

PART I: PHYSIOLOGICAL CHANGES AND SYMPTOM MANAGEMENT DURING THE DYING PROCESS

As a person dies, many different physiological changes present as signs and symptoms. Each one can be alarming if it is not understood. To control each symptom effectively, physicians need to have an understanding of:

- The symptom's cause
- The underlying pathophysiology
- The appropriate pharmacology to use

Commonly encountered physiological changes during the dying process include:

- Weakness/Fatigue
- Decreasing Appetite/Food Intake, Wasting
- Decreasing Fluid Intake, Dehydration
- Decreasing Blood Perfusion, Renal Failure
- Neurological Dysfunction: An Overview
 - Decreasing Level of Consciousness
 - Terminal Delirium
 - Changes in Respiration
 - Loss of Ability to Swallow
 - Loss of Sphincter Control
- Pain
- Loss of Ability to Close Eyes
- Changes in Medication Needs

Weakness/Fatigue: Signs and Symptoms

- Weakness and fatigue usually increase as the patient gets closer to death
- In the last hours of life, it is likely that the patient will not be able to move around in the bed or raise his or her head
- Joints may become uncomfortable if they are not moved
- Continuous pressure on the same area of skin, particularly over bony prominences, will increase the risk of skin ischemia and the development of pressure ulcers
 - These may become painful or odoriferous if they become infected
 - They are more easily prevented than treated (see Module 10: Common Physical Symptoms)

Weakness/Fatigue: Management

- At the end of life, fatigue need not be resisted and most treatment to alleviate it can be discontinued
- Patients who are too fatigued to move and have joint position fatigue may require passive movement of their joints every 1 to 2 hours
- To minimize the risk of pressure ulcer formation:
 - Turn the patient from side to side every 1 to 1.5 hours
 - Protect areas of bony prominence with hydrocolloid dressings and special supports
 - A draw sheet can assist caregivers to turn the patient and minimize pain and shearing forces to the skin
 - If turning is painful, consider a pressure-reducing surface (air mattress or airbed)
 - As the patient approaches death, the need for turning lessens as the risk of skin breakdown becomes less important
- Intermittent massage before and after turning, particularly to areas of contact, can both
 - Be comforting
 - Reduce the risk of skin breakdown by improving circulation and shifting edema
- Avoid massaging areas of erythema or actual skin breakdown

Decreasing Appetite/Food Intake, Wasting: Signs and Symptoms

- Most patients lose their appetite and reduce food intake long before they reach the last hours of their lives
- There are many causes, most of which become irreversible close to death (see Module 10: Common Physical Symptoms)
- Families and professional caregivers often:
 - Interpret cessation of eating as "giving in"
 - Worry that the patient will "starve to death"

Decreasing Appetite/Food Intake, Wasting: Management of Family Concerns

- Physicians can help families understand that loss of appetite is normal at this stage. Remind them that:
 - The patient is not hungry
 - Food either is not appealing or may be nauseating
 - The patient would likely eat if he or she could
 - Clenching of teeth may be the only way for the patient to express desires
- Educate families about the studies that demonstrate that parenteral or enteral feeding of patients at the end of their lives neither improves symptom control or lengthens life
- Help them to understand that anorexia may be protective, as the resulting ketosis can lead to a greater sense of well being and diminish pain
- Whatever the degree of acceptance of these facts, it is important for physicians to help families and caregivers realize that food pushed upon the unwilling patient may cause problems (e.g., aspiration) and increase tensions
- Above all, help them to find alternate ways to provide appropriate physical care and emotional support to the patient so that they can continue to participate and feel valued during the dying process

Dehydration: Signs and Symptoms

- Most patients also reduce their fluid intake, or stop drinking entirely, long before they die
- If they are still taking some fluid but are not eating, salt-containing fluids such as soups, soda water, sport drinks, and red vegetable juices can:
 - Help to maintain electrolyte balance
 - Minimize the risk of nausea from hyponatremia
- Decreased fluid intake usually heightens onlookers' distress as they worry that the dehydrated patient will suffer, particularly if he or she becomes thirsty

Dehydration: Management

- As with feeding, families and professional caregivers will need support to understand that this is an expected event. It may help families to understand that:
 - Most experts in the field feel that dehydration in the last hours of living
 - Does not cause distress
 - May stimulate endorphin release that adds to the patient's sense of well being
 - Low blood pressure or weak pulse is part of the dying process and not an indication of dehydration
 - Patients who are not able to move off the bed do not get light-headed or dizzy
 - Patients with peripheral edema or ascites have excess body water and salt and are not dehydrated
- Parenteral fluids, either intravenously or subcutaneously using hypodermoclysis, are sometimes considered, particularly when the goal is to reverse delirium. However, parenteral fluids may have adverse effects that are not commonly considered:
 - Intravenous lines can be cumbersome and difficult to maintain
 - Moving the angiocatheter can be uncomfortable, particularly if the access site needs to be changed frequently and the patient is cachectic or has no veins
 - Excess parenteral fluids can lead to fluid overload with consequent peripheral or pulmonary edema, worsened breathlessness, cough, and orotracheobronchial secretions, particularly if there is significant hypoalbuminemia
 - They also have the potential to prolong the dying process, which may be undesirable

Dehydration: Mucosal/Conjunctival Care

- To maintain patient comfort and minimize the sense of thirst, even in the face of dehydration, maintain moisture in mucosal membranes with meticulous oral, nasal and conjunctival hygiene
- Moisten and clean oral mucosa every 15 to 30 minutes with either baking soda mouthwash (1 teaspoon salt, 1 teaspoon baking soda, 1 quart tepid water) or an artificial saliva preparation to minimize the sense of thirst and avoid bad odors or tastes and painful cracking
- Treat oral candidiasis with topical nystatin or systemic fluconazole (if the patient is able to swallow)
- Coat lips and anterior nasal mucosa hourly with a thin layer of petroleum jelly to reduce evaporation
- Avoid perfumed lip balms and swabs containing lemon and glycerin, as these can be both desiccating and irritating, particularly on open sores
- If eyelids are not closed, moisten conjunctiva with an ophthalmic lubricating gel every 3 to 4 hours, or artificial tears or physiological saline solution every 15 to 30 minutes to avoid painful dry eyes

Decreasing Blood Perfusion, Renal Failure

- As cardiac output and intravascular volume decrease toward the end of life, there will be evidence of diminished peripheral blood perfusion
- Normal symptoms include:
 - Tachycardia
 - Hypotension
 - Peripheral cooling
 - Mottling of the skin (livedo reticularis)
 - Venous blood may pool along dependent skin surfaces
 - Urine output falls as perfusion of the kidney diminishes
 - Oliguria or anuria
- Parenteral fluids will not reverse this circulatory shut down

Overview of Neurological Dysfunction in the Dying Process

- The neurological changes associated with the dying process are the result of multiple concurrent nonreversible factors, including:
 - Hypoxemia
 - Metabolic imbalance
 - Acidosis
 - Toxin accumulation due to liver and renal failure
 - Adverse effects of medication
 - Sepsis
 - Disease-related factors
 - Reduced cerebral perfusion
- The neurological changes associated with the dying process may manifest in 2 different patterns that have been described as the "two roads to death"

1) The "usual road" that most patients follow presents as decreasing level of consciousness that leads to coma and death

2) The "difficult road" that a few patients follow presents as an agitated delirium due to CNS excitation, with or without myoclonic jerks that leads to coma and death. Based on clinical observation, it is likely that the risk of focal or grand mal seizures is increased along the "difficult road", particularly when cerebral metastases are present

Decreasing Level of Consciousness: Signs and Symptoms

- The majority of patients traverse the "usual road to death"
- They experience increasing drowsiness, sleep most if not all of the time, and eventually become unrousable
- Absence of eyelash reflexes on physical examination indicates a profound level of coma equivalent to full anesthesia

Decreasing Level of Consciousness: Management (Communication with the Unconscious Patient)

1. Plan ahead to reduce family distress

- Families will frequently find that their decreasing ability to communicate is distressing
- The last hours of life are the time when they most want to communicate with their loved one
- As many clinicians have observed, the degree of family distress seems to be inversely related to the extent to which advance planning and preparation occurred
- Time spent preparing families is likely to be very worthwhile

2. Assume the unconscious patient can hear everything

- While we do not know what unconscious patients can actually hear, experience suggests that at times their awareness may be greater than their ability to respond
- Given our inability to assess dying patient's comprehension and the distress that talking "over" the patient may cause, it is prudent to presume that the unconscious patient hears everything
- Advise families and professional caregivers to talk to the patient as if he or she was conscious

3. Encourage families to create an environment that is familiar and pleasant

- Surround the patient with the people, children, pets, things, music, and sounds that he or she would like
- Include the patient in everyday conversations
- Encourage family to say the things they need to say
- At times, it may seem that a patient may be waiting for permission to die
 - If this is the case, encourage family members to give the patient permission to "let go" and die in a manner that feels most comfortable to them
 - The physician or other caregivers might suggest to family members other words like:
 - "I know that you are dying, please do so when you are ready"
 - "I love you. I will miss you. I will never forget you. Please do what you need to do when you are ready"
 - "Mommy and Daddy love you. We will miss you, but we will be OK"
- As touch can heighten communication:
 - Encourage family members to show affection in ways they are used to
 - Let them know that it is okay to lie beside the patient in privacy to maintain as much intimacy as they feel comfortable with

Terminal Delirium: Signs and Symptoms

- Delirium may be the first sign to herald the "difficult road to death"
- It frequently presents as confusion, restlessness, and/or agitation, with or without day-night reversal
- It may result from any of the standard causes of delirium listed in DSM-IV (American Psychiatric Association, 1994) that can accompany the dying process
- Agitated terminal delirium can be very distressing to family and professional caregivers who do not understand it
- Although previous care may have been excellent, if the delirium goes misdiagnosed or unmanaged, family members will likely remember a horrible death "in terrible pain" and may worry that their own death will be the same

Terminal Delirium: Aspects of Management

1. Prepare Family/Caregivers

- In anticipation of the possibility of terminal delirium, educate and support family and professional caregivers to understand:
 - The causes of terminal delirium
 - The finality and irreversibility of the situation
 - Approaches to its management
 - That what the patient experiences may be very different from what onlookers see

2. Treat underlying causes only if death is NOT imminent

- If delirium presents and the patient is not perceived to be actively dying, it may be appropriate to evaluate and try to reverse treatable contributing factors
 - However, if the patient is close to the last hours of his or her life, this is only effective in a minority of cases
 - Standard approaches to managing delirium are discussed in Module 6: Anxiety, Delirium, Depression
- If death is imminent, it will not be possible to reverse the underlying causes. Focus on:
 - The management of the symptoms associated with the terminal delirium
 - Settling the patient and the family

3. Use Opioids with Caution

- When moaning, groaning, and grimacing accompany agitation and restlessness, they are frequently misinterpreted as pain
- However, it is a myth that pain suddenly develops during the last hours of life when it has not previously been out of control
- While a trial of opioids may be beneficial in the unconscious patient who is difficult to assess, physicians must remember that opioids may accumulate and add to delirium when renal clearance is poor
- If the trial of increased opioids does not relieve the agitation or makes the delirium worse by increasing agitation or precipitating myoclonic jerks or seizures (rare), then pursue alternate therapies directed at suppressing the symptoms associated with the delirium

4. Medication Management of Delirium

- **Benzodiazepines** are used widely as they are anxiolytics, amnestics, skeletal muscle relaxants, and antiepileptics
 - Oral lorazepam 1–2 mg as an elixir or the tablet predissolved in 0.5–1.0 ml of water and administered against the buccal mucosa q 1h prn will settle most patients with 2–10 mg/24 hours. It can then be given in divided doses, q 3–4h to keep the patient settled
 - For a few extremely agitated patients, high doses of lorazepam 20–50+ mg/24 hours, may be required
 - A midazolam infusion of 1–5 mg SC or IV q 1h, preceded by repeated loading boluses of 0.5 mg q 15min to effect, may be a rapidly effective alternative
- **Neuroleptic medications** may be required to control delirium for patients for whom benzodiazepines prove excitatory and not have the desired settling effect
 - Haloperidol (0.5–2.0 mg q hs to q 6h to start and titrated) given intravenously, subcutaneously, or rectally may be effective
 - Chlorpromazine (10–25 mg PO q hs to q 6h to start and titrated), given intravenously or rectally, is a more sedating alternative
- Seizures may be managed with high doses of benzodiazepines. Other antiepileptics such as phenytoin PR or IV, fosphenytoin SC, or phenobarbital 60–120 mg PR, IV, or IM q 10–20min prn may become necessary until control is established

Changes in Respiration: Signs and Symptoms

- Changes in a dying patient's breathing pattern may be indicative of significant neurological compromise
- Breaths may become very shallow and frequent with a diminishing tidal volume
- Periods of apnea and/or Cheyne-Stokes pattern respirations may develop
- Accessory respiratory muscle use may become prominent
- A few (or many) last reflex breaths may signal death
- Families and professional caregivers may frequently:
 - Find changes in breathing patterns to be one of the most distressing signs of impending death
 - Fear that the comatose patient will experience a sense of suffocation

Changes in Respiration: Management

- Educate and support family and caregivers, helping them to understand that:
 - The unresponsive patient may not be experiencing breathlessness or "suffocating"

- Oxygen may actually prolong the dying process
- Low doses of opioids or benzodiazepines are appropriate to manage any perception of breathlessness (see Module 10: Common Physical Symptoms)

Loss of Ability to Swallow: Signs and Symptoms

- In the last hours of life, weakness and decreased neurological function frequently impair the patient's ability to swallow
- The gag reflex and reflexive clearing of the oropharynx decline and secretions from the tracheobronchial tree accumulate
- These conditions may become more prominent as the patient loses consciousness
- Buildup of saliva and oropharyngeal secretions may lead to gurgling, crackling or rattling sounds with each breath
 - Some have called this the "death rattle" (a term frequently disconcerting to families and caregivers)
 - For unprepared families and professional caregivers, it may sound like the patient is choking

Loss of Ability to Swallow: Management

1. Cease oral intake

- Once the patient is unable to swallow, cease oral intake
- Warn families and professional caregivers of the risk of aspiration

2. Reduce saliva and secretion production

- Use of medications to reduce the production of saliva and other secretions:
 - Will minimize or eliminate the gurgling and crackling sounds, and
 - May be used prophylactically in the unconscious dying patient
- Anecdote suggests that the earlier treatment is initiated, the better it works, as larger amounts of secretions in the upper aerodigestive tract are more difficult to eliminate
- However, premature use in the patient who is still alert may lead to unacceptable drying of oral and pharyngeal mucosa
- Recommended medications and dosages include:
 - Scopolamine 0.2–0.4 mg SC q 4h or 1–3 transdermal patches q 72h or 0.1–1.0 mg/h by continuous IV or SC infusion
 - Glycopyrrolate 0.2 mg SC q 4–6h or 0.4–1.2 mg/day by continuous IV or SC
 - While atropine may be equally effective, it has an increased risk of producing undesired cardiac and/or CNS excitation

3. Use repositioning to clear accumulated fluids

- If excessive fluid accumulates in the back of the throat and upper airways, it may need to be cleared by repositioning the positioning or postural drainage
- Turning the patient onto one side or a semiprone position may reduce gurgling
- Lowering the head of the bed and raising the foot of the bed while the patient is in a semi-prone position may cause fluids to move in the oropharynx from which they can be easily removed
- Do not maintain this position for more than a few minutes at a time as stomach contents may also move unexpectedly

4. Avoid suctioning

- Oropharyngeal suctioning is not recommended
- It is frequently ineffective as fluids are beyond the reach of the catheter
- Suctioning may have only undesirable effects, such as:
 - Stimulating an otherwise peaceful patient
 - Causing distress for family members who are watching

Loss of Sphincter Control: Signs and Symptoms

- Fatigue and loss of sphincter control in the last hours of life may lead to incontinence of urine and/or stool
- Both can be very distressing to patients and family members, particularly if people are not warned in advance that these problems may arise

Loss of Sphincter Control: Management

- If incontinence occurs, attention needs to be paid to cleaning and skin care
- A urinary catheter may:
 - Minimize the need for frequent changing and cleaning
 - Prevent skin breakdown
 - Reduce the demand on caregivers
- However, catheterization is not always necessary if urine flow is minimal and can be managed with absorbent pads or surfaces
- If diarrhea is considerable and relentless, a rectal tube may be similarly effective

Pain: Signs and Symptoms

- While many fear that pain will suddenly increase as the patient dies, there is no evidence to suggest this occurs
- Though difficult to assess, continuous pain in the semiconscious or obtunded patient may be associated with:
 - Grimacing and continuous facial tension, particularly across the forehead and between the eyebrows
 - Physiologic signs, such as transitory tachycardia, that may signal distress
- Do not over-diagnose pain when fleeting forehead tension comes and goes with movement or mental activity (e.g., dreams or hallucinations)
- Do not confuse pain with the restlessness, agitation, moaning, and groaning that accompany terminal delirium
- If the diagnosis is unclear, a trial of a higher dose of opioid may be necessary to judge whether pain is driving the observed behaviors

Pain: Management

- Knowledge of opioid pharmacology becomes critical during the last hours of life
- The liver conjugates codeine, morphine, oxycodone, and hydromorphone into glucuronides
 - Some of their metabolites remain active as analgesics until they are renally cleared, particularly morphine
 - As dying patients experience diminished hepatic function and renal perfusion, and usually become oliguric or anuric, routine dosing or continuous infusions of morphine may lead to:
 - Increased serum concentrations of active metabolites
 - Toxicity
 - Increased risk of terminal delirium
- To minimize this risk:
 - Discontinue routine dosing or continuous infusions of morphine when urine output and renal clearance stops
 - Titrate morphine breakthrough (rescue) doses to manage expressions suggestive of continuous pain
 - Consider the use of alternative opioids with inactive metabolites
 - Fentanyl
 - Hydromorphone

Loss of Ability to Close Eyes: Signs and Symptoms

- Advanced wasting leads to loss of the retro-orbital fat pad, and the orbit falls posteriorly within the orbital socket
- As eyelids are of insufficient length to both extend the additional distance backward and cover the conjunctiva, they may not be able to fully appose
- This may leave some conjunctiva exposed even when the patient is sleeping
- Eyes that remain open can be distressing to onlookers unless the condition is understood

Loss of Ability to Close Eyes: Management

- If conjunctiva remains exposed, maintain moisture by using ophthalmic lubricants, artificial tears, or physiological saline as previously discussed

Changes in Medication Needs

- As patients approach the last hour of their lives, reassess the need for each medication and minimize the number that the patient is taking
- Leave only those medications to manage symptoms such as pain, breathlessness, excess secretions, and terminal delirium and reduce the risk of seizures
- Choose the least invasive route of administration:
 - The buccal mucosa or oral routes first
 - The subcutaneous or intravenous routes only if necessary
 - The intramuscular route almost never

National Cancer Institute grant (R25 CA76449) to Sara J. Knight, Ph.D., at the Robert H. Lurie Comprehensive Cancer Center provided the funding for the development of this program. This material was adapted from the EPEC project (Education for Physicians on End-of-life Care).