes. Aside from writing a DNR order without patient or family agreement, other options at this time include:

- Transfer care to another physician chosen by the patient/family.
- Plan to perform CPR at the time of death – *but don't end the discussion*. Engage the patient about her or his wishes if she or he survive the resuscitation attempt. Tell the patient that you need guidance because it is very likely that if she or he survives CPR, they will be on life support in the ICU, and they may not be able to make decisions for themselves; ask them (or the family) to help you determine guidelines for deciding whether to continue life-support measures. If not already done, clarify if there is a legal surrogate decision-maker.

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FAST FACTS AND CONCEPTS #42
BROACHING THE TOPIC OF A PALLIATIVE CARE CONSULTATION WITH PATIENTS AND FAMILIES

Robert Arnold MD and David E Weissman MD

Introduction Palliative care consultative services are becoming commonplace in academic and community hospitals and clinics. Patients and families may have negative perceptions of palliative care and hospice – viewing such a discussion as signaling that the physician is "giving up on the patient" and that the reality of impending death must be faced. For the attending physician, the decision to convey to a patient and family that a consultation is needed can provoke anxiety. Physicians may fear such a discussion will provoke anxiety, anger or a sense of hopelessness. This *Fast Fact* provides tips for beginning a discussion leading to a visit by a palliative care consultation team.

First, decide why you want assistance from the palliative care team. Typically, physicians seek assistance in four domains: 1) pain and non-pain symptom assessment and management; 2) assistance in making difficult decisions, usually about continued use or withdrawal of potentially life-prolonging treatments such as feeding tubes, antibiotics, dialysis, or ventilators; 3) assistance in planning for the most appropriate care setting to meet patient/family goals for end-of-life care; and 4) providing psychological support to patients, families and the health care team.

Second, contact the palliative care team. Discuss your reason(s) for consultation along with pertinent details of the patient's history and family support structure. Describe both what your goals are for the consultation, as well as what the family's/patient's goals may be. This is a good time to discuss any concerns you have about using the term *palliative care* with the patient or family.

Third, engage the patient/family in a discussion of the current medical condition and goals of care. Introduce the topic of a consultation by saying: *To best meet some of the goals we've been discussing (*fill in with the goals mentioned by the family/patient*) I'd like to have some consultants from the Palliative Care Team visit with you.* You can follow this by saying, *They are experts in treating the symptoms you are experiencing* (fill in symptom*). They are also good at helping your family deal with all the changes brought on by your illness; they can answer your questions about* (fill in previously discussed patient questions*).*

You should not say that the reason you are asking Palliative care to be involved is "that there is nothing more to do" or because "I have nothing more to offer." Talk about the positive goals Palliative Care can help you and the patient achieve.

Finally, emphasize your continued involvement*: You and I will talk about the recommendations of the palliative care experts. I'll make sure all your questions are answered.* This can help relieve fears of abandonment. If a patient or family reacts negatively to the suggestion for a consultation, explore their concerns. Someone may have mentioned palliative care and this may have negative connotations to them. Ask, *What experience do you have with hospice/palliative care? What are your concerns?* It may be important to discuss that palliative care is compatible with aggressively treating the underlying disease. Emphasize the positive aspects of what palliative care can do, rather than focusing on how the palliative care team will help them accept death and dying. After all, the goal of palliative care is to achieve the best possible quality of life through relief of suffering, control of symptoms and restoration of functional capacity, while remaining sensitive to the patient and family's values. Palliative Care guides the patient and family as they face disease progression and changing goals of care, and helps those who wish to address issues of life completion and life closure.

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FAST FACTS AND CONCEPTS #55
DECISION MAKING CAPACITY
ROBERT ARNOLD MD

Background Informed consent is based on the principle that patients should be allowed to make decisions for themselves. Decision making capacity thus serves as a gatekeeper concept. Patients who have it can make decisions for themselves; conversely, a surrogate is needed for patients who lack decision-making capacity. *Competency* is a legal term referring to a decision made by judge, although a physician's opinion carries considerable weight in a competency hearing. In contrast, *decision making capacity* ('decisionality') refers to a physician's determination, based on clinical examination, that a patient is able to make medical decisions for him- or herself. Most state Power of Attorney for Health Care documents require a physician (or similarly qualified individual such as a psychologist) to document that a patient has lost decision making capacity for the surrogate to become the legal agent for medical decisions.

Assessing decision making capacity

- To be deemed 'decisional,' a physician must be satisfied that a patient is able to do three tasks:
  - Receive information (e.g. must be awake, but not necessarily oriented x 4),
  - Evaluate, deliberate, and mentally manipulate information, and
  - Communicate a treatment preference (e.g. the comatose patient by definition is not decisional).
- Physicians should look for:
  - **Understanding.** Does the patient adequately understand the information about the risks, benefits, and alternatives of what is being proposed? The patient does not have to agree with your interpretation, but should be able to repeat what you have said. Ask, *Can you repeat to me the options for treating X I have just discussed with you? Can you explain to me why you feel that way? What is your understanding of what will happen if we don't do Y?*
  - **Logic.** Is the logic the patient uses to arrive at the decision "not-irrational"? One wants, as much as possible to make sure the patient's values are speaking, rather than an underlying mental or physical illness. Note: Severe depression or hopelessness will make it difficult to interpret decisionality; consult psychiatry for assistance with this or other complex cases.
  - **Consistency.** Is the patient able to make a decision with some consistency? This means not changing one's mind every time one is asked. Is the decision consistent with the patient's values? If there is a change in the patient values, can the patient explain the change?

Decision making capacity is contingent

- **Task specific.** Deciding if the patient is decisional means weighing the degree to which the patient has decision making capacity against the objective risks and benefits to the patient. Some decisions are more complex than others, requiring a higher level of decision-making capacity. Thus a moderately demented patient may be able to make some decisions (e.g. antibiotics for pneumonia) but not others (e.g. chemotherapy for metastatic lung cancer). This sliding scale view of decisionality holds that it is proper to require a higher level of certainty when the decision poses great harm.
- **Time specific.** When encephalopathic a patient may not be decisional; after treatment decisionality may be regained.

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FAST FACTS AND CONCEPTS #59
DEALING WITH THE ANGRY DYING PATIENT
Rebekah Wang-Cheng MD, FACP

Background Anger is a common emotion expressed by seriously ill patients and their families. A typical reaction by the health professional, confronted by the angry patient or family, is to either *get angry back* or to physically and psychologically withdraw; neither are particularly helpful coping strategies. A guide to managing these situations is presented below.

Look for the underlying source of anger. Fear is probably the most common source of anger, especially in the dying and their families – fear of the unknown, being in pain or suffering, the future well-being of family members, abandonment, leaving unfinished business, losing control of bodily functions or cognition, being a burden to the family, and dying alone.
Other sources of anger include: 1) a genuine insult – so called "rational anger" (e.g. waiting six hours to see the doctor); 2) organic pathology: frontal lobe mass, dementia or delirium; and 3) personality style/disorder – the person whose approach to much of life is via anger or mistrust.

Recognize the direction of anger. Recognizing the difference between internal and external anger is critical to effective management, because internal anger may lead to potentially harmful patient consequences. When the patient directs anger internally because of fear and guilt (e.g. *I didn't take care of myself; I'm abandoning my family.*), this can lead to withdrawal, self-neglect, anxiety, depression, or a combination of these. Others direct their anger outward at physicians, hospitals, family members or a deity. Particularly in the case of an angry parent of a dying child, he or she may feel helpless and guilty about many things – not bringing the child for medical care soon enough, not being a loving enough or "great" parent (1). This internal guilt and blame can then be displaced towards health care professionals.

Engage rather than withdraw from the patient. The natural tendency for clinicians is to cut short the office or hospital visit, find ways to avoid contact with the angry patient or family member, or to try to mask his/her own anger in order to continue to interact with the patient. Robert Houston MD has written a very helpful article listing 10 rules for engaging the dying patient which will have a beneficial impact on the physician/patient relationship and the quality of the patient's end-of-life experience (2). One of his most important tips is to refrain from personalizing the anger when the patient accuses you of "missing the diagnosis" or under treating the pain. Some of his rules which are pertinent to this discussion are:

- Engage the patient, but do not enmesh with and do the emotional work for the patient.
- Maintain adult-adult communication rather than fostering the patient's dependency.
- Do not personalize the patient's anger.
- Adopt a patient-centered worldview by ascertaining his/her values, priorities, hopes.
- Normalize anger so that the patient can move through this stage.

Use the "BATHE" approach to create an empathic milieu (3). As with any difficult patient situation, communication techniques are especially important so that both the patient and physician do not become further embittered and frustrated.

- Background: Use active listening to understand the story, the context, the patient's situation.
- Affect: Name the emotion; for instance, *You seem very angry….* It is crucial to validate feelings so the angry person feels that you are listening. Attempting to defuse it, counter it with your own anger or ignore it, will be counter-productive. Acknowledging their right to be angry will help start the healing process and solidify the therapeutic relationship.
- Troubles: Explore what scares or troubles them the most about their present and future. Just asking the question *Tell me what frightens you?* will help them to focus on circumstances they may not have considered.
- Handling: Knowledge and positive action can help mitigate fears and reduce anger. How are they handling the dying – are they making concrete plans about their finances, their things, their family? Have they thought about formal counseling to help deal with the depression, the anger?

- Empathy: By displaying empathy and concern you can help the person feel understood, less abandoned and alone. Avoid trite statements such as *I know what you're going through.* Paraphrasing the patient's comments is an effective way to convey that you heard and are seeking to understand: *You feel like it's so unfair that the cancer appeared out of nowhere after all these years.*

Summary The journey from life to death almost always is accompanied by some degree of anger. A caring, patient clinician can assist the patient and the family in recognizing, mobilizing, and modifying the anger into positive emotional energy. Established communication approaches are available such as BATHE which have shown improvements in self-efficacy for communicating with angry patients.

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FAST FACTS AND CONCEPTS #136
MEDICAL FUTILITY
Joy E Cuezze MD and Christian T Sinclair MD

Medical futility is commonly used by health professionals in reference to the appropriateness of a medical treatment option. Increasingly hospitals and nursing homes are developing their own futility policies and Texas has developed a statewide futility policy. This *Fast Fact* will explore bioethical issues with the term futility and as well as recommendations from the American Medical Association (AMA) on how to approach medical futility concerns.

The Problem with 'Futility' The public, policymakers, ethicists, and the medical profession have been unable to agree on a clear, concise definition of futility that can be applied to all medical situations. One commonly used definition is that a futile intervention is one that a) is unlikely to be of any benefit to a particular patient in a particular medical situation, and b) will not achieve the patient's intended goals. The sticking point in all futility definitions is the concept of *benefit*, as the perception of benefit is highly subjective. Physicians, patients and families often have very different views on what is potentially beneficial. For example, a physician may believe that renal dialysis in an elderly demented patient is futile, while the family that views preservation of life at all costs as part of their cultural ethos, may view dialysis as a beneficial intervention. Furthermore, medical futility can be easily misunderstood as health care rationing. While economic issues may impact shared decision making, the ultimate question is not *How much does this therapy cost?* Rather, it is *Do the advantages of this therapy outweigh the disadvantages in a given patient?*

Types of 'Futility' *Quantitative futility* refers to the intervention that has a very small chance of benefiting the patient; the most commonly used number is less than 1% chance of success. Q*ualitative futility* describes a situation in which the quality of benefit an intervention will produce is exceedingly poor. However, neither approach is adequate as there is no consensus on either numeric thresholds for quantitative futility nor shared understanding of what constitutes qualitative benefits.

Medical Futility Policies Despite these challenges with the concept of medical futility, many large organizations recommend that health care institutions adopt a clear policy that outlines a due process for approaching futility disputes which provides both patient protections and clinician options in cases where continuing life-prolonging treatments serves no appreciable medical benefit. Suggestions from an AMA Council on Ethical and Judicial Affairs on the content of such a medical futility policy include:

- Earnest attempts should be made in advance to negotiate between patient, proxy, and physician on what constitutes futile care for the patient.
- Joint decision making between patient or proxy and physician should occur to the maximum extent.
- Assistance of consultants such as ethics committees should be pursued to negotiate disagreements.
- If a dispute remains unresolved and the institutional review supports the patient's position and the physician is unpersuaded, transfer of care to another physician within the institution may be arranged.
- If the institutional review supports the physician's position and the patient remains unpersuaded, transfer to another institution should be sought.
- If no transfer of care can be arranged, halting futile treatment is ethically acceptable.

Institutional Medical Futility Policies Although recommended by the AMA (see above), most hospitals do not have a medical futility policy outlining a process of resolution. Since physicians are not legally, professionally or ethically required to offer medically futile treatments, a defined policy can serve as a method to outline a clear process that honors both patient rights and clinician professionalism.

Other Suggestions
- Check with your health care institution regarding the presence of an existing futility policy.
- Ethics committees and medical organizations (local/state/national) can provide resources to understand medical futility and professional responsibilities in one's practice area.
- Avoid using the term 'futility' in discussion with patients/families. Rather, speak in terms of 'benefits'/'burdens' of treatment and patient or family-specific goals of care.

- Involve a palliative care and/or ethics consultant in any situation where 'futility' will be invoked as a process step in formulating decisions.
- See *Fast Facts* #183 and #184 for more information on conflict resolution strategies.

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FAST FACTS AND CONCEPTS #183
CONFLICT RESOLUTION I: CAREFUL COMMUNICATION
Adam Kendall MD, MPH and Robert Arnold MD

Background Conflicts about medical care occur frequently at the end of life. These conflicts threaten therapeutic relationships and lead to patient, healthcare provider, and family dissatisfaction. Conflict between the patient/family and physician may arise from simple factual misunderstandings about medical care. Frequently, however, conflict is driven by a patient's or family's emotions such as feeling unheard or ignored, as well as having goals that conflict those of the medical team. In these instances, attempting to convince a patient or family through providing additional medical information will not work. This *Fast Fact* provides an alternative approach to conflict resolution based on understanding a patient's or family's story, attending to their emotions, and establishing shared goals. A subsequent *Fast Fact* (#184) will focus on conflict resolution employing the techniques of *Principled Negotiation*.

1. Learn the patient's and family's story

- Begin discussions with a genuine curiosity to learn what they perceive to be the course of events during the illness.
- Explore the context of the patient's illness narrative with attention paid to their relationships with doctors, their sources of medical information, and their life goals (see *Fast Fact* #26)
- Avoid presenting agenda items for a meeting that are defined by the medical team's priorities. Instead, focus on the patient's and family's concerns.
- If a patient or family is asking for treatment against the recommendation of the medical team, focus on the context of the request. Have they been let down by the medical system in the past? Have they found that others in their family have benefited from the treatment they request?
- Find out how they want information presented to them. Do they want specific benefits and risks? Do they want written information?

2. Attend to emotions

- Conflict can cause strong emotions in healthcare providers including guilt, anger, and resentment. Acknowledge these emotions to yourself and other professionals, but strive to prevent them from interfering with your interactions with the patient and family.
- Patient and family emotions such as grief, disappointment, and anger are to be expected in these situations. Compassionately acknowledge and address these emotions as they arise, and allow the patient and family to express what is making a situation frustrating for them (see *Fast Facts* #29, #59). When people are emotionally stressed, they may have trouble cognitively processing information. Empathically attending to emotions often allows a patient or family to move on to understanding medical information.
- If a family is focusing on what they believe was an error in care, be transparent about where a mistake may have been made (see *Fast Facts* #194, 195). Apologize. Even if it was not an error, one can acknowledge how frustrating the situation is. Saying "I can tell that this situation is frustrating for you," is not an admission of error—it is empathic.

3. Establish shared goals for treatment

- Use the patient's core values as a foundation for developing a treatment plan. "I would like to know more about your mother and what her values have been during her life."
- Ask about a patient's goals including what they would want if they were dying or if there were no curative treatments available for their condition.
- When there are requests for ineffectual treatment, describe instead where the medical team can make a difference for the patient, in relation to their goals. "Please correct me if I'm wrong, but it sounds like your mother really values her independence and freedom from being in pain. Let's try to figure out how we can best help her achieve these goals."

Summary Providing medical information to patients and families may seem at first to be the most natural approach to resolving conflict. Addressing the underlying roots of conflict will have a longer

lasting effect. The above approach emphasizes resolving conflict through finding mutual trust and shared goals between physicians, patients, and families.

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FAST FACTS AND CONCEPTS #184
CONFLICT RESOLUTION II: PRINCIPLED NEGOTIATION
Adam Kendall MD, MPH and Robert Arnold MD

Background When conflicts about medical care persist despite gaining mutual trust and a deep understanding of goals (see *Fast Fact* #183), it may be effective to use principled negotiation. *Principled negotiation* is an approach to resolving conflict that avoids power struggles and unwanted compromises. The following is an illustration of the steps that are involved. Within each step, we will refer to a case example: a family who is requesting artificial feeding against medical advice for their father who is dying from end-stage dementia.

1. Separate people from the problem. Identify the fundamental problem, separating that from individuals'—on both sides—intentions and culpability.

- The problem is not that the family members are "in denial" that their loved one is dying or "uneducated" when they do not hear the medical team's recommendations.
- The problem is not that the family is acting out their frustration by making unreasonable demands.
- Nor is the problem that the medical team and hospital are trying to withhold treatment from the patient or "giving up" on him.
- The problem *is* that the patient is dying, no longer able to eat properly, and that artificial nutrition does not improve quality or quantity of life in this situation.

2. Focus on interests. Listen to requests and demands but try to look into underlying interests. In addition, express the intentions and goals of the medical team.

- The family wants what is best for the patient. Their intent may be to provide comfort and to build up the patient's strength, and to prevent a painful starvation.
- The medical team wants to provide the best medical care for the patient. Their intent may be to avoid an intervention that has no clear benefit for the patient, may cause harm, and may not have been desired by the patient.

3. Invent solutions. Avoid contrasting different philosophies of medical care. Instead, propose a plan of care that meets a family's expectations without detracting from good medical care. Consideration could be given to:

- Meeting the family's goals of providing food by allowing for the patient to taste home cooked meals.
- A short trial of tube-feeding with the plan to continue only if the overall quality of life for the patient improves.
- A trial of attentive oral feeding with a plan to reconsider tube feeding if the patient appears to be hungry or otherwise suffering.
- Solutions that do not promote mutual interests are: placing a feeding tube without a plan to measure its success or failure at meeting a goal, arranging for another medical team to take over the patient's care, or referring the case to an ethics committee.

4. Outline objective criteria. If a time trial is being pursued, agree upon what the deciding factors would be in determining a trial's success. Provide objective information to substantiate medical recommendations.

- Establish signs of improvement or worsening such as functional ability, weight, ability to interact, and level of consciousness.
- Establish criteria for harm such as infections, restraint or sedative use, hospitalizations or emergency department visits.
- Consider providing publications from organizations that advocate for patients and families, and are not associated with physicians or hospitals.
- Provide opinions or guidance from individuals outside of the conflict. These could include social workers, case managers, chaplains, or therapists.

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FAST FACTS AND CONCEPTS #219
RESPONDING TO REQUESTS FOR NON-DISCLOSURE OF MEDICAL INFORMATION
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Background What do you do when a family member asks you not to tell your patient important medical information such as a diagnosis or prognosis? Requests for non-disclosure can represent a loving family's efforts to protect a patient from emotional harm, an inaccurate assessment by the family about a patient's preferences or emotional resilience, or an accurate reflection of how the patient would prefer to make decisions. This *Fast Fact* will introduce readers to a practical approach to these clinical dilemmas.

The Problem Contemporary medical ethics and professional standards dictate that patients have the right to choose the medical care that best allows them to meet their life goals. To make such choices requires they be fully informed of their condition, prognosis, and reasonable treatment options (see *Fast Facts* #164, 165). One needs to differentiate the right to such information from the duty to hear the information, however. Patients have different preferences for medical decision-making, ranging from individualistic, to paternalistic (doing whatever the physician recommends), to communal (sharing, or deferring, important medical decisions to family members or religious/community leaders). Truly respecting patient autonomy requires clinicians to identify and respect patient wishes to share or defer decision-making, including a patient's preference to not be informed of key medical information.

Prevention Negotiate with the patient *before* the results of testing arrive as to how much information they would like and who they would like to have present for information sharing*. Are you the kind of person who wants to know the results of the test or would you rather I talk to your children?*

Managing Requests for Non-Disclosure (adapted from Hallenbeck and Arnold, 2007):

- *Stay Calm*. These situations can be confusing and emotional for clinicians. The calmer you remain the more information you will gain from the family as to why they do not want their loved one to be informed of the bad news. Demonstrating frustration or implying that the request is inappropriate can break trust and derail your efforts to resolve the situation.
- *Try to understand the family's viewpoint*. They know the patient best and can provide insight into the cause of the request. Politely ask questions to understand the nature of the request. *Can you tell me more about why you feel this way? How does your family typically handle difficult information? How are important decisions made by your family?* Ask about how the patient has responded in the past to bad news and if they have made specific statements to others about what they want to know. Is the family more worried more about *how* the information is given rather than the information itself (e.g. given to the patient when alone, use of 'death' or 'dying,' the disclosure of specific prognostic time-frames)?
- *Clarify what the patient already knows.* Politely ask questions to understand what the family believes the patient already knows. Does the family think the patient already knows or strongly suspects what is going on and would rather not talk further about it, or is the patient completely in the dark? Have other clinicians already told or implied to the patient what is going on? How did the patient respond to that? Is the patient talking with the family about their concerns? A patient's reluctance to talk with family members may represent an attempt to protect them.
- *Respond empathically.* A family's request to not tell their loved ones usually comes from a kind and loving place; they are often frightened for themselves and the patient. Responding empathically (see *Fast Fact* #29) allows them to recognize that you care about them. It may allow them to see your ability to give information to their loved one in a compassionate way.
- *State your views openly, but as your own views.* Disclose any discomfort you have with the family's request; explain your professional obligation to ensure the patient is able to make informed decisions in the manner they prefer. Disclose this specifically in the context of you wanting what is best for the patient, including respecting how she or he would like to hear information.
- *Be willing to brainstorm possible solutions.* Rigidly informing the family that you must tell the patient breaks trust and is inaccurate. There is no 'one-size-fits-all' solution to these scenarios. Often, there are solutions neither of you have thought about that will meet everyone's goals. In other cases, the

family may not have thought about the implications of the request (e.g. giving Mom chemotherapy but not telling her she has cancer).

- *Negotiate a solution.* Recommend to the family that you, in their presence, share with the patient a limited amount of information, and then specifically ask the patient if they would like to hear more. Tell the family what you plan on saying, i.e. – *You came to the hospital because you were not eating well and became dehydrated. We have been trying to figure out what is going on. Some people want to know everything about their medical condition, others prefer the doctors talk with family members about what is happening and the best way to help a patient. What would you prefer?* Contract with the family that they, and you, will respect the patient's decision.

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FAST FACTS AND CONCEPTS #222
PREPARING FOR THE FAMILY MEETING
David E Weissman MD, Timothy E Quill MD, and Robert M Arnold MD

Background A cornerstone procedure in Palliative Medicine is leadership of family meetings to establish goals of care, typically completed at a time of patient change in status, where the value of current treatments needs to be re-evaluated. As with any procedure, preparation is essential to ensure the best outcome. This *Fast Fact* reviews how to prepare for a Family Meeting. See also *Fast Fact* #16 for a concise overview of family meetings, as well as *Fast Facts* 223-227 for discussion of additional aspects of family conferences.

Data Review

- Review the medical history relevant to the current medical situation (e.g. history of disease progression, symptom burden, past treatments, treatment-related toxicity, and prognosis).
- Review all current treatments (e.g. renal dialysis, artificial nutrition, antibiotics) and any positive and/or negative treatment effects.
- Review all treatment options being proposed.
- Determine the prognosis with and without continued disease-directed treatments. Prognostic information includes data concerning future patient function (physical/cognitive), symptom burden, and time (longevity).
- Solicit and coordinate medical opinions about the utility of current treatments among consultants and the primary physician. If possible, families need to hear a single medical consensus—all relevant clinicians should be contacted and consensus reached prior to the meeting. If the consultants do not agree, then prior to the family meeting they should meet to negotiate these differences and attempt to reach consensus regarding the plan. If there is no consensus, a plan should be developed for how to describe these differences to families.
- If the patient lacks capacity, review any Advance Directive(s), with special attention to discover if the patient has named a surrogate decision maker, and if the patient has indicated any specific wishes (e.g. DNR status, 'no feeding tubes').
- Seek out patient/family psychosocial data. Focus on psychological issues and family dynamics (e.g. anger, guilt, fear) potentially impacting decision making. These issues may be long-standing, or due to the current illness. **Note:** talking to the patient's social worker, bedside nurses, and primary and consulting physicians can help you get a better sense of the family and how they make decisions.
    - Review what transpired in prior family meetings.
    - Learn about particular cultural/religious values and/or or social/financial issues that may impact decision making.

Information Synthesis Based on your review of the medical and prognostic data, make an independent determination of which current and potential tests/treatments will improve, worsen, or have no impact on the patient's function/quality of life (physical/cognitive) and time (longevity).

Meeting Leadership Leading a family meeting requires considerable flexibility to ensure that all relevant participants have the opportunity to have their points of view expressed. Though it is useful to have one person designated as the main orchestrator and coordinator of the meeting, the essential skills for making a family meeting successful can come from more than one participant. These skills include:

- Group facilitation skills.
- Counseling skills.
- Knowledge of medical and prognostic information.
- Willingness to provide leadership/guidance in decision making.

Invitations A decisional patient can be asked who he/she wants to participate from his/her family/community, including faith leaders; in general it is wise not to set any arbitrary limits on the number of attendees. The medical care team should likewise decide who they want to participate. **Note:** it is important not to overwhelm a family with too many health professionals. On the other hand, a physician from the primary team as well as a nurse and social worker should attend when possible; these individuals can help ensure the consistency of information as well as help deal with complicated dynamics. If the patient has a long-time treating physician whom he/she trusts, this person should ideally be present.

Setting The ideal setting is private and quiet, with chairs arranged in a circle or around a table. Everyone should be able to sit down if they wish. For non-decisional patients, the clinical team should negotiate with the surrogate whether or not to have the meeting in the presence of the patient.

The Pre-Meeting Meeting The participating health care members should meet beforehand to confirm: a) the goals for the meeting (e.g. information sharing, specific decisions sought), b) who will be the meeting leader to start the meeting, and c) likely sources of conflict and initial management strategies.

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FAST FACTS AND CONCEPTS #223
THE FAMILY MEETING: STARTING THE CONVERSATION
David E Weissman MD, Timothy Quill MD, and Robert M Arnold MD

Background *Fast Fact* #16 gives a concise overview of running a family meeting. *Fast Fact* #222 provides a list of preparatory steps in planning for a family meeting to discuss end-of-life goals; this *Fast Fact* reviews the early steps of the actual meeting.

1. Introductions & setting goals for the meeting

- The meeting leader begins the meeting by introducing him or herself, and suggesting that each person present (medical team and family/community) introduce themselves including their relationship to the patient.
- The meeting leader should summarize the meeting goals (e.g. *We are here to discuss next steps in the care of Mr. Jones*) and ask the family to confirm these goals and/or add other agenda items.
- **Note:** if you do not know the patient or family well, take a moment to build relationship. Ask a non-medical question such as *I am just getting to know you. I had a chance to look at your chart and learn about your medical condition but it does not say much about your life before you got sick. Can you tell us about the things you liked to do before you got sick?* Similarly, if the patient is not able to participate in the meeting, ask family to describe the patient prior to his becoming ill: *As we get started, can you describe what Mr. Jones was like before he became ill?*

2. Determine what the patient/family already knows This step is essential as it guides you in providing a synthesis of the medical information (see below). Always invite the patient and all family members to provide their understanding of the medical information. Examples of opening lines:

- *Tell me what the doctors have told you about your condition?*
- *Can you describe for me your sense of how things are going?*
- For patients who have been declining from a chronic illness, you can ask*: Tell me about the past 3-6 months: what types of changes have you noted?* The patient or family will typically describe changes in terms of function (physical or cognitive) and quality of life.

3. The Medical Review Once you know what the patient/family understands, you are in a good position to confirm their understanding, or provide new information/correct misunderstandings. First, ask if you can bring them up-to-date about what is going on; asking shows politeness and also signals that they should attend to what you are trying to say. The clinician most closely aligned with the patient's ongoing treatment should begin this discussion, supplemented with information from consulting services if relevant. Do not provide information using medical jargon or in an organ system approach (e.g. *The creatinine is improving, but there is a new pleural effusion and the heart rate has become irregular*). A more patient-centered approach is to provide a succinct summary of the current condition, without any medical jargon, focusing on the issues of most importance, which are usually function/quality/time. Give a 'bottom-line' statement: 'getting worse,' 'not going to improve,' 'dying and time is likely very short.'

- *The worsening weakness and pain you describe is from the cancer which is growing despite the chemotherapy.*
- *You are telling me that despite the recent hospitalization, you are not able to do as much around the house; unfortunately your lung disease is getting worse despite all our best treatments.*
- *Despite our best efforts, your wife's brain injury from the car crash is getting worse. She can no longer stay awake or move her arms/legs.*

Using the 'D word' if relevant: when a patient is clearly deteriorating and death is likely within the next days to weeks, or even a few months, it is appropriate to use the word *dying* in the conversation. Both patients and surrogates find that saying the word *dying*, if done compassionately, is helpful in clearing what is often a confusing and frightening situation. *I'm afraid we have run out of options to shrink the cancer. Based on your declining function, I believe you are dying.*

4. Silence Whether or not you use the word *dying*, when you have presented bad news (such as information about disease progression), the next step is for you to allow silence, and let the family/patient

respond. In truth, no matter what you might imagine the response from the patient/family to be once the bad news is delivered, you really cannot predict their emotional reaction (e.g. relief, anxiety, anger, regret, fear). This silence can be uncomfortable; resist the urge to fill it with more facts as they will not be heard. Not all patients/families express emotions at this point and instead respond practically (*Well, what happens next then?*). This is fine, but you need to wait, silently, to see what response the patient/family demonstrates. In addition, even practical questions have underlying emotions (*Are you sure?* Or – *There must be something you can do?*). It is important to respond to both the factual aspect of the question (*Yes I am sure.* Or – *There are no more effective treatments available*.), as well as the emotional level (*I wish I had better news for you.* Or – *I wish our treatments worked better than they do.).*

When the patient/surrogates openly acknowledge that current treatments are no longer effective, that death is coming, they will generally ask one or all of the following questions: *How long? What will happen? Will there be suffering? What do we do now?* Your response at this point should be to address prognosis in terms of time, function, and symptoms, as best you can (see *Fast Facts* #13,141,143,149,150). This will answer the first two questions; the last questions will require more discussion of patient-centered goals (see *Fast Fact* #227).

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FAST FACTS AND CONCEPTS #224
RESPONDING TO EMOTION IN FAMILY MEETINGS
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Background Family meetings are stressful events, often provoking strong emotional reactions. *Fast Fact* #29 presents a general outline on the topic of how clinicians can respond to emotions. The *Fast Fact* will provide a more detailed approach to emotions that arise during family meetings.

Consider your role. It is important to reflect on the role of clinicians in responding to patient/family emotions at the time life-altering information is shared. The goal is not to prevent a patient/family from having those emotions. Sadness, fear, anger, and loss are normal responses to unwelcome news. Instead your role is: 1) to maintain a trusting therapeutic relationship and safe/supportive environment that allows emotions to be expressed in a way that meets the patient's/family's needs; and 2) not to worsen the experience for the patient/family by ignoring or delegitimizing their responses, or confusing them with medical information when they are not ready to hear it. Recognize that most families find clinicians' expressions of empathy tremendously supportive and these are associated with family satisfaction.

Acknowledge that emotion is being expressed. If you have a good sense of what the emotion is, then it is useful to name it. If not, using more general language is preferable.

- *I can see this is really affecting you.*
- *This information is very upsetting.*

Legitimize the appropriateness and normalcy of the reaction. Medical professionals are in a powerful position to help patients and families feel that strong emotions under these circumstances are normal and to be expected.

- *Anyone receiving this news would feel devastated.*
- *It is completely expected to be very distressed by this kind of news.*

Explore more about what is underneath the emotion. It is tempting to try to limit the emotion, and be prematurely reassuring. But it is generally more helpful and ultimately more time-efficient to allow the patient and family to more deeply explore their feelings and reactions.

- *Tell me what is the scariest (most difficult) part for you.*
- *Tell me more about that….* (Keep the exploration going until it is fully expressed and understood.)

Empathize (if you genuinely feel it). Empathy means being able to emotionally imagine what the patient is going through. Clinicians can initiate the prior responses (acknowledge, legitimize, explore) without having a clear feeling for the patient's experience. These responses can be adequate in themselves. If the clinician cannot imagine the patient's experience, he or she can still sensitively explore the experience and provide caring and support. But if you have a strong sense of what the patient is experiencing, it can be very therapeutic to express it.

- *This seems really unfair.*
- *I can imagine that you might feel very disappointed.*

Explore strengths/coping strategies. This may occur at this phase of the interview, or it may be postponed to a later phase when planning for next steps begins.

- *In past circumstances, what has helped?*
- *How have you adapted to difficult circumstances in the past?*
- *What are you hoping for now?*

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FAST FACTS AND CONCEPTS #225
THE FAMILY MEETING: CAUSES OF CONFLICT
David E Weissman MD, Timothy E Quill MD, and Robert M Arnold MD

Background When family meetings are conducted with the goal of helping a patient/family cope with a shift in goals from life-sustaining treatments to a more comfort focused approach, communication can break down. This *Fast Fact* reviews the common causes of conflict.

Recognizing Conflict When the patient/surrogates are not psychologically ready to accept the limits of medical interventions or the finality of the impending death, you will hear comments such as these: *There must be some mistake; I know there are other treatments available; We want a second opinion; We believe in miracles; She is fighter, she will never give up; There must be something (medically) you can do.* Health professionals may interpret these statements as 'denial.' But the term denial, by itself, is insufficient to help the clinician understand what is causing the impasse. Understanding the cause is essential in planning an effective strategy to move beyond the conflict to meet the needs of the patient and surrogates.

Information Gaps

- Inaccurate understanding of the patient's medical condition (e.g. overly optimistic/pessimistic prognosis).
- Inconsistent information (*One doctor tells us one thing and another something else.*).
- Confusing information (e.g. use of medical jargon, multiple treatment options presented without a clear recommendation).
- Excessive information (well-meaning family/friends/clinicians providing information without full awareness of the problems).
- Genuine uncertainty (e.g., predicting functional outcome from a brain injury in its immediate aftermath may be impossible).
- Language/translation/cultural issues (*We never tell someone they are dying in our culture.*).

Treatment Goal Confusion

- Inconsistent treatments and unclear goals, often due to physician/patient/surrogate emotional issues (see below):
    - Clinician initiated: *We will keep your husband on blood pressure raising medicine but stop antibiotics.*
    - Family initiated: *We want you to do CPR, but not intubate her.*
- Differing priorities about disease-directed treatment and comfort-oriented treatment between clinicians and patient/family.
- Lack of clarity about goals when several things are going on simultaneously (advanced cancer, severe infection, respiratory failure – *Isn't the pneumonia potentially treatable?*)

Emotions

- Grief (*I don't know how I will live without him.*)
- Fear/anxiety (*I don't want to be responsible for ending my father's life. My family will be angry at me for doing this.*)
- Guilt (*I haven't visited my sister in 20 years. I should have been here for her.*)
- Anger (*My mother was very abusive, I've never forgiven her; you are just giving up on her.*)
- Hope (*I'm still hoping and praying she can pull through this.*)

Family/Team dynamics

- Patient/family conflicted within themselves; may want different things at different times
- Dysfunctional family system (family members unable to put the patient's needs/values/priorities above their own).
- Surrogate lack of ability (cognitive deficit, psychological/psychiatric trait/illness). In pediatrics, this can be conflict between what is in the best interest of a child vs. a caregiver or family.

- Consulting teams disagree about the optimal approach, putting the patient/family in the middle of the dispute.

Relationship between the Clinician and the Patient/Surrogate

- Lack of trust in the health care team/health care system.
- Past experiences where the patient has had a better outcome than predicted.
- Genuine value differences:
    - Cultural/religious values concerning life, dying, and death.
    - Clinician value to protect the patient from invasive, non-beneficial treatment while the family values wanting to prolong life no matter how much suffering it might entail.

All of these issues represent a degree of conflict and will need to be addressed before proceeding to set end-of-life goals. See *Fast Facts* #183,184 for additional discussion on managing conflict.

Debriefing Conflicts are stressful for all involved health professionals. It is helpful to debrief the process – what went well, what could have been improved, and – most importantly – addressing the emotional reaction and needs of the care team. See *Fast Fact* # 203 on managing clinician emotions.

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FAST FACTS AND CONCEPTS #226
HELPING SURROGATES MAKE DECISIONS
David E Weissman MD, Timothy E Quill MD, and Robert M Arnold MD

Background Surrogate decision makers are often placed in the difficult position of making what feels to them as life or death decisions. This *Fast Fact* reviews an approach to help surrogates through the decision process when patients cannot participate in decision-making themselves.

Surrogate decision making The surrogate's role is clearly to exercise "substituted judgment" – that is, to make decisions as the patient would make them using the patient's values and preferences as previously expressed. The challenge was clearly expressed by the New Jersey Supreme Court in the Quinlan case: *if (the patient) could wake up for 15 minutes, understand his current medical situation completely, and then had to go back into it, what would he tell us to do?* In the case of children, surrogate decision makers (usually parents) are expected to make decisions that represent the child's 'best interests'; depending on the age and capacity of the child to participate in his/her own healthcare decision making, the applied 'best interest' judgment by the surrogate and healthcare providers may incorporate the patient's values and preferences to the extent possible, or may be solely based on the decision maker's interpretation of best interest. If there is conflict about what is in a child's best interest, or in cases of developmentally disabled adults who have never had capacity, consultation from ethics and law may be appropriate, as the rules governing decision-making vary considerably.

Helping surrogates

1. Before making a recommendation, make sure there is a common understanding of the patient's condition and prognosis. Following this, the next step is to try to understand the patient's goals in light of these medical facts.
2. Bring the patient's "voice" into the decision process even if he/she cannot participate directly: *If your father were sitting here with us, what would he say?* If available, share a copy of any advance care planning document with the surrogate. Realize that it is common for the surrogate never to have seen the document.
3. Whenever possible, frame the decision around the treatment goals (e.g. life prolongation, allowing a peaceful death) in light of the patient's current condition, rather than focusing on very specific treatments (e.g. thoracentesis, antibiotics). The details of the medical plan should flow from the overall goals of care.
4. Do not make the surrogate feel that they are taking full responsibility for medical decisions, especially those which may result in the death of their loved one (*We can do option a or b; what would like me to do?*). Once you have a sense of the patient's goals in light of his/her medical condition, offer to make a recommendation that reflects those goals. **Note:** Many families are looking for support and guidance from medical professionals, especially the physician. *Given what you have told me about your mother, and what we know about her medical condition, I would recommend….* Start with what you *are* going to do to achieve the patient's goals and then talk about what does not make sense given those goals. Remember, however, that some families may want information but not your recommendation. It is therefore important to offer your recommendation (*Would it be helpful for me to say what medically makes the most sense, given what you've told me about your Dad?).*
5. Remember that we are talking about the potential death of the surrogate's loved one. Emotions – sadness, frustration and guilt – are appropriate and to be expected. Use previously discussed emotion management skills to acknowledge, legitimize, empathize and support the family's emotional response (see *Fast Facts* #29 and #224).
6. Do not argue over the facts; repeating the facts over and over again is not likely to be effective. When the surrogate says *He is a fighter*, acknowledge that he is and has really fought hard. The surrogate saying *I want you to do everything* is as much a sign of emotional desperation as it is a factual request. Respond with empathy: *It seems this is really hard for you*. If hope for a miracle is expressed, it is appropriate to acknowledge that you hope for an unanticipated recovery as well, but that a miracle is truly what it would take at this point.
7. Rather than reiterating what medicine cannot do, consider using "*I wish"* statements to keep you in touch with the surrogate's feelings, while simultaneously expressing medicine's limitations (*I wish our medicines were more effective; I wish we had more medical treatment to offer than we do…).*

8. Recognize the importance of time and support for surrogates to do their necessary grief-work. Offer counseling services, either informal through the work of a palliative care team, or more formal resources available at your institution. Bring together your clinical care team and strategize potential resources for support such as chaplaincy, social services, psychology, palliative care or ethics consultation.

Remember that time is your ally. The surrogate needs to process that their loved one is dying and conceptualize what life will be like without him or her. This grief work takes time and psychological support. Often, letting people think about what you have said and talking again over subsequent days provides them the space to do grief work. It also allows them to see for themselves that what you have advised is coming true (e.g. the patient is not getting better).

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FAST FACTS AND CONCEPTS #227
THE FAMILY MEETING: END OF LIFE GOAL SETTING AND FUTURE PLANNING
David E Weissman MD, Timothy E Quill MD, and Robert M Arnold MD

Background End-of-life goal setting is a key palliative care skill, typically occurring as part of a family meeting (see *Fast Facts* #16, 65, 222-226). This *Fast Fact* discusses an approach to goal setting when the expected length of life is short.

Establishing patient-centered goals Here is an example of how to start the conversation (the patient should be given sufficient time to respond to each of these questions):

I/we have discussed your current condition and that time may be short. With that in mind –

- *What are you hoping for now?*
- *What is important to you?*
- *What do you need to accomplish?*
- *Who do you need to see in the time that is left?*

Common responses invoke family, home, and comfort; often surviving until a specific future family event/date or visit with a key family member is described as an important goal. Re-state your understanding: *What I hear you saying is that you want to be home, comfortable, and survive until your daughter gives birth – you hope to meet your next grandchild*. **Note:** if you believe the patient's goal of survival to a specific event/date is not practical, it is important to say so and discuss alternative plans.

Recommend a care plan based on the goals Once the goal(s) is/are established, you can then review the patient's current treatments (e.g. antibiotics, chemotherapy), monitoring (e.g. pulse oximetry), planned tests (e.g. colonoscopy), and medications (e.g. anti-hypertensives), and decide which will help meet, or not, the patient's goals. Anything that will not help meet the goals should be discussed for potential discontinuation. Depending on the specific disease/patient condition, other issues that are naturally discussed at this point include:

- Future hospitalizations, ICU admissions, laboratory and radiology tests.
- Resuscitation orders/code status (see *Fast Facts* #23-24).
- Current/future use of blood products, antibiotics, artificial hydration/nutrition.
- If present, the potential continuation or stopping of dialysis or cardiac devices.
- Role of a second (or third) opinion.
- Exploration of experimental therapy.
- Exploration of treatment options the patient or family may bring into the conversation.
- Disposition options to best meet the goals (e.g. home hospice referral).

Note: There is *no* need to ask about each option as a yes/no question (*Do you want blood products?*). Based on what you know about the patient's goals, make a recommendation about what should and should not be done in light of the patient's goals, condition and prognosis. If you are unsure, you can explore the issue with the patient/family (*Given that your dad wanted to get home as soon as possible and yet he was also willing to do easy things that might help him live longer, I am unsure whether it makes sense to stay in the hospital an extra day or two to finish the antibiotics. What do you think he would say?*).

'Long-shot' goals If patients are going to pursue 'long-shot' or experimental therapy, perhaps even against the recommendation of the treating team, it is useful to ensure the following:

- Reinforce the team's respect for the decision, and desire to make sure the treatment has the best possible chance of working.
- Simultaneously try to maximize quality of life *in the present*, including the best possible pain and symptom management and support.
- Encourage the patient and family to prepare in case treatment is not successful and the patient dies sooner rather than later. Useful language is to say, *I'd encourage us all to hope for the best, but prepare for the worst*.

- Reinforce that the team will not abandon the patient and family even if the decision is not what is being recommended.

Close the meeting Following this discussion, restate your understanding of the patient's goals and agreed-upon next steps to meet those goals, invite and answer questions, and close the meeting.

Discussion & documentation Discuss the goals with key staff not in attendance (e.g. consulting physicians, patient's nurse, discharge planner, primary care provider). Document the goals, preferably using a templated family meeting note (see Reference 1): who was present, what was discussed (e.g. treatment options, prognosis), what was decided, next steps.

Debriefing A useful step after every family meeting is to debrief the process – what went well, what could have been improved and, most importantly, addressing the emotional reaction and needs of the care team.

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FAST FACTS AND CONCEPTS #3
SYNDROME OF IMMINENT DEATH
David E Weissman MD

Background Virtually all dying patients go through a stereotypical pattern of symptoms and signs in the days prior to death. This trajectory is often referred to as "actively dying" or "imminent death". Prompt recognition of this trajectory is key for clinicians to provide the most appropriate interventions for both the patient and family.

1. Stages

- ***Early***
  - Bed bound
  - Loss of interest and/or ability to drink/eat
  - Cognitive changes: increasing time spend sleeping and/or delirium (see *Fast Fact* #1)
- ***Middle***
  - Further decline in mental status to obtundation (slow to arouse with stimulation; only brief periods of wakefulness)
- **Late**
  - Death rattle – pooled oral sections that are not cleared due to loss of swallowing reflex
  - Coma
  - Fever – usually from aspiration pneumonia
  - Altered respiratory pattern – periods of apnea, hyperpnea, or irregular breathing
  - Mottled extremities

2. Time Course The time to traverse the various stages can be less than 24 hours or as long as ~14 days. Patients who enter the trajectory who are nutritionally intact, with no infection (e.g. acute stroke), are apt to live longer than cachectic cancer patients

3. Common Family Concerns Family members present during the dying process often express the following concerns/questions. Clinicians can best help families by expecting these questions, providing education, reassurance, and responding to emotions (see also *Fast Fact* # 29; #149).

- Is my loved one in pain; how would we know?
- Aren't we just starving my loved one to death?
- What should we expect; how will we know that time is short?
- Should I/we stay by the bedside?
- Can my loved one hear what we are saying?
- What do we do after death?

4. Treatment

- Confirm treatment goals; recommend stopping treatments that are not contributing to comfort – pulse oximetry, IV hydration, antibiotics, finger sticks, etc.
- Communicate clearly to others what is going on. Write in progress notes: "patient is dying," not "prognosis is poor".
- Treat symptoms/signs as they arise: common among these are: oral secretions (see *Fast Fact* #109, #158); delirium (#1, 60); dyspnea (# 27), fever (#256) and pain (# 53, 54).
- Provide excellent mouth and skin care.
- Provide daily counseling and support to families.

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FAST FACTS AND CONCEPTS #13
DETERMINING PROGNOSIS IN ADVANCED CANCER
David E Weissman MD

Background *How long do I have, Doc?* is among the most common questions asked by cancer patients, especially when informed that there are no further effective anti-neoplastic treatment options. Although prognostication is not an exact science, there are data to help clinicians provide useful information to patients and families – information critical to making realistic end-of-life decisions and referrals for home hospice service (see *Fast Fact* #30).

Performance Status The single most important predictive factor in cancer is *Performance Status* ('functional ability,' 'functional status'): a measure of how much a patient can do for themselves, their activity and energy level. Patients with solid tumors typically lose ~ 70% of their functional ability in the last 3 months of life. The most common scales used to measure functional ability are the Karnofsky Index (100 = normal; 0 = dead) and the ECOG scale (Eastern Cooperative Oncology Group), (0 = normal; 5 = dead). A median survival of 3 months roughly correlates with a Karnofsky score $\leq$40 or ECOG $\geq$ 3. Newer prognostic scales have been developed to help provide prognostic information (See *Fast Facts* #124, 125).

The simplest method to assess functional ability is to ask patients: *How do you spend your time? How much time do you spend in a chair or lying down?* If the response is >50% of the time, and is increasing, you can roughly estimate the prognosis at 3 months or less. Survival time tends to decrease further with increasing numbers of physical symptoms, especially dyspnea, if secondary to the cancer.

Other Factors Several common cancer syndromes have well-documented short median survival times:

- Malignant hypercalcemia: 8 weeks, except newly diagnosed breast cancer or myeloma (see *Fast Fact* #151)
- Malignant pericardial effusion: 8 weeks (see *Fast Fact* #209)
- Carcinomatous meningitis: 8-12 weeks (see *Fast Fact* #135)
- Multiple brain metastases: 1-2 months without radiation; 3-6 months with radiation.
- Malignant ascites (see *Fast Fact* #176), malignant pleural effusion (#209), or malignant bowel obstruction: < 6 months.
- Modified Glasgow Prognostic Score (mGPS): multiple studies have shown that an increased mGPS -- meaning an elevated serum c-reactive protein and a reduced serum albumin – is associated with a reduced cancer specific survival curve irrespective of cancer type.

Other Comments In general, a patient with metastatic solid cancer, acute leukemia or high-grade lymphoma, who will not be receiving systemic chemotherapy (for whatever reason), has a prognosis of *less than 6 months*. Notable exceptions to this are patients with metastatic breast or prostate cancer with good performance status, as these cancers may have an indolent course. In these patients additional features suggesting short prognosis are needed (declining functional status, dyspnea, weight loss).

Discussing Prognosis When discussing prognosis with patients/families, the following four step approach is recommended: *Preparation; Content; Patient's Response; Close*. Remember to:

- Confirm that the patient/family are ready to hear prognostic information.
- Present information using a range: *a few days to weeks; 2-4 months*, etc.
- Allow silence after you provide information; respond to emotion (see *Fast Fact* #29).
- Use prognostic information for eliciting end-of-life goals (see *Fast Fact* #65).

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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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FAST FACTS AND CONCEPTS #143
PROGNOSTICATION IN HEART FAILURE
Gary M Reisfield MD and George R Wilson MD

Background This *Fast Fact* reviews prognostication data in Heart Failure (HF). Although the Framingham Heart Study (1990-1999) showed a 5-year mortality rate of 50% for newly identified cases, providing accurate prognostic data for 6-12 month mortality in HF has been nearly impossible. Reasons cited include: 1) an unpredictable disease trajectory with high incidence (25-50%) of sudden death; 2) disparities in the application of evidence-based treatment guidelines; 3) inter-observer differences in New York Heart Association (NYHA) classification; and 4) heterogeneous study populations

NYHA Classification The NYHA classification remains the major gauge of disease severity. Based on data from SUPPORT, Framingham, IMPROVEMENT, and other studies, 1-year mortality estimates are:

- Class II (mild symptoms): 5-10%.
- Class III (moderate symptoms): 10-15%.
- Class IV (severe symptoms): 30-40%.

General Predictors of Shorter Prognosis:

- Cardiac hospitalization (triples 1-year mortality; nearly 1 in 10 die within 30 days of admission).
- Intolerance to neurohormonal therapy (i.e. beta-blockers or ACE-inhibitors) is associated with high 4 month mortality
- Elevated BUN (defined by upper limit of normal) and/or creatinine ≥1.4 mg/dl (120 µmol/l).
- Systolic blood pressure <100 mm Hg and/or pulse >100 bpm (each doubles 1-year mortality).
- Decreased left ventricular ejection fraction (linearly correlated with survival at LVEF ≤ 45%).
- Ventricular dysrhythmias, treatment resistant.
- Anemia (each 1 g/dl reduction in hemoglobin is associated with a 16% increase in mortality).
- Hyponatremia (serum sodium ≤135-137 mEq/l).
- Cachexia or reduced functional capacity.
- Orthopnea.
- Co-morbidities: diabetes, depression, COPD, cirrhosis, cerebrovascular disease, and cancer

Hospice Eligibility Guidelines The National Hospice and Palliative Care Organization's 1996 guidelines for heart disease admission criteria include: a) symptoms of recurrent HF at rest (NYHA class IV) *and* b) optimal treatment with ACE inhibitors, diuretics, and vasodilators (*contemporary optimal treatment now includes β-blockers, aldosterone antagonists, and device therapies*). The NHPCO guide indicates that an ejection fraction ≤ 20% is "helpful supplemental objective evidence," but not required. The NHPCO guidelines also assert that each of the following further decreases survival: treatment resistant ventricular or supraventricular arrhythmias, history of cardiac arrest in any setting, history of unexplained syncope, cardiogenic brain embolism, and concomitant HIV disease.

Prognostic Models Since publication of the NHPCO's guidelines, several models have been developed for predicting short- and/or long-term mortality among HF patients. Two recent models purport to predict mortality among patients *hospitalized with acutely decompensated HF.* Fonarow et al (2005), using a model based on admission BUN (≥ 43 mg/dl), creatinine (≥ 2.75 mg/dl), and systolic BP (< 115 mmHg), identified in-hospital mortality rates ranging from about 2% (0/3 risk factors) to 20% (3/3 risk factors). Lee et al (2003), using a model based on admission physiologic variables and co-morbidities (almost all from above list of indicators) identified 30-day mortality and 1-year mortality rates ranging from <1% and <10%, respectively, for the lowest risk patients to >50% and >75%, respectively, for the highest risk patients. While both models are applicable to bedside use, neither has been applied prospectively or in independent patient samples, nor do they address HF treatments as predictive variables. More recently, Levy et al (2006) developed a 24-variable risk model using the PRAISE1 (*n*=1125) database and validated it on preexisting ELITE2, ValHeFT, UW, RENAISSANCE, and IN-CHF (*n*=9942) databases. The model purports to accurately estimate mean 1-, 2-, and 3-year survival and, importantly, *dynamically* incorporates clinical and laboratory variables, HF medications, and device therapies. It awaits independent, prospective evaluation in unselected HF patients. A web-based interactive calculator can be accessed at http://www.seattleheartfailuremodel.org.

Bottom Line Meticulous application of medication and device therapies can and will continue to change HF prognosis. HF follows an unpredictable disease trajectory, one which is highly mutable by application of evidence-based therapies, yet still marked by a high incidence of sudden death. The 1996 NHPCO criteria are not accurate predictors of 6-month mortality. Several models have recently been developed to aid in determining short- and long-term mortality in HF patients. These models await independent, prospective validation in unselected ambulatory HF patients and will need periodic updating to control for continually evolving standards of HF care. At present, accurate prognostication remains problematic.

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FAST FACTS AND CONCEPTS #150
PROGNOSTICATION IN DEMENTIA
Sing Tsai MD and Robert Arnold MD

Background Dementia is a syndrome of acquired and persistent impairment in cognition and intellectual functioning (1). When caused by certain diseases or injury, dementia is irreversible, leading to progressive brain failure and death. This *Fast Fact* reviews issues of prognostication in dementia.

Natural history of dementia Olson (2003) classifies dementia into four functionally defined categories: mild, moderate, severe, and terminal. 'Terminal dementia' is defined as loss of communication, ambulation, swallowing, and continence. Others use the term "end-stage" or "advanced" making interpretation of prognostic data challenging. Many prognostic factors have been associated with shortened survival: male gender, age, diabetes mellitus, CHF, COPD, cancer, cardiac dysrhythmias, peripheral edema, aspiration, bowel incontinence, recent weight loss, dehydration, fever, pressure ulcers, seizures, shortness of breath, low oral intake, not being awake for most of the day, low Body Mass Index, and recent need for continuous oxygen. A 2012 systematic review found that malnutrition, feeding issues, and dysphagia were the strongest associated factors with 6 month mortality in elderly patients with advanced dementia. Simply being admitted to the hospital with acute illness and end-stage or terminal dementia is associated with a particularly poor prognosis: the six month mortality after hospitalization for pneumonia was 53% compared with 13% for cognitively intact patients. For patients with a new hip fracture, 55% of end-stage dementia patients died within 6 months compared with 12% for cognitively intact patients (Morrison 2000).

Prognostic Systems (see table below):
The National Hospice and Palliative Care Organization (NHPCO) recommends the ***Functional Assessment Staging*** **(FAST)**, a 7-step staging system, to determine hospice eligibility. The FAST identifies progressive steps and sub-steps of functional decline. NHPCO guidelines state that a FAST stage 7A is appropriate for hospice enrollment, based on an expected six month or less prognosis, if the patient also exhibits one or more specific *dementia-related co-morbidities* (aspiration, upper urinary tract infection, sepsis, multiple stage 3-4 ulcers, persistent fever, weight loss >10% within six months). Luchins (1997) studied the relationship of FAST to survival in 47 patients enrolled in hospice with advanced dementia and one or more dementia-related co-morbidities. The median survival for all patients was 6.9 months; 38% survived beyond six months. Of note, 41% of patients did not demonstrate dementia progression in a manner that allowed for assigning a FAST stage. For those patients who could be assigned a FAST stage (n = 12), and who were at stage 7C or greater, mean survival was 3.2 months. The generalizability and clinical relevance of this data are greatly compromised by this very low patient number.

The *Mortality Risk Index* (MRI), a composite score based on 12 risk factor criteria obtained from using the MDS (Minimum Data Set), has been suggested as an alternative to FAST. Mitchell (2004) developed and then validated the MRI by examining data from over 11,000 newly admitted nursing home patients. Among patients with a MRI score of ≥ 12, 70% died within 6 months (mean survival time not reported). Compared to FAST Stage 7C, the MRI had greater predictive value of six month prognosis. The MRI as only been evaluated in newly admitted nursing home residents; it has yet to be validated in the community setting or for previously established long-term nursing home residents.
Medical Interventions Estimation of prognosis in severe/terminal dementia is in part dependent on the goals of care and decisions regarding the level of intervention that will be provided to treat acute medical problems such as urosepsis and malnutrition.

Summary Although many prognostic risk factors have been identified there is no gold standard to help clinicians determine a less than six months prognosis with any degree of certainty. The criteria adopted by NHPCO for hospice eligibility is based on very limited research and lacks important studies to determine FAST scale reliability and validity among referring physicians and hospice staff. The MRI is a promising new scale but more research is needed. Physicians can best help their patients by working with families to help them establish goals of care and levels of medical intervention that are most consistent with current medical research and family/patient preferences.

Functional Assessment Staging (FAST)

Stages

1. No difficulties
2. Subjective forgetfulness
1. Decreased job functioning and organizational capacity
4. Difficulty with complex tasks, instrumental ADLs
5. Requires supervision with ADLs
6. Impaired ADLs, with incontinence
7. A. Ability to speak limited to six words
   B. Ability to speak limited to single word
   C. Loss of ambulation
   D. Inability to sit
   E. Inability to smile
   F. Inability to hold head up

Mortality Risk Index Score (Mitchell)

Points	Risk factor
1.9	Complete dependence with ADLs
1.9	Male gender
1.7	Cancer
1.6	Congestive heart failure
1.6	O_2 therapy needed w/in 14 day
1.5	Shortness of breath
1.5	<25% of food eaten at most meals
1.5	Unstable medical condition
1.5	Bowel incontinence
1.5	Bedfast
1.4	Age > 83 y
1.4	Not awake most of the day

Risk estimate of death within 6 months

Score	Risk %
0	8.9
1-2	10.8
3-5	23.2
6-8	40.4
9-11	57.0
≥ 12	70.0

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FAST FACTS AND CONCEPTS #234
PROGNOSIS OF ANOXIC-ISCHEMIC ENCEPHALOPATHY
James Fausto MD

Introduction Cardiac arrest, experienced by approximately 450,000 Americans annually, has a very poor survival rate (see *Fast Fact* #179). Some patients who initially survive cardiopulmonary resuscitation remain comatose, demonstrating obvious impairments in consciousness and neurologic function. This syndrome, called anoxic-ischemic encephalopathy (AIE, also known as 'anoxic brain injury,' or 'hypoxic-ischemic coma'), can result in outcomes ranging from full recovery to permanent unconsciousness to death. This *Fast Fact* discusses prognostic factors in adults with AIE after cardiac arrest.

"Neurologic Outcome" A challenge in interpreting the literature on AIE is the use of variable or imprecise definitions of a 'poor neurologic outcome.' The American Academy of Neurology practice parameter paper defines poor outcome as: death, persistent unconsciousness (such as a vegetative state), or severe disability requiring full nursing care after 6 months (6). This is the definition used in this *Fast Fact*.

Predictors of Neurologic Outcome A review of the current literature reveals that data obtained by careful neurologic exam, electrophysiological studies, and biochemical markers are most predictive of outcome (see below). Other factors not strongly predictive of outcome include: age, sex, cause of arrest, type of arrhythmia, total arrest time, duration of CPR, geographic location of arrest, elevated body temperature, elevated intracranial pressure, concurrent respiratory failure, and early brain imaging findings (3,6,7,8).

Note: the data below assume patients are not receiving medications which would significantly confound their neurologic examination such as high-dose barbiturates. In all cases, specialist neurologic examination and input is advised.

Strong Indicators of Poor Outcome (false positive rates of 0% based on current literature):

- Absent pupillary light reflexes 24 hours after CPR, or 72 hours after CPR for those who initially had intact papillary light reflexes (3,6,7).
- Absent corneal reflexes 72 hours post-CPR (6,7).
- Short-latency Somatosensory Evoked Potentials (SSEP, an electrophysiologic study): bilateral absence of the N20 potentials on SSEP of the median nerve in AIE patients greater than 24 hours post-CPR (1,6,7,8).
- Neuron-Specific Enolase (NSE, a blood test): serum NSE > 33 mcg/L on day 1 to 3 (6,7,8). While this biomarker is promising, it has not been studied in large trials, nor is the assay itself standardized, so its current clinical role remains undefined (7).

Moderate Predictors of Poor Outcomes (these all predict a poor outcome, but not as invariably as the above factors based on current literature):

- Clinical exam findings: no spontaneous eye movements or absent oculocephalic reflexes at 72 hours post-arrest (3,6,7). No, or extensor-only, motor response to painful stimuli at 72 hours also implies a very poor chance of recovery (3,6).
- Electroencephalogram findings: certain findings can be strongly associated with poor outcomes but are highly subject to institutional/technician variability. Myoclonic status epilepticus within 1 day of cardiac arrest is the most predictive of a poor outcome (3,6,7,8).

The Therapeutic Hypothermia Protocol The majority of the evidence for prognosis in the comatose patient after CPR predates the widespread use of therapeutic hypothermia in patients after cardiac arrest. It remains unclear how this intervention will change prognostication. While the above factors will likely still indicate poor prognosis, the timing of when the evaluations should be done, as well as if they will predict a *uniformly* poor outcome is uncertain. One European study advises that patients have an initial neurological assessment as soon as possible, but that the second assessment occurs *no earlier* than 48-72 hours after the return of normal blood temperature and not 48-72 hours after the discontinuation of

active cooling (2). Zandbergen et al suggest that serum NSE >33 mcg/L occurring while hypothermic still consistently predicts poor outcomes accurately (8). Initial data (4,8) on the predictive value of SSEPs in patients who underwent hypothermia confirmed that bilateral absent N20 responses is highly predictive of a poor outcome. There has been a case report of an isolated patient with absent N20 responses who made a full recovery, highlighting the importance of ongoing investigation into the impact of the hypothermia protocol on the prognosis of AIE (4).

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FAST FACTS AND CONCEPTS #10
TUBE FEED OR NOT TUBE FEED?

James Hallenbeck MD

Background Tube feeding is frequently used in chronically ill and dying patients. The evidence for much of this use is weak at best. The Fast Fact reviews data on the use of tube feeding in advanced illness.

For prevention of aspiration pneumonia

- Numerous observational studies have demonstrated a high incidence of aspiration pneumonia in those who have been tube fed. Reduction in the chance of pneumonia has been suggested for non-bed-ridden post-stroke patients in one prospective, non-randomized study. For bedridden post-stroke patients, no reduction was observed.
- Three retrospective cohort studies comparing patients with and without tube feeding demonstrated no advantage to tube feeding for this purpose.
- Swallowing studies, such as videofluoroscopy, lack both sensitivity and specificity in predicting who will develop aspiration pneumonia. Croghan's (1994) study of 22 patients undergoing videofluoroscopy demonstrated a sensitivity of 65% and specificity of 67% in predicting who would develop aspiration pneumonia within one year. In this study no reduction in the incidence of pneumonia was demonstrated in those tube fed.
- Swallowing studies may be helpful in providing guidance regarding swallowing techniques and optimal food consistencies for populations amenable to instruction. See *Fast Fact* #128 for discussion of the role of swallowing studies.

For life prolongation via caloric support

- Data is strongest for patients with reversible illness in a catabolic state (such as acute sepsis).
- Data is weakest in advanced cancer. No improvement in survival has been found (see exceptions noted below).
- Individual patients may have weight stabilization or gain with tube feeding. However, when cohorts of patients have been studied in non-randomized retrospective or prospective studies, no survival advantage between tube fed and hand fed cohorts has been demonstrated.
- Tube feeding may be life-prolonging in select circumstances:

  → Patients with good functional status and proximal GI obstruction due to cancer
  → Patients receiving chemotherapy/XRT involving the proximal GI tract.
  → Selected HIV patients
  → Patients with Amyotrophic Lateral Sclerosis

For enhancing quality of life

- Where true hunger and thirst exist, quality of life may be enhanced (such as in very proximal GI obstruction).
- Most actively dying patients (see *Fast Fact* #3) do not experience hunger or thirst. Although dry mouth is a common problem, there is no relation to hydration status and the symptom of dry mouth – see *Fast Fact* #133.
- A recent literature review using *palliative care* and *enteral nutrition* as search terms found no studies demonstrating improved quality of life through tube feeding (results were limited to a few observational studies).
- Tube feeding may adversely affect quality of life if patients are denied the pleasure of eating.

Summary

Although commonly used, current data does not provide much support for the use of artificial enteral nutrition in advanced dementia, or in patients on a dying trajectory from a chronic illness. A recommendation to use, or not use, tube feeding should be made only after first establishing the overall *Goals of Care* (see *Fast Fact* #16). Recommendations for how to discuss the issue tube feeding with patients/families can be found in *Fast Fact* #84.

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FAST FACTS AND CONCEPTS #133
NON-ORAL HYDRATION IN PALLIATIVE CARE
Robin Fainsinger MD

Background At the center of the debate with regard to hydration in terminally ill patients is the desire to maintain comfort and avoid unnecessary/distressing procedures. There is no controversy that terminally ill patients should be encouraged to maintain adequate oral hydration for as long as possible. However there is debate and controversy around the use of parenteral hydration. This *Fast Fact* discusses medical decision-making about non-oral hydration in palliative care settings; *Fast Fact* #134 discusses techniques of hydration.

Arguments Against Hydration

- Comatose patients do not experience symptom distress.
- Parenteral fluids may prolong dying.
- With less urine there is less need to void and use catheters.
- With less gastrointestinal fluid there can be less nausea and vomiting.
- With less respiratory tract secretions there can be less cough and pulmonary edema.
- Dehydration can help reduce distressing edema or ascites.
- Dehydration may be a "natural" anesthetic to ease the dying process.
- Parenteral hydration can be uncomfortable (e.g. needles/catheters) and limit patient mobility.

Arguments For Hydration

- Dehydration can lead to pre-renal azotemia, which in turn can lead to accumulation of drug metabolites (notably opioids), leading to delirium, myoclonus and seizures. Hydration can reverse these symptoms in some patients leading to improved comfort.
- There is no evidence that fluids prolong the dying process.
- Providing hydration can maintain the appearance of "doing something," even though there may be no medical value, and thus ease family anxiety around the time of death.

Ethical/Legal Issues In the United States, the following ethical/legal standards exist:

- Competent patients or their surrogates can accept or refuse hydration based on relevant information.
- Non-oral hydration is considered a *medical intervention*, not *ordinary care. A*s such, there is no legal or ethical imperative to provide it unless the benefits outweigh the burdens.

Recommendation There is published medical literature to support both the use of, and the withholding of, non-oral hydration in patients near death; thus, there is no consensus on the single best approach to care. A Cochrane review of 6 relevant studies showed that sedation and myoclonus were improved with hydration in adult palliative care patients; however, discomfort from fluid retention was significantly higher in the hydration group and survival seemed to be the same between the groups. Key issues to be considered when determining the role of non-oral hydration include the following:

- Expressed wishes of the patient or surrogate decision-maker regarding use of hydration.
- Patient-defined goals; the presence of a specific goal may direct the clinician to use hydration as a means to improve delirium and potentially delay death.
- Symptom burden: symptoms related to total body water excess may improve by withholding hydration, while delirium may lessen with hydration.
- Burden to the patient and caregivers of maintaining the non-oral route of hydration.
- Family distress concerning withholding hydration/nutrition.
- When in doubt, a time limited hydration trial is an appropriate recommendation.

Clinician Self-Reflection Finally, it is important to recognize that health care providers often have biases for or against non-oral hydration near the end-of- life. Self-reflection upon these biases is crucial to help patients and families make decisions that are based on the best interests and goals of the patient/family unit.

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FAST FACTS AND CONCEPTS #82
MEDICARE HOSPICE BENEFIT – PART I: ELIGIBILITY AND TREATMENT PLAN
Robin Turner MD and Drew A Rosielle MD

Background In the United States, the Medicare Hospice Benefit (MHB) pays for 80% of all hospice care. Established in 1983, the MHB pays for medical, nursing, counseling, and bereavement services to terminally ill patients and their families. The original goal of the MHB was to support families caring for a dying relative at home. Under certain circumstances, hospice services under the MHB can also be provided in a nursing home or the acute care hospital. Referral for hospice care is appropriate when the overall plan of care is directed toward comfort rather than reversing the underlying disease process. *Fast Facts* #87, 90, 139, and 140 further discuss the MHB.

Eligibility—Medicare Hospice Benefit

1. The patient must be entitled to Medicare Part A (hospital payments); once the patient decides to enter hospice care, they sign off Part A and sign on (elect) the MHB. Note: this process is reversible—patients may at a future time elect to return to Medicare Part A.
2. The patient must be *certified* by the Hospice Medical Director and primary physician to have a life expectancy < 6 months "*if the patient's disease runs its natural course*." Patients can continue to be eligible if they live beyond 6 months as long as the physicians believe death is likely within 6 months.
3. Under the MHB, DNR status **cannot** be used as a requirement for admission.

Covered Services (100% coverage with no co-pay)

- Case oversight by the physician Hospice Medical Director
- Nursing care: symptom assessment, skilled services/treatments and case management. The nurse visits routinely; 24-hour/7-day per week emergency contact is also provided.
- Social work: counseling and planning (living will, DPOA).
- Counseling services including chaplaincy.
- All medications and supplies *related* to the terminal illness. The hospice can charge a $5 copay per medication, but most choose not to charge this. Medications for conditions not related to the terminal condition are not covered.
- Durable medical equipment: hospital bed, commode, wheelchair, etc.
- Home health aid and homemaker services.
- Speech, nutrition, physical, and occupational therapy services as determined by the plan of care (see below).
- Bereavement support to the family after the death of the patient.
- Short term *General Inpatient Care* for problems that cannot be managed at home—most commonly intractable pain, delirium, or caregiver breakdown.
- Short term *Respite Care*—up to 5 days to permit family caregivers to take a break.
- *Continuous care* at home for short episodes of acute need.

Not Covered: Continuous nursing assistance (i.e. extended supervisory care) or nursing home room and board charges.

Plan of Care (POC): The hospice team and the patient's physician work together to maximize quality of life by jointly developing the *Plan of Care.* The POC is based on the patient's diagnosis, symptoms, and other needs. The hospice program and the patient's physician must together approve any proposed tests, treatments, and services. In general, only those treatments that are necessary for palliation and/or management of the terminal illness will be approved.

Non-Medicare Hospice Plans: Medicaid hospice benefits closely mirror the MHB. Private insurance plans generally emulate the MHB but occasionally depart from it dramatically (e.g. capping the total number of days a patient may receive hospice care).

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FAST FACT AND CONCEPT # 87
MEDICARE HOSPICE BENEFIT – PART II: PLACES OF CARE AND FUNDING, 2ND EDITION
Robin Turner MD and Drew A Rosielle MD

Introduction *Fast Fact* #82 described eligibility for the Medicare Hospice Benefit (MHB) and the services it covers. This *Fast Fact* will review where services are provided and the reimbursement system for hospice care. *Fast Fact* #90 reviews special interventions under the MHB, and #140 further discusses levels of care.

Places of Care

- **Home:** The majority (~95%) of hospice care takes place in the home. Hospice team members visit the patient and family on an intermittent basis determined by the Plan of Care (see *Fast Fact* #82), which changes based on the patient's needs. Medicare rules do not require a primary caregiver in the home, but as death nears, it becomes increasingly difficult to provide care for a patient who does not have someone (family, friends, hired caregivers) who can be present 24 hours a day in the home.
- **Long-term care facility:** 25% of patients in the US die in nursing homes. Medicare recognizes that this can be the resident's 'home' and that the patient's 'family' frequently includes the nursing home staff. Hospice care under the MHB can be provided to residents *in addition* to usual care provided by the facility. Individual hospice programs must establish a contract with the facility to provide hospice care. The MHB does not pay for nursing home room and board charges.
- **Hospice inpatient unit:** Dedicated units, either free-standing or within other facilities (such as nursing homes or hospitals) are available in some regions. Patient eligibility (e.g, whether or not a patient requires general inpatient care or not), permitted length-of-stay, and fees for room and board vary between facilities.
- **Hospital:** When pain or other symptoms related to the terminal illness cannot be managed at home, the patient may be admitted to a hospital for more intensive management, still under the MHB. The inpatient facility must have a contract with the hospice program to provide this service.

Payment Medicare pays for covered services using a per diem capitated arrangement in one of four categories (see *Fast Fact* #140). The rates below reflect 2015 Medicare and Medicaid reimbursements.

- **Routine Home Care:** care at home or nursing home (~$159/day).
- **Respite Care:** care in an inpatient setting (nursing home, hospice facility, or hospital) for up to 5 days to give caregivers a rest (~$164/day).
- **General Inpatient Care**: acute inpatient care (at a hospital or hospice facility) for conditions related to the terminal illness such as pain and symptom control, caregiver breakdown, or impending death that requires inpatient-level interventions (~$709/day).
- **Continuous Home Care:** provides acute care at home with around-the-clock nursing for a crisis that might otherwise lead to inpatient care (~$930/day).

The rates of reimbursement are fixed for each category of care on an annual basis, but they vary by geographical location. Cited rates are approximate and are intended to convey general orders of magnitude of payment. Payment is made from Medicare to the hospice agency, which then pays the hospital or nursing home (for respite or acute care), depending on the specifics of the contractual arrangement between the hospice agency and the facility.

Physician Services Direct patient care services by physicians, for care related to the terminal illness, are reimbursed by Medicare, and are not included in the per diem. If the attending physician is not associated with the hospice program via employment or similar contract, the physician bills Medicare Part B in the usual fashion. The bill must indicate that the physician is not associated with the hospice program or the claim may be denied. If the attending is associated with the hospice program (e.g. as a medical director) the physician submits the bill to the hospice program, which in turn submits the claim to Medicare under Part A. The physician is then reimbursed based on a contract with the hospice program. Patients can see consulting physicians under the MHB if the hospice agency contracts with the consultant to do so. The hospice agency submits the claim under Medicare Part A and reimburses the consultant per their contract.

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FAST FACTS AND CONCEPTS #14
PALLIATIVE CHEMOTHERAPY
David E Weissman MD

Introduction One often hears the term *palliative chemotherapy*, but what exactly does it mean and how can a non-oncologist decide if it has potential value?

Why is chemotherapy used? From the perspective of the patient with locally advanced or metastatic cancer, chemotherapy is used with one of two intents: Hope for cure or hope for life-prolongation. Oncologists use the term *palliative chemotherapy* as a euphemism for chemotherapy that is not expected to be curative. What about chemotherapy used solely for symptom control—is that a realistic goal? Oncologists will occasionally recommend chemotherapy for symptom control, as there are some clinical trial data that in selected cancers chemotherapy may improve quality of life and/or symptom control, without impacting survival. However, as a general rule, physical symptoms related to the cancer highly correlate with tumor burden; chemotherapy that does not effect tumor growth will generally not improve physical symptoms caused by the tumor.

What information do you need from the consulting oncologist to help a patient decide on the value of chemotherapy in advanced cancer?

1. What is the *Response Rate* of the proposed chemotherapy? *Response Rate* = (# of complete responses + # of partial responses)/total # of treated patients; as studied in clinical trials. To qualify as a Response, the reduction in tumor must last for at least one month:

- *Complete Response* = complete eradication of measurable tumor
- *Partial Response* = $\geq$ 50% reduction in measurable tumor
- *Progressive Disease* = $\geq$ 25% growth in measurable tumor
- *Stable Disease* = anything between partial response and progressive disease

Note: response rate data that are generally quoted to patients comes from clinical trials involving closely monitored patients with good performance statuses. The response rates for patients outside of clinical trials can be expected to be lower – See *Fast Fact* # 99.

2. What is the *Median Duration of Response* of the proposed chemotherapy regimen? This number is vital for patients to make an informed decision and roughly correlates to months of added life to be expected if the chemotherapy is effective. The MDR, also known as *Time to Progression* (TTP), can be explained to the patient as: *if the chemotherapy is effective at shrinking or stabilizing your cancer (if you are a chemotherapy responder), you can expect it will work for X-X months.*

3. What is the potential treatment burden? Including acute and delayed toxicities, direct and indirect costs (lost work for family members), need for clinic visits or inpatient stays, need for treatment monitoring (e.g. blood tests, x-rays). See *Fast Facts* # 276 and 277 for a discussion of the role of targeted cancer therapies in limiting the potential treatment burden.

4. How long must treatment be continued? Standard practice is to wait for two full cycles of treatment before assessing response. However, if a patient is progressing during the first cycle, they will almost always continue to progress through a second cycle. For responding patients, chemotherapy is generally continued until there is disease progression or intolerable toxicities.

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FAST FACTS AND CONCEPTS #112
IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS AT END-OF-LIFE
Harrington MD, Luebke DL, Lewis WR, Aulisio MP, Johnson NJ

Background
Recent clinical trials and advances in device technology have expanded the indications for implantation of cardiac devices. According to 2011 data published by the ICD Registry, more than 12,000 implantable cardioverter-defibrillators (ICDs) implantations were reported to them from US hospitals per month. It is estimated that over 3 million patients in North America could now be eligible for an ICD, with over 400,000 additional patients meeting the criteria every year. However, near the end of life, decisions as to how best to use these devices can be the source of much anguish for patients, families and palliative care/hospice staff.

Current Devices
ICDs are somewhat larger than pacemakers and are usually implanted in the upper chest under the clavicle. They monitor cardiac rhythm and can either cardiovert or defibrillate (electrically 'shock' a heart) when certain rapid abnormal cardiac rhythms are identified. These shocks can be painful and are inconsistent with comfort care in a dying patient. ICDs can also deliver pacing therapy. Pacing increases heart rate when slow heart rhythms are detected and can promote comfort as slow heart rhythms can cause heart failure symptoms. The shocking and pacing functions of an ICD can be independently turned off and a decision to discontinue a device's ICD function should be considered separately from a decision to discontinue its pacing functions (see *Fast Fact* #111 about discontinuation of pacemakers).

Indications for deactivation of ICD therapy
- Continued use of an ICD is inconsistent with patient goals.
- Withdrawal of anti-arrhythmic medications: if anti-arrhythmic medications are withdrawn consider turning off the ICD to avoid frequent shocks.
- Imminent death.
- The patient has a DNR order. The functioning of an ICD is generally inconsistent with a 'Do-Not-Resuscitate' order since ICDs attempt to resuscitate the patient by shocking their hearts back into a life-sustaining rhythm.

Discussing deactivation of the ICD
1. Consult the clinician who manages the ICD (usually a cardiologist or associated clinician); that individual is often the person to assume responsibility for deactivation. Patients are usually followed in a device clinic and probably have an established relationship with the physician and staff. The involvement of these professionals can provide a sense of comfort and closure for the patient and family. Note: The device manufacturers will not send representatives to patient's homes for deactivation.
2. Discuss expectations of "turning off" the ICD. The following should be made clear:
    a. Turning off the ICD means that the device will no long provide life-saving therapy in the event of a ventricular tachyarrhythmia.
    b. Turning off the ICD will not cause death.
    c. Turning off the ICD will not be painful, nor will its failure to function cause pain.
3. Establish a plan of care that will ensure availability for addressing new questions or concerns that might arise (patient/family should not feel abandoned once the device is turned off).
4. If there are conflicts among providers or family members, consultation with a palliative care expert or ethics team can be helpful.

Ethical/Legal issues
A patient's right to request withdrawal of life sustaining medical interventions, including ICDs, is both legal and ethical. Withdrawal of a life sustaining medical intervention with the informed consent of a patient or legal surrogate is not physician-assisted suicide or euthanasia.

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FAST FACTS AND CONCEPTS #269
DEACTIVATION OF A LEFT VENTRICULAR ASSIST DEVICE AT THE END-OF-LIFE
Ellin F Gafford MD, Angela J Luckhardt RN, CNS, and Keith M Swetz MD, MA

Introduction The increased use of left ventricular assist devices (LVADs) is expected, particularly as destination therapy for patients with advanced heart failure who are not transplant candidates. *Fast Fact* #205 discusses LVAD technology in general. This *Fast Fact* discusses important considerations at the time of LVAD deactivation. **Note:** published clinical outcomes with LVAD therapy have improved further after the initial publication of *Fast Fact* #205, please refer to the updated version of #205 for current information (1). A general review of contemporary LVAD management, including images regarding common devices currently in use can be found in Reference (2). *Fast Fact* # 296 addresses palliative care issues regarding total artificial hearts.

Common clinical scenarios leading to LVAD deactivation Clinical situations leading to LVAD deactivation include catastrophic complications of the LVAD (e.g. stroke, sepsis and multiorgan failure); poor quality of life despite LVAD treatment (e.g. chronic infections, intolerance of or a decision to forego hemodialysis); and developing serious secondary comorbidities (e.g. cancer, dementia) (3, 4). As with other life-sustaining treatments, patients may request withdrawal of life-sustaining treatments that are no longer consistent with their goals of care.

Important Process Steps in Deactivating LVADs

- Since part of the device is implanted within the patient, an LVAD is 'turned-off,' akin to deactivating an implantable defibrillator. However, LVADs have an external power source and associated controlling unit which are removed from a patient, analogous to removing a ventilator.
- The process regarding LVAD deactivation should be clearly outlined and understood by those who are participating. Any patient/family or professional ethical concerns should be addressed. Families and loved ones should have ample opportunities for visitation. *Family members' presence can be based on patient preferences, and a description of what can be expected should be shared.*
- DNR and DNI status should be confirmed and documented in the chart and orders, as well as the goals of care and overall medical plan of care.
- Survival after LVAD deactivation at the end-of-life ranges from a few minutes to a few days (5). Providers should carefully explain this variability to families as it can be upsetting if a patient lives *longer* or *shorter* than what family expects.
- Many patients will also be on other forms of life-sustaining treatments such as renal replacement therapy, vasopressors, tube feeds, implantable cardioverter-defibrillators (see *Fast Fact* #112), and mechanical ventilation that generally should be discontinued at the time of LVAD deactivation. Once the care goals are clear, it is usually best to make direct recommendations to the patient/family about the medical plan of care including what treatments should be stopped, as opposed to asking families treatment-by-treatment what they want done. Families should be reassured that patients can be kept comfortable without such treatments.
- All non-symptom-directed monitoring should be discontinued.

Practical LVAD Deactivation Tips

- Clinicians should think of LVAD deactivation as analogous to ventilator withdrawal. They should be prepared to prevent and treat the potentially rapid onset of dyspnea/labored respirations, agitation, or other signs of discomfort. Pharmacologic principles are similar to ventilator withdrawal – see *Fast Facts* # 33, 34.
- Work closely with the individuals in your institution responsible for LVAD management, such as the LVAD nurse coordinators. There are many different LVAD models which have different steps in their deactivation.
- Familiarity with the alarm functions of LVAD devices, and how to turn them off, is critical to prevent unsettling alarming during what is hoped to be a peaceful and intimate process for patients and loved ones. Tips to deactivate the alarms for the HeartMate II device, one of the most commonly implanted adult LVAD devices today, are included in the box below.
- Once the LVAD is deactivated, cardiovascular circulation may greatly diminish. Therefore, clinicians should strongly consider bolusing with comfort medications *prior* to deactivation to ensure adequate

circulation of the drugs. Due to diminished drug circulation, the time to peak effect of an opioid or benzodiazepine bolus may be delayed after LVAD discontinuation.

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Box: Basic Deactivation Sequence Checklist for HeartMate II LVAD

a. Unscrew small black nickel-sized battery in “System Driver” (also called controller) to disable back-up alarms.
b. Press alarm silence button on controller.
c. Remove power from controller by removing both cables coming from the main power base unit (simultaneous removal of both cables will limit alarms).
d. Detach controller from patient (cord going from LVAD driveline exiting patient to the controller).

If deactivation occurs sequentially and not simultaneously, there is the risk of the device alarming due to low power or low flow, which can be distressing to families.

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FAST FACTS AND CONCEPTS #266
CONSULTATION ETIQUETTE IN PALLIATIVE CARE
Charles F von Gunten MD, PhD and David E Weissman MD

Background There are generally agreed upon rules for consultation (just as there are in social life) that can have profound consequences if they are breached. For those just starting to provide consultation services, it is wise to follow the rules until you develop enough familiarity to know when they can be breached. This *Fast Fact* reviews the rules of consultation etiquette for palliative care (PC) clinicians. See *Fast Fact* #298 for more specific guidance on PC consultation in the Emergency Department.

1) Remember your stakeholders. Although the focus of the consultation is a patient/family issue, your primary stakeholder is the attending physician that requested the consultation. Unhappy referring physicians mean fewer palliative care consultations!

2) Make contact/clarify request. Before you see the patient, contact the referring service to acknowledge that you received the request and to clarify the nature of the request. Determine what questions the managing service wants answered. The phrasing of this is important. '*Please tell me a little about Patient X so we can be most helpful to you'* is an excellent open-ended query. Determine if there are areas that are "off-limits" and find out who the consulting team should talk with following your assessment – the referring clinicians or someone else on the care team. Remember, no matter what is written in the chart, the real story exceeds what is written, and the referring clinicians often have concerns/needs that are not evident from the chart. Particularly for palliative care consultations, this has an important secondary importance; in telling you about the patient, the service will receive emotional support in the telling the story. Be quiet and actively listen; acknowledge the underlying distress. **Cultural corollary:** in *some* institutions the rank of the person calling should match or exceed the rank of the person called. Strictly applied, for instance, an attending speaks to an attending. This is not true of all institutions or physicians, but it is wise to know your local culture. When in doubt, or conflict occurs, following the cultural corollary of your institution connotes respect.

3) Negotiate roles. Many referring clinicians will want the palliative care service to play an ongoing role in the management of the patient and family. This may range from providing information and counseling, to actively managing symptoms including writing medication orders, to assuming principal care for the patient and family. Others will want the palliative care service to maintain a strictly consulting role while the primary service implements recommendations.

4) See the patient & gather your own data. This includes reviewing the medical record, pertinent laboratory and diagnostic tests, interviewing the patient and family, examining the patient, and offering information and counseling if that was part of the nature of the request.

5) Call the referring service. Before you write in the chart, call the referring service with details of your findings and recommendations. With experience and familiarity with frequent referrers, this step may not be necessary. If appropriate, contact other consultants and clinicians involved with the patient (housestaff, nurses, discharge planners, etc.).

Additional Tips

- **Brevity** (in general, try to limit your recommendations to $\leq$ 5) and **specificity** (e.g., exact morphine dose/route/schedule) are important to both communicate your key messages and increase the likelihood that your recommendations will be acted upon.
- **Plan ahead** – you are often in the best position to recognize likely future needs beyond the hospitalization; plan ahead to meet expected symptom control and other patient/family needs. Helping to expedite and simplify patient discharge is an easy and high-yield way of demonstrating your service's value to referring clinicians.
- **Honor turf** – you may be one of many consultants; when in doubt about the expectations and plans of the referring clinician, clarify by personal contact.
- **Be accessible** – a referring physician or service needs to know how to reach you easily. He or she will be put off if they can't reach your service. Indicate how you can be reached in your consult note.

- **Be responsive** – acknowledge receipt of the request as immediately as possible and plan to see the patient the same day or within 24 hours. If unable to do this, contact the referring clinician directly to discuss.

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FAST FACTS AND CONCEPTS #267
WRITING THE CONSULATION NOTE
Charles F von Gunten MD, PhD and David E Weissman MD

Background Documentation the consultation serves to: a) communicate your findings, b) document the service you provided and c) support your coding and billing activity. In *Fast Fact* # 266, the basic principles of consultation ettiquete were reviewed as they apply to palliative care clinicians. This *Fast Fact* reviews key elements of the palliative care consutation note.

1) Reason for Consultation *I was asked to see this 87 year old man for problems related to shortness of breath and setting goals-of-care by Dr. Bligh.* An older etiquette form that is appreciated is to begin the consultation note with the phrase: *Thank you for asking me to see this….*

2) Summarize the Case, including your activities

- I have reviewed the medical record and the chest radiographs, interviewed the patient and family, and examined the patient. The following aspects are pertinent:
- Pertinent Current and Past History
- Pertinent Social/Family/Spiritual History
- Pertinent Medications and their effects
- Pertinent Review of Systems
- Pertinent Examination Findings
- Pertinent lab/x-ray/pathology
- Prognosis/Advance care planning/Goal setting information

3) Your Assessment Clearly and prominently indicate your assessment. This is where those who want to know "the bottom line" will look first. It is common practice in some institutions to put your assessment and recommendations at the very top of the note for readability. Encapsulate the case from your point of view. This should be as concise as possible, however it should contain adequate accounting of your medical decision making, particularly if your discussion could be surprising or unfamiliar to other clinicians (e.g., hospice eligibility in 'borderline' cases, opioid hyperalgesia).

- *This 87 year old man has dyspnea due to a combination of COPD and metastatic adenocarcinoma of the lung. He understands his diagnosis and prognosis. He and his wife made it quite clear that they do not want to suffer and would like to be cared for at home. They would like no heroic or extraordinary measures used to keep him alive. They agree to a hospice plan of care.*

4) Recommendations Number, bullet, and/or **bold** your recommendations; don't bury them in a dense paragraph. Be as specific as possible with recommendations and avoid vague statements like "start morphine for dyspnea."

1. *Initiate oral morphine 5 mg po q 1h to relieve dyspnea*
2. *Initiate dexamethasone 8 mg orally q am to diminish inflammation and add to relief of dyspnea*
3. *Enter a DNR order in the chart and give the patient documentation to take with him at discharge.*
4. *Refer the patient to Pershing Hospice which serves the area where he lives. Their telephone number is 111-222-2222. We would be happy to arrange this if you would like.*

5) Closure Indicate with whom you have discussed the recommendations and your plan for following-up the patient; conclude with the conventional etiquette.

- *I have discussed these recommendations with Dr. Bligh who concurs. Further, I have discussed my findings with the housestaff, nursing and social work staff caring for this gentleman.*
- *Dr. Bligh has asked us to continue to follow this patient during his hospitalization to supervise titration of morphine and to continue to provide counseling and information. If you need us, it is best to contact our nurse, Betty Blythe, RN at 444-4444,*
- *Thank you for permitting us to participate in the care of this patient.*

6) Signature Clearly indicate your name and a way that the service can contact you.

- *Charles Feelbetter, MD; Office 333-3333; Pager 111-1111*

7) Coding and Billing For coding and billing purposes, if you are using time to justify the level of coding, you should include start/stop times of your face to face patient contact (see *Fast Fact* #48).

- *I spent a total of 90 minutes on this consultation. 50 minutes of this time was spent in counseling and information giving to the patient and his wife, starting at 1530 and ending at 1620.*

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