Pediatric Palliative Care

Jeffrey C. Klick, MD,[a] and Julie Hauer, MD[b]

Palliative care has always been a part of the care of children. It includes any intervention that focuses on relieving suffering, slowing the progression of disease, and improving quality of life at any stage of disease. In addition, for even the child with the most unpredictable disease, there are predictable times in this child's life when the child, family, and care team will be suffering in ways that can be mitigated by specific interventions.

Rather than defining pediatric palliative care in terms of a patient base, severity of disease, or even a general philosophy of care, palliative care can best be understood as a specific set of tasks directed at mitigating suffering. By understanding these tasks; learning to identify predictable times and settings of suffering; and learning to collaborate with multidisciplinary specialists, use communication skills, and identify clinical resources, the pediatrician can more effectively support children with life-threatening illnesses and their families.

In this article, we define palliative care as a focus of care integrated in all phases of life and as a set of interventions aimed at easing suffering associated with life-threatening conditions. We detail an approach to these interventions and discuss how they can be implemented by the pediatrician with the support of specialists in hospice and palliative medicine. We discuss common and predictable times of suffering when these interventions become effective ways to treat suffering and improve quality of life. Finally, we discuss those situations that pediatricians most commonly and intensely interface with palliative care—the care of the child with complex, chronic conditions and severe neurologic impairment (SNI).

Curr Probl Pediatr Adolesc Health Care 2010;40:120-151

Palliative care has always been a part of the care of children. Whether we are talking about end-of-life care, effective pain prevention and management, or communication and decision-making in difficult circumstances, the pediatrician is asked to help children and families with palliative tasks daily. While all pediatricians have a knowledge base and skill set in these situations, everyone's abilities are challenged in some of the extreme situations often identified as part of palliative care. In these situations, fostering a more developed understanding of the principles and tasks associated with pediatric palliative care can help us relieve suffering and help find a better quality of life for the child, family, and even the practitioners caring for them.

Pediatric palliative care can best be understood as a specific set of tasks directed at mitigating suffering.

Approximately 55,000 infants, children, and adolescents die each year in the USA of complications of prematurity, congenital defects, injuries, malignancies, and a wide variety of other illnesses.[1,2] Tens of thousands of others live with chronic, life-threatening conditions that may result in death before they reach adulthood. Of these children, most will die in a hospital, with a large proportion cared for in a hospital during the days or weeks before their deaths.[3] These children and their families are at very high risk for suffering.

Traditionally, however, care for these children and their families has been focused on the cure of disease or the restoration of health status. While this focus is clearly an indispensable approach, they also deserve care to ensure that the children are as comfortable as possible and that their families receive the support and guidance

From [a]The University of Pennsylvania School of Medicine, Pediatric Hospice and Palliative Medicine, Division of General Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania; and the [b]Division of Pediatric Palliative Care, Dana-Farber Cancer Institute, Boston, Massachusetts.

Curr Probl Pediatr Adolesc Health Care 2010;40:120-151
1538-5442/$ - see front matter

doi:10.1016/j.cppeds.2010.05.001

necessary to make decisions, cope, and maintain family functioning. They deserve effective, timely, and compassionate palliative care.

The World Health Organization (WHO) defines palliative care as "the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social, and spiritual problems is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families." Many clinicians also consider the principles and tasks of palliative care as a viable part of the care of any child with a life-threatening illness and their family; care that should be initiated at the time of diagnosis, offered in conjunction with treatments of curative intent, and continue throughout the illness and even after the child dies in supporting the family in bereavement. In 2000, the American Academy of Pediatrics supported this approach to care by stating that "the components of palliative care are offered at diagnosis and continued throughout the course of illness, whether the outcome ends in cure or death" and should be available in any setting, including home, hospital, and school.[4] In short, palliative care is about treating suffering and improving quality of life in all phases of life, not about death.

Each phase or period of change presents a challenge . . . and an opportunity to improve that child's, family's, and even the care team's lives by addressing and performing specific interventions.

The practice of palliative care grew out of the hospice movement with a focus on treating the suffering at the end of life. Due to these origins, palliative care has historically been held synonymous with end-of-life care. While these phases of life are clear opportunities for care directed at treating suffering, limiting palliative care interventions to the last stages of life misses a profound number of opportunities to improve the lives of children and their families.

The importance of palliative care in the care of pediatric patients has been emphasized in the Institute of Medicine landmark report, *When Children Die*, which delineated the need for significant improvement in the palliative, end-of-life, and bereavement care received by this population.[5] In 2006, with accreditation of fellowship training programs by the Accreditation Council of Graduate Medical Education, the American Board of Medical Specialties initiated a pathway that has established a subspecialty board of Hospice and Palliative Medicine.

Growing evidence demonstrates that families of children with life-threatening conditions benefit from palliative care.[6-8] Earlier initiation of palliative care and discussions that allow parents to prepare can improve symptom management and quality of life[6,9] and provide a positive benefit to later bereavement.[8] In contrast, patients and families who are poorly prepared tend to choose more aggressive care at the end of life.[6,10] In a study of bereaved family members of adult cancer patients, half indicated that palliative care was provided too late in the disease course, while less than 5% thought palliative care referrals occurred too early.[11]

Palliative care specialists are an invaluable resource in the care of children with life-threatening illnesses and their families. It is important, however, to recognize that the use of palliative care interventions should not be limited to the specialist. By integrating the assessment methods and interventions described in this article in the everyday care of children with life-threatening conditions, the pediatrician can most effectively improve the quality of life of the child, family, and the team taking care of them.

In the remainder of this article, we define palliative care as a focus of care integrated in all phases of life and as a set of interventions aimed at easing suffering associated with life-threatening conditions. We detail an approach to these interventions and discuss how they can be implemented by the pediatrician with the support of specialists in hospice and palliative medicine. We discuss common and predictable times of suffering—physical, emotional, and psychosocial suffering in the child, family, and care providers—when these interventions become effective ways to treat suffering and improve quality of life. Finally, we discuss those situations that pediatricians most commonly and intensely interface with palliative care—the care of the child with complex, chronic conditions and SNI.

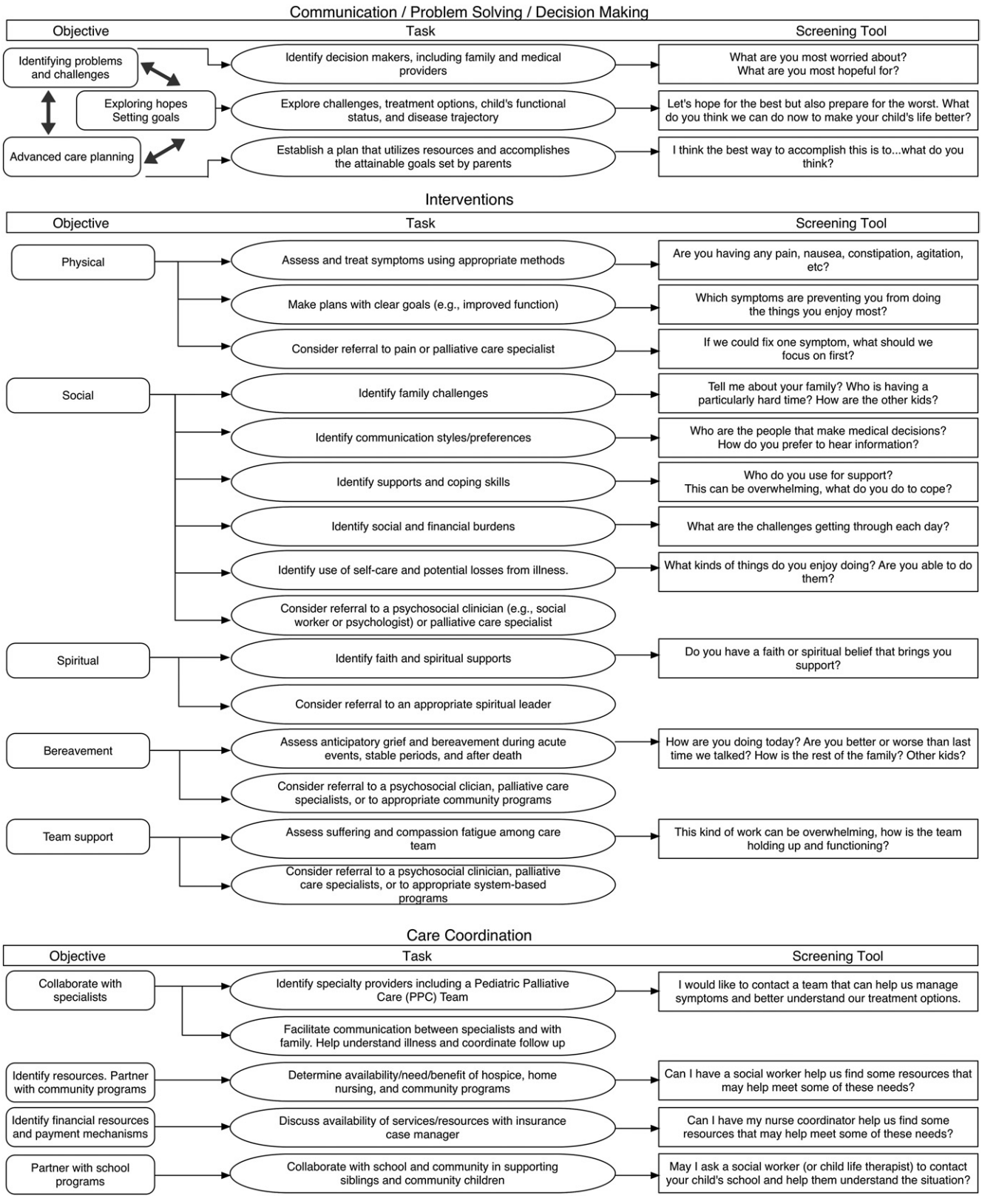

FIG 1. Tasks in pediatric palliative care.

Defining Palliative Care as a Set of Tasks

Pediatric palliative care includes any intervention that focuses on reducing the morbidity of illness, slowing the progression of disease, and improving quality of life at any stage of disease.[12] Rather than defining pediatric palliative care in terms of a patient base, severity of disease, or even a general philosophy of care, pediatric palliative care can best be understood as a specific set of tasks directed at mitigating suffering. By understanding these tasks; learning to identify predictable times and settings of suffering; and learning to collaborate with multidisciplinary specialists, use communication skills, and identify clinical resources, the pediatrician can more effectively support children with life-threatening illnesses and their families.

Figure 1 depicts the specific tasks and goals of palliative care.[5,12-16] As the cornerstone of good palliative care is effective and supportive communication, each task described in the figure is paired with word choices for assessing the child's and family's needs within each task.

Predictable Opportunities to Initiate Palliative Tasks

Consider a child with a metabolic disease. Unfortunately, these diseases are fraught with uncertainty. Sometimes the diagnosis and severity of disease is unclear. The undulating course of illness and unsure prognosis makes predicting the timing of setbacks and ultimate life span difficult, if not impossible. Often most distressing is the inability to predict how ill the child will get with even a simple illness, what will happen with each cough or sneeze, and what the child will have to go through for even a chance of recovery.

There are, however, predictable times in this child's life when the child, family, and care team will be suffering in ways that can be mitigated by specific interventions. Figure 2 is a graphical depiction of the health status of a child with a life-limiting disease. The beginning of the figure represents a child's initial baseline before any decline in health or changes in function. At this time, the child, family, and care team are at the least risk of suffering. Over time, however, this child's health status changes—sometimes acutely during acute illnesses, depicted by A, and sometimes more insidiously, depicted by D.

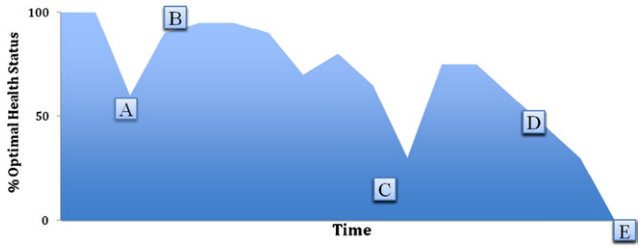

FIG 2. A child's health status over time. (Color version of figure is available online.)

Rather than considering the general life-trajectory as a whole, recognize that each phase or period of change presents a challenge to the child, family, and care team. At these times there is a higher risk of suffering. There is also an opportunity to improve that child's, family's, and even the care team's lives by addressing and performing specific interventions. When caring for children with life-threatening conditions and their families, attempt to recognize the isolated events described below as predictable periods or phases of illness in which the type of suffering is also predictable.

Acute Decompensation and Hearing Bad News (Point A)

In this figure, point A represents a period of acute decline. Often, when this is the presenting event, this can be a severe shock to children and families. This may be the first time they will hear of a life-threatening or chronic diagnosis; the first time the child will suffer physical symptoms, and the first time they will have to picture their child's life with disease.

At this point, predictable sources of suffering include pain or other symptoms associated with the acute decompensation; family psychosocial distress associated with seeing their child suffer and from trying to understand and accommodate to the new diagnosis; sibling distress from the change in family dynamics and difficulty understanding what is going on; and care team distress from trying to collaborate together to efficiently work up the child's illness, help the family cope with the new diagnosis, and help maintain hope for recovery.

There are opportunities to treat pain and other symptoms; to facilitate communication between care providers and the family; to collaborate with psychosocial clinicians (eg, social work, child life therapists, chaplains/spiritual leaders, child psychologists); and to

help the child and siblings better cope with the disease and the associated suffering. Importantly, as we discuss in further detail, all of these interventions can have dramatic effects on quality of life without compromising the pursuit of cure or recovery from the acute illness.

Recovery and Accommodating to a New Life (Point B)

As a child recovers from an acute episode or decompensation—depicted at point B—the child and family are suddenly faced with many new challenges. The child may not have reached his or her previous level of function and may still be suffering from lingering symptoms. Many families will be faced with coordinating multiple clinic appointments where they are often asked to manage the differing opinions of the subspecialists. They are still coming to grips with the new diagnosis, often bereaving the loss of their "well" child, and experiencing guilt from having those feelings despite the survival of their child. They will suffer from anticipatory grief from not having a clear picture of what this disease will do to their family, what their child will have to go through in the future, and if each cough or sneeze could lead to another life-threatening event. Siblings will often suffer from a feeling of loss, from a change in function of their sibling, or from a lack of attention as their parents focus on the sibling with the new illness.

In these times of relative stability, it is easy to assume that family functioning is stable as well. This point, however, is an opportunity to address and normalize the anticipatory grief associated with a chronic disease, identify physical suffering associated with long-term or permanent loss of health status or function, support the family in coordinating care between multiple subspecialists, and help the family manage the distress of siblings as they adjust to a different level of attention from parents. These points of stability also provide an opportunity to build the therapeutic relationship that will be essential later in the child's life.

Acute Decompensations and Unexpected Recoveries (Point C)

As the child's disease progresses, the ability to recover from severe decompensations may be uncertain. At these times, many care providers often discuss the possibility of severe impairment and death with the family. Despite our best predictions in even the most dire of situations, however, the child may survive. These episodes of recovery can be a time of great suffering for the family and will change the way they approach decision-making in the future.

At these times, the child will suffer significantly from physical symptoms. Depending on age and cognitive ability, the child may also suffer from trying to understand the disease and questions regarding death. The family will be asked to make decisions that have significant long-term effects on their child's life, from adding technology (such as a feeding tube or tracheostomy) to considering focusing on comfort care only. If the child then recovers, the family may struggle, potentially feeling guilty for their child's suffering or for considering limiting invasive life-sustaining therapy. They may redefine their approach to decision-making, often gaining an increased understanding of the suffering their child may have to endure or that their child may recover even when clinicians predict otherwise.

In this time of great intensity, there are significant opportunities for addressing suffering and assisting with decision-making. The child's symptoms must be managed. Families will need support in decision-making—help identifying hopes, setting goals, making plans that help achieve these goals, and living with the consequences of their decisions. They may need support helping other family members understand the illness and why the decisions they are making are appropriate. They may simply need permission to communicate that "though the doctors cannot make Jacob's disease better they can help us keep him comfortable." Siblings continue to need support coping with the upheaval in their lives, processing their feelings of loss and confusion, and understanding the change in availability of their parents.

Slow Decline Preceding Death (Point D)

Some children with life-threatening conditions will reach a phase of life where they have an insidious decline in health status and function. This period may last days, weeks, months, or even years. It is often punctuated by acute, more minor, losses than previous severe decompensations. There is, however, less recovery. Often in this stage, parents are faced with the decision of implementing invasive technology (such as feeding tubes and tracheostomies) or invasive surger-

ies (such as spinal rod surgery or fundoplications) in an effort to maintain function as long as possible. These interventions may help in the short term, although in the long term many children continue to lose health status and eventually die.

In these times, children often suffer from increasingly difficult to control physical symptoms. Families must coordinate the opinions of multiple specialists in making difficult decisions regarding interventions or limitations of care. They are likely to be anxious about their child's decline and fearful of their ability to manage clinical changes outside the hospital. Often, they will need significant help with the daily care of their child. For families with a child with SNI, the intensity of the care provider role can naturally result in care providers feeling responsible for acute decompensations. Sibling's distress may be significant at this time as they continue to struggle to understand the sick child's illness, loss of function, and eventual death.

At this point in life, children will need significant attention to symptoms, even anticipating and establishing plans to address symptoms not yet present. Families will need significant support in decision-making and would benefit from help exploring their hopes, setting goals, and making consistent plans. They will need support collaborating with specialists and understanding options for care. They will benefit from reassurance that they are not at fault for any decline in health. It is also important to address the family's feelings of "giving up." The child and siblings will need help understanding the medical issues, communicating with their family, and learning to process and understand their emotions and concerns. If the child dies, the family will need ongoing bereavement support.

End of Life (Point E)

The last stages of life are a time of great risk for suffering. For some children and their families, the burden of disease and poor quality of life outweigh the potential benefit of longer duration of life. In these situations, a family may choose to pursue comfort measures only and forgo any life-sustaining therapy. The focus of care is then on ensuring the child's comfort and that the family is able to spend as much quality time with the child as possible. The details of care are based on the individual child, family, and nature of suffering and may include limitations on interventions that cause suffering in the child, including limitations on invasive procedures, discontinuing life-sustaining therapies, and discontinuing artificial nutrition and hydration.

Other children and families may choose to pursue some life-sustaining therapy as they balance the burden of disease with quality of life. They may feel that the degree of suffering is balanced by an equal or greater quality of life. While the focus of care may still be on ensuring that the child is in no discomfort, the details of care become much less constant as the child's disease progresses. The decisions of the family may seem conflicted and unclear. Care plans may include interventions that cause some suffering but also prolong life. This conflict, however, simply stems from the family's and care team's attempts to balance quality of life with duration of life.

In any situation, regardless of the family's goals of care, suffering may change daily. As they cope with the impending death of their child, see the effects of the disease on their child's suffering, and recognize how the interventions affect their child, families may change their mind on the type of care they feel will best meet their child's needs. Open, compassionate communication, frequent re-evaluation with consideration of the above interventions, and partnerships with pediatric palliative care teams and hospice services become essential to care.

Unique to this phase of life is planning the location of death based on family preferences and available resources. The opportunity to plan and prepare for the location of death has a significant impact on where the death of a child occurs. Such planning for parents who lost a child to cancer resulted in 72% home deaths for those who planned versus 8% for those who did not plan.[17] For children who died in the hospital, planning resulted in more deaths outside the intensive care unit and fewer children being intubated.[17]

Planning location of death including the option of home care requires an honest discussion of care plans that will meet goals of care, identify current and future care needs, and determine what resources in the community are available to meet these needs. Discharge planners and social workers are essential members of the team to help identify these resources. Involving the child when appropriate is another very important part of this planning process.

While the tasks listed in Figure 1 are essential components in care at the end of life, Figure 3 describes additional, more specific tasks in end-of-life care.

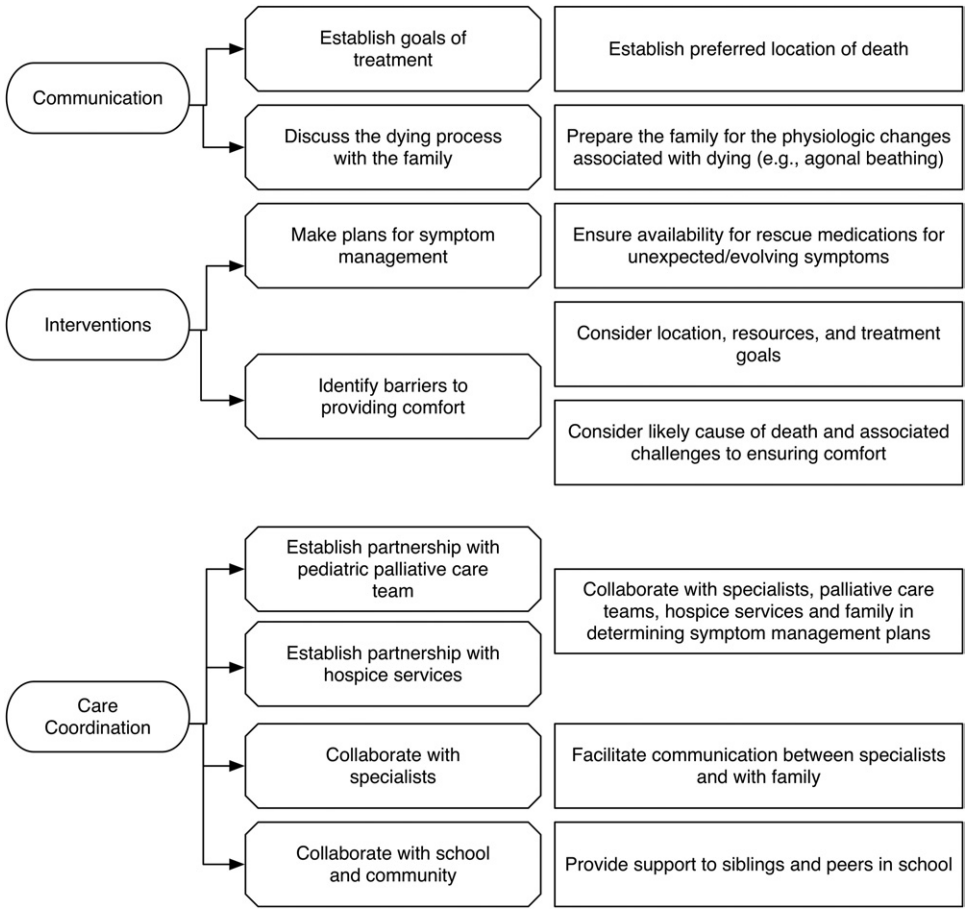

FIG 3. Specific tasks of end-of-life care.

The Care Team

The Role of the Pediatrician

Regardless of the phase of life, the pediatrician must recognize and initiate treatment for suffering. Many children with cancer, congenital heart disease, cystic fibrosis, and other specific life-threatening diseases may have these issues addressed by the subspecialist. For these children, pediatricians remain slightly removed from the subspecialist's role of determining treatment options of curative intent. This role leaves them in a position to discuss the broader context of decisions. They must also maintain a central role in assessing the physical, emotional, spiritual, and social suffering and need for palliative care interventions. They should be able to facilitate decision-making and planning for future care; efficiently anticipate, assess, and manage the child's symptoms; provide front-line bereavement care to the family; and assess when the suffering requires referral to a specialist.

One group of children that primarily looks to their pediatrician for palliative interventions is children with complex chronic conditions. These children often employ multiple specialists in their care, with none primarily in charge of the child's medical home. Children with metabolic diseases, genetic syndromes, and congenital anomalies, and conditions associated with neurologic devastation often fall into this group.[1,2,5]

The Interdisciplinary Team

A dedicated, well-trained pediatrician can initiate many of the tasks listed in Figure 1. When symptoms become more severe, coordination more complicated, communication more intense, and decisions more life-changing, however, even the most experienced palliative care specialist must rely on an interdisciplinary team to help meet the needs of children and their families.

The most successful team is one that can most effectively accomplish the tasks listed in Figure 1. Subspe-

cialty level palliative care includes, at a minimum, the services of a physician, nurse coordinator, and a psychosocial clinician, such as a social worker trained in family counseling.[2] In addition, children and their families benefit from access to a chaplain/spiritual leader, child psychologist, child life specialist, and art therapist—all practitioners trained at performing the different tasks listed in Figure 1. Other services (such as pain management specialists, psychiatrists, bereavement counselors, etc) should be used when specific children and families require more specialized care.

Most importantly, the interdisciplinary team must function as a single unit. Physical, emotional, spiritual, and social distress all cause suffering. Aggressively managing only 1 aspect of this complex suffering will provide little relief for the patient and family. By working together, using each team member's expertise in assessing and managing the different sources of suffering, the team can provide significant relief in the child's and family's suffering.

Hospice

Hospice care is an essential component of palliative care often associated with the end-of-life phase of an illness. The main role of hospice for children is to improve quality of life at the end of life. In general, hospice agencies provide in-home assessment for ongoing symptom management, ongoing psychosocial and decision-making support for the child and family, and grief and bereavement care for the family after the child dies.

While many hospice agencies rarely care for children, they can still be extraordinary resources. Hospice providers maintain an expertise in the last stages of life. They are comfortable with the dying process and the associated physical and psychosocial suffering. They are experienced with the rapid clinical and psychosocial changes and the required frequent reevaluation and treatment changes that can occur in this phase of life. They may simply need some guidance in applying these principles to children such as suggestions for pediatric medication dosage and thinking through strategies in symptom management. A good collaborative relationship between a practitioner who may be less comfortable with end-of-life care and hospice agency less experienced in the care of children can effectively meet the needs of children and their families.

Misconceptions about hospice, however, can limit families' and practitioners' acceptance of this resource. Careful investigation into the family's perceptions of hospice is important before introducing their services. If appropriate, detailing hospice services and their ability to help accomplish the family's goals is often the most effective way to introduce them to families.

Specific Tasks in Palliative Care

In the remainder of this article we discuss, in detail, the specific tasks in pediatric palliative care listed in Figure 1. We go on to discuss the challenges often present in this type of care. Finally, we focus on the children the pediatrician is most often managing, children with SNI.

Communication in Palliative Care

Effective communication is the cornerstone of palliative care.[16,18,19] In this effort, communication should be seen as a specific tool to help build relationships; resolve conflict; deliver bad news; foster a common understanding of challenges, hopes, and goals; and improve collaboration in decision-making and in determining care plans that are consistent with these hopes and goals. The task of communication in palliative care is to relieve the suffering of conflict, confusion, and decision-making by creating a sense of teamwork and facilitating collaboration. In performing this task, the pediatrician must learn to manage oneself, family meetings, and the information coming from other members of the medical team.

Good communication is most effective when the clinician is calm, clear, empathetic, accurate, and centered on the family's needs and preferences. Discussing the difficult topics associated with children with life-threatening illnesses, however, can be very difficult for everyone involved. Too often we underestimate the anxiety that open discussion—and the inevitably associated emotions—can bring out in us. Fortunately, there are some simple and evidenced-based methods that can help the clinician foster a sense of calm, clear, empathetic, and accurate communication that is supportive to the family.

We present an algorithm for developing a therapeutic plan, but, first, the clinician should understand steps that are key when discussing difficult information with families.

Key Steps for Effective Communication with Families

1. *Prepare*: the best way to facilitate good communication is to prepare. First, determine who the decision-makers are in the family and then limit people to those that are important to the family or essential to the topic being discussed. Determine a setting that is centered on the family's wishes although most often a small quiet room with a minimal number of people is beneficial. Touch base with specialists to ensure you have a clear understanding of the child's illness, the clinical problems and potential treatment options, and the decisions that need to be discussed. When there is conflict or an impasse in decision-making, make sure to illicit the points of view of all of the clinical team but reserve judgment until you understand the family's perspective. Discuss how the family is coping. Actively think through the different directions that the conversation may go and prepare for those possibilities. Finally, ensure that you have enough time to sit down and have a calm, unrushed conversation.
2. *Assess*: Always ask the family to recap the situation so you have a clear understanding of where they are coming from ("All of this has been pretty complicated, can you help me make sure we are on the same page by explaining to me your understanding of the situation?). It is essential to use this as the starting point to any conversation as families often perceive a very different concern than the clinical team. These concerns may demonstrate a different understanding of the same problem or a different problem all together. Regardless, you must develop a therapeutic relationship with the family by first addressing their concerns. You must then reframe your clinical concerns to match the family's understanding ("I know you are worried that medications may make her sleepy. Let's talk about what we can do to manage her pain and also allow her to interact").
3. *Deliver*: At this point you should clarify any challenges the family presented in describing the illness and their understanding of the situation. When delivering news or explaining topics, be clear, concise, and empathetic. State the facts simply and in language the family can understand. When breaking bad news, consider using phrases starting with "I wish" ("I wish I had better news.") This offers empathy without accepting blame for a situation. When discussing prognosis or outcomes, consider using the phrase "I am worried" ("I am worried that this medication will not help" or "I am worried that we are looking at days rather than months.") This phrase also offers empathy and helps define your thoughts without being confrontational or overly specific.
4. *Allow silence and acknowledge emotion*: Often in discussion of difficult topics, families will flood with emotion. The best way to remain calm and support the family is to simply name the emotion ("I can see how upset you are" or "I can hear how angry you are") and allow for silence. While this silence can feel uncomfortable, it allows time for the family and the care team to regroup and prepare for the remainder of the meeting.
5. *Plan*: This point in a conversation is a key time to assess the family's ability to continue. If they are flooded with emotion, they are likely to process very little of the remaining conversation. It is, however, important to give a vision of what the future may look like. This discussion may include decision-making, detailed long-term treatment plans, or simply the logistics of the rest of the day and deciding when to meet for the rest of the conversation. The focus should center on the family's ability to continue on in the conversation. Do not expect the family to retain much detail from initial discussions and always plan to repeat the information in future meetings.
6. *Do not abandon*: The clinician can accomplish this by simply explaining to the family the next time they will be in contact with you and how they can reach you if they have any concerns prior to that meeting.

Goals of Care Conversations

A common approach to family meetings is to present a set of choices, explain those choices, and ask the family to make a decision. This construct, however, places the emphasis of the conversation on understanding the choices rather than on gaining understanding of why the family would make those decisions. For example, when a family is faced with deciding on a Do Not Attempt Resuscitate (DNAR) order, they are often asked if they would like someone to intubate their child or to perform cardiopulmonary resuscitation. With this presentation, even the most

TABLE 1. Framework for therapeutic planning conversation

Steps	Comment
1. Review the major problems	A shared understanding of what the major problems are confronting the child and family is essential: "I think we all find it useful to hear what each of you think are the most important problems and challenges that we need to confront."
2. Discuss goals, objectives, hopes	The compass by which the course of therapy will be set depends on a clear sense of purpose and the values that underwrite that purpose. A question that can initiate this phase of the discussion is, "Given the problems and challenges, I am thinking about how we can best care for your child. What are your major hopes or goals?" Encourage each participant to state all of their hopes or goals, which may not be entirely consistent (such as "to be cured by a miracle" and "to not suffer before dying"). The aim of this phase is simply to air all the hopes, goals, or objectives, and to summarize them for the group when everyone has spoken.
3. Spell out alternative actions	In as nonjudgmental and succinct a manner as possible, clarify the main alternative ways of caring for the child, such as: "I feel that we have 2 major ways we can proceed, namely, continue to have your child stay in the hospital or work to have your child go home with the help of hospice-home care nursing." Check to see if anyone has another major option.
4. Examine consequences of options	Typically, no therapeutic option is perfect. Once the main options are spelled out, explore as a group the pros and cons of each alternative. "If we keep your child in the hospital, there are some good and not-so-good things I can foresee happening, such as . . ." The judgments of "good and not-so-good" should refer back to the discussion regarding hopes and goals. Solicit other participants' perspectives.
5. Explore tradeoffs	Often a central pattern of tradeoffs between 2 goals emerges in the discussion of options. Addressing this tradeoff explicitly can be helpful: "We seem to be struggling with the goal of feeling secure, a sense of which the hospital provides, being at odds with the goal of being at home." Stating these tradeoffs can help people clarify which goal is more important, or devise new alternatives to accomplish both goals (such as enhancing the sense of security at home by augmenting the nursing coverage).
6. Formulate a plan	By this point, the broad elements of a plan have typically emerged by consensus. If so, spell it out and assess whether everyone agrees. If not, acknowledge the disagreement and seek agreement to continue to work together to formulate a mutually acceptable plan.
7. Specify next-steps and follow-up assessment	Before ending the conversation, clarify who will do what next, and when the next discussion will occur.

Reprinted with permission from Kang and coworkers.[19]

advanced families may see this as choosing to let their child die rather than ensuring that their child does not suffer from an intervention with minimal likely benefit.

Another approach may be to focus the discussion on what the family does want for their child, focusing on things that we have control over. The family can then set goals that they can achieve. These goals then become the "true north on a compass" that can help them make decisions in the future ("The last time we had to discuss this, you made the difficult and loving decision to focus on ensuring that she was comfortable. Do you still feel that is the best way to support and love your child?"). The clinician then partners with the family by describing the clinical interventions that most effectively achieve the family's hope and goals.

At early stages of many illnesses, the goals of care are likely to include aggressive and invasive interventions. As the disease worsens, the burden of disease becomes more intense, and the likelihood of survival decreases, the family may choose less aggressive measure with an increasing focus on comfort and quality of life. Even when the likelihood of survival is extremely low, some families may still wish to pursue therapies of curative intent. As long as there is no harm to the child, families must be supported in deciding the focus of care for their child. The clinician must make medical plans that best balance the therapies with intent at cure and restoration with those directed at providing comfort. Partnering with the family in finding this balance can be very effective shared decision-making.

Table 1 provides a framework for therapeutic planning conversations.

Resuscitation Orders

DNAR/Allow Natural Death and Do Not Intubate

DNAR/DNI orders simply dictate that a child not have certain interventions should they have a cardiopulmonary arrest. In practice, these orders are nonspecific and the details of the goals of care need to be spelled out. Unfortunately, these orders can be a source of confusion for many families and clinicians

as some treat them as a declaration that the focus of care is on comfort. These orders, however, do not preclude life-sustaining, restorative, or curative measures. They are not permanent and should be rescinded if the clinical issues change. An out-of-hospital DNAR does not preclude the child from returning to the hospital.

When discussing resuscitation with families, it is essential to focus the conversation on what they are hoping for in their child's life. These goals should be detailed in the child's chart or care plan to provide a much clearer guide to medical interventions than a simple DNAR/DNI order.

Out-of-hospital DNAR

In an effort to support the wishes of children and their families outside the hospital, some states provide for a provision of an out-of-hospital DNAR. In an effort to make these orders accepted and honored in many different clinical settings, these orders come on official forms that state the resuscitation wishes of the child and family. Unfortunately, as most clinicians are rarely faced with the impending death of a child, they may not feel comfortable honoring the order and limiting interventions. In addition, in some states, the interpretation of laws has made it difficult for families to be supported with an out-of-hospital DNAR. In these situations, the clinician must provide the family with clear documentation that succinctly describes the child's medical status, poor prognosis, and the details of the goals of care.

Autopsy, Organ, and Tissue Donation

Autopsy and organ or tissue donation is a topic that must be discussed at the end of life. The most family-centered approach to this decision is to first decide the clinical and psychosocial utility of autopsy and organ/tissue donation. One study suggested that autopsy results helped clarify the cause of a child's death in 53% of cases and contributed to patient care quality control in 36% of cases. In contrast, autopsies were only helpful in informing the family regarding future reproductive choices and the future health care of siblings in 6%-10% of cases.[20] In addition, discussions regarding autopsy results may allow lingering questions or concerns that are causing parental distress to be addressed.[21]

Symptom Management

Aggressive, empiric, developmentally appropriate symptom management is core to any palliative care intervention. Children with life-threatening conditions suffer from many types of symptoms. In this article, we discuss the most common symptoms the pediatrician is faced with and is the most equipped to manage.

There are several guiding principles when assessing and treating symptoms with a palliative approach.

Guiding Principles in Symptom Management

1. *Partnering with the child and parents is essential*: Establish clear goals of therapy with a focus on improving physical function, if possible, and decreasing suffering. Provide clear guidance regarding the benefits and side effects of the medications; this is especially important with opioids due to the cultural stigma of these medications. Partnering with the child and family allows them to have some control over the situation. This will relieve a significant source of suffering and is likely to increase adherence to care plans.
2. *Emotional, spiritual, and social suffering can be significant confounders in the experience of symptoms*: Children do not separate the physical and emotional nature of suffering and may have extreme anxiety due to anticipated pain or other symptoms. If the symptom is nonresponsive to seemingly appropriate management, consider evaluating for other sources of suffering and drawing on the expertise of the interdisciplinary team.
3. *The child's self-report of symptoms is the "gold standard"*: Parental report, physiologic indicators, and behavioral indicators are less reliable assessment methods. Most young children, however, are not able to provide a historical context to their pain. Other children, such as infants or children with neurocognitive disabilities, cannot communicate effectively. In these situations, parental report becomes an important additional tool for assessing pain.
4. *Assessment and communication must be developmentally appropriate*: Children will only answer questions if asked in language that is understandable to them. In addition, children must be asked if they are having pain, as they may not know to report what they are experiencing. When available, validated assessment tools based on age and cognitive ability, when appropriate, should be used.

Ultimately, however, the child's interpretation of the experience is the "gold standard."

5. *Anticipate symptoms, react expediently, and reassess frequently*: Many forms of acute pain are predictable. In addition, there are easily predictable times when a child is at increased risk for pain, such as during or after procedures; at times when medications are wearing off or the dose is being changed; and at times of peak effect of the medication. When unanticipated pain is present, management should be initiated promptly. Predicting management needs at initiation of therapy, however, is difficult and symptoms will also evolve over time. Frequent reassessment of the plan is essential. In addition, emergency rescue plans should be available, especially at the end of life.
6. *As symptoms escalate or become difficult to control, early referral to a pain or palliative care specialist is essential*.

The traditional focus on symptom management has been on using pharmacologic solutions. Nonpharmacologic modalities, however, can be very helpful, especially when used in conjunction with pharmacologic options. Effective strategies include guided imagery, distraction and relaxation, massage, acupuncture and acupressure, and play. Pain or palliative care specialists, child life therapists, and psychosocial clinicians can be effective resources to implementing these strategies.

The WHO developed a simple, effective pain-management strategy based on the four principles described.

Pain

Pain is one of the most common symptoms experienced by children with life-threatening conditions. Unfortunately, a substantial percentage of children's pain is undertreated.[22,23] The experience of pain is inherently a subjective experience with sensory, emotional, cognitive, and behavioral components interwoven with environmental, developmental, social, spiritual, and contextual factors.[22] Children suffer from the experience of pain differently, depending on a variety of factors. Pain causes suffering when the child and family have no sense of control over the symptoms, when the pain is overwhelming, when the source is unknown, when the meaning of the pain is perceived to be dire, and when the pain is chronic.[24] In addition, the perception of pain can be dramatically affected by the child's age and cognitive ability, previous experiences with pain, expectations for relief and recovery, and ability to control the pain themselves.[25]

The pediatrician must address and treat all types of pain, including acute pain, chronic pain, recurring pain, procedure-related pain, and pain associated with end of life.[22] To effectively accomplish this task, pediatricians must understand a simple approach to assessing and initiating pain management. They must also understand that psychosocial issues associated with suffering complicate treatment, and they must develop effective ways to screen and refer for support. Finally, they must understand the need to frequently re-evaluate symptoms and management plans, to partner with families to improve their sense of control in managing symptoms, and to refer to a pain or palliative specialist when control proves difficult.

Assessment of Pain

Table 2 lists the validated assessment tools to assess physical pain based on age and cognitive ability. Importantly, many of these tools were validated following postprocedural pain, and different clinical circumstances may call for different methods. In addition, when assessing pain at different points—as in assessing the effectiveness of a dose of medication—the same assessment method should be used for each assessment.

Management of Pain

The goal of pain management is simply for the child to be pain free and functional. There are two core constructs in meeting these goals—first, identifying and treating the underlying pathology or source of the pain and, then, treating the suffering associated with the experience of pain. While both are essential to a good pain management strategy, the sources of underlying pathology are dependent on the evaluation of many clinical features centered on the specific disease or condition. This article focus on treating the suffering associated with pain.

Mild pain is often effectively managed with acetaminophen, ibuprophen, or naproxen. As pain becomes more severe and these medications become less

TABLE 2. Pain assessment scales

Age	Scale	Notes
Neonate	CRIES[a]	Uses physiologic measures, including: the degree of Crying, Required oxygen, Increased vital signs (heart rate and/or blood pressure), Expression (for example, grimace), and Sleeplessness.[1]
Infant and toddler	FLACC[a]	Uses physiologic measures in the following categories: Face (degree of grimace); Legs (degree of restlessness or tension); Activity (degree of agitation); Cry (degree of crying); and Consolability (amount of physical consoling needed to comfort child).[2,3]
School-aged children	Faces	Uses visual images that represent levels of pain. Tell the child that the face on the left side shows no pain and the face on right shows the worst pain. The child then points to the face that shows his/her current level of pain.[4]
Age 7 years or older	Numeric	Uses a rating of pain on a scale. This scale can be a line, a number between one and ten, etc. The practitioner grounds the child by describing that one end of the scale represents no pain with the other representing the worst pain.
Cognitively impaired	R-FLACC	The R-FLACC was developed by revising the FLACC tool to include behaviors specific to children with cognitive impairment. In addition, it allows parents to individualize by adding behaviors specific to their child.[5]
Cognitively impaired	NCCPC-R	The Non-Communicating Children's Pain Checklist-Revised.[6,7]
Cognitively impaired	PPP	The Paediatric Pain Profile is available to download from the web following registration at www.ppprofile.org.uk.[8,9]

[a]Note. Children with chronic pain rapidly adapt and may not show the features in these tools, making them less reliable. In this setting, child and parental report are essential.

effective, opioids become the standard therapy. There are many different formulations of opioids, all having slightly different properties that make them slightly more or less effective in specific clinical circumstances. In an effort to improve consistency of practice, this article recommends using a single agent—morphine—until the practitioner is comfortable with its use. After gaining comfort with the single agent, the practitioner can then learn the benefits of other opioids, such as the rapid metabolism of fentanyl or the long half-life and steady state of methadone.

In an effort to improve pain control in children with life-threatening conditions, the WHO developed a simple, effective pain-management strategy based on the four principles described below.[26] While the strategy was developed for children with cancer, the methods are applicable to any child with a life-threatening condition and persistent pain.

By the ladder: analgesics should be started and escalated in a stepwise approach based on the severity of symptoms.

By the clock: analgesics should be given on a scheduled basis to provide stable blood levels of the medication. Rescue doses should then be available for breakthrough pain.

By the mouth: analgesics should be given by the least invasive route available that allows for effective pain control.

By the child: analgesics should be based on the individual child's circumstances and tailored to that child's response to therapy.

Table 3 depicts an approach to pain control adapted from the WHO guidelines. While the opioid used in this algorithm is morphine, another can be substituted.

Breakthrough Pain. Breakthrough pain is pain that "breaks through" despite scheduled doses of an analgesic. This may occur due to an insufficient dose, dosing that is too infrequent, worsening of the source of pain, or episodes of incident pain. Rescue medications are analgesics that are prescribed on an as-needed basis and should be available to any child at risk for pain. The goal, however, is for the child to be pain free. Frequent use of rescue medications should prompt a re-evaluation of a pain plan that is insufficient.

Scheduled Medications. Scheduled medications make up the backbone of good pain control. Giving the medication on a sustained, scheduled basis allows for stable blood levels of analgesic and more stable pain management. The dose and frequency should be titrated to allow the child to be pain free and functional.

Rescue Medications. In managing breakthrough pain, the practitioner should anticipate episodes and always have rescue doses available. The medication should be the same analgesic offered for scheduled analgesia. The frequency should be based on the route and time to peak effect—every hour for oral, every 30 minutes for subcutaneous, and every 15 minutes for intravenous. The dose should be based on the scheduled dosing—50%-200% of the hourly dose for infusions and 25%-50% of the every 4-hour dosing equivalent for scheduled oral or intravenous boluses. Most

TABLE 3. Pain management algorithm

Pain level		Rescue medication	Sustained medication
Step 1	Mild pain	**Start rescue medication:** Start a nonopioid analgesic (NSAID or acetaminophen) as needed	**Consider sustained therapy:** Consider a standing dose for short period of time
Step 2	Moderate pain	**Start or Escalate rescue medication:** Tramadol oral 1-2 mg/kg/dose PO q 4-6 hr prn	**Consider sustained therapy:** Tramadol oral (same dosage on scheduled basis)
Step 3	Severe pain	**Start or escalate rescue medication:** Morphine oral immediate release preperation Opioid naive: 0.2-0.3 mg/kg/dose q 3-4 hrs prn Opioid exposed: increase previous dose 25-50% for moderate pain and 50-100% for severe pain	**Start or escalate sustained medication:** Morphine oral immediate release preperation Opioid naive: 0.2-0.3 mg/kg/dose q 3-4 h Opioid exposed: total daily morphine dose divided every 3-4 hours If meant for prolonged use should consider sustained release formulation morphine, methadone, or a fentanyl patch
Step 4	Severe-persistent pain	**Start or increase rescue medication:** Morphine: IV, SQ Opioid naive <6 mos: 0.05-.1 mg/kg every 3-4 hours prn Opioid naive >6 mos: 0.1-0.2 mg/kg every 3-4 hours prn Opioid exposed: Previous total daily oral dose, converted to IV morphine equivalent, and divided by frequency	**Initiate or escalate sustained medication:** Transition sustained medication to IV equivalent Consider an infusion
		Consider patient controled Analgesia (PCA): Morphine Opioid naive: Basal infusion: 0-0.02 mg/kg/hour; Demand dose: 0.015-0.02 mg/kg/dose; Lockout interval: 5-10 minutes Opioid exposed: Basel infusion: daily dose divided over 24 hrs; Demand dose: 50-100% of the hourly dose; Lockout interval: 5-10 minutes	

Escalation information:

- If poor control with a rescue opioid medication, increase dose by 25-50% for moderate pain and 50-100% for severe e pain
- If frequent use of the rescue dose in a 24-48 hour period, increase sustained dose by adding up daily mg of rescue medication, divide by frequency of sustained release, and add to the sustained dose. Alternatively, may also increase sustained dose by 25-50%
- If persistent or worsening symptoms or frequent use of rescue medication, consider increasing dose or advance to step 3
- If no effective benefit, frequent use of recue doses, or worsening/persistent symptoms, continue escalation of dosage until the patient is free of pain

Additional information:

- The suggested starting dose of morphine is listed. The medication can be titrated beyond this amount based on pain control and side effects
- A typical breakthrough/rescue dose is 10% of the 24 hour opioid requirement
- Adjuvant medication should be considered at any step
- Consider initiating/continuing non-opioid analgesics at any step to maximize pain control
- Evaluate for constipation and initiate prevention plan when starting an opioid
- Only use a single opioid agent at a time
- Consider early referral to a pain or palliative care specialist

Adapted from McGrath.[26]

importantly, if the child is requiring frequent rescue dosing, the scheduled analgesic should be increased by either increasing the dose or decreasing the frequency of administration followed by a reassessment of the scheduled analgesic dose and frequency.

Special Circumstances

Procedure-Related Pain. Pain experienced in anticipation of, during, and after a procedure can be easily anticipated and prevented, as inadequate management can cause increased morbidity and mortality.[27,28] Fortunately, there are a few, simple methods for improving pain control in this setting including sucrose for infants, topical analgesia, benzodiazepines, and conscious sedation.

Incident Pain. Incident pain is pain that is typically short-lived and can easily be anticipated, such as with nursing care or trips to the bathroom. Rescue medica-

tions should be provided when this type of pain is anticipated. The nature of this pain—the rapid onset and relief—however, makes it difficult to manage. Ideally the use of fast-acting analgesics with rapid metabolism is most beneficial (eg, transmucosal preparations of fentanyl).

Opioid Rotation. Extreme and refractory side effects may limit the use and escalation of opioids. In these circumstances, improved pain control with fewer side effects may be accomplished by switching to a different opioid.[29] When rotating opioids, consider consulting with a pain or palliative care specialist, as the dosage calculations can be complex. In addition, there are significant risks of incomplete pain control during the period of rotation and rescue medications should be readily available until the second opioid is in steady state.

Benefits of Other Opioids

Tramadol. Tramadol is considered a weak opioid that is useful for moderate pain. Along with being a mu-receptor agonist, it is a serotonin-releasing agent and norepinephrine-reuptake inhibitor, properties that may indicate theoretical benefit of tramadol for neuropathic pain.

Fentanyl. Advantages of fentanyl include that it has a shorter onset of action compared with other opioids, has a shorter duration of action (benefit during certain procedures), is available as a transmucosal "lozenge," and is available as a transdermal patch for around the clock opioid dosing (should only be initiated after establishing daily opioid dose). Fentanyl and methadone are the preferred opioids in patients with renal insufficiency.

Methadone. Methadone is the only long-acting opioid available as a liquid. As an NMDA receptor antagonist, methadone may be beneficial for neuropathic pain. The main disadvantage is its biphasic elimination, which can result in drug accumulation and toxicity 2-5 days after starting or increasing methadone.[30] For these reasons, methadone requires expertise in use.

Management of the Toxic Effects of Opioids

Constipation. All opioids cause decreased intestinal motility that can lead to constipation. Proper management includes prophylactic therapy.

Nausea and Vomiting. Nausea and vomiting is sometimes associated with the initiation of opioids. This side effect often resolves after several days, although it may last weeks.[31] During this period, odansetron or metoclopramide may be effective. If severe, the practitioner can consider rotating to another opioid. Importantly, constipation is commonly associated with the long-term use of opioids and can also lead to significant nausea and even vomiting. Constipation should be assessed and relieved before adding medications or rotating opioids.

Pruritis. Pruritis is often misconstrued as an allergic reaction, although it is more often a benign side effect that will likely resolve after several days. Until resolution occurs, the child may benefit from diphenhydramine or hydroxyzine.

Fatigue. This side effect often improves a few days after initiation or titration of the opioid. If persistent or intolerable, the most effective therapy is rotating the opioid. The practitioner may try a trial of stimulant such as methylphenidate.

Confusion or Odd Feelings Associated With Opioids. This clinically benign side effect can be very distressing to children and parents. They may refuse to take/give the medication as it makes them feel and act differently. If persistent or intolerable, the practitioner may try a trial of stimulant such as methylphenidate.

Delirium. Delirium most commonly occurs when a child is receiving multiple medications or is critically ill. If present, the practitioner must first determine if there is another cause of the delirium. If so, the practitioner can consider a trial of haloperidol, a trial of a decreased dose of the same opioid, or, if these prove ineffective, rotation to a different opioid.

Myoclonus. Myoclonus—brief, involuntary twitching—is most often due to the accumulation of metabolites and is often only seen in patients receiving very high doses of opioids for a prolonged duration. Treatment of this distressing symptom includes benzodiazepines, muscle relaxants, or rotation of the opioid.

Respiratory Depression. True respiratory depression is very rare when opioids are dosed appropriately. Pain itself causes alterations in breathing patterns and release of a catecholamine response. When pain intensity is decreased, metabolic and respiratory demand are also decreased, giving the perception of a decreased respiratory drive. Some patients may fall into a deep sleep and may show signs of obstructive apnea, including desaturations on pulse oximetry. The child, however, remains arousable. True respiratory depression is preceded by sleepiness, decreased consciousness, decreased respiratory rate, and, finally, central

apnea. Once true respiratory depression is identified, it can often be managed by closely monitoring the child and providing respiratory support, decreasing the opioid dose, and waiting for resolution. Rarely is an opioid antagonist (such as nalaxone) necessary. When needed in critical situations, it should be used with extreme caution, as sudden opioid antagonism can lead to life-threatening withdrawal.

Urinary Retention. Alleviating interventions include external bladder pressure, intermittent bladder catheterization, or bethanechol to stimulate bladder contraction. If these methods are ineffective, low-dose nalbuphine or rotating the type of opioid can be considered.

Adjuvant Medications

An adjuvant medication can be used in specific clinical circumstances to modify the pain experience and decrease the amount of analgesic necessary to treat pain. These medications are best when used in addition to opioid and nonopioid analgesics. When considering adjuvant medications, the practitioner must first determine the type of pain that the child is experiencing. The best adjuvant medication is directed at that specific type of pain and has limited side effects.

Types of Pain

Nociceptive/Somatic Pain. Somatic pain is caused by inflammation or actual damage to tissue. This results in stimulation of nociceptors in skin, soft tissue, skeletal muscle, and bone. The child experiences an aching or gnawing pain that is very well localized, often located at a point of tissue injury. Anti-inflammatory agents (NSAIDs and steroids) and opioids are effective for pain treatment. When possible, treating the underlying tissue damage is the most effective therapy.

Neuropathic Pain. Neuropathic pain comes from central or peripheral nervous system dysfunction secondary to direct injury to the nervous system or as a side effect of medications. The child may experience numbness, itching, burning, or pins-and-needles sensations, as well as sudden, sharp, and shooting pain. The pain may also be associated with sensation changes and feelings of weakness. Effective adjuvant therapy may include opioids, gabapentin, amitriptyline, and transcutaneous electrical nerve stimulation. This type of pain can also be refractory to standard therapy and referral to a pain or palliative care specialist should be considered early.

Special Considerations

Neonates and Children Younger Than 3 Months. Neonates and premature infants may have an exaggerated sense of pain[32] but are also at an increased risk of respiratory depression.[33] The initial dose of an opioid should be about 30% of that for older children. The efficacy of treatment should then be reassessed frequently and rapid titration of the medication is very important.

Fixed Combination Products (eg, Percocet, Vicodin). Escalating these medications becomes difficult owing to side effects of the nonopioid component. These formulations should then be avoided by simply separating the components if both medications are necessary.

Specific Opioids With Toxic Metabolites (eg, Propoxyphene and Merperidine). Some opioids have metabolites that are neurotoxic and should be avoided in pediatric patients.

Codeine Should Be Avoided. Codeine is not recommended as it has a poor side-effect profile, is ineffective in some individuals because of their inability to metabolize codeine to the active metabolite morphine,[34] and can result in toxicity in others who are ultrarapid-metabolizers.[35]

Steroids. Steroids can be of significant benefit to both pain and nonpain symptoms. While they likely have many effects on treating the experience of these symptoms, they most notably decrease inflammation and edema and increase energy levels. These medications have short-lived beneficial effects, significant and severe long-term side effects, and a profound effect on the primary illness. They should, therefore, be used with caution.

Nausea and Vomiting

Nausea and vomiting are very common symptoms in children with life-threatening conditions, especially at the end of life.[36-38] Proper management includes a detailed history describing timing, quality, volume, frequency, and triggers. Review of systems should include a detailed history of abdominal pain, oral intake and hydration, stooling pattern, headaches, anxiety and depression, medications focused on recent changes, and any recent illnesses suggestive of a metabolic or electrolyte derangement. Physical examination should focus on the abdomen—noting any

TABLE 4. Sources and treatment of nausea and vomiting

Source	Intervention/medication choice
Envornmental triggers	Small, more frequent meals Remove pungent odors/smells
Toxic effects of drugs (eg., chemotheraputics, opioids, antibiotocs)	Stop offending agent if possible Odansetron 0.45 mg/kg oral/IV daily or divided q8 hrs
Biochemical abnormality (eg., Hypercalcemia, uremia, liver failure)	Metoclopramide 0.5-1 mg/kg/dose oral/IV q6 hours prn — Consider adding diphenhydramine to prevent dystonic reaction Opioid rotation if caused by opioids
Anxiety or anticipatory	Lorazepam 0.25 mg/kg/dose oral/IV q6 hrs
Movement	Scopolamine (>40 kg) 1.5 mg patch behind ear q72 hrs
Increased ICP	Dexametasone 10 mg/m^2 oral/IV (max 40 mg/day)
Constipation	Fleets Enema daily (up to 3 doses) until stooling Mirilax 1/2 to 1 cap QD to BID till stool loose
Gastroesophogeal reflux	Ranitadine 2-4 mg/kg/dose PO BID Omeprazole (5-10 kg) 5 mg daily; (10-20 kg) 10 mg daily; (>20 kg) 20 mg daily
Gastrointestinal obstruction (noncomplete or functional)	Surgical intervention if consistent with goals of care Dexametasone 10 mg/m^2 oral/IV daily (max 20 mg/day) Scopolamine (>40 kg) 1.5 mg patch behind ear q72 hrs Haloperidol 0.01-0.02 mg/kg/dose PO TID prn (max start dose 0.5-1 mg)
Gastritis, Gastric ulcer, Mucocytis	Protective measure (sucralfate, zantac, or PPI)
Idiopathic or unclear	Metoclopramide 0.5-1 mg/kg/dose oral/IV q6 hours prn Scopolamine (>40 kg) 1.5 mg patch behind ear q72 hrs Odansetron 0.45 mg/kg oral/IV daily or divided q8 hrs Dronabinol (>6 yrs) 2.5-5 mg/m^2/dose q4-6 hrs
Other	Prochlorperazine 0.1-0.15 mg/kg PO/NG/PR q6-8 hrs Dronabinol (>6 y) 2.5-5 mg/m^2/dose q4-6 hrs Cyproheptadine 0.08 mg/kg/dose PO q8 hr (max start dose 4 mg) If no benefit in 3-5 days, increase each dose by 0.04-0.08 mg/kg/dose Consider referral for acupuncture or hypnosis

pain, masses, or signs of anatomic or functional obstruction—and neurologic examinations.

As with pain, the core steps in managing nausea and vomiting include treating the underlying cause when possible and managing the suffering associated with the symptoms. In managing the suffering, the medication choice should match the most likely cause of the vomiting, as described in Table 4. Many medications work by blocking the receptors that trigger the emetic process including acetylcholine, histamine (H_1), serotonin (5-HT_3 and 5-HT_2), and dopamine (D_2) receptors. When a single drug regimen is not effective, a second agent with a different mechanism and location of action should be used. Once a medication is proven ineffective, it should be stopped as another is added. If a medication is partially effective, consider continuing it while avoiding adding multiple medications all with limited efficacy.

Special Considerations

Steroids. Steroids are often very helpful in the short-term treatment of nausea and vomiting for selected patients and conditions. As previously mentioned, they should be used with caution.

Constipation

Constipation is a common symptom in children with life-threatening conditions—especially at the end of life—due to medications, decreased fluid intake, slowed intestinal motility, and decreased physical activity.[36-39] It can be difficult to assess, as many children underreport their symptoms until the problem is severe—a particular problem in children with neurocognitive impairment. Preventive measures—especially when using opioid analgesics—and frequent assessment of the stooling pattern are, therefore, the best approach to management.

Proper management includes a detailed history of stooling pattern, stool quality and volume, and bowel routine/behaviors. Review of systems includes a history of abdominal pain, nausea, vomiting, and anorexia. Difficulty with urination, weakness, and paresthesias are important, as they may be associated with neurologic compromise. A detailed medications history, including those that can cause constipation and those that have helped the child in the past, is also important. Physical examination centers on ensuring there is no neurologic

TABLE 5. Management strategies for anxiety

Intervention	Notes
Share control	Perceived loss of control is a significant source of suffering. Give the child some control, such as a choice of which arm for blood draws. Give parents control by giving detailed anticipatory guidance and specific features to monitor that would change therapy.
Provide control over symptoms	Communicating clearly and teaching cognitive/coping strategies, such as guided imagery and relaxation/distraction techniques, can facilitate the child's and family's participation in the care plan, mastery over the illness, and sense of control.
Avoid separation	Fear of separation from family for the young child and peers for adolescents can be distressing and should be limited as much as possible. When separation is necessary, a psychosocial clinician should be available to help the child cope.
Prevent painful experiences	Children will anticipate pain from procedures and side effects from medications. Effective therapy includes pain control, procedural pain control and anxiolysis, guided imagery, and sharing control.
Manage physical symptoms	A major source of suffering from symptoms is the anticipation of the symptoms. Prompt, aggressive, and effective symptom management can mitigate this anxiety.
Improve physical functioning	Functional ability is a significant source of coping. Loss of function is often associated with difficulty with activities of daily living. Maintaining function should be a core goal of any symptom-management plan, especially focused on treating pain, fatigue, and nausea and by providing physical aids such as walkers or wheelchairs and home nursing to help with activities of daily life.
Distract and relax	Distraction (focusing the child's mind on something else, such as a toy) and relaxation (as simple as focused deep breathing and guided imagery) will ease anticipatory anxiety. Child life specialists and child psychologists can be very effective at teaching these strategies.
Use pharmacotherapy	Anxiolysis is very effective in acute procedures for the treatment and prevention of anxiety. For chronic anxiety, medications should be reserved for severe situations. The most commonly used anxiolytics for this indication are the benzodiazepines, including oral or intravenous lorazepam or diazepam.
Refer to a specialist	When the standard approach to therapy is not sufficient to control symptoms, the child should be referred to a psychosocial clinician (eg, child life therapist or child psychologist) or palliative care specialist.

compromise or a source of pain, such as an anal fissure, that is preventing the child from stooling.

Effect prevention, especially when using opioids, starts with stimulants (senna). If a regimen proves ineffective, medications with differing mechanisms should be used together. Other options include stool softeners (ducosate), osmotic agents (lactulose), osmotic hydrants (polyethylene glycol), as well as suppositories (Bisacodyl) and enemas (Fleet). Severe constipation may require evacuation with polyethylene glycol and enemas. If the child has a history of an effective management plan, it should be initiated after ensuring there is no distal obstruction. Once evacuated, an aggressive regimen and close follow-up should continue.

Anxiety

Anxiety occurs commonly in children with life-threatening illnesses. Even though the symptoms may not fit psychiatric criteria for an anxiety spectrum disorder, they can be very distressing to the child, family, and even the care team. Anxiety complicates the management of other symptoms, making the associated experience of suffering significantly worse.

Sources of anxiety are very different depending on the developmental stage and cognitive ability of the child. Often anxiety stems from many anticipated issues. For the infant and young child, it may be from anticipation of separation from family, pain or distressing symptom, loss of control, or perceived meaning of symptoms (eg, "I must have done something wrong to deserve this"). For the adolescent it may come from loss of contact with peers, self-image issues, loss of control, or perceived meaning of the symptoms. Concurrently, using pharmacologic, nonpharmacologic, and alternative approaches to management can have benefits to the child's quality of life and significantly simplify assessment and treatment of other issues.

Table 5 describes the key issues in the management of anxiety. Importantly, nonpharmacologic modalities and using child psychologists, child-life therapists, or social workers are often the most effective modality.

Palliative Care for Children with Complex Chronic Conditions

Children with complex, chronic medical conditions—including genetic disorders, congenital anomalies, metabolic disorders, and injuries to the central nervous system—pose a unique challenge to the pediatric practitioner. First, these children often have some degree

of neurologic impairment. Second, in part due to this impairment, these children are at risk for frequent acute decompensations and a general long-term decline in health status (as described in Fig 2). They suffer from a multitude of nonspecific and difficult-to-assess symptoms. While the principles and algorithms previously presented in this article clearly apply to these children and their families, this section reviews some of the unique clinical challenges common to all children with severe neurological impairment (SNI), focusing on symptom management.

Pain and Distressing Symptoms

General Approach to Treating Symptoms in Children with Severe Neurologic Injury

Children with SNI experience pain and other distressing symptoms at a significantly higher rate than the general pediatric population.[40-45] In addition, they are at risk for many complications that can lead to pain-like behaviours—neurologic (spasticity, seizures, autonomic dysfunction), gastrointestinal (vomiting, retching, constipation, "feeding intolerance"), and respiratory (recurrent illnesses, secretions, and dyspnea).[41,42]

Determining the primary source of pain behaviors can be challenging. As an example, it can be difficult to know if a nonverbal child with SNI appears uncomfortable because of spasticity or if the increase in spasticity is secondary to underlying pain. When the primary source of suffering is unclear, the practitioner is often faced with empirically treating, expectantly watching, or performing an extensive workup. In better understanding the sources of pain-like behaviors, clinicians can be more directed in their understanding of treatment options. Figure 4 highlights some of the more common pain and nonpain sources that can lead to pain behaviors.

Evaluation and Treatment of Symptoms in Children with Severe Neurologic Injury

Answering the question "Is it pain?" is clearly complicated in the nonverbal child with SNI. The behaviors associated with pain (Fig 4) have been identified in validated pain assessment tools for nonverbal children with SNI[43-47]; yet, each child will display a unique set of behaviors that can range from crying to being withdrawn. They may also show idiosyncratic behaviors such as laughing, clapping, and blunted facial expressions.[47-50] Although observational pain-assessment tools (Table 2)[43-47] can assist with identifying the presence of pain, they cannot replace the input of a parent or caregiver who is involved with the child daily.

Pain management begins with an assessment of and treatment for sources of tissue injury and inflammation, while simultaneously considering interventions that target symptoms [opioids, tricyclic antidepressants, gabapentin, anticholinergics]. It is also critical to consider whether a persistent symptom—despite comprehensive evaluation, management of contributing problems, and use of symptom management strategies—is a "marker" of an irreversible decline in a child's overall neurologic function and health status.

When considering treatment of pain in children with SNI, the clinician should consider the different types of pain, the common clinical features, and the effective management strategies for the sources of pain that are common to these children.

Nociceptive Pain. Commonly recognized pain sources in children with SNI include acute sources such as fracture, urinary tract infection, nephrolithiasis or pancreatitis[51] and chronic sources such as gastroesophageal reflex (gastroesophageal reflux (GER)), constipation, feeding difficulties from delayed gut motility, positioning, spasticity, hip pain from subluxation, or dental pain.

Neuropathic Pain. Neuropathic pain is an important pain source to consider in children with SNI who have unexplained persistent pain behaviors. Terms such as "screaming of unknown origin,"[52] agitation, cerebral irritation, and neuro-irritability are used to describe such children. Neuropathic pain in children with SNI can be secondary to disease and medication but is also associated with repeated injury or surgery.[53,54] Medications used for neuropathic pain include opioids, tricyclic antidepressants (nortriptyline), and anticonvulsants (such as gabapentin and carbamazepine).[55,56] Treatment with gabapentin in children with SNI can lead to a significant reduction in pain symptoms, improvement in feeding intolerance, and improved sleep.[57] Transcutaneous electrical nerve stimulation may also be helpful if tolerated by the child, especially following orthopedic surgery.[53]

Central Pain. Central pain is caused by dysfunction of the central nervous system, causing malfunction of the pain system such as from multiple sclerosis or cerebral vascular accident.[58] Although historically referred to as thalamic pain syndrome, central pain is not limited to injury of the thalamus.[58] In addition to such pain descriptors as burning and aching, the child may

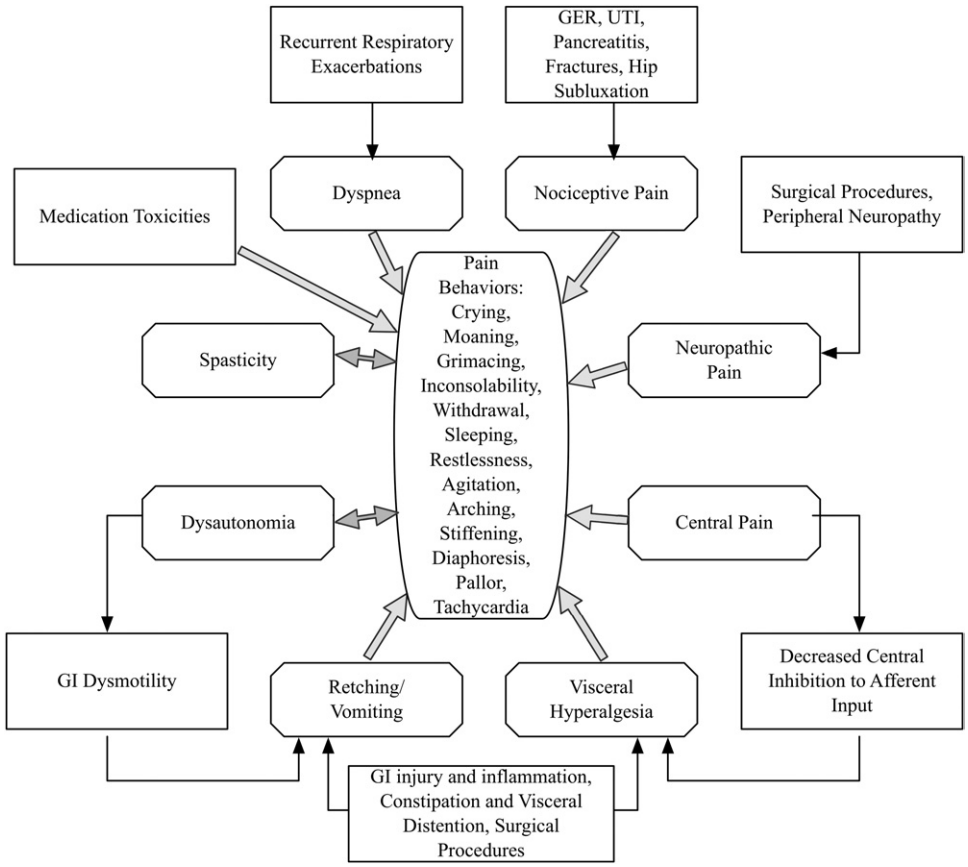

FIG 4. Sources of pain behaviors in children with severe neurologic injury.

experience visceral pain, such as an exaggerated sensation of painful fullness from bladder and visceral distention.[58,59] Symptoms are a mixture of poorly localized and constant discomfort with brief bursts of intense pain. Although not described in children, central pain is a source for consideration in children with impairment of the central nervous system. Interventions include nortriptyline, gabapentin, and lamotrigine.[58]

Visceral Hyperalgesia. Visceral hyperalgesia is an altered response to visceral stimulation resulting in a decreased activation threshold for pain in response to a stimulus such as intraluminal pressure.[60] Pain in children with SNI was commonly localized to the bowels, gastrointestinal tract, and digestion despite treatment of problems such as constipation and GER.[40,43] Visceral hyperalgesia and central pain are another potential source of such pain. Treatment of visceral hyperalgesia includes gabapentin and nortriptyline.[61-63]

Neuropathic pain is an important pain source to consider in children with SNI who have unexplained persistent pain behaviors.

Special Considerations

Medication Toxicities. It is essential to consider medication toxicities when first assessing a child with SNI, as many of the associated features are the same as the behaviors associated with pain. Children with SNI are commonly on multiple medications, increasing the risk of adverse effects.[44] Although the features are commonly described as developing over hours, case reports in children with SNI indicate a significant delay in recognition.[64,65] It is important to understand drug–drug interactions (such as how 1 medication may alter the metabolism of another) and the receptor properties of medications to avoid duplication.[66]

Empiric Therapy for Symptoms of Unclear Etiology. When the source of the symptoms cannot be identified, the clinician should consider the most-likely source as the "working diagnosis." In the setting of persis-

TABLE 6. Medications used for treatment of common symptoms (maximum weight 50 kg)

Medications	Mechanisms of action	Usual starting dose (maximum starting dose)
Neuropathic pain and neuro-irritability (including central pain and visceral hyperalgesia)		
Gabapentin	Thought to inhibit excitation by binding to the alpha-2-delta subunit of voltage-dependent Ca ion channels in the CNS	Day 1-3: 5 mg/kg/dose PO qhs Day 4-6: 2.5 mg/kg/dose am and midday and 5 mg/kg qhs Day 7-9: 2.5 mg/kg/dose am and midday and 10 mg/kg qhs Day 10-12: 5 mg/kg/dose am and midday and 10 mg/kg qhs Increase every 4th day by 5 mg/kg/d until (1) effective analgesia (titrating to minimum dose of 30-40 mg kg^{-1} d^{-1} for children >5 years and 40-60 mg/kg/d for children <5 years); (2) side effects experienced; (3) total dose of 60-75 mg kg^{-1} d^{-1} reached (maximum 3600 mg/d); (4) consider half of total dose as the evening dose; (5) titrate more rapidly if tolerated
Nortriptyline	Presynaptic reuptake inhibition of norepinephrine and serotonin, both inhibitors of pain transmission	Day 1-4: 0.2 mg/kg PO qhs Day 5-8: 0.4 mg/kg PO qhs Increase every 5th day by 0.2 mg/kg/d until (1) effective analgesia; (2) dosing reaches 1 mg/kg/d (maximum 50 mg/d); (3) obtain plasma level and ECG before further dose escalation beyond 1 mg/kg/d
Agitation/pain adjuvant (?)		
Clonazapam	Increases affinity of GABA for $GABA_A$ receptors	0.005-0.01 mg/kg PO q 8-12 h (0.25-0.5 mg)
Dysautonomia (features include flushing, sweating, tachycardia, retching, agitation, and stiffening)		
Clonidine	Centrally acting alpha 2 adrenergic receptor agonist, reducing sympathetic outflow	Day 1-3: 0.002 mg/kg PO qhs (maximum 0.1 mg) Day 4-6: 0.002 mg/kg q 12 h Day 7-9: 0.002 mg/kg q 8 h In addition: (1) 0.002 mg/kg q 4 h prn "autonomic storm" (2) doses may be increased to 0.004 mg/kg (3) titrate more rapidly if tolerated
Gabapentin	See above	See neuropathic pain section
Cyproheptadine	5-HT_2, H_1, and ACH receptor antagonist	0.08 mg/kg PO Q 8 h (4 mg) If no benefit in 3-5 d, increase each dose by 0.04-0.08 mg/kg
Morphine sulfate	CNS opioid receptors	0.3 mg/kg PO/SL Q 3-4 h prn "autonomic storm"
Diazepam	See above	0.05-0.2 mg/kg PO/IV q 6 h prn "autonomic storm" (2.5-10 mg)
Dyspnea		
Morphine	CNS opioid receptors	0.1 mg/kg PO or 0.05 mg/kg IV/Sq q 3-4 h prn (5 mg PO, 2.5 mg IV) (10 mg/5 ml, 20 mg/mL)
Lorazepam	See above	0.025-0.05 mg/kg PO/SL/IV/SQ q 6 h prn (max dose 2 mg)
Midazolam	See above	0.2 mg/kg PO/SL (10 mg)
Respiratory secretions		
Ipratropium	All are ACH receptor antagonists	250-500 μg nebulization Q 4-6 h prn
Glycopyrrolate		0.04-0.05 mg/kg PO q 4-8 h (1-2 mg)
Hyoscyamine		<2 y 4 drops PO/SL Q 4 h prn (0.125 mg/mL) 2-12 y 8 drops PO Q 4 h prn (0.125 mg/mL)
Retching and vomiting (mechanism of action indicated as receptor antagonist)		
Cyproheptadine	5-HT_2, H_1, and ACH	See dysautonomia above (children with SNI and retching)
Ondansetron	5-HT_3	0.15 mg/kg PO/IV q 8 h prn (4-8 mg)
Metoclopramide	D_2-prokinetic	Prokinetic: 0.1-0.2 mg/kg PO/IV q 6 h (max dose 10 mg)

Abbreviations: HT, serotonin; H1, histamine; ACH, acetylcholine; D2, dopamine.
Modified from Schechter and coworkers,[23] and Goldman A, Hain R, Liben S, editors. Oxford Textbook of Palliative Care for Children. Oxford University Press, Oxford, 2006.

tent distress without a clear source, children with SNI often benefit from a medication trial that targets peripheral neuropathic pain, central pain, and visceral hyperalgesia. Table 6 provides recommendations for gabapentin and nortriptyline. Empiric therapy should be initiated with clear goals to measure effective management and then evaluated for effectiveness and titrated to effect if insufficient or discontinued if not helpful. It is very important to stop a medicine that is ineffective, as medication toxicities are a significant problem for these children.

Nonpharmacological Management. This is a critical part of symptom management in children with SNI. Parents often become very adept at identifying comfort strategies such as rocking, massaging, and repositioning. Other interventions include venting gastrostomy feeding tubes and altering tube feedings. Supportive equipment can minimize positional pain, such as seating systems and supportive pillows. Other modalities include aromatherapy and acupuncture.[67]

Benzodiazepines. Benzodiazepines are commonly used in children with SNI, including for spasticity, dystonia, dysautonomia, seizures, agitation, irritability, and sleep. They are generally safe and effective in the short term, although sedation and paradoxical effects, including agitation and irritability, do occur.[68] Limitations of daily, prolonged use are a result of tolerance, with a decrease of benzodiazepine binding sites. This can be prevented using intermittently (prolonged seizure, intermittent muscle spasms, or "autonomic storms") or short term as other medications are initiated (gabapentin, clonidine), ideally less than 4 weeks. Sudden cessation with prolonged use can result in a withdrawal syndrome.

Spasticity, Hypertonia, and Muscle Spasms

In isolation, spasticity—an increased resistance to stretch[69]—and hypertonia are often not painful. They can, however, increase with acute illness and sources of discomfort (pain, constipation, and reflux). In addition, increased tone can cause musculoskeletal injury and inflammation. Intermittent muscle spasms, in contrast, can be painful and increase also in frequency because of other illnesses and pain.

While there are various therapeutic interventions available—including physical therapy, medications, and surgery—it is important to search for sources of pain that can increase spasticity and frequency of muscle spasms. Symptom-management trials should be considered for persistent and troublesome spasticity. Effective inteventions include botulinum toxin A for localized/segmental spasticity and pain; diazepam for short-term treatment of generalized spasticity; intrathecal baclofen pump for severe generalized spasticity: and tizanidine.[70-72] Baclofen, dantrolene, and clonidine may be beneficial as well.[73] Side effects include sedation, drowsiness, and muscle weakness, are dose-related, and improve with dose reduction.

Autonomic Dysfunction

Autonomic dysfunction, also called dysautonomia, autonomic storm, sympathetic storm, and paroxysmal sympathetic hyperactivity, includes features such as tachycardia or bradycardia; hyperthermia or hypothermia; pallor, flushing and redness of the face and body; retching, vomiting, bowel dysmotility, and constipation; urinary retention; abnormal sweating; increased salivation; posturing and agitation; generalized discomfort; and abdominal pain.[74]

Unfortunately, treatment of dysautonomia in children with SNI has been limited to case reports predominantly in patients with hypoxic and traumatic brain injury, with mixed results from benzodiazepines, bromocriptine, clonidine, oral and intrathecal baclofen, beta antagonists, and morphine sulfate.[75,76] Case reports of hypothalamic dysfunction with hypothermia have indicated improvement from cyproheptadine, with a decrease or elimination in associated symptoms, including diaphoresis, vomiting, and abdominal pain.[77,78] Gabapentin was beneficial in children with traumatic brain injury when symptoms persisted despite treatment with bromocriptine, benzodiazepine, morphine, clonidine, intrathecal baclofen, and metoprolol.[79] Pregabalin showed a decrease in symptoms in individuals with familial dysautonomia.[74] In addition to a trial of gabapentin or cyproheptadine, children with intermittent "autonomic storms" (often manifested by an acute onset of facial flushing, sweating, tachycardia, retching, agitation, and stiffening) may benefit from as needed clonidine, morphine sulfate, or diazepam during episodes.

Recurrent Respiratory Illness

Children with SNI have a high incidence of respiratory problems.[80] Recurrent respiratory illness leading to respiratory compromise and failure is the most common cause of mortality in children with severe cerebral palsy,[81] with aspiration being a frequent factor.[82] While often referred to as an "aspiration pneumonia," respiratory exacerbations and compromise in neurologically impaired children is better understood as an acute exacerbation resulting from chronic contributing factors, including the following:

1. Diminished effectiveness of cough
2. Shallow breathing from inactivity and motor impairment

3. Chronic aspiration of oral secretions resulting in inflammation and infection
4. Impaired ability to mobilize pulmonary secretions
5. Development of mucous plugs with ventilation/perfusion (V/Q) mismatch
6. Concomitant medical problems (such as GER and neuromuscular scoliosis).

In children with SNI and recurrent respiratory illnesses, it is misleading to parents to label respiratory exacerbations as "aspiration pneumonia" as this can give the impression of a reversible problem. Instead, it can be helpful to acknowledge that the goal of chronic and acute treatment is to minimize the effect of these factors and maximize maintenance and recovery of health while we prepare for diminishing benefit. When considering an intervention, it is essential to determine what the intervention will improve in the context of the degree of ongoing benefit from chronic and acute interventions such as outlined in Table 7. Unfortunately, especially for the available invasive procedures, the evidence suggests that many of the interventions that were traditionally felt to be definitive therapy for these problems may not be as effective as thought.

Special Considerations

Antireflux Surgery. Antireflux surgery does not routinely alter frequency of pneumonia in children with SNI, although it is often offered for this purpose.[83-88] It can result in retching or worsen preexisting retching, a distressing symptom seen in children with SNI.[89]

Tracheotomy. Neurologically impaired children had increased mortality with tracheotomies when compared with children with conditions of airway obstruction.[90,91] This likely reflects greater benefit for airway obstruction vs the multifactoral issues for children with SNI.

Salivary Duct. Although studies are not as clear, surgical ligation or botulinum toxin injection decreases drooling and suctioning but does not seem to alter the frequency of lower respiratory tract infection in children with chronic pulmonary aspiration.[92]

Dyspnea

Dyspnea is the experience of shortness of breath, difficulty of breathing, or uncomfortable breathing.

TABLE 7. Respiratory Home Management—Medical and Symptom Treatment Strategies

Chronic Interventions	
Suctioning	As needed for comfort
Oxygen	Assessed by appearance of patient or by oximeter
Albuterol nebulizer	Every 3-4 h for coughing, wheezing, congestion
Ipratropium (Atrovent) nebulizer	Every 3-4 h for coughing, wheezing, congestion
Saline or Mucomyst nebulizer	As needed for thick secretions
Chest physiotherapy or vest	2 times/day, increase to 4 times/day with increased symptoms[a]
Nebulized budesonide (Pulmicort)	2 times/day, increase to 4 times/day with increased symptoms[a]
Acute interventions for respiratory exacerbations from chronic aspiration	
Clindamycin, Augmentin, or Levofloxacin/Moxifloxacin[b]	10-14 d
Systemic steroids (prednisone)[c]	5 d
Additional interventions for symptom management and end-of-life care	
Fan on face	Relieves sensation of breathlessness
Morphine sulfate	Use for respiratory distress[d] Starting dose 0.1 mg/kg/dose PO/SL/Gtube (max 5 mg) May increase by 30%-50% until comfortable
Glycopyrrolate (Robinul), Scopalamine, hyoscyamine	May contribute to mucous plugging; decreases oral and respiratory secretions in end-of-life care

[a]Symptoms include increased coughing, secretions, congestion, respiratory rate, and breathing effort.
[b]Use when respiratory symptoms persist or worsen despite an increase in chronic interventions.
[c]Include with third or fourth exacerbation, sooner if recurrence within 2 months of antibiotic course.
[d]Features suggesting respiratory distress include facial expression such as grimacing, appearing restless, having an anxious look, stiffening, tears, or becoming withdrawn.
Adapted from Hauer[93] (Table 1). Reprinted with permission from Journal of Palliative Medicine.

Strategies for identifying dyspnea in a nonverbal child with SNI are similar to pain assessment of such children, although physiologic markers do not necessarily correlate with the patient's perception of breathlessness. Assessment includes asking a family if they have observed their child to be in distress or appear anxious during a respiratory exacerbation.

Importantly, breathlessness can increase the appearance of respiratory distress and work of breathing. A single-dose trial of low-dose morphine can be very effective in assessing and treating for dyspnea when the situation is unclear. If distress improves and other physiologic parameters remain stable, consider continuing on an as-needed basis. Table 7 outlines chronic

and acute home-care strategies for children with SNI and recurrent respiratory illnesses.[93]

Secretions

When evaluating and managing oral and pulmonary secretions in children with SNI, it is helpful to consider sialorrhea separately from respiratory secretions. Sialorrhea involves thin, watery secretions that can pool out of the mouth because of diminished oral sensation of saliva. Glycopyrrolate and interventions to the salivary ducts are effective in diminishing sialorrhea.

In contrast, an increase in lower respiratory secretions in children with SNI may be due to impaired mobilization, an increase in pulmonary mucus due to chronic silent aspiration, and increased saliva production from autonomic dysfunction. Management includes secretion mobilization with chest physiotherapy or pulmonary vest therapy[94] and interventions to the salivary ducts to decrease frequency of suctioning. Inhaled corticosteroids, with a 5-day course of prednisone during acute exacerbations, may improve pulmonary inflammation. Decreasing total fluid intake by 25% or greater is another simple intervention to consider for management of excessive respiratory secretions. Finally, anticholinergic medications (Table 6) are available to decrease secretions but should be used with caution in this population, as they can result in thicker secretions that are more difficult to mobilize.

Retching, Vomiting, and Feeding Intolerance

Gastrointestinal problems and symptoms are common in children with SNI, including retching, vomiting, and pain.[40,95] Vomiting in these children is commonly attributed to GER;[95] however, dysautonomia, visceral hyperalgesia/central pain, and activation of the emetic reflex[89,96] are likely underrecognized sources.

Visceral Hyperalgesia as a Source of Vomiting, Retching, and Feeding Intolerance

Zangen et al.[61] speculate that repeated painful gastrointestinal experiences contribute to sensitization of visceral afferent pathways. Children with SNI have an increased frequency of sensitizing experiences such as GER, constipation, gastrostomy tube placement, and antireflux surgery.[95] In nonverbal children with SNI, visceral hyperalgesia is suggested by pain behaviors and feeding intolerance from routine gastric and intestinal distention associated with tube feedings and intestinal gas, from colonic distention associated with flatus and bowel movements, and in response to a noxious stimulus such as prolonged crying spells associated with GER.

Treatment

The clinician should first empirically treat common concomitant problems, such as constipation and GER. If no improvement, self-limited empiric trials directed at the potential sources may include medications for visceral hyperalgesia/central pain (gabapentin, nortriptyline), retching (cyproheptadine), dysautonomia (cyproheptadine, gabapentin, clonidine), and the emetic reflex (ondansetron). Other intervention strategies include an empiric trial of an elemental formula, an empiric trial of metronidazole or rifaximin for small bowel bacterial overgrowth, and a trial of J-tube feedings. Experience shows that J-tube feedings may not improve the pain associated with vomiting. Finally, some children will benefit from a decrease by 25%-30% or greater in the total amount of nutrition and fluids provided by feeding tube. As there is limited evidence to guide in these empiric trials, the medication should be continued only if helpful, titrated to effect if insufficient, or discontinued if not helpful. As mentioned earlier, it is very important to stop a medicine that is ineffective, as medication toxicities are a significant problem for these children.

Special Considerations

Retching After Anti-Reflux Surgery. Children with SNI have a higher failure rate and increased incidence of pain, retching, and vomiting following antireflux surgery.[61,89,96,97] In addition, antireflux surgery may cause retching in these children.[89,96,97] Visceral hyperalgesia plays a role in this setting,[89] making tricyclic antidepressants, gabapentin, cyproheptadine, and dicyclomine reasonable treatment strategies.[61,97] It is essential that medical and symptom-management modalities be maximized before considering surgical intervention in these children.

Persistent Feeding Intolerance

As with recurrent respiratory exacerbations, the initial benefit from treatment interventions may lessen

over time. This may reflect irreversible changes in the nervous system including autonomic dysfunction, visceral hyperalgesia, or central pain and may account for why some children with SNI develop feeding intolerance that is not amenable to medical interventions.[98] Management strategies should include treating these forms of pain, as discussed previously.

Special Considerations

Fluids. Calculating "maintenance" fluids by weight assumes an average amount of insensible loss, although a child with limited activity may not "require" the amount calculated. Some children with SNI, in contrast, may have less gastrointestinal pain, feeding intolerance, and secretions if the amount of fluids is "restricted."

Nutrition. Children with SNI who receive nutrition by a feeding tube are at risk for excessive weight gain. Those requiring total care, including transfers, may benefit from a weight to length goal of the 10th percentile. This can be accomplished by monitoring weight, reducing caloric intake by decreasing volume, and supplementing with micronutrients and protein as needed.

Discontinuing Medical Nutrition and Hydration. Discontinuing medical nutrition and hydration remains challenging and controversial. A feeding tube is a life-sustaining technology in the same sense as a ventilator. While these tubes, once in place, are generally well tolerated, sometimes feeding can be a significant source of pain, particularly for children with SNI, as discussed. In these circumstances, it is permissible to discontinue medical nutrition/hydration when it is prolonging or contributing to suffering.[99-101] Navigating the ethical, legal, clinical, and self-care issues surrounding the discontinuation of nutrition and hydration can be challenging, and the clinician should illicit the support of a palliative care team.

Psychosocial Issues

Communicating with Children

Developmentally, appropriate communication can improve a child's understanding of a disease, lessen stress and anxiety, facilitate comfort, and facilitate a child's involvement in care and decision-making. Children benefit from simple, concrete, factual information to explain their health status and care plan. Euphemisms about illness, death, and dying can lead to greater confusion. It is important to be clear and honest but not overwhelm the child with information. Information must be delivered in language that is appropriate to the child's developmental age and individual preferences.[19] Parents play a crucial role throughout this process yet can feel confused and uncertain about the amount of information to share with their child. Helping parents navigate these challenges can allow them to be open and available to their seriously ill child and the child's siblings.[102] Table 8 further describes some of the communication, emotional, and coping needs of children at different ages.

Child Participation in Decision Making

Children suffer when they do not feel a sense of control over what is happening to them. Traditionally, children were considered minimal participants in medical decisions. Even young children, however, often know that they are dying despite never being directly told[103] and may have the ability to voice their preferences about treatment and care decisions.[104] Most adolescents with life-threatening conditions have considered the potentially life-limiting nature of their disease and their preferences should be considered, especially regarding end-of-life care.[105] Paternalistic approaches toward the preferences and decisions of older children and adolescents' will undermine respect for their emerging autonomy and the emotional investment they have in their current values.[106]

Except in extreme circumstances, parents have the legal right and obligation to act as surrogate decision makers for their children less than 18 years of age. There is growing recognition, however, of a child's right to be informed and actively involved in decisions pertaining to care.[107,108] Children older than 14 years of age are generally viewed as having the ability to reason as well as a competent adult. Children as young as 9 years are able to express reasonable preferences regarding treatment that render them capable of participating in decisions about their own health.[108,109] Children with more prolonged conditions (eg, cystic fibrosis, certain kinds of cancer, complicated types of heart disease) will have a range of physical and psychologic experiences, such as experiencing the death of a friend with a similar condition. Such experience deserves a voice at the table.

Having the capacity to provide consent requires that a person have the ability to (1) understand the information, (2) understand the implications to treatment, (3) weigh risks and benefits, and (4) communicate a

TABLE 8. Cognitive concepts and emotional, communication, and coping strategies

	Infants and toddlers (age 0-3)	Preschool age (age 3-6)	School-age (age 7-12)	Adolescents (age 13-17)
Major Characteristics	Interactions initially limited to sensory and motor actions. Achieves object permanence.	Egocentric. Uses magical and animistic thinking. Understanding centers on interweaving fact and fantasy. Can engage in symbolic play.	Begin to differentiate between self and others. Concrete thoughts with beginning transition to more logical thinking.	Capable of abstract thoughts; reality becomes objective. Body image and self-esteem paramount. Begins to identify with cultural specificity and to challenge parental views. Separate by developing peer-group identity.
Concept of spirituality	Needs a sense of trust and hope in others. Developing need for self-worth and love.	Spirituality is magical and imaginative. Participation in rituals becomes important.	Develops concern over right and wrong. Start connecting ritual with personal identity and accepting external interpretation as truth.	Searches for meaning, purpose, hope, and value of life. Begins to accept internal interpretations as truth. Evolution of relationship with higher power.
Concept of death	No concept of death.	Death is a temporary separation and reversible.	Death is irreversible and personal. Interested in physiology and details of death.	Explores nonphysical explanations of death.
Concept of illness	Limited concept of reality and may simply sense something is wrong.	Illness perceived as the result of a "contagion" or from contact with an object or person and benefit from reassurance.	Understands illness as something separate from oneself that is capable of injuring ones body. May feel responsible and need reassurance. Begin to demonstrate mature understanding of illness.	Very self-conscious of physical change. Struggle with need for independence and physical dependence due to illness.
Emotional strategies	Focused on providing maximal physical relief of suffering.	May feel responsible for illness and misinterpret emotions (eg, think sadness is disappointment). Benefits from clarification of misconceptions and reassurance.	Should be invited to share their emotions when they are ready. May exhibit stoic responses in an attempt to protect their parents and caregivers.	Should be helped to communicate feelings and invited to share their thoughts and sadness when they are ready. May turn to a nonparental adult to share sadness.
Communication strategies	Benefits from simple physical communication (consoling).	Use precise language (avoid euphemisms). Evaluate for feelings of guilt and anger at self or others. Correct improper attribution ("I must have done something to deserve this"). Benefits from exploring the child's understanding of the cause of illness and correcting misconceptions, and dispeling guilt.	Should have some participation in decision making. Evaluate for fears of abandonment and perception of body mutilation. Benefits from open, honest communication and concrete details of treatments. Also benefits from indirect communication such as cards, tapes, and gifts.	Key participant in decision making. Benefits from clear, direct, honest communication.
Coping strategies	Benefits from physical touch, maintaining routines, and safe environment.	Benefits from minimizing separation from family and maintaining consistency in daily routine. Utilizes play, puppets, dolls, expressive therapies and story telling in coping and learning.	Benefits from maintaining access to peers and fostering a sense of control/mastery over the illness. Benefits from maintaining usual activities as much as possible.	Benefits from reinforcement of body image and fostering self-esteem by providing privacy and promoting independence. Benefits from access to peers and support groups and utilizing creative outlets. Is at risk for developing depression and risk-taking behaviors

choice.[110] Assent is considered a child's agreement to treatment without having the legal capacity to consent. Key features of assent include (1) providing a developmentally appropriate description of the illness and the treatments, 2) assessing the child's understanding of this information, and (3) soliciting the patient's willingness to accept treatment.[107] Core to the idea of assent is the knowledge that the child's cognitive

ability to understand the disease and consequences of medical decisions. By collaborating with parents and communicating with the child and adolescent in a developmentally appropriate way, the pediatrician can facilitate an appropriate transition from surrogate decision making to assent and autonomy.

Both consent and assent can be facilitated using language and descriptions that the child and family can understand, tailoring the information to the abilities of the individual, breaking information down into parts, allowing time to process the impact of treatment, and providing emotional support throughout the process. As the child's ability develops, support can be given to the adolescent's preferences and decisions with the parent taking the role of educator, challenger, and shared decision-maker.[111] The goal is to create a supportive environment that allows decisions to be made cooperatively between the child, parents, and care team.

Spirituality

Spirituality represents how an individual seeks connectedness, meaning, and understanding in life and, in its most fundamental form, represents a child's approach to understanding life.

The way in which children express an awareness of spirituality varies based on age (Table 8).[112] Spirituality is closely tied to the fears and uncertainties experienced in life. For most patients and parents, serious illness naturally raises thoughts of fairness, anger, and blame with a desire to seek meaning at such times.[113] Attending to the spiritual needs of the child and family can help the child with expression of such thoughts, prepare parents for questions from children, help bring meaning to what the family is enduring, and provide hope and comfort at end of life.[114] Interdisciplinary care that explores these spiritual needs can provide an avenue for expression of the beliefs, values, hopes, and fears that often guide decisions and impact grieving.

Developmental Understanding of Death

Children understand death as a changed state as early as 3 years of age, universality by about 5 to 6 years of age, and personal mortality by 8 to 9 years of age.[115,116] In addition, the concept of death is influenced by personal experiences and culture. Details that can help a parent understand how to support their child with serious illness and other children in the family based on developmental age are included in Table 8.[115-117]

Care in the School

Children with life-threatening conditions and severe neurologic impairment routinely attend school. As these conditions progress, many children choose to remain in school as long as possible in an effort to maintain social relationships and daily routines. Schools are now caring for children with a significant health care needs at risk of a potentially life-threatening event. The pediatrician must collaborate with school nurses, teachers, and administrators in developing an individualized plan of care that addresses emergency and symptom management challenges. Social workers and child life specialists can work with school systems to assist the other children in the classroom, including preparing students before a child's return to school or assisting bereavement following the death of a child.

Bereavement is described as a process of "relearning the world."

Grief and Bereavement

Bereavement of parents is considered the most intense grief known.[118] Many parents who have lost a child describe that a part of them has also been lost. Parents describe adjusting to the loss of the physical presence of holding and touching their child as well as the loss of what their child will not experience.[119] Parents who indicated that they have not worked through their grief have an increased risk of long-term mental and physical morbidity, an increased health service use, and an increased amount of sick leave.[120] Despite our understanding of the intensity of the loss and the subsequent associated risks, there is still much to understand, including what experiences fall within an expected course following the loss of a child and what interventions can impact the long-term outcome following such a loss.

Bereavement is poignantly described by Attig as a process of "relearning the world."[121] The process of bereavement has been described to include experiencing the pain and emotional aspects of the loss, adjusting to an environment in which the deceased is missing, finding ways to memorialize that person, accepting the reality of the loss, and relocating the

dead person within one's life. It has been described as a dual process in which an individual oscillates between focusing on loss/grieving and restoration/coping.[122] Parents identify the process of living "without closure" as part of "being a good parent" and "keeping the memories alive."[123] Parents' ability to maintain a continued bond with their deceased child and integrate memories into a new reality is considered central to parental bereavement and adjustment.[124]

Anticipatory Grief

Anticipatory grief is the emotional preparatory experience leading up to the time of death.[125] It describes the process of coping, interaction, psychosocial reorganization, planning, balancing of conflicting demands, and facilitation of an appropriate death. Parents who shared and sought support during their child's illness and during the last month of the child's life identified better coping following the loss.[126] Support provided by health care staff, the attitudes of staff, and satisfaction with end-of-life care can have a positive impact on the parental grief response.[126,127]

Sibling Grief

Studies of bereaved siblings have shown that they may experience social isolation and withdrawal that can have a lifelong impact.[128] Interventions that can be helpful include addressing their fears and concerns about the cause of death, including them throughout the illness trajectory, allowing them to have safe outlets for their feelings such as expressive arts, and creating opportunities for their needs to be identified and met.[128] Table 8 shows the emotional, communication, and coping strategies of children that can be beneficial for siblings.

Bereavement Support

Parents and siblings can be supported through their loss by knowing the community resources available through palliative care and hospice programs. These resources may include access to mental health specialists, clergy and spiritual support, self-help groups, and bereavement programs often through hospice agencies and religious groups. Such services have been identified by families as beneficial.[129,130] Children and parents most appreciate the support and understanding they receive, the freedom to express themselves, a diminished sense of isolation, and the normalization of their emotions.[129] Parents identified using a hospice child bereavement support service for advice and reassurance, support for their children while they grieved, and advice on ameliorating behavioral difficulties at home and school.[130] Even those who did not use the service identified that it was helpful to know that the service existed so their children's needs could be addressed. Children and their parents felt they benefited from talking to a nonfamily member and being involved in social events that reduced feelings of isolation.[130]

Contacting a family following the death of a child can have a positive impact on families. After a child dies, parents also lose a support network they developed in the hospital and may feel cut off from the people with whom they developed an intense bond.[131] When a clinician has become close to the patient and family, writing a condolence card[132] and attending the memorial or funeral service may be appropriate. This allows a family to recognize the concern and caring of the clinician as well as provide an opportunity for healing and closure for the clinician.

References

1. Arias E, MacDorman MF, Strobino DM, Guyer B. Annual summary of vital statistics. Pediatrics 2002:112(6 Pt. 1): 1215-30.
2. Himelstein BP, Hilden JM, Boldt AM, Weissman D. Pediatric palliative care. N Engl J Med 2004;350(17):1752-62.
3. Feudtner C, diGiuseppe DL, Neff JM. Hospital care for children and young adults in the last year of life: A population-based study. BMC Med 2003;1:3.
4. American Academy of Pediatrics. Committee on Bioethics and Committee on Hospital Care. Palliative care for children. Pediatrics 2000;106(2 Pt 1):351-7.
5. Field MJ, Behrman RE, editors. Institute of Medicine (U.S.). In: Committee on Palliative and End-of-Life Care for Children and Their Families. When Children Die: Improving Palliative and End-of-Life Care for Children and Their Families. Washington, D.C.: National Academies Press; 2003.
6. Wolfe J, Klar N, Grier HE, Duncan J, Salem-Schatz S, Emanuel EJ, et al. Understanding of prognosis among parents of children who died of cancer: Impact on treatment goals and integration of palliative care. JAMA 2000; 284(19):2469-75.
7. Mack JW, Wolfe J, Cook EF, Grier HE, Cleary PD, Weeks JC. Hope and prognostic disclosure. J Clin Oncol 2007;25(35):5636-42.
8. Valdimarsdóttir U, Kreicbergs U, Hauksdóttir A, Hunt H, Onelöv E, Henter JI, et al. Parents' intellectual and emotional awareness of their child's impending death to cancer: A population-based long-term follow-up study. Lancet Oncol 2007;8(8):706-14.
9. Stromgren AS, Sjogren P, Goldschmidt D, Petersen MA,

Pedersen L, Hoermann L, et al. A longitudinal study of palliative care: Patient-evaluated outcome and impact of attrition. Cancer 2005;103(8):1747-55.
10. Weeks JC, Cook EF, O'Day SJ, Peterson LM, Wenger N, Reding D, et al. Relationship between cancer patients' predictions of prognosis and their treatment preferences. JAMA 1998;279(21):1709-14.
11. Morita T, Akechi T, Ikenaga M, Kizawa Y, Kohara H, Mukaiyama T, et al. Late referrals to specialized palliative care service in Japan. J Clin Oncol 2005;23(12):2637-44.
12. Liben S, Papadatou D, Wolfe J. Paediatric palliative care: challenges and emerging ideas. Lancet 2008;371(9615):852-64.
13. Levetown M, editor. Compendium of Pediatric Palliative Care. Children's International Project on Palliative/Hospice Services (ChIPPS). Alexandria, VA: National Hospice and Palliative Care Organization, 2000.
14. Last Acts Palliative Care Task Force. Precepts of palliative care for children/adolescents and their families (Accessed March 29, 2004 at: http://www.lastacts.org/files/publications/pedprecept.pdf).
15. Kane JR, Himelstein BP. Palliative care in pediatrics. In: Berger AM, Portenoy RK, Weissman DE, editors. Principles and Practice of Palliative Care and Supportive Oncology, 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2002.
16. Feudtner C. Collaborative communication in pediatric palliative care: A foundation for problem-solving and decision-making. Pediatr Clin North Am 2007;54(5):583-607, ix.
17. Dussel V, Kreicbergs U, Hilden JM. Looking beyond where children die: Determinants and effects of planning a child's location of death. J Pain Symptom Manage 2009;37(1):33-43.
18. Hays RM, Haynes G, Geyer JR, et al. Communication at the end of life. In: Carter BS, Levetown M, editors. Palliative Care for Infants, Children, and Adolescents: A Practical Handbook. Baltimore (MD): Johns Hopkins University Press, 1992.
19. Kang T, Hoehn KS, Licht DJ, Mayer OH, Santucci G, Carroll JM, et al. Pediatric palliative, end-of-life, and bereavement care. Pediatr Clin North Am 2005;52(4):1029-46, viii.
20. Feinstein JA, Ernst LM, Ganesh J, Feudtner C. What new information pediatric autopsies can provide: A retrospective evaluation of 100 consecutive autopsies using family-centered criteria. Arch Pediatr Adolesc Med 2007;161(12):1190-6.
21. Riggs D, Weibley RE. Autopsies and the pediatric intensive care unit. Pediatr Clin North Am 1994;41(6):1383-93.
22. Committee on Psychosocial Aspects of Child and Family Health. The assessment and management of acute pain in infants, children, and adolescents. Pediatrics 2001;108(3):793-97.
23. Schechter NL, Berde CB, Yaster M. Pain in infants, children, and adolescents: An overview. In: Schechter NL, Berde CB, Yaster M, editors. Pain in Infants, Children, and Adolescents. Baltimore (MD): Williams & Wilkins; 1993.
24. Cassell EJ. The nature of suffering and the goals of medicine. N Engl J Med 1982;306:639-45.
25. McGrath PA. Pain control. In: Doyle D, HG Cherny N, Calman K editors. Oxford Textbook of Palliative Medicine, 3rd ed. New York: Oxford University Press; 2005.
26. McGrath PA. Development of the World Health Organization Guidelines on cancer pain relief and palliative care in children. J Pain Symptom Manage 1996;12(2):87-92.
27. Bellieni C. Pain definitions revised: Newborns not only feel pain, they also suffer. Ethics Med 2005;21(1):5-9.
28. Fitzgerald M, Anand KJS. Developmental neuroanatomy and neurophysiology of pain. In: Schecter NL, Berde CB, Yaster M, editors. Pain in Infants, Children, and Adolescents. Baltimore, MD: Williams and Wilkins, 1993. p. 11-3.
29. Portenoy RK. Opioid tolerance and responsiveness: Research findings and clinical observations. In: Gebhardt G, editor. Progress in Pain Research and Management. Seattle (WA): IASP Press; 1994. p. 615-19.
30. Strouse TB. Pharmacokinetic drug interactions in palliative care: Focus on opioids. J Palliat Med 2009;12(11):1043-50.
31. Abraham J. A Physicians's Guide to Pain and Symptom Management in Cancer Patients. Baltimore (MD): Johns Hopkins University Press; 2000.
32. Anand K. Physiology of pain in infants and children. In: Pain in Infancy and Childhood. Ann Nestle 1999;1-12.
33. Berde CB, Sethna NF. Analgesics for the treatment of pain in children. N Engl J Med 2002;347(14):1094-103.
34. Williams DG, Patel A, Howard RF. Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability. Br J Anaesth 2002;89(6):839-45.
35. Ciszkowski C, Madadi P, Phillips MS, Lauwers AE, Koren G. Codeine, ultrarapid-metabolism genotype, and postoperative death. N Engl J Med 2009;361(8):827-28.
36. Jalmsell L, Kreicbergs U, Onelov E, Steineck G, Henter JI. Symptoms affecting children with malignancies during the last month of life: A nationwide follow-up. Pediatrics 2006;117(4):1314-20.
37. Wolfe J, Grier HE, Klar N, Levin SB, Ellenbogen JM, Salem-Schatz S, et al. Symptoms and suffering at the end of life in children with cancer. N Engl J Med 2000;342(5):326-33.
38. Carter BS, Howenstein M, Gilmer MJ, Throop P, France D, Whitlock JA. Circumstances surrounding the deaths of hospitalized children: Opportunities for pediatric palliative care. Pediatrics 2004;114(3):e361-6.
39. Santucci G, Mack JW. Common gastrointestinal symptoms in pediatric palliative care: Nausea, vomiting, constipation, anorexia, cachexia. In: Pediatr Clin North Am 2007;54(5):673-89.
40. Breau LM, Camfield CS, McGrath PJ, Finley GA. The incidence of pain in children with severe cognitive impairments. Arch Pediatr Adolesc Med 2003;157(12):1219-26.
41. Drake R, Frost J, Collins JJ. The symptoms of dying children. J Pain Symptom Manage 2003;26(1):594-603.
42. Hunt A, Burne R. Medical and nursing problems of children with neurodegenerative disease. Palliat Med 1995;9(1):19-26.
43. Hunt A, Goldman A, Seers K, Crichton N, Mastroyannopoulou K, Moffat V, et al. Clinical validation of the paediatric pain profile. Dev Med Child Neurol 2004;46(1):9-18.
44. Hunt A, Wisbeach A, Seers K, Goldman A, Crichton N, Perry L, et al. Development of the paediatric pain profile: Role of video analysis and saliva cortisol in validating a tool

to assess pain in children with severe neurological disability. J Pain Symptom Manage 2007;33(3):276-89.
45. Breau LM, Camfield C, McGrath PJ, Rosmus C, Finley GA. Measuring pain accurately in children with cognitive impairments: Refinement of a caregiver scale. J Pediatr 2001;138(5):721-27.
46. Breau LM, McGrath PJ, Camfield CS, Finley GA. Psychometric properties of the non-communicating children's pain checklist-revised. Pain 2002;99(1-2):349-57.
47. Malviya S, Voepel-Lewis T, Burke C, Merkel S, Tait AR. The revised FLACC observational pain tool: Improved reliability and validity for pain assessment in children with cognitive impairment. Paediatr Anaesth 2006;16(3):258-65.
48. Oberlander TF, Gilbert CA, Chambers CT, O'Donnell ME, Craig KD. Biobehavioral responses to acute pain in adolescents with a significant neurologic impairment. Clin J Pain 1999;15(3):201-9.
49. Fanurik D, Koh JD, Schmitz ML, Harrison RD, Conrad TM. Children with cognitive impairment: Parent report of pain and coping. J Dev Behav Pediatr 1999;20(4):228-34.
50. Hadden KL, von Baeyer CL. Pain in children with cerebral palsy: Common triggers and expressive behaviors. Pain 2002;99(1-2):281-8.
51. Hauer JM. Central hypothermia as a cause of acute pancreatitis in children with neurodevelopmental impairment. Dev Med Child Neurol 2008;50(1):68-70.
52. Greco C, Berde CB. Pain management for the hospitalized pediatric patient. Pediatr Clin North Am 2005;52:995-1027.
53. Lauder GR, White MC. Neuropathic pain following multilevel surgery in children with cerebral palsy: A case series and review. Paediatr Anaesth 2005;15(5):412-20.
54. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: Risk factors and prevention. Lancet 2006;367:1618-25.
55. Berde CB, Lebel AA, Olsson G. Neuropathic pain in children. In: Schechter NL, Berde CB, Yaster M, editors. Pain in Infants, Children, and Adolescents, 2nd ed. Philadelphia: Lippincott Williams and Wilkins; 2003.
56. Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, et al. Pharmacologic management of neuropathic pain: Evidence-based recommendations. Pain 2007;132:237-51.
57. Hauer J, Wical B, Charnas L. Gabapentin successfully manages chronic unexplained irritability in children with severe neurologic impairment. Pediatrics 2007;119(2): e519-22.
58. Klit H, Finnerup NB, Jensen TS. Central post-stroke pain: Clinical characteristics, pathophysiology, and management. Lancet Neurol 2009;8(9):857-68.
59. Canavero S, Bonicalzi V. Central Pain Syndrome: Pathophysiology, Diagnosis, and Management. Cambridge (NY): Cambridge University Press, 2007.
60. Delgado-Aros S, Camilleri M. Visceral hypersensitivity. J Clin Gastroenterol 2005;39(Suppl 3):S194-203.
61. Zangen T, Ciarla C, Zangen S, Di Lorenzo C, Flores AF, Cocjin J, et al. Gastrointestinal motility and sensory abnormalities may contribute to food refusal in medically fragile toddlers. J Pediatr Gastroenterol Nutr 2003;37(3): 287-93.
62. Hasler ML. Pharmacotherapy for intestinal motor and sensory disorders. Gastroenterol Clin North Am 2003;32(2): 707-32, viii-ix.
63. Lee KJ, Kim JH, Cho SW. Gabapentin reduces rectal mechanosensitivity and increases rectal compliance in patients with diarrhoea-predominant irritable bowel syndrome. Aliment Pharmacol Ther 2005;22(10):981-8.
64. Taddio A, Oberlander TF. Pharmacological management of pain in children and youth with significant neurological impairments. In: Oberlander TF, Symons F, editors. Pain in Children and Adults with Developmental Disabilities. Baltimore (MD): Brookes; 2006.
65. van Maldegem BT, Smit LM, Touw DJ, Gemke RJ. Neuroleptic malignant syndrome in a 4-year-old girl associated with alimemazine. Eur J Pediatr 2002;161(5):259-61.
66. Bernard SA, Bruera E. Drug interactions in palliative care. J Clin Oncol 2000;18(8):1780-99.
67. Liptak GS. Complementary and alternative therapies for cerebral palsy. Ment Retard Dev Disabil Res Rev 2005;11(2):156-63.
68. Kalachnik JE, Hanzel TE, Sevenich R, Harder SR. Benzodiazepine behavioral side effects: Review and implications for individuals with mental retardation. Am J Ment Retard 2002;107(5):376-410.
69. Sanger TD, Delgado MR, Gaebler-Spira D, Hallett M, Mink JW. Classification and definition of disorders causing hypertonia in childhood. Pediatrics 2003;111:e89-97.
70. Delgado MR, Hirtz D, Aisen M, Ashwal S, Fehlings DL, McLaughlin J, et al. Practice parameter: Pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2010;74(4):336-43.
71. Rivard PF, Nugent AC, Symons FJ. Parent-proxy ratings of pain before and after botulinum toxin type a treatment for children with spasticity and cerebral palsy. Clin J Pain 2009;25:413-17.
72. Hoving MA, van Raak EP, Spincemaille GH, van Kranen-Mastenbroek VH, van Kleef M, Gorter JW, et al. Safety and one-year efficacy of intrathecal baclofen therapy in children with intractable spastic cerebral palsy. Eur J Paediatr Neurol 2009;13:247-56.
73. Krach LE. Pharmacotherapy of spasticity: Oral medications and intrathecal baclofen. J Child Neurol 2001;16(1):31-6.
74. Axelrod FB, Berlin D. Pregabalin: A new approach to treatment of the dysautonomic crisis. Pediatrics 2009;124(2): 743-6 [Epub;2009, July 20].
75. Baguley IJ, Cameron ID, Green AM, Slewa-Younan S, Marosszeky JE, Gurka JA. Pharmacological management of dysautonomia following traumatic brain injury. Brain Inj 2004;18(5):409-17.
76. Baguley IJ. Autonomic complications following central nervous system injury. Semin Neurol 2008;28(5):716-25 [Epub; 2008, December 29].
77. Ruiz C, Gener B, Garaizar C, Prats JM. Episodic spontaneous hypothermia: A periodic childhood syndrome. Pediatr Neurol 2003;28(4):304-6.
78. Kloos RT. Spontaneous periodic hypothermia. Medicine (Baltimore) 1995;74(5):268-80.

79. Baguley IJ, Heriseanu RE, Gurka JA, Nordenbo A, Cameron ID. Gabapentin in the management of dysautonomia following severe traumatic brain injury: A case series. J Neurol Neurosurg Psychiatry 2007;78(5):539-41.
80. Seddon PC, Khan Y. Respiratory problems in children with neurological impairment. Arch Dis Child 2003;88:75-8.
81. Strauss D, Cable W, Shavelle R. Causes of excess mortality in cerebral palsy. Dev Med Child Neurol 1999;41(9):580-85.
82. Taniguchi MH, Moyer RS. Assessment of risk factors for pneumonia in dysphagic children: Significance of videofluoroscopic swallowing evaluation. Dev Med Child Neurol 1994;36:495-502.
83. Kawahara H, Okuyama H, Kubota A, Oue T, Tazuke Y, Yagi M, et al. Can laparoscopic antireflux surgery improve the quality of life in children with neurologic and neuromuscular handicaps? J Pediatr Surg 2004;39(12):1761-4.
84. Cheung KM, Tse HW, Tse PW, Chan KH. Nissen fundoplication and gastrostomy in severely neurologically impaired children with gastroesophageal reflux. Hong Kong Med J 2006;12(4):282-8.
85. Bui HD, Dang CV, Chaney RH, Vergara LM. Does gastrostomy and fundoplication prevent aspiration pneumonia in mentally retarded persons? Am J Ment Retard 1989;94(1): 16-9.
86. Srivastava R, Downey EC, O'Gorman M, Feola P, Samore M, Holubkov R, et al. Impact of fundoplication versus gastrojejunal feeding tubes on mortality and in preventing aspiration pneumonia in young children with neurologic impairment who have gastroesophageal reflux disease. Pediatrics 2009;123(1):338-45.
87. Srivastava R, Berry JG, Hall M, Downey EC, O'Gorman M, Dean JM, et al. Reflux related hospital admissions after fundoplication in children with neurological impairment: Retrospective cohort study. BMJ 2009;339:b4411 [10.1136/bmj.b4411].
88. Lee SL, Shabatian H, Hsu JW, Applebaum H, Haigh PI. Hospital admissions for respiratory symptoms and failure to thrive before and after Nissen fundoplication. J Pediatr Surg 2008;43(1):59-63; Discussion 63-5.
89. Richards CA, Milla PJ, Andrews PL, Spitz L. Retching and vomiting in neurologically impaired children after fundoplication: Predictive preoperative factors. J Pediatr Surg 2001;36(9):1401-4.
90. Carron JD, Derkay CS, Strope GL, Nosonchuk JE, Darrow DH. Pediatric tracheotomies: Changing indications and outcomes. Laryngoscope 2000;110(7):1099-104.
91. Berry JG, Graham DA, Graham RJ, Zhou J, Putney HL, O'Brien JE, et al. Predictors of clinical outcomes and hospital resource use of children after tracheotomy. Pediatrics 2009;124(2):563-72.
92. Vijayasekaran S, Unal R, Schraff SA, Johnson RF, Rutter MJ. Salivary gland surgery for chronic pulmonary aspiration in children. Int J Pediatr Otorhinolaryngol 2007;71(1): 119-23.
93. Hauer JM. Respiratory symptom management in a child with severe neurologic impairment. J Palliat Med 2007;10(5): 1201-7.
94. Plioplys AV, Lewis S, Kasnicka I. Pulmonary vest therapy in pediatric long-term care. J Am Med Dir Assoc 2002; 3(5):318-21.
95. Del Giudice E, Staiano A, Capano G, Romano A, Florimonte L, Miele E, et al. Gastrointestinal manifestations in children with cerebral palsy. Brain Dev 1999;21(5):307-11.
96. Richards CA, Andrews PL, Spitz L, Milla PJ. Nissen fundoplication may induce gastric myoelectrical disturbance in children. J Pediatr Surg 1998;33(12):1801-5.
97. Antao B, Ooi K, Ade-Ajayi N, Stevens B, Spitz L. Effectiveness of alimemazine in controlling retching after Nissen fundoplication. J Pediatr Surg 2005;40(11):1737-40.
98. Siden H, Tucker T, Derman S, Cox K, Soon GS, Hartnett C, et al. Pediatric enteral feeding intolerance: A new prognosticator for children with life-limiting illness? J Palliat Care 2009;25(3):213-7.
99. Nelson LJ, Rushton CH, Cranford RE, Nelson RM, Glover JJ, Truog RD. Forgoing medically provided nutrition and hydration in pediatric patients. J Law Med Ethics 1995;23(1):33-46.
100. Stanley AL. Withholding artificially provided nutrition and hydration from disabled children—Assessing their quality of life. Clin Pediatr 2000;39(10):575-9.
101. Diekema DS, Botkin JR, The Committee on Bioethics. Clinical report forgoing medically provided nutrition and hydration in children. Pediatrics 2009;124(2):813-22.
102. Duncan J, Joselow M, Hilden JM. Program interventions for children at the end of life and their siblings. Child Adolesc Psychiatr Clin N Am 2006;15(3):739-58.
103. Waechter EH. Children's awareness of fatal illness. Am J Nurs 1971;7(6):1168-72.
104. Hinds PS, Drew D, Oakes LL, Fouladi M, Spunt SL, Church C, et al. End-of-life care preferences of pediatric patients with cancer. J Clin Oncol 2005;23(36):9146-54.
105. Edwards J. A model of palliative care for the adolescent with cancer. Int J Palliat Nurs 2001;7:485-8.
106. Ladd RE, Forman EN. Adolescent decision-making: Giving weight to age-specific values. Theor Med 1995;16(4): 333-45.
107. Committee on Bioethics, American Academy of Pediatrics. Informed consent, parental permission, and assent in pediatric practice. Pediatrics 1995;95(2):314-17.
108. Weir RF, Peters C. Affirming the decisions adolescents make about life and death. Hastings Cent Rep 1997;27(6):29-40.
109. Doig C, Burgess E. Withholding life-sustaining treatment: Are adolescents competent to make these decisions? CMAJ 2002;162(11):1585-88.
110. Appelbaum PS. Clinical practice. Assessment of patients' competence to consent to treatment. N Engl J Med 2007; 357(18):1834-40.
111. King NM, Cross AW. Children as decision-makers: Guidelines for pediatricians. J Pediatr 1989;115(1):10-6.
112. Davies B, Brenner P, Orloff S, Sumner L, Worden W. Addressing spirituality in pediatric hospice and palliative care. J Palliat Care 2002;18(1):59-67.
113. Stuber ML, Houskamp BM. Spirituality in children confronting death. Child Adolesc Psychiatr Clin N Am 2004;13(1): 127-36, viii.
114. Hufton E. Parting gifts: The spiritual needs of children. J Child Health Care 2006;10(3):240-50.

115. Himebauch A, Arnold RM, May C. Grief in children and developmental concepts of death #138. J Palliat Med 2008; 11(2):242-3.
116. Poltorak DY, Glazer JP. The development of children's understanding of death: Cognitive and psychodynamic considerations. Child Adolesc Psychiatr Clin N Am 2006;15(3):567-73.
117. Rauch PK, Muriel AC. The importance of parenting concerns among patients with cancer. Crit Rev Oncol/Hematol 2004; 49(1):37-42.
118. Rando TA. Parental Loss of a Child. Champaign (IL): Research Press, 1986.
119. Barrera M, O'Connor K, D'Agostino NM, Spencer L, Nicholas D, Jovcevska V, et al. Early parental adjustment and bereavement after childhood cancer death. Death Stud 2009;33(6):497-520.
120. Lannen PK, Wolfe J, Prigerson HG, Onelov E, Kreicbergs UC. Unresolved grief in a national sample of bereaved parents: Impaired mental and physical health 4 to 9 years later. J Clin Oncol 2008;26(36):5870-6 [Epub;2008, November 24].
121. Attig T. How we grieve: relearning the world. New York: Oxford University Press, 1996.
122. Stroebe MS, Schut H. The dual process model of coping with bereavement: Rationale and description. Death Stud 1999; 23(3):197-224.
123. Woodgate RL. Living in a world without closure: Reality for parents who have experienced the death of a child. J Palliat Care 2006;22(2):75-82.
124. Barrera M, D'Agostino NM, Schneiderman G, Tallett S, Spencer L, Jovcevska V. Patterns of parental bereavement following the loss of a child and related factors. Omega 2007;55(2):145-67.
125. Rini A, Loriz L. Anticipatory mourning in parents with a child who dies while hospitalized. J Pediatr Nurs 2007;22(4):272-82.
126. Kreicbergs UC, Lannen P, Onelov E, Wolfe J. Parental grief after losing a child to cancer: Impact of professional and social support on long-term outcomes. J Clin Oncol 2007;25(22):3307-12.
127. Meert KL, Thurston CS, Thomas R. Parental coping and bereavement outcome after the death of a child in the pediatric intensive care unit. Pediatr Crit Care Med 2001; 2(4):324-8.
128. Davies B. Shadows in the Sun: The Experiences of Sibling Bereavement in Childhood. Philadelphia (PA): Taylor and Francis, 1999.
129. Davies B, Collins J, Steele R, Cook K, Distler V, Brenner A. Parents' and children's perspectives of a children's hospice bereavement program. J Palliat Care 2007;23(1):14-23.
130. Wilkinson S, Croy P, King M, Barnes J. Are we getting it right? Parents' perceptions of hospice child bereavement support services. Palliat Med 2007;21(5):401-7.
131. Meyer EC, Burns JP, Griffith JL, Truog RD. Parental perspectives on end-of-life care in the pediatric intensive care unit. Crit Care Med 2002;30(1):226-31.
132. Bedell SE, Cadenhead K, Graboys TB. The doctor's letter of condolence. N Engl J Med 2001;344(15):1162-64.