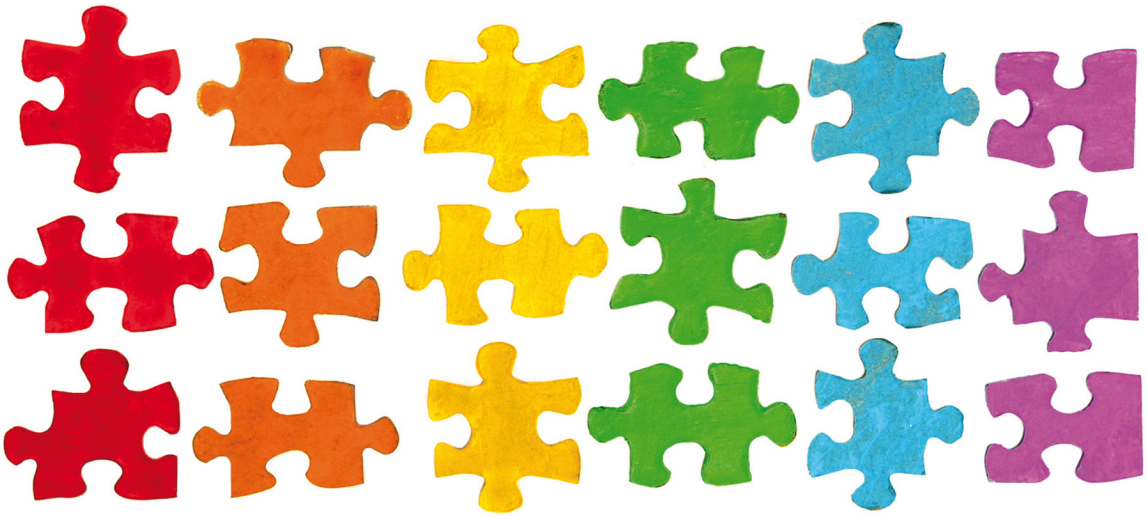
Ninth edition, 2013

together for short lives



Basic Symptom Control in Paediatric Palliative Care

The Rainbows Children's Hospice Guidelines

www.togetherforshortlives.org.uk

Basic Symptom Control in Paediatric Palliative Care
The Rainbows Children's Hospice Guidelines
Ninth Edition, 2013

ISBN: 1 898447284

Author: Dr Satbir Singh Jassal B.Med Sci, B.M., B.S., DRCOG, Dip Pall Med, DFSRH, MRCGP, FRCPCH (Hon), Medical Director Rainbows Children's Hospice and General Practitioner
Production: Myra Johnson and Katrina Kelly, Together for Short Lives
Design: Qube Design Associates Ltd

Certified by the Information Standard

Together for Short Lives is the leading UK charity that speaks for all children with life-threatening and life-limiting conditions and all those who support, love and care for them. When children are unlikely to reach adulthood, we aim to make a lifetime of difference for them and their families.

Together for Short Lives
4th Floor, 48-52 Bridge House, Baldwin Street,
Bristol BS1 1QB

T: 0117 989 7820
info@togetherforshortlives.org.uk
www.togetherforshortlives.org.uk

Together for Short Lives is a registered charity in England and Wales (1144022) and Scotland (SC044139) and a company limited by guarantee (7783702)

About Together for Short Lives

Together for Short Lives is the leading UK charity for all children with life-threatening and life-limiting conditions and all those who support, love and care for them – families, professionals and services, including children's hospices. Our work helps to ensure that children can get the best possible care, wherever and whenever they need it.

From the moment of diagnosis, for whatever life holds, we help to ensure that families make the most of their precious time together.

There are an estimated 49,000 children and young people in the UK living with a life-threatening or life-limiting condition that may require palliative care services. We are there for every single one of these children, and their families, so they know where to go for help and are aware of the support available to them. With the right kind of information, it can become easier to access care and support, as well as practical and emotional help for the whole family when it's needed most. We help families to access this information so they know what to expect at different stages throughout their journey and can make informed choices about their child's care.

We work closely with the organisations and professionals that provide important lifeline services to children and families. We support, lobby, and raise funds for children's hospices and a range of other voluntary organisations to enable them to sustain the vital work they do. We offer resources and training to help them maintain consistent, high quality care from the moment a child is diagnosed, until their eventual death, and to continue supporting families for as long as they need it.

We campaign for equal provision of specialised services for children with life-threatening and life-limiting conditions and families across the UK; and better co-ordination of health, social care and education. By working nationally we give a powerful voice to children, families and the organisations that support them, ensuring their views are heard by the government and that they influence policy.

T: 0117 989 7820
info@togetherforshortlives.org.uk
www.togetherforshortlives.org.uk

Call the helpline: **0808 8088 100**

Contributions and peer review

Dr Justin Amery, GP in Oxford, Hospice Doctor at Keech Hospice

Nigel Ballantine, Specialist Clinical Pharmacist, Haematology Oncology, Birmingham

Ann Booth, RSCN, Rainbows Children's Hospice

Dr Lynda Brook, Macmillan Consultant in Paediatric Palliative Care, Alder Hey Children's Hospital

Dr Michael Capra, Lecturer in Paediatric Oncology, QMC

Susan Carr, Senior Pharmacist, Regional Drug Information Centre LRI

Vanessa Chapman, Regional Prescribing and Drug Information Development Pharmacist, LRI

Dr Finella Craig, Consultant in Children's Palliative Care, Great Ormond Street Hospital

Dr Jonathan Cusack, Consultant Neonatologist, University Hospitals of Leicester

Chris Cutts, Paediatric Pharmacist, LRI

Dr Henry Davis, Hospice Doctor, Acorns Hospice, Birmingham

Lynne Demelo, Clicinal Nurse Specialist, Rainbows Children's Hospice

Francis Edwards, Independent Nurse Consultant

Dr Richard Hain, LATCH Senior Lecturer and Honorary Consultant in Paediatric Palliative Medicine, University Hospital of Wales

Dr Clare Hale, Deputy Medical Director, Rainbows Children's Hospice

Lucy Hawkes, Neonatal Pharmacist, University Hospitals of Leicester

Dr Anne Hunt, Senior Research Fellow in Children's Palliative Care, University of Central Lancashire

Dr Patrick Ireland, Retired

Helen Kenney, Respiratory Nurse Specialist, Rainbows Children's Hospice

Dr Nicola King, Demelza House Hospice, Kent

Dr Susie Lapwood, Lead Doctor, Helen and Douglas House Hospices for children and young adults, Oxford

Julia Martin, RSCN Children's Gastroenterology Nurse Specialist, LRI

Dr Renee McCulloch, Dr Renee McCulloch, Paediatric Palliative Care Consultant, Great Ormond Street Hospital/Institute of Child Health, London

Dr George Murty, Consultant ENT, Leicester Royal Infirmary

Dr Jill Platt, Retired

Dr Peter Sullivan, Consultant Paediatrician, Oxford

Dr Angela Thompson, Associate Specialist, Palliative Care Lead Paediatrician, Coventry and Warwickshire

Dhiraj D Vara, Head of Respiratory Physiology Unit Glenfield Hospital Leicester

Dr David Walker, Consultant Paediatric Oncologist, (Senior Lecturer) QMC

The authors have made every effort to check current data sheets and literature up to July 2013, but the dosages, indications, contraindications and adverse effects of drugs change over time as new information is obtained. It is the responsibility of the prescriber to check this information with the manufacturer's current data sheet and we strongly urge the reader to do this before administering any of the drugs in this document. In addition, palliative care uses a number of drugs for indications or by routes that are not licensed by the manufacturer. In the UK such unlicensed use is allowed, but at the discretion and with the responsibility of the prescriber.

Contents

A word from the editor

Welcome to the ninth edition of the Rainbows Symptom Control Manual. There is a new chapter on End of life, and major rewrites on Pain and Gastrostomy as well as some minor corrections.

The formulary has been updated to the second edition of the APPM master formulary.

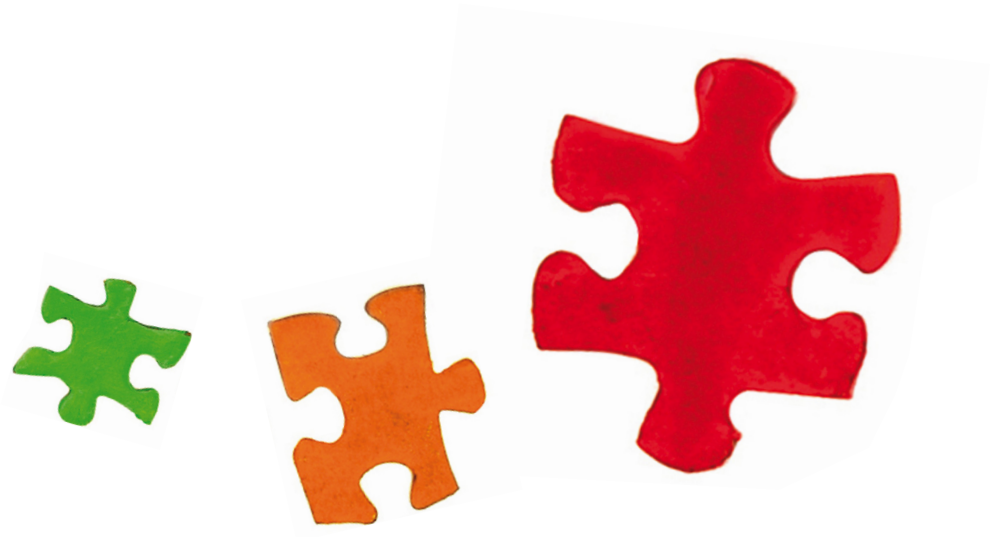
Following feedback from previous editions, I now include my references for the manual. I have put the references at the back so those who wish to have a lighter version can avoid printing them.

I wish to thank Together for Short Lives for agreeing to provide the considerable administrative support needed to revise the manual.

Please let me know if you would like additional chapters on particular themes or if you have any comments on the work by emailing me at sat.jassal@gmail.com.

We now give all the parents of our children who are receiving end of life care a copy to keep at home, to help visiting health professionals. We hope you find it useful.

Dr Satbir Jassal
August 2013



Foreword: Barbara Gelb

Together for Short Lives is delighted to publish the ninth edition of *Basic Symptom Control in Paediatric Palliative Care*. This is the key clinical tool used by children's palliative care doctors and nurses across the world and the only resource of its kind that provides comprehensive guidelines for treating a wide range of symptoms experienced by children with life-limiting or complex health conditions. Indeed this manual has earned the reputation of being the 'industry bible' for professionals working in the field.

Providing pain and symptom management is the cornerstone of good palliative care. Getting this right for babies, children and young people can be challenging and anxiety provoking, perhaps even more so for those general practitioners and paediatricians who may only encounter a small number of life-limited children throughout their working lives.

The resource has been pioneered and written by Dr Satbir Jassal, GP and Medical Director at Rainbows Children's Hospice, with contributions and peer reviews from 29 leading paediatric and palliative care specialists. It is written in an accessible style and helpfully brings together clinical information with practical support and tips. The first section of the resource provides an A-Z of common symptoms and tried and tested treatments with the second section setting out a specialist children's palliative care drug formulary developed by the Association of Paediatric Palliative Medicine.

I commend this vital resource to you.

Barbara Gelb
CEO, Together for Short Lives

Foreword: Joan Marston

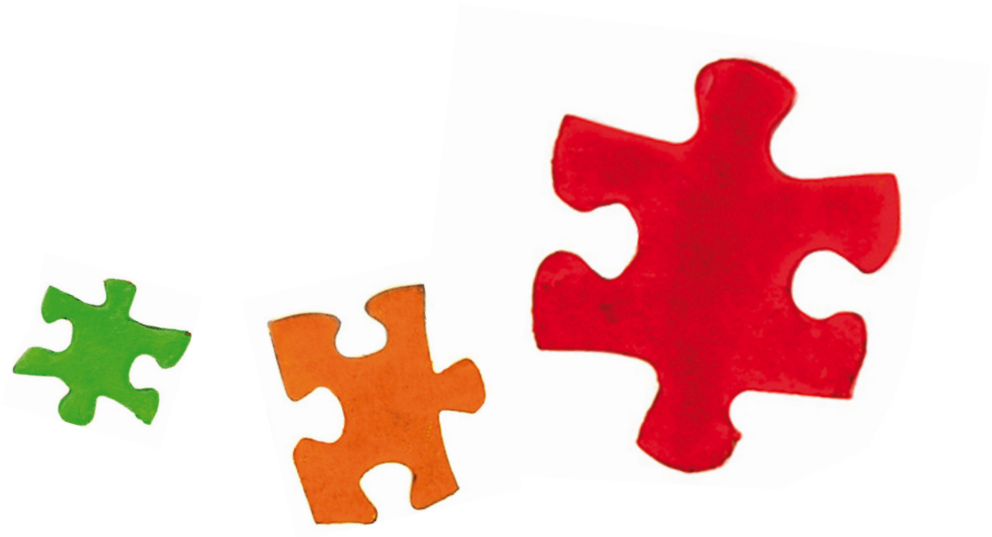
Basic Symptom Control in Paediatric Palliative Care is an outstanding resource for professionals delivering care and vital pain and symptom management for babies, children and young people with life-limiting and life-threatening health conditions. Its strength lies in its long heritage, collective knowledge and experience of some of the world's leaders and specialists in children's palliative care. Its thorough peer review process adds weight; you know that this is a tried and tested resource that you can rely on.

Although it has been developed and published in the UK, *Basic Symptom Control in Paediatric Palliative Care* has international resonance. The approaches and symptom management techniques know no boundaries and translate to any setting across the world. Whether you are caring for a child in one of the top UK specialist hospitals, or caring for a baby with HIV in a rural clinic in Malawi, this resource is sure to provide clear, unbiased guidance.

In my role as CEO of the International Children's Palliative Care Network, I know that many countries have little or no knowledge of children's palliative care, let alone specialist services and trained clinicians. But there is still a hunger to provide the very best care to children with palliative care needs. Resources are few and far between and many clinicians operate in remote parts of the world, making do with the few resources they have. This publication has the power to give professionals the tools and confidence to provide good symptom management. Plus, it is completely free and available as an interactive PDF that will perform on portable devices anywhere in the world.

My message to all professionals is to read and make good use of this resource, and to share it as widely as possible.

Joan Marston
CEO, International Children's Palliative Care Network (ICPCN)



Introduction

This protocol has been written to allow doctors (both GPs and Paediatricians) and nursing staff in specialised units and in the community, an understanding of the basis of symptom control in paediatric palliative care. This topic normally instils tremendous anxiety in professional people.

Quite rightly if we think that the average GP will have to look after only one or two children with life-limiting disorders in their entire working life. Fortunately, provided we remember the basic skills we were all taught, care of a child follows a very similar pathway to that used in adult palliative care. This protocol assumes a narrative style deliberately, as distinct from a textbook, as it is designed to provide more practical support and hands on clinical information in the acute setting. There is much more to supporting the terminal child and family than just the symptom control outlined in this paper: we must also remember the important emotional, social and spiritual needs of the child, siblings, parents, grandparents, family and society around the child.

Unless the child is older and can describe their symptoms, we need to glean an understanding of how the illness is affecting the child from all possible sources. Remember to read the notes from hospital consultants, ward nursing notes, question any specialist community health visitors and ask the opinion of the nursing staff supporting you. Doctors will spend on average five to thirty minutes a day looking at a child. It therefore follows that palliative care can only be done as a team approach.

The first rule is don't panic, do not dive in blindly, keep your hands tucked behind your back, your mouth shut and listen to the parents. In terminal care the parents assume a pivotal role in the care for their child. They have often experienced a variety of levels of medical and nursing care ranging from excellent to pathetic, and have a much deeper understanding of their child's medical, nursing and social needs then we give them credit for. Only once you have obtained a good history from all sources should you start an examination. Remember the laying on of hands is as important as anything you may discover on your examination. Be methodical, logical and above all professional: the parents have allowed you into their lives because they perceive that you may be able to help them. Once you have formulated a plan of action go through it with the parents in language that they understand. Parents may well feel that they want more or even less than has been recommended to them. Explanation, compromise and the knowledge that decisions can be amended as the child's condition changes, allows the parents to feel that they have informed choice in the care of their dying child. This particular point is also very important in post bereavement support.

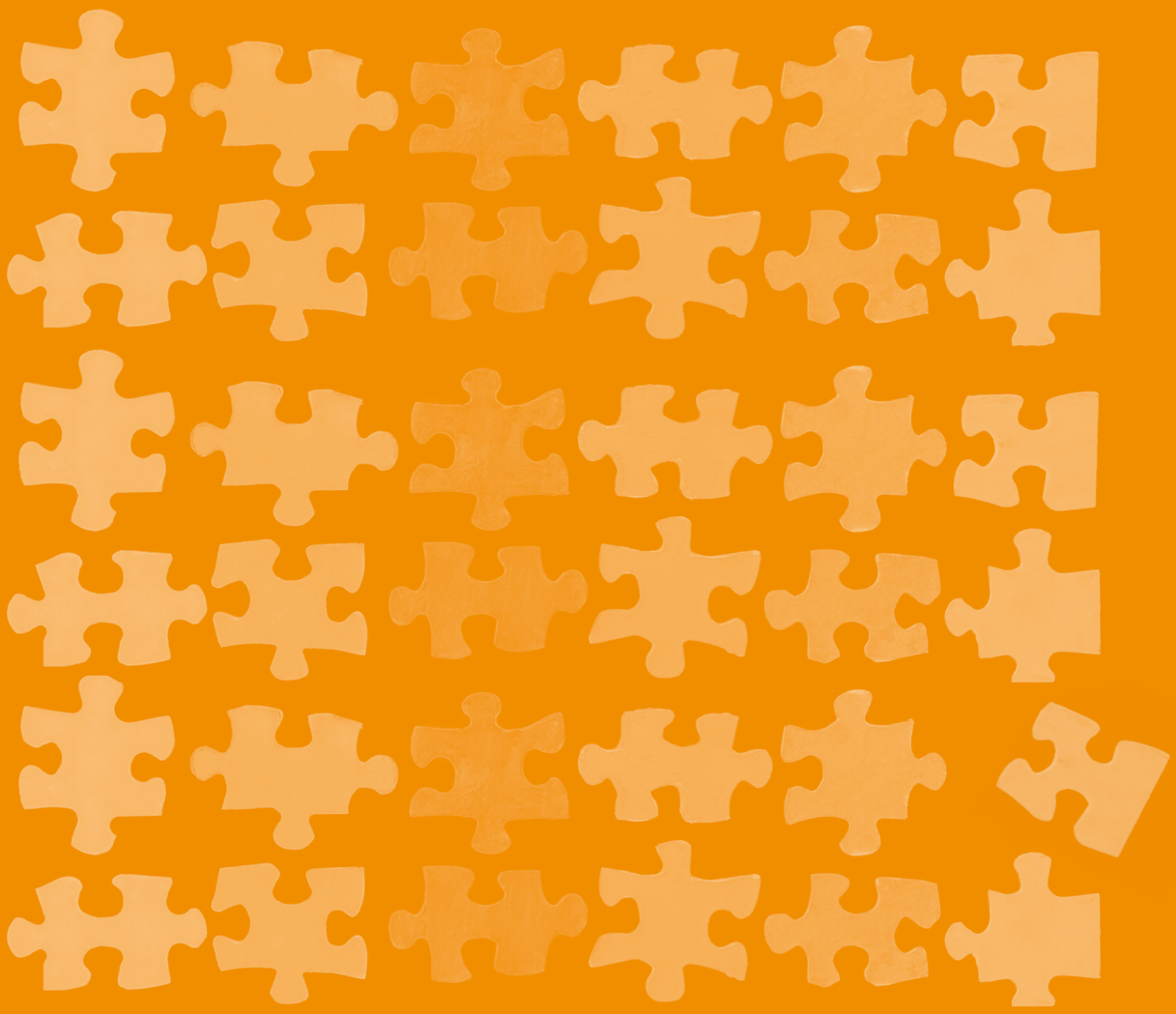
The second rule is to document and disseminate information to all your care team. Check that they are happy about the care plan and that everyone is clear about their role. Unfortunately, care at the terminal phase cannot be conducted by numerous junior doctors, deputising services or half a dozen different key workers. We as health care professionals have to make ourselves available even at short notice.

The third rule is beware that you do not fall into the same trap as Icarus (who flew too close to the sun). The intensity of emotion surrounding a dying child would make even the sun pale. Many nurses and doctors get so personally attached that they burn out emotionally. This unfortunately will be of little or no benefit for the next family they have to look after. Remember to retain a sensitive professional distance.

How to use *Basic Symptom Control in Paediatric Palliative Care*

The symptoms included in this manual are listed alphabetically. Under each symptom you will find an orange banner containing a series of numbers referring to evidence, such as Ref: [128,197-200]. The numbers in square brackets refer to the references which can be found on pages 160-172.

Symptoms



Anorexia

[3-10]

One of the primeval instincts all parents have is to feed their children. So when children, particularly those with malignancy, stop eating it generates considerable anxiety in their parents. Anorexia can be caused by:

- Pain
- Anxiety
- Nausea or vomiting
- Thrush in the mouth or oesophagus
- Drugs
- Depression
- Dyspepsia
- Constipation
- Radiotherapy
- Certain smells
- Altered taste
- Anorexia/Cachexia syndrome

It is always worth hunting out and treating these conditions, and involving a dietician. Otherwise it is important to reassure the parents that the inactive child may need less food and will not be feeling hungry. There are other common-sense approaches, such as presenting small meals on a small plate, spending some time on the presentation and remembering that many of children's favourite meals, such as Macdonald's, are in fact very high in calories.

The only therapeutic approach is small dose steroids used in 5 to 7 day courses. However the side effect profile is often so profound that it is normally difficult to justify.

Bladder

[11]

Although one need not get too concerned about falling urinary output in the terminal phase of illness one should remember two special cases.

1. A number of children with neurodegenerative disorders may have problems with emptying their bladder.

2. Children on opiates may go into retention.

Urinary retention due to opioids may improve with Bethanechol. Fentanyl causes less urinary retention than other opiates and a change to Fentanyl may be helpful. In these children gentle bladder massage, warm baths or catheterisation can easily alleviate the obstruction. Catheterisation of children is similar to adults with due regard to catheter size and depth of insertion. The loss of bladder function in a child who has previously been continent can often be a source of great distress to parents; another 'loss' that needs to be mourned, another indignity the child must suffer. The use of pads is non-invasive and simple, although may require a careful approach of tact and sensitivity to introduce.

Bleeding

[12-14]

The sight of blood is very distressing to patient, parent and carer alike. If bleeding is likely, or if it has already started, gentle warning of the possibility that it could happen, or get worse, may help to reduce the distress and shock that the parents' experience. Bleeding can be a major problem in a number of malignancies and liver diseases. Although it is a subject that should normally be dealt with in specialist units, in the terminal phase heroics are often inappropriate.

- Small bleeds can often be dealt with by using oral tranexamic acid or topical Adrenaline 1:1000 on a gauze and applied directly to the wound.

- Bleeding gums can be helped with tranexamic acid mouthwashes or absorbable haemostatic agents such as Gelfoam or Gelfilm.

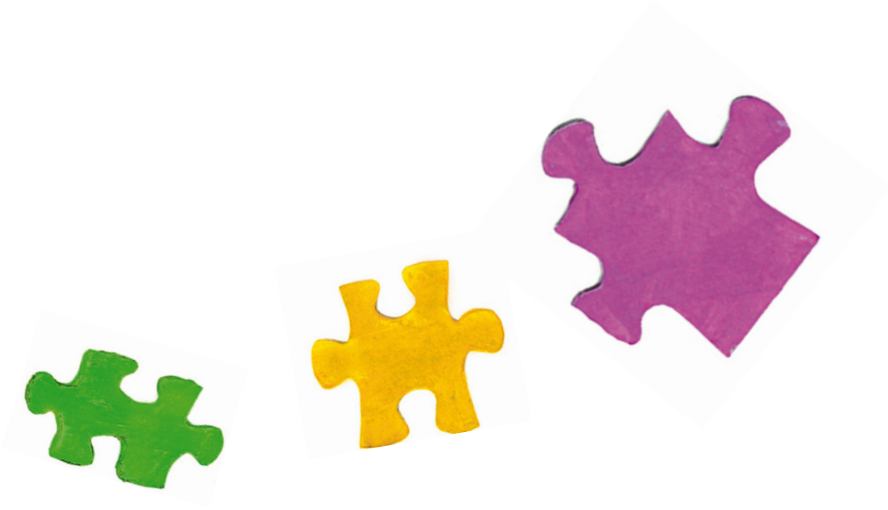
- Liver dysfunction with coagulation abnormalities can be helped with Vitamin K both orally (prevention) or by injection (acute bleed).

- Vaginal bleeding can respond to oral progestogen.

- Platelet or blood transfusion if necessary.

To minimise the shock of seeing their child's blood, the use of red towels and blankets may be tried.

In the face of a catastrophic haemorrhage, some authors recommend the use of intravenous Diamorphine and Diazepam or Midazolam. If no intravenous route is available then subcutaneous Diamorphine with rectal Diazepam can be given. However it is important to recognise that haemorrhage of this type is normally painless and that the principle of double intent for the use of Diamorphine may apply in this situation.



Constipation

[4, 7, 10, 15-27]

The management of constipation in paediatrics follows many of the same principles as in adult care, but there are certain important differences.

- The definition of constipation in paediatrics can be difficult. A newborn baby may not open its bowels for three days. A breast-fed baby may not open its bowels for seven days. However they would not be thought of as being constipated. It is better perhaps in paediatrics to think of alteration in bowel habits as a way of detecting constipation.

- The ability of a medication to relieve constipation is often linked less to pathophysiology than to the flavour. If it tastes bad then it's not going to go down that child's mouth without a fight. After a week of fighting, the parents will be knocking on the doctor's door.

- Oral preparations are generally preferable to rectal. Because of the number of medications that can be given to children rectally, some nurses and parents are often keen to jump into using rectal treatment very early. One should try to resist this pressure, trying to remember that this may not be in the best interests of the child.

- It is important in paediatrics to recognise the specific sensitivities of the child. Rectal examination in adults is fairly straightforward. In children it should be done only when absolutely necessary and then only by experienced physicians or nurses. The little finger should be used in most cases. A child with an anal tear may well have anal spasm of a level that makes it impossible to insert a finger without causing significant pain. Children who have had repeated rectal examinations in the past may become very distressed if they need to be re-examined. This can make the examination technically very difficult and emotionally traumatic for both the child and doctor. It is important to explain the reasons for a rectal examination to the parents, especially from a medico-legal position.

- Although much is made of diet in the management of constipation, many of the children that we see in paediatric palliative care fall under the heading of special needs. These children will have disorders that limit their ability to chew food or even swallow their food easily. The food often has to be puréed and it can take up to an hour to feed that child a single meal. Many of the children will have gastrostomies and feeds specially designed and calculated for them by dietitians.

Before rushing in to prescribe, one should consider the possible causes of constipation in children.

- **Inactivity:** some children with neurodegenerative or genetic disorders can find themselves becoming wheelchair bound, for example boys with muscular dystrophy.

- **Neurological:** as some of the neurodegenerative disorders progress they can affect the nerve pathways and musculature required for defecation, for example myotonic dystrophy. Due to the rarity of many of these conditions we are often unaware of the actual mechanism involved.

- **Metabolic:** dehydration can affect all children very quickly. Cystic fibrosis (meconium ileus equivalent) can cause constipation. Hypercalcaemia and hypokalaemia can cause problems in paediatric oncology.

- **Decreased food intake:** as any parent will know, any child who feels unwell may go off their food. Children in the paediatric oncology field are particularly susceptible as they are affected both by the disease process and the treatment modalities.

- **Fears of opening bowels:** a child who is constipated may well get significant pain when he does actually defecate. For the child the best way not to have pain is to hold back the urge to empty his bowels for as long as possible.

- **Rectal tears:** when children pass hard, large stools, these stools can, through stretching, cause superficial rectal tears. This results in two problems. The tears are very painful when the child tries to empty its bowels. The tears produce anal spasm and so emptying the bowels require the child to exert even greater pressure and strain than normal.

- **Social:** many children are shy or nervous about using toilets outside the home or away from their parents. They may not know where the toilets are, or may be too shy to ask a nurse to help them.

- **Drugs:** one of the major causes of constipation in the hospice is iatrogenic. Doctors continue to fail to appreciate the side effect profiles of the drugs that they use. Although the constipation side effects of the opioids are well recognised many physicians fail to remember that anticholinergics (Hyoscine etc.) and anticonvulsants can also induce constipation.

- **Liaise with parents:** they know their child and his/her habits, also they may have misconceptions about defecation and use of laxatives. Co-operation is needed for treatment to be successful.

Types of laxatives

The types of laxatives used in paediatrics are often limited by special factors such as taste. Laxatives can be divided into predominantly softening or peristalsis stimulating, also whether they are used orally or rectally.

Softening laxatives given rectally

Type	Mechanism	Notes
Lubricant, e.g. *Arachis oil, olive oil*	Penetrates stools and softens.	Used as retention enemas overnight to soften stool. *Be careful of nut allergy as arachis oil is made from peanuts.*
Surfactant, e.g. *sodium docusate*	Act like detergents and increase water penetration into stool.	Can be used by itself. Other similar compounds found in mini-enemas.
Osmotic, e.g. *glycerine*	Soften stool by osmosis and act as a lubricant.	Very useful as they come in various sizes.
Saline, e.g. *sodium phosphate*	Release bound water from faeces and may stimulate peristalsis.	Very effective in difficult cases. Also has an osmotic mechanism of action. Repeated use is inappropriate and can cause biochemical imbalance.

Softening laxatives given orally

Type	Speed of onset	Mechanism	Notes
Lubricant, e.g. *Paraffin*	1 to 3 days	Penetrates stools and softens.	Taste and risk of inhalation particularly in children with gastro-oesophageal reflux limits use. No longer recommended for internal use.
Surfactant, e.g. *docusate or poloxamer*	1 to 3 days	Act like detergents and increase water penetration into stool.	Docusate can be used by itself. Poloxamer is combined to make co-danthramer.
Bulk forming, e.g. *Fybogel*	2 to 4 days	Act as stool normalisers.	Very limited use in paediatric palliative care.
Osmotic, e.g. *lactulose macrogol*	1 to 2 days	Exert an osmotic influence in the small bowel and so retain water in lumen.	Lactulose is first line treatment. Sickly taste can be a problem.
Saline, e.g. *Magnesium hydroxide or sulphate, sodium sulphate*	1 to 6 hours	Osmotic effect in all of gut. Increase water secretion and stimulate peristalsis.	Not used very much in ill children because of their strong purgative action.

Peristalsis stimulating

Type	Speed of onset	Mechanism	Notes
Anthracene, e.g. *senna and danthron*	Orally 6 to 12 hours or rectally 15 to 60 minutes	Directly stimulate the myenteric plexus	Senna is very commonly used as the liquid. It combines well with lactulose. Danthron is used in combinations e.g. co-danthramer.
Polyphenolics, e.g. *bisacodyl and sodium picosulphate*			Bisacodyl can be given orally or rectally. It is particularly useful in its suppository form. Sodium picosulphate should be reserved for the most difficult cases.

Having developed an understanding of the special needs of children with constipation and the types and mode of action of the medication, we can now outline a simple strategy (see the steps below).

Step 1
Take a history and examine the child. Abdominal examination may reveal a sausage shaped mass in the left iliac fossa. Rectal examination may reveal a rectum that is full of hard stools, soft stools or empty. Assess possibility of impaction and overflow presenting as diarrhoea or faecal soiling.

Step 2
Start with lactulose, building up the dose over a week.

Step 3
If no improvement add senna.

Special Step 4
If the child is on an opioid then ignore steps 2 and 3 and start a macrogol such as Movicol or sodium picosulphate.

Step 5
If the child is distressed with the constipation, then from the rectal examination follow the guidance:
If stool hard – use glycerine suppository.
If stool soft – use bisacodyl suppository.
If rectum empty – use bisacodyl suppository to *bring stool down* or high phosphate enema.

Step 6
If severely constipated use MiraLax or phosphate enema or if you have time Movicol (see table below).

Movicol is an iso-osmotic laxative only licensed for children over the age of two years. It is flavour and sweetener free but most importantly it is highly effective.

Number of sachets of Movicol to use in severe constipation

Number of sachets of Movicol							
Age	**Day 1**	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**	**Day 7**
2-4yrs	2	4	4	6	6	8	8
5-11yrs	4	6	8	10	12	12	12

Step 7
If manual removal is necessary then use a topical anaesthetic gel or discuss the possibility of a general anaesthetic with the local hospital.

As with so many conditions in medicine, prevention is better than cure. The physician should attempt to predict the possibility of constipation and treat it prophylactically.

Novel approaches
It is helpful to know about a number of alternative approaches to constipation, although all of these are unlicensed uses of these agents. The use of prokinetic drugs such as Metoclopramide or Domperidone (less effective but less dystonic) have been shown to be helpful. The side effects of increased bowel motility with Erythromycin can be effective. Oral Naloxone can help with opioid induced constipation, whilst its poor absorption from the gut limits its effects systemically.

Cough

[4, 28-39]

The management of cough involves accurate diagnosis of the various causes of cough. Often the underlying illness will give clues to the cause, but be wary of dual pathology.

Causes

- Cystic fibrosis
- Heart failure
- Lung metastases
- Infections
- Neurodegenerative disorders
- Gastro-oesophageal reflux
- Seizure activity

Initial treatment consists of treating the underlying cause, i.e. diuretics for heart failure or antibiotics for infections etc. Clues to coughing being driven by subclinical seizure activity are its paroxysmal and episodic clustering, its association with retching and/or screaming together with a background of poorly controlled epilepsy. Hyoscine patches can help dry excessive secretion particularly in the neurodegenerative disorders.

However, we are often confronted with situations when symptomatic treatment is required. Humidified air or oxygen can help in a number of cases. It is often worth trying nebulised Salbutamol or Atrovent although sometimes nebulised normal saline works just as well. Sometimes a child unaccustomed to masks and nebulizers may become distressed with this treatment, and staff along with parents may have to judge whether the efficacy of this treatment is worth the distress caused to the child.

Physiotherapy with or without suction can often settle a child down. One of the most effective treatments is to hold the child propped up: parents and carers are very good at this and it may help them to feel involved in the care of the child. Cough suppressants can also be used starting with simple Linctus or Pholcodine (often not very effective at this level), then Codeine Linctus, and if necessary Morphine or Diamorphine Linctus. Coughing can be very exhausting for the child and family and warrants aggressive management from the care team. An adult approach is to use nebulised local anaesthetics such as Lignocaine or Bupivacaine. However, this is much less appropriate in children both because of the unpleasant taste and numbness that it leaves in the mouth and because in the presence of neurological compromise, there is risk of aspiration when the gag reflex is anaesthetised.

Cough itself is a very important reflex and without it mucous would soon build up in the lungs. In a number of conditions, particularly neurodegenerative disorders, the loss of the ability to cough is a major problem. Good physiotherapy, posture drainage and suction can be very helpful. With the advent of new technologies we are finding increasing benefits of using cough assist machines in many of these cases.

Diarrhoea

[19, 40-43]

Diarrhoea in children can occur for various reasons and requires a detailed history of past illness, diet, medication and treatments.

Causes

- Gastroenteritis
- Faecal impaction with overflow
- Malabsorption/diet
- Drug induced, e.g. antibiotics
- Post radiation/chemotherapy
- Concurrent illness, e.g. colitis

Simple reassurance, and clear fluids, can deal with most cases. Dioralyte can be helpful to replace sugar and salts in the short term. Faecal loading and impaction would need appropriate treatment. Nappy rashes are common and barrier creams should be used early to prevent rashes. Subsequent rashes can be treated with exposure of the skin to air and Daktacort cream. Stool cultures and reducing substance screens are sometimes needed to make an appropriate diagnosis. The use of live yoghurt or soya milk can sometimes help with malabsorption. If, however, simple methods fail, then a pharmacological approach is needed.

Both Imodium and Lomotil can be used medically to control persistent diarrhoea.

Dyspnoea

[44-47]

Dyspnoea refers to a subjective sensation that breathing has become unpleasant, rather than an objective observation that it has become fast or difficult. This is an important distinction as it underlines the importance of discrimination in investigating and treating.

Dyspnoea can be a frightening symptom; the idea that their child is suffocating to death would terrify any parent. Correct early treatment can be very rewarding and helps parents to develop confidence in the care team. As in all symptoms a good understanding of pathology and physiology makes management a simple and logical process.

Causes

- Anaemia
- Anxiety, fear or claustrophobia
- Ascites
- Cerebral tumours
- Congenital heart disease
- Cystic fibrosis
- Hepatic or renal impairment
- Infection
- Metabolic
- Mechanical
- Pain
- Pleural effusion, left ventricular failure or pneumothorax
- Raised intracranial pressure
- Respiratory muscle dysfunction, e.g. neurodegenerative disorders
- Secondary tumours, i.e. lymphoma

Anaemia is often seen in the haematological malignancies, and towards the terminal phase can cause mild to moderate dyspnoea. The decision to give blood transfusions is often difficult. Transfusion is an invasive process, which limits parent child contact and is not without a degree of discomfort for the child. Transfused blood itself, for various reasons of storage, is not always as successful as expected at reducing dyspnoea. Communication between the hospital specialist unit, the care team and parents is therefore essential in making the appropriate decision.

Anxiety and dyspnoea is the proverbial chicken and egg. Anyone who cannot breathe will feel anxious. The process of anxiety itself will lead to hyperventilation. This in itself will make the dyspnoea feel worse. It is therefore important that initial management should be to calm the situation down and reassure both the child and parents. Small dose Diazepam, Midazolam or chloral hydrate can be helpful without necessarily suppressing respiration.

Cerebral tumours can affect the respiratory centres either directly through local invasion or indirectly by raising intracranial pressure. Dexamethasone is helpful in the short term, but eventually the progression of the disease or side effects from the steroids reduce its benefit.

A child propped up by a calm parent or carer with oxygen via a nasal tube will help most cases of dyspnoea. In palliative care higher than normal flow rates are perfectly acceptable. However we will often see children on heroic doses of oxygen (10-14L/min). This is very rarely necessary for the child and appears to be more for the doctors and parents. It is often helpful to measure oxygen saturation (pulse oximeter), but probably better to look at the child and their condition in the context of their illness.

The oxygen cylinders used in the community are smaller than those in hospitals, so with higher rates of flow it is always worth ordering more cylinders than normal.

1360L cylinder lasts 11 hrs @ 2L/min

Nasal cannulae	1L/min	24% delivered
	2L/min	28% delivered
Ventimask	2L/min	24% delivered

Oxygen concentrator	X1 = 2-4L/min
	X2 = 4-8L/min

Dyspnoea is commonly seen in the neurodegenerative disorders due to weakened respiratory muscles and inability to clear secretions. Physiotherapy should be done very gently in these often fragile children. Suction can cause more distress than benefit and should in such cases be undertaken by experienced staff or not at all.

Thick secretions can sometimes be managed with mucolytics such as N-acetyl Cysteine. The use of nebulised normal saline can also be helpful in difficult cases (be aware that some children can have reflex bronchospasm).

Pleural effusions are thankfully rare, tending to occur in lymphoma and other malignancies. Pleural taps are invasive, can be distressing for the child and may only give temporary relief.

Two other empirical treatments that should be considered are nebulised bronchodilators and analgesia.

Even without the presence of wheeze, nebulised Salbutamol or Ipratropium can produce symptomatic benefit. The use of oral Morphine or subcutaneous Diamorphine **(in half-analgesic doses)** can help settle dyspnoea. They reduce anxiety and pain, settle down the respiratory centres and reduce pulmonary artery pressure, which is the cause of a lot of breathlessness (this effect is more marked with Diamorphine).

Emergencies in paediatric palliative care

[48-57]

Uncontrolled and distressing symptoms are a medical emergency and need to be actively treated.

Types of emergency in paediatric palliative care

- Severe pain
- Difficulty breathing and airway obstruction
- SVC obstruction
- Spinal cord compression
- Agitation
- Haemorrhage
- Seizures
- Urinary retention

Most emergencies can be anticipated by knowing the natural history of a disease (for example, anticipate breathlessness in disease that metastasises to lungs), and from a knowledge of the individual child (for example, anticipate haemoptysis in a child with pulmonary Aspergillus).

Proactive planning and preparation for medical emergencies is essential

- Discuss possible events with the family.
- Discuss how events could be managed at home, in hospital or in a hospice. Management can sometimes vary according to location (e.g. a chest drain would not be inserted at home to manage a pneumothorax, but could be done in hospital).
- Find out where the child and family want to be in an emergency situation, for example moving to a hospice, staying at home.
- Have a management plan which parents can initiate.
- Appropriate drugs available and usable.
- Make sure parents have professionals they can contact.
- Make sure the professionals they will contact have a plan.

Investigation, management and treatment of palliative care emergencies

With all emergencies it is important to consider:

- Do I need to know the underlying cause or can I manage the symptom effectively without confirming the cause?
- Is the underlying cause likely to be treatable?
- Are investigations of the underlying cause appropriate, (for example, are they invasive, do they require being in hospital etc).
- Will treating the underlying cause improve prognosis or quality of remaining life?
- How effective could any potential treatment be?
- How toxic could any potential treatment be?

- Will the child have to move to another location for the investigation and/or treatment? Will this be possible, will they be willing to do this?

- Wishes of the child and family.

It is essential to adopt a holistic approach to symptom management, as medication alone is rarely sufficient.

Uncontrolled or poorly controlled pain

Good early pain control is the best way to avoid severe uncontrolled pain at the end of life. It is essential that drug doses are increased quickly enough to manage rapidly escalating pain, and that the right analgesic is used. Inadequately treated neuropathic pain is perhaps one of the hardest to manage emergencies, yet one that is potentially preventable when tackled early.

Sudden onset rapidly escalating opiate-sensitive pain

This type of pain is often seen in children with cardiac disease associated with pulmonary constriction. It is also seen in children with malignant disease who have rapid onset of break-through pain that is opiate responsive, but where oral opiates take too long to be effective.

Intranasal or buccal Morphine:

- Use the IV solution.

- Start with a dose of 0.05mg/kg if the child is opiate naïve; 0.1mg/kg if the child is already on opiates.

- Make sure the parents are able to draw up and administer the medication. It is useful to mark the syringe clearly with the volume of Morphine they will need to give.

- Advise the parents to repeat the dose every 10-15 minutes up to a maximum of the dose you would give if you were giving an IV breakthrough dose. It is unusual for a child to need as much as this.

- If a child needs two to three doses, increase the starting dose for the next episode to the total dose that was needed in the previous episode.

- If you do not get good pain relief, despite titrating the dose up, then this is unlikely to be purely opiate sensitive pain.

Neuropathic pain

Neuropathic pain should always be considered in the following groups of children:

- Any solid tumour.
- Epidermolysis bullosa.
- Rapidly progressive spinal curvature.
- Dislocated/displaced hip.

We also suspect that some children with encephalocoele and hypoxic ischaemic encephalopathy experience neuropathic pain.

It is absolutely essential that neuropathic pain is treated early, particularly in children with malignant disease, before a crisis situation arises.

For children with severe neuropathic pain that needs emergency treatment the following options should be considered:

- For solid tumours: high dose Dexamethasone and radiotherapy.
- Methadone: either added in as an additional analgesic or by converting all opiates to Methadone.
- Ketamine: sublingual or by continuous subcutaneous infusion.
- Lidocaine: by continuous subcutaneous infusion.
- Regional nerve block.
- Intrathecal and epidural analgesia: this is best considered ahead of a crisis situation. In the right situations it can be extremely effective and children with severe uncontrolled neuropathic pain can become completely pain free.

We strongly advise that Methadone, Ketamine and Lidocaine are only considered with the support of a specialist palliative care or pain team.

Breathlessness

Breathlessness should be anticipated in the following situations:

- Reduced lung volume, for example tumour growth, chronic lung disease.
- Upper airway obstruction, for example from tumour.
- Pneumothorax, for example in children with lung metastases.
- Superior vena cava obstruction.
- Pulmonary oedema, for example in children with cardiac failure.
- Chest infection.
- Anaemia.

Treatment of the underlying cause should always be considered, but may not be appropriate or possible:

- Steroids and radiotherapy or chemotherapy for malignant disease.
- Chest drain for pneumothorax.
- Diuretics in pulmonary oedema.
- Antibiotics for chest infection.

Severe sudden onset breathlessness:

When this occurs, it is often a terminal event. The goal of care is to get the child settled and comfortable as quickly as possible.

- Give buccal Midazolam 0.5mg/kg and buccal Morphine 0.1mg/kg.
- Repeat every 10 minutes until the child is settled.
- As soon as possible, set up a continuous subcutaneous or intravenous infusion of Midazolam 0.3mg/kg/24hrs and Morphine or Diamorphine at a dose that is at least the equivalent of an intravenous breakthrough pain dose. If pulmonary oedema is likely to be a contributing factor to the breathlessness, consider adding Furosemide, either 0.5mg/kg (od-qds) stat or into the continuous infusion. (NB at high opiate doses, Furosemide may precipitate out.)

Superior Vena Cava (SVC) obstruction

SVC obstruction is most likely to occur in children with mediastinal tumours.

Typical signs of SVC obstruction are:

- Breathlessness
- Headache
- Visual changes
- Dizziness
- Swelling of face, neck, arms.

Emergency treatment is usually with steroids, usually Dexamethasone (1-2mg/kg/day up to 16mg maximum).

Radiotherapy and/or chemotherapy may then be considered.

Symptomatic management of breathlessness before the tumour shrinks is essential.

Spinal cord compression

This is a real medical emergency and prompt appropriate treatment is essential. By the time clinical signs are classic, treatment is unlikely to reverse the disability.

Most usually seen in children with intramedullary metastases, intradural metastases or extradural compression (vertebral body metastases, vertebral collapse, interruption of vascular supply).

Early signs of spinal cord compression:

- Back pain
- Leg weakness
- Vague sensory disturbance in legs

Late signs of spinal cord compression:

- Profound weakness.
- Sensory level.
- Sphincter disturbance.
- Emergency treatment is with steroids, usually Dexamethasone (1-2mg/kg/day up to 16mg maximum).
- Radiotherapy and/or chemotherapy may then be considered.
- Spinal surgery may also be an option.

Agitation

Consider and treat underlying causes where appropriate, for example:

- Fear, anxiety, bad dreams
- Pain
- Medication
- Constipation
- Dehydration
- Hypoxia
- Anaemia

Sudden onset severe agitation can be relieved with intranasal or buccal Midazolam 0.2-0.5mg/kg. The buccal preparation is not always easy to get hold of quickly, so the IV solution can be used instead (given intranasally or buccally at the same dose).

Cerebral irritability

This is not always easy to diagnose and is often a diagnosis of exclusion. It is most frequently a problem in children with severe birth asphyxia. Whilst not strictly something that occurs acutely, these children can cry for hours, without any response to comfort or analgesia.

Medication that can be helpful includes:

- Phenobarbital (1-4mg/kg once to twice daily).
- Levomepromazine (0.25 - 1mg/kg up to 4x day).
- Buccal Midazolam (0.5mg/kg as needed). Midazolam can be used in a crisis situation when the baby needs something to break the cycle of crying and help him/her relax and go to sleep. It should not be considered as 'treatment' for the irritability, but as an essential drug for crisis management.

Acute pulmonary haemorrhage

Children most at risk from this are those with pulmonary Aspergillus, often following bone marrow transplant. It can be a dramatic and catastrophic terminal event. Families must be warned if this is a risk.

- Use coloured towels to soak up blood, so the visual bleeding is less dramatic.
- Give buccal or intranasal Midazolam 0.5mg/kg and buccal or intranasal morphine 0.1mg/kg. Repeat these every 10 minutes until the child is settled. Giving buccal drugs can be very difficult during an acute haemorrhage, so if in hospital give stat IV or S.C. doses.
- As soon as possible, start a continuous subcutaneous or intravenous infusion of Midazolam 0.3mg/kg and Morphine at a dose that is at least the equivalent of an IV breakthrough dose. In an acute severe haemorrhage, the child is likely to die before this is possible.

Seizures

Seizures should be treated according to local seizure management protocols, for example using PR Diazepam, buccal Midazolam, paraldehyde and/or IV Lorazepam.

Resistant seizures can become a medical emergency:

- First line treatment should be with a continuous infusion of Midazolam 0.25-3mg/kg/24hrs. We would recommend starting at a low dose and incrementing every four to six hours as necessary.
- If seizures continue, add in s.c. Phenobarbital. If the child has not recently been on similar drugs, give a loading dose of 15mg/kg over 30-60 mins, then start a continuous infusion at 500mcg/kg/hr. Increment by 20% increases every six hours until seizures stop.
- For children with severe neurological disorders who have been on multiple anticonvulsants, we have found Midazolam is not always helpful and tend to omit this step.

Urine retention

The most usual causes of urine retention are:

- Side effect of morphine.
- Spinal cord compression.
- Constipation.
- Solid tumours.

Treating the underlying cause can be effective, such as switching to an alternative opiate or using Dexamethasone and/or radiotherapy to shrink a solid tumour.

Having a warm bath and encouraging the child to pass urine in the bath is often the most effective crisis management for children with opioid-induced retention. Creating a relaxed atmosphere and gentle bladder massage are also helpful.

Catheterisation may be necessary to relieve the discomfort of a full bladder. This will usually only be needed for a short time in opioid-induced retention. Be very cautious if considering catheterisation in a child with a solid tumour obstructing urinary outflow; it is likely they will need a suprapubic catheter.

End of life management

Introduction

One of the major concerns that doctors and nurses who look after children with a life-limiting or life-threatening condition profess to having, is how to manage the final stages of their lives. This is not surprising when one considers some of the fundamental problems of dealing with end of life; from being able to predict the time of death, to how the death will occur when dealing with children whose diagnoses are uncertain. In addition, this subject also brings about the concept of a good or bad death, as well as issues around where a child wishes to die, and communication issues with the family. The key point on this subject is that one does not require a specialist paediatric palliative care consultant and team to look after all children who are dying. In the majority of cases, good compassionate care from a primary health care team or local paediatric team can be just as effective. The secret lies in using basic common sense medical practice, with sound holistic care and sensitive communication skills.

Many doctors and nurses who work in paediatric palliative care will talk about a good or bad death. For doctors, a 'good death' may mean that a child has had optimal symptom control and a painless death. To the nursing team this may mean a child has received good holistic care, there has been adequate time to look after the child and family, and supportive medical backup was in place. To a child and family, all of these things are equally important, but in addition they also need to feel in control, without fear, and with a sense of ease of access to medical and nursing support.

Although the ideology of helping a child achieve a good death is sound in practice, this is sometimes not achieved. There are many reasons cited for this including finance, resources and access to technology. However it has been shown by units all over the world in both the West and Third World countries, that these problems can often be overcome by simple solutions. In parts of Africa, healthcare assistants are taught by experienced palliative care doctors to look after children within distant rural communities. In parts of Eastern Europe, excellent community services are delivered on shoestring budgets. In places such as India, the challenges will stem from the diversity of environments, from the technology-rich major cities to the socially deprived rural areas.

Discussion

Prognosis

Probably the most common question asked by parents of doctors is 'how long does my child have left to live?' This is actually one of the most difficult questions in children's palliative care to answer, with the difficulty stemming from some fundamental differences between children and adults. An adult approaching death may be suffering from a number of possible medical conditions which over time doctors have grown to understand and can predict in terms of course. This allows the doctor to estimate fairly accurate timeframes, particularly towards the end of life, for an adult dying from either cancer or noncancerous conditions. Children however are much more difficult to predict. Firstly, a child with cancer can often do very well with current aggressive chemotherapy and adjunct treatments. Conditions that were previously thought of as terminal can sometimes revert into long-term remission.

Unfortunately if other factors such as infection intervene, the child may well suddenly succumb to death. In other circumstances a child with cancer may go through various levels of chemotherapy treatment before the paediatric oncologist finally accepts that the child has entered the terminal phase. Sadly this can lead to the paediatric palliative care team having only a few days to develop a relationship with the family and child, before the child subsequently dies.

In noncancerous conditions there is often a deterioration curve for the child which involves slow progressive deterioration with increasingly frequent episodes of dipping, associated with other intercurrent illnesses such as infection. During these episodes, a child may succumb to their illness, whilst others may subsequently pick up. This is often associated with the fact that unlike adults, children's organs may be damaged by certain types of illness, but their other organs tend to be very healthy and resilient. The difficulty for parents when their child goes through this type of disease process, is that they often have to be warned that they may lose the child during the specific episode, only to then find the child improving and going home. This puts a major emotional strain on the family and parents as they have to relive the process of watching the child potentially dying over and over again.

So when presented with parents requesting a timeframe for the child's death how should one proceed? It is important to let the parents know that you are uncertain. Parents do not perceive this as a negative, but more as an honest approach. We would recommend that the parents take each day as it comes, and try and tackle the issues within the day, with the knowledge that you as their doctor will regularly communicate with them as to the progress of their child's condition.

Indicators of poor prognosis and deterioration include [58]

- deteriorating vital signs
- loss of interest in surroundings
- decreased interactions with others
- loss of appetite
- decreased urine and stool output
- increased periods of sleep and/or withdrawal
- worsening laboratory tests (if being monitored)

The final mode of death to consider is that of sudden unexpected death. In many neurodegenerative and genetic disorders, situations arise where a child, although relatively well, may suddenly deteriorate and die within a matter of a few hours or days. This is often linked to the development of resistant infections. It is important in these situations to be clear with the parents that this type of event does happen, and is not linked with anything that they, or any other health care professional, may or may not have done. These types of deaths tend to be particularly distressing for the family as they often have not had time to prepare emotionally for the loss of the child, and this is often linked to recriminations and regret.

Management

When first presented with a child who is entering the final stages of their life, it is useful to consider various issues of symptom management, communication and planning. The following discussion uses Together for Short Lives' philosophy for end of life care as its basis.

- **The child's needs should be assessed and a plan of care should be discussed and developed with the child and their family or carers.**

When first presented with a child who has end of life needs, it is important that as the healthcare professional you do not panic. The parents will have sufficient anxiety in their minds without the healthcare professional adding to their concerns. A clear, calm approach will help to settle both the child and the parents and help establish the initial rapport that is required for good communication. In paediatric palliative care, assessment cannot be done in 5 to 10 minutes. It is important to set aside sufficient time to do a detailed and thorough assessment of the child, allowing for discussion with the child, parents and surrounding support system. Within the UK a system of palliative care called the Gold Standards Framework [60] recommends a management plan called 'PEPSI COLA'. This is both simple to use and covers all the main subject matters.

- Physical issues.
- Emotional issues.
- Personal issues.
- Social issues.
- Information: does everybody know what they need to know?
- Control: place of death, dignity, autonomy.
- Out of hours/emergency.
- Late: what is the end of life management plan? Has non-palliative treatment been stopped?
- Afterwards: bereavement support for the family.

It is very important at this stage to involve any other healthcare professionals within the assessment and discussion process. This reassures parents that there is a multidisciplinary team approach to their child's care. The family can then ask questions of the healthcare team even when the doctor is not present, which can be answered with a unified approach if there is a clear understanding of the plan.

- **Communication and information should be provided for the child, siblings and parents appropriate to age and understanding.**

One of the key differences between adult and paediatric palliative care is the need to understand the importance of age and development of the child when trying to communicate with them. This is further complicated by the effect on cognition from many neurodegenerative conditions, disease progression and drugs. It is therefore beholden to the doctor to take all of these factors into account as they endeavour to communicate with a particular child. Parents' understanding of medical conditions will be influenced by many factors, including their education, language difficulties, religious and social beliefs. There is little point in giving any written plan to a parent who is unable to read. It's far better to consider who may be able to read the plan to the parents to allow them to fully understand and follow the management plan.

- **The religious and spiritual needs of the child, family and carers should be considered.**

Religious beliefs are very important in almost all cultures. The issues around dying and subsequent death vary between all the different religions. Each faith has only slightly different ways of dealing with things, but if these differences are not upheld then this can cause offence. Any healthcare professional dealing with end of life issues in children should make themselves fully aware of the appropriate religious and spiritual needs of the child and family. It is important to remember that within any one religion there may be a diverse range of views and opinions regarding appropriate protocol. It is also unwise to assume that a family from a particular religious group would wish to follow the beliefs of that faith. The health care professional should make every effort to discuss with the family what their individual belief systems are.

- **The child's, family's and carers' understanding of the child's condition should be considered.**

It is very important that when the doctor first does his/her assessment of the child, they endeavour to find out just how informed the family and carers are of the child's condition. Sadly there are many situations where the child is sent for end of life care to a specialist team, only for the team to discover that the parents have not been informed of why they were sent across, the seriousness of the child's medical condition, or the fact that the child is expected to die. In these situations it is important to show care and compassion towards the family, as you explain the fundamental issues around the child's medical condition.

Some cultures feel that entering the end of life phase may be a case of giving up on the child, and their beliefs are such that they are obliged to continue to preserve life at all costs. In these situations it is very important to communicate effectively with the parents to help them to understand that this is not giving up, but a continuation of medical care for the child.

In other situations difficulties may arise from denial by the family and carers of the severity of the child's condition. There may be seeking behaviour where parents will try alternative practitioners and therapies. It is important to allow them to do this, whilst still maintaining a presence to support the family should these fail.

- **The child's and family's wishes and views should be incorporated into the end of life care plan.**

When one considers the issues around the causes of a bad death, a common theme is that the family feel that their wishes were not considered by the healthcare team. It is critical that the family's wishes and views are not only listened to, but form a critical pillar within the end of life care plan. This enablement of the family gives them a sense of ownership of the care plan and a feeling of control in a situation which they otherwise have very little ability to affect.

- **Ensure that the family has all the relevant and up to date emergency contact details of staff and agencies that they may need to get in touch with.**

The ability to provide 24hour emergency backup for the family is an issue which affects units throughout the world. In many cases there are significant logistical issues, such as the distance between the child and health care teams. There are also issues of access to local expertise and fear amongst other healthcare professionals of getting involved. In the majority of cases, a child with an end of life problem can be managed by local healthcare professionals with basic access to, and telephone support from a specialist team. The key to this is good care planning, with effective planning for the worst case scenarios and the appropriate actions that should be taken. Palliative care cannot be conducted on a 9 to 5 weekday basis, and the end of life plan must incorporate information about how the parents can obtain support out of hours.

- **The child's current medication should be re-assessed. If appropriate consider discontinuing any non-essential medication.**

Over a period of time, a child can develop a long list of medications that various specialists have instigated. This polypharmacy, although appropriate through the child's medical journey, may no longer be appropriate towards the end of life. It is helpful at this stage to go through all the drugs to see which may be stopped or reduced. There are situations where parents may have strong feelings towards the continuation of certain types of drugs, even when they would no longer be considered beneficial, and in these situations the priority is to maintain one's relationship with the parents – therefore it may be advisable to continue with the medication in question.

- **It is important to anticipate and prescribe for a range of possible symptoms.**

This will be discussed in further detail towards the end of this chapter.

- **Consider, discuss and decide whether to discontinue inappropriate interventions such as blood tests, intravenous fluids and routine observations of vital signs.**

As a child enters their end of life stage, one needs to assess what tests and interventions are actually of any benefit to the management of the child. Most children require very little in the way of interventions, and often these can be disruptive or cause discomfort to a child within the final days of their lives. As the doctor, it is important to consider what difference any interventions that you request will actually make to your care of the child. It is often better to use your eyes to observe a deterioration in a child, rather than to do repeated blood tests. A natural part of the dying process is the need for less and less food and fluids, and use of intravenous fluids may just prolong the agony of dying rather than provide any increase in quality of life. Most routine observations of vital signs are of little or no benefit, although it can be very difficult sometimes to get parents to move away from using technology that they have used to monitor their child, such as oxygen saturation monitors. It is always best in these situations to present your case but to avoid conflict and allow the parents to continue using these technologies if they feel it gives them a sense of control.

- **Ensure the family and carers are given appropriate written information to back up your discussions and plans.**

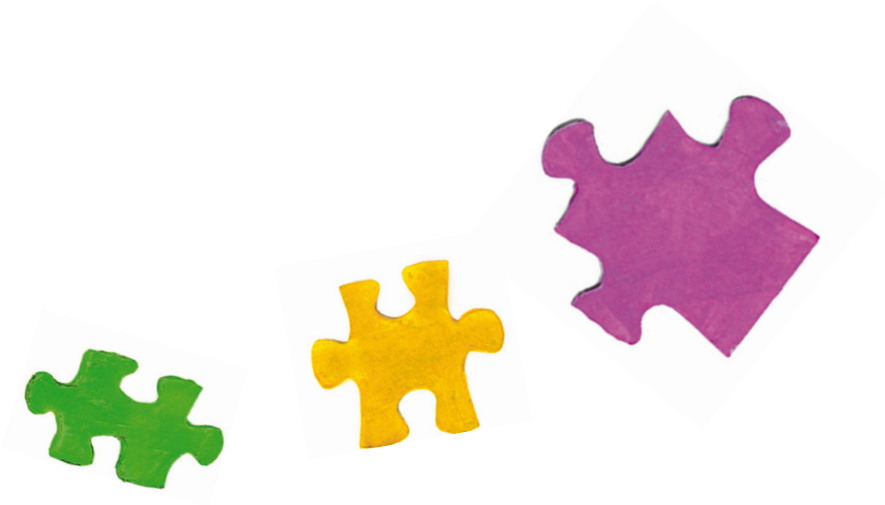
After the initial assessment, it is important to develop a plan of action and to write this plan down rather than keeping it in one's head. There is a difference between medical notes and a care plan in terms of the language and jargon used. It is important that the information in the care plan is written in such a form that doctors, health care professionals and family can all read and understand it. This may require a healthcare professional to read and interpret the plan for an illiterate family or for the plan to be translated into their preferred language.

- **The primary care team, specialist community services, hospital specialists, ambulance services and out of hours services should be made aware of the child's condition and that they are now at the end of life phase.**

It is critical that good communication operates throughout all levels of the healthcare service. This will allow everyone to follow the care plan through correctly. It should also prevent situations whereby a child is rushed into hospital inappropriately as part of an ambulance protocol, to be managed within the hospital aggressively but inappropriately.

- **The family should be given the opportunity to discuss their plans for death care.**

The family should have information about who to call when a child dies, what should be done immediately and what can wait. They should also be able to discuss their wishes regarding what happens after the death and subsequent funeral arrangements.



- **Help the family to think about support systems after their child's death and who they might like to support them.**

The emotional trauma felt by a family after the death of their child cannot be underestimated. It is important to consider the support systems that may be required by the family after the loss of a child. These support systems do not necessarily have to be related to the health care profession. Family, friends and religious support can all be very effective. Although counselling can be of great benefit to certain individuals, it does not automatically follow that all parents require counselling after the death of their child. In fact many would choose to use the local support systems in preference.

Symptom management at end of life

Symptom management in paediatric palliative care is extensively covered throughout this book within its individual chapters. In this section we will consider the specific symptoms that may occur towards the end of the life. Details of the drug usage and dosages can be found in individual chapters. The chapter on emergencies in paediatric palliative care covers many of these issues in detail.

As a child approaches end of life, there will be considerable anxiety amongst family and healthcare professionals to ensure that all symptoms are adequately controlled. Pre-planning around the type of symptoms that may occur and the management of these individually is essential. An emergency box of drugs can also be helpful if financially feasible.

Pain

It is not unusual to see an increase in pain towards the end of the child's life although it should be recognised that some children actually will die without experiencing any significant degree of pain. The key to managing pain in these situations is to have pre-planned management, with access to fast acting opioids. Most children's pain can be managed with morphine elixir, used every four hours and increased in increments of 30 to 50% as required. Detailed use of morphine is outlined in the chapter on pain. Be cautious when using slow release preparations as any change in dosages can take a long time to become effective. When a child is unable to swallow and there is no access via a nasogastric tube or gastrostomy, then morphine can be used either buccally or rectally. If facilities allow, then the use of syringe drivers can be most effective. They facilitate the provision of fast, effective control of pain and other symptoms, avoiding the peak and trough effect of oral opioids. Where breakthrough pain occurs, then a dose of 1/10 to 1/6 of the 24 hour morphine dose can be given as required. There is no maximum dose of morphine. The dosages if increased correctly will neither cause nor postpone death.

Death rattle

The death rattle is often seen in the terminal phase. This can sound very distressing to the family and it is important that they are pre-warned regarding this. The rattle is caused by noisy secretions when the child is no longer able to cough up or swallow secretions within the large airways. As this tends to occur when the child has dropped their level of consciousness, it is not a direct cause of distress to the child. Management should consist of the following:

- Positioning of the child's head to allow secretions to drain
- If linked with dyspnoea then treat with opioids and/or benzodiazepines
- Use hyoscine either subcutaneously or in the form of a patch
- Gentle suction only

Seizures

The management of epileptic seizures is covered in a previous chapter. However in the acute situation a seizure can be controlled with either buccal midazolam or rectal diazepam. Occasionally rectal paraldehyde can be helpful. In situations where seizures are recurring and a syringe driver is available then a subcutaneous infusion of either midazolam or phenobarbitone can be used.

Dyspnoea

The first priority when presented with a child with dyspnoea is to rule out any treatable causes such as heart failure or asthma. When the dyspnoea is purely due to the terminal condition, then a low dose of opioids or benzodiazepines can be helpful.

Fluids

The ethical issues concerning withholding fluids are covered in the chapter on ethics. In general terms giving fluids via intravenous lines is normally inappropriate towards the end of life. There is a general multi-organ failure and shut down of the body, and as such the fluid requirements of a child are considerably diminished. Running the child slightly dry can also help reduce respiratory secretions. There is a natural shutdown by the body of renal function, and so urine output falls naturally. Thirst is rarely an issue towards the end of life, however it is important to continue to give the child small volumes of water even if this is just wetting the mouth or lips. Parents find this action comforting and reassuring.

Summary

The actions that one takes as a healthcare professional when managing a child who is approaching the end of their life can have a profound effect on whether a child has a good or bad death. This will subsequently either help the parents cope with the loss of a child, or cause them great distress. The key to successful management rests with professional assessment, planning, communication and access to adequate resources. It is important that all the appropriate members of the team develop their knowledge and expertise within the subject, whether this involves symptom management, nursing care or understanding the religious and spiritual needs of the family. The death of a child is not the end of the journey for the parents or family and it can take many years for the parents to come to terms with the loss of a child, if they ever truly do so.

Ethics and the law

UK law is determined in two ways:

- Laws passed through Acts of Parliament.
- Case law arising from Law Lords ruling in the High Court. This then becomes legally binding for subsequent similar cases.

This guidance has been prepared in line with UK law including relevant case law up until November 2010. The scope of this guidance includes babies, children and young people including adults over 18 years. For the purposes of this guidance the term 'child' will be used to describe any baby, child or young person regardless of age unless otherwise specified.

Case law is often complex and often contradictory. Specialist advice is strongly recommended if the issue is beyond the scope of this guidance or there is significant disagreement.

Applied clinical ethics in paediatric palliative care

The primary **duty of care** of any healthcare professional is to the child who is your patient. Consideration of the wellbeing of the parents, carers and wider family is likely to have a direct impact on the child but their needs must not take precedence over that of your patient.[1]

Decision making model

Decision making must be made on the grounds of the **best interests**[2] of the child. The best interests standard refers to what is best for the patient and the option that is likely to result in overall benefit.

1 General Medical Council. *Treatment and Care Towards the End of Life,* 2010.

2 The concept of best interests is used England, Wales (*Mental Capacity Act* 2005) and common law in Northern Ireland. A similar interpretation is attributed to "benefit" in the *Adults with Incapacity (Scotland) Act* 2000.

The **responsible physician** must use their specialist knowledge, experience, clinical judgement, and their understanding of the patient, to identify which investigations or treatments are clinically appropriate and likely to result in overall benefit for the patient. The responsible physician must explain the options setting out the potential benefits, burdens and risks of each option. The responsible physician may recommend a particular option that they believe to be best for the patient, but they must not put pressure on the patient or their carer to accept their advice.

The **person with decision making-responsibility** should weigh up the potential benefits, burdens and risks of the various options as well as any non-clinical issues that are relevant. The person with decision-making responsibility should then evaluate the patient's best interests and decide which, if any of the options to accept.

Person with decision-making responsibility

Adults with capacity

Where the patient is an adult with capacity the patient is assumed to be able to determine their best interests and has responsibility for decision making, including giving or refusing consent to treatment.

Tests for capacity

An adult of 18 years or over is assumed to have **capacity** to decide what is in their best interests unless proven otherwise. An adult with capacity has the right to accept or refuse an option for a reason that may seem irrational to the doctor or for no reason at all. An adult has capacity to consent to or refuse an investigation or treatment if they are able to understand, retain, use and weigh information regarding treatment options and consequences of each option including refusal of treatment and to communicate their decision to others.

Adults who lack capacity

If an adult patient lacks capacity to decide, decisions made on the patient's behalf must be based on their best interests (as determined below) and which option (including the option not to treat) would be least restrictive of the patient's future choices.

In England and Wales[3] an adult with capacity may apply for another adult to have Lasting Power of Attorney to make decisions on their behalf should they subsequently lose capacity. The Courts can also appoint a Court Appointed Deputy to make decisions on behalf of an adult who lacks capacity.

In circumstances in which there is no legal proxy with authority to make a particular decision for the patient, the treating physician is responsible for making the decision. In England and Wales, if there is no legal proxy, close relative or other person who is willing or able to support or represent the patient and the decision involves serious medical treatment, the treating physician must approach their employing or contracting organisation to appoint an Independent Mental Capacity Advocate (IMCA).[4] The IMCA will have authority to make enquiries about the patient and contribute to the decision by representing the patient's interests, but cannot make a decision on behalf of the patient.

Children and young people who may have capacity

Where the patient is a child or young person with capacity for decision making they should be allowed to do so. A child or young person may have capacity to consent to an investigation or treatment if they are able to understand, retain, use and weigh information regarding treatment options including refusal of treatment and consequences of each option and communicate their decision to others. Capacity depends more on a child's or young person's ability to understand and weigh up options than on age. A higher level of capacity is generally considered to be required to refuse treatment options, particularly where the consequence may shorten life or restrict future choices.

Where a child or young person may have capacity they should be involved as much as possible in discussions about their care, whether or not they are able to make decisions for themselves. Information about their diagnosis and prognosis that they are able to understand should not be withheld, unless they specifically request it, or if it is felt that giving such information might cause serious harm. In this context 'serious harm' means more than that the child or young person might become upset or decide to refuse treatment.[5]

3 *Mental Capacity Act* 2005.
4 *Mental Capacity Act* 2005.
5 General Medical Council, *Treatment and Care Towards End of Life*, 2010.

Children and young people who lack capacity

If a child or young person lacks capacity to consent, the responsible physician should discuss the investigations or treatments that are deemed clinically appropriate and likely to result in overall benefit for the patient with their parents or those with parental responsibility. The child's parents or those with parental responsibility should evaluate the child's best interests and decide whether to consent to any of the options and, if so, which. The parents must be kept fully involved.[6]

The child's parents or those with parental responsibility are usually considered to be in the best position to advocate for the child or young person and advise regarding their best interests. However this may be influenced by the direct consequences including bereavement and secondary losses arising from the outcome of the decision. Specialist advice should be sought if it is unclear whether the parents or those with parental responsibility themselves have capacity. Specialist advice should also be sought if there are doubts regarding ability of the parents or those with parental responsibility to act in the best interests of the child.

Best interests

Decisions must be made on the grounds of the **best interests** of the patient. Best interests is a complex construct closely related to, but not limited exclusively to, quality of life. A patient's best interests are not always limited to clinical considerations and it is important to take account of any other factors relevant to the circumstances of each individual.[7]

A patient with capacity is assumed to be able to determine their own best interests.

The Nuffield Council on Bioethics[8] suggests that for a neonate up to 28 days of age evaluation of best interests should include consideration of:

- What degree of pain suffering and mental distress will/might the treatment inflict on the child?
- What benefits will/might the future child get from the treatment?
- What kind of support is likely to be available to provide optimum care for the child?
- What are the views and feelings of the parents?
- For how much longer is it likely that the baby will survive if life sustaining treatment is continued?

Determination of best interests for a child, young person or adult without capacity should include:

- All reasonable attempts to elicit the views of the patient themselves. Even if the patient lacks capacity, if they are able to express a view and take part in decision making, it is essential to listen to them and take account of what they have to say about things that affect them.[9]

- Considering an independent advocate on behalf of the child or young person. For an adult who lacks capacity an Independent Mental Capacity Advocate (IMCA) must be appointed if there is no legal proxy, close relative or other person who is willing or able to support or represent the patient and the decision involves serious medical treatment.

- Considering whether the child, young person or adult may gain capacity at some point in the future and if this is the case, whether it is possible to postpone decision making until this time.

- The views of the child's or young person's parents or those with parental responsibility.

- The views of those who have an interest in the welfare of the child, young person or adult.

6 General Medical Council, *Treatment and Care Towards End of Life,* 2010.
7 General Medical Council, *Treatment and Care Towards End of Life,* 2010.
8 Nuffield Council on Bioethics. *Critical care decisions in fetal and neonatal medicine: ethical issues.* 2007.
9 General Medical Council. *Treatment and Care Towards the End of Life,* 2010.

- The views of the treating multi-disciplinary. Professionals must be careful not to rely on their personal views about a patient's quality of life and to avoid making judgements based on poorly informed or unfounded assumptions about the healthcare needs of particular groups, such those with disabilities.

- When discussing the issues with people who do not have legal authority to make decisions on behalf of a patient who lacks capacity, it should be emphasised that their role is to advise the healthcare team about the patient's known or likely wishes, views and beliefs. They are not being asked to make the decision.[10]

- Views of the wider multi-disciplinary team and those who have an interest in the wellbeing of the child or young person are important. These views should be taken into account but must not be allowed to take precedent over the views of those with primary responsibility for decision making.

It should be possible to justify decisions made in the best interests of the child or young person by articulating the balance between potential benefits and harm [dis-benefits] to the child or young person.[11] If the decision making process is robust it will not be overly influenced by considerations of what the parents or carers want for themselves. For example, if it is not in a child's best interests to receive cardiopulmonary resuscitation the decision not to provide cardiopulmonary resuscitation should not be directly influenced by whether the child's parents are present at the time of the cardiopulmonary arrest. The presence or absence of the parents during a cardiac arrest situation will not have any direct or indirect influence on the potential benefits or harms of the treatment proposed, in this case cardiopulmonary resuscitation.

Uncertainty about whether a particular treatment will provide overall benefit

The exact consequences for the individual child or young person of a particular course of action are often unclear. In such circumstances, all reasonable attempts should be made to evaluate possible consequences, both positive and negative, including consideration of seeking a second opinion or deferring the decision making until the likely outcomes are clearer.

Where the person with decision making responsibility is not the patient there is a need to consider which option would be least restrictive of the patient's future choices.

If there is a reasonable degree of uncertainty about whether a particular treatment will provide overall benefit, the treatment should be started in order to allow a clearer assessment to be made. Treatment must be monitored and reviewed, and may be withdrawn at a later stage if it proves ineffective or too burdensome for the patient in relation to the benefits. Prior to commencing treatment of uncertain benefit the basis on which the decision will be made about whether the treatment will continue or be withdrawn should be clearly articulated.

In circumstances where the balance between benefits and harms of proposed treatment is very delicate, it is likely that the views of the person with responsibility for decision making will be the deciding factor.

Impact on the family and wider healthcare team

Some members of the healthcare team, or people who are close to the patient, may find it more difficult to contemplate withdrawing a life prolonging treatment than to decide not to start the treatment in the first place. This may be because of the emotional distress that can accompany a decision to withdraw life-prolonging treatment, or because they would feel responsible for the patient's death. These anxieties must not override clinical judgement and allow continuation of treatment that is of no overall benefit or failure to initiate treatment that may be of some benefit to the patient.

Parents may feel responsible for any adverse outcomes and want reassurance that all appropriate treatment for their child is being offered. This does not necessarily mean that they are requesting full cardiopulmonary resuscitation, intensive care or other aggressive life prolonging treatment. It may be that they are simply expressing fear of abandonment and their need for ongoing support.[12]

10 General Medical Council, *Treatment and Care Towards End of Life*, 2010.
11 An NHS Trust v MB [2006] EWHC 507 (Fam).
12 Gillis, J. "We want everything done" Archives of Disease in Childhood; 93(3): 191-6 2008.

The wider multi-disciplinary team, particularly carers with a longstanding and close relationship with the child or young person and their family, may require additional support in order to understand the decision making process leading to withholding or withdrawing. They may require psychological support to enable them to express and share their views and emotions in a 'safe' environment away from the child and family.

Specific situations

Information giving

Apart from circumstances in which a patient refuses information, you should not withhold information necessary for making decisions, (including when asked by someone close to the patient), unless you believe that giving it would cause the patient serious harm. In this context 'serious harm' means more than that the patient might become upset or decide to refuse treatment.

If you withhold information from the patient, you must record your reasons for doing so in the medical records, and be prepared to explain and justify your decision. You should regularly review your decision and consider whether you could give information to the patient later, without causing them serious harm.

A patient cannot have capacity to consent to or refuse treatment unless they are fully appraised of the treatment options and potential consequences.

Consent to treatment

A young person of 16 or over can be presumed to have capacity to consent. A young person under 16 years old may have the capacity to consent, depending on their maturity and ability to understand. A young person who has the capacity to consent to straightforward, relatively risk-free treatment may not necessarily have the capacity to consent to complex treatment involving high risks or serious consequences.

Refusal of treatment

A young person under 18 years old who has capacity to consent may not necessarily have capacity to refuse treatment. A child or young person may have capacity if they are able to understand, retain, use and weigh information regarding treatment options including refusal of treatment and consequences of each option and communicate their decision to others. Capacity depends more on a young person's ability to understand and weigh up options than on age. A higher level of capacity is generally considered to be required to refuse treatment options, particularly where the consequence may shorten life or restrict future choices. A number of high court rulings have overturned refusal of treatment by a young person including on the grounds that the young person lacked capacity. Are these the only grounds, or do the courts just want to retain the power to have refusal by a competent young person overridden? For example because they were not fully cognisant of the consequences of refusal of treatment.[13]

Advance refusal of treatment

Advance refusals of treatment can only be made by an individual with capacity to do so. Adults with capacity can make provision for future decisions by appointing attorneys, recording statements of their preferences and by making advance decisions or directives refusing treatment.

Children of any age who are assessed as being 'Fraser' competent can validly give/refuse consent to treatment offered to them, including advance decisions.

If a child (under 18) refuses treatment, this can be legally overridden by parental consent to the treatment and/or a court order.

There is no legal precedent in UK law for an advance refusal of treatment to be made by an individual with capacity on behalf of another individual, even if they have responsibility for decision making for that person. Likewise there is no legal precedent for an adult with parental responsibility to make a legally binding advance refusal of treatment for their child. Furthermore the Mental Capacity Act specifies that advance decisions can only be made by persons over 18 years old.

13 Re M (Medical Treatment: Consent) [1999] 2 FLR 1097.

The individual with capacity can change their mind, at any time, which will override the previous refusal of treatment. This will include a refusal of treatment revoked by a young person with capacity and regardless of the parent's views.

A valid advance refusal that is clearly applicable to the patient's present circumstances will be legally binding in England and Wales[14] (unless it relates to life-prolonging treatment, in which case further legal criteria must be met). Valid and applicable advance refusals are potentially binding in Scotland[15] and Northern Ireland[16], although this has not yet been tested in the courts.

Written and verbal advance refusals of treatment that are not legally binding, should still be taken into account as evidence of the person's wishes.

Assessing the validity and applicability of advance refusals

If there is doubt or disagreement about the status of advance refusals made by an adult over 18 years professionals should start from a presumption that the patient had capacity when the decision was made. Both the validity and the applicability of any advance refusal should be assessed.

An advance refusal of treatment will be valid if:

(a) The patient was an adult when the decision was made (16 years old or over in Scotland, 18 years old or over in England, Wales and Northern Ireland see above).

(b) The patient had capacity to make the decision at the time it was made (UK wide).

(c) The patient was not subject to undue influence in making the decision (UK wide).

(d) The patient made the decision on the basis of adequate information about the implications of their choice (UK wide).

(e) If the decision relates to treatment that may prolong life it must be in writing, signed and witnessed, and include a statement that it is to apply even if the patient's life is at stake (England and Wales only).

(f) The decision has not been withdrawn by the patient (UK wide).

(g) The patient has not appointed an attorney, since the decision was made, to make such decisions on their behalf (England, Wales and Scotland).

(h) More recent actions or decisions of the patient are clearly inconsistent with the terms of their earlier decision, or in some way indicate they may have changed their mind.

An advance refusal of treatment will be applicable if:

(a) The decision is clearly applicable to the patient's current circumstances, clinical situation and the particular treatment or treatments about which a decision is needed.

(b) The decision specifies particular circumstances in which the refusal of treatment should not apply.

(c) There is not an excessive time interval between the time the decision was made or it has been reviewed or updated (this may also be a factor in assessing validity).

14 The code of practice supporting the Mental Capacity Act 2005, which uses the legal term 'advance decision', sets out detailed criteria that determine when advance decisions about life-prolonging treatments are legally binding.

15 The code of practice supporting the Adults with Incapacity (Scotland) Act 2000, which uses the legal term 'advance directive', gives advice on their legal status and how advance directives should be taken into account in decisions about treatment.

16 In Northern Ireland there is no statutory provision or case law covering advance refusals, but it is likely that the principles established in English case law precedents would be followed.

(d) There are no reasonable grounds for believing that circumstances exist which the patient did not anticipate and which would have affected their decision if anticipated.

Advance care plan

In circumstances where an advance refusal of treatment is not applicable, an advance care plan may nevertheless provide appropriate guidance regarding the most appropriate care for a child in specific circumstances such as sudden collapse or cardiopulmonary arrest.

Where the advance care plan suggests specific circumstances when it is not in that particular child's 'best interests' to receive aggressive life prolonging treatment, staff may, in theory, be vulnerable to allegations of assault if this treatment is provided.

However if there is any doubt as to whether the care plan applies in any given situation, those caring for the child should provide life-sustaining treatment until it is possible to obtain further advice from the child's parents and the clinical team.

In an emergency

If there is no time to investigate further, the presumption should be in favour of providing treatment, if it has a realistic chance of prolonging life, improving the patient's condition, or managing their symptoms.

Reviewing decisions

The patients' condition may deteriorate, improve unexpectedly, or may not progress as anticipated. The views of the patient, those with an interest in their welfare or those with decision making-responsibility about the benefits, burdens and risks of treatment may change over time. It is essential that there are clear and robust arrangements in place to review decisions on regular basis.

Requests for treatment

If the person with decision-making responsibility asks for a treatment that would not be clinically appropriate and of overall benefit to the patient, the issues should be discussed and the reasons for their request explored. If, after discussion, it is still considered that the treatment would not be clinically appropriate and of overall benefit to the patient, the treatment does not have to be provided. The reasons for not providing the treatment should be explained together with other options that are available, including the option to seek a second opinion or access legal representation.

Conscientious objection

A healthcare professional can withdraw from providing care on the grounds of their religious, moral or other personal beliefs. However this does not override the duty of care to the patient and alternative arrangements to providing ongoing care must be ensured.

Withholding or withdrawing life-prolonging treatment

If after discussion, there is a consensus that life-prolonging treatment would not be in the child's best interests and the treatment is withdrawn or not started, any distressing symptoms must be addressed and the child must be is kept as comfortable as possible. It is essential to monitor the child's condition and reassess the benefits, burdens and risks of treatment in light of changes in their condition.

Resource constraints

If available treatment options are subject to resource constraints such as funding restrictions on certain treatments in the NHS, or lack of availability of intensive care beds, it is essential that the patient continues to receive as good a standard of care as possible. This will include the need to balance sometimes competing duties towards the wider population, funding bodies and employers. There will often be no simple solution.

Ideally, decisions about access to treatments should be made on the basis of an agreed local or national policy that takes account of the human rights implications. Decisions made on a case by case basis, without reference to agreed policy, risk introducing elements of unfair discrimination or failure to consider properly the patient's legal rights.

If resource constraints are a factor, it is essential to:

(a) Provide the best service possible within the resources available.

(b) Be familiar with any local and national policies that set out agreed criteria for access to the particular treatment (such as national service frameworks and NICE and SIGN – Scottish Intercollegiate Guidelines Network – guidelines).

(c) Make sure that decisions about prioritising patients are fair and based on clinical need and the patient's capacity to benefit, and not simply on grounds of age, race, social status or other factors that may introduce discriminatory access to care.

Acrimonious parental relationships, parental disagreement, inability to contact one parent
It is usually sufficient to have consent from one parent, but if more than one person holds parental responsibility you should encourage them to reach a consensus.

When treatment proposed carries a significant risk of mortality, or when discussions include the possibility of withholding or withdrawing life-sustaining treatment, it is strongly recommended that every reasonable attempt is made to contact all those with parental responsibility. If this is impossible, the circumstances including attempts made to contact all those with parental responsibility must be carefully documented.

It has been argued that if an individual with parental responsibility has not had contact with the child or family for a number of years they are not, in practical terms, exerting their parental responsibility. However this has not been tested in a court of law.

Clinically assisted hydration and nutrition
The terms 'clinically assisted nutrition' and 'clinically assisted hydration' do not refer to help given to patients to eat or drink, for example by spoon feeding. Nutrition and hydration provided by tube or drip are regarded in law as medical treatment, and should be treated in the same way as other medical interventions.

Clinically assisted hydration and nutrition are can be ethically and legally withdrawn or withheld if it is considered to be in the best interests of the child. However in these circumstances a second opinion, from a physician not previously involved in the care of the child or young person must be sought.[17]

For this reason it is especially important that you listen to and consider the views of the patient and of those close to them (including their cultural and religious views) and explain the issues to be considered, including the benefits, burdens when clinically assisted nutrition or hydration would be of overall benefit, it will always be offered; and that if a decision is taken not to provide clinically assisted nutrition or hydration, the patient will continue to receive high-quality care, with any symptoms addressed.

If a consensus is reached that clinically assisted nutrition or hydration would not be of overall benefit to the patient and the treatment is withdrawn or not started, it is essential to ensure that patient is kept comfortable and that any distressing symptoms are addressed. The patient's condition must be monitored and the benefits, burdens and risks of providing clinically assisted nutrition or hydration must be reassessed in light of changes in their condition.

Patients in a persistent vegetative state
In England, Wales and Northern Ireland a court ruling is required before withholding or withdrawing artificial fluids or nutrition for a patient in a persistent vegetative state or a condition closely resembling a persistent vegetative state. The courts in Scotland have not specified such a requirement.

17 General Medical Council. *Treatment and Care Towards the End of Life*, 2010.

Cardiopulmonary resuscitation

Cardiopulmonary resuscitation is like any other potentially life-prolonging medical treatment and the same principles of decision making in the patient's best interests apply. If cardiopulmonary resuscitation may be successful in restarting a patient's heart and breathing and restoring circulation, the benefits of prolonging life must be weighed against the potential burdens and risks. Accurate information must be provided about the potential the burdens and risks of cardiopulmonary resuscitation interventions including the likely clinical and other outcomes if cardiopulmonary resuscitation is successful.

Some patients or those with decision-making responsibility may request cardiopulmonary resuscitation to be attempted when there is only a small chance of success. As with any other request for treatment, the issues should be discussed and the reasons for the request explored. If, after discussion, it is still considered that the treatment would not be clinically appropriate and of overall benefit to the patient, the treatment does not have to be provided. The reasons for not providing the treatment should be explained together with other options that are available, including the option to seek a second opinion or access legal representation.

Where there is disagreement

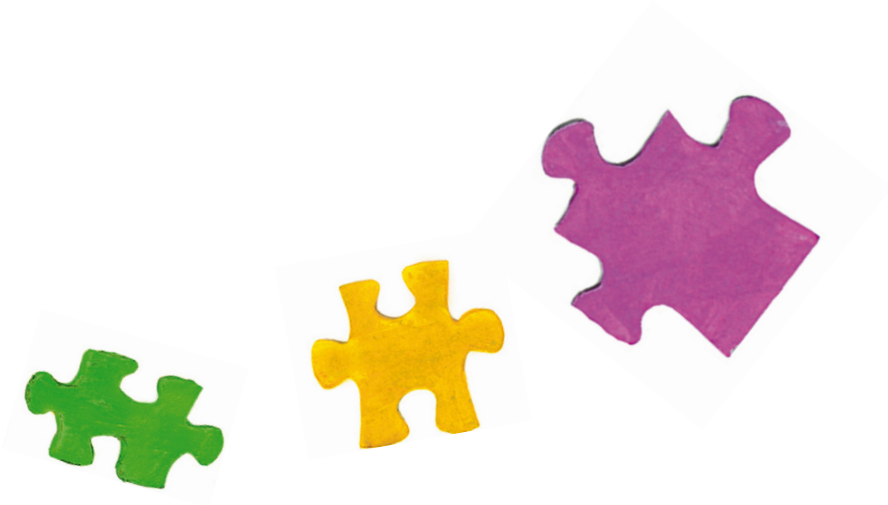
In circumstances where the balance between benefits and harms of proposed treatment is very subtle it is likely that the views of the person with responsibility for decision-making will be the deciding factor.

Even when the medical facts are certain, individual interpretation of the facts may lead to different conclusions regarding the best interests of the child or young person.

Depending on the seriousness of any disagreement, it is usually possible to resolve it; for example, by involving an independent advocate, seeking advice from a more experienced colleague, obtaining a second opinion, holding a case conference, or using local mediation services. It may also be possible to consider deferring decision-making until the situation is clearer or until the patient themselves has capacity to make a decision regarding their own best interests.

If disagreements cannot be resolved in an appropriate and timely fashion there must be an application to the courts.

An application to the courts is mandatory in England, Wales or Northern Ireland, when considering withholding or withdrawing clinically assisted feeding or hydration for a patient in a persistent vegetative state.



Fluid and electrolytes management

[61-63]

Patient weight and blood pressure (BP) are useful parameters in assisting with fluid balance interpretation, but it should be borne in mind that BP may be elevated due to causes other than fluid overload. Also, insensible losses need to be considered, so a positive balance on a chart is usually not strictly accurate as it does not account for this loss.

For practical purposes, 1kg of weight = 1L of fluid.

No action should usually be taken on the basis of a single parameter (for example, fluid balance alone). The child should be fully assessed, including BP, heart rate, respiratory rate, capillary refill time, temperature, weight and general condition.

Remember, older children can tolerate a larger positive fluid balance than younger ones.

Normal fluid requirements

Blood volume is about 100ml/kg at birth, falling to about 80ml/kg at one year of age. Total body water varies from about 800ml/kg in the neonate to about 600ml/kg at one year, and subsequently varies very little. Of this, approximately $^{2}/_{3}$ (or 400ml/kg) is intracellular fluid, the rest is extracellular fluid.

Normal daily fluid **maintenance** requirement is calculated on the basis of the amount of fluid required to keep a patient well hydrated and passing reasonable amounts of urine. The standard calculation (based on APLS recommendations) **includes the following considerations:**

1. Baseline maintenance requirements.

2. Replacement of **insensible losses** through sweating, respiration, normal stool loss (usually 10ml/kg in an adult, 20ml/kg in a child & 30ml/kg in a baby <1 year).

3. Replacement of **essential urine output** (= minimal urine output required for waste excretion).

4. Some extra fluid to maintain a modest amount of diuresis.

The calculation is by weight and thus applies to all age ranges.

Total daily fluid requirement consists of:

Maintenance + Replacement of deficit (existing/ongoing loss) + Resuscitation (if required).

Calculation of maintenance fluid requirement

(Includes 1+2+3+4 above)

Body Weight	**Fluid Requirement per 24 hours**	**Fluid Requirement per hour**
First 10kg	100ml/kg/24 hrs	4ml/kg/hr
Second 10kg	50ml/kg/24 hrs	2ml/kg/hr
Each subsequent 1kg	20ml/kg/24 hrs	1ml/kg/hr
e.g., 24kg =	(100x10kg) + (50x10kg) + (20x4kg) = 1000 + 500 + 80	**or** (4x10kg) + (2x10kg) + (1x4kg) = 40 + 20 + 4 = 64ml per hour x 24
	=1580ml per 24 hours	**= 1536ml per 24 hours**

This shows that either method of calculating fluids is acceptable, giving reasonably close answers for fluids for a 24kg child over a 24 hour period. (Indeed, the difference between the two methods is less than 2ml/hr).

In addition to the above, maintenance fluid requirements, **ongoing losses** (for example, due to significant gastrointestinal losses i.e. diarrhoea or vomiting, polyuria) need to be considered and replaced. In **febrile** patients, **insensible losses through sweating and respiration will be higher than usual**; add approximately 13% extra fluid for each 1 degree C > 37.5 degrees C.

Replacement Fluid (Deficit = existing + ongoing losses)

Ongoing losses, for example, due to significant diarrhoea or vomiting, may be replaced intravenously on an ml-for-ml basis or as part-replacement if the patient is also tolerating some oral fluids.

Existing losses (i.e. dehydration)

Percentage dehydration can be estimated clinically using the following parameters:
(APLS guidelines)

Signs and symptoms of dehydration

Sign/Symptom	**Mild** (<5%)	**Moderate** (5-10%)	**Severe** >10%
Decreased urine output	+	+	+
Dry mouth	+/-	+	+
Decreased skin turgor	-	+/-	+
Tachypnoea	-	+/-	+
Tachycardia	-	+/-	+

NB: Tachypnoea may be due to, or worsened by, metabolic acidosis and pyrexia.
Tachycardia may be due to hypovolaemia, but also due to other causes e.g. pyrexia, pain or irritability.
A low blood pressure is a serious sign in a child: it may be due to hydration/hypovolaemia or due to other causes e.g. septic shock. ***It is a late/peri-arrest sign, and preventative action should be taken prior to the child reaching this stage.***

To Calculate Replacement Fluids (according to % dehydration):

Fluid deficit (ml) = Percentage dehydration x Weight (kg) x 10

e.g. A 24kg child is 7.5% dehydrated, calculated fluid requirement. (Assuming no resuscitation required).

Fluid deficit	=	7.5 x 24 x 10
	=	1800ml
Maintenance	=	(100 x 10kg) + (50 x 10kg) + (20 x 5kg)
	=	1000 + 500 + 80
	=	1580ml
Thus **Total** fluid requirement	=	Maintenance + Deficit + Resuscitation fluids
	=	1580ml + 1800ml + 0
	=	3380ml over 24 hours
		(+ addition for ongoing losses on a ml-for-ml basis)

Normal daily electrolyte requirements

Sodium	2-4mmol/kg/day
Potassium	2mmol/kg/day
Calcium	3mmol/kg/day
Magnesium	0.75mmol/kg/day

To calculate electrolyte deficit:

Deficit (mmol) = (Normal level - actual level) x weight (in kg) x 0.7

e.g. 24kg child with serum potassium of 2.5mmol/L

Deficit	= (4-2.5) x 24 x 0.7 = 25.2mmol
Maintenance	= 2mmol/kg/day = 2 x 24 = 48mmol
Thus, total requirement	= Deficit + Maintenance = 25 + 48 = 73mmol

If not taking oral fluids will need maintenance hydration containing 73mmol over the next 24 hours.
If taking diet, and hence maintenance electrolytes, needs 25mmol extra potassium over next 24 hours.

Gastro-oesophageal reflux

[19, 30, 64-74]

Gastro-oesophageal reflux (GOR) is a very common and probably under recognised problem in neurologically impaired children, perhaps around 50% (15-75%) in this group. The most common GOR associated symptoms are shown in bold type. The symptoms are particularly significant if multiple, and if during or after feeds.

Gastro-intestinal: **Food refusal**.
Vomiting (especially during/after feeds and supine at night).
Dysphagia/difficulty swallowing.
Weight loss/failure to thrive.
Haematemesis/melaena.

Respiratory: Troublesome secretions.
Aspiration pneumonia.
Recurrent RTIs/bronchitis.
Cough.
Wheezing.
Choking/gagging.

Other symptoms, especially with temporal relation to feeding:

Irritability (especially when supine).
Pain.
Hyperextensive posturing.
Sandifer's syndrome (neck extension and head rotation during/after meals in infant/young child, associated with iron deficiency anaemia and severe oesophagitis).

Non-drug treatments

- Adjust posture.
- Alter feeding regime from large bolus to frequent small volume, or if nasogastric/gastrostomy fed, overnight feeding/continuous feeding (sometime this may aggravate symptoms: try it and see).
- Check for overfeeding, especially if nasogastric/gastrostomy fed.
- Thicken feed with gum or starch. However, this may aggravate symptoms by osmotic effect.

Drug treatments

- Antacids, especially Gaviscon for its raft as well as antacid effects.
- Omeprazole reduces noxious effects of reflux via its actions as a proton pump inhibitor.
- Ranitidine can be used as second line, but can give problems with rebound nocturnal acid secretion.
- Prokinetic, for example Domperidone or Metoclopramide.

If, despite maximal medical therapy, vomiting, weight loss or distress continues then surgery needs to be considered. Fundoplication with or without pyloroplasty is effective in over 80% of cases, but has a high morbidity (26-59% post-operative complications, 6-70% get recurrent GOR and 5-15% need repeat surgery). If the child has severely compromised nutrition, inefficient feeding, NGT dependency or swallowing problems, then gastrostomy should be considered simultaneously.

Omeprazole
For children who cannot swallow tablets or capsules then the following can be tried:

- Open capsule and mix granules with acidic drink (orange or apple juice) and swallow without chewing.

- MUPS tablets can be dispersed in water, fruit juice or yogurt.

- For PEG and NG tubes the MUPS tablets can be dispersed in a large volume of water.

- For PEG and NG tubes the granules can be mixed with 10ml of sodium bicarbonate 8.4% and left to stand for 10 minutes until a turbid suspension is formed. The suspension is given immediately then flushed with water.

- For older children Lansoprazole fastabs dissolve very well in water and do not block the tubes as badly as Omeprazole.

Gastrostomy care

[75-88]

Gastrostomy tubes

A gastrostomy is a surgical opening through the abdomen into the stomach. This allows feeding directly into the stomach, bypassing the mouth and throat.

A gastrostomy may be inserted because a child or young person has difficulty eating and/or drinking. This may be due to neurological disorders or gastro-intestinal disorders. Difficulty in swallowing leading to an increased risk of aspiration may also require gastrostomy feeding.

Percutaneous endoscopy gastrostomy (PEG)

- A flexible polyurethane tube passed down the throat and in to the stomach. The end of the tube is brought out through a small incision in the abdomen to allow feeding.
- It can stay in place for about 18 months.
- It is held in place using a disc inside the stomach.

Malecot tube

- Flexible rubber tube inserted through an incision in the abdomen.
- Usually a temporary device for the first 6-8 weeks, then replaced by a balloon device.
- Held in place using wide, flat wings inside the stomach, but may need to be temporarily stitched to the skin.
- Must be secured with tape and the position of the tube tested prior to each feed.

Balloon device (tube or button)

- Two types available, gastrostomy tube or button.
- Tube stays in place for three months and the button for six months to a year.
- Both are held in stomach using a balloon filled with water.

Most of the children and young people have a MIC-KEY button. The external base holds the tube in place yet allows air circulation to the skin underneath. The bottom of the base should rest 3mm above the skin.

Liquids are delivered through the tube and into the stomach through the feed and medication port. This is covered by the attached feeding port cover when not in use.

An anti-reflux valve is located inside and towards the top of the feeding port. This helps prevent stomach contents leaking out of the tube. The use of the extension set will open the valve. The extension set is used for feeding and venting (air release).

It is important to keep the feeding port and anti-reflux valve clean. Dried milk/feed may lodge inside the recess and hold the valve open. To prevent this, flush thoroughly with enough water to clear all residue.

The button has a balloon inside the stomach which is inflated to hold the tube in place. This is filled with water. The balloon volume should be checked once a week.

The balloon holding the tube in place is inflated and deflated by inserting a leuer lock syringe into the balloon valve. It should only be used when checking the balloon volume or replacing the MIC-KEY. Never attempt to feed through the balloon valve. Ensure valve is kept clean.

Clean the MIC-KEY feeding tube daily. The tube and skin around the stoma site should be kept clean and dry. Check water volume in balloon once a week. Attach leuer lock syringe to balloon port and withdraw all the water, leaving the feeding tube in place. If there is less fluid than there should be, replace it with the correct amount. Distilled or sterile water is best but cooled boiled water can be used. Never fill balloon with air.

Rotate tube a full 360 degrees when carrying out daily tube care. This will prevent tube or balloon adhering to skin.

Always wash hands before touching tube. Inspect the skin around the stoma after feeding. It should be clean and dry. Observe stoma post-feed for gastric leakage. Clean around site using mild soap and warm water, rotate tube 360 degrees and clean again.

It is not necessary to use a dressing around stoma site but some families prefer to. Never allow a wet dressing to remain in contact with the skin.

Oral hygiene

- If a child has reduced or no oral feeds, plaque can build up on their teeth rapidly. Poor oral hygiene will cause soreness and pain.
- Teeth need to be cleaned twice daily and artificial saliva or mouthwash can be used where appropriate.

Problem solving

Stomach contents leak out around the tube

- Ensure that the balloon inside the stomach is filled by gently pulling on the tube and checking for resistance.
- Check how much the prescribed balloon fill volume is.
- Test the balloon by attaching a leuer slip syringe to the inflation valve. Withdraw the fluid from the balloon and note the volume in the syringe. If the amount is less than prescribed, refill the balloon with the prescribed amount of water, wait 10 to 20 minutes and repeat the procedure. If the prescribed volume of water is still in the balloon, try increasing the volume by 2ml at a time until the leak stops. The maximum fill volume is 10ml. Do not exceed this.
- Aspirate tube prior to feeding to remove excessive air from stomach:
  PEG- use 50ml syringe ensuring leuer port is closed.
  MIC-KEY- as above or use decompression tube provided with the kit.
- If child/young person is inactive encourage sitting upright if possible following feed or position on right side with head elevated to promote gastric emptying.
- Consider reducing rate of feed or giving smaller, more frequent feeds.
- Gastric contents will quickly cause excoriation and soreness. Protect the skin with water proofing product such as Cavilon while establishing and correcting cause.
- If leakage persists contact medical staff.

Leakage may be due to

Granulation tissue:

- Looks like a raised red lip or cauliflower type growth(s) around the stoma site.
- Produces a copious, sticky, mucous type discharge, often mistaken for infection.

Balloon leaks or ruptures:

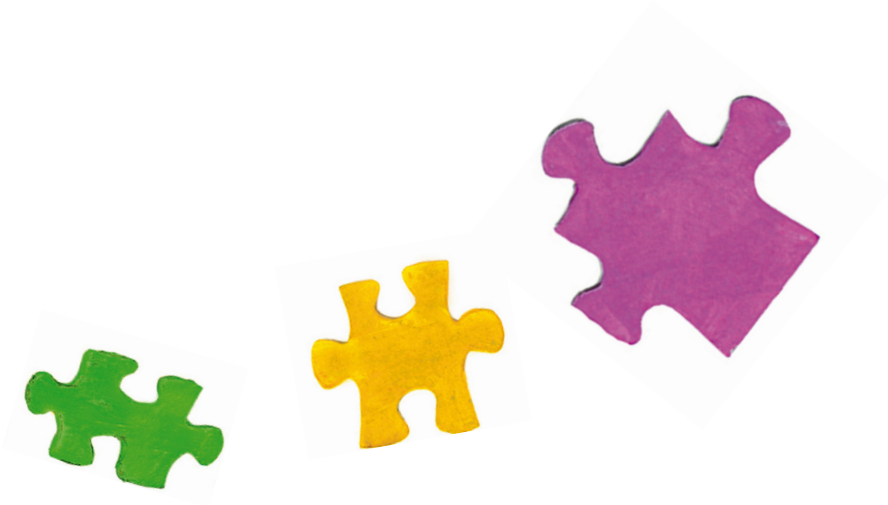
- A replacement MIC-KEY feeding tube should always be available. The life span of the balloon varies according to several factors. Medication, volume of water used to fill the balloon, gastric PH and tube care.

Tube blockage

- Flush the tube before and after each feed, before and after giving medication and every three to four hours if receiving continuous feeds.
- Small children and babies may require less flush and some children/young people will require minimal intake. It may therefore be necessary to be flexible with flushes.
- Medication should not be mixed with milk feeds.
- Medication should be in liquid form where possible. If tablets need to be used they should be crushed finely and well dispersed in water.
- Multiple medications must be given one at a time.
- Ideally the tube should be flushed between each medicine but this may not be possible due to the increased volume required to do this.
- Cola, soda water or pineapple juice can be used to remove persistent blockages.
- If blockage does persist, gently draw back on syringe and flush as before.
- Gently squeeze the tube between your fingers along its length to 'milk' the tubing.

Stoma and skin problems

- If a stoma is bleeding, seek help.
- Redness or soreness around the stoma may be the result of gastric leakage. Wash and dry the area frequently.
- Rotate the feeding tube 360 degrees during daily tube care.
- Check stoma site for signs of irritation, redness or swelling.



Hiccough

[89-94]

Hiccough is a common occurrence in normal individuals, and only becomes a symptom when it becomes troublesome, severe or intractable, which can occur in palliative care situations.

In terminal care the most common cause of hiccough is gastric distension. The first line of treatment is often a defoaming antiflatulent containing Simeticone (active dimeticone such as Asilone or Maalox Plus). If this fails to settle the hiccough a prokinetic drug such as Metoclopramide can be added to tighten the lower oesophageal sphincter and promote gastric emptying. Sometimes peppermint water is helpful, by relaxing the lower oesophageal sphincter to facilitate belching, but as this works in opposition to the action of Metoclopramide these two should not be given together.

Gastrointestinal reflux can sometimes cause hiccough, and this can be reduced by the use of prokinetics such as Metoclopramide, or by H2 antagonists or proton pump inhibitors.

Diaphragmatic irritation is another cause of hiccough seen in palliative care. Baclofen is seen as the drug of choice with its muscle relaxant properties.

There are also single case reports in adults for the use of Gabapentin, Nifedipine and Haloperidol supporting their potential benefit for intractable hiccough.

Stimulation of the pharynx may help with the management of hiccough, and this is the basis for how a lot of the traditional 'folk' remedies for hiccough may work. Such advice includes swallowing crushed ice, a cold key down the back of the neck, and drinking from the wrong side of the cup.

More medically based treatments that stimulate the pharynx include normal saline 2mls nebulized over five minutes, and oro-pharyngeal stimulation with an NG tube, both of which suggested a reduction in hiccough. A similar method is by massaging the junction between the hard and soft palate with a cotton bud. Forced traction of the tongue to stimulate a gag reflex is also thought to potentially work by pharyngeal stimulation.

Central suppression of the hiccough reflux can be achieved in several ways. Re-breathing air out of a paper bag and breath holding are both thought to inhibit processing of the hiccough reflex in the brain stem by elevating PaCO2.

Dopamine antagonists such as Metoclopramide may help by both their central action and if there is associated gastric distension.

Other drugs to centrally suppress hiccough include Haloperidol, or Chlorpromazine. GABA agonists such as Sodium Valproate 200-500mg daily are also potentially effective by central suppression.

Potential biochemical causes of hiccough should be sought and corrected appropriately if possible, including hyponatraemia, hypocalcaemia (for example, after bisphosphonate treatment), and in renal failure.

If hiccoughs persist, the possibility of infection or a brain stem lesion/intra-cranial lesion should be considered.

In summary, if hiccoughs become a persistent and distressing symptom, effort should be made to relieve treatable causes such as gastric distension and reflux or correct biochemical causes, whilst considering infection and neurological causes.

Simple 'folk' remedies and attempts at other methods of pharyngeal stimulation should then be tried, followed by specific drug treatment if the above remedies have proved ineffective.

HIV and AIDS

[95-111]

Introduction

AIDS is by far the biggest the main non-acute cause of childhood death in the world, bringing a huge physical, psychological and social burden to infected children and their families. Even in the era of anti-retroviral therapy (ARTs), palliative care remains a crucial part of HIV/AIDS care, because treatment sometimes fails, and more often is not available or affordable. Palliative care also has an important role to play in the relief of distressing symptoms (some which may be as a result of side effects to ARVs) and immune reconstitution illnesses.

It is important to realise that HIV/AIDS is a multi-system, multi-organ disease; not just a disease of the immune system. Fortunately, most symptoms caused by HIV/AIDS can be managed successfully, using the same principles as with symptoms due to other pathologies. It is not necessary to be an HIV/AIDS expert to provide good children's palliative care, but you do need to know about side effects and interactions of ARVs, which can be significant in palliative care settings.

Facts and figures

Most infections in African children are caused by mother-to-child-transmission (MTCT). These result from a variety of factors: the high HIV infection rate in women of childbearing age, the high birth rates/fertility rates, and low uptake and coverage of PMTCT (preventing mother to child transmission).

There are approximately 2.1 million children under the age of 15 years living with HIV worldwide, at least 90% of these live in Africa. UNAIDS estimated that in 2003 there were 630,000 new paediatric HIV infections. It is currently estimated that in developing countries 1,600 children are infected daily by their HIV-infected mothers and in Africa, more than 400,000 children under 15 died of AIDS in 2003 alone. In 2004 there were over 13 million orphans worldwide who have lost one or both parents from AIDS and this is projected to rise to 25 million by 2010.

The impact of AIDS on families and communities also affects non-orphaned children. With the deepening poverty that results from sick and dying parents, children are the first to suffer. They suffer mental, psychological, and social distress and increasing material hardships. The children may be the only caregivers for their sick or dying parents/guardians, may drop out of or interrupt school, and are at risk of discrimination and abuse, both physical and sexual. Children with HIV/AIDS in resource-constrained countries experience high rates of morbidity and mortality relatively early in their lives, with up to 75% mortality by five years of age.

Improvements in basic HIV care, and more recently antiretroviral therapy, have improved survival among HIV-infected children in developed countries. On the other hand, HIV-infected children in resource-limited settings continue to have little access to even basic HIV and supportive care. Globally, but particularly in resource-constrained settings, the terminal care needs and services for children with life-threatening illnesses are poorly understood and poorly developed.

Relevant information about HIV and its pathology

HIV attacks the immune system of the individual leading to decline in CD4 cell counts. CD4 cells are a group of T-lymphocytes vital in fighting infections and immunosurveillance. HIV infection may be asymptomatic for a number of years whilst the virus insidiously damages the immune system. As the level of immunity falls children become susceptible to specific types of infections.

In children immunosuppression is defined according to age group since children usually have higher cell counts in all blood lines than adults. In children in the developed world, the median time from the onset of severe immunosuppression to an AIDS defining illness is 12-18 months in children not receiving antiretroviral drugs. HIV-infected infants frequently present with clinical symptoms in the first year of life, and by one year of age an estimated one-third of infected infants will have died, and about half by two years of age. There is thus a critical need to provide antiretroviral therapy (ART) for infants and children who become infected.

It is important to look for opportunistic infections as a cause of pain and symptoms in HIV positive children. Treating them may enable a patient to stop analgesics and improve their quality of life greatly, even returning to school and normal activities. Many of these infections (for example, candida, toxoplasmosis, tuberculosis, and pneumonia) can be treated with inexpensive medications, although some treatments are more expensive, such as treatment of cryptococcal meningitis.

Pathophysiology of HIV/AIDS

It is important to understand that the HIV virus causes pathology in two ways:

1. By suppressing the immune system.

2. By directly infecting and damaging organs and systems.

Organs and systems that can be directly infected and damaged include:

- **The central nervous system:** The HIV virus damages the central and peripheral nervous system causing HIV encephalopathy and both central and peripheral neuropathies. These can cause a range of problems from subtle developmental and cognitive delay through to global neuro-degeneration with severe disability and ultimately death. Other less common problems include vascular myelopathy of the spinal cord and a sensory polyneuropathy affecting the hands and feet which can cause severe pain.

- **The gastrointestinal system:** HIV enteropathy is used to describe a syndrome of diarrhoea, mal-absorption and weight loss for which no other explanation is found. Villous atrophy is a common histological finding and small bowel permeability is increased.

- **The heart:** Causing HIV related cardiomyopathy.

- **The kidneys:** Causing HIV related nephropathy.

- **The respiratory system:** Causing lymphocytic interstitial pneumonitis (LIP) and debilitating chronic lung disease often complicated by cor pulmonale.

Psychosocial issues in HIV/AIDS

Children with HIV/AIDS are liable to suffer with all of the psychosocial problems of children with any other life-limiting condition, but there are additional issues that HIV-infected children face because of the nature of the HIV virus: its infectivity, its long latent period, its tendency to decimate whole families, and the fact that is still highly stigmatizing.

Symptoms in AIDS

Incidence of different symptoms

HIV-related conditions in children that are observed to cause pain particularly in children include:

- Meningitis and sinusitis (headaches).
- Pneumonia and chest pain.
- Otitis media.
- Shingles.
- Cellulitis and abscesses.
- Severe candida dermatitis.
- Oral lesions such as herpes, acute necrotizing gingivitis and severe dental caries.
- Intestinal infections, such as mycobacterium avium intracellulare (MAI) and cryptosporidium.
- Hepatosplenomegaly.
- Oral and esophageal candidiasis.
- Disseminated Kaposi's Sarcoma.
- Dystonic pain secondary to encephalopathy.

Pain

Pain in AIDS can be caused by:

1. The effects of specific opportunistic infections (e.g. headache with cryptococcal meningitis, visceral abdominal pain with disseminated Mycobacterium Avium complex).

2. The effects of HIV itself or the body's immune response to it (e.g. distal sensory polyneuropathy, HIV-related myelopathy).

3. The effects of medications used to treat HIV disease (for example, dideoxynucleoside-related peripheral neuropathy, zidovudine-related headache, protease inhibitor-related gastrointestinal distress).

4. The non-specific effects of chronic debilitating illness.

5. Procedural pain due to repeated procedures such as venesection, tube feeding, lumbar punctures and so on.

AIDS pain syndromes and most common pain diagnoses in AIDS

It should be noted that in some instances the incidence and/or prevalence of pain may have actually increased with the advent of ART (anti-retroviral therapy). As is often the case with AIDS, the irony of decreased mortality rates is that by surviving longer some children may thus be vulnerable to new complications and pain, as in the observed increasing prevalence of peripheral neuropathy which occurred with longer survival according to the Multi-Centre AIDS Cohort Study.

Despite the high prevalence of pain in AIDS, several studies have also demonstrated that pain in children with AIDS is likely to be under-diagnosed and under-treated. This failure to diagnose and treat pain may reflect both the general under-recognition of pain by most physicians and/or the additional reluctance to consider seriously any self-report of pain in children.

In addition to pain, children with AIDS have been found to have a high prevalence of other symptoms, particularly but not exclusively in the advanced stages of the disease. Moreover, one recent study suggested that physicians frequently also fail to identify and under-treat common non-pain symptoms reported by children with AIDS. Symptoms include a mixture of physical and psychological conditions, such as fatigue, anorexia, weight loss, depression, agitation and anxiety, nausea and vomiting, diarrhoea, cough, dyspnoea, fever, sweats and pruritus.

Other symptoms

The prevalence of the most common ten symptoms for children with HIV/AIDS in Africa has been reported as follows:

- Fever, sweats, or chills (51%)
- Diarrhoea (51%)
- Nausea or anorexia (50%)
- Numbness, tingling, or pain in hands/feet (49%)
- Headache (39%)
- Weight loss (37%)
- Vaginal discharge, pain, or irritation (36%)
- Sinus infection or pain (35%)
- Visual problems (32%)
- Cough or dyspnoea (30%)

Management of symptoms in children with AIDS

Individual symptom management advice is covered more fully in the relevant chapters of this book. However, to demonstrate the overlap between disease specific treatment and palliative treatment that is a feature of AIDS, the following table will give an overview.

Practical management of symptoms in HIV/AIDS

Symptom	Causes	Disease specific therapy	Palliative therapy
Fatigue, weight loss, anorexia	HIV infection Opportunistic infections Malignancy Anaemia	ART. Treat infections. Transfusions. Nutritional support.	Explanation and reassurance. Lifestyle modifications. Steroids.
Pain	See above	ART. Treat specific diseases using antibacterials/antifungals/antivirals.	Treat underlying cause. Remember non-pharmacological approaches. Consider ART. Use WHO pain ladder.
Nausea and vomiting	Drugs. Gastrointestinal infections.	Stop drugs. Treat infections using antifungals, antiparasitics, antivirals and antibiotics.	Antiemetics. Prokinetic. H2 blockers (e.g. Ranitidine) or PPI (e.g. Omeprazole). Small frequent feeds, fluids between meals, offer cold foods, eat before taking medications, dry foods, avoid sweet, fatty salty, or spicy foods.
Dysphagia	Candidal Oesophagitis	Antifungals	If severe, reduce inflammation by giving steroids initially (may need IV initially). The ideal treatment is Fluconazole which may need to be given intravenously. If this is not available, we have had some success using Clotrimazole pessaries -500mgs to be sucked daily for five days. Use analgesic ladder for pain.
Sore mouth	Herpes simplex Aphthous Ulcers Thrush Gingivitis	Acyclovir	Keep mouth clean; clean with soft cloth or gauze in clean salt water. Give clear water after each feed. Avoid acidic drinks and hot food. Give sour milk or porridge, soft and mashed. Ice cubes may help; ice cream or yoghurt.
Chronic diarrhoea	Infections (gastroenteritis, parasites, MAC, cryptosporidium, CMV), malabsorption, malignancies, drug-related.	Antibiotics/antivirals/antiparasitics	Rehydration (Bowie's regimen), Vitamin A and Zinc. Diet modification (e.g. yoghurt rather than fresh milk if lactose intolerance is a possibility), micronutrient supplements. Kaolin (cosmetic only) or Bismuth. Oral morphine can alleviate intractable diarrhoea as can Loperamide if available.
Constipation	Dehydration Tumours Drugs	Rehydrate. Treat tumours with DXT or chemo if appropriate. Adjust medication.	Activity. Diet modification. Laxatives.
Ano-genital ulceration	Commonly due to herpes simplex virus. Candidiasis.	Herpes: Acylovir (oral) or an emulsion mixture of Nystatin 5 ml, metronidazole powder 400mgs and Acyclovir 1 tablet. Antifungals.	Crush a tablet of Prednisolone and apply the powder to the affected part.

Breathlessness	Pneumonia. Anaemia. Tumour. Effusion. Weakened respiratory muscles.	Treat cause. Antibiotics. Iron or transfusion if severe. Treatment of tumour (if appropriate). Drainage (if appropriate).	Fan and maximize airflow. Counselling. Distraction. Relaxation. Guided imagery. Opioids. Benzodiazepines.
Persistent cough	Infections LIP Bronchiectasis TB Effusion Tumour	Antibiotics. PCP treatment. Anti-TB treatment. Treatment of tumour (if appropriate). Drainage.	Nebulisation with physiotherapy. Suppressant (e.g. low-dose morphine). Physiotherapy. Humidification. Steroids (LIP).
Severe dermatitis	Seborrhoea dermatitis Infestations Folliculitis Fungal infection Hypersensitivity Renal and liver disease	Antibacterials/antifungal/antiparasitics. Hydration. Steroids.	Emollients. Antihistamines. Aantiseptics. Topical steroids. Antimuscarinic antidepressants (e.g. Amitriptyline). Anxiolytics. Keep nails short to minimize trauma and secondary infection from scratching.
Shingles and post-herpetic neuralgia	Herpes Zoster	Aciclovir if caught early	Liquid from frangipani tree when applied to the vesicles (before they break) causes paralysis of nerves for up to eight hours. Break off a small branch and collect the white fluid into a clean jar. Paint this onto the area. (This fluid can be kept up to 24 hours).[18] Post herpetic neuralgia: use Amitriptyline, Valproate, Phenytoin or Carbamazepine for shooting pain (but beware interactions with ARTs). Add Morphine if necessary.
Convulsions	Infections and infestations Encephalopathy Malignancies PMLE		Diazepam or Phenobarbitone or paraldehyde for acute control, then convert to longer term therapy. Beware interactions between anticonvulsants and ART's.
Metabolic disorders	Anticonvulsants Dextrose Mannitol Steroids		Rehydrate. Ensure good oxygenation. Give high energy, low protein feeds until disorder resolves. Treat individual cause.
Fevers, sweats	HIV MAC CMV Lymphoma	HAART. Azithromycin. Aciclovir. Chemotherapy.	NSAIDS. Steroids. Hyoscine. Cimetidine.
Pressure sores	Malnutrition Reduced mobility	Nutrition. Mobilisation.	Wound dressing: metronidazole powder to control odour, honey applications on clean, debridement if necessary.
Delirium, agitation	Electrolytes disturbances Toxoplasmosis Cryptococcal meningitis IC sepsis	Correct imbalances and rehydrate. Antifungals and antibiotics.	Assist orientation. Haloperidol or Promazine. Benzodiazepines.
Depression	Reactive Chronic illness	Play therapy. Counselling. Distraction. (Role of antidepressants in children still uncertain)	Counselling. Distraction.

18 The frangipani tree is not native in Europe and may not be available. The plant is native to Central and South America, South East Asia, the Caribbean and East Africa.

Antiretroviral therapy in children's palliative care

A significant proportion of children with HIV/AIDS receiving children's palliative care will be on ARTs, usually including nucleoside reverse transcriptase inhibitors (NRTI), non-reverse transcriptase inhibitors (NNRTI) and a few on protease inhibitors (PI). It is very important to understand that significant drug interactions can occur in children receiving palliative care drugs who are also on ARTs. Furthermore most of these medications may need to be administered in the presence of other co-morbid conditions such as hepatitis, pancreatitis, gastritis, hypertriglyceridaemia, hyperglycaemia, lipodystrophies, HIV-associated nephropathies and opportunistic infections. These can increase the risk of and the effects of interactions and adverse effects of drugs.

It is beyond the boundaries of this book to deal with the whole pharmacology of ARTs. If you are regularly prescribing and managing ARTs, or of you do not have ready access to advice and support from professional ART providers, you should familiarise yourself with the relevant pharmacology using other more detailed sources. The aim of this chapter is to highlight at least the major risks.

The key system to understand is the cytochrome P450 (CYP) enzyme system. This group of enzymes is largely located in the liver, but also in the kidneys, lungs, brain, small intestine and placenta. The CYP system is responsible for the metabolism of almost all clinically useful medications, most importantly the antiretroviral agents (PIs and NNRTIs), several drugs used in the management of opportunistic infections in advancing HIV disease, many of the newer serotonin-specific reuptake inhibitors (SSRIs) and other psychotropic agents, endogenous substances such as steroids and prostaglandins, environmental toxins, anti-malarial and dietary components.

The primary role of the CYP system is to make the drugs more water-soluble and less fat-soluble, so that biliary excretion of the drugs can take place. As a result, these enzymes can affect the amount of active drug in the body at any given time. Such changes can be positive, enhancing efficacy, or negative, worsening toxicity and adverse events.

Recognising significant interactions and adverse effects

Any child with seemingly exaggerated toxicities on usual doses of medications or manifesting treatment failure in the absence of factors such as resistance or poor adherence/compliance should be considered to be suffering from an unidentified drug-drug interaction until proven otherwise. In such cases, careful review of the child's medication profile is necessary. Fortunately, the majority of drug-drug interactions are minor in nature and do not require extensive changes to the child's drug regimen. However, the minority of drug interactions that can be clinically important can reduce the effectiveness of both HIV/AIDS treatment and palliative care treatment, and so need to be addressed.

Common effects of children's palliative care drugs on ARTs

Certain drugs commonly used in children's palliative care can induce or inhibit the CYP system. Those that induce CYP can reduce the amount of available ARTs in the system, thereby making treatment failure more likely. Those that inhibit CYP can increase the amount of available ARTs in the system, thereby making ART toxicity more likely.

Known CYP Inducers	Known CYP Inhibitors
Carbamazepine (Tegretol)	Ketoconazole
Rifampin (Rifadin)	Itraconazole
Phenobarbital	Erythromycin
Phenytoin	Fluoxetine
Prednisolone	Diltiazem
Cigarette smoke	Verapamil
Omeprazole	Clarithromycin
Isoniazid	Omeprazole
	Ciprofloxacin
	Fluconazole
	Metronidazole
	Trimethoprim/Sulfamethoxazole (Septrin)
	Haloperidol
	Cimetidine

Common effects of ART's on children's palliative care drugs

Some PI's and NRTIs can induce or inhibit the CYP, thereby increasing or reducing the effects of certain drugs commonly used in children's palliative care. Different PI's and NRTI's have different effects on the CYP system; some are more powerful inducers or inhibitors than others. The most potent inhibitor is Ritonavir. Where the child is taking CYP inducers or inhibitors, you may find you need to use different starting and continuation doses than would otherwise be the case. As a general rule, drugs that inhibit the CYP system cause the most dangerous interactions as they increase the level of toxic drugs thereby making dangerous toxic effects more likely. Some of these interactions are potentially very harmful. These are outlined below.

Highest risk drugs when used with CYP inhibitors

- **Tricyclic antidepressants (e.g. Amitriptyline):** risk of prolonged QT interval and sudden cardiac deaths.
- **Macrolides (for example, Erythromycin):** risk of prolonged QT interval and sudden cardiac deaths.
- **Newer antihistamines (e.g. Terfenadine):** risk of prolonged QT interval and sudden cardiac deaths.
- **Cisapride:** risk of prolonged QT interval and sudden infant death syndrome.
- **Quinine and Chloroquine:** risk of prolonged QT interval and sudden cardiac deaths.
- **Chloral Hydrate:** risk of prolonged sedation and respiratory depression.
- **Benzodiazepines:** risk of prolonged sedation and respiratory depression.
- **Methadone:** risk of prolonged sedation and respiratory depression.
- **Rifabutin (Mycobutin):** Ritonavir increases the risk of rifabutin-induced hematological toxicity by decreasing its metabolism.
- **Clotrimoxazole/Sulfamethoxazole (Septrin):** risk of increase in allergic reactions, especially rash.
- **Beta blockers:** risk of significant falls in blood pressure and heart rate.
- **Haloperidol:** risk of increased dystonic side effects and drowsiness.

Counselling children and families about potential cardiac interactions

While children are generally less prone to cardiotoxicity than adults, this is not always the case, particularly where there are co-morbid cardiac conditions. All children using these drug combinations should be counselled to immediately report tachycardia, light-headedness, palpitations, vomiting or diarrhoea and avoid use of street drugs, substances of abuse, or excessive use of alcohol.

Ethics and communication

Fuller discussion of ethics can be found in this book. However, there are particular issues that apply in children's palliative care in children with HIV/AIDS. These arise partly because ARTs are so effective, even in children who are apparently moribund (the so-called 'Lazarus effect') and partly because ARTs can be quite toxic, burdensome and expensive. Common dilemmas include:

- **Balancing risks versus harms at the end of life:** Should a child with very advanced HIV neuropathy causing global neurological and functional loss be given ARTs, thereby potentially extending lifespan when the quality of life could be argued to be overly burdensome to the child?
- **Benefits versus harms of treatment:** Should we treat severe side-effects of ARTs with more drugs, such as anti-emetic therapy for protease inhibitor-induced nausea and vomiting or alternatively to stop/change the ARTs?

- **Withdrawing life-sustaining treatment:** Should we withdraw drugs such as PCP prophylaxis or ARTs when a child is clearly at the end of life?

- **Justice:** Should life-sustaining treatments such as ARTs be limited either to children whose families can afford them or, where ARTs are available, on a rationing system?

Prognostication

With the advent of ART, prognostication in HIV/AIDS has become extremely unreliable, as children apparently on death's door can make dramatic recoveries. It requires a very good understanding of both the evidence and the specifics of the individual child (his or her nature, history, investigations, previous management and so on). Even then, prognostication is little more than educated guesswork, but the guess is often crucial to a decision which literally has life and death consequences. To help you, here are some indicators of a poor prognosis in HIV/AIDS.

Laboratory markers

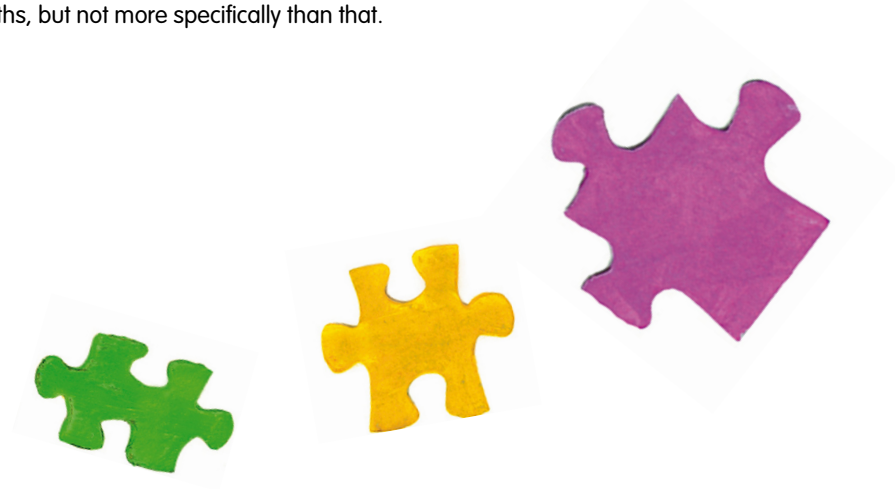
CD4 + T-lymphocyte count < 25cells/mm^3
Cd4 < 15%
Serum albumin < 2.5gm/dl

Clinical conditions

- CNS lymphoma
- PML
- Cryptosporidiosis
- Severe wasting
- Visceral Kaposi's sarcoma
- Advanced AIDS dementia (more in adults)
- Toxoplasmosis
- Severe cardiomyopathy
- Chronic severe diarrhoea
- Life-threatening malignancies
- Advanced end-organ failure (for example, liver failure, congestive heart failure, COPD, renal failure, chronic lung disease).

Note: All of these factors may potentially be over-ridden in the setting of effective antiretroviral therapy.

Ultimately, it is almost certain that you will be called upon by a child's family to give your opinion as to the child's likely prognosis, because it is very stressful and exhausting not to know when death is going to occur. This stress and exhaustion can be complicated by guilt and anxiety triggered by wishing that everything could be all over with. In the author's experience, as long as you explain that you cannot be certain, it is usually possible to talk in terms of hours, days, weeks or months, but not more specifically than that.



Managing opportunistic infections in children with HIV/AIDS

Arguably, this section does not belong in a book on palliative care. However, opportunistic infections (OI's) are a source of common and highly distressing symptoms and so should be treated as part of a palliative approach.

Symptom	Treatment
Bacterial Pneumonia (non severe)	Follow national or IMCI guidelines. If no guidelines: Oral Amoxycillin or Penicillin (10y 125mg tds, >10y 250-500mg tds) Or Cotrimoxazole (<5month 120mg bd, 6m-5y 240mg bd, 6-12y 480mg bd, >12y 960mg bd) Plus Paracetamol 15mg/kg/dose qds or Ibuprofen If recurrent (>3x/y) investigate for TB, foreign body, or chronic lung disease.
Severe Pneumonia	Admit if possible. **Supportive Care:** Supplemental oxygen Correct severe anaemia (Hb <5g/dL) by transfusion Oral or IV hydration Monitor fluid input/output Analgesic/antipyretic Vitamin A supplementation **Specific Therapy:** Unknown organism: Amoxicillin 50-100mg/kg/day IV divided doses or third generation Cephalosporin (for example, Ceftriaxone 100mg/kg IV or IM once a day) or Ampicillin *plus* Cloxacillin *plus* Gentamicin. If <1 year old: consider PCP (see below). If staphylococcal skin lesions or bullae on CXR or post measles, or with poor response to first line add Cloxacillin or Vancomycin. If repeated pneumonia, poor response, bronchiectasis, or chronic lung disease; suspect gram negatives and add Gentamicin or Ceftazidime.
Pneumocystis Pneumonia Major cause of severe pneumonia (15-30%) and death (30-50%) in HIV-infected infants, peaking at 3 to 6 months of age	*Pneumocystis carinii* pneumonia (PCP): If PCP is suspected, continue to treat for bacterial pneumonia, but also treat for PCP: **Supportive Management:** See section on cough and dyspnoea. Hydration Vitamin A supplementation Correct severe anaemia by transfusion Oxygen Prednisone at 2mg/kg/day for 7-14 days. **Specific Care:** High dose Cotrimoxazole 20mg/kg Trimethoprim/day. (OR 80 mg/kg/day of Sulphamesoxazole) tds for 21 days.
Tuberculosis	NB Treatment for TB should be started two months (two weeks to one month) prior to starting ART to avoid the immune reactivation syndrome. Treat as recommended by national guidelines. Take care with possible interactions between antiretroviral, antifungal, and antituberculous drugs.
Lymphocytic Interstitial Pneumonitis	Oxygen Pulsed steroid (2mg/kg for seven days, tailed to 5mg/day over a month. Bronchodilators (e.g. nebulised salbutamol 2.5-5mg four hourly). Start ART if available. Physiotherapy Treat associated cor pulmonale with diuretics (for example, Furosemide) and potassium supplementation.

Scabies	Children <1yr 25% benzyl benzoate for 12 hours or gamma benzene hexachloride. 2.5% sulphur ointment three times daily for three days. Screen and treat other household contacts where appropriate. Wash and iron bedding and clothing or hang it out in the sun.
Ringworm	Whitfield's ointment (benzoic acid with salicylic acid). 2% miconazole cream: twice daily for two to five weeks. For scalp lesions give oral Ketoconazole if available. If not use Griseofulvin 10mg/kg/day for eight weeks, but beware side effects.
Herpes zoster	Analgesia (for example, Paracetamol or Ibuprofen and add adjuvant, for example Carbamazepine or Amitriptyline if necessary). IV acyclovir 30mg/kg/day in three doses every eight hours for seven days. Prevention in exposed child: varicella-zoster immune globulin (VZIG) 125U per 10kg (max 625U) within 48-96 hours of exposure.
Impetigo Treatment	Hygiene 10% iodine solution 3x daily or zinc oxide cream. If pyrexial or resistant: Flucloxacillin or Erythromycin for 7-10 days.
Chickenpox	Topical calamine lotion. If available; all HIV infected children should receive acyclovir 20mg/kg PO four or five times daily for 21 days. Where supplies are limited, it should be used for disseminated chicken pox with complications.
Herpes simplex	Local antiseptic (e.g. gentian violet) Analgesia: Paracetamol or Ibuprofen and add adjuvant for example, Amitriptyline if necessary. If disseminated: acyclovir 5mg/kg intravenously three times a day or 200-400mg orally five times a day, for seven to ten days.
Oral candidiasis (present in 75% of patients)	Nystatin drops 5ml qds Nystatin lozenges qds Fluconazole (loading dose 6mg/kg then 3mg/kg/24h) Amphotericin (0.3mg/kg/24h)
Recurrent herpes simplex	Acyclovir
Bacterial meningitis	1st line: chloramphenicol IV 50-100mg/kg/day IV in 24 divided doses or third generation Cephalosporin (e.g. Ceftriaxone 100 mg/kg IV or IM once a day).
Cryptococcal meningitis	Treat pain using WHO ladder. Amphotericin B 0.7-1mg/kg/day IV for two weeks followed by fluconazole 3-6 mg/kg/day for eight weeks or until CSF is sterile Fluconazole requires an induction dose especially in children (10-12mg/kg PO or IV in two divided doses). Maintain prophylaxis with Fluconazole unless the child is on ART and with sustained immune recovery (3-6mg/kg/day PO or IV).
Tuberculous meningitis	12 months of Rifampicin and Isoniazid plus Pyrazinamide and a fourth drug (Ethambutol, Ethionamide, or Streptomycin) for at the first two month. Corticosteroids as adjunctive therapy in more serious cases.
CMV infection	IV ganciclovir 10mg/kg per day in two divided doses for two to three weeks. Foscarnet 180mg/kg/day in three divided doses for 14-21 days may be used when there is sight threatening CMV retinitis.
Cryptococcus	Induction with Amphotericin B (0.7-1.0 mg/kg/day) for two weeks followed by fluconazole 400mg/day for a minimum of 10 weeks, then 200mg/kg maintenance therapy.
Toxoplasmosis	Pyrimethamine loading dose 2mg/kg/day (max 50mg) for two days then maintenance, 1mg/kg/day (max 25mg) plus sulphadiazine 50mg/kg every 12 hours/folinic acid 5-20mg three times weekly. Treat until one to two weeks beyond resolution of signs and symptoms.

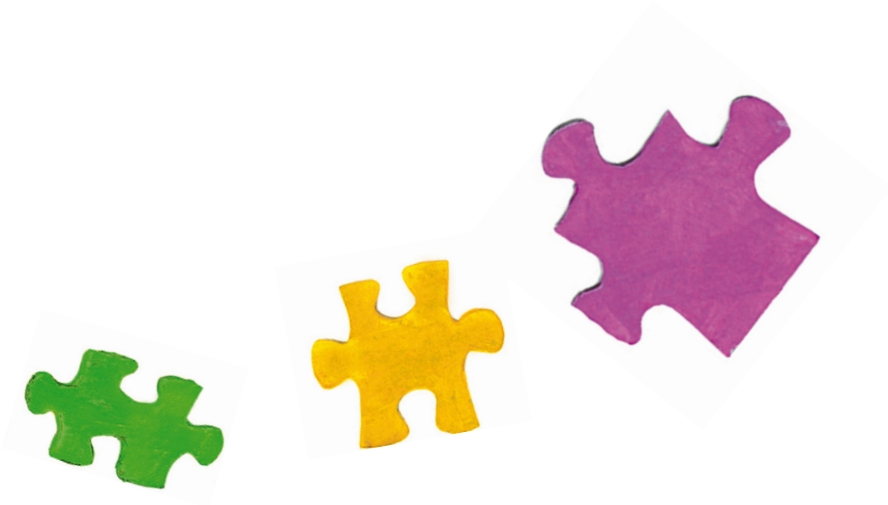
Infections

Any infection causing symptoms and affecting quality of life should be treated. Antibiotic resistance and allergies are a common problem. In the palliative care setting rules may be bent; hence antibiotics not normally recommended for children, e.g. tetracycline could be given. Other antibiotics not normally available in liquid form for children can be given. Hospital pharmacies and traditional retail pharmacies can be very helpful in providing such information. Remember to record in the notes and discuss with the parents what you are doing to protect yourselves medico-legally.

Pneumonia is sometimes called the 'old man's friend'. It is also the most common cause of the terminal event in many children with life-threatening conditions. The use of antibiotics can present the parents and care team with an ethical dilemma. It is best to sit down and discuss the pros and cons of treatment together. Oral treatment in the terminal phase does not extend the life expectancy of the child but can allow the parents to feel that they tried their best to the last. Most parents will accept that intravenous antibiotics are normally inappropriate at this stage.

It is worth remembering that while we cannot insist on treating an infection if the parents refuse, neither are we forced to give treatment that we consider is inappropriate. This type of dilemma is best resolved by negotiation with parents and, where appropriate, the child.

Sometimes antibiotics are necessary, e.g. pain relief in acute ear infections or severe tonsillitis, even when the parents of the child have decided on no more active treatment.



Mouthcare

[4, 9, 42, 112-117]

This is an overlooked aspect of palliative care but correct management can easily enhance the quality of life for a dying child. As in all cases take a good history and look inside the mouth. Establishing the cause of the mouth problem helps to direct the correct treatment.

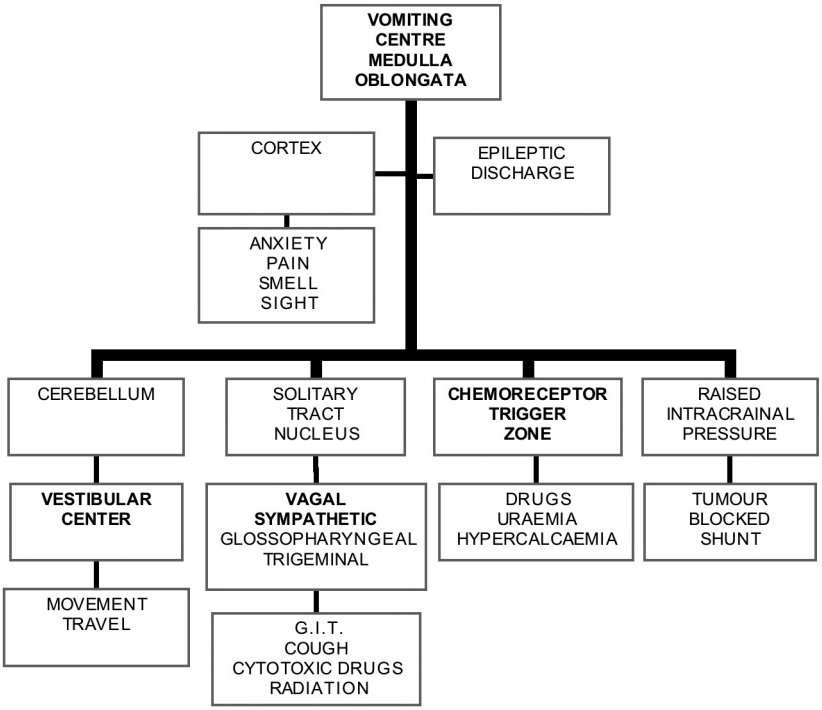
Causes

- Oral candidiasis
- Poor oral hygiene
- Dry mouth from
  a) Mouth breathing
  b) Oxygen that has not been humidified
  c) Drugs i.e. Morphine, Hyoscine or Amitriptyline
  d) Radiotherapy
- Mouth ulcer
  a) Traumatic
  b) Aphthous
- Bleeding gums from
  a) Haematological cancers
  b) Liver disease
  c) Clotting disorders
- Oral hygiene can be maintained by careful and gentle cleaning of teeth and gums. This is a task that the parents may like to carry out as part of the child's daily routine.
- Pink sponges dipped in mouthwash can be applied to the gums and teeth to keep the mouth moist and cream applied to the lips to prevent dryness and cracking. This attention to mouth care will go a long way to maintaining hygiene, preventing some of the complications and aiding the child's comfort.
- Oral thrush can be cleared using various anti-fungal agents. Nystatin drops are really not very effective in these cases and Miconazole oral gel applied gently around the mouth is better. Fluconazole, which is a once daily oral anti-candidal agent, is often more effective than topical agents.
- Artificial saliva, e.g. Glandosane comes in various forms and the spray is particularly effective. KY Jelly is very effective for dry mouths and is well tolerated.
- Community dentists can advise regarding traumatic ulcers.
- Aphthous ulcers can be treated with Adcortyl in Orabase applied locally.
- Bleeding gums can be helped with tranexamic acid mouthwashes or haemostatic agents such as Gelfoam or Gelfilm. Bleeding from blood malignancies may require platelet transfusions even in the palliative setting. Oral Ethamsylate decreases capillary bleeding and has been used in adults at a dose of 500mg qds in a palliative care setting.

Nausea and vomiting

[7, 117-127]

The management of nausea and vomiting highlights the importance of understanding the cause of a symptom to determine the appropriate therapeutic course.



Whilst nausea and vomiting can be effectively managed with medication, common sense principles must not be forgotten:

- Identify and manage the correctable causes e.g. pain, infection, drugs, biochemical, etc.
- Certain smells may antagonise the nausea.
- Leftover food must be removed immediately.
- Staff and parents advised against the use of strong perfumes.
- Strong odours avoided.
- Meals kept small but often, if the child's appetite allows.

Once we have an understanding of the cause we can then target anti-emetics according to their mode of action. It may be necessary to use a number of different anti-emetics, and logic dictates that we use medications from different groups. Many of the drugs used will overlap in their site of action.

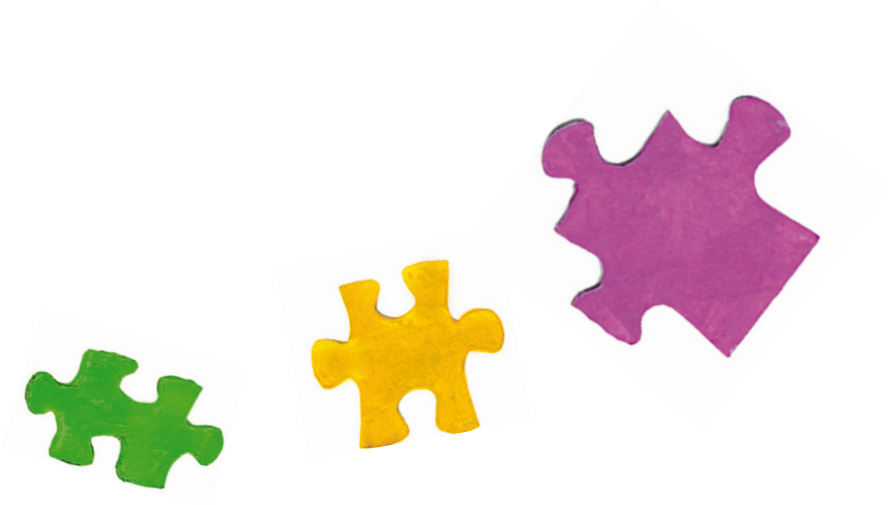
There is no evidence to support any particular dosage of Dexamethasone when used as an anti-emetic. Another rule of thumb is 8mg/m^2/day. Remember this is not for long-term use because of side effects and altered body image.

Octreotide has been used in adults for vomiting secondary to obstruction but its benefits in children is unknown.

If you need to use more than one anti-emetic then make sure they are complementary e.g. Cyclizine and Haloperidol and not antagonist e.g. Cyclizine and Domperidone.

Site of action of anti-emetic drugs

Drug	Site of action	Notes
Haloperidol	Chemoreceptor trigger zone.	Anxiolytic benefits.
Thioridazine	Chemoreceptor trigger zone.	May have some benefits in epilepsy, although generally Phenothiazine can exacerbate epilepsy.
Chlorpromazine	Chemoreceptor trigger zone.	Sedation benefits. Contra-indicated in epilepsy.
Prochlorperazine	Vestibular centre and chemoreceptor trigger zone.	Side effects in children, limit use.
Ondansetron	Chemoreceptor trigger zone. Medulla oblongata. Also may work at vagal level.	Side effects of flushing, headaches and constipation. More effective combined with corticosteroids (dexamethasone). Onset of action 30 minutes, peak one to two hours, duration 12 hours.
Cyclizine	Medulla oblongata.	Commonly used and highly effective. Sedating antihistamine with antimuscarinic properties. May crystallise with Diamorphine in s/c infusion. Side effects drowsiness, dry mouth, blurred vision, urinary retention. Onset 30 minutess, peak two hours, duration four to six hours.
Levomepromazine	Effects at all levels.	Phenothiazine. Broad spectrum. Use when there is failure of specific anti-emetic. Stable with Diamorphine in s.c. infusion. Side effects sedative and postural hypotension.
Domperidone	Vagal sympathetic.	Prokinetic in upper gut. Good for dysmotility in neurological conditions.
Metoclopramide	Vagal sympathetic.	Crosses blood brain barrier. Causes extrapyramidal side effects in children limit use.
Dexamethasone	Intracranial pressure.	Use in short bursts due to side effects. Reduces permeability of chemoreceptor trigger zone and blood brain barrier to emetogenic substances and reduce GABA in brainstem.



Neonatal palliative care

[128-132]

Introduction

There have been many advances both in antenatal diagnosis and neonatal intensive care over recent times. However there still remain a number of babies where full intensive care is not indicated, or is futile.

There are a number of common reasons that neonatal intensive care may be withheld or withdrawn after discussion with the family including:

- Genetic problems with a limited life expectancy – for example Trisomy 18.
- Severe congenital abnormalities – for example spina bifida or cardiac problems that are not amenable to surgery.
- Complications of extreme prematurity – for example, low blood pressure that fails to respond to inotropic medication, or extensive bowel damage that is incompatible with life following necrotizing enterocolitis.
- Perinatal hypoxic brain injury with a poor prognosis.

Some babies, particularly preterm babies, will already be receiving intensive care support when the decision is made to withdraw or withhold intensive care.

The intensive care support received may include:

- Support of the respiratory system, either via an endotracheal tube, or via nasal continuous positive airway pressure (CPAP).
- Support of the blood pressure with inotropic medication.
- Infusion of opiate medications or muscle relaxants to facilitate artificial ventilation.
- Organ support (renal replacement therapy etc.).

Following discussion with the family, a decision may be made not to escalate the intensive care support further, or more commonly, to withdraw support, keep the baby comfortable and allow the baby to die with their family.

Many parents will have built up a relationship with the team on the neonatal unit, and will choose to spend time with their baby on the intensive care unit, supported by the staff that they know. Some families may prefer for the baby to die at home, or in the hospice setting.

It is usual practice on the intensive care unit to discontinue muscle relaxant medications, and allow these to 'wear off,' but to continue any other sedative or analgesic medications after removing the baby from the ventilator. Intravenous access is often left in place to allow for the administration of palliative medications, but oral and subcutaneous medications can be given, even to the smallest of infants.

There are a number of issues that need to be thought about when caring for the dying baby, and the principles of care are similar to those for an older child. It is important to remember that simple comfort measures, such as positioning the baby with suitable boundaries, gentle rocking and swaddling, can be very effective.

Feeds

Most full term babies will feed around 120ml per kilogram per day of breast or formula milk if left to their own devices. Most babies feed six to seven times per day, but many breast fed infants feed more frequently than this.

Preterm babies start to learn to suck and swallow at around 33-34 weeks gestation, and babies younger than this are usually fed via a nasogastric tube.

Babies who are receiving palliative care should be allowed to feed orally if they wish to do so. They are likely to find breast feeding comforting even if they are not able to take much milk. If a baby is unable to take oral feeds, it is usually appropriate to offer feeds via a nasogastric tube. Providing around 50ml/kg/day of milk, split into six to eight feeds, will keep the baby hydrated, and may produce less vomiting and feed intolerance than using higher volumes. The aim of this approach is to reduce distress from hunger, rather than to provide calories for growth.

Gastro-oesophageal reflux

A small amount of vomiting or posseting following feeds is normal for babies. Antiemetics are not often required or used in small babies because of the significant side effect profile.

Gastro-oesophageal reflux is fairly common, particularly in babies with neurological problems. This can be distressing for the infant and can be dealt with by:

- Feeding with the head of the cot slightly elevated, and the baby lying with the left side down.
- Giving nasogastric feeds slowly (sometimes it is best to remove the plunger from the syringe and allow the milk to flow in 'by gravity').
- Giving smaller volume feeds more regularly (two hourly instead of four hourly for instance).
- Considering anti-reflux medications:

Drugs commonly used as anti-reflux medications in neonates:

Drug	Use
Gaviscon Infant	'feed thickener'/alginate
Ranitidine oral solution	H2 antagonist
Domperidone	prokinetic

Constipation

Constipation can be a problem, particularly for babies taking long term opioids.

Lactulose syrup 2.5ml twice daily titrated to response can be helpful, and ensuring adequate hydration is important. Lactulose may take 36-48 hours to act.

Distressing constipation in babies can be relieved by administering the 'tip' of a glycerine suppository rectally (it is easiest to slice a small chip off a 1gram suppository with a blade).

Pain

It is imperative that all babies receiving palliative care have close attention paid to their analgesia. The assessment of pain in babies is very difficult.

There are many pain 'scoring systems' that have been widely used for neonates, but the scores given are often subjective and not always clinically useful.

The following features are the most reliable indicators of pain in small babies:

- Persistent crying (although remember that a silent baby may be suffering from severe pain).
- Furrowing or bulging of the brow.
- Furrowing of the nasolabial folds (the folds between the lips and nose).
- Tight squeezing of the eyes.

Simple environmental methods may be very effective for relieving pain in babies.

Babies (particularly preterm babies) will often settle simply with a dark, quiet, warm environment. Other methods include swaddling of the baby in a blanket, allowing the baby to suck at the breast or on a dummy (see below), gentle rocking, stroking and massage of the baby.

There is good evidence that sucking on a syringe or dummy containing glucose or sucrose provides short term pain relief. This is particularly useful for procedural pain, including dressing/stoma changes for example. Glucose 30% solution 1ml orally as required can be used.

Non-opioid analgesia

Paracetamol:
Paracetamol can be given orally, or PR if needed by cutting up suppositories.

Non steroidal anti-inflammatory drugs:
Ibuprofen suspension after feeds.

Diclofenac is not usually recommended below six months of age because of the significant side effects. However, if the oral route is unavailable, rectal Diclofenac may be useful in neonates weighing 3.125kg or greater. The smallest dose that can practically be given is 3.125mg (by cutting a 12.5mg suppository into quarters.

Opioids

Morphine remains the most commonly used medication for neonatal analgesia.

Morphine can be given intravenously for acute pain, using a dose of 40-100micrograms/kg as needed.

Intravenous Morphine infusions are used, even in the smallest preterm infants, and doses of 10-40micrograms/kg/hour are often used. In unventilated babies the initial dose is 10-20micrograms/kg/hour and is then titrated to response. High doses of morphine can lead to a change in the respiratory pattern, and occasionally respiratory depression.

Subcutaneous infusions of morphine can be used in small babies, but are often problematic in small preterm infants, because of a lack of subcutaneous tissue.

Diamorphine is useful for subcutaneous use as it is more water soluble than morphine so smaller infusion volumes can be achieved, and is the preferred opioid for subcutaneous use. Intravenous Diamorphine has been extensively used in ventilated neonates, a dose of 100micrograms/kg is useful for acute pain, and an initial infusion of 2.5-7micrograms/kg/hour can be used safely in non-ventilated babies and then titrated to response.

Morphine sulphate oral solution is the most common oral opioid used. The total daily intravenous opioid requirements can be calculated and converted to an oral regime, giving the morphine every four hours initially. Breakthrough analgesia (PRN doses) should also be prescribed and given in-between the regular doses if required. The dose is then adjusted to response – there is no maximum dose of morphine for neonatal palliative care – high doses of morphine will often change the breathing pattern, and may cause respiratory suppression.

Opioids may also help to relieve breathlessness at rest.

Fentanyl has been associated with chest wall muscle spasm in neonates, and is not often used. It is difficult to cut Fentanyl patches into small enough pieces for use with small babies.

Seizures

Seizures are a common problem encountered in neonatal palliative care. These are often secondary to a perinatal hypoxic insult to the brain or a primary brain problem and can be distressing for the family to see. Seizures can manifest in subtle ways in babies, common features are cycling movements of the arms and legs, unusual mouth movements or lip smacking.

There are a number of medications used for seizures in neonates – most neonatologists start with Phenobarbital.

Drugs used to treat seizures in neonates

Drug	Comments
Phenobarbital (Phenobarbitone)	Most commonly used first line medication in neonates – causes sedation and may suppress respiration in high doses. Can be given IV or orally.
Phenytoin	Commonly used as a second line agent in neonates – can be given IV or orally. May cause blood and skin disorders with long term use.
Clonazepam	Very effective anticonvulsant – significant sedation which can be useful in palliative care. Can be given orally or IV - IV dose associated with respiratory depression. Can be used to ameliorate distressing gasping.
Midazolam	Midazolam is not often used for IV or subcut infusions in neonates as it tends to accumulate, and can cause respiratory depression. It is not licensed for sedation below six months but is still occasionally used, with good effect. Can be used to ameliorate distressing gasping.

Sedation

It is important to ensure that babies who are 'unsettled' are not in pain.

Occasionally babies benefit from oral sedative drugs to help them sleep.

The most commonly used sedatives in babies are:

- Chloral Hydrate orally or rectally at night, or as required.
  May be used up to QDS for continuing sedation.
  The oral solution can be given rectally if suitably sized suppositories are unavailable.
  (Chloral can accumulate if used regularly in babies. It is also an irritant to the stomach if given orally so should ideally be given with or after milk feeds).

- Alimemazine (Trimeprazine) orally as required (maximum four times daily).

Excessive secretions

Many babies with neurological problems have difficulties clearing secretions from their mouth and pharynx.

Some babies are managed at home, or in the hospice setting with oral suction.

Hyoscine patches (quarter of a patch, applied behind the ear, every 72 hours) are often useful for excessive respiratory secretions.

Mouthcare

Opioids and hyoscine may cause dry mouth – regular mouth care should be performed.

Syringe drivers

In palliative care, when the parenteral route becomes necessary for symptom control, the use of syringe drivers to administer continuous subcutaneous infusions can be useful to reduce the discomfort of repeated injections. Commonly used drugs given via continuous subcutaneous infusion include opioid analgesics, antiemetics, sedatives and anti-secretory agents. Most drugs can be diluted with water for injection for continuous subcutaneous infusion. Luer-Lok syringes should be used.

When given subcutaneously, Diamorphine is preferred over Morphine because it is more soluble so can be made up in smaller volumes which are suitable for subcutaneous use.

Daily oral or IV Morphine requirements can be used to calculate equivalent daily subcutaneous Diamorphine doses;

Total daily dose of oral Morphine: total daily dose of subcutaneous Diamorphine = 1: 0.33

Total daily dose of IV Morphine: total daily dose of subcutaneous Diamorphine = 1: 0.66

If a patient is receiving several subcutaneous infusions, it may be possible to mix both drugs in one syringe to avoid multiple infusion sites – check the compatibility of the combination with a pharmacist before proceeding.

The site of subcutaneous infusion should be monitored to check for precipitation of drug, local reactions, fluid accumulation and inflammation.

Summary

The palliative care of infants is important, and follows the same principles as in older children. There should be a focus on relieving pain and distress, and opioids remain the most commonly used medication. Unfortunately, many of the other medications used in older children accumulate in babies and this can cause problems if these medications are used in the longer-term.

The treatments discussed are by no means comprehensive – in difficult cases it would be advisable to seek the advice of a neonatologist or a neonatal pharmacist.

Neurological

(See specific text)

Epilepsy

Definition

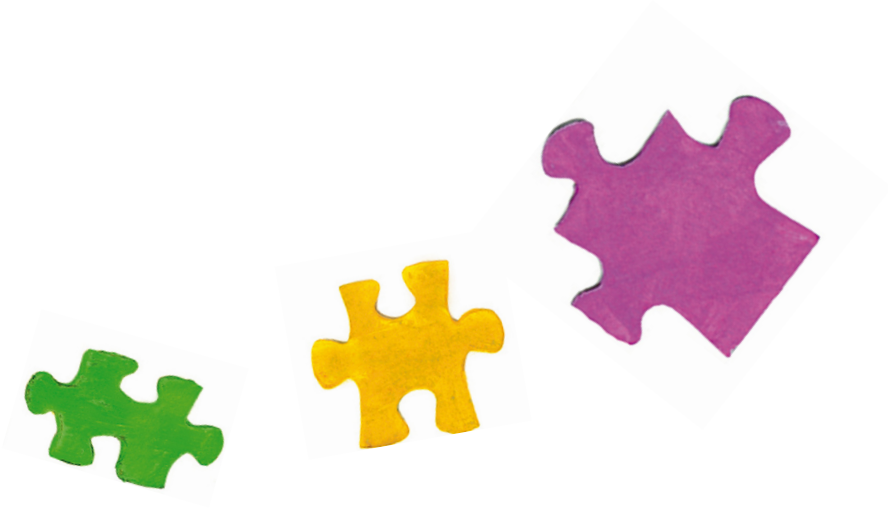
Recurrent convulsive or non-convulsive seizures caused by partial or generalised epileptogenic discharges in the cerebrum.

General points

- Not all seizures are grand-mal epileptic seizures; they come in many forms and it is important to recognise the different types.
- Not all seizures require immediate administration of medication. The majority of seizures will settle given five to ten minutes, particularly in children with neurodegenerative disorders.
- Look for the reversible causes of increased seizures and attempt to correct them.
- Seizures can be very frightening for the child, family and carers. Try to remain calm and give the parents an explanation of what is happening.

Reversible causes of increased seizures

- Infection
- Renal failure
- Hepatic failure
- Electrolyte imbalance (sodium, calcium or magnesium)
- Hypoglycaemia
- Raised intracranial pressure
- Inappropriate epilepsy management
- Too rapid an increase or decrease of epilepsy medication



General principles of management [2, 133]

- Correctly diagnose the type of epileptic seizure [2, 134].
- Know which drugs are used to treat the different types of seizures.
- Start with one drug, working up the dose gradually until seizure control or side effects occur [2].
- Add second drug only if seizure control not achieved with first drug alone.
- Remember to weigh up the benefits vs side effects of the treatments. 30% of children have behavioural problems whilst on anticonvulsants [135, 136].
- Change doses gradually.
- Regular re-calculation of drug dosage as the child grows and puts on weight.
- Metabolism of drugs can be affected by hepatic and renal failure [137].
- Children under the age of three years may need higher doses of drugs due to their more efficient drug metabolism.
- Blood levels are generally unhelpful.
- If in doubt ask a paediatric neurologist.

Intractable epilepsy

The management of intractable epilepsy is beyond the scope of this manual. However it is worth remembering a few points [2, 138-142].

40% of children with intractable epilepsy are misdiagnosed. This can be due to:

- Underlying aetiology overlooked.
- Misdiagnosis of syndrome or seizure type.
- Poor EEG recording or interpretation.
- Non-epileptic disorders that mimic epileptic disorders.

There are often errors in therapy due to:

- Inappropriate choice of drugs.
- Inappropriate dose and dosing interval.
- Inappropriate polytherapy.

In all cases of intractable epilepsy check:

- That child has actually seen a paediatric neurologist and has had a formal diagnosis of type of epilepsy.
- If on polytherapy, has this decision been made by a paediatric neurologist, and if not, what is the rationale for the polytherapy.

Status epilepticus

Definition

When seizures occur so frequently that over the course of thirty or more minutes, they have not recovered from the coma produced by one attack, before the next attack supervenes.

Management [52]

In the community or smaller units (major hospitals have established protocols that should be followed).

- Secure airway.
- Give oxygen.
- Establish cause.
- Check for hypoglycaemia.
- If facilities available, check FBC, U+E, glucose, calcium, magnesium, liver function tests, blood cultures. If possible check urine for infection.

***First line treatment** [48, 143, 144]*

Diazepam

- Intravenously: getting new access site is difficult, onset of action in one to three minutes, effective in 80% of cases within five minutes, short duration of action 15-20 minutes.
- Rectally: as a solution (suppositories take too long to work) works within six to eight minutes.
- Nasogastric tube or gastrostomy: best mode if available.

Midazolam

- Buccally: increasingly popular due to ease of administration, works within six to eight minutes.
- Rectally.

Lorazepam

- Intravenously: as infusion, give slowly to avoid apnoea.
- Rectally.
- Orally.
- Sublingually.

The metabolites of diazepam are active. Furthermore, diazepam accumulates in lipid stores. When these stores saturate, then the levels rise rapidly leading to unexpected side effects (secondary peak phenomenon). This is not true of Lorazepam.

Second line treatment

If still fitting then repeat first line treatment after 10-15 minutes.

Third line treatment

If there is still no response then rectal paraldehyde should be administered.
Paraldehyde should be mixed in an equal volume of arachis oil (or olive oil if there is any nut allergy), drawn up into a glass syringe and given via a quill (if urgent, a plastic syringe can be used provided it is drawn up and given immediately).

Fourth line treatment

Hospitalise the child for advanced management, paralysis and ventilation.

Terminal seizures or if not appropriate to hospitalise

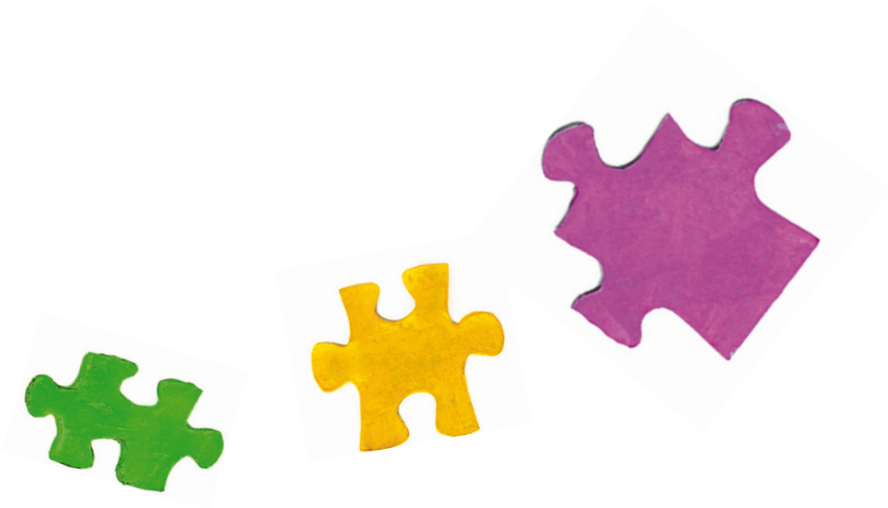
In the terminal phase seizures can become more severe and frequent. The child at this stage is normally not able to take or absorb oral anti-epileptics, and in such cases continuous subcutaneous Midazolam or Phenobarbitone can be used. The physician needs to balance the heavily sedating effects of treatment against the benefits of seizure control. It may not be possible to control all the seizures, and an explanation is needed to the parents that some minor seizures may breakthrough and do not necessarily require escalation of treatment.

Midazolam subcutaneous infusion [48, 143, 144]

- Onset of action one to five minutes.
- Duration of action one to five hours.
- Easier to titrate than phenobarbitone.
- Good anxiolytic.
- Dose can be steadily increased (up to 150mg/24 hours then consider changing to Phenobarbitone).
- Only available in one strength so volume in smaller Graseby syringe drivers can be a problem.
- Anecdotal evidence suggests that a small dose of Diamorphine added to syringe driver can help with seizures requiring increasing doses of Midazolam.
- Clonazepam is an alternate to Midazolam.

Phenobarbitone subcutaneous infusion

- Sedating.
- Anxiolytic.
- Do not combine with other drugs in syringe driver (only miscible with Diamorphine and Hyoscine).
- Should be diluted with water.



Spasticity

Definition
Is a condition of increased tone, spasms, clonus, weakness and loss of dexterity.

Causes
- Cerebral palsy
- Brain haemorrhage
- Brain tumours
- Anoxia
- Vegetative state

Management [145]
- Multidisciplinary
- Physiotherapy
- Surgical
- Botulinum A injections [146]
- Drugs [147], not always very successful:
  - Baclofen, orally or by pump
  - Diazepam
  - Tizanidine
  - Dantrolene
  - Quinine
  - Gabapentin

Myoclonus

Definition
Brief, abrupt, involuntary, non-suppressible, and jerky, contractions involving a single muscle or muscle group [148].

Causes
- Normal; onset of sleep, exercise, anxiety.
- Neuro-degenerative disorders.
- Secondary to opioid overdose.

Management
- Opioid rotation.
- Benzodiazepines:
  - Diazepam
  - Lorazepam
  - Clonazepam

Chorea

Definition
Frequent, brief, purposeless movements that tend to flow from body part to body part chaotically and unpredictably [148].

Causes
- Rheumatic fever.
- Neuro-degenerative disorder.
- Encephalopathy.
- Hypo – and hypernatraemia.
- Drugs including [149]:
  - Haloperidol
  - Phenytoin
  - Phenothiazines

Management
- Bed rest in quiet darkened room.
- Sodium Valproate.

Dystonia

Definition
Syndrome of sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures [148].

Causes
- Neuro-degenerative disorders.
- Metabolic disorders.
- In drug induced reactions producing extrapyramidal reactions.
- Drugs including [149]:
  - Dopamine antagonists
  - Antipsychotics
  - Antiemetics
  - Antidepressants
  - Antiepileptics

Management
- Anti-cholinergic drugs such as Benztropine or Diphenhydramine (in collaboration with neurologist).
- Review medication and reduce or stop drugs if possible.

Akathisia

Definition
Motor restlessness, in which the patient feels compelled to pace up and down, or to change body position frequently [148].

Causes
- Drugs including Haloperidol and Prochlorperazine [149].

Management
- Review medication and reduce or stop drugs if possible.
- Propranolol.

Noisy breathing

[150-152]

Noisy breathing from excessive secretions or a death rattle in an unconscious child is very distressing. Excessive respiratory secretions are a dose-related side effect of all the benzodiazepines.

Hyoscine hydrobromide can be used to dry secretions and its sedative effects can be helpful. It can be given as patches or by subcutaneous infusion. It has a tendency to inflame subcutaneous sites after 24-48 hours and so the site should be moved regularly. Officially the patches should not be cut but instead occluded to produce the half and quarter patch, in reality most users tend to cut the patches.

The anticholinergic drug Glycopyrronium has been used in children with chronic handicap to reduce hypersalivation.

The 'death rattle' can be treated with Diamorphine, Midazolam subcutaneously or Diazepam rectally.

Pain assessment

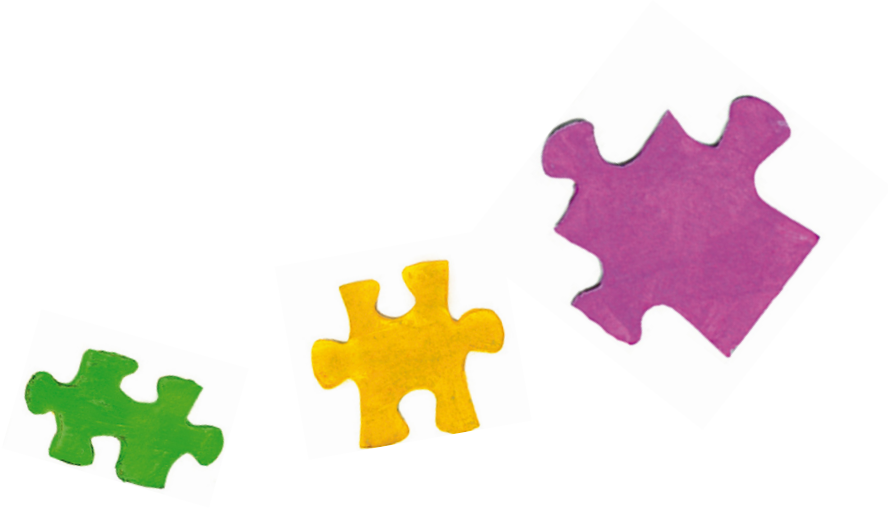
[31, 153-173]

Assessing pain in children with life-limiting illness can be complex but is assisted by:

- Building a relationship with the child and family;
- Understanding the context in which pain occurs; and
- Being familiar with the child's medical condition.

The object of pain assessment is to capture the various dimensions of the pain, including:

- Location;
- Intensity;
- Character (for instance is it burning or sharp?);
- The significance or meaning of the pain for the child and family.



Pain measurement

The main purposes of pain measurement are to:

- Quantify the experience;
- Monitor the effects of treatment;
- Provide a shared medium through which the child can communicate the experience to others.

Children's self-report of pain
Children are less able than adults to quantify and qualify abstract phenomena so any measures of pain need to be appropriate to the child's cognitive and developmental level. It should be kept in mind that during illness children may be less able to use tools designed for their age and cognitive ability.

There are several tools that can help the child to communicate their pain to others. It is sensible to have a few that are well known to your practice.

Pain location

Body map
The child can be asked to indicate on a body outline (or themselves) where the pain is. Children could also be asked to choose colours which signify different levels of pain and use these to colour in the painful areas.

Pain intensity

Faces pain rating scales
Faces scales consist of a number of cartoon type faces in which the facial expression varies on one end with either a smiling face or a neutral (no pain) face to an expression which signifies extreme pain. The child is asked to identify their own pain intensity from the faces offered. Faces pain scales are suitable for children who are at a developmental age of five or above. Adolescents may find the tool tiresome if used over the longer term and may prefer a straightforward Numerical Rating Scale (NRS).

The Wong-Baker Faces pain rating scale is probably the most commonly used. Copies can be downloaded from the internet for clinical use from: www.wongbakerfaces.org

Numerical rating scales
Children must have a sound understanding of language, order and number to be able to use either the verbal or the numerical scales, probably seven to eight years upwards. Ask the child how bad their pain is on a zero to ten scale, with zero being no pain and ten being as much pain as you can imagine.

Verbal pain rating scales
Four to five point categorical scale with pain ratings from no pain to severe, or very severe pain. For example, pain could be none, mild, moderate, severe, very severe.

Parents as proxy reporters of their child's pain
When children are unable to rate their pain, parents or clinicians can provide a proxy rating. The source of these ratings is usually the child's behaviour in relation to their non-pain behaviour, the context in which the behaviour is taking place, and the provider of the ratings own attitude towards pain. As with the children themselves, parents may place particular meaning on a change in the child's behaviour and this can be explored. Assessments can sometimes vary between proxy raters of the child's pain, and it is helpful to discuss and explore the reasons for any differences.

Behaviours that signal pain

There are categories of pain cues that, whilst the emphasis may change with age, are common across all ages. These include changes in:

- facial expression
- vocal sounds
- bodily posture
- movements
- mood

Facial expression and cry are widely discussed in the literature on neonatal and infant pain, but their importance as indicators of pain appears to decrease with age. This downward trend is associated with, in normal circumstances, the development of a wider repertoire of behaviour which includes language. Consequently, older children are normally less likely to emit behaviours with high 'signal value' such as crying and grimacing [174]. In addition, as children mature they learn to moderate their behaviour in line with the expectations of the culture within which they live.

Children who are unable to communicate verbally or by augmentative means are wholly dependent upon their carers correctly interpreting their behavioural cues of pain. The Paediatric Pain Profile (PPP) has been developed for children with severe neurological impairments. The 20-item behaviour rating scale is incorporated into a parent-held document which can be downloaded here: **www.ppprofile.org.uk**

Pain diaries and flow sheets

Ask parents, children or carers to keep a pain diary or a flow sheet, where space is provided to write the time, duration, context in which pain has occurred, pain measurement on one of the above tools or suitable alternative, the intervention and the outcome of the intervention using the same pain measure. The use of a standard pain measure will help to evaluate the effectiveness of different interventions.

Some useful web resources

International Association for the Study of Pain. Pain assessment in children **www.iasp-pain.org**

Wong Baker Faces Pain Rating Scale **www.wongbakerfaces.org**

Paediatric Pain Profile: A behaviour rating scale for children with severe to profound neurological impairments **www.ppprofile.org.uk**

Institute of Child Health: Children's pain assessment project **www.ich.ucl.ac.uk/cpap**

World Health Organisation book: Cancer Pain in Children, available to buy from: **www.tso.co.uk/bookshop/bookstore.asp?FO=1160671&DI=352971**

Pain

(See specific text)

Introduction

Pain is one of the most prevalent symptoms in children requiring palliative care support [175]. It is also one of the most feared by parents [176]. A child in pain can be a very distressing experience for everyone: child, parent and professional alike. Fortunately, in most cases, pain is quite straightforward to manage. The majority of children respond well to good pain management based upon a few simple pharmacological principles, and application of the skills of the multidisciplinary team. A sensible and empiric approach, with thorough assessment and good understanding of disease process, will enable safe and effective therapeutic management.

The study of pain in children started with recognition that pain is undertreated in children [177]. The last 25 years have seen significant gains in the understanding and management of pain in children.

We know:

- Infants and children suffer prolonged pain due to disease, trauma and psychological factors.
- Infants can experience pain at birth and failing to alleviate their pain causes adverse physiological consequences and needless suffering.
- Children can experience many different types of acute, recurrent and persistent pain.
- Children can describe their pain.
- Children's pain must be regularly monitored, evaluated and assessed.
- Children in severe pain require potent analgesics for relief.
- Administration of opioids in children does not lead to addiction (adapted from PJ McGrath [178]).

Although pain in children's palliative care is receiving significant attention in literature, clinical practice is currently influenced by extrapolation of evidence from studies in acute pain in children and adult palliative care. Despite this literature providing sound knowledge and comparable similarities, there should be caution in extrapolating data from different populations. Although the core principles of pain management can be shared between the adult and paediatric specialties, there are many differences that determine distinct practice. 'Paediatric' patients represent an incredibly variable and diverse subset of individuals from the premature neonate to the fully-grown, sexually mature young adult. Anatomy, physiology and cognitive responses differ, disease types differ, and social, psychological and environmental factors differ [179]. This should be kept in mind, particularly when prescribing.

Children treated by palliative care teams have pain that is usually a result of multiple causes. As professionals in the field we need to be competent in managing a variety of pain experiences: acute pain, chronic pain, recurring pain, procedural related pain and pain at the end of life.The study of pain in children is a vast subject and so this section can only represent a synopsis of pain management in this field.

Essential to achieving effective pain control is the development of a solid, trusting relationship based upon effective communication (between professionals, parents/carers/family and child) and, attention to detail. The aim must always be for excellent pain control. Meticulous assessment and treatment using the varied skills of the multidisciplinary team is essential. Taking the time to fully understand the child's pain in the context of their developmental level, what they understand to be happening, how they think and what they associate their pain with, and the wider picture of the impact of the pain, not only on the individual child, but also on their parents/carers/family, is the is key to success [180].

Pain is a 3D film not a 2D picture. Behind the 'scenes', there is a life-long history, a set of social, behavioural and psychological factors, and a cultural and social framework all influencing the pain experience. The complexities surrounding pain management arise from the wider issues regarding pain: myths and misconceptions, social issues surrounding the coping skills of the child and family, compliance with treatment, acknowledgement about escalating pain in a sick child and interpretation of the meaning of pain [181]. What children think, what they do and what they might sense or feel, deeply influences their pain experience. The combination of situational factors [178] (for example worsening physical function associated with disease progression, sleep deprivation, upset parents, feeling worried and scared) that influence the meaning of the pain experience for the child, impacts upon the physiological response of the body. [182]

As pain is always multidimensional, involving the emotional and sensory experience of the child, an honest and open approach will allow discussion about anxieties and misunderstandings, which without being addressed may prevent successful treatment. Being able to provide accurate age appropriate information increases a child's sense of control and has a direct impact on their experience of pain. Offering children reasonable options and choices (e.g. would you like tablets or liquid? would you like a heat pack or a massage?) With explanations about how treatments work and what to expect (e.g. this medicine might make you feel a bit sleepy, but this feeling should get better in a couple of days) also supports this process.

Evaluation of pain is the cornerstone of good pain management in children. This process includes a detailed pain history, examination, and diagnosis of the causes and subsequent measurement of pain. Evaluating pain involves trying to establish the various dimensions of pain including location, intensity and characteristics (for instance is it a stabbing or throbbing pain?). The consequence of pain upon the child's activity and daily routine is one of the most important things to establish. Age and cognitive development influence how pain is perceived and expressed in children and it is helpful to have a baseline knowledge of this spectrum of understanding from infants to teenagers.

Remember...

- Children may decide not to disclose information or under-report pain if they associate the outcome as having a negative impact; for example requiring a hospital visit or inpatient stay, an unpleasant intervention or causing upset or worry to their parents.
- Absence of signs and absence of reporting, does not equate to absence of pain.

How parents/carers/family respond to their child in pain is critically important to how both they and the child attempt to cope with pain [183]. Parental education of pain mechanisms and management is important in making sure that parents are not only able to understand and comply with a pain management plan, but are also equipped with the correct information to pass on to their child. Educating parents regarding rationale for treatments, how disease processes and emotional/behavioural/cognitive factors impact upon pain, what to expect from medication in terms of benefits and side effects and non pharmacological pain control techniques is absolutely vital.

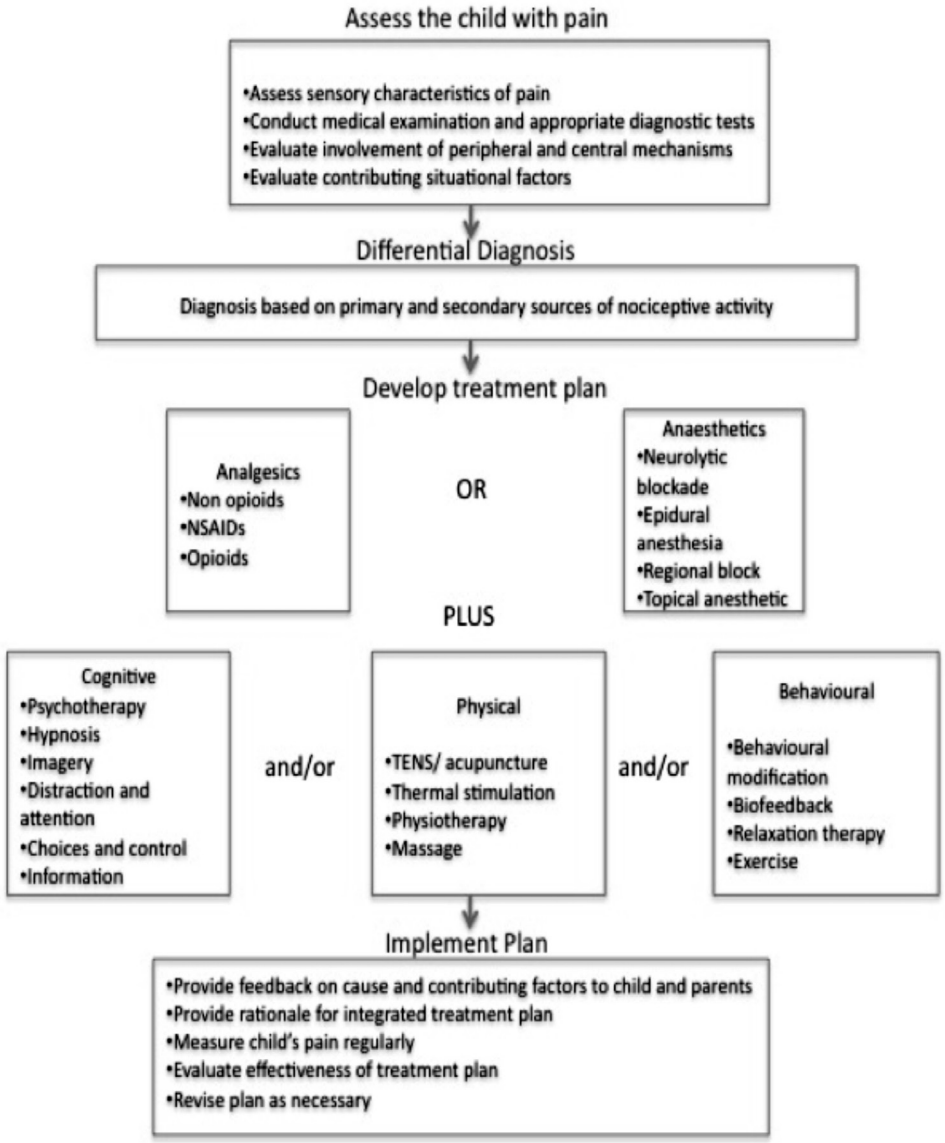
The latest initiative from the World Health Organisation (WHO), 'WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illness' 2012 [184] has taken the best available evidence and developed a new guideline to improve the management of persisting pain in children. Persisting pain in children is a global phenomenon and is described as "duration of pain lasting beyond what one would expect from an acute injury". This definition intends to cover longer-term pain related to medical illness and has no defined time frame. The new guidelines are based upon the principle that, irrespective of whether an underlying cause can be identified, pharmacological and non-pharmacological techniques should be used to treat pain in children. This document replaces the previous guideline 'Cancer Pain and Palliative Care in Children' 1998.

Pain Management

Before reading about pain management the previous chapter about pain assessment will need to be read. Optimal pain relief in children's palliative care is only achieved through thorough holistic assessment and an integrative approach to treatment. Without attention to the psychological and spiritual wellbeing of the child, pharmacological management alone will not achieve the desired result.

Modern medical practice has evolved over the past 10-15 years to include non-drug techniques that not only improve the experience of pain, but also the ability to cope with pain [180] [185]. Integrating cognitive, behavioural and physical interventions into a pain management plan (see below) has been shown to have a positive impact upon a child's pain experience and gain better analgesia.

Figure 1: A model of Integrated pharmacological and non-pharmacological approach for controlling children's pain. From [178] (Originally adapted from PA McGrath. *Pain Control in Children. In Innovations in Pain Management; A Practical Guide for Clinicians,* RS Weiner, editor. Paul M. Deutsch 1992 32-43 with permission).



Non-pharmacological (non-drug) interventions can alter factors that are known to exacerbate pain and improve the child's control. They also directly activate endogenous (built in) pain-inhibitory systems: pain pathways which are able to block incoming pain signals at the level of the spinal cord [178]. Going beyond standard 'drug-based' medical practice addresses the psychosocial and spiritual elements of pain and suffering and provides an individualised approach to the child, which in the palliative care setting cannot be underestimated.

The Pharmacological Management of Pain in Children: The 2012 WHO Approach

The WHO 2012 guidelines reiterate the key principles of pain management in children:

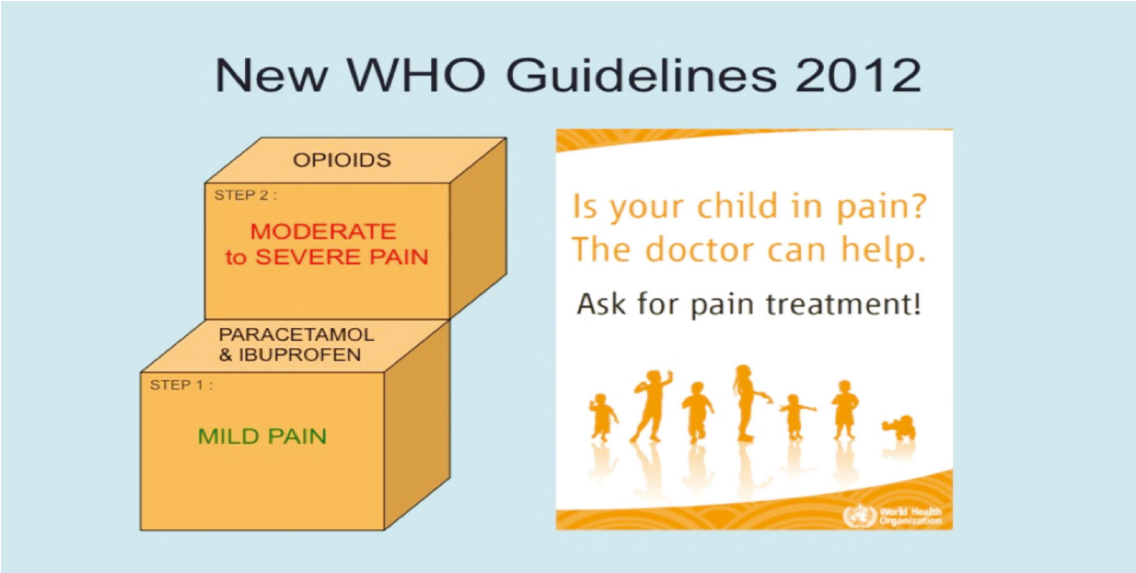
- Ensure that detailed assessment has occurred.
- Dose analgesia at regular intervals when pain is constant ("by the clock").
- Make sure medication is available for 'break through" pain episodes.
- Use the simplest route of administration ("by the appropriate route").
- Tailor treatment to the individual ("by the child").

Using a Two-Step Strategy

Modifications of the original WHO guidelines have included moving from the 'three-step analgesic ladder' (mild vs. moderate vs. severe pain) to a 'two-step analgesic approach' (mild pain vs. moderate to severe pain). A strong recommendation by the expert group (but with very low quality evidence) this change was centered on expert experience and a simplified, more effective strategy for pain management in children in combination with various concerns regarding efficacy of "weak" opioids.

In summary new recommendations from the WHO include:

- Exclusion of Tramadol and codeine from the guidelines based upon the safety and efficacy of these medications in children:
  - There is no available evidence for the effectiveness and safety of tramadol in children.
  - Codeine has varied metabolism across the population and in neonates and children; it has a very low analgesic effect but a significant side effect profile.
- In effect the 'weak' opioids are not recommended for use in children and have been replaced with a low dose of a major opioid.
- Concern regarding the use of strong opioids in children is offset by poor efficacy and unknown response to the weak opioids.
- The 'level' of approach is determined by severity of pain, classified as either 'mild' or 'moderate to severe'.



Step one: Mild Pain

Non-opioids

Paracetamol

Paracetamol (acetaminophen)

- Provides effective relief from mild pain and is widely available and well tolerated.
- One of the few analgesics that can be used safely in neonates and children under the age of three months.
- Administration is aided by the fact that it comes in so many strengths and forms (available in syrup, tablets, suppositories and parenteral formulations).
- Has a low adverse effect profile when used in appropriate doses.
- Antipyretic effects are also very helpful with concurrent infections.
- Hepatotoxicity is rare but can occur in vulnerable children at therapeutic doses. Risk factors that increase toxicity are those that can frequently be present in the children requiring palliative care support: hepatic or renal disease, malnutrition and enzyme induction with various drugs (Including carbamazepine; rifampicin and phenobarbitone amongst others).

Ibuprofen

Ibuprofen

- A safe and familiar medication used frequently in children.
- Side effect risk of renal, gastrointestinal and cardiovascular is low, although care must be taken in children who are dehydrated.
- Has a mild antiplatelet effect and should be used with caution in patients with a bleeding tendency.

Step two: Moderate to Severe Pain

Children assessed with moderate to severe pain should have an opioid analgesic administered. The second step recommends the use of low dose opioids for moderate pain. The WHO guidelines reiterate that fear and lack of knowledge regarding the use of opioids in children should not be a barrier for effective analgesia.

Opioids

Myths and Misconceptions

There is often hesitancy shown from professionals, parents and carers about initiating an opioid drug, usually morphine. There are a great many fears and myths surrounding its use. It is very important that before starting any treatment these issues are openly addressed and explored and correct information is provided. Many parents need support in understanding the difference between tolerance and dependence.

Tolerance occurs when the body becomes accustomed to a certain dose of the medicine and an increased dose is required to obtain the same effect

Dependence involves a strong desire to take a drug for its psychoactive properties (rather than analgesic properties) continuing with its use despite harmful potentially consequences, and giving a higher priority to drug use than to other activities and responsibilities.

Significant investment in time and education is often needed, usually on repeated consults; to dispel fears and misconceptions and enable enough understanding for adherence to pain management plans.

Myth: It will shorten the child's life.
Truth: Pain control does not shorten a child's life; it only brings comfort and improves the quality of experiences that the child can enjoy, rather than being exhausted and sad from fighting pain.

Myth: It will suppress a child's breathing.
Truth: Respiratory depression can be avoided by steady increases of dose.

Myth: It will give the child nausea.
Truth: Nausea rarely occurs in children and will normally settle in five to seven days.

Myth: It will make the child even more constipated.
Truth: Constipation can be prevented by the early use of prophylactic laxatives.

Myth: They will develop addiction to it.
Truth: Addiction is very rare in children taking opioids for pain and is not a problem encountered in paediatric palliative care.

Myth: Sedation will affect the quality of the child's life in the final days.
Truth: Sedation will normally improve within a few days of taking morphine.

Myth: It is the beginning of the end.
Truth: Our experience is that children will often live longer than we expect. Also dosage can be reduced or increased depending on the child's state.

Opioid Prescribing

There are a variety of opioids available to the physician in some countries however there are no proven benefits of using alternatives to morphine in children. Internationally the availability of child appropriate dosage formulations is limited and can make pain management very challenging in smaller children.

Morphine is well established as a first line opioid in children as it is inexpensive and has a wide range of formulations, however alternative strong opioids can be considered based upon pain pathophysiology, safety and availability.

Individualised opioid prescribing: 'by the child'

Finding the right dose of opioid for a child involves three phases:

Initiation: the initial starting dose of medication in an opioid naïve child is usually calculated per kilogram of body weight (up to a maximum dose of 50 kg). The WHO guidelines have added a specified age range to allow for changes in pharmacokinetics in the growing child (see formulary). In a child already receiving opioids the current total daily dose of opioid should be used as a basis for calculation.

Titration: the dose of analgesia is titrated on an individual basis. Opioid analgesics must be increased in steps until the correct dose is achieved, based on the child's response to medication. The correct dose of opioid is determined in partnership with the child and carers until the best possible pain relief is achieved, with the least side effects.

Generally the maximum dose increase is approximately 30-50% of the previous total daily dose, however in an inpatient setting with careful monitoring and repeated assessment experienced practitioners may increase doses more rapidly.

Maintenance: is established once a dose that provides adequate relief of pain is achieved. A long acting opioid is usually commenced at this point, if available. For many children long acting morphine preparations (granules) are convenient and offer flexible dosing. Fentanyl patches should only be used once a child is stabilized on morphine as it can take approximately 12-24 hours to reach a steady state using a patch. (Note: A minimum total daily dose of oral morphine 30-40mg is required prior to commencing the lowest available dose of Fentanyl 12 microgram patch which can prohibit use in many small children.)

Careful distinction between end of dose failure, breakthrough pain and incident pain must always be made. Assessment of patterns of pain behavior and analgesic requirements will help the clinician to determine if the child requires more frequent or increased dosing of opioid (end of dose failure), if pain is related to movement or procedures or if true pain exacerbations occur on a background of reasonable analgesia (such as in cancer pain). When breakthrough pains become more frequent, the background dose of opioid may need to be increased.

An additional dose of opioid should always be prescribed as required as a 'rescue' dose. Recommended calculation of the rescue dose of morphine is varied; the WHO Guidelines 2012 (p80) recommend 1/5th to 1/10th of the total daily dose, however, historical practice has been based upon adult palliative care prescribing and calculated as 1/6th of the total daily dose of opioid. The benefit of a lower breakthrough dose (1/20th -1/10th) enables closer and probably safer, titration of dosing in children.

Other helpful guidance to prescribing opioids

- Opioid analgesia must be prescribed on a regular basis when pain is frequent or constant rather than 'as needed'.
- Effective analgesia is achieved through gradual increase in opioid until pain relief is achieved.
- In practice a four hourly dosing schedule for immediate release opioid works well although there is wide inter-individual variability.
- Theoretically the dosage interval of morphine is shorter than that of adults as the half-life of morphine in children is reduced compared to adults as such some children may benefit from an eight hourly dose of long acting opioid preparations rather than the standard 12 hourly regime.
- Incremental increases in dose should be of the level of 30-50% of the total daily dose or based on previous days breakthrough pain dose.
- Be aware of when the half-life of an opioid is increased: occurs in neonates and infants up to the age of 12 months (have reduced renal clearance of morphine) and in renal failure (morphine/oxycodone) and liver failure (methadone).
- Neonates and infants (under 12 months) are prescribed a lower starting dose of opioid at longer intervals, for example 6 or 8 hourly.
- The least invasive route, the oral route, is usually preferable in children. Palatability, availability of oral solutions, size of tablets and frequency of dosing become important factors to consider ensuring compliance, and consequently good symptom management.
- Choice of alternative routes of administration when the oral route is not possible should be based on clinical judgment, availability of drugs, feasibility and patient preference.
- Situations when the enteral route might not be suitable and an alternative route must be sought include:
  – pain crisis requiring rapid titration of intravenous opioids
  – poor absorption: vomiting, disordered gastrointestinal motility
  – inability to comply: unconscious; severe nausea, poor swallow; risk of aspiration, medication refusal.

Opioid Switching and Rotation

Opioid switch: change in opioid early in treatment as doesn't appear to be effective, or side effects intolerable

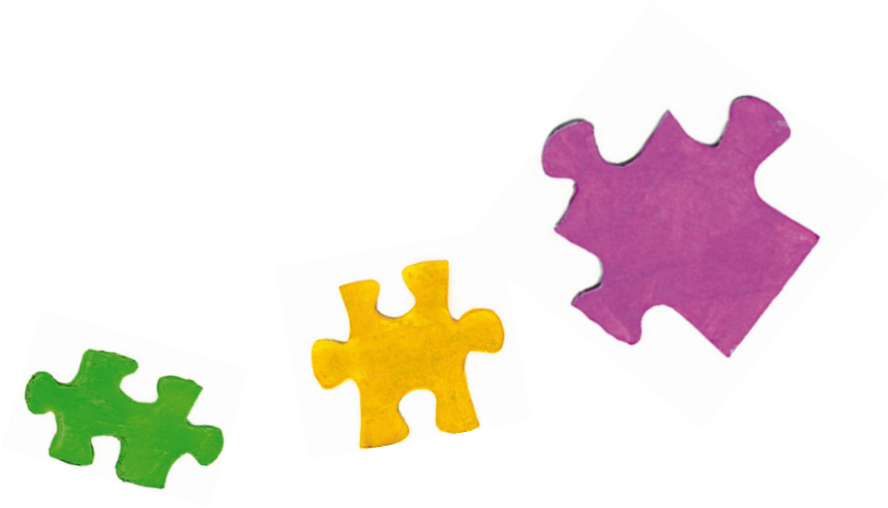
Opioid rotation: change in opioid after a period of benefit when tolerance appears to be developing

Opioid switching should be considered in children if:

- analgesia is inadequate
- dose limiting side-effects occur
- there are unpleasant side effects despite adequate analgesia (for example itch not resolving)
- an alternative opioid might offer specific advantage over the current one (for example changing from enteral morphine to transdermal fentanyl).

The new dose is calculated on an equi-analgesic dose based upon oral morphine equivalency. A reduction in the dose of the new opioid by approximately 25-30% is recommended to reduce toxicity and counter the possibility of incomplete cross-tolerance.

Opioid Side Effects	
Sedation	One of the first side effects to occur in opioid naïve patient or when opioids are significantly increased. May last a few days but then subsides. Warning parents/carers avoids unnecessary worry.
Constipation	Very common in children. Regular laxatives (stimulant and softener) are required prophylactically. Good evidence in adults that opioid antagonists naloxone and methylnaltrexone are effective in opioid induced constipation without causing opioid withdrawal. Fentanyl has been reported as causing less constipation than other opioids.
Pruritus	Not uncommon in children. Usually occurs around the nose and face.
Nausea	Less common in children than adults but possibly under-reported.
Myoclonus	Not infrequent in children and usually prompts opioid switching or dose reduction.
Urinary retention	Seen in children particularly after rapid dose escalation and spinal or epidural opioids. Anecdotally, children seem to experience urinary symptoms (usually hesitancy) not infrequently. External bladder massage/pressure, heat packs, voiding in a warm bath and if necessary intermittent catheterization or cholinergic agent may be required.
Respiratory depression	Very rare occurrence if opioids are titrated appropriately. Narcotism more likely to occur if sudden removal of pain stimulus (following radiotherapy or intrathecal pump insertion – revert to short acting opioid/infusion to avoid this) with addition of adjuvant or opioid switch resulting in improved analgesia (should be anticipated) onset of inability to excrete opioid metabolites (e.g. renal failure). Inadvertent overdose.
Consider opioid switch or opioid reduction for troublesome side effects.	



Common side effects of opioids should be anticipated and managed aggressively. If children associate unpleasant side effects with medication, it is likely that compliance will be affected and refusal to continue with the medication might become a problem. Children may not report adverse effects, such as constipation, nausea and itching, voluntarily so careful attention must be paid to identify these problems early when assessing opioid efficacy.

Non malignant pain and the use of opioids

Using opioids for persisting non malignant pain is a practice that requires specialist pain and palliative care knowledge and skill. Close monitoring is necessary and although there are few robust studies and historically it has been a controversial area of prescribing, there is growing expertise and knowledge within children's pain and palliative medicine with positive anecdotal results.

Adjuvant analgesics

An adjuvant analgesic is a medication that has a primary indication other than pain, but is analgesic in some painful conditions.

The WHO recently reviewed the evidence for the use of adjuvant analgesic medicines in pain management for children and found insufficient or very poor quality evidence to support the use of many commonly prescribed adjuvants in children's palliative care including antidepressants, anticonvulsants, corticosteroids and bisphosphonates. Although frequently used for the management of neuropathic pain in children, it was also not possible to make evidence-based recommendations for or against the use of tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), or anticonvulsants as adjuvant medicines. Also no recommendation was made regarding the risks or benefits of ketamine or systemic local anesthetics' as adjuvants to opioids for the treatment of neuropathic pain in children. The quality of current evidence, and risks and benefits of different treatments, is summarised in the WHO Document. [184] It is sometimes helpful to discuss this with parents and carers, particularly when prescribing medication off license or off use as it can cause anxiety (therefore it can be helpful to obtain informed consent for the use of these medications).

In reality, however, when faced with the symptoms of very sick and dying children, many of these adjuvant medications are trialled with anecdotal benefit to patients reported. Small case reports and series have been published but robust data is unavailable due to the scientific, ethical and practical challenges of drug related research in this area of practice.

Pain Syndromes

Bone Pain

Bone pain is a common symptom in children seen by palliative care teams. Its association with cancer is well known, but what is often overlooked is that it is also an important problem for many children with non-malignant conditions.

Bone pain associated with secondary distortion of the normal skeletal structures may occur in children with chronic neurological conditions (such as cerebral palsy or those with neuromuscular weakness) and can be exacerbated during periods of growth. Non-ambulatory children with chronic conditions can also have low bone density and an increased tendency to non-traumatic fracture, or fracture with minimal trauma, such as that caused by moving and handling.

Pathological involvement of bone from systemic disease, e.g. mucopolysaccharhidosis, or primary defects of structural bone proteins, e.g. osteogenesis imperfecta, often results in bone pain as a prominent feature. Other causes of bone pain in children includes osteopenia from systemic treatments such as prolonged steroid use in cancer. Children in sub-Saharan Africa with HIV/AIDs often have decreased bone mineral density likely to be a result of malnutrition and mineral and vitamin deficiency. Bone pain in this group can be due to multiple causes including: osteopenia as a result of bone loss and altered bone metabolism; cancer; and infections such as osteomyelitis or septic arthritis.

Cancer induced bone pain has been reported to be the most frequent single symptom of malignant disease and is associated with primary bone tumours, metastatic tumour and infiltrative bone marrow disease in haematological malignancy. The effective management of bone pain relies upon an individualised treatment to the identified cause and the clinical condition. Treatment of bone cancer pain usually requires a multidisciplinary approach such as an orthopaedic intervention, palliative radiotherapy alongside disease modifying treatment (chemotherapy) and supportive care (analgesic and integrative therapies). Newer approaches such as the use of radiopharmaceuticals and interventional techniques (radioablation, magnetic resonance-guided ultrasound) have shown promising results in relieving pain in focal metastatic disease in adults and if accessible, might be considered if other treatments fail.

Although there is little evidence for the use of bisphosphonates as an adjuvant, there is increasing experience with use in children with congenital and acquired forms of osteopenia, but little data in terms of analgesic efficacy and safety with long term use.

Muscle spasm

Episodic pain related to muscle spasm is common. A significant source of discomfort in children with neuromuscular conditions and severe neurological impairment, triggers for muscle spasm might include: constipation, seizures, gastro esophageal reflux, and discomfort from orthotic supports. Management is often multimodal and requires understanding the child's baseline tone and directing treatment at probable triggers. For example, manging simple issues, such as constipation and increased seizure activity, may be effective Use of non pharmacological strategies are often particularly helpful. Antispasmodic agents, such as baclofen and dantrolene are also useful but can have detrimental side effects (including sedation and hypersalivation) especially in children who have focal hypertonia or mixed tone disorders. Targeted therapies such as botulinum toxin, surgical intervention and intrathecal drug delivery are becoming more common and reduce the systemic side effects of medication. Although anecdotal practice supports the use of opioid prescribing in children with muscle spasm and non-malignant disorders, trial withdrawal of long-term opioids should be considered on a regular basis as the cause for the spasm may dissipate with time.

Neuropathic pain

Neuropathic pain arises as a consequence of a lesion or disease affecting the somatosensory system [186]. Neuropathic pain can be exceptionally severe and disabling. It is a particularly challenging diagnosis in children due to heterogeneity of conditions, diagnostic uncertainty and unknown trajectories.

If available the child's own description provides the best indication that the pain may be neuropathic. Children may describe sensory anomalies such as numbness, itching, tingling or burning sensations. Unusual expressions such as 'shivering', 'fizzing', 'tickling' or 'pricking' should be a signal that there is a neuropathic component to the pain.

In adult practice, assessment and diagnosis is becoming more rigorous, with amongst other things, the presence of pain with a distinct sensory distribution in a corresponding body part, indication of sensory signs within the area and confirmation of the lesion by a diagnostic test [187, 188]. Paediatric practice is some way behind as many children and infants with a possible diagnosis are not able to communicate making it very difficult to elicit sensory changes.

Any damage to the nervous system presents a potential risk of the development of neuropathic pain. Damage can range from single nerve involvement to complex genetic disorders that are thought to compromise the normal working of the nervous system and result in abnormal pain signals.

Cerebral Irritability

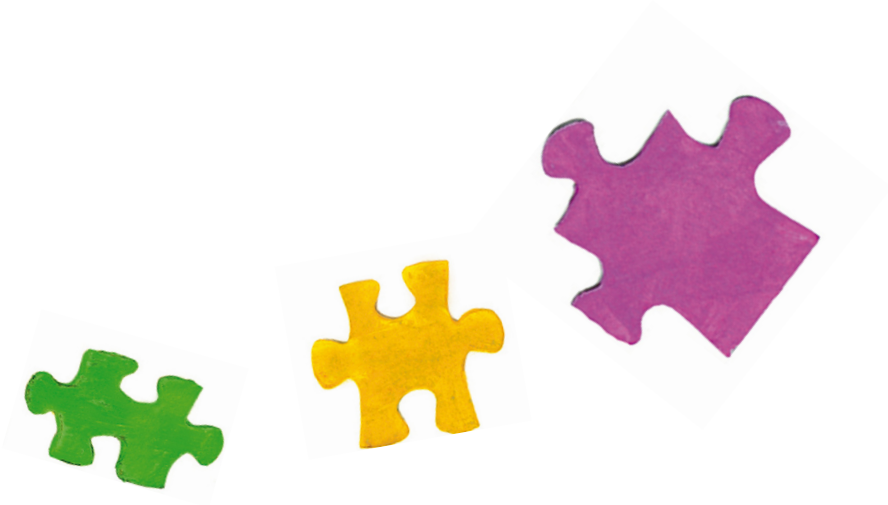
Cerebral irritability is a term used to describe the clinical presentation of persistent, unremitting agitation and distress. In the children's palliative care setting cerebral irritability is most often associated with the nonverbal child with severe neurological impairment but may also be seen in infants presenting with an acute illness, children with progressive, often neurodegenerative disorders (adrenoleukodystrophy, AIDS encephalopathy) and occasionally towards the end of life in children with malignancy. Cerebral irritability can be confused with an agitated delirium at the end of life although clinical management, at this stage, is very similar.

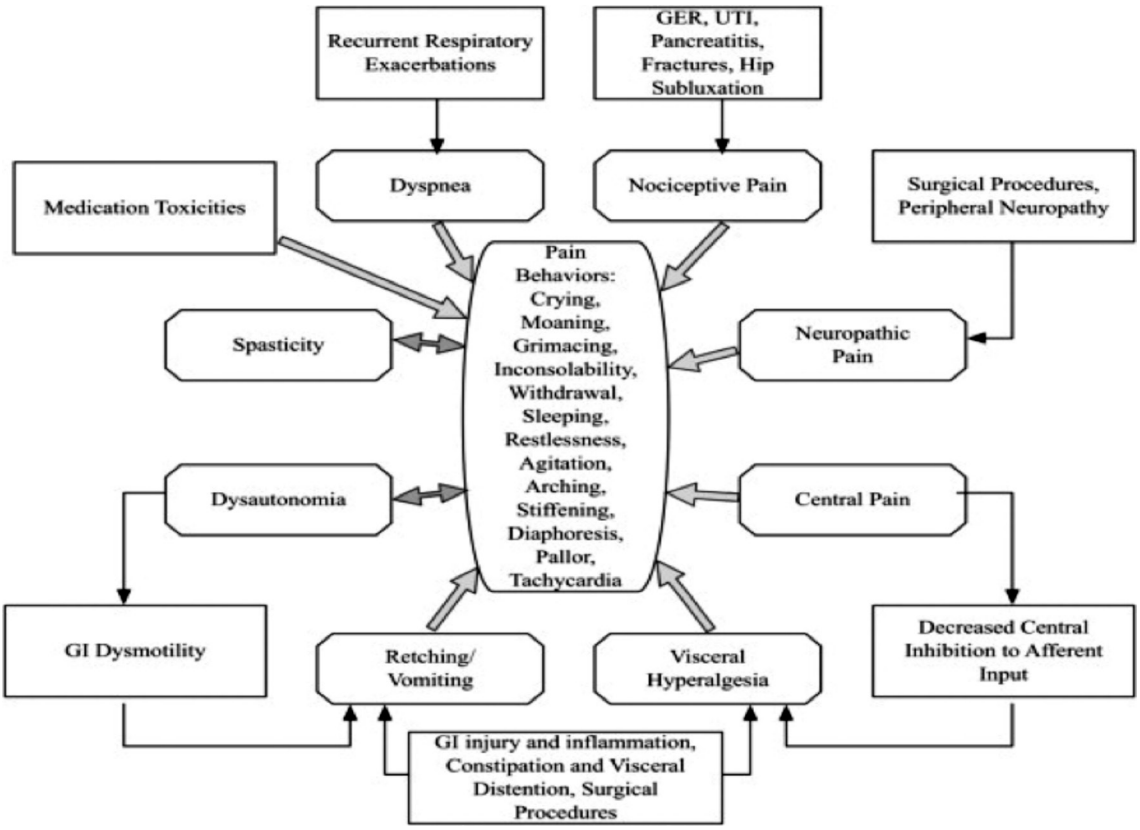
Cerebral irritability describes a constellation of features, which are thought to be the end point of a variety of different processes resulting in similar clinical symptoms and signs. These processes may be pathological or, as in many children with severe neurological conditions, of unknown aetiology. There are various hypotheses as to potential causes in this particular group of patients including central pain and visceral hypersensitivity (see below).

Classical symptoms in an infant or non verbal child with severe neurological impairment include an unrelenting high pitched scream and other pain related behaviours such as an increase in tone (spasticity) and/or seizures, sleep-wake cycle disruption, autonomic dysfunction (sweating, paradoxical bradycardia), increase in secretions, vomiting, retching and 'feed intolerance'. If these symptoms present as a sudden change in behaviour, a hospital review may be required with appropriate investigations to identify the source and exclude a reversible cause. However, in the neurologically impaired child, this behaviour can evolve over time and become a chronic problem.

It is a commonly held belief that cerebral irritability in a neurologically impaired child in the absence of pathology is due to an abnormal brain, and abnormal neurological processing. In this situation it is difficult to know whether the child with severe neurological impairment and cerebral irritability is also experiencing pain. [189] Morally and ethically the assumption has to be that pain is a factor in cerebral irritability until proven otherwise. This is reinforced by the fact that most of these children will be known to have an alternative baseline behaviour when they are not distressed, that the reversible causes of irritability have been excluded and the pattern of cerebral irritability mimics previous pain behaviours that have had a bona fide cause.

The most important aspect of managing this condition is recording a detailed history and evaluation of the child. In the case of chronic cerebral irritability, it may be necessary to request a symptom diary to establish temporal factors relating to the irritability and to understand the impact upon the child and family. Exclusion of all other causes of pain and irritability, with relevant investigations should be undertaken. If the cause of the cerebral irritation is known and reversible, then treatment will obviously be directed towards the cause.





Sources of Pain Behaviour in Children with Severe Neurological Injury. From [189] (with permission).

Central Pain

Central pain arises from damage to any part of the central somatosensory system, that is, those parts of the central nervous system (CNS) that are specialised for pain perception.

Conditions known to cause central neuropathic pain in adults, for example multiple sclerosis and stroke are rare in children. However, many other life-limiting conditions in childhood could potentially be the cause of central pain. [190] Neurodegenerative conditions and the consequences of hypoxic or traumatic brain injury can cause a range of different types of damage to the CNS, including disordered structure, abnormal neuronal migration and myelination, and/or abnormalities of normal neurological systems at the cellular level. A familiar clinical picture in paediatric palliative care is one of persistent screaming and distress, and alongside visceral hyperalgesia, central pain is an important differential diagnosis of 'cerebral irritiability'. However, it is usually a diagnosis of exclusion and as yet with little or no evidence base, only exists as a theoretical diagnosis within the field when considering causes of cerebral irritability in the neurologically impaired child.

Visceral Hyperalgesia

Visceral hypersensitivity or hyperalgesia is an altered response to visceral stimulation resulting in activation of pain sensation.

Visceral hypersensitivity has been hypothesized to be a possible cause of cerebral irritability in children with severe neurological impairment and may manifest as feeding intolerance presenting with symptoms of irritability. [191] Chronic cerebral irritability in children with neurological impairment is often temporally related to gastrointestinal symptoms and signs indicating feed intolerance (gastro oesophageal reflux, malabsorption and gut dysmotility), including flatus, retching and vomiting and spasmodic pain are frequently seen despite adequate treatment of constipation and gastro oesophageal reflux. [189, 192]

Drug management directed at central neuropathic pain and visceral hypersensitivity has been poorly studied and, in adults, central neuropathic pain has been classically difficult to treat. Approaches with medication would usually involve a trial of adjuvant agents including tricyclic anti-depressants, anti-convulsants and NMDA receptor antagonists.

Cancer pain

As cancer progresses, increasing disease burden results in numerous symptoms with evidence showing pain to be a very common problem, particularly towards the end of life. Understanding and diagnosing the cause(s) of pain is based upon knowledge of disease pathology and clinical signs. Pain can be a mixture of pain types, both neuropathic and nociceptive (somatic or visceral) pain, depending on pathology. Frequently, the anticipation of pain or the assumption that pain must be present, particularly in the non-verbal child who is quiet and withdrawn, can lead to trialing analgesia and assessing behavioural response.

With locally advanced disease palliative radiotherapy can improve analgesic requirements particularly when it is offered in combination with other treatment modalities. Not infrequently palliative chemotherapy may also be offered in the hope of slowing disease progression and improving symptoms but there is little evidence to show that it improves analgesia.

There is increasing experience with anaesthetic or neurosurgical analgesic options, for example epidural/ intrathecal infusions or neurolytic blocks, in children with advanced cancer. Generally these are offered when medication has failed. Epidural and peripheral nerve catheters can be used successfully despite typical contraindications (thrombocytopenia, fever, spinal metastasis, vertebral fracture) and, depending on local community service support, does not necessarily prevent patients from being cared for in their preferred setting.

Use of multiple drugs and the continual addition or increment of medication, without consideration for withdrawal or efficacy of drugs, should be avoided. Of particular concern can be the phenomena of opioid induced hypersensitivity (OIH). This may well go unrecognized and is significantly under reported in children. OIH is broadly defined as a state of hypersensitisation caused by exposure to opioids. The state is characterised by a paradoxical response whereby a person receiving opioids for the treatment of pain may become more sensitive to pain. It is thought to be due to adaptive (neuroplastic) changes in the central and peripheral nervous system.

It is important to note that OIH and opioid tolerance are two distinct pharmacological phenomena that can result in similar net effects on opioid requirements. However, increasing the dose of opioid in OIH will paradoxically aggravate the problem and worsen the patient's pain. Considerable diagnostic confidence is required to reduce the opioid consumption in a child with end stage cancer. It is therefore recommended to rotate the opioid, potentially in combination with an NMDA receptor antagonist. Methadone has been reported to have efficacy in reducing high dose OIH.

Intractable Pain

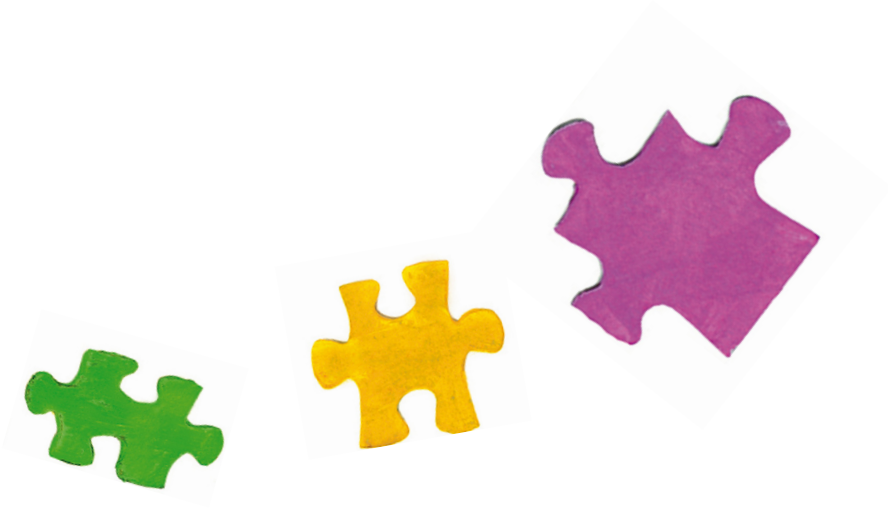
Palliative sedation in end of life care is an accepted but controversial means of providing relief from otherwise refractory and intolerable symptoms and distress. The European Association for Palliative Care defines palliative sedation as 'the monitored use of medications intended to induce a state of decreased or absent awareness in order to relieve the burden of otherwise intractable suffering in an ethically acceptable manner'. The use of sedation in the setting of refractory pain assumes that all possible analgesic therapies have been employed and that there is no acceptable means of providing analgesia without compromising consciousness.

There is little information regarding the practice of palliative sedation in children. A recent review of the paediatric literature offers some insight into practice by stating that sedation in children remains controversial and is influenced by educational, cultural, legal, moral and health policy issues- so the interplay of both internal and external factors is complex. Importantly, it highlighted that physical symptoms are described as an indication for the practice of sedation but existential suffering must also be considered in the evaluation of refractoriness of symptoms [193]. Existential suffering of parents must also be acknowledged and addressed, as their distress behaviour may impact upon the child and the clinical team.

For the specific cohort who requires sedation for intractable pain recommended therapeutic modalities include neuroleptics, opioids, benzodiazepines, and anaesthetic agents such as propofol.

Conclusion

Although managing pain in children is only one of the aspects of palliative care, it is a core task that must be approached with meticulous attention. A child's pain should be considered in the context of the child as a whole person; their family, their environment, their developmental level, reasoning and understanding and the existential depth of their suffering. Pain management must address both the cause and the contributing factors, use medication and non pharmacological approaches and be continually reviewed and evaluated to make sure that the absolute best that can be done is achieved.



Psychological

[194-206]

The whole subject of child psychiatry in paediatric palliative care is vast and complex. The symptoms that present themselves are often a reflection of the internal stresses and strains within a family. Helping the parents cope with a particular illness is as important as helping the child itself. All parents with healthy children who have been up with them a few nights during a trivial illness will have a brief understanding of the tiredness, fatigue, frustration and worry that is constantly felt by the parents of life-limited children. The children themselves can also be left feeling frightened and guilty about their illness. There is no magical secret in helping these children and families. It requires good old-fashioned care and compassion. We need to give the family our time and we need to be prepared to listen. Giving honest answers to straight questions can allay fears and anxieties. A doctor or specialist counsellor is not necessarily the best or only person to tackle these issues. Our experience is that children and their families often prefer to talk to the nurses, teachers or priests. All these carers will need support to cope with the issues.

When, however, despite our best efforts, a child is manifesting clinical symptoms of anxiety or depression, we must not be afraid of using medication as an adjuvant to our counselling and support. Symptoms manifested by children are not the same as those manifested by adults. They are also very dependent on the age and development of the child. Younger children tend to regress and develop behavioural problems; older children may have nightmares, insomnia or become introspective. It is very difficult without experience to diagnose many of the psychological problems that these children can get. Fortunately a child psychiatrist can be very helpful and supportive. Also it is worth trusting the natural instincts of the parents and nurses who often know the children better than we do.

Anxiety

Particularly in the terminal stages, anxiety can be helped with a number of drugs each of which can have different benefits. Midazolam and Methotrimeprazine are two of the first line drugs for treating anxiety (although Midazolam can cause paradoxical agitation). Chlorpromazine works well and its sedating effects can be helpful in certain cases. Diazepam also has sedative effects and its rectal form can be used in urgent cases when agitation is a major problem. Haloperidol has an important role in treating confusion.

Insomnia

A problem not only for the child but also for the parents. Parents may benefit from the use of complimentary therapies, particularly aromatherapy and massage, which can help to reduce tension and anxiety and promote relaxation and hopefully sleep. Temazepam can be used for the older child. Triclofos or Choral are useful in the younger child. The antihistamine Promethazine can be used in the milder cases. Melatonin can help in managing insomnia and appears to be used increasing in children with special needs. However it is unlicensed in the UK for this and so many general practitioners may feel unhappy about prescribing it.

Depression

Treatment has the disadvantage of taking two to three weeks to work. The older child may benefit from serotonin re-uptake inhibitors such as Fluoxetine. Paroxetine has been used in the past but is now no longer licensed for use in children due to its side effects. There is currently a lot of controversy about the other forms of serotonin re-uptake inhibitors (except for Fluoxetine) and in view of this it is probably best to avoid them unless there is no other option.

Parents and other family members may also require medical treatment.

Respiratory ventilation and management

[207-213]

Physiology of breathing

During normal respiration an increase in CO2 levels and decrease in O2 levels in the blood triggers a response in the brain. Information is then transmitted to the muscles used in respiration.

The intercostal muscles, between the ribs, contract which causes the ribs to move upwards and outwards. At the same time the diaphragm contracts and moves downwards. The lung tissue is enclosed in the pleura, which is a thin covering that protects and cushions the lungs; it is made up of two thin layers which are separated by a small amount of fluid. The pleura is attached to the ribcage and diaphragm, as the ribcage moves upwards and outwards and the diaphragm moves downwards the pleura follows. This movement increases the space inside the lungs with the same amount of gas present. The pressure inside the lungs falls, whilst the pressure outside the lungs, in the atmosphere is higher, air is then sucked in to the lungs to try to equalise the pressure.

Children/young people can have blocks on this process of information and action at various levels.

Neurologically

Interference in information being sensed, interpreted or transmitted can create a need for mechanical ventilation. If the part of the brain which controls breathing is damaged or affected by disease, e.g. Congenital Central Hypoventilation Syndrome (Ondine's Curse) or a spinal cord injury at, or above the level at which messages are relayed, then the information is not processed.

Physically

Muscle weakness or deformity, such as scoliosis, Duchenne muscular dystrophy or spinal muscular atrophy, can prevent effective movement and breathing, therefore reducing lung volume.

Respiratory

Prolonged periods of low volume breathing can result in the chest wall becoming less compliant and making it more difficult for respiratory muscles to expand; the loss of elasticity can prevent air from being drawn in. Children/young people with low lung volume become more prone to chest infections, which are slower to clear due to ineffective coughing. Also, there is an increased risk of aspiration if their swallowing reflex is weak.

Breathing out is usually a passive process and does not require strong muscles. However, coughing does require effective contraction of expiratory muscles and normal function of upper airway muscles.

With prolonged periods of low lung volume the chest wall becomes stiff and less compliant and it becomes increasingly more difficult for respiratory muscles to expand.

This is usually the reason people are offered life enhancing ventilation at night when they do not normally require ventilation during the day.

Hypoventilation

During sleep, inspiratory and expiratory muscles relax and breaths become smaller and oxygen levels reduce. If respiratory muscles are already weak then oxygen levels which are already low decrease even more which is known as under ventilation or hypoventilation.

Mild cases of hypoventilation do not display any symptoms and is only noticed during REM sleep with a drop in oxygen levels and a rise in carbon dioxide levels. However, if the condition progresses, it can lead to low oxygen and high carbon dioxide levels during the day.

Symptoms of hypoventilation

- Morning headaches
- Lethargy
- Breathlessness
- Disturbed sleep
- Sweating at night
- Poor appetite
- In young children, failure to thrive/poor weight gain

Ventilation

Positive pressure ventilation-pressurised gas is forced into the lungs from the ventilator, forcing them to expand due to the air movement. There is a risk of lung damage if the pressure is too high, which can cause barotrauma or a pneumothorax.

After a short pause, the ventilator lowers the pressure and the lungs return to their previous size and air leaves the lungs.

A small amount of pressure is kept in the lungs so the alveoli remain slightly inflated making the process of breathing easier.

Terminology

PIP (Positive Inspired Pressure/IPAP-Inspired Positive Airway Pressure)
The airway pressure that the alveoli expand to, during inspiration.

PEEP (Peak End Expired Pressure/EPAP – Expired Positive Airway Pressure)
The pressure in the airway, at which the alveoli are kept open to at the end of expiration.

Trigger
The level of negative pressure generated by the child/young person, which will trigger the ventilator to support a breath. This is used as a way to build up the muscles required for respiration.

Inspiratory Period
The length of time, in seconds, in which the breath is delivered into the lungs.

I:E ratio (Inspiratory:Expiratory ratio)
The time, in seconds, for the inspiratory and expiratory periods of ventilation.

Tidal volume
The volume of gas generated on each breath, measured in millilitres.

Minute volume
The volume of gas generated over a minute, it is calculated by multiplying the tidal volume by the respiratory rate per minute. This is measured in litres.

Modes of ventilation

CPAP (Continuous Positive Airway Pressure)
A constant flow of positive pressure on inspiration and expiration allows less work by the respiratory muscles. The bronchioles and alveoli do not collapse at the end of expiration so significant pressure is not required to re-expand them. This is a support mode of ventilation and requires the child/young person to trigger every breath.

BiPAP (Bi-level Positive Airway Pressure)
This is also a support mode of ventilation, airflow is strongest when the young person breaths in, encouraging increased air into the lungs. Airflow pressure is lowered when they breathe out but remains positive. The continual positive pressure "splints" the airway open. However this is not suitable for young children as a negative pressure needs to be generated to alter the pressure level for inspiration.

Pressure Control Ventilation
A control form of ventilation; where a prescribed number of breaths are delivered to a maximum pressure setting. However if compliance in the lungs changes due to secretions or tension in the lungs then a reduced volume of gas is delivered, which will affect oxygen uptake and carbon dioxide clearance. This is the preferred form of ventilation in small children as setting a maximum target for pressure will reduce the risk of barotraumas and pneumothorax.

Volume Control Ventilation
A control form of ventilation; where a prescribed volume of gas is administered. The ventilator will administer the volume at whatever pressure it needs to generate to get the gas in. It is usually used in older children and those who have stiff lungs. It is not recommended in young children as it could result in barotraumas and pneumothorax.

Pressure Support
This is used in conjunction with forms of support ventilation which have a prescribed number of breaths with a set PIP and PEEP. When the child/young person takes a spontaneous breath on the ventilator, this breath is then supported by the pressure support which is added to the PEEP, creating a PIP value which will differ from the prescribed level. This allows the child/young person to take bigger spontaneous breaths than they would normally be able to manage unsupported, improving oxygen intake and carbon dioxide clearance.

SIMV (Synchronized Intermittent Mandatory Ventilation)
This is a support form of ventilation. The length of each breath is calculated by a Continuous Mandatory Ventilation (CMV) rate, an SIMV rate is then set and these are administered by the ventilator, the SIMV rate will be less than the CMV rate. A gap is then given to allow the child/young person to instigate breaths themselves, these breaths are supported by the pressure support which will also have been prescribed.

Observations

It is recommended that any child/young person who is on full face mask CPAP or BiPAP should have saturation monitoring even if they are not on any additional oxygen. As they are wearing a full mask which is securely fixed to their face they are at risk of aspiration if they vomit. The ventilator will not always alarm as it will continue to deliver the gas at the prescribed settings. The only indicator will be a drop in oxygen saturations due to aspiration.

Hourly observations of ventilator settings should be recorded to ensure the ventilator is delivering the prescribed settings. Delivered settings may be different to prescribed settings if there are physiological changes in the child/young person. These can include compliance changes in the child's/young person's lungs, position of the mask or PEEP valve, or airway obstruction with the position of their head or neck. These will not always trigger the alarms if the delivered setting are borderline acceptable to the alarm settings.

- Look at chest movement to see if it is good or poor. Listen to breath sound, do they sound steady and regular or restless?

- Check whether the child's/young person's colour is appropriate to their oxygen saturations.

- Listen to the noise of the ventilator, are there any change to sound level or pattern?

- Is there a leak from the circuit or mask?

- Check that the machine is not overheating.

Care needs to be taken with the positioning of the face mask in CPAP or BiPAP. The mask needs to fit securely, but does not need to be over tightened. This could result in skin ulceration or eye irritation if the masks are fitted incorrectly. If straps are used rather than a hat, it is usually beneficial to put gauze dressings over their ears to prevent irritation from straps which may be tight. If the CPAP or BiPAP is given without humidification there is an increased likelihood of a dry mouth, nasal congestion and nose bleeds. Regular mouth care is required.

Face mask ventilation will also blow air into the stomach as well as the lungs, this can result in bloating and stomach ache.

If a child/young person is on life-enhancing ventilation they will only have one ventilator which should be kept in a working condition and charged up at all times. If they have life-sustaining ventilation they will have two ventilators which should be with them. One will usually be a dry circuit with a HME (Heat Moisture Exchange) device which uses the heat and moisture from the expired breath to warm and humidify the inspired breath. The other on warmed humidification, the humidified ventilator is used at night for at least eight hours.

Life-sustaining ventilation is invasive ventilation via a tracheostomy which bypasses the body's normal route of warming and humidifying the air breathed in via the nasal passages. This can cause problems with cold dry air going straight to the lungs which can cause irritation and thick secretions. However, it is not practical to use a humidifier with the ventilator during the day so ventilation is provided via the dry circuit with a HME device alternating at night with a humidified ventilator. Both ventilators should be checked daily, kept in working condition and charged up.

Signs of poor ventilation

- Poor chest movement.
- Child/young person is restless.
- Colour is pale, possibly with cyanosed fingers and toes.
- Low saturation levels, but they may not be low enough to trigger the alarms.
- Increase in heart rate.
- Change in noise from the ventilator.

Troubleshooting

- Change the child/young person's position to improve the airway.

- Check the child for other issues, whether too hot/too cold/unwell.

- Ensure their nose is not blocked.

- Ensure mask is fitted correctly.

- Ensure oxygen saturation probe is fitted correctly.

- Check ventilator settings are correct and remain locked.

- Check that there are no kinks or splits in the ventilator tubing and that all connections are secure.

- If a full face mask is used ensure that the blow off valve is clear and working (or else there is no way to release the CO2 the child/young person is breathing out).

- Do not replace the mask or change connections to a ventilator that does not have a blow off valve.

Alarms

Different ventilators will have slight variations in the type and sound of alarms. It is important to familiarise yourself with the ventilators used and their alarms, how to correct the problem, reset the system and silence them.

Common alarms can include:

Power failure: If there is an interruption to the electrical supply.

Low battery level: When running on a battery the alarm will trigger when there is only 10 minutes of battery life left.

Empty battery: Once the battery is completely discharged and an external electrical supply is required.

High pressure alarm: When pressure in the circuit is higher than the high pressure limits setting. The ventilator will stop generating a breath. This can be the result of a change in the physical condition of the child, such as increased secretions, or due to a kink in the circuit.

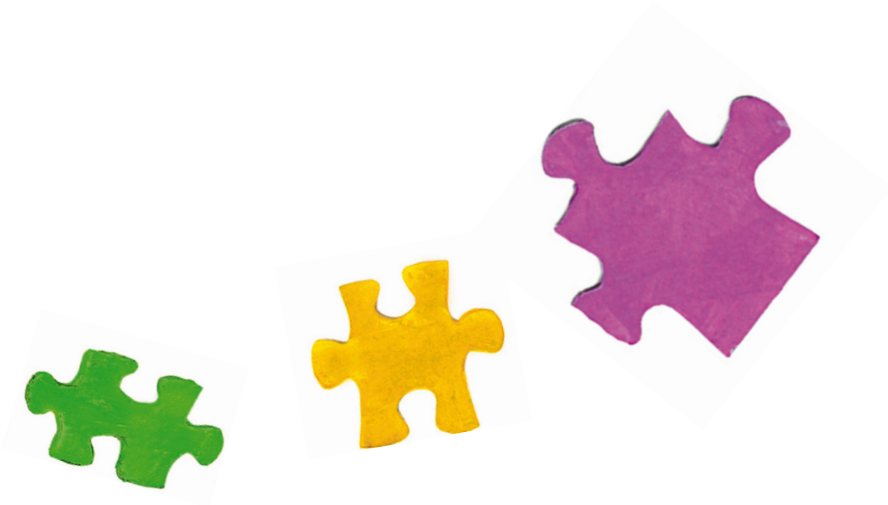
This will require an urgent review of the child/young person, and an alternative form of ventilation may be required, such as a bagging circuit, to ensure ventilation is maintained until the cause is ascertained.

Low pressure alarm: When pressure in the circuit falls below the pre-set low pressure alarm. Usually caused by a disconnection from the ventilator, this will require an urgent review of the child/young person.

Low minute alarm: Can occur on ventilators with a prescribed volume of gas to be delivered. If the child/young person does not take as many breaths when asleep, this alarm may occur as the volume of gas inspired per minute is lower than the alarm setting.

This will also occur when the ventilator is disconnected and the low pressure alarm is triggered.

Fault: May be triggered by an internal fault.



Skin

[214-216]

Management of skin problems is often challenging. This is one subject where prevention is better than cure. Our children are often wasted and immobile. Because the metabolism of the body enters a catabolic phase during severe illness the skin becomes very vulnerable to breakdown and subsequent poor healing. Good nursing care is required to predict where potential problems may occur. Special mattresses, aids and appliances can be organised. Turning of the child needs to be frequent and regular. Skill is also required in knowing how to move the child. Hoists and harnesses may be needed.

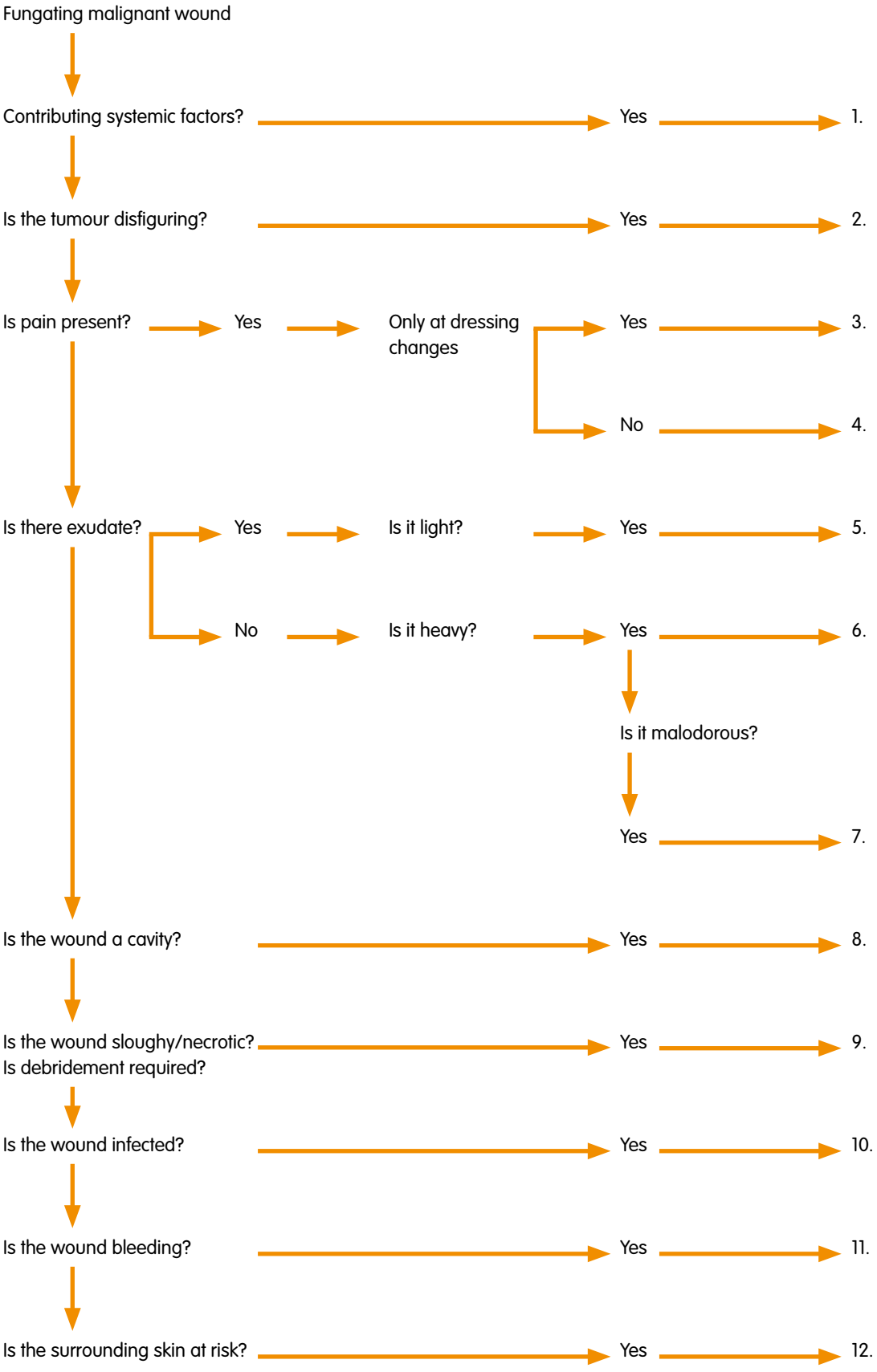
- Initial problems tend to start from pressure sores or friction burns.
- The skin at this stage can be protected with OpSite, Tegaderm or Cutifilm.
- Care must be taken when removing these dressings so as not to further damage the skin.
- Once it breaks down then DuoDerm or Spyrosorb can be used.
- Infected skin ulceration will require IntraSite gel or Lodosorb paste to remove discharge or necrotic tissue (top dressings can be OpSite or Tegaderm).
- Cavities can be packed with Kaltostat or Sorbsan. Re-dressings are done as required depending on the amount of exudate.
- Oral antibiotics may be necessary if cellulitis or discharging pus is present. Because many of the children may be on anti-epileptic drugs, Erythromycin must be used with caution.
- Fungating tumours when infected can be very smelly. This causes great distress to the child and family. Metronidazole orally or topically is very effective and a deodoriser can help. The skin can also be dressed with Actisorb (charcoal dressing) to help reduce the smell. Honey and sugar can be used topically to reduce the smell of ulcers and they are also bacteriostatic.

Types of dressings and their use

Type	Example	Benefit	Notes
Films	OpSite, Tegaderm, Cutifilm.	Semipermeable, totally occlusive, allow observation.	Cannot absorb exudates.
Hydrocolloids	Granuflex, Comfeel, DuoDerm, Spyrosorb.	Occlusive but absorb exudates.	Facilitate autolysis of slough and eschar.
Hydrogels	IntraSite gel, Lodosorb.	Absorb large amounts of exudates.	Useful for cavities. Can damage healing tissue if allowed to dry.
Alginates	Kaltostat, Sorbsan.	Highly absorbent, haemostatic.	
Foams	Lyofoam, Silastic.	Highly absorbent, good for deep cavities.	Not for wounds with sinuses.
Low adherent	Release, Mepore.	Protects wound surface, absorb some exudates.	If dried out then wet to remove.

(Table adapted from commonly used dressing Symptom Management in Advanced Cancer by Robert Twycross [217]).

Flow chart of management of fungating tumours



1. Consider potentially treatable factors:
- Reducing or stopping steroids.
- Improving nutrition.

2. Modify the size and appearance of the tumour:
- Surgery by debulking or excision.
- Radiotherapy.
- Chemotherapy.

3. If pain present at dressing changes:
- Short acting analgesic e.g. buccal Diamorphine.
- Topical anaesthetic agents e.g. Lignocaine.
- Entonox.

4. If pain present all the time:
- Review analgesia.
- Consider topical Diamorphine in dressing.

5. For light exudates:
- Semi-permeable film dressing.
- Hydrocolloid interactive dressing.
- Low adherent dressing.
- Alginate dressing.
- Hydrophilic foam dressing.

6. For heavy exudates:
- Hydrocolloid interactive dressing.
- Hydrogel with secondary dressing.
- Alginate dressing.
- Hydrophilic foam dressing.
- Use of paediatric stoma bags.

7. For malodour consider:
- A counter odour e.g. household air freshener, ostomy agents, aromatherapy oils.
- A deodorant e.g. Naturcare or electric deodoriser.
- Metronidazole either topically or systemically.
- Live yoghurt.
- Charcoal impregnated alginate or foam dressing.
- Totally occlusive dressing e.g. OpSite or almost totally occlusive dressing e.g. Granuflex.

8. If a cavity is present consider:
- Cavity dressing e.g. alginate.
- Silastic foam if wound is clean.
- Foam dressing.

9. If debridement is required consider:
- Surgery.
- Enzymes e.g. Varidase.
- Hydrocolloid paste with dressing.
- Hydrogel.

10. If the wound is infected:
- Topical Metronidazole.
- Irrigate with IV Metronidazole solution.
- Systemic antibiotics.
- Honey and icing sugar dressing.

11. If the wound is bleeding:
- Calcium alginate dressing (haemostatic properties).
- Topical adrenaline 1:1000 solution.
- Radiotherapy.
- Use non-adherent dressings and soak dressings off with normal saline.

12. If the surrounding skin at risk:
- Protect surrounding skin with barrier ointment.

Care must be taken with dressing to:
- Remove dressings without pain.
- Make dressings cosmetically acceptable to the child.
- Lengthen the time required between dressing changes.
- Understand the cost effectiveness in terms of time and money for all the different types of dressings.

Spiritual pain

This chapter is taken from information written for parents of life-limited and life-threatened children. Although it is not directed primarily at practitioners, it will be useful for talking to parents about addressing spirituality with their children, and will also help you find a suitable approach when talking to children about their illness, and about their death.

Introduction

Spirituality and spiritual care are the proper concern of all who work with you as a family. It should be recognised that the issues of spirituality and religion are very important. However, they are two different aspects of care. It has been suggested that we all have a spiritual dimension and needs, and some people also have religious needs. It is possible to have spiritual needs independently of religious needs. Religious needs are to do with a shared faith, beliefs, practices and rituals that help a person make a connection with their 'god'. Spiritual needs are to do with our search for meaning and purpose and a sense of well-being and wholeness.

These next few pages are not about answering all the questions you may now have about 'Why my child' or 'Why our family' or 'What is the meaning of life' and all those very difficult questions you now face with your child and family. Nobody can give you the answers to these profound questions you, your family or your child now ask.

Within this section no answers are given, but it is suggested that you do something that is far from easy for anyone to do. That is to sit with your child and try and stay in that difficult place and listen to your children's questions and hear their fears. You will not be failing your children by not knowing the answers to some of the questions they may now have. Not knowing can be a place of strength and maybe even reassuring for your child.

I once read a book which that was called, *"Failure, the gate way to hope"*, which I found very reassuring in itself. We won't always get it right, so don't expect to. Don't go looking for perfection. You will struggle with your own doubts as well as those of your child and family, but the struggle will be worth it.

This advice focuses on the needs of your child who is ill, but they are just as applicable to you as parents or to your other children. I would suggest that we all have spiritual needs to which we must attend. Our spirituality is something that cannot be turned on and off at will, it is a part of us and is always present. Your spirituality cannot be isolated from all that makes you who you are.

As a parent, you now find yourself on a journey, a journey that you have had no choice in taking, and would have preferred not to have started.

I have suggested that spirituality is about a 'journey' to the centre, to the heart of the matter, to our 'deep centre',

where sometimes we meet our pain and have to address it. Children do come readily equipped for their spiritual journey, in so far as they have an openness and awareness, which is often unique to a child's early years. As we get older this openness and awareness gets pushed to one side.

Definition

Spirituality is what gives a person's life meaning. It is about how people view the world they find themselves in and this may or may not include a god figure or a religious faith. Spirituality is about how we view the world and how we react within it.

In talking about spirituality we need to bear in mind that we all come from different social and cultural contexts, that we each have a past and a future; and it is out of this setting that our spiritually will manifest itself. It is from this background or setting that your child's questions will flow. Therefore, you may well be the best person to offer this aspect of care, with help and support from others around you.

I have found that children with a life-limiting or life-threatening condition have a highly developed sense of their own spirituality, though they may not say or show it directly. It may well be deeper and more mature, than other children of their age and development. However, they may not always have the words or means of expressing it. Therefore, you as parents are very important, because you will be able to understand your child's language and play far better than anyone else.

Practicalities

If we are to understand our children, their spirituality and their needs, we must first reflect on our own spirituality and be prepared to question our own assumptions about spirituality and religion. How do we see spirituality in our own lives and the psychological influence it may have had on us coming from our past? The current situation in which you find yourself will challenge your value systems and notions of spirituality and cause you to reflect deeply. This process of questioning often happens and you need to know that it is not unusual and you should not be wracked with guilt for questioning.

Spiritual care is about responding to the uniqueness of your children and accepting their range of doubts, beliefs and values as they arise. It means responding to the spoken or unspoken statements from the very core of your children's being as valid expressions of where they are and who they are. It means being their friend, companion and their advocate in their search for identity on their journey and in the particular situation in which they now find themselves. It is to respond to them without being prescriptive, judgemental or dogmatic and without preconditions, acknowledging that your child and other members of the family will be at different stages on this very painful spiritual journey. In order to be able to respond to this call, you need to try and create a safe and secure place, which I have come to call a 'sacred space', where your children can express their inner suffering and know that it is alright to do so, that they will be heard and taken seriously. You can help them best by just sitting with them, watching with them, waiting with them and just letting them wonder. Take your lead from them, go with them, do not try to direct them, and use the language and imagery they use.

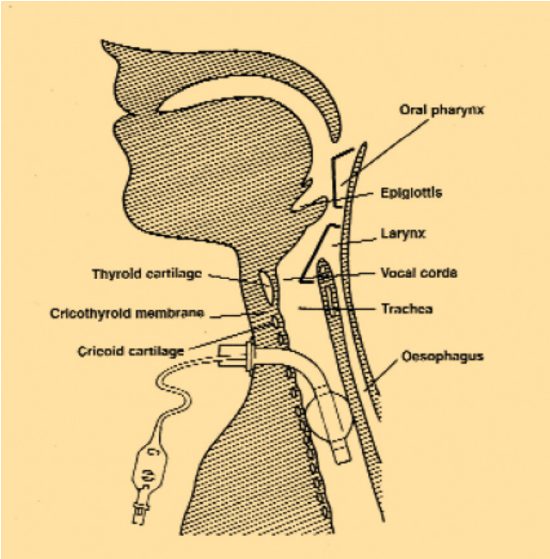
We need to be open to what our children have to teach us. We need to be prepared to learn from them. The skill here, as in other aspects of your children's care, is to be able to understand or 'crack' their code. We can start to do this, if we just sit with them, if we learn to watch, wait and wonder with them, if we take our lead from them, and be responsive to their needs, not the needs we think they may have, or our own needs. Never underestimate your child's understanding of what is going on. You may be surprised at how your child has an unclouded, clear way of thinking and their "take" on abstract ideas is often quirky, but relentlessly practical. This is the way in which they can help us with our struggle in trying to understand their suffering.

You may have discovered for yourself by now that you cannot fill the hole in a doughnut as much as you try to fill it, it just keeps disappearing out the back into some black hole. What you need to remember is that when you are with your child, the spaces or the gaps in the conversation do not need to be filled. This may be the centre of their journey and you just need to hold that space with your child and be present with them. *"Suffering is not a question that demands an answer; it is not a problem that demands a solution; it is a mystery that demands a presence."* (Source unknown.)

Tracheostomy care

What is a tracheostomy?

This is an artificial opening into the windpipe (trachea) which is held open by a tracheostomy tube. This helps the child to breathe easily; air now goes in and out through the tracheostomy, bypassing the mouth.



Indications for a tracheostomy

- A narrow upper airway.
- The need for long-term ventilation.
- Bronchial toilet.

There are several types of tracheostomy. They can be made of plastic or metal, may be cuffed (avoided in children), uncuffed, or fenestrated (with a hole in the canula to facilitate speech). The child will be given the one most suitable for his/her needs.

All children that have a tracheostomy must at all times have with them the following:

- Suction machine and charger.
- Appropriate size suction catheters.
- Change of tracheostomy tube – same size and one size down.
- Change of ties/tapes.
- Scissors.
- Water based lubricant.
- Normal saline and gauze.
- Water to clear tubing.
- Gloves.
- Change of Swedish nose.
- Most importantly, a capable adult to change a tracheostomy in the event of an emergency.

Prior to any procedure in relation to the tracheostomy it is important to reassure the child and explain as much as possible about the procedure to be performed.

Daily care

The tracheostomy stoma needs cleaning daily as tracheal secretions can infect the stoma site. Cleaning may need to be increased if child unwell or there are a lot of secretions. The stoma site is cleaned with normal saline and a cotton wool applicator. This is a time to inspect the stoma for any signs of redness or the presence of granulation tissue (excess new skin). If there is redness/irritation a sterile keyhole dressing can be applied between the skin and the flanges, taking care not to cover the tracheostomy tube.

The dressing should be changed regularly as wet dressings can cause irritation and infection.
BARRIER CREAM SHOULD NOT BE APPLIED.

If there is granulation tissue present discuss with a tracheostomy nurse specialist as this will need to be cauterised or removed.

Tape changes

The tracheostomy tube is held in place by either cotton ties or velcro tapes. These need to be changed daily or more frequently if soiled.

This is a two person procedure; one person secures tracheostomy in place, while the other person changes the ties or tapes.

Prior to any procedure ensure that all the necessary equipment is at hand:

- Two lengths of 1/4 inch cotton tape or Velcro ties.
- Normal saline and gauze to clean the skin.
- Tracheostomy tubes.
- Suction if necessary.

1. Position child on his/her back with the neck extended over a rolled towel.

2. One person secures tube in place, the other cuts and removes the soiled tapes.

3. Thread the end of one of the tapes through the tracheostomy tube flange on the far side and tie it to the other with three knots.

4. Repeat the procedure on the other side but instead of securing the tapes with a knot, just tie in a bow. Keep the tapes as unwrinkled as possible and try to achieve the correct tension before tying the bow.

5. Continuing to hold the tube, sit the child forward and with child's head bent forward it should be possible to place one finger between the ties and the skin. This is the safest recommended tension.

6. If tension is correct then change the bow to three knots securely.

7. If Velcro tapes used, remove soiled tapes, position new tapes, thread the Velcro part through the flange of tracheostomy, fasten and repeat on the other side, ensuring that the safe tension is maintained at all times.

Suctioning

Why suction?

- If secretions are allowed to accumulate they will block the tube.
- Secretions left in the tube could lead to infection.

When to suction?

- Noisy breathing (sound of air bubbling through secretions).
- Visible secretions.
- A cough that sounds like secretions are in the tube.
- Restlessness/crying.
- Increased respiratory rate.

Suctioning instructions

Make sure you have at hand all the equipment you need:

- Suction unit.
- Catheter (correct size) – new one for each suction.
- Connecting tubes if needed.
- Syringe of saline
- Bowl or bottle of water to clean the catheter.

1. Turn on suction pump and check pressure is correct as instructed.
2. Gently insert catheter into tracheostomy, ensure thumb is off port of suction catheter.
3. Apply suction, by covering the port with thumb and withdraw catheter. This should only take five or six seconds.
4. Repeat if necessary but allow child time to settle in-between.
5. Disconnect the catheter from the tubing and dispose of safely. Clear the tubing with the water provided.
6. Attach a new catheter to be ready for next time.

Each time you suction it is important to observe the secretions:
- Have they changed colour?
- Are they thicker than usual?
- Are you suctioning more frequently?
- Unpleasant smell?
- Tinged with blood?

If so, the child may have an infection. Their GP needs to be informed in case the child needs antibiotics.
Be aware that when a child has a chest infection he/she will require more frequent suctioning.

Changing tracheostomy tube

In a non-emergency situation leave tube change for one and a half hours after feed as child may vomit when upset. Tracheostomy tubes are usually changed weekly.

Prepare equipment

- Round ended scissors.
- Two lengths of 1/4 inch cotton tapes or Velcro tapes.
- New tube, check correct size and that the tube is intact.
- A smaller sized tube in case the correct size does not go in.
- Water based lubricant.
- Prepare tube, insert introducer, apply a small amount of lubricant on the outer tubing away from end of tube, place tube ready to use.

1. Position child as for tape change, older child can sit up.

2. Hold the tube (one person).

3. Second person cut and remove the dirty tapes and place clean tapes behind child's head.

4. First person holds tube; second person holds the new tube by flanges and positions the tip near the child's neck.

5. Gently remove the old tube following the curve of the tube. Same person firmly and gently slide in the new tube following the curve of the tube so as not to damage the trachea. Remove introducer if used.

6. Hold new tube securely.

7. If child is coughing allow to settle.

8. Check air flow through tube, child's breathing pattern and colour, suction if necessary.

9. Clean the skin around the tube. Tie the tapes.

10. Do not let go of the tube until the tapes are securely tied.

Humidification

The normal mechanism of warming and humidifying air is removed with a tracheostomy. Therefore most children have a Swedish nose applied to the tracheostomy to give dry humidification. Wet humidification may also be given by using nebulised saline.

Nebulising with a tracheostomy?

Medication checked and instilled into nebuliser as prescribed. The most important thing to remember is to stand next to the child with the nebuliser near the tracheostomy, to allow the nebulised medication to be given, but NOT to attach the nebuliser to the tracheostomy as this will cause major damage and restrict breathing.

How to recognise blocked tube

- Childs may be coughing vigorously.
- Difficulty breathing.
- Change in colour leading to unconsciousness.

Immediate action is required

1. Try suctioning.

If no better:

2. Cut tapes and remove tracheostomy tube. In long standing tracheostomies the tract will be well developed and no immediate action is required.

If still no better:

3. Insert new tube same size or if necessary a smaller size.

If still no better:

4. Insert a cut off piece of suction catheter to allow some air to pass through, call for help and phone 999.

If changing tube has resolved the problem, hold tracheostomy tube in place until another person arrives to help. Reassure child and allow to settle.

Suction only if necessary.

If a child stops breathing

1. Call for help if someone within earshot.
2. Check if child responsive.
3. Turn child onto back on firm flat surface.
4. Tilt head back slightly to expose tracheostomy.
5. Is tracheostomy blocked? Attempt suction.
6. Still seems blocked? Attempt to change tube.
7. Look, listen and feel for breathing.
8. If not breathing, shout for help get someone to dial 999.
9. Commence basic life support immediately.

DO NOT LEAVE CHILD ALONE, EVEN IF BREATHING RETURNS TO NORMAL.

Travel abroad

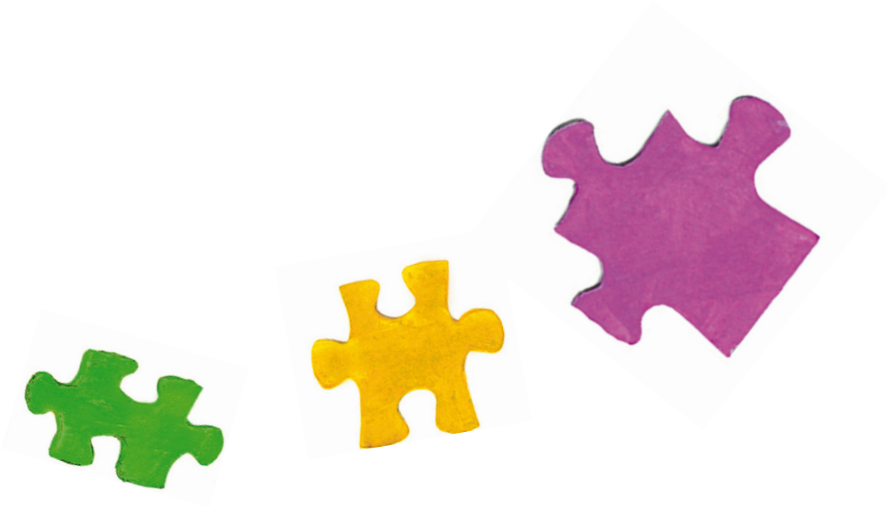
Many of our patients will have a desire to travel abroad during their limited life span. This can present particular problems in terms of carrying medication across borders. There are strict rules laid down by the UK Home Office in relation to which medication can be carried and which requires a special Home Office personal export license. These restrictions not only concern controlled drugs but can affect other types as well. There are also rules in terms of the limit of quantity. Each country visited will also have their own rules and the family must contact the appropriate embassy to find out exactly what these are. The Home Office license is for crossing UK borders only; many countries prohibit the import of diamorphine, morphine or methadone for personal use.

It is important to check all these details. To find out more information then contact the Home Office:

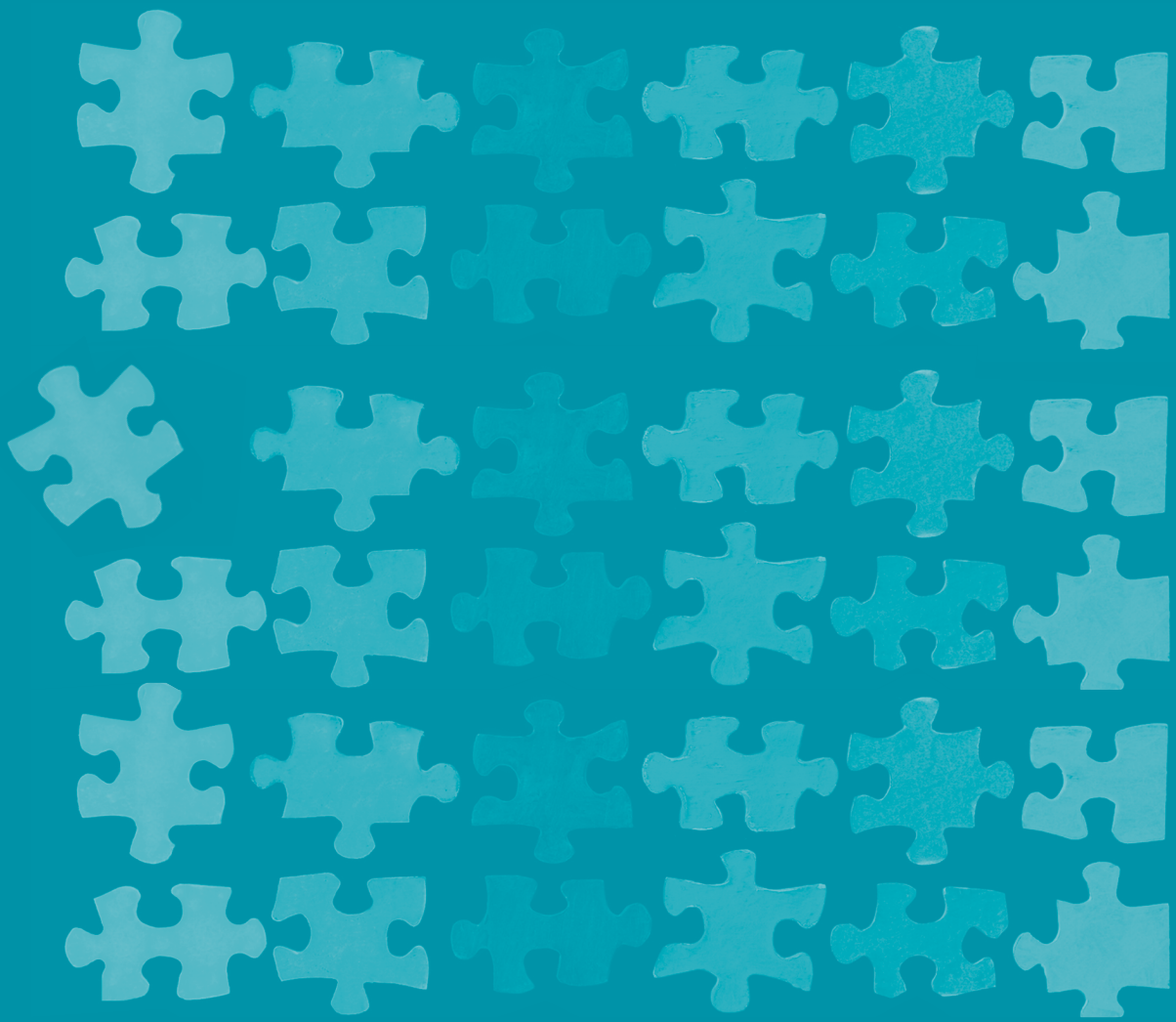
Home Office
Drugs Licensing & Compliance Unit
4th Floor Fry Building
2 Marsham Street
London SW1P 4D

Tel: 0207 035 4848 (9-5 Monday to Friday).
Email: public.enquiries@homeoffice.gsi.gov.uk
Web: www.homeoffice.gov.uk/drugs/licensing/nds

Please be aware that this web link is subject to change, please do use the search facility of the Home Office website if the address above becomes outdated.



Formulary



How to use the formulary

The medicines included in this formulary are listed alphabetically. Under each medicine heading you will find:

The name of the drug and evidence references – You will find a series of numbers referring to evidence, such as [128, 197-200]. The numbers in square brackets refer to the references which can be found on pages 160-172. For some medicines you will also see abbreviations next to the evidence, such as CC, EA and RC. These refer to the seven abbreviations detailed on this page (below).

Use – This details what the specific medicine is used for in children's palliative care.

Dose and routes – This details different routes and appropriate doses for each medicine depending on the age/ weight of the child.

Notes – This provides any additional relevant notes, cautions, information on compatibility etc. We have also included a note that explains what form and size each medicine is available in.

Abbreviations

RE Strong research evidence
SR Some weak research evidence
CC No published evidence but has clinical consensus
EA Evidence (research or clinical consensus) with adults
SC Subcutaneous
IV Intravenous
IM Intramuscular

This formulary includes doses used in palliative care as those recommended in the British National Formulary (BNF)[218], British National Formulary for Children (BNFC) [128], Neonatal Formulary[129], WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses[219], Palliative Care Formulary[220] and Medicines for Children[221]. Readers outside the UK are advised to consult local prescribing guidelines (where they exist) as well.

The authors have made every effort to check current data sheets and literature up to May 2012, but the dosages, indications, contraindications and adverse effects of drugs change over time as new information is obtained. It is the responsibility of the prescriber to check this information with the manufacturer's current data sheet and we strongly urge the reader to do this before administering any of the drugs in this document. In addition, palliative care uses a number of drugs for indications or by routes that are not licensed by the manufacturer. In the UK such unlicensed use is allowed, but at the discretion and with the responsibility of the prescriber.

Adrenaline (topical)

Evidence: [128] CC

Use:
- Small external bleeds.

Dose and routes:
Soak gauze in 1:1000 (1 mg/mL) solution and apply directly to bleeding point.

Alfentanil

Evidence: [128, 221-224]
EA, RC (for PICU settings), CC (in palliative care settings outside ICU)

Use:
- Short acting synthetic opioid analgesic derivative of fentanyl.
- Useful for breakthrough pain, procedure-related pain, and by SC/IV infusion.
- Used as analgesic especially for patients in intensive care and on assisted ventilation (adjunct to anaesthesia).
- Alternative opioid if intolerant to other strong opioids; useful in renal failure if neurotoxic on morphine, or stage 4 to 5 severe renal failure.

Dose and routes:
Titrate from other opioids but note poor relationship between effective PRN dose and regular background dose.

Buccal/intranasal dose is equivalent to bolus SC/IV dose. Used for incident and breakthrough pain. If possible, give 5 minutes before event likely to cause pain, and repeat (and increase) dose if needed.

By IV/SC bolus (**these doses presume** assisted ventilation)
- **Neonate:** 5-20 micrograms/kg initial dose, supplemental doses up to 10 micrograms/kg.
- **1 month to 18 years:** 10-20 micrograms/kg initial dose, up to 10 micrograms/kg supplemental doses.

By continuous IV or SC infusion (**these doses presume** assisted ventilation)
- **Neonate:** 10-50 micrograms/kg over 10 minutes then 30-60 micrograms/kg/ hour.
- **1 month to 18 years:** 50-100 microgram/kg loading dose over 10 minutes, then 30-60 micrograms/kg/ hour as continuous infusion.

Notes:
- Potency: 10-20 times stronger than parenteral morphine, approx ¼ as strong as fentanyl.
- Has the best evidence of all opioids to support its use in severe renal failure. May need to reduce dose in severe hepatic failure.
- To avoid prolonged respiratory depression, administer last bolus dose 10 minutes before end of procedure; discontinue infusion 30 minutes before end of procedure.
- Best dosage information available for anaesthetic adjunct use. Analgesic doses mostly extrapolated from fentanyl.
- Compatible with sodium chloride, dextrose and compound sodium lactate infusion fluids.
- Useful in high doses as can be dissolved in small volumes (as diamorphine).
- Available as: injection (500 microgram/mL in 2ml and 10ml ampoule), Intensive care injection (5 mg/mL in 1ml ampoule). Nasal spray with attachment for buccal/SL use (5 mg/5 mL bottle available as special order from Torbay Hospital).
- Alfentanil injection is licensed for use in children as an analgesic supplement for use before and during anaesthesia. Buccal or intranasal administration of alfentanil for incident/breakthrough pain is an unlicensed formulation and route of administration.
- With the recent availability of commercial buccal fentanyl preparations, and increasing experience with their use in children, there may be less place for alfentanil in children's palliative care outside intensive care settings.

Amitriptyline

Evidence: [128, 218, 225, 226]

Use:
- Neuropathic pain.

Dose and routes:
By mouth:
- **Child 2-12 years:** initial dose of 0.2 mg/kg (maximum 25 mg) given once daily at night. Dose may be increased gradually, if necessary, to a suggested maximum of 1 mg/kg/dose twice daily (under specialist supervision). Do not exceed 150 mg/day.
- **Child 12-18 years:** initial dose of 10 mg at night increased gradually, if necessary, every 3-5 days to a suggested initial maximum of 75 mg/day. Higher doses up to 150 mg/day in divided doses may be used under specialist advice.

Notes:
- Not licensed for use in children with neuropathic pain.
- Available as: tablets (10 mg, 25 mg, 50 mg) and oral solution (25 mg/5 mL, 50mg/5mL).
- Analgesic effect unlikely to be evident for several days. Potential improved sleep and appetite which are likely to precede analgesic effect.
- Main side effects limiting use in children include; constipation, dry mouth and drowsiness.

Arachis Oil Enema

Evidence: [128, 221] CC

Use:
- Faecal softener.
- Faecal impaction.

Dose and routes:
By rectal administration:
- **Child 3-7 years:** 45-65 mL as required (~1/3 to 1/2 enema).
- **Child 7-12 years:** 65 mL - 100 mL as required (~1/2 to 3/4 enema).
- **Child 12 years and over:** 100-130 mL as required (~3/4 – 1 enema).

Notes:
- Caution: as arachis oil is derived from peanuts, do not use in children with a known allergy to peanuts.
- Generally used as a retention enema to soften impacted faeces. May be instilled and left overnight to soften the stool.
- Warm enema before use by placing in warm water.
- Administration may cause local irritation.
- Licensed for use in children from 3 years of age.
- Available as: enema, arachis (peanut) oil in 130 mL single dose disposable packs.

Arthrotec®

Evidence: [218]

Use:
- Anti-inflammatory pain killer (Diclofenac) combined with gastroprotective drug (Misoprostol).
- For musculoskeletal pain and bone pain caused by tumour.
- Prophylaxis against NSAID-induced gastroduodenal ulceration in patients requiring diclofenac.

Dose and routes:
By mouth:
- Arthrotec® 50, **Adults:** 1 tablet 2-3 times a day.
- Arthrotec® 75, **Adults:** 1 tablet 2 times a day.

Notes:
- Not licensed for children.
- Above doses only for adults.
- Available as: tablets (Arthrotec 50 = diclofenac 50 mg and misoprostol 200 micrograms and Arthrotec 75 = diclofenac 75 mg and misoprostol 200 micrograms).

Aspirin

Evidence: [128, 218]

Use:
- Mild to moderate pain.
- Pyrexia.

Dose and routes:
By mouth:
- > **16 years of age:** Initial dose of 300 mg every 4-6 hours when necessary. Dose may be increased if necessary to a maximum of 900 mg every 4-6 hours (maximum 4 g/day).

Notes:
- Available as: tablets (75 mg, 300 mg), dispersible tablets (75 mg, 300 mg), and suppositories (150 mg).
- Contraindicated in children due to risk of Reye Syndrome.
- May be used in low dose under specialist advice for child with some cardiac conditions.

Baclofen

Evidence: [128, 145, 218, 227-233]

Use:
- Chronic severe spasticity of voluntary muscle.
- Considered as third line neuropathic agent.

Dose and routes:
By mouth:
- **Initial dose for child 1-10 years:** 0.3 mg/kg/day in 4 divided doses (maximum single dose 2.5 mg) increased gradually to a usual maintenance dose of 0.75-2 mg/kg/day in divided doses or the following ranges:
- **Child 1-2 years:** 10-20 mg daily in divided doses.
- **Child 2-6 years:** 20-30 mg daily in divided doses.
- **Child 6-10 years:** 30-60 mg daily in divided doses.
- **Child 10-18 years:** initial dose 5 mg three times daily increased gradually to a usual maintenance dose up to 60 mg/day (maximum 100 mg/day).

Notes:
- Not licensed for children < 1 year old.
- Avoid abrupt withdrawal.
- Available as: tablets (10 mg) and oral solution (5 mg/5 mL).
- Monitor and review reduction in muscle tone and potential adverse effects on swallow and airway protection.

Bethanechol

Evidence: [11, 234]

Use:
- Opioid induced urinary retention.

Dose and routes:
By mouth:
- **Child over 1 year:** 0.6 mg/kg/day in 3 or 4 divided doses. Maximum single dose 10 mg.
- **Adult dose:** 10-50 mg per dose 3 to 4 times a day.

Subcutaneous:
- **Child over 1 year:** 0.12 to 2 mg/kg/day in 3 or 4 divided doses. Maximum single dose 2.5 mg.
- **Adult dose**: 2.5 to 5 mg per dose 3 to 4 times a day.

Notes:
- The safety and efficacy of bethanechol in children has not been established (bethanechol is not licensed for use in children).
- Available as: tablets (10 mg and 25 mg), injection for subcutaneous injection only.
- (5 mg/mL – not licensed in the UK but may be possible to import via a specialist importation company).

Bisacodyl

Evidence: [128, 218]

Use:
- Constipation.

Dose and routes:
By mouth:
- **Child 4-10 years:** 5 mg at night; adjust according to response.
- **Child 10-18 years:** 5-10 mg at night; increase if necessary to maximum of 20 mg per dose.

By rectum (suppository):
- **Child 2-10 years:** 5-10 mg in the morning.
- **Child 10-18 years:** 10 mg in the morning.

Notes:
- Tablets act in 10-12 hours. Suppositories act in 20-60 min. Must be in direct contact with mucosal wall.
- Stimulant laxative.
- Available as: tablets (5 mg) and suppositories (5 mg, 10 mg).

Buprenorphine

Evidence: [128, 223, 235, 236]

Use:
- Moderate to severe pain.

Dose and routes:
By sublingual route (starting doses):
- **Child body weight 16-25 kg:** 100 microgram every 6-8 hours.
- **Child body weight 25-37.5 kg:** 100-200 microgram every 6-8 hours.
- **Child body weight 37.5-50 kg:** 200-300 microgram every 6-8 hours.
- **Child body weight over 50 kg:** 200-400 microgram every 6-8 hours.

By transdermal patch:
- By titration or as indicated by existing opioid needs.

Notes:
- Caution with hepatic impairment and potential interaction with many drugs including antiretrovirals.
- Sublingual tablets not licensed for use in children < 6 years old.
- Available as: tablets (200 microgram, 400 microgram) for sublingual administration. Tablets may be halved.

Available as: two types of patches:

1. BuTrans® – applied every 7 days. Available as 5 (5 microgram/hour for 7 days),10 (10 microgram/hour for 7 days), and 20 (20 microgram/hour for 7 days)
2. TransTec® – applied every 96 hours. Available as 35 (35 microgram/hour for 96 hours), 52.5 (52.5 microgram/hour for 96 hours), and 70 (70 microgram/hour for 96 hours).

- Patches not licensed for use in children.
- Has both opioid agonist and antagonist properties and may precipitate withdrawal symptoms, including pain, in children dependant on other opioids.
- Sublingual duration of action 6-8 hours.

For patches, systemic analgesic concentrations are generally reached within 12-24 hours but levels continue to rise for 32-54 hours. If converting from:
  - 4-hourly oral morphine - give regular doses for the first 12 hours after applying the patch.
  - 12-hourly slow release morphine - apply the patch and give the final slow release dose at the same time.
  - 24-hourly slow release morphine - apply the patch 12 hours after the final slow release dose.
  - Continuous subcutaneous infusion - continue the syringe driver for about 12hours after applying the patch.
- Effects only partially reversed by naloxone.
- Rate of absorption from patch is affected by temperature, so caution with pyrexia or increased external temperature such as hot baths: possibility of accidental overdose with respiratory depression.
- Patches are finding a use as an easily administered option for low dose background opioid analgesia in a stable situation, for example in severe neurological impairment.

Carbamazepine

Evidence: [128, 237-240]

Use:
- Neuropathic pain.
- Some movement disorders.

Dose and routes:
By mouth:
- **Child 1 month-12 years:** initial dose of 5 mg/kg at night or 2.5 mg/kg twice daily, increased as necessary by 2.5-5 mg/kg every 3-7 days; usual maintenance dose 5 mg/kg 2-3 times daily. Doses up to 20 mg/kg/DAY in divided doses have been used.
- **Child 12-18 years**: initial dose of 100-200 mg 1-2 times daily; increased slowly to usual maintenance of 200-400 mg 2-3 times daily. Maximum 1.8 g/DAY in divided doses.

By rectum:
- **Child 1 month-18 years:** use approximately 25% more than the oral dose (maximum single dose 250 mg) up to 4 times a day.

Notes:
- Not licensed for use in children with neuropathic pain.
- Can cause serious blood, hepatic, and skin disorders. Parents should be taught how to recognise signs of these conditions, particularly leucopoenia.
- Numerous interactions with other drugs including chemotherapy drugs.
- Different preparations may vary in bioavailability so avoid changing formulations or brands.
- Available as: tablets (100mg, 200mg, 400mg), chew tabs (100mg, 200mg), liquid (100mg/5mL), suppositories (125mg, 250mg), and modified release tablets (200mg, 400mg).

Celecoxib

Evidence: [241-243] SR

Use:

- Pain, inflammatory pain, bone pain, stiffness. Not used first line.
- Dose based on management of juvenile rheumatoid arthritis.

Dose and routes:

By mouth:

- **Child over 2 years:**
  - Weight 10-25 kg: 50 mg twice daily.
  - Weight more than 25 kg: 100 mg twice daily.

Notes:

- Tablets may be crushed for oral administration.
- Tablets not licensed for use in children.
- Celecoxib interacts with a great many commonly used drugs, check BNF.
- Available as: tablets (50 mg).

Chloral hydrate

Evidence: [128, 129, 195, 221, 244, 245]

Use:

- Insomnia.

Dose and routes:

By mouth or rectum:

- **Neonate:** initial dose of 30 mg/kg as a single dose at night. May be increased to 45 mg/kg at night if necessary.
- **Child 1 month-12 years:** initial dose of 30 mg/kg as a single dose at night. May be increased to 50 mg/kg at night if necessary. Maximum single dose 1 g.
- **Child 12-18 years:** initial dose of 500 mg as a single dose at night. Dose may be increased if necessary to 1-2 g at night. Maximum single dose 2 g.

Notes:

- Oral use: mix with plenty of juice, water, or milk to reduce gastric irritation and disguise the unpleasant taste.
- For rectal administration use oral solution or suppositories (available from 'specials' manufacturers).
- Accumulates on prolonged use and should be avoided in severe renal or hepatic impairment.
- Available as: tablets (chloral betaine 707 mg = cloral hydrate 414 mg- Welldorm®), oral solution (143.3 mg/5 mL-Welldorm®; 200 mg/5 mL, 500 mg/5 mL both of which are available from 'specials' manufacturers or specialist importing companies), suppositories (available as various strengths 25mg, 50 mg, 60 mg, 100 mg, 200 mg, 500 mg from 'specials' manufacturers).

Chlorpromazine

Evidence: [89-92, 94, 121, 123, 126, 128, 246]

Use:

- Hiccups.
- Nausea and vomiting of terminal illness (where other drugs are unsuitable).

Dose and routes:

Hiccups

By mouth:

- **Child 1-6 years:** 500 micrograms/kg every 4-6 hours adjusted according to response (maximum 40 mg daily).
- **Child 6-12 years:** 10 mg 3 times daily, adjusted according to response (maximum 75 mg daily).
- **Child 12-18 years:** 25 mg 3 times daily (or 75 mg at night), adjusted according to response, to usual maintenance dose of 75-300 mg daily (but up to 1 g daily may be required).

Nausea and vomiting of terminal illness (where other drugs are unsuitable)

By mouth:

- **Child 1-6 years:** 500 micrograms/kg every 4-6 hours; maximum 40 mg daily.
- **Child 6-12 years:** 500 micrograms/kg every 4-6 hours; maximum 75 mg daily.
- **Child 12-18 years:** 10-25 mg every 4-6 hours.

By deep intramuscular injection:

- **Child 1-6 years:** 500 micrograms/kg every 6-8 hours; maximum 40 mg daily.
- **Child 6-12 years:** 500 micrograms/kg every 6-8 hours; maximum 75 mg daily.
- **Child 12-18 years:** initially 25 mg then 25-50 mg every 3-4 hours until vomiting stops.

Notes:

- Caution in children with hepatic impairment (can precipitate coma), renal impairment (start with small dose; increased cerebral sensitivity), cardiovascular disease, epilepsy (and conditions predisposing to epilepsy), depression, myasthenia gravis.

- Caution is also required in severe respiratory disease and in children with a history of jaundice or who have blood dyscrasias (perform blood counts if unexplained infection or fever develops).
- Photosensitisation may occur with higher dosages; children should avoid direct sunlight.
- Antipsychotic drugs may be contra-indicated in CNS depression.
- Available as: tablets, coated (25 mg, 50 mg, 100 mg); oral solution (25 mg/5 mL, 100 mg/ 5mL); injection (25 mg/mL in1mL and 2mL ampoules).

Clobazam

Evidence: [128, 221]

Use:

- Benzodiazepine.
- Adjunctive therapy for epilepsy.

Dose and routes:

For oral administration:

- **Child 1 month-12 years:** initial dose of 125 microgram/kg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 250 microgram/kg twice daily. Maximum dose 500 microgram/kg (15 mg single dose) twice daily.
- **Child 12-18 years:** initial dose of 10 mg twice daily. Increase every 5 days as necessary and as tolerated to a usual maintenance dose of 10-15 mg twice daily. Maximum 30 mg twice daily.

Notes:

- Not licensed for use in children less than 3 years of age.
- Tablets should not be chewed.
- Available as: tablets (10mg), tablets (5mg – unlicensed and available on a named-patient basis), oral liquid (various strengths may be prepared as extemporaneous formulations or are available from 'specials' manufacturers or specialist importing companies – unlicensed).
- NHS black-listed except for epilepsy and endorsed 'SLS'.

Clonazepam

Evidence: [128, 129, 196, 232, 239, 247]

Use:

- Tonic-clonic seizures.
- Partial seizures.
- Cluster seizures.
- Myoclonus.
- Status epilepticus (3rd line, particularly in neonates).
- Neuropathic pain.
- Restless legs.
- Gasping.
- Anxiety and panic.

Dose and routes:

By mouth (anticonvulsant doses: reduce for other indications):

- **Child 1 month-1 year:** initially 0.25 mg at night for 4 nights, increased over 2-4 weeks to usual maintenance dose of 0.5-1 mg at night (may be given in 3 divided doses if necessary).
- **Child 1-5 years:** initially 0.25 mg at night for 4 nights, increased over 2-4 weeks to usual maintenance of 1-3 mg at night (may be given in 3 divided doses if necessary).
- **Child 5-12 years:** initially 0.5 mg at night for 4 nights, increased over 2-4 weeks to usual maintenance dose of 3-6 mg at night (may be given in 3 divided doses if necessary).
- **Child 12-18 years:** initially 1 mg at night for 4 nights, increased over 2-4 weeks to usual maintenance of 4-8 mg at night (may be given in 3 divided doses if necessary).

For status epilepticus: (SR)
Continuous subcutaneous Infusion:

- **Child 1 month-18 years:** starting dose 20-25 microgram/kg/24 hours.
- Maximum starting doses:
  1-5 years: 250 microgram/24 hours.
  5-12 years: 500 microgram/24 hours.
- Increase at intervals of not less than 12 hours to 200 microgram/kg/24 hours (maximum 8 mg/24 hours).
- Doses of up to 1.4 mg/kg/24 hours have been used in status epilepticus in PICU environment.

By intravenous injection over at least 2 minutes, or infusion:

- **Neonate:** 100 microgram/kg intravenous over at least 2 minutes, repeated after 24 hours if necessary (avoid unless no safer alternative). Used for seizures not controlled with phenobarbital or phenytoin.
- **Child 1 month-12 years:** loading dose 50 micrograms/kg (maximum 1 mg) by IV injection followed by IV infusion of 10 microgram/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour.
- **Child 12-18 years:** loading dose 1 mg by IV injection followed by IV infusion of 10 microgram/kg/hour adjusted according to response; maximum 60 micrograms/kg/hour.

Notes:

- Licenced for use in children for status epilepticus and epilepsy. Not licensed for neuropathic pain. Tablets licensed in children. Oral liquid is unlicensed in UK and is available from 'specials' manufacturers.
- Check preparation's suitability if administering via Jejunostomy tubes.
- Stability of diluted clonazepam is up to 12 hours so prescribers should consider 12 hourly infusions.
- Very effective anticonvulsant, usually 3rd line due to side effects and development of tolerance.
- Use lower doses for panic, anxiolysis, terminal sedation, neuropathic pain, and restless legs.
- As anxiolytic/sedative approximately 20 times as potent as diazepam (i.e. 250 microgram clonazepam equivalent to 5 mg diazepam orally).
- Multiple indications in addition to anticonvulsant activity can make it particularly useful in palliative care for neurological disorders.
- Many children with complex seizure disorders are on twice daily doses and on higher dosages.
- Increase for short periods 3-5 days with increased seizures e.g. from viral illness.
- Elimination half life of 20-40 hours means that it may take up to 6 days to reach steady state; risk of accumulation and toxicity with rapid increase of infusion; consider loading dose to reach steady state more quickly.
- Compatible with most drugs commonly administered via continuous subcutaneous infusion via syringe driver.
- Available as: tablets (500 microgram scored, 2 mg scored); liquid (0.5 mg in 5 mL and 2 mg in 5 mL now available as licensed preparations); injection (1 mg/mL).

Co-danthramer

Evidence: [128, 218]

Use:

- Constipation in terminal illness only.

Dose and routes:

By mouth:
Co-danthramer 25/200 suspension 5mL = one co-danthramer 25/200 capsule:

- **Child 2-12 years:** 2.5-5 mL at night.
- **Child 6-12 years:** 1 capsule at night.
- **Child 12-18 years:** 5-10 mL or 1-2 capsules at night. Dosage can be increased up to 10-20 mL twice a day.

Strong co-danthramer 75/1000 suspension 5 mL = two strong co-danthramer 37.5/500 capsules:

- **Child 12-18 years:** 5 mL or 1-2 capsules at night.

Notes:

- Co-danthramer is made from danthron and poloxamer '188'.
- Acts as a stimulant laxative.
- Avoid prolonged skin contact due to risk of irritation and excoriation.
- Danthron can turn urine red/brown.
- Rodent studies indicate potential carcinogenic risk.

Co-danthrusate

Evidence: [128, 218]

Use:

- Constipation in terminal illness only.

Dose and routes:

By mouth:
Co-danthrusate 50/60 suspension 5 mL = one co-danthrusate 50/60 capsule:

- **Child 6-12 years:** 5 mL or 1 capsule at night.
- **Child 12-18 years:** 5-15 mL or 1-3 capsules at night.

Notes:

- Co-danthrusate is made from danthron and docusate sodium.
- Acts as a stimulant laxative.
- Avoid prolonged skin contact due to risk of irritation and excoriation.
- Danthron can turn urine red/brown.
- Rodent studies indicate potential carcinogenic risk.

Codeine phosphate

Evidence: [128, 129, 218, 239, 248, 249]

Use:

- Mild to moderate pain in patients known to be able to benefit. For prn use only – not suitable for management of background pain.
- Marked diarrhoea, when other agents are contra-indicated or not appropriate, with medication doses and interval titrated to effect.
- Cough suppressant.

Dose and routes:

By mouth, rectum, SC injection, or by IM injection:

- **Neonate:** 0.5-1 mg/kg every 4-6 hours.
- **Child 1 month-12 years:** 0.5-1 mg/kg every 4-6 hours; maximum 240 mg daily.
- **Child 12-18 years:** 30-60 mg every 4-6 hours; maximum 240 mg daily.

As cough suppressant in the form of pholcodine linctus/syrup (NB different strengths are available):

- **Child 6-12 years:** 2.5 mg 3-4 times daily.
- **Child 12-18 years:** 5-10 mg 3-4 times daily.

Notes:

- Not licensed for use in children < 1 year old.
- Codeine is effectively a pro drug for morphine, delivering approximately 1 mg of morphine for every 10 mg of codeine.
- Conversion to morphine is subject to pharmacogenetic variation.
- Pharmacologically, codeine is no different from morphine except that it is weaker and less consistently effective. This has led the WHO to recommend that it is better replaced by low doses of morphine.
- 5-34% of population have an enzyme deficiency that prevents activation of codeine to active metabolite and so is ineffective in this group.
- Individuals who are ultra-rapid metabolisers can develop life threatening opioid toxicity.
- Seems relatively constipating compared with morphine/diamorphine, particularly in children.
- Rectal administration is an unlicensed route of administration using an unlicensed product.
- Must *not* be given IV.
- Reduce dose in renal impairment.
- Available as: tablets (15 mg, 30 mg, 60 mg), oral solution (25 mg/5 mL), injection (60 mg/mL), suppositories of various strengths available from 'specials' manufacturers. Pholcodine as linctus 2 mg/5 mL, 5 mg/5 mL and 10 mg/5 mL.
- Some retail pharmacies do not stock codeine phosphate solution at 25 mg/5 mL. They usually do stock codeine phosphate linctus at 15 mg/5 mL and this is worth enquiring of if a practitioner is working in the community and wishes to prescribe this medication. BE CAREFUL WITH DIFFERING STRENGTHS OF LIQUIDS.

Cyclizine

Evidence: [128, 250]

Use:

- Nausea and vomiting and particularly useful in vomiting associated with raised intracranial pressure.

Dose and routes:

By mouth or by slow IV injection over 3-5min:

- **Child 1 month-6 years:** 0.5-1 mg/kg up to 3 times daily; maximum single dose 25 mg.
- **Child 6-12 years:** 25 mg up to 3 times daily.
- **Child 12-18 years:** 50 mg up to 3 times daily.

By rectum:

- **Child 2-6 years:** 12.5 mg up to 3 times daily.
- **Child 6-12 years:** 25 mg up to 3 times daily.
- **Child 12-18 years:** 50 mg up to 3 times daily.

By continuous IV or SC infusion:

- **Child 1 month-5 years:** 3 mg/kg over 24 hours (maximum 50 mg/24 hours).
- **Child 6-12 years:** 75 mg over 24 hours.
- **Child 12-18 years:** 150 mg over 24 hours.

Notes:

- Tablets may be crushed for oral administration.
- Tablets not licensed for use in children < 6 years old.
- Injection not licensed for use in children.
- Rapid SC or IV bolus can lead to 'lightheadness' – disliked by some and enthralling to others leading to repeated quests for IV Cyclizine.
- Care in subcutaneous or intravenous infusion: Important to use in water for injections rather than saline. Can precipitate with diamorphine at high concentrations, and can cause injection site reactions.
- Suppositories must be kept refrigerated.
- Available as: tablets (50 mg), suppositories (12.5 mg, 25 mg, 50 mg, 100 mg from 'specials' manufacturers) and injection (50 mg/mL).

Dantrolene

Evidence: [128, 147, 228, 229, 233, 251]

Use:

- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

Dose and routes:

By mouth:

- **Child 5-12 years:** initial dose of 500 microgram/kg once daily; after 7 days increase to 500 microgram/kg/dose 3 times daily. Every 7 days increase by further 500 microgram/kg/dose until response. Maximum recommended dose is 2 mg/kg 3-4 times daily (maximum total daily dose 400 mg).
- **Child 12-18 years:** initial dose of 25 mg once daily; after 7 days increase to 25 mg 3 times daily. Every 7 days increase by further 500 microgram/kg/dose until response. Maximum recommended dose is 2 mg/kg 3-4 times daily (maximum total daily dose 400 mg).

Notes:

- Not licensed for use in children.
- Hepatotoxicity risk, consider checking liver function before and at regular intervals during therapy.
- Avoid in liver disease or concomitant use of hepatotoxic drugs.
- Available as: capsules (25 mg, 100 mg), oral suspension (extemporaneous formulation).

Dexamethasone

Evidence: [126, 221, 252-254]

Use:

- Headache associated with raised intracranial pressure caused by tumour.
- Anti-inflammatory in brain and other tumours causing pressure on nerves, bone or obstruction of hollow viscus.
- Analgesic role in nerve compression, spinal cord compression and bone pain.
- Antiemetic either as an adjuvant or in highly emetogenic cytotoxic therapies.

Dose and routes:

Prescribe as dexamethasone base.

Headache associated with raised intracranial pressure

By mouth or IV:

- **Child 1 month-12 years:** 250 microgram/kg twice a day for 5 days; then reduce or stop.

To relieve symptoms of brain or other tumour

Numerous other indications in palliative medicine such as spinal cord compression, some causes of dyspnoea, bone pain, superior vena caval obstruction etc, only in discussion with specialist palliative medicine team.

Antiemetic

By mouth or IV:

- **Child < 1 year:** initial dose 0.25 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 1 mg 3 times daily.
- **Child 1-5 years:** initial dose 1 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 2 mg 3 times daily.
- **Child 6-12 years:** initial dose 2 mg 3 times daily. This dose may be increased as necessary and as tolerated up to 4 mg 3 times daily.
- **Child 12-18 years:** 4 mg 3 times daily.

Notes:

- Not licensed for use in children as an antiemetic.
- Dexamethasone 1 mg = dexamethasone phosphate 1.2 mg = dexamethasone sodium phosphate 1.3 mg.
- Dexamethasone 1 mg = 7 mg prednisolone (anti-inflammatory equivalence).
- Problems of weight gain and Cushingoid appearance are major problems specifically in children. All specialist units therefore use pulsed dose regimes in preference to continual use. Regimes vary with conditions and specialist units. Seek local specialist advice.
- Other side effects include; diabetes, osteoporosis, muscle wasting, peptic ulceration and behavioural problems particularly agitation.
- Tablets may be dispersed in water or injection solution given by mouth.
- Available as: tablets (500 microgram, 2 mg), oral solution (2 mg/5 mL and other strengths available from 'specials' manufacturers) and injection as dexamethasone sodium phosphate (equivalent to 4 mg/1 mL dexamethasone base (Organon® brand) or 3.3 mg/mL dexamethasone base (Hospira® brand).

Diamorphine

Evidence: [128, 143, 221, 239, 255]

Use:

- Pain of all types unless opioid insensitivity has been shown (Step 2 WHO Pain Ladder, second line).
- Background pain relief (maintenance phase)
- Dyspnoea.

Dose and routes:

Normally convert using OME from previous analgesia. Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

Acute or Chronic pain

By continuous subcutaneous or intravenous infusion:

- **Neonate:** Initial dose of 2.5 microgram/kg/hour which can be increased as necessary to a suggested maximum of 7 micrograms/kg/hour.
- **Child 1 month-12 years:** 1 month-18 years: 7-12.5 microgram/kg/hour (maximum 10 mg/24 hours) adjusted according to response.

By intravenous injection:

- **Neonate:** 15 micrograms/kg every 6 hours as necessary, adjusted according to response.
- **Child 1-3 month:** 20 micrograms/kg every 6 hours as necessary, adjusted according to response.
- **Child 3-6 months:** 25-50 micrograms/kg every 6 hours as necessary, adjusted according to response.
- **Child 6-12 months:** 75 micrograms/kg every 4 hours as necessary, adjusted according to response.
- **Child 1-12 years:** 75-100 micrograms/kg every 4 hours as necessary, adjusted according to response (maximum total 10 mg over 24 hours).
- **Child 12-18 years:** 2.5-5 mg every 4 hours as necessary, adjusted according to response.

By SC or IM injection:

- **Child 12-18 years:** 5 mg every 4 hours as necessary.

By intranasal or buccal route:

- **Child over 10kg**: 50-100 micrograms/kg; maximum single dose 10 mg.

Breakthrough

By buccal or subcutaneous routes:

- 5-10% of total diamorphine dose over 24 hours, as needed 1-4 hourly.

Dyspnoea

By buccal or subcutaneous routes:

- Prescription as for pain, but at 50% of breakthrough dose.

Notes:

- Morphine injection is rapidly taking over from diamorphine as the only benefit of diamorphine over morphine is solubility and this is rarely a problem in paediatric doses.
- Available as : injection (5 mg, 10 mg, 30 mg, 100 mg, 500 mg ampoules).
- Diamorphine injection is licensed for the treatment of children who are terminally ill.
- Administration of diamorphine by the intranasal or buccal routes is not licensed.
- For intranasal or buccal administration of diamorphine use the injection powder reconstituted in water for injections.
- In neonates, dosage interval should be extended to 6 or 8 hourly depending on renal function and the dose carefully checked, due to increased sensitivity to opioids in the first year of life.
- In poor renal function, dosage interval may be extended or opioids given as required only to titrate against symptoms. Or consider Fentanyl.
- Reduce dose accordingly where respiratory insufficiency exists.
- Significant tolerance to opioids is unusual. If it occurs, the best solution is simply to increase the opioid dose to overcome tolerance (being mindful that the dose is not increased inappropriately too high when it would be better to opioid rotate earlier). If this is limited by adverse effects, opioid substitution should be carried out with a 25-50% reduction in oral morphine equivalence (OME). Adjuvants such as ketamine intended to reduce opioid tolerance are rarely indicated in paediatric palliative care.

Diazepam

Evidence: [48, 52, 54, 128, 196, 218, 221, 228, 233, 256-258]

Use:

- Short term anxiety relief.
- Agitation.
- Panic attacks.
- Relief of muscle spasm.
- Treatment of status epilepticus.

Dose and routes:

Short term anxiety relief, panic attacks and agitation

By mouth:

- **Child 2-12 years:** 2-3 mg 3 times daily.
- **Child 12-18 years:** initial dose of 2 mg 3 times daily increasing as necessary and as tolerated to a maximum of 10 mg 3 times daily.

Relief of muscle spasm

By mouth:

- **Child 1-12 months:** initial dose of 250 microgram/kg twice a day.
- **Child 1-5 years:** initial dose of 2.5 mg twice a day.
- **Child 5-12 years:** initial dose of 5 mg twice a day.
- **Child 12-18 years:** initial dose of 10 mg twice a day; maximum total daily dose 40 mg.

Status epilepticus

By IV injection over 3-5 minutes:

- **Neonate:** 12 years: 0.3-0.4 mg/kg as a single dose (maximum 10 mg) repeated once after 10 minutes if necessary (In hospital 0.5 mg/kg up to maximum of 20 mg as single dose).
- **Child 12-18 years:** 10 mg repeated once after 10 minutes if necessary (In hospital 20 mg as single dose).

By rectum (rectal solution):

- **Neonate:** 1.25-2.5 mg repeated once after 10 minutes if necessary.
- **Child 1 month-2 years:** 5 mg repeated once after 10 minutes if necessary.
- **Child 2-12 years:** 5-10 mg repeated once after 10 minutes if necessary.
- **Child 12-18 years:** 10 mg repeated once after 10 minutes if necessary (in hospital up to 20 mg as a single dose may be used).

Notes:

- Available as: tablets (2 mg, 5 mg, 10 mg), oral solution (2 mg/5 mL, 5 mg/5 mL), rectal tubes (2.5 mg, 5 mg, 10 mg), and injection (5 mg/mL solution and 5 mg/ml emulsion).
- Rectal tubes not licensed for children < 1 year old.

Diclofenac Sodium

Evidence: [128, 221, 246]

Use:

- Mild to moderate pain and inflammation, particularly musculoskeletal disorders.

Dose and routes:

By mouth or rectum:

- **Neonates weighing 3.125 kg or greater – Child 18 years:** initial dose of 0.3 mg/kg 3 times daily increasing if necessary to a maximum of 1 mg/kg 3 times daily (maximum 50 mg single dose).

By IM or IV infusion:

- **Child 2-18 years:** initial dose of 0.3 mg/kg 1-2 times daily; maximum of 150 mg/day and for a maximum of 2 days.

Notes:

Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease

- Not licensed for use in children < 1 year old.
- Suppositories not licensed for use in children < 6 years old (except in children > 1 year old with juvenile idiopathic arthritis).
- Smallest dose that can be given practically by rectal route is 3.125 mg by cutting a 12.5 mg suppository into quarters (CC).
- Injection not licensed for use with children. Voltarol injection is for IM or IV infusion only.
- Solid dosage forms of 50 mg or more are not licensed for use in children.
- Available as: tablets/capsules (25 mg, 50 mg, 75 mg modified release), dispersible tablets (10 mg from a 'specials' manufacturer, 50 mg), injection (25 mg/mL Voltarol® for IM injection or IV infusion only), and suppositories (12.5 mg, 25 mg, 50 mg and 100 mg).

Dihydrocodeine

Evidence: [128, 149, 223, 239, 246] EA, CC for injection

Use:

- Mild to moderate pain in patients known to be able to benefit.

Dose and routes:

By mouth or subcutaneous or deep intramuscular injection:

- **Child 1-4 years:** 0.5 mg/kg every 4-6 hours.
- **Child 4-12 years:** initial dose of 0.5 mg/kg (maximum 30 mg/dose) every 4-6 hours. Dose may be increased if necessary to 1 mg/kg every 4-6 hours (maximum 30 mg/dose).
- **Child 12-18 years:** 30 mg (maximum 50 mg by intramuscular or deep subcutaneous injection) every 4-6 hours.
- Modified release tablets used 12 hourly (use 1/2 of previous total daily dose for each modified release dose).

Notes:

- Most preparations not licensed for children under 4 years.
- Available as: tablets (30 mg, 40 mg), oral solution (10 mg/5 mL), injection (CD) (50 mg/mL 1 mL ampoule) and m/r tablets (60 mg, 90 mg, 120 mg).
- Relatively constipating compared with morphine/diamorphine and has a ceiling analgesic effect.
- Dihydrocodeine is itself an active substance, not a pro-drug like codeine.
- Oral bioavailability 20%, so probably equipotent with codeine by mouth (but opinion varies), twice as potent as codeine by injection.
- Time to onset 30 minutes, duration of action 4 hours for immediate release tablets.
- Side effects as for other opioids, plus paralytic ileus, abdominal pain, paraesthesia.
- Precautions: avoid or reduce dose in hepatic or renal failure.

Docusate

Evidence: [128]

Use:

- Constipation (faecal softener).

Dose and routes:

By mouth:

- **Child 6 months-2 years:** initial dose of 12.5 mg 3 times daily; adjust dose according to response.
- **Child 2-12 years:** initial dose of 12.5 mg 3 times daily. Increase to 25 mg 3 times daily as necessary and then further adjust dose according to response.
- **Child 12-18 years:** up to 500 mg/DAY in divided doses; adjust dose according to response.

By rectum:

- **Child 12-18 years:** 1 enema as single dose.

Notes:

- Adult oral solution and capsules not licensed in children < 12 years.
- Oral preparations act within 1-2 days.
- Rectal preparations act within 20min.
- Mechanism of action is emulsifying, wetting and mild stimulant.
- Doses may be exceeded on specialist advice.
- Available as capsules (100 mg), oral solution (12.5 mg/5 mL paediatric, 50 mg/5 mL adult), and enema (120 mg in 10 g single dose pack).

Domperidone

Evidence: [19, 69, 71, 118, 120, 128, 129, 221]

Use:

- Nausea and vomiting where poor GI motility is the cause.
- Gastro-oesophageal reflux resistant to other therapy.

Dose and routes:

For nausea and vomiting

By mouth:

- **> 1 month and body-weight ≤ 35 kg:** initial dose of 0.25 mg/kg 3-4 times daily increasing if necessary to 0.5 mg/kg 3-4 times daily. Maximum 2.4 mg/kg in 24 hours.
- **Body-weight > 35 kg:** initial dose of 10 mg 3-4 times daily increasing if necessary to 20 mg 3-4 times daily. Maximum 80 mg in 24 hours.

By rectum:

- **Body-weight 15-35 kg:** 30 mg twice a day.
- **Body-weight > 35 kg:** 60 mg twice a day.

For gastro-oesophageal reflux and gastrointestinal stasis

By mouth:

- **Neonate:** initial dose of 0.1 mg/kg 4-6 times daily before feeds. Dose may be increased, if necessary, to maximum of 0.3 mg/kg 4-6 times daily.
- **Child 1 month-12 years:** initial dose of 0.2 mg/kg (maximum single dose 10 mg) 3-4 times daily before food. Dose may be increased, if necessary, to 0.4 mg/kg 3-4 times daily. Maximum single dose 20 mg.
- **Child 12-18 years:** initial dose of 10 mg 3-4 times daily before food. Dose may be increased, if necessary, to 20 mg 3-4 times daily.

Notes:

- Only licensed in children for the management of nausea and vomiting following radiotherapy or chemotherapy.
- Not licensed for use in gastro-intestinal stasis; not licensed for use in children for gastro-oesophageal reflux disease.
- Domperidone may be associated with an increased risk of serious ventricular arrhythmias. Use at lowest effective dose. Domperidone should be avoided in patients who are taking concomitant medication known to cause QT prolongation (e.g. erythromycin, ketoconazole).
- Reduced ability to cross blood brain barrier, so less likely to cause extrapyramidal side effects compared with metoclopramide.
- Promotes gastrointestinal motility so diarrhoea can be an unwanted (or useful) side effect.
- Available as: tablets (10 mg), oral solution (5 mg/5 mL), and suppositories (30 mg).

Entonox (nitrous oxide)

Evidence: [128, 259]

Use:

- As self-regulated analgesia without loss of consciousness.
- Particularly useful for painful dressing changes.

Dose and routes:

By inhalation:

- **Child usually > 5 years old:** self-administration using a demand valve. Up to 50% in oxygen according to child's needs.

Notes:

- Is normally used as a light anaesthesia.
- Rapid onset and then offset.
- Should only be used as self-administration using a demand valve; all other situations require specialist paediatric anaesthetist.
- Is dangerous in the presence of pneumothorax or intracranial air after head injury.
- Prolonged use can cause megaloblastic anaemia.
- May be difficult to make available in hospice settings especially if needed infrequently, due to training, governance and supply implications.

Erythromycin

Evidence: [15, 128, 260] SR

Use:

- Gastrointestinal stasis (motilin receptor agonist).

Dose and routes:

By mouth:

- **Neonate:** 3 mg/kg 4 times daily.
- **Child 1 month-18 years:** 3 mg/kg 4 times daily.

Notes:

- Not licensed for use in children with gastrointestinal stasis.
- Available as: tablets (250 mg, 500 mg) and oral suspension (125 mg/5 mL, 250 mg/5 mL).
- Interacts with many antiepileptics by reducing their metabolism.

Etamsylate

Evidence: [218]

Use:

- Treatment of haemorrhage, including surface bleeding from ulcerating tumours.

Dose and routes:

By mouth:

- **> 18 years:** 500 mg 4 times daily, indefinitely or until a week after cessation of bleeding.

Notes:

- Not licensed for use with children with haemorrhage.
- Available as: tablets (500 mg).

Fentanyl

Evidence: [25, 128, 219, 223, 224, 255, 262-271]

Use:

- Step 2 WHO pain ladder once dose is titrated.

Dose and routes:

Normally convert using OME from previous analgesia. Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By transmucosal application (lozenge with oromucosal applicator):

- **Child 2-18 years and greater than 10 kg:** 15 micrograms/kg as a single dose, titrated to a maximum dose 400 micrograms (higher doses under specialist supervision).

By intranasal:

- **Child 2-18 years:** 1-2 micrograms/kg as a single dose, with initial maximum single dose of 50 micrograms.

By transdermal patch or continuous infusion:

- Based on oral morphine dose equivalent (given as 24-hour totals).

By intravenous injection:

- **Neonate or infant:** 1-2 micrograms/kg per dose slowly over 3-5 minutes; repeated every 2-4 hours.
- **Child:** 1-2 micrograms/kg per dose, repeated every 30-60 minutes.

By continuous intravenous infusion:

- **Neonate or infant:** initial IV bolus of 1-2 micrograms/kg (slowly over 3-5 minutes) followed by 0.5-1 microgram/kg/hour.
- **Child:** initial IV bolus of 1-2 micrograms/kg (slowly over 3-5 minutes) followed by 1 microgram/kg/hour.

Product monograph:

- Oral morphine 45 mg = 12 micrograms/hour patch of fentanyl.
- Oral morphine <90 mg = 25 micrograms/hour patch of fentanyl.
- Oral morphine 135-189 mg = 50 micrograms/hour patch of fentanyl.
- Oral morphine 225-314 mg = 75 micrograms/hour patch of fentanyl.

Notes:

- Injection not licensed for use in children less than 2 years of age. Lozenges and nasal sprays are not licensed for use in children.
- The injection solution can be administered by the intranasal route for doses less than 50 micrograms which is the lowest strength of nasal spray available.
- Injection solution could be administered drop wise (may be unpleasant) or using an atomiser device that A+E units use for intranasal diamorphine.
- The main advantage of fentanyl over morphine in children is its availability as a transdermal formulation.
- It can simplify analgesic management in patients with poor, deteriorating or even absent renal function.
- Avoid or reduce dose in hepatic impairment.
- It is a synthetic opioid, very different in structure from morphine, and therefore ideal for opioid substitution.
- Evidence that it is less constipating than morphine has not been confirmed in more recent studies [261].
- The patch formulation is not usually suitable for the initiation or titration phases of opioid management in palliative care since the patches represent large increments and because of the time lag to achieve steady state.
- The usefulness of lozenges in children is also limited by the dose availability. Opioid morphine equivalence of the smallest lozenge (200 microgram) is 30 mg, meaning it is probably suitable to treat breakthrough pain only for children receiving a total daily dose equivalent of 180 mg morphine or more. Older children will often choose to remove the lozenge before it is completely dissolved, giving them some much-valued control over their analgesia. Note lozenge must be rotated in buccal pouch, not sucked. Unsuitable for pain in advanced neuromuscular disorders where independent physical rotation of lozenge not possible.

- Pharmacokinetics of fentanyl intranasally are favourable but it is not always practical and/or well tolerated in children.

Available as fentanyl citrate:
- Intranasal spray(50 micrograms/metered spray, 100 micrograms/metered spray, 200 micrograms/ metered spray InstanylR). Also available as PecFent 100 microgram/metered spray and 400 microgram/ metered spray.
- Lozenge with oromucosal applicator (200 micrograms, 400 micrograms, 600 micrograms, 800 micrograms, 1.2 mg, 1.6 mg ActiqR).
- Patches (12 microgram/hour, 25 microgram/hour, 50 microgram/hour, 75 microgram/hour, 100 microgram/hour).

Fluconazole

Evidence: [128, 272]

Use:
- Mucosal candidiasis infection.

Dose and routes:
By mouth or intravenous infusion:
- **Neonate under 2 weeks:** 3-6 mg/kg on first day then 3 mg/kg every 72 hours.
- **Neonate over 2 weeks:** 3-6 mg/kg on first day then 3 mg/kg every 48 hours.
- **Child 1 month-12 years:** 3-6 mg/kg on first day then 3 mg/kg (maximum 100 mg) daily.
- **Child 12-18 years:** 50 mg/DAY. Increase to 100 mg/ DAY in difficult infections.

Notes:
- Use for up to 7-14 days in oropharyngeal candidiasis.
- For 14-30 days in other mucosal infection.
- Different duration of use in severely immunocompromised patients.
- Available as: capsules (50 mg, 150 mg, 200 mg) and oral suspension (50 mg/5 mL, 200 mg/mL).

Fluoxetine

Evidence: [128, 194, 202-206, 218, 273, 274]

Use:
- Major depression.

Dose and routes:
By mouth:
- **Child 8-18 years:** initial dose 10 mg once a day. May increase after 1-2 weeks if necessary to a maximum of 20 mg once daily.

Notes:
- Licensed for use in children from 8 years of age.
- Use with caution in children ideally with specialist psychiatric advice.
- Increase in anxiety for first 2 weeks.
- Onset of benefit 3-4 weeks.
- Consider long half-life when adjusting dosage.
- May also help for neuropathic pain and intractable cough.
- Available as: capsules (20 mg) and oral liquid (20 mg/5 mL).

Gabapentin

Evidence: [128, 218, 237, 239, 275, 276] CC, SR

Use:
- Adjuvant in neuropathic pain.

Dose and routes:
By mouth:
- **Child >2years:**
  - Day 1 10 mg/kg as a single dose (maximum single dose 300 mg).
  - Day 2 10 mg/kg twice daily (maximum single dose 300 mg).
  - Day 3 onwards 10 mg/kg three times daily (maximum single dose 300 mg).
  - Increase further if necessary to maximum of 20 mg/kg/dose (maximum single dose 600 mg).
- **From 12 years:** the maximum daily dose can be increased according to response to a maximum of 3600 mg/day.

Notes:
- Not licensed for use in children with neuropathic pain.
- Speed of titration after first 3 days varies between increases every 3 days for fast regime to increase every one to two weeks in debilitated children or when on other CNS depressants.

- No consensus on dose for neuropathic pain. Doses given based on doses for partial seizures and authors' experience.
- Capsules can be opened but have a bitter taste.
- Available as: capsules (100 mg, 300 mg, 400 mg) and tablets (600 mg, 800 mg).

Gaviscon®

Evidence: [128, 129, 218]

Use:

- Gastro-oesophageal reflux, dyspepsia, and heartburn.

Dose and routes:

By mouth:

- **Neonate – 2 years, body weight < 4.5 kg:** 1 dose (half dual sachet) when required mixed with feeds or water for breast fed babies, maximum 6 doses in 24 hours.
- **Neonate – 2 years body weight > 4.5 kg:** 2 doses (1 dual sachet) when required mixed with feeds or water for breast fed babies, maximum 6 doses in 24 hours.
- **Child 2-12 years:** 2.5-5 mL or 1 tablet after meals and at bedtime.
- **Child 12-18 years:** 5-10 mL or 1-2 tablets after meals and at bedtime.

Notes:

- Available as: tablets, liquid (Gaviscon® Advance), and infant sachets (comes as dual sachets, each half of dual sachet is considered one dose).
- Gaviscon Infant not to be used with feed thickeners, nor with excessive fluid losses, (e.g. fever, diarrhoea, vomiting).

Glycerol (glycerin)

Evidence: [128, 218, 246]

Use:

- Constipation.

Dose and routes:

By rectum:

- Neonate: tip of a glycerol suppository (slice a small chip of a 1 g suppository with a blade).
- Child 1 month-1 year: 1 g infant suppository as required.
- Child 1-12 years: 2 g child suppository as required.
- Child 12-18 years: 4 g adult suppository as required.

Notes:

- Moisten with water before insertion.
- Hygroscopic and lubricant actions. May also be a rectal stimulant.
- Response usually in 20 minutes to 3 hours.
- Available as: suppositories (1 g, 2 g, and 4 g).

Glycopyrronium bromide

Evidence: [128, 150-152]

Use:

- Control of upper airways secretion and hypersalivation.

Dose and routes:

By mouth:

- **Child 1 month-18 years:** initial dose of 40 microgram/kg 3-4 times daily. The dose may be increased as necessary to 100 microgram/kg 3-4 times daily. Maximum 2 mg/dose given 3 times daily.

Subcutaneous:

- **Child 1 month-12 years:** initial dose of 4 micrograms/kg 3 to 4 times daily. The dose may be increased as necessary to 10 microgram/kg 3-4 times daily. Maximum 200 microgram/dose given 4 times daily.
- **Child 12-18 years:** 200 micrograms every 4 hours when required.

Continuous subcutaneous infusion:

- **Child 1 month-12 years:** initial dose of 10 micrograms/kg/24 hours. The dose may be increased as necessary to 40 microgram/kg/24 hours (maximum 1.2 mg/24 hours).
- **Child 12-18 years:** initial dose of 0.6 mg/24 hours. The dose may be increased as necessary to 1.2 mg/24 hours. Maximum recommended dose is 2.4 mg/24 hours.

Notes:

- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Excessive secretions can cause distress to the child, but more often cause distress to those around them.
- Treatment is more effective if started before secretions become too much of a problem.
- Glycopyrronium does not cross the blood brain barrier and therefore has fewer side effects than hyoscine hydrobromide, which is also used for this purpose. Also fewer cardiac side effects.
- Slower onset response than with hyoscine hydrobromide or butylbromide.
- For oral administration injection solution may be given or crushed tablets suspended in water.
- Available as: tablets (1 mg, 2 mg via an importation company as the tablets are not licensed in the UK): dosing often too inflexible for children, costly and can be difficult to obtain. Injection (200 microgram/mL 1mL ampoules) can also be used orally (unlicensed route).Oral solution can also be prepared extemporaneously from glycopyrronium powder and obtained from a 'specials' manufacturer.

Haloperidol

Evidence: [128, 197-199, 218, 221, 254, 277, 278]

Use:

- Nausea and vomiting where cause is metabolic or in tricky or difficult to manage cases.
- Restlessness and confusion.
- Intractable hiccups.
- Psychosis, hallucination.

Dose and routes:

By mouth for nausea and vomiting:

- **Child 12-18 years:** 1.5 mg once daily at night, increasing as necessary to 1.5 mg twice a day; maximum 5 mg twice a day.

By mouth for *restlessness and confusion*:

- **Child 12-18 years:** 10-20 microgram/kg every 8-12 hours; maximum 10 mg/day.

By mouth for *intractable hiccups*:

- **Child 12-18 years:** 1.5 mg 3 times daily.

By continuous IV or SC infusion (for any indication):

- **Child 1 month-12 years:** initial dose of 25 microgram/kg/24 hours (initial maximum 1.5mg/24hrs). The dose may be increased as necessary to a maximum of 85 microgram/kg/24 hours.
- **Child 12-18 years:** initial dose of 1.5 mg/24 hours. The dose may be increased as necessary to a suggested maximum of 5 mg/24 hours although higher doses may be used under specialist advice.

Notes:

- D2 receptor antagonist and typical antipsychotic.
- The cBNF in UK recommends caution in high doses or IV. The FDA in the USA recommends EKG monitoring if Haloperidol is given IV.
- 'Extra caution when giving Haloperidol to patients with other QT-prolonging conditions, including electrolyte abnormalities (particularly hypokalemia and hypomagnesaemia), underlying cardiac disease, familial prolonged QTc, or taking other drugs known to prolong the QT interval'.
- Dosages for restlessness and confusion are often higher.
- Adult dosages can exceed 15 mg/24 hours in severe agitation.
- Not licensed for use in children with nausea and vomiting, restlessness and confusion or intractable hiccups.
- Useful as long acting – once daily dosing often adequate.
- Available as: tablets (500 microgram, 1.5 mg, 5 mg, 10 mg, 20 mg), capsules (500 microgram), oral liquid (1 mg/mL, 2 mg/mL), and injection (5 mg/mL).

Hydromorphone

Evidence: CC, EA, [128, 218-220, 236, 239, 265, 266, 279, 280]

Use:

- Alternative opioid analgesic for severe pain (Step 2 WHO Pain Ladder) especially if intolerant to other strong opioids.
- Antitussive.

Dose and routes:

Normally convert using OME from previous analgesia. Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth:

- **Child 12-18 years:** initially 1.3 mg/dose or 30-80 micrograms/kg per dose every 3-4 hours increasing as required. Modified release capsules: initially 4 mg/dose every 12 hours increasing if necessary.

By IV or SC infusion:

- **Child:** initially 15 micrograms/kg per dose slowly over at least 2-3 minutes every 3-6 hours.
- Convert from oral (halve dose for equivalence).

Notes:

- Hydrated morphine ketone effects are common to the class of mu agonist analgesics.
- Injection is not licensed in the UK. May be possible to obtain via a specialist importation company but as hydromorphone is a CD this is not a straightforward process.
- Oral bioavailability 37-62% (wide inter-individual variation), onset of action 15 min for SC, 30 min for oral. Peak plasma concentration 1hour orally. Plasma half life 2.5 hours early phase, with a prolonged late phase. Duration of action 4-5 hours.
- Oral form licensed for use in children from 12 years of age with cancer pain.
- Potency ratios seem to vary more than for other opioids. This may be due to inter-individual variation in metabolism or bioavailability.
- Caution in hepatic impairment, use at reduced starting doses.
- Conversion of oral morphine to Hydromorphone: divide morphine dose by 5
- Conversion of IV Morphine to Hydromorphone: Divide morphine dose by 5
- Modified release capsules given 12 hourly.
- Capsules (both types) can be opened and contents sprinkled on soft food.
- Available as: capsules (1.3 mg, 2.6 mg) and modified release capsules (2 mg, 4 mg, 8 mg, 16 mg, 24 mg).

Hyoscine butylbromide

Evidence: [128, 151, 152, 218]

Use:

- Adjuvant where pain is caused by spasm of the gastrointestinal or genitourinary tract.
- Management of secretion, especially where drug crossing the blood brain barrier is an issue.

Dose and routes:

By mouth:

- **Child 1 month-2 years:** 300-500 micrograms/kg (maximum 5 mg/dose) 3-4 times daily.
- **Child 2-5 years:** 5 mg 3-4 times daily.
- **Child 5-12 years:** 10 mg 3-4 times daily.
- **Child 12-18 years:** 10-20 mg 3-4 times daily.

By IM or IV injection:

- **Child 1 month-4 years:** 300-500 micrograms/kg (maximum 5 mg) 3-4 times daily.
- **Child 5-12 years:** 5-10 mg 3-4 times daily.
- **Child 12-18 years:** 10-20 mg 3-4 times daily.

By continuous subcutaneous infusion

- **Child 1 month-4 years:** 1.5 mg/kg/24 hours (max 15 mg/24 hours).
- **Child 5-12 years:** 30 mg/24 hours.
- **Child 12-18 years:** up to 60-80mg/24 hours.
- Higher doses may be needed; doses used in adults range from 20-120 mg/24 hours (maximum dose 300 mg/24 hours).

Notes:

- Does not cross blood brain barrier (unlike hyoscine hydrobromide), hence no central antiemetic effect and doesn't cause drowsiness.
- Tablets are not licensed for use in children < 6 years old.
- Injection is not licensed for use in children.
- The injection solution may be given orally. Injection solution can be stored for 24 hours in the refrigerator.
- IV injection should be given slowly over 1 minute and can be diluted with glucose 5% or sodium chloride 0.9%.
- Available as: tablets (10 mg) and injection (20 mg/mL).

Hyoscine hydrobromide

Evidence: [128, 150-152, 218, 246]

Use:

- Control of upper airways secretion and hypersalivation.

Dose and routes:

By mouth or sublingual:

- **Child 2-12 years:** 10 micrograms/kg (maximum 300 micrograms single dose) 4 times daily.
- **Child 12-18 years:** 300 micrograms 4 times daily.

By transdermal route:

- **Neonate:** quarter of a patch every 72 hours.
- **Child 1 month-3 years:** quarter of a patch every 72 hours.
- **Child 3-10 years:** half of a patch every 72 hours.
- **Child 10-18 years:** one patch every 72 hours.

By SC or IV injection or infusion:

- **Child 1 month-18 years:** 10 micrograms/kg (maximum 600 micrograms) every 4-8 hours. Maximum suggested dose is 2.4 mg in 24 hours although higher doses are often used by specialist units.

Notes:

- Not licensed for use in children for control of upper airways secretion and hypersalivation.
- Higher doses often used under specialist advice.
- Can cause delirium or sedation (sometimes paradoxical stimulation) with repeated dosing. Constipating.
- Apply patch to hairless area of skin behind ear.
- The patch can cause alteration of the pupil size on the side it is placed.
- Some specialists advise that transdermal patches should not be cut – however, the manufacturers of Scopoderm TTS patch state that it is safe to do this.
- Injection solution may be administered orally.
- Available as: tablets (150 micrograms, 300 micrograms), patches (releasing 1 mg/72hours), and injection (400 microgram/mL, 600 microgram/mL).

Ibuprofen

Evidence: [128, 129, 218, 281]

Use:

- Simple analgesic.
- Pyrexia.
- Adjuvant for musculoskeletal pain.

Dose and routes:

By mouth:

- **Neonate:** 5 mg/kg/dose every 12 hours
- **Child 1-3 months:** 5 mg/kg 3-4 times daily preferably after food.
- **Child 3-6 months:** 50 mg 3 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3-4 divided doses.
- **Child 6 months-1 year:** 50 mg 3-4 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3-4 divided doses.
- **Child 1-4 years:** 100 mg 3 times daily preferably after food; in severe conditions up to 30 mg/kg daily in 3-4 divided doses.
- **Child 4-7 years:** 150 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3-4 divided doses. Maximum daily dose 2.4 g.
- **Child 7-10 years:** 200 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3-4 divided doses. Maximum daily dose 2.4 g.
- **Child 10-12 years:** 300 mg 3 times daily, preferably after food. In severe conditions, up to 30 mg/kg daily in 3-4 divided doses. Maximum daily dose 2.4 g.
- **Child 12-18 years:** 300-400 mg 3-4 times daily preferably after food. In severe conditions the dose may be increased to a maximum of 2.4 g/day.

Pain and inflammation in rheumatic diseases, including idiopathic juvenile arthritis:

- **Child aged 3 months-8 years and body weight > 5 kg:** 30-40 mg/kg daily in 3-4 divided doses preferably after food. Maximum 2.4 g daily.

In systemic juvenile idiopathic arthritis:

- Up to 60 mg/kg daily in 4-6 divided doses up to a maximum of 2.4 g daily (off-label).

Notes:

- **Will cause closure of ductus arteriosus; contraindicated in duct dependent congenital heart disease.**
- Orphan drug licence for closure of ductus arteriosus in preterm neonate.
- Caution in asthma and look out for symptoms and signs of gastritis.
- Consider use of proton pump inhibitor in prolonged use of ibuprofen.
- Liquid and plain tablets are not licensed for use in children < 7kg or < 1 year old.
- Topical preparations and granules are not licensed for use in children.
- Available as: tablets (200 mg, 400 mg, 600 mg), capsule (300 mg MR), oral syrup (100 mg/5 mL), granules (600 mg/sachet), and spray, creams and gels (5%).

Ipratropium Bromide

Evidence: RE [128]

Use:

- Wheezing/Breathlessness caused by bronchospasm.

Dose and routes:

Nebulised solution:

- **Child less than 1 year:** 125 micrograms 3 to 4 times daily.
- **Child 1-5 years:** 250 micrograms 3 to 4 times daily.
- **Child 5-12 years:** 500 micrograms 3 to 4 times daily.
- **Child over 12 years:** 500 micrograms 3 to 4 times daily.

Aerosol Inhalation:

- **Child 1 month-6 years:** 20 micrograms 3 times daily.
- **Child 6-12 years:** 20-40 micrograms 3 times daily.
- **Child 12-18 years:** 20-40 micrograms 3-4 times daily.

Notes:

- Available as: nebuliser solution (250 micrograms in 1mL, 500 micrograms in 2mL), aerosol inhaler (20 microgram per metered dose).
- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training.
- In acute asthma, use via an oxygen driven nebuliser.
- In severe acute asthma, dose can be repeated every 20-30 minutes in first two hours, then every 4-6 hours as necessary.

Ketamine

Evidence: [266, 282-289] CC, EA

Use:

- Adjuvant to a strong opiate for neuropathic pain.
- To reduce NMDA wind-up pain and opioid tolerance.

Dose and routes:

By mouth or sublingual:

- **Child 1 month-12 years:** Starting dose 150 microgram/kg, as required or regularly 6-8 hourly: increase in increments of 150 microgram/kg up to 400 microgram/kg as required. Doses equivalent to 3 mg/kg have been reported in adults.
- **Over 12 years and adult:** 10 mg as required or regularly 6-8 hourly; increase in steps of 10 mg up to 50 mg as required. Doses up to 200 mg 4 times daily reported in adults.

By continuous SC or IV infusion:

- **Child 1 month-adult:** Starting dose 40 microgram/kg/hour. Increase according to response; usual maximum 100 microgram/kg/hour. Doses up to 1.5 mg/kg/hour in children and 2.5 mg/kg/hour in adults have been reported.

Notes:

- NMDA antagonist.
- Specialist use only.
- Not licensed for use in children with neuropathic pain.
- Higher doses (bolus injection 1-2 mg/kg, infusions 600-2700 microgram/kg/hour) used as an anaesthetic e.g. for short procedures.
- Sublingual doses should be prepared in a maximum volume of 2ml. The bitter taste may make this route unpalatable. Special preparations for sublingual use are available in UK.
- Enteral dose equivalents may be as low as 1/3 IV or SC dose because ketamine is potentiated by hepatic first pass metabolism.
- Agitation, hallucinations, anxiety, dysphoria and sleep disturbance are recognised side effects. These may be less common in children and when sub-anaesthetic doses are used.
- Caution in severe hepatic impairment, consider dose reduction.
- Dilute in 0.9% saline for subcutaneous or intravenous infusion.
- Can be administered as a separate infusion or by adding to opioid infusion/PCA/NCA.
- Can also be used intranasally and as a topical gel.
- Available as: injection (10 mg/mL, 50 mg/mL, 100 mg/mL) and oral solution 50 mg in 5 ml (from a 'specials' manufacturer). Injection solution may be given orally. Mix with a flavoured soft drink to mask the bitter taste.

Lactulose

Evidence: [17, 24, 128, 218, 221, 223, 246]

Use:

- Constipation.
- Hepatic encephalopathy and coma.

Dose and routes:

Constipation

By mouth: initial dose twice daily then adjusted to suit patient:

- **Neonate:** 2.5 ml/dose twice a day.
- **Child 1 month to 1 year:** 2.5 ml/dose 1-3 times daily.
- **Child 1 year to 5 years:** 5 ml/dose 1-3 times daily.
- **Child 5-10 years:** 10 ml/dose 1-3 times daily.
- **Child 10-18 years:** 15 ml/dose 1-3 times daily.

Hepatic encephalopathy

- **Child 12-18 years:** use 30-50 ml three times daily as initial dose. Adjust dose to produce 2-3 soft stools per day.

Notes:

- Side effects may cause nausea and flatus, with colic especially at high doses. Initial flatulence usually settles after a few days.
- Precautions and contraindications; Galactosaemia, intestinal obstruction. Caution in lactose intolerance.
- Use is limited as macrogols are often better in palliative care.
- Sickly taste.
- Onset of action can take 36-48 hours.
- May be taken with water and other drinks.
- Relatively ineffective in opioid induced constipation: need a stimulant.
- 15 ml/day is 14kcal so unlikely to affect diabetics.
- Does not irritate or directly interfere with gut mucosa.
- Available as oral solution 10 g/15 ml. Cheaper than Movicol (macrogol).
- Licensed for constipation in all age groups. Not licensed for hepatic encephalopathy in children.

Levomepromazine

Evidence: [127, 128, 200, 218, 223] CC, EA

Use:

- Broad spectrum antiemetic where cause is unclear, or where probably multifactorial.
- Second line if specific antiemetic fails.
- May be of benefit in a very distressed patient with severe pain unresponsive to other measures.
- Sedation for terminal agitation, particularly in end of life care.

Dose and routes:

Used as antiemetic

By mouth:

- **Child 2-12 years:** initial dose 0.1 mg/kg given once or twice daily. This dose may be increased as necessary to a maximum of 1 mg/kg given once or twice daily. Maximum 25 mg once or twice daily.
- **Child 12-18 years:** initial dose 6.25 mg once or twice daily. This dose may be increased as necessary to a maximum of 25 mg once or twice daily.

By continuous IV or SC infusion over 24 hours:

- **Child 1 month-12 years:** initial dose of 0.1 mg/kg/24 hours increasing as necessary to a maximum of 0.4 mg/kg/24 hours. Maximum 25 mg daily.
- **Child 12-18 years:** initial dose of 5 mg/24 hours increasing as necessary to a maximum of 25 mg/24 hours.

Used for sedation

By SC infusion over 24 hours:

- **Child 1 year-12 years:** initial dose of 0.35 mg/kg/24 hours (maximum initial dose 12.5 mg), increasing as necessary up to 3 mg/kg/24 hours.
- **Child 12-18 years:** initial dose of 12.5 mg/24 hours increasing as necessary up to 200 mg/24 hours.

Analgesia

- In adults stat dose 12.5 mg/dose by mouth or SC. Titrate dose according to response; usual maximum daily dose in adults is 100 mg SC or 200 mg by mouth.

Notes:

- Licensed for use in children with terminal illness for the relief of pain and accompanying anxiety and distress.
- Low dose often effective as antiemetic. Titrate up as necessary. Higher doses very sedative.
- Low dosages are often very effective for nausea and vomiting. If child not stable on high dosage for nausea and vomiting, reconsider cause and combine with other agents.
- For SC infusion dilute with sodium chloride 0.9%.
- Some experience in adults with low dose used buccally as antiemetic (e.g. 1.5mg three times daily as needed).
- Can cause hypotension particularly with higher doses.
- Available as: tablets (25mg) and injection (25mg/mL). An extemporaneous oral solution may be prepared.

Lidocaine (Lignocaine) patch

Evidence: [218, 290-292] CC, EA

Use:
- Localised neuropathic pain.

Dose and routes:
Topical:
- **Child 3-18 years:** apply 1-2 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hour plaster free period.
- **Adult 18 years or above:** up to 3 plasters to affected area(s). Apply plaster once daily for 12 hours followed by 12 hour plaster free period.

Notes:
- Not licenced for use in children or adolescents under 18 years.
- Available as 700 mg/medicated plaster (5% w/v lidocaine).
- Cut plaster to size and shape of painful area. Do NOT use on broken or damaged skin. If skin is unbroken and normal hepatic function risk of systemic absorption is low.
- Maximum recommended number of patches in adults currently is 3 per application.
- Doses extrapolated from BNF 2012 March.

Loperamide

Evidence: [128, 218, 293, 294]

Use:
- Diarrhoea from non-infectious cause.

Dose and routes:
By mouth:
- **Child 1 month-1 year:** initial dose of 0.1 mg/kg twice daily given 30 minutes before feeds. Increase as necessary up to a maximum of 2 mg/kg/DAY given in divided doses.
- **Child 1-12 years:** initial dose of 0.1 mg/kg (maximum single dose 2 mg) 3-4 times daily. Increase as necessary up to a maximum of 1.25 mg/kg/DAY given in divided doses (maximum 16 mg/DAY).
- **Child 12-18 years:** initial dose of 2 mg 2-4 times daily. Increase as necessary up to a maximum of 16 mg/DAY given in divided doses.

Notes:
- Not licensed for use in children with chronic diarrhoea.
- Capsules not licensed for use in children < 8 years.
- Syrup not licensed for use in children < 4 years.
- Available as tablets (2 mg) and oral syrup (1 mg/5 mL).

Lomotil® (co-phenotrope)

Evidence: [40, 41, 43, 128, 218]

Use:
- Diarrhoea from non-infectious cause.

Dose and routes:
By mouth:
- **Child 2-4 years:** half tablet 3 times daily.
- **Child 4-9 years:** 1 tablet 3 times daily.
- **Child 9-12 years:** 1 tablet 4 times daily.
- **Child 12-16 years:** 2 tablets 3 times daily.
- **Child 16-18 years:** initially 4 tablets then 2 tablets 4 times daily.

Notes:
- Not licensed for use in children < 4 years.
- Available only as tablets Co-Phenotrope (2.5 mg diphenoxylate hydrochloride and 25 microgram atropine sulphate).
- Tablets may be crushed.

Lorazepam

Evidence: [128, 197, 295] CC, EA

Use:
- Background anxiety.
- Agitation and distress.
- Adjuvant in cerebral irritation.
- Background management of dyspnoea.
- Muscle spasm.
- Status epilepticus.

Dose and routes for all indications except status epilepticus:
By mouth:
- **Child < 2 years:** 25 microgram/kg 2-3 times daily.
- **Child 2-5 years:** 0.5 mg 2-3 times daily.
- **Child 6-10 years:** 0.75 mg 3 times daily.
- **Child 11-14 years:** 1 mg 3 times daily.
- **Child 15-18 years:** 1-2 mg 3 times daily.

Sublingual:
- **Children of all ages:** 25 micrograms/kg as a single dose. Increase to 50 microgram/kg (maximum 1 mg/dose) if necessary.
- **Usual adult dose:** 500 microgram – 1 mg as a single dose, repeat as required.

Notes:
- Well absorbed sublingual, fast effect.
- Potency in the order of 10 times that of diazepam per mg as anxiolytic/sedative.
- Most children will not need more than 0.5 mg for trial dose.
- Injectable form can also be given sublingual in same doses (off-label).
- May cause drowsiness and respiratory depression if given in large doses.
- Caution in renal and hepatic failure.
- Available as tablets (1 mg, scored, 2.5 mg) and injection (4 mg in 1mL).
- Not licensed for use in children for these indications.
- Tablets licensed in children over 5 years for premedication, injection not licensed in children less than 12 years except for treatment of status epilepticus.

Melatonin

Evidence: [128, 218, 296-311]

Use:
- Sleep disturbance due to disruption of circadian rhythm (not anxiolytic).

Dose and routes:
By mouth:
- **Child 1 month-18 years:** initial dose 2-3 mg, increasing every 1-2 weeks dependent on effectiveness up to maximum 10 mg daily (higher doses have been used).

Notes:
- Not licensed for use in children.
- Specialist use only.
- Some prescribers use a combination of immediate release and m/r tablets to optimise sleep patterns.
- Only licensed formulation in the UK is 2 mg m/r tablets (Circadin). Various unlicensed formulations, including an immediate release preparation are available from 'specials' manufacturers or specialist importing companies.

Methadone

Evidence: [128, 218, 219, 223, 236, 246, 312-323]

(WARNING: requires additional training for dosing)

Use:
- Major opioid moderate to severe pain, particularly neuropathic pain and pain poorly responsive to other opioids.
- Not normally used as first line analgesia.

Caution:
Methadone should only be commenced by practitioners experienced in its use.
This is due to wide inter-interindividual variation in response, very variable conversion ratios with other opioids, complex pharmacokinetics and a long half life. Initial close monitoring is particularly important.

Dose and routes:
In opioid naïve children
By mouth, SC and IV injection:
- **Child 1-12 years:** 100-200 micrograms/kg every 4 hours for first 2-3 doses then every 6-12 hours (maximum dose 5 mg/dose initially).
- Methadone should initially be titrated like other major opioids.
- **Doses may need to be reduced by up to 50% 2-3 days after the effective dose has been found to prevent adverse effects** due to methadone accumulation. From then on increments in methadone dosing should be approximately at weekly intervals, with a maximum increase of 50% (experienced practitioners may increase more frequently).
- Titration of methadone dosing must be done under close clinical observation of the patient particularly in the first few days. Due to large volume of distribution, higher doses are required for the first few days whilst body tissues become saturated. Once saturation is complete, a smaller dose is sufficient. Continuing on initial daily dose is likely to result in sedation within a few days, possible respiratory depression and even death.
- Methadone has a long and variable half-life with potential to cause sedation, respiratory depression and even death from secondary peak phenomenon.
- Continued clinical reassessment is required to avoid toxicity as time to reach steady state concentration following a change in dosing may be up to 12 days.
- The breakthrough dose of oral methadone will be 5-10% of the total 24 hour dose. Caution is required here as the total number of daily doses (regular plus breakthrough doses) rarely exceeds six doses per day.
- *Administer IV methadone slowly over 3-5 minutes.*

In opioid substitution/rotation or switch
Caution: Substitution, rotation or switch to methadone is a specialist skill and should only be undertaken in close collaboration with practitioners experienced in its use. There is a risk of unexpected death through overdose.

Equianalgesic doses:
Dose conversion ratios from other opioids are not static but are a function of previous opioid exposure, and are highly variable.

Published tables of equianalgesic doses of opioids, established in healthy non-opioid tolerant individuals, indicate that methadone is 1-2 times as potent as morphine in single dose studies, but in individuals on long-term (and high dose) morphine, methadone is closer to 10 times as potent as morphine; it can be 30 times more potent or occasionally even more. The potency ratio tends to increase as the dose of morphine increases. If considering methadone, thought should be given to the potential difficulty of subsequently switching from methadone to another opioid.

Other opioids should be considered first if switching from morphine due to unacceptable effects or inadequate analgesia.

Consultation with a pain clinic or palliative-care service is advised.

Ref [219]

In adults there are several protocols for opioid rotation to methadone which are not evidence based in paediatrics.

- In one approach, previous opioid therapy is completely stopped and restarted with a fixed dose of methadone at variable dose intervals.
- The other approach incorporates a transition period where the dose of the former opioid is reduced and partially replaced by methadone.

It can be difficult to convert patients to methadone, or from methadone to other opioids. Current practice is usually to admit to a specialist inpatient unit for 5-6 days of regular treatment or titrate orally at home with close supervision.

Converting oral methadone to SC/IV or CSCI/CIVI methadone

- Approximate dose ratios for switching between oral dosage and parenteral/subcutaneous form 1:1 - 2:1 (oral: parenteral).
- Calculate the total daily dose of oral methadone and halve it (50%). This will be the 24hour parenteral/subcutaneous methadone dose.
- Seek specialist guidance if mixing with any other drug [312].
- If CSCI methadone causes a skin reaction, double the dilution and change the syringe every 12 hours.

Notes:

- Not licensed for use in children with neuropathic pain.
- Data on methadone in paediatric patients is limited; known to have wide inter-individual pharmacokinetic variation.
- Use methadone with caution, as methadone's effect on respiration lasts longer than analgesic effects.
- Side effects include: nausea, vomiting, constipation, dry mouth, biliary spasm, respiratory depression, drowsiness, muscle rigidity, hypotension, bradycardia, tachycardia, palpitation, oedema, postural hypotension, hallucinations, vertigo, euphoria, dysphoria, dependence, confusion, urinary retention, ureteric spasm and hypothermia.
- Following concerns regarding methadone and sudden death from prolongation of QT interval or torsade de pointes (especially at high doses) it is recommended that patients have an ECG prior to initiation of treatment, particularly if they have any risk factors or are having intravenous treatment.
- Methadone has potentially lethal drug interactions with other drugs (for example: naltrexone; naloxone; monoamine oxidase inhibitors).
- Carbamazepine, phenobarbital, phenytoin and rifampicin increase the metabolism of methadone; amitriptyline, cimetidine, ciprofloxacin, fluconazole and SSRIs decrease its metabolism.
- Efavirenz, lopinavir-ritonavir, nelfinavir, nevirapine and ritonavir (all antiretroviral agents) may reduce plasma methadone concentrations.
- Renal impairment: severe (GFR <10 ml/min or serum creatinine >700 micromol/l) – reduce dose by 50% and titrate according to response; significant accumulation is not likely in renal failure, as elimination is primarily via the liver.
- As methadone has a long half-life, infusion of naloxone may be required to treat opioid overdose.
- Available as: linctus (2 mg/5 mL), mixture (1 mg/mL), solution (1 mg/mL, 5 mg/ml, 10 mg/mL, and 20 mg/mL), tablets (5 mg), and injection (10 mg/mL).

Methylnaltrexone

Evidence: [218, 324]

Use:
- Opioid induced constipation in palliative care not responsive to other laxatives.

Dose and routes:
- Subcutaneous injection:
  Body weight < 38 kg: 150 microgram/kg on alternate days.
  Body weight 38-62 kg: 8 mg on alternate days.
  Body weight 62-114 kg: 12 mg on alternate days.
- Patients may receive two consecutive doses 24 hours apart, only when there has been no response (bowel movement) to the dose on the preceding day.

Notes:
- Constipation in palliative care is usually multifactorial and other laxatives are often required in addition; reduce dose by 50% in severe renal impairment.
- Does not cross blood brain barrier.
- Not licensed for use under 18 years.
- Available as subcutaneous injection 20 mg/ml.
- Contraindicated in bowel obstruction.

Metoclopramide

Evidence: [19, 67, 91, 93, 94, 120, 123, 128, 129, 218, 246, 325, 326]

Use:
- Antiemetic if vomiting caused by gastric compression or hepatic disease.
- Prokinetic for slow transit time (not in complete obstruction or with anticholinergics).
- Hiccups.

Dose and routes:
By mouth, IM injection, or IV injection:
- **Neonate:** 100 microgram/kg every 6-8 hours (by mouth or IV only).
- **Child 1 month-1 year and body weight up to 10 kg:** 100 microgram/kg (max. 1 mg/dose) twice daily.
- **Child 1-3 years and body weight up to 10-14 kg:** 1 mg 2-3 times daily.
- **Child 3-5 years and body weight up to 15-19 kg:** 2 mg 2-3 times daily.
- **Child 5-9 years and body weight up to 20-29 kg:** 2.5 mg 3 times daily.
- **Child 9-10 years and body weight up to 30-60 kg:** 5 mg 3 times daily.
- **Child 15-18 years and body weight over 60 kg:** 10 mg 3 times daily.

Notes:
- Not licensed for use in neonates as a prokinetic.
- Available as: tablets (10 mg), oral solution (5 mg/5 mL) and injection (5 mg/mL).
- Use may be limited by dystonic side effects.

Metronidazole topically

Evidence: [128, 218]

Use:
- Odour associated with fungating wound or lesion.

Dose and routes:
By topical application:
- Apply to clean wound 1-2 times daily and cover with non-adherent dressing.
- Cavities: smear gel on paraffin gauze and pack loosely.

Notes:
- Anabact® not licensed for use in children < 12 years.
- Metrogel® not licensed for use with children.
- Available as: gel (Anabact® 0.75%, Metrogel® 0.75%, Metrotop® 0.8%).

Miconazole oral gel

Evidence: [128]

Use:
- Oral and intestinal fungal infection.

Dose and routes:
By mouth:
- **Neonate:** 1 mL 3-4 times a day.
- **Child 1 month-2 years:** 2.5 mL twice daily.
- **Child 2-6 years:** 5 mL 2 times daily.
- **Child 6-12 years:** 5 mL 4 times daily.
- **Child 12-18 years:** 5-10 mL 4 times daily.

Notes:
- After food retain near lesions before swallowing.
- Treatment should be continued for 48 hours after lesions have healed.
- Not licensed for use in children under 4 months.
- Available as: oral gel (24 mg/mL in 15 g and 80 g tube).

Micralax® Micro-enema (sodium citrate)

Evidence: [128, 218]

Use:

- Constipation where osmotic laxative indicated.

Dose and routes:

By rectum:

- **Child 3-18 years:** 5 mL as a single dose.

Notes:

- Not recommended in children < 3 years.
- Available as: micro-enema (5 mL).

Midazolam

Evidence: [48, 52, 53, 128, 143, 144, 221, 327-330]

Use:

- Status epilepticus and terminal seizure control.
- Breakthrough anxiety, e.g. panic attacks.
- Adjuvant for pain of cerebral irritation.
- Anxiety induced dyspnoea.
- Agitation at end of life.

Dose and routes:

By buccal or intranasal administration for status epilepticus, should wait 10 minutes before repeating dose:
By oral or gastrostomy administration for anxiety or sedation:

Buccal doses for status epilepticus:

- **Neonate:** 300 microgram/kg as a single dose, repeated once if necessary.
- **Child 1-6 months:** 300 microgram/kg (maximum initial dose 2.5 mg), repeated once if necessary.
- **Child 6 months-1 year:** 2.5 mg, repeated once if necessary.
- **Child 1-5 years:** 5 mg, repeated once if necessary.
- **Child 5-10 years:** 7.5 mg, repeated once if necessary.
- **Child 10-18 years:** 10 mg, repeated once if necessary.

Buccal doses for acute anxiety:

- **Any age:** 100 microgram/kg as a single dose (maximum initial dose 5 mg).

By SC or IV infusion over 24 hours for terminal seizure control:

- **Neonate (seizure control):** 150 microgram/kg IV loading dose followed by a continuous IV infusion of 60 microgram/kg/hour. Dose can be increased by 60 microgram/kg/hour every 15 minutes until seizure controlled (maximum dose 300 microgram/kg/hour).
- **Child 1 month-18 years:** Initial dose 50 microgram/kg/hour increasing up to 300 microgram/kg/hr (maximum 100 mg/24 hours or 150 mg/24 hours in specialist units).

By SC or IV infusion over 24 hours for anxiety:

- Dosages of 30-50% of terminal seizure control dose required to control anxiety, terminal agitation and terminal breathlessness.

Notes:

- Not licensed for use in children with these conditions.
- In single dose for sedation midazolam is 3 times as potent as diazepam, and in epilepsy it is twice as potent as diazepam. (Diazepam gains in potency with repeated dosing because of prolonged half life).
- Recommended doses vary enormously in the literature. If in doubt, start at the lowest recommended dose and titrate rapidly.
- Onset of action by buccal and intranasal route 5-10 minutes.
- Onset of action by oral or gastrostomy route 10-30 minutes.
- Onset of action by IV route 2-3 minutes.
- Midazolam has a short half life.
- High doses can lead to paradoxical agitation.
- Available as oral solution (2.5 mg/mL), buccal liquid (10 mg/mL), and injection (1 mg/mL, 2 mg/mL, 5 mg/mL). Oral and buccal liquids are available from 'specials' manufacturers or specialist importing companies (unlicensed). A licensed buccal formulation Buccolam® is now available. NOTE The buccal formulations available may differ in strength – take care with prescribing.
- First dose in community may be given as two aliquots.

Morphine

Evidence: [11, 128, 129, 218, 221, 236, 255, 265, 282, 331-347]

Use:

- Major opioid (step 2). First line oral opioid for breakthrough and background.
- Dyspnoea.
- Cough suppressant as morphine linctus.

Dose and routes:

Normally convert using OME from previous analgesia. Use the following **starting** doses in opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth or rectum:

- **Child 1-3 months:** initially 50 micrograms/kg every 4 hours adjusted to response.
- **Child 3-6 months:** initially 100 micrograms/kg every 4 hours adjusted to response.
- **Child 6 months-12 years:** initially 200 micrograms/kg every 4 hours adjusted to response, maximum initial dose of 5mg.
- **Child 12-18 years:** initially 5-10 mg every 4 hours adjusted to response.

By continuous SC or IV infusion:

- **Neonate**: 5 micrograms/kg/hour adjusted according to response.
- **Child 1-6 months:** 10 micrograms/kg/hour adjusted according to response.
- **Child 6 months - 18 years:** 20 micrograms/kg/hour (maximum 20 mg/24 hours) adjusted according to response.

By single SC injection:

- **Neonate:** initially 25 micrograms/kg every 6 hours adjusted to response.
- **Child 1-6 months:** initially 100 micrograms/kg every 6 hours adjusted to response.
- **Child 6 months-2 years:** initially 100 micrograms/kg every 4 hours adjusted to response.
- **Child 2-12 years:** initially 100 micrograms/kg every 4 hours adjusted to response, maximum initial dose of 2.5mg.
- **Child 12-18 years:** initially 2.5-5 mg every 4 hours adjusted to response (maximum 20 mg/24 hours).

By single IV injection (over at least 5 minutes):

- **Neonate:** initially 25 micrograms/kg every 6 hours adjusted to response.
- **Child 1-6 months:** initially 100 micrograms/kg every 6 hours adjusted to response.
- **Child 6 months-12 years:** initially 100 micrograms/kg every 4 hours adjusted to response maximum initial dose of 2.5 mg.
- **Child 12-18 years:** initially 5 mg every 4 hours adjusted to response.

Parenteral dose: 30-50% of oral dose if converting from oral dose of morphine

Dyspnoea
30-50% of the dose used for pain.

Notes:

- Oramorph® solution not licensed for use in children < 1 year.
- Oramorph® unit dose vials not licensed for use in children < 6 years.
- Sevredol® tablets not licensed for use in children < 3 years.
- MXL capsules not licensed for use in children <1 year.
- Caution in renal or hepatic impairment.
- Where opioid substitution or rotation is to morphine: use oral morphine equivalency.
- Particular side effects include urinary retention and pruritus in paediatric setting, in addition to the well recognised constipation, nausea and vomiting.
- Morphine toxicity often presents as myoclonic twitching.
- Rectal route should be avoided if possible, and usually contraindicated in children with low platelets and/or neutropenia.
- In an emergency, when oral intake not appropriate, MST tablets can be administered rectally.

Available as:

- Tablets (10 mg, 20 mg, 50 mg).
- Oral solution (10 mg/5 mL, 100 mg/5 mL).
- Modified release tablets and capsules (5 mg, 10 mg, 15 mg, 30 mg, 60 mg, 100 mg, 200 mg).
- Modified release capsules 24 hourly (30 mg, 60 mg, 120 mg, 200 mg).
- Modified release suspension (20 mg, 30 mg, 60 mg, 100 mg, 200 mg).
- Suppositories (10 mg, 15 mg, 20 mg, 30 mg).
- Injection (10 mg/mL, 15 mg/mL, 20 mg/mL and 30 mg/mL).

Movicol® Macrogol

Evidence: [17, 20, 128, 218]

Use:
- Constipation.
- Faecal impaction.
- Suitable for opioid-induced constipation.

Dose and routes (Movicol® paediatric plain):
By mouth for constipation or prevention of faecal impaction:
- **Child under 1 year:** ½-1 sachet daily.
- **Child 1-6 years:** 1 sachet daily (adjust dose according to response; maximum 4 sachets daily).
- **Child 6-12 years:** 2 sachets daily (adjust dose according to response; maximum 4 sachets daily).
- **Child 12-18 years:** 1-3 sachets daily of adult Movicol®.

By mouth for faecal impaction:
- **Child under 1 year:** 1/2-1 sachet daily.
- **Child 1-5 years:** 2 sachets on first day and increase by 2 sachets every 2 days (maximum 8 sachets daily). Treat until impaction resolved.
- **Child 5-12 years:** 4 sachets on first day and increase by 2 sachets every 2 days (maximum 12 sachets daily). Treat until impaction resolved.
- **Child 12-18 years:** 8 sachets daily of adult Movicol® for a usual maximum of 3 days.

Notes:
- Not licensed for use in children < 5 years with faecal impaction and < 2 years with chronic constipation.
- Need to maintain hydration. Caution if fluid or electrolyte disturbance.
- Mix powder with water: Movicol® paediatric 60mL per sachet and adult Movicol® 125 mL per sachet.

Nabilone

Evidence: EA [128, 218, 223]

Use:
- Antiemetic if vomiting caused by anxiety/anticipation (e.g. chemotherapy) and unresponsive to conventional antiemetics.

Dose and routes:
By mouth:
- **Adult dose:** 1-2 mg twice a day as required; maximum dose 6 mg/day in divided doses.

Notes:
- Not licensed for use in children.
- Medication is a cannabinoid.
- For specialist use only.
- Available as: capsules (1 mg). Schedule 2 controlled drug.

Naloxone

Evidence: [23, 128, 348] EA

Use:
- Emergency use for reversal of opioid-induced respiratory depression or acute opioid overdose.
- Constipation when caused by opioids if Methylnaltrexone not available.

Dose and routes:
Reversal of respiratory depression due to opioid overdose
By intravenous injection: (review diagnosis, further doses may be required if respiratory depression deteriorates)
- **Neonate:** 10 micrograms/kg; if no response give a subsequent dose of 100 microgram/kg (then review diagnosis).
- **Child 1 month-12 years:** 10 micrograms/kg; if no response give a subsequent dose of 100 microgram/kg (then review diagnosis).
- **Child 12-18 years:** 0.4-2 mg; if no response repeat at intervals of 2-3 minutes to maximum of 10 mg total dose (then review diagnosis).

By subcutaneous or intramuscular injection only if intravenous route not feasible
- As per intravenous injection but onset slower.

By continuous intravenous infusion, adjusted according to response
- **Neonate:** Rate adjusted to response (initially, rate may be set at 60% of the initial resuscitative intravenous injection dose per hour).
- **Child 1 month-18 years:** Rate adjusted to response (initially, rate may be set at 60% of the initial resuscitative intravenous injection dose per hour).
- *The initial resuscitative intravenous injection dose is that which maintained satisfactory ventilation for at least 15 minutes.*

Opioid-induced constipation
By mouth:
- In adults the following doses have been used: total daily dose oral naloxone = 20% of morphine dose; titrate according to need; maximum single dose 5 mg.

Notes:
- Not licensed for use in children with constipation.
- Although oral availability of naloxone is relatively low, be alert for opioid withdrawal symptoms, including recurrence of pain, at higher doses.
- Available as: injection (400 microgram/mL).

Nystatin

Evidence: [116, 128, 272]

Use:
- Oral and perioral fungal infection.

Dose and routes:
By mouth:
- **Neonate:** 100 000 units 4 times a day.
- **Child 1 month-18 years:** 100 000 units 4 times a day.

Notes:
- After food retain near lesions before swallowing.
- Treatment for 7 days and should be continued for 48 hours after lesions have healed.
- Licensed from 1 month of age. Not licensed for use in neonates for treatment of infection but licensed once daily for prophylaxis.
- Available as oral suspension 100 000 units/mL, 30 mL with pipette.

Octreotide

Evidence: [128, 223, 246]

Use:
- Bleeding from oesophageal or gastric varices.
- Nausea and vomiting.
- Intestinal obstruction.
- Intractable diarrhoea.
- Also used for hormone secreting tumours, ascites, bronchorrhoea.

Dose and routes:
Bleeding from oesophageal varices
By continuous intravenous infusion:
- **Child 1 month-18 years:** 1 microgram/kg/hour, higher doses may be required initially. When no active bleeding reduce dose over 24 hours. Usual maximum dose is 50 micrograms/hour.

Nausea and vomiting, intestinal obstruction and intractable diarrhoea
By continuous intravenous or subcutaneous infusion:
25 microgram/kg/24 hours.

Notes:
- Not licensed for use in children.
- Administration: for IV injection or infusion, dilute with sodium chloride 0.9% to a concentration of 10-50% (i.e. not less than 1:1 and not more than 1:9 by volume). For SC bolus injections, may be administered neat but this can be painful (this can be reduced if the ampoule is warmed in the hand to body temperature before injection). For SC infusion may be diluted with 0.9% NaCl.
- Avoid abrupt withdrawal.
- Available as: injection for SC or IV administration (50 micrograms/mL, 100 micrograms/ml, 200 micrograms/ml, 500 micrograms/mL). Also available as depot injection for IM administration every 28 days (10 mg, 20 mg and 30 mg Sandostatin Lar®). Recommend specialist palliative care advice.

Omeprazole

Evidence: [30, 68, 128, 129, 218, 349, 350]

Use:
- Gastro-oesophageal reflux.
- Treatment of peptic ulcers.
- Gastrointestinal prophylaxis (e.g. with combination NSAID/steroids).

Dose and routes:
By mouth:
- **Neonate:** initial dose of 700 microgram/kg once daily; increase if necessary to a maximum of 2.8 mg/kg once daily.
- **Child 1 month-2 years:** initial dose of 700 microgram/kg once daily; increase if necessary to a maximum of 3 mg/kg once daily.
- **Child body weight 10-20 kg:** initial dose of 10 mg once daily; increase if necessary to a maximum of 20 mg once daily.
- **Child body weight > 20 kg:** initial dose 20 mg once daily; increase if necessary to a maximum of 40 mg once daily.

Intravenous (by injection over 5 minutes or by infusion):
- **Child 1 month-12 years:** initially 500 micrograms/kg (maximum 20 mg) once daily, increased, if necessary to 2 mg/kg (maximum 40 mg) once daily.
- **Child 12-18 years:** 40 mg once daily.

Notes:

- Oral formulations not licensed for use in children except for severe ulcerating reflux oesophagitis in children > 1 year.
- Injection not licensed for use in children under 12 years.
- Many children with life limiting conditions have GORD and may need to continue with treatment long term.
- Can cause agitation.
- Occasionally associated with electrolyte disturbance.
- For oral administration tablets can be dispersed in water or with fruit juice or yoghurt. Capsules can be opened and mixed with fruit juice or yoghurt.
- Administer with care via gastrostomy tubes to minimise risk of blockage. Seek advice.
- Available as: MUPS tablets (10 mg, 20 mg, 40 mg), capsules (10 mg, 20 mg, 40 mg), intravenous injection (40 mg) and intravenous infusion (40 mg), oral suspension available as special order 10 mg/5 mL.

Ondansetron

Evidence: [119, 121, 128, 221, 254, 325, 351]

Use:

- Antiemetic, if vomiting caused by chemotherapy or radiotherapy.
- May have a use in managing opioid induced pruritus.

Dose and routes:

During chemotherapy

By mouth:

- **Child 1-12 years:** 4 mg by mouth every 8-12 hours for up to 5 days after chemotherapy.
- **Child 12-18 years:** 8 mg by mouth every 8-12 hours for up to 5 days after chemotherapy.

By slow intravenous injection or by intravenous infusion:

- **Child 1-12 years:** 5 mg/m^2 every 8-12 hours. Maximum single dose 8 mg.
- **Child 12-18 years:** 8 mg every 8-12 hours.

Nausea and vomiting

By mouth or slow intravenous injection or by intravenous infusion:

- **Child 1-18 years:** 0.1-0.15 mg/kg/dose every 8-12 hours. Maximum single dose 8 mg.

Notes:

- Not licensed for use in children < 2 years.
- Causes constipation.
- Available as: tablets (4 mg, 8 mg), oral lyophilisate (4 mg, 8 mg), oral syrup (4 mg/5 mL), injection (2 mg/mL, 2 mL and 4 mL amps).
- For slow intravenous injection, give over 2-5 minutes.
- For intravenous infusion, dilute to a concentration of 320-640 micrograms/mL with Glucose 5% or Sodium Chloride 0.9% or Ringer's Solution; give over at least 15 minutes.

Oxycodone

Evidence: [25, 128, 218, 220, 223, 352-356]

Use:

- Pain of all types unless opioid insensitive. Step 2 WHO pain ladder.

Dose and routes:

Normally convert using OME from previous analgesia. Use the following **starting** doses In opioid naive patient. The maximum dose stated applies to **starting** dose only.

By mouth:

- **Child 1-12 months:** initial dose 50-125 micrograms/kg every 4 hours.
- **Child 1-12 years:** initial dose 125-200 micrograms/kg (maximum single dose 5 mg) every 4 hours.
- **Child 12-18 years:** starting dose 5 mg every 4-6 hours.
- Titrate as for morphine.
- **m/r tablets Child 8-12 years:** initial dose 5 mg every 12 hours, increased if necessary.
- **m/r tablets Child 12-18 years:** initial dose 10 mg every 12 hours, increased if necessary.

By intravenous injection, subcutaneous injection or continuous subcutaneous infusion:

- To convert from oral to IV or SC Oxycodone injection, divide the dose of oral Oxycodone by 2.
- For conversion from oral Oxycodone to a continuous subcutaneous infusion of Oxycodone, divide the total daily dose of oral Oxycodone by 1.5.
- To convert from SC/IV morphine to SC/IV Oxycodone ratio is 1:1. i.e. use same dose.

Notes:
- Not licensed for use in children.
- It is important to prescribe breakthrough analgesia which is 5-10% of the total 24 hour dose given every 1 to 4 hours.
- It is moderately different from morphine in its structure, making it a candidate for opioid substitution.
- It is significantly more expensive than morphine.
- Caution in hepatic or renal impairment.
- Controlled drug schedule 2.
- Available as: tablets and capsules(5 mg, 10 mg, 20 mg), liquid (5 mg/5 ml, 10 mg/ml) and m/r tablets (5 mg, 10 mg, 20 mg, 40 mg, 80 mg), injection (10 mg/ml and 50 mg/ml).

Oxygen

Evidence: [44, 46, 128, 218, 357-359]

Use:
- Breathlessness caused by hypoxaemia.
- Placebo in other causes of breathlessness.

Dose and routes:
By inhalation through nasal cannula:
- Flow rates of 1-2.5L/min adjusted according to response. This will deliver between 24-35% oxygen depending on the patient's breathing pattern and other factors. Lower flow rates may be appropriate particularly for preterm neonates.

By inhalation through facemask:
- Percentage inhaled oxygen is determined by the oxygen flow rate and/or type of mask. 28% oxygen is usually recommended for continuous oxygen delivery.

Notes:
- Oxygen saturations do not necessarily correlate with the severity of breathlessness. Where self-report is not possible observation of the work of breathing is a more reliable indicator of breathlessness.
- Frequent or continuous measurement of oxygen saturations may lead to an over-reliance on technical data and distract from evaluation of the child's over-all comfort and wellbeing.
- Target oxygen saturations 92-96% may be appropriate in acute illness but are not necessarily appropriate for palliative care. More usual target oxygen saturations are above 92% in long-term oxygen therapy and 88-92% in children at risk of hypercapnic respiratory failure.
- Moving air e.g. from a fan maybe equally effective in reducing the sensation of breathlessness when the child is not hypoxaemic.
- Nasal cannula are generally preferable as they allow the child to talk and eat with minimum restrictions. However continuous nasal oxygen can cause drying of the nasal mucosa and dermatitis.
- Oxygen administration via a mask can be claustrophobic.
- The duration of supply from an oxygen cylinder will depend on the size of the cylinder and the flow rate.
- An oxygen concentrator is recommended for patients requiring more than 8 hours oxygen therapy per day.
- Liquid oxygen is more expensive but provides a longer duration of portable oxygen supply. Portable oxygen concentrators are now also available.
- If necessary two concentrators can be Y-connected to supply very high oxygen concentrations.
- Higher concentrations of oxygen are required during air travel.
- Home oxygen order forms (HOOF) and further information available from www.bprs.co.uk/oxygen.html

Pamidronate (Disodium)

Evidence: CC, EA [218, 223, 360]

Use:
- Bone pain caused by metastatic disease or osteopaenia.
- Acute hypercalcaemia.

Dose and routes:
For *bone pain* (metastatic bone disease or osteopaenia):
By IV:
- 1 mg/kg infused over 6 hours, repeated daily for 3 days. Can be given 3 monthly.

For *malignant hypercalcaemia*:
By IV:
- 1 mg/kg infused over 6 hours, then repeated as indicated by serum calcium.

Notes:
- Not licensed for use in children.
- May have worsening of pain at first.
- Many bisphosphonates available in different formulations, including oral.
- Risk of osteonecrosis, especially of jaw if pre-existing pathology.
- Recommend dental check pre administration.
- Anecdotal risk of iatrogenic osteopetrosis with prolonged use (if prolonged use is likely, precede with DEXA scan and investigation of calcium metabolism).

Paracetamol

Evidence: [128, 129, 218, 221]

Use:

- Mild to moderate pain.
- Pyrexia.

Dose and routes:

Oral:

- **Neonate 28-32 weeks postmenstrual age:** 20 mg/kg as a single dose then 10-15 mg/kg every 8-12 hours as necessary (maximum 30 mg/kg/DAY in divided doses).
- **Neonates over 32 weeks postmenstrual age:** 20 mg/kg as a single dose then 10-15 mg/kg every 6-8 hours as necessary (maximum 60 mg/kg/DAY in divided doses).
- **Child 1 month-6 years:** 20-30 mg/kg as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY in divided doses).
- **Child 6-12 years:** 20-30 mg/kg (max 1 g) as a single dose then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY or 4 g/DAY in divided doses).
- **Over 12 years:** 1 g every 4-6 hours as necessary (maximum 4 g/DAY in divided doses).

Rectal:

- **Neonate 28-32 weeks postmenstrual age:** 20 mg/kg as single dose then 15 mg/kg every 12 hours as necessary (maximum 30 mg/kg/DAY in divided doses).
- **Neonates over 32 weeks postmenstrual age:** 30mg/kg as a single dose then 20 mg/kg every 8 hours as necessary (maximum 60 mg/kg/DAY in divided doses).
- **Child 1-3 months:** 30 mg/kg as a single dose, then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY in divided doses).
- **Child 3 months to 12 years:** 30 mg/kg as a single dose (maximum 1g) then 15-20 mg/kg every 4-6 hours as necessary (maximum 90 mg/kg/DAY or 4 g/DAY in divided doses).
- **Over 12 years:** 1 g every 4-6 hours as necessary (maximum 4 g/DAY in divided doses).

IV: as infusion over 15 minutes:

- **Preterm neonate over 32 weeks postmenstrual age:** 7.5 mg/kg every 8 hours, maximum 25 mg/kg/DAY.
- **Neonate:** 10 mg/kg every 4-6 hours (maximum 30 mg/kg/DAY).
- **Child bodyweight <50 kg:** 15 mg/kg every 4-6 hours (maximum 60 mg/kg/DAY).
- **Bodyweight over 50 kg:** 1g every 4-6 hours (maximum 4 g/DAY).

Notes:

- Hepatotoxic in overdose or prolonged high doses.
- In moderate renal impairment use maximum frequency of 6 hourly; in severe renal impairment maximum frequency 8 hourly.
- Onset of action 15-30 minutes orally, 5-10 minutes IV (analgesia), 30 minutes IV (antipyretic). Duration of action 4-6 hours orally and IV. Oral bioavailability 60-90%. Rectal bioavailability about 2/3 of oral.
- Dispersible tablets have high sodium content (over 14 mmol per tablet), so caution with regular dosing.
- Available as: tablets and caplets (500 mg), capsules (500 mg), soluble tablets (120 mg, 500 mg), oral suspension (120 mg/5 mL, 250 mg/5 mL), suppositories (60 mg, 125 mg, 250 mg, 500 mg and other strengths available from 'specials' manufacturers or specialist importing companies) and intravenous infusion (10 mg/mL in 50mL and 100mL vials).
- Oral and licensed rectal preparations are licensed for use in infants from 2 months for post immunisation pyrexia and from 3 months as antipyretic and analgesic.
- IV paracetamol is licensed for short term treatment of moderate pain, and of fever when other routes not possible.

Paraldehyde (rectal)

Evidence: [128, 221, 361] CC

Use:

- Treatment of prolonged seizures and status epilepticus.

Dose and routes:

By rectal administration (dose as undiluted paraldehyde):

- **Neonate:** 0.4 mL/kg paraldehyde as a single dose.
- **1 month-18 years:** 0.4 mL/kg paraldehyde (maximum 10mL) as a single dose.

Notes:

- Available as: paraldehyde ampoules (5mL containing 100% paraldehyde which must be diluted with at least an equal volume of olive oil before administration) or paraldehyde enema may be extemporaneously prepared or is available from 'special-order' manufacturers or specialist importing companies.
- Note – if using a ready-prepared special, be aware that the paraldehyde is already diluted and dose accordingly. The usual strength of paraldehyde enema is 1:1 with olive oil.
- Rectal administration may cause irritation.
- Paraldehyde enema for rectal use is an unlicensed formulation and route of administration.

Phenobarbital

Evidence: [50, 52, 128, 129, 362]

Use:

- Adjuvant in pain of cerebral irritation.
- Control of terminal seizures.
- Sedation.
- Epilepsy including status epilepticus. Commonly used first line for seizures in neonates (phenytoin or benzodiazepine are the main alternatives).
- Agitation refractory to midazolam in end of life care.

Dose and routes:

Loading dose: Oral, intravenous or subcutaneous injection:
All ages: 20 mg/kg/dose over 20 minutes

By mouth:

- **Neonates for control of ongoing seizures:** 2.5-5 mg/kg once or twice daily as maintenance (SR).
- **Child 1 month-12 years:** 1-1.5 mg/kg twice a day, increased by 2 mg/kg daily as required (usual maintenance dose 2.5-4 mg/kg once or twice a day).
- **Child 12-18 years:** 60-180 mg once a day.

Subcutaneous or intravenous injection or infusion:

- **Neonates for control of ongoing seizures:** 2.5-5 mg/kg once or twice daily as maintenance; (SR).
- **Child 1 month-12years:** 2.5-5 mg/kg (maximum single dose 300 mg) once or twice daily or may be given as a continuous infusion over 24 hours.
- **Child 12-18 years:** 300 mg twice daily or may be given as a continuous infusion over 24 hours.

Notes:

- Not licensed for agitation in end of life care.
- Tablets may be crushed.
- Single loading dose required for initiation; administer via enteral route if possible. Loading dose can be administered intravenously over 20 minutes or as a slow subcutaneous loading dose however volume of resultant solution will limit the rate at which a subcutaneous bolus can be administered. Use a separate site to commence subcutaneous infusion. SC bolus injections should be avoided because they can cause tissue necrosis due to the high pH.
- Essential to dilute injection in 10 times volume of water for injection before intravenous or subcutaneous injection (i.e. to concentration of 20 mg/mL).
- Elimination half life of 2-6 days in adults, 1-3 days in children.
- Loading dose essential to reach steady state quickly and avoid late toxicity due to accumulation.
- For patients already on phenobarbital, doses equivalent to the patient's usual total daily dose of enteral phenobarbitone have been used. Doses up to 20 mg/kg maximum 1200 mg/24 hours.
- Available as: tablets (15 mg, 30 mg, 60 mg), oral elixir (15 mg/5 mL) and injection (200 mg/mL).

Phenytoin

Evidence: [128, 129, 221, 223, 240, 355, 363]

Use:

- Epilepsy (3rd or 4th line oral antiepileptic) including status epilepticus.
- Rarely used for neuropathic pain.

Dose and routes:

All forms of epilepsy except absence seizures.
Status epilepticus and acute symptomatic seizures due to head trauma or neurosurgery:
Oral:

- **Neonate:** Initial loading dose by slow IV injection 10 mg/kg THEN by mouth 2.5-5 mg/kg twice daily adjusted according to response and plasma phenytoin levels. Usual maximum 7.5 mg/kg twice daily.
- **1 month to 12 years:** initial dose of 1.5-2.5 mg/kg twice daily then adjust according to response and plasma phenytoin levels to 2.5-5 mg/kg twice daily as a usual target maintenance dose. Usual maximum dose of 7.5 mg/kg twice daily or 300 mg daily.
- **12 to 18 years:** initial dose of 75-150 mg twice daily then adjusted according to response and plasma phenytoin levels to 150-200 mg twice daily as a usual target maintenance dose. Usual maximum dose of 300 mg twice daily.

Intravenous (Status epilepticus, acute symptomatic seizures):

- **Neonate:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg/dose (over 30 minutes) every 12 hours as a usual maintenance dose. Adjust according to response and older babies may need higher doses.
- **1 month to 12 years:** 20 mg/kg loading dose over at least 20 minutes, then 2.5-5 mg/kg twice daily usual maintenance dose.
- **12 to 18 years:** 20 mg/kg loading dose over at least 20 minutes, then up to 100mg (over 30 minutes) 3 to 4 times daily usual maintenance dose.

Notes:

- Recommend prescriptions for oral preparations should include brand name to ensure consistency of drug delivery as not all preparations are equivalent in bio-availability.
- Reduce dose in hepatic impairment. Monitor carefully if reduced albumin or protein binding e.g. in renal failure.
- Avoid abrupt withdrawal.
- Bioavailability may be reduced by enteral feeds and/or nasogastric tube feeds, so flush with water, and interrupt enteral feeding for at least 1-2 hours before and after giving phenytoin.
- Oral bioavailability roughly equivalent to intravenous.
- Oral bioavailability 90-95%, plasma half-life 7-42 hours. Poor rectal absorption.
- Available as tablets (phenytoin sodium 100 mg, generic), capsules (phenytoin sodium 25 mg, 50 mg,100 mg, 300 mg EpanutinR), infatabs (chewable tablets of phenytoin base 50 mg), oral suspension (phenytoin base 30 mg/5 mL Epanutin® and 90 mg/5 mL available as an 'unlicensed special') and injection (phenytoin sodium 50 mg/mL generic and EpanutinR).
- Licensed status: suspension 90 mg in 5 mL is a 'special' and unlicensed. Other preparations are licensed for use in children as anticonvulsant (age range not specified).

Phosphate (rectal enema)

Evidence: [128, 218]

Use:

- Constipation intractable to other treatments.

Dose and routes:

By rectal enema:

- **Child 3-7 years:** 45-65 mL once daily.
- **Child 7-12 years:** 65-100 mL once daily.
- **Child 12-18 years:** 100-128 mL once daily.

Notes:

- Watch for electrolyte imbalance.
- Use only after specialist advice.
- Available as Phosphate enema BP formula B in 128 mL with standard or long rectal tube (do not confuse with Fleet enema).

Promethazine

Evidence: [128, 195, 343]

Use:

- Sleep disturbance.
- Mild sedation.
- Antihistamine.

Dose and routes:

By mouth:

- **Child 2-5 years:** 15-20 mg at night.
- **Child 5-10 years:** 20-25 mg at night.
- **Child 10-18 years:** 25-50 mg at night.

Notes:

- Available as: tablets (10 mg, 25 mg) and oral solution (5 mg/5 mL).

Quinine Sulphate

Evidence: [218]

Use:

- Leg cramps.

Dose and routes:

By mouth:

- Not licensed or recommended for children as no experience.
- **Adult dose:** 200-300 mg at night.

Notes:

- Not licensed for use in children for this condition.
- Available as: tablets (200 mg, 300 mg quinine sulphate).

Ranitidine

Evidence: [128, 129, 218, 364]

Use:

- Gastro-oesophageal reflux.
- Treatment of peptic ulcers.
- GI prophylaxis (e.g. with combination NSAID/ steroids).

Dose and routes:

By mouth:

- **Neonate:** 2-3 mg/kg 3 times daily.
- **Child 1-6 months:** 1 mg/kg 3 times daily increasing if necessary to maximum 3 mg/kg 3 times daily.
- **Child 6 months-3 years:** 2-4 mg/kg twice a day.
- **Child 3-12 years:** 2-4 mg/kg (maximum single dose 150 mg) twice a day. Dose may be increased up to 5 mg/kg (maximum 300 mg/dose) twice daily in severe gastro-oesophageal reflux disease.
- **Child 12-18 years:** 150 mg twice a day or 300 mg at night. May be increased if necessary in moderate to severe gastro-oesophageal reflux disease to 300 mg twice a day or 150 mg 4 times daily for up to 12 weeks.

Notes:

- Oral formulations not licensed for use in children < 3 years.
- Available as: tablets (150 mg, 300 mg) and oral solution (75 mg/5 mL).
- May cause rebound hyperacidity at night.

Risperidone

Evidence: CC [128, 199]

Use:

- Dystonia and dystonic spasms refractory to first and second line treatment.
- Psychotic tendency/crises in Battens disease.

Dose and routes:

Oral:

- **Child 5-12 years (weight 20-50 kg):** 250 microgram once daily; increasing, if necessary, in steps of 250 microgram on alternate days to maximum of 750 microgram daily.
- **Child 12 years or over (>50 kg):** 500 microgram once daily; increasing in steps of 500 microgram on alternate days to maximum of 1.5 mg daily.

Notes:

- Not licensed for this indication. Not licensed for children under 15 years.
- Caution in epilepsy and cardiovascular disease; extrapyramidal symptoms less frequent than older antipsychotic medications; withdraw gradually after prolonged use.
- Available as: tablets (0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg), orodispersible tablets (0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg), Liquid 1 mg/mL.

Salbutamol

Evidence: [128, 129, 218]

Use:

- Wheezing/Breathlessness caused by bronchospasm.

Dose and routes:

Nebulised solution:

- **Neonate:** 1.25-2.5 mg up to four times daily.
- **Child 1 month-18years:** 2.5-5 mg up to four times daily.

Aerosol Inhalation:

- **Child 1 month-18years:** 100-200 micrograms (1-2 puffs) for persistent symptoms up to four times a day.

Notes:

- Many paediatricians now advise multi-dosing of salbutamol 100 microgram up to 10 times, via a spacer, instead of a nebuliser.
- Available as nebuliser solution (2.5 mg in 5 mL, 5 mg in 2.5 mL), respirator solution (5 mg in 1 mL), aerosol inhalation (100 micrograms/puff). Other types of dry powder inhaler are also available.
- For nebulisation dilute the nebulised solution with a suitable volume of sterile sodium chloride 0.9% according to the nebuliser type and duration; can be mixed with nebulised solution of ipratropium bromide.
- Salbutamol may not be effective in very young children due to the immaturity of the receptors; ipratropium may be more helpful in those less than 1 year.
- Inhaled product should be used with a suitable spacer device, and the child/carer should be given appropriate training.
- Side effects: increased heart rate; feeling "edgy" or agitated; tremor.

- The side effects listed above may prevent use, in which case ipratropium bromide is a good alternative.
- Nebuliser solution and inhalers are licensed for children for this use.

Senna

Evidence: [19, 128, 221]

Use:

- Constipation.

Dose and routes:

By mouth:

Initial doses which can be adjusted according to response and tolerance

- **Child 1 month-2 years:** 0.5 mL/kg (maximum 2.5 mL) of syrup once a day.
- **Child 2-6 years:** 2.5-5 mL of syrup a day.
- **Child 6-12 years:** 5-10 mL a day of syrup or 1-2 tablets at night or 2.5-5 mL of granules.
- **Child 12-18 years:** 10-20 mL a day of syrup or 2-4 tablets at night or 5-10 mL of granules.

Notes:

- Syrup is not licensed for use in children < 2 years and tablets/granules are not licensed for use in children <6 years.
- Stimulant laxative.
- Onset of action 8-12 hours.
- Initial dose should be low then increased if necessary.
- Doses can be exceeded on specialist advice.
- Granules can be mixed in hot milk or sprinkled on food.
- Available as: tablets (7.5 mg sennoside B), oral syrup (7.5 mg/5 mL sennoside B) and granules (15 mg/5 mL sennoside B).

Sodium Picosulphate

Evidence: [128, 218]

Use:

- Constipation.

Dose and routes:

By mouth:

- **Child 1 month-4 years:** initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 10 mg daily.
- **Child 4-18 years:** initial dose of 2.5 mg once a day increasing if necessary according to response to a suggested maximum of 20 mg daily.

Notes:

- Available as: elixir (5 mg/5 mL) and capsules (2.5 mg).
- Acts as a stimulant laxative.
- Onset of action 6-12 hours.
- Elixir is licensed for use in children of all ages; capsules are not licensed for use in children less than 4 years of age.
- Effectiveness dependent upon breakdown by gut flora – previous effectiveness may therefore be lost during courses of antibiotics and ensuing altered gut flora.

Sucralfate

Evidence: [128, 221]

Use:

- Stress ulcer prophylaxis.
- Prophylaxis against bleeding from oesophageal or gastric varices; adjunct in the treatment of: oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration, upper GI bleeding of unknown cause.

Dose and routes:

Oral:

Stress ulcer prophylaxis, prophylaxis against bleeding from oesophageal or gastric varices

- **Child 1 month-2 years:** 250 mg four to six times daily.
- **Child 2-12 years:** 500 mg four to six times daily.
- **Child 12-15 years:** 1 g four to six times daily.
- **Child 15-18 years:** 1 g six times daily (maximum 8 g/day).

Oesophagitis with evidence of mucosal ulceration, gastric or duodenal ulceration

- **Child 1 month-2 years:** 250 mg four to six times daily.
- **Child 2-12 years:** 500 mg four to six times daily.
- **Child 12-15 years:** 1 g four to six times daily.
- **Child 15-18 years:** 2 g twice daily (on rising and at bedtime) or 1 g four times daily (1 hour before meals and at bedtime) taken for 4-6 weeks (up to 12 weeks in resistant cases); maximum 8 g daily.

Notes:

- Administer 1 hour before meals.
- Spread doses evenly throughout waking hours.
- Tablets may be crushed and dispersed in water.
- Administration of sucralfate suspension and enteral feeds via a NG or gastrostomy tube should be separated by at least 1 hour. In rare cases bezoar formation has been reported when sucralfate suspension and enteral feeds have been given too closely together.
- Caution – sucralfate oral suspension may block fine-bore feeding tubes.
- Caution – absorption of aluminium from sucralfate may be significant in patients on dialysis or with renal impairment.
- Not licensed for use in children less than 15 years; tablets are not licensed for prophylaxis of stress ulceration.
- Available as: oral suspension (1 g in 5 mL), tablets (1 g).

Temazepam

Evidence: [218]

Use:

- Sleep disturbance where anxiety is a cause.

Dose and routes:

By mouth:

- **Adult:** 10-20 mg at night. Dose may be increased to 40 mg at night in exceptional circumstances.

Notes:

- Not licensed for use with children.
- Available as: tablets (10 mg, 20 mg) and oral solution (10 mg/5 mL).

Tizanidine

Evidence: [218, 228, 229, 233, 365-368]

Use:

- Skeletal muscle relaxant.
- Chronic severe muscle spasm or spasticity.

Dose and routes:

Children doses based on SR [365]

- **Child 18 months-7 years:** 1 mg/day; increase if necessary according to response.
- **Child 7-12 years:** 2 mg/day; increase if necessary according to response.
- **Child >12 years:** as per adult dose [218]: Initially 2 mg increasing in increments of 2 mg at intervals of 3-4 days. Give total daily dose in divided doses up to 3-4 times daily. Usual total daily dose 24 mg. Maximum total daily dose 36 mg.

Notes:

- Not licensed for use in children.
- Timing of dose individual to specific patient as maximal effect is seen after 2-3hours and is short-lived.
- Caution – in liver disease, monitor liver function regularly.
- Usually prescribed and titrated by neurologists.
- Available as: tablets (2 mg, 4 mg).

Tramadol

Evidence: [128, 218, 236, 239]

Use:

- Minor opioid with additional non-opioid analgesic actions.

Dose and routes:

By mouth:

- **Child 5-12 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum of 4 doses in 24 hours). Increase if necessary to a maximum dose of 3 mg/kg (maximum single dose 100 mg) every 6 hours.
- **Child 12-18 years:** initial dose of 50 mg every 4-6hours. Increase if necessary to a maximum of 400 mg/day given in divided doses every 4-6 hours.

By IV injection or infusion:
- **Child 5-12 years:** 1-2 mg/kg every 4-6 hours (maximum initial single dose of 50 mg; maximum 4 doses in 24 hours). Increase if necessary to a maximum dose of 3 mg/kg (maximum single dose 100mg) every 6 hours.
- **Child 12-18 years:** initial dose of 50 mg every 4-6 hours. Dose may be increased if necessary to 100 mg every 4-6 hours. Maximum 600 mg/DAY in divided doses.

Notes:
- Not licensed for use in children < 12 years.
- Not a controlled drug.
- By mouth about 1/10 as potent as morphine.
- Onset of action after oral dose 30 to 60 minutes. Duration of action 4-9hours.
- Causes less constipation and respiratory depression than equivalent morphine dose.
- Analgesic effect is reduced by ondansetron.
- Available as tablets (100 mg), capsules (50 mg, 100 mg), soluble tablets (50 mg), orodispersible tablets (50 mg), m/r tablets and capsules (100 mg, 150 mg, 200 mg, 300 mg, 400 mg) and injection (50 mg/mL).

Tranexamic acid

Evidence: [13, 14, 128, 221, 369-371]

Use:
- Oozing of blood (e.g. from mucous membranes/ capillaries), particularly when due to low or dysfunctional platelets.
- Menorrhagia.

Dose and routes:
By mouth:
Inhibition of fibrinolysis
- **Child 1 month-18 years:** 15-25 mg/kg (maximum 1.5 g) 2-3 times daily.

Menorrhagia
- **Child 12-18 years:** 1 g 3 times daily for up to 4 days. If very heavy bleeding a maximum daily dose of 4 g (in divided doses) may be used. Treatment should not be initiated until menstruation has started.

By intravenous injection over at least 10 minutes:
Inhibition of fibrinolysis
- **Child 1 month -18 years:** 10 mg/kg (maximum 1 g) 2-3 times a day.

By continuous intravenous infusion:
Inhibition of fibrinolysis
- **Child 1 month -18 years:** 45 mg/kg over 24 hours.

Mouthwash 5% solution:
- **Child 6-18 years:** 5-10 mL 4 times a day for 2 days. Not to be swallowed.

Topical treatment:
- Apply gauze soaked in 100mg/mL injection solution to affected area.

Notes:
- Parenteral preparation can be used topically.
- Available as: tablets (500 mg), syrup (500 mg/5mL available from 'specials' manufacturers) and injection (100 mg/mL 5 mL ampoules). Mouthwash only as extemporaneous preparation.

Vitamin K (Phytomenadione)

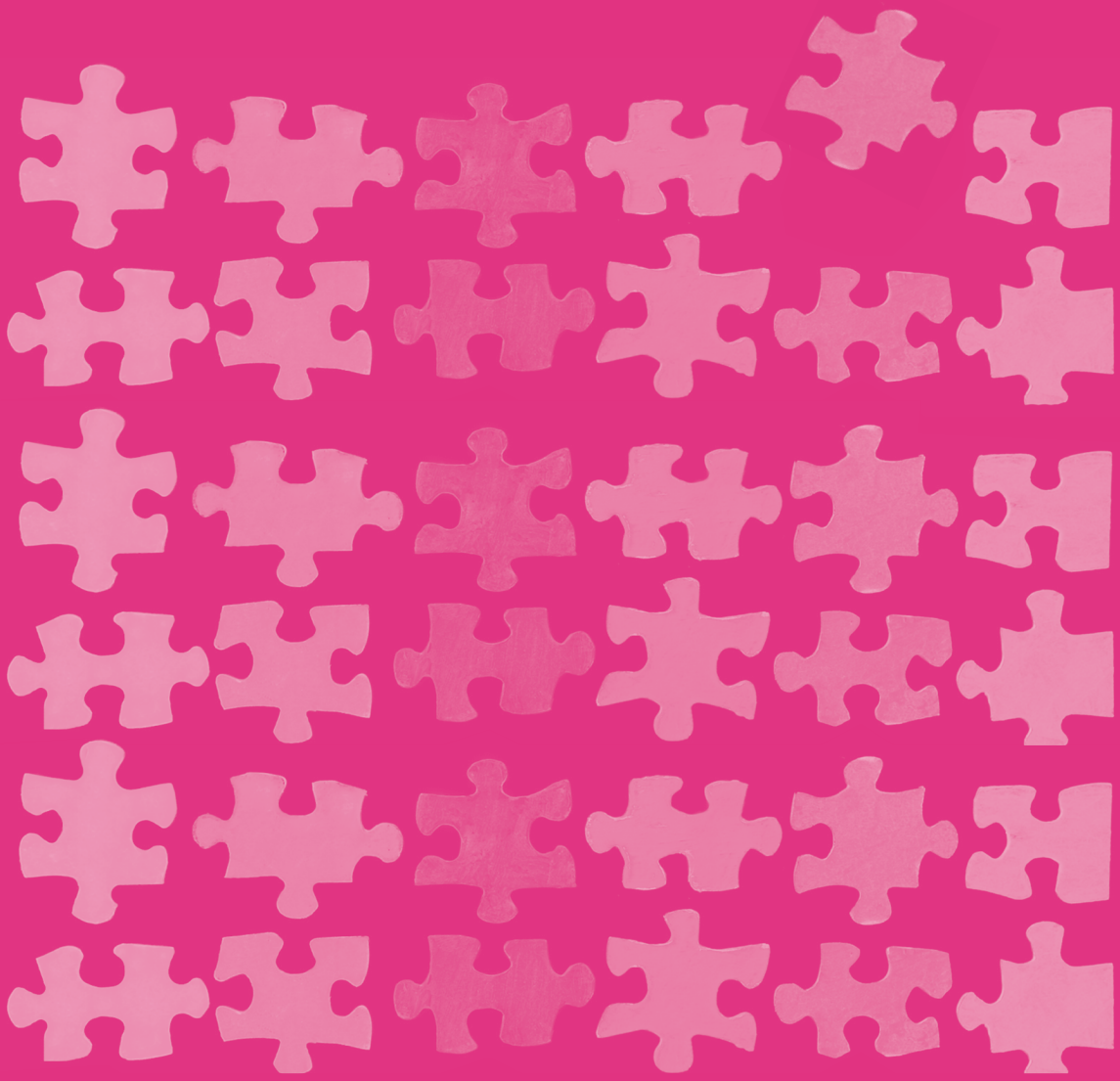
Evidence: [128, 129, 218, 221]

Use:
- Treatment of haemorrhage associated with vitamin-K deficiency (seek specialist advice).

Dose and routes:
By mouth or intravenous:
- **Neonate:** 100 micrograms/kg
- **Child 1 month-18 years:** 250-300 micrograms/kg (maximum 10 mg) as a single dose.

Notes:
- Available as Konakion MM injection 10 mg/mL (1 mL amp) for slow intravenous injection or intravenous infusion in glucose 5%; NOT for intramuscular injection.
- Available as Konakion MM Paediatric 10 mg/mL (0.2 mL amp) for oral administration or intramuscular injection. Also for slow intravenous injection or intravenous infusion in glucose 5%.
- There is not a UK licensed formulation of Vitamin K tablets currently available. Possible to obtain 10 mg phytomenadione tablets via a specialist importation company.
- Caution – with intravenous use in premature infants <2.5 kg.

Appendices



Appendix 1a: Morphine equivalence single dose [128, 218, 220]

Analgesic	Dose
Morphine oral	10mg
Morphine subcutaneous	5mg
Diamorphine subcutaneous	3mg
Hydromorphone oral	2mg
Oxycodone oral	6.7mg
Methadone	Variable

Appendix 1b: Dose conversion of morphine to Fentanyl patches

Dose conversion of Fentanyl patches							
Four hourly oral morphine (mg)	<20	25-35	40-50	55-65	70-80	85-95	100-110
Fentanyl patch strengh	25	50	75	100	125	150	175
24 hour oral morphine dose (mg)	<135	135-224	225-314	315-404	405-494	495-584	585-674

Appendix 2: Subcutaneous infusion drug compatibility

Evidence suggests that during end of life care in children, where the enteral route is no longer available, the majority of symptoms can be controlled by a combination of six "essential drugs" [372]. Compatibility for these six drugs is given in the table 1 below [223]. For more detailed information professionals are advised to consult an appropriate reference source [130].

Table 1: Syringe driver compatibility for two drugs in water for injection

diamorphine						
-	morphine sulphate					
+	+	midazolam				
A+	+	+	cyclizine			
A+	+	+	+	haloperidol		
+	?	+	-	-	levomepromazine	
+	+	+	?	?	?	hyoscine hydrobromide

A	Laboratory data; physically and chemically compatible but crystallization may occur as concentrations of either drug increase.
+	Compatible in water for injection at all usual concentrations.
-	Combination not recommended; drugs of similar class.
?	No data available.

Table 2: The compatibility of drugs with OxyNorm injection

Drug	Compatible with OxyNorm injection
Dexamethasone	Yes
Haloperidol	Yes
Hyoscine butylbromide	Yes
Hyoscine hydrobromide	Yes
Levomepromazine	Yes
Metoclopramide	Yes
Midazolam	Yes
Cyclizine	Incompatible in concentrations >3mg/ml of cyclizine (i.e. 30mg in standard 10ml syringe). Use water for injection as diluent.
Prochlorperazine	No

Appendix 3: Don't panic: where to get help

Dr Lynda Brook
Macmillan Consultant in Paediatric Palliative Care
Royal Liverpool Children's Hospital
Alder Hey
Eaton Road
Liverpool L12 2AP
Tel: 0151 252 5187
Mobile: 07881 788903
Long range bleep via switchboard: 0151 228 4811
Lynda.Brook@RLC.NHS.UK

Dr Pat Carragher
Deputy Chief Executive (Medical)
Children's Hospice Association Scotland
Canal Court
42 Craiglockhart Avenue
Edinburgh
EH14 1LT
Tel: 0131 444 1900
Tel: 0131 444 4015 DDL
F: 0131 444 4001

Rachel House
Kinross
KY13 8AA
Tel: 01577 865777
p.carragher@chas.org.uk

Dr Finella Craig
Paediatric Palliative Care Consultant
Great Ormond Street Children's Hospital
Symptom Care Team (x8678)
Tel: 020 7829 8678
CraigF@gosh.nhs.uk

Dr Richard Hain
Consultant and Lead Clinician
Wales Managed Clinical Network in Paediatric Palliative Care
Children's Hospital
Heath Park
Cardiff CF14 4XN
Tel: (+44) 29 2074 3373
Tel: (+44) 29 2074 5395
richard.hain@southwales.ac.uk

Dr Satbir Singh Jassal
Medical Director
Rainbows Children's Hospice
Lark Rise
Loughborough
Leicestershire
LE11 2HS
Tel: 01509 638000
Tel: 01509 263018
sat@jassal.f9.co.uk

Dr Susie Lapwood
Lead Doctor
Helen & Douglas House
14a Magdalen Road
Oxford
OX4 1RW
Tel: 01865 794749
susie.lapwood@bigfoot.com

Dr Mike Miller
Consultant in Paediatric Palliative Medicine
Martin House
Grove Road
Clifford
Wetherby
LS23 6TX
Tel: 01937 845 045
Mobile: 07802448890
mmiller@martinhouse.org.uk

Together for Short Lives
4th Floor
Bridge House
48-52 Baldwin Street
Bristol
BS1 1QB
Tel: 0117 989 7820
Fax: 0117 929 1999
info@togetherforshortlives.org.uk
www.togetherforshortlives.org.uk

APPM: Association of Paediatric Palliative Medicine
Chairman – Dr Pat Carragher
Secretary – Dr Mike Miller
appm@togetherforshortlives.org.uk
www.appm.org.uk

Diploma in Paediatric Palliative Medicine
Dippallmed@velindre-tr.wales.nhs.uk

Palliative Drugs.Com
(Website hosts the latest version of the Palliative Care Formulary, as well as an active bulletin board for drug-related questions).
www.palliativedrugs.com

Medical resources: paper-based

- *Care of the Dying Child* (2nd edition): Ann Goldman.
- *A Guide to Symptom Relief in Palliative Care* (5th edition): Claud Regnard 2003. User friendly and practical.
- *Oxford Handbook of Paediatric Palliative Medicine*: Richard Hain and Satbir Singh Jassal. A wealth of resources in a small space.
- *Medicines for Children*: 3rd edition RCPCH 2006.
- *BNF for Children 2010* (and the standard BNF).
- *Palliative Care Guidelines 2006*: Max Watson et al. This was the precursor to the Oxford Handbook. It was produced for the SW London Cancer network, has both adult and paediatric sections, and copies are available very cheaply from Princess Alice Hospice, Esher, Surrey, and from the handbook website (www.greenbox.net/palliative; 0870 163 0073
- *Oxford Textbook of Palliative Medicine* (3nd edition) Doyle et al 2005.
- *Oxford Textbook of Palliative Care for Children*: Goldman, Hain, Liben (2nd edition) 2012.
- *Symptom Management in Advanced Cancer*: Twycross.
- *Palliative Care Formulary*: Twycross (same as is available online through Palliative Drugs site): 3rd edition Oct 07.

Medical resources: online

Child-specific:

Canadian Paediatric Palliative Care
Lots of useful links and resources.
www.cnpcc.ca

Great Ormond Street Hospital
Useful for clinical guidelines and patient information.
www.gosh.nhs.uk/health-professionals

Together for Short Lives
Together for Short Lives produces various resources to help professionals in practice. You can view them all, and order online at **www.togetherforshortlives.org.uk/resources**

Palliative care:

Palliative Drugs
Excellent palliative drugs website and bulletin board. Very active and helpful international palliative medicine community: post a query here and you should get a useful answer within the day. Also hosts the electronic version of Palliative Care Formulary (Palliative version of the BNF, which includes syringe driver compatibility charts etc), and a 'RAG' section with lots of useful guidelines and protocols from elsewhere.
www.palliativedrugs.com

Palliative Medicine Handbook
A useful UK site, which includes the 'Palliative Care Matters' handbook.
www.book.pallcare.info

Palliative Info
Canadian palliative care website with a lot of useful links and protocols.
www.palliative.info

Association for Palliative Medicine
www.apmonline.org

Help the Hospices
Help the Hospices site is useful, in particular the education section has a very full listing of courses available, and the 'e-learning' section has helpful modules based on the CLIP programme.
hwww.helpthehospices.org.uk/our-services/education-training

For information regarding specific diseases:

National Organization for Rare Diseases
Holds a rare diseases database and very useful for looking up rare syndromes.
www.rarediseases.org

National Institute for Neurological Diseases and Stroke
Holds a good disease database for medical information (US site).
www.ninds.nih.gov/disorders/disorder_index.htm

Contact a Family
Includes very useful information for families about specific conditions and offers access to support and information.
www.cafamily.org.uk

Appendix 4: Protocol for subcutaneous drug administration

In palliative care the sub-cutaneous route of drug administration is often the most convenient. It has many advantages, including being seen as less invasive than intravenous therapy, not requiring venous access where such access may be difficult or impossible, being easily monitored for local irritation, and being easily relocated if such problems occur.

The network of small blood vessels provide good absorption of medication and parenteral drugs are often absorbed more rapidly than oral drugs. The sub-cutaneous tissue lies between the skin and the underlying muscle, it is made up of loose connective tissue and varying amounts of fat. It also contains cutaneous nerves, small lymph vessels and blood vessels.

It is also widely acceptable in the community setting, making it possible to manage patients at home when more invasive devices would preclude this.

Sub-cut treatment can be given when it is not possible or desirable for it to be given orally.

Indications for its use may be:
- Persistent nausea and vomiting.
- Dysphagia.
- Mouth/throat/oesophageal lesions.
- Intestinal obstructions.
- Malabsorption of oral medication.
- Unconscious child/young person.
- Profound weakness when child/young person unable to swallow medication.

Advantages to this method of administration are:
- Constant serum plasma levels ensuring better pain control.
- Usually reloaded once every 24 hours.
- No repeated injections.
- Permits better control of nausea and vomiting.
- Control of multiple symptoms with a combination of drugs.

If possible involve the child or young person in the choice of site. This may increase compliance and acceptability.

The most frequently used sites are:
- Abdomen or chest wall.
- Thighs; upper and lateral aspects.
- Buttocks.
- Upper arms.

Preparation of child and family

- Explain the full procedure to the child and family including the purpose and any possible side effects and allow them to ask questions.
- Assess the child for the most suitable infusion site.
- Offer topical anaesthetic. EMLA or Ametop.
- Apply topical anaesthetic cream according to manufacturers' instructions and allow maximum time for it to take effect.
- If possible involve the parents, particularly if the treatment is being given at home. This will offer security to the child and assist with distraction.

Preparation of medication and equipment

- Check the prescription is written correctly to comply with local policy.
- Check child/young person's allergies.
- Wash hands according to standard (universal) precautions to reduce the risk of cross infection.
- Prepare a tray or suitable working surface.

Equipment required

- Syringe driver policy.
- Syringe driver that has been serviced in the last 12 months.
- Medication to be administered.
- Luer lock syringe appropriate to the infusion volume, usually 10 or 20ml.
- Blue or green needles for drawing up the medication.
- Butterfly needle appropriately sized depending on age/size of child/young person and amount of sub-cutaneous tissue they have.
- Opsite or tegaderm dressing to secure butterfly.
- Portable syringe pump. Graseby MS26 or Mckinley T34 depending on child to ensure their comfort and ease of movement.
- Sharps bin to ensure equipment is disposed of safely.
- Prepare the drug and diluents, checking name, dose and expiry date.
- Draw up the injection with the blue or green needle and luer lock syringe.
- Remove needle and discard in sharps bin.
- Complete label to attach to syringe with drug name(s), strength, batch number, child/young person's name and date of birth and initialled by two nurses.
- Connect the syringe to the infusion needle. Prime extension and ensure medication at tip of butterfly needle.

Administration

- Remove anaesthetic cream 2-5 minutes before needle insertion to allow skin to dry and to maximise its effect.
- Check child/young person's details with parents and second nurse.
- Ensure the child is comfortable and if appropriate, encourage them to participate. This may help the child to co-operate and ensure their safety.
- Wash hands.
- Lift a skin fold and insert the needle into the sub-cutaneous tissue at approximately a 45 degree angle.
- Ensure the needle and extension line are connected to the syringe and the syringe is fitted into the pump correctly.
- Start infusion ensuring rate corresponds to prescription.

Graseby MS26

- Insert 9 volt battery into pump and listen for alarm. Press and hold start/test button for ten seconds; the motor will then run and stop. Release the button. Observe for the flashing light.
- Ensure you have protective plastic cover for pump.
- Ensure you have a rate adjuster and a Graseby ruler to measure length of syringe contents.
- Wash hands.
- Draw up the prescribed medication and the diluents and make up to **48mm** within the syringe barrel. Check the solution for clouding or crystallisation. If this occurs, do not use and check with pharmacist regarding compatibility of drugs. Whatever syringe size used the total volume should measure **48mm**.
- Connect syringe to butterfly tubing. Prime the line and the butterfly with the prescribed medication. DO NOT PRIME THE LINE WHEN ATTACHED TO THE CHILD/YOUNG PERSON.
- **By loading the syringe and then priming the infusion line it is recognised that this will reduce the duration of the infusion by approximately 2-4 hours.**
  This will occur each time a new infusion line is primed, i.e. on each re-siting of the needle.
  Do not make up the fluid lost in the infusion line as this will dilute the drug concentration and thus reduce the amount of medication the child/young person receives each hour.

NB. If the combination of drugs is changed it is essential to replace the infusion line. This prevents a delay in the child or young person receiving the new prescription and possible drug incompatibility occurring in the infusion line.

- Hold the syringe driver with the battery side facing you. Press the square actuator button to move the actuator to the far right hand side. Put the syringe on top of the driver with the barrel in the shallow V shaped recess. The finger grip on the syringe barrel must be in the slot in the case.
- Move the actuator up to the syringe plunger by pressing and holding in the button on the side and sliding it along. The push button on the plunger of the syringe must be fitted in the slot in the actuator. Be careful not to push the plunger forwards.
- Put the rubber securing strap over the syringe barrel and pull it tight. Hook and then press it into the groove in the side of the case.
- Slide the syringe driver into the clear plastic cover with the front facing the side of the cover with the hole in it. NEVER PUT THE SYRINGE DRIVER IN FACING THE OTHER WAY.

Setting the correct rate for the MS26 and starting the infusion

- Fill the syringe with the required volume of medication.
- Connect and fill the infusion line. Make sure the connection is secure and the air is expelled.
- Measure the distance in millimetres (mm) from the empty line on the syringes scale up to the line where the plunger piston is.
- In the hospice we draw up 8ml of medication and diluents which runs at 48mm in 24 hours.
- Press and hold the START button. The motor will turn and stop after ten seconds, then the alarm will sound. This will continue for about 15 seconds longer if the button is not released.
- Releasing the button starts the syringe driver. The indicator lamp will begin to flash: once every 25 seconds.

During the administration

- It is recommended that procedures are established for regular checks on the progress of the administration. In the hospice or hospital environment this should be done hourly. In a patients home it should be done twice in 24 hours.

Parents or carers can be made aware of a few simple checks that can be made:
- The volume is being delivered as expected
- The rate set is the correct value
- The indicator lamp is flashing
- The syringe driver is in good condition.

A family must know who to contact in an emergency.

Stopping the syringe driver

- When the syringe is empty the syringe driver will stop automatically and the alarm will sound for about 15 seconds.
- There is no OFF switch to stop the driver before the syringe is empty. To stop it move the rate switches to 00 – the indicator lamp will still flash, or take the battery out.

Alarms

The syringe driver will give an audible alarm lasting about 15 seconds:
- When a battery is put in.
- When the START/TEST button is pressed for longer than ten seconds.
- When the syringe is empty.
- When the syringe driver has stopped. This may be caused by a blocked or trapped infusion line.

The indicator lamp will stop flashing:
- When the syringe driver has stopped and switched off.
- When the battery needs replacing.

Troubleshooting

The syringe driver will not start:
- The START button has not been pressed in enough. Press again.
- There is no battery. Fit a battery.
- The battery is in the wrong way round. Refit battery.
- The battery is exhausted. Fit a new battery.
- The syringe driver is faulty. Service needed.

The infusion is going too quickly or has ended early:
- Wrong rate set. Correct error.
- Wrong syringe brand or size. Correct error.
- Syringe plunger push-button or finger grips were not held in the actuator or case correctly. Correct error.
- Plunger position measured wrongly. Correct error.
- Line was filled after the plunger position was measured. Correct error.
- Syringe driver has got wet. Remove from use immediately.

The infusion is going too slowly:
- Wrong rate set. Correct error.
- Wrong syringe brand or size. Correct error.
- Plunger position measured wrongly. Correct error.

T**he syringe driver has stopped before emptying the syringe:**
- Exhausted battery. Fit new battery.
- Blocked or trapped infusion line. Clear line.

The syringe driver has stopped with the lamp still flashing:
- The mechanism for pushing the plunger has worn out. Listen for a faint click when the motor turns a few times. Service needed.

McKinley T34 Pump

Batteries

Always use a 9 volt battery. When setting up the pump always check there is enough charge in the battery to cover the infusion being set up. To do so follow this procedure:

- Switch the pump ON.
- Press INFO key.
- Select BATTERY LIFE from the menu and press YES to confirm.
- Verify sufficient battery charge is available to complete the current programme. If not, change the battery.

Access codes and keypad lock

Program lock
Always use the program lock when the pump is used in a home environment to prevent patient or family changing the prescription.

Keypad lock
To activate the keypad lock:

- With the pump infusing, press and hold the INFO key until a chart is displayed showing a bar moving from left to right.
- Hold the key until the bar has moved completely across the screen and a beep is heard to confirm the lock has been activated.
- To turn off repeat this procedure. The bar will now move from right (ON) to left (OFF) and a beep will be heard to confirm.

Infusion set up and programming

Always use luer lock syringes.

Priming the infusion set

After filling the syringe attach the infusion set, prime manually to remove all air from the syringe and extension set and apply clamp to the line.

Pre-loading and syringe placement

- Before placing the syringe into the pump ensure the barrel clamp arm is down then press and hold the ON/OFF key until the SELF TEST screen appears. Do not label the syringe or apply anything that changes its external diameter at the point where the barrel clamp is applied as incorrect syringe recognition may result.
- Check the remaining battery life is sufficient to cover the infusion you are about to program. Press the INFO key and use the UP or DOWN arrow keys to select battery level. Press YES/START to confirm and view battery status.
- Load the syringe into the pump prior to connecting the syringe to the child/young person.
- The LCD display will show PRE-LOADING and the actuator will start to move. Wait until it stops moving and the syringe detection screen appears.
- If the actuator is not in the correct position to accommodate the syringe leave the barrel arm clamp down and use the FF or BACK buttons on the keypad to move the actuator to the required position. Forward movement of the actuator is limited, therefore repeated presses of the FF key may be required when moving the actuator forward. Backwards movement is not restricted.
- Lift the barrel arm clamp and load the syringe into the pump. Note that the syringe graphic on the screen flashes in three places, the barrel, ear/collar and plunger, denoting the position and status of each sensor. Seat the collar/ear and plunger first. As you correctly seat each point of the syringe note that the flashing indicator for that sensor becomes solid on the display.
- Lower the barrel arm clamp. If the syringe is correctly loaded the syringe graphic will become solid (no flashing components) and the pump will display the next screen – size and brand of the syringe detected.

Syringe detection and confirmation

- Check the LCD display to ensure the pump has correctly identified the syringe size and brand. If it is not correct use the UP or DOWN arrow keys to scroll between brands.
- Press YES/START to confirm.
- If the pump was stopped and turned off before the last program reached End Program, the Resume Prompt screen will appear. Press NO to continue programming the new regime.
- Once the syringe brand and size are confirmed the pump calculates and displays the deliverable volume in the syringe.
- The pump cannot deliver the full contents of all syringe brands/sizes so in some cases there may be a slight residual volume left in the pump when the actuator has travelled to the zero position. So when the syringe is loaded, the VTBI may read 17.5ml when 18ml has been drawn up.
- Press YES/START key to confirm the volume to be infused (VTBI).
- Set duration of infusion. Will read 24:00. Use UP and DOWN arrow keys to set desired duration or press YES to confirm 24:00.

Setting the infusion rate

- The pump calculates and displays the rate (in millilitres per hour) required to deliver the VTBI over the infusion duration confirmed.
- Press YES to confirm the calculated rate or use the UP and DOWN arrow to adjust. Changing the rate will alter the duration confirmed at the previous step.

Starting the infusion

- The summary screen confirms the volume to be infused, duration and infusion rate. **You must always check the details on this screen match the prescription.**
- Press YES/START to confirm the infusion parameters.
- Pump prompts, 'START INFUSION?' Check infusion set is attached to patient access device and the clamp is released. Press YES/START to commence infusion.
- While running, the LCD displays infusion 'Time Remaining' (top line), 'Infusion Rate' (in bold on the middle line) and the bottom line will alternate between 'Syringe Size and Brand' and 'Pump Delivering.'

Recommended checks during infusion

- CHECK THE LCD DISPLAY to confirm the pump is still running at the same infusion rate as originally set (unless the titration option has been enabled and the user has been authorised to adjust the rate within the programmed limits).
- CHECK THE GREEN LED IS FLASHING and/or pump delivering animation appears intermittently on the bottom line of the LCD display.
- CHECK FOR SIGNS OF PHYSICAL DAMAGE to the pump or accessories.
- PRESS THE INFO KEY TO CHECK:

Single Press: Volume to be Infused (VTBI) & Volume Infused (VI).
Double Press: for battery life remaining.

This information is for a quick reference only. You must refer to the pump manufacturer's booklet for the full information and instructions.

Subcutaneous Infusion Chart

Name **Age** **D.O.B** **WT**

Syringe size BD **Total volume in syringe** **Dilutent**

Date	Time Started	Drug-Prescription	Total dose in syringe	Rate	Rate variations allowed	Dr sign	Checked	

Time																							
Rate: mm/24hr																							
Hourly infusion mm/hr completed																							
Site check																							
Respiration rate																							
Pain assessment																							
Sedative effect																							
Suctioning																							
Postion change																							
Boosts given																							

Pain

 = 0

 = 1

 = 2

 = 3

 = 4

 = 5

Sedative effects

Unconscious	= 1
Asleep/Rousable	= 2
Awake/Comfortable	= 3
Upset	= 4

Site check

Clean/no redness	= 1
tracking/warm	= 2
Blood/inflamation	= 3
Infiltration	= 4

Respiratory pattern

Tachypnoea	= T
Wheezing	= W
Dyspnoea	= D
Cheyne stokes	= C

References

1. Mattson, R.H., *The role of the old and the new antiepileptic drugs in special populations: mental and multiple handicaps.* Epilepsia, 1996. 37 Suppl 6: p. S45-53.
2. Udani, V., *Evaluation and management of intractable epilepsy.* Indian J Pediatr, 2000. 67(1 Suppl): p. S61-70.
3. Davis, M.P., et al., *Appetite and cancer-associated anorexia: a review.* J Clin Oncol, 2004. 22(8): p. 1510-7.
4. Duval, M. and C. Wood, *[Treatment of non-painful symptoms in terminally ill children].* Arch Pediatr, 2002. 9(11): p. 1173-8.
5. Goldman, A., et al., *Symptoms in children/young people with progressive malignant disease: United Kingdom Children's Cancer Study Group/Paediatric Oncology Nurses Forum survey.* Pediatrics, 2006. 117(6): p. e1179-86.
6. Peng, J.K., et al., *What can family physicians contribute in palliative home care in Taiwan?* Fam Pract, 2009. 26(4): p. 287-93.
7. Santucci, G. and J.W. Mack, *Common gastrointestinal symptoms in pediatric palliative care: nausea, vomiting, constipation, anorexia, cachexia.* Pediatr Clin North Am, 2007. 54(5): p. 673-89, x.
8. Theunissen, J.M., et al., *Symptoms in the palliative phase of children with cancer.* Pediatr Blood Cancer, 2007. 49(2): p. 160-5.
9. Walsh, D., S. Donnelly, and L. Rybicki, *The symptoms of advanced cancer: relationship to age, gender, and performance status in 1,000 patients.* Support Care Cancer, 2000. 8(3): p. 175-9.
10. Wolfe, J., et al., *Symptoms and suffering at the end of life in children with cancer.* N Engl J Med, 2000. 342(5): p. 326-33.
11. Durant, P.A. and T.L. Yaksh, *Drug effects on urinary bladder tone during spinal morphine-induced inhibition of the micturition reflex in unanesthetized rats.* Anesthesiology, 1988. 68(3): p. 325-34.
12. Cartoni, C., et al., *Hemorrhagic complications in patients with advanced hematological malignancies followed at home: an Italian experience.* Leuk Lymphoma, 2009. 50(3): p. 387-91.
13. Frachon, X., et al., *Management options for dental extraction in hemophiliacs: a study of 55 extractions (2000-2002).* Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2005. 99(3): p. 270-5.
14. Morimoto, Y., et al., *Haemostatic management of intraoral bleeding in patients with von Willebrand disease.* Oral Dis, 2005. 11(4): p. 243-8.
15. Bellomo-Brandao, M.A., E.F. Collares, and E.A. da-Costa-Pinto, *Use of erythromycin for the treatment of severe chronic constipation in children.* Braz J Med Biol Res, 2003. 36(10): p. 1391-6.
16. Brown, E., A. Henderson, and A. McDonagh, *Exploring the causes, assessment and management of constipation in palliative care.* Int J Palliat Nurs, 2009. 15(2): p. 58-64.
17. Candy, D.C., D. Edwards, and M. Geraint, *Treatment of faecal impaction with polyethelene glycol plus electrolytes (PGE + E) followed by a double-blind comparison of PEG + E versus lactulose as maintenance therapy.* J Pediatr Gastroenterol Nutr, 2006. 43(1): p. 65-70.
18. Chong, S.K., *Gastrointestinal problems in the handicapped child.* Curr Opin Pediatr, 2001. 13(5): p. 441-6.
19. Demol, P., H.J. Ruoff, and T.R. Weihrauch, *Rational pharmacotherapy of gastrointestinal motility disorders.* Eur J Pediatr, 1989. 148(6): p. 489-95.
20. Hanson, S. and N. Bansal, *The clinical effectiveness of Movicol in children with severe constipation: an outcome audit.* Paediatr Nurs, 2006. 18(2): p. 24-8.
21. Hongo, T., et al., *Analysis of the circumstances at the end of life in children with cancer: symptoms, suffering and acceptance.* Pediatr Int, 2003. 45(1): p. 60-4.
22. Selwood, K., *Constipation in paediatric oncology.* Eur J Oncol Nurs, 2006. 10(1): p. 68-70.
23. Tofil, N.M., et al., *The use of enteral naloxone to treat opioid-induced constipation in a pediatric intensive care unit.* Pediatr Crit Care Med, 2006. 7(3): p. 252-4.
24. Urganci, N., B. Akyildiz, and T.B. Polat, *A comparative study: the efficacy of liquid paraffin and lactulose in management of chronic functional constipation.* Pediatr Int, 2005. 47(1): p. 15-9.
25. Weschules, D.J., et al., *Toward evidence-based prescribing at end of life: a comparative analysis of sustained-release morphine, oxycodone, and transdermal fentanyl, with pain, constipation, and caregiver interaction outcomes in hospice patients.* Pain Med, 2006. 7(4): p. 320-9.
26. Woolery, M., et al., *A constipation assessment scale for use in pediatric oncology.* J Pediatr Oncol Nurs, 2006. 23(2): p. 65-74.

27. Zernikow, B., E. Michel, and B. Anderson, *Transdermal fentanyl in childhood and adolescence: a comprehensive literature review*. J Pain, 2007. 8(3): p. 187-207.
28. Awqati, N.A., et al., *Causes and differentials of childhood mortality in Iraq*. BMC Pediatr, 2009. 9(1): p. 40.
29. Cash, S. and A. Shinnick-Page, *Basic life support and children with profound and multiple learning disabilities*. Paediatr Nurs, 2008. 20(8): p. 38-9.
30. Chang, A.B., et al., *Gastro-oesophageal reflux treatment for prolonged non-specific cough in children and adults*. Cochrane Database Syst Rev, 2005(2): p. CD004823.
31. Collins, J.J., et al., *The measurement of symptoms in children with cancer*. J Pain Symptom Manage, 2000. 19(5): p. 363-77.
32. de Groot, I.J. and L.P. de Witte, *Physical complaints in ageing persons with spinal muscular atrophy*. J Rehabil Med, 2005. 37(4): p. 258-62.
33. Fogarasi, A., J. Janszky, and I. Tuxhorn, *Autonomic symptoms during childhood partial epileptic seizures*. Epilepsia, 2006. 47(3): p. 584-8.
34. Hanayama, K., et al., *Dysphagia in patients with Duchenne muscular dystrophy evaluated with a questionnaire and videofluorography*. Disabil Rehabil, 2008. 30(7): p. 517-22.
35. Kravitz, R.M., *Airway clearance in Duchenne muscular dystrophy*. Pediatrics, 2009. 123 Suppl 4: p. S231-5.
36. Laub, M., S. Berg, and B. Midgren, *Symptoms, clinical and physiological findings motivating home mechanical ventilation in patients with neuromuscular diseases*. J Rehabil Med, 2006. 38(4): p. 250-4.
37. Miske, L.J., et al., *Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough*. Chest, 2004. 125(4): p. 1406-12.
38. Simonds, A.K., *Recent advances in respiratory care for neuromuscular disease*. Chest, 2006. 130(6): p. 1879-86.
39. Zylicz, Z. and M. Krajnik, *The use of antitussive drugs in terminally ill patients*. European Journal of Palliative Care, 2004. 11(6): p. 225-9.
40. Bala, K., S.S. Khandpur, and V.V. Gujral, *Evaluation of efficacy and safety of lomotil in acute diarrhoeas in children*. Indian Pediatr, 1979. 16(10): p. 903-7.
41. Karan, S., *Lomotil in diarrhoeal illnesses*. Arch Dis Child, 1979. 54(12): p. 984.
42. Lavy, V., *Presenting symptoms and signs in children referred for palliative care in Malawi*. Palliat Med, 2007. 21(4): p. 333-9.
43. Waterston, A.J., *Lomotil in diarrhoeal illnesses*. Arch Dis Child, 1980. 55(7): p. 577-8.
44. Cachia, E. and S.H. Ahmedzai, *Breathlessness in cancer patients*. Eur J Cancer, 2008. 44(8): p. 1116-23.
45. Collins, J.J. and D.A. Fitzgerald, *Palliative care and paediatric respiratory medicine*. Paediatr Respir Rev, 2006. 7(4): p. 281-7.
46. Currow, D.C., et al., *Does palliative home oxygen improve dyspnoea? A consecutive cohort study*. Palliat Med, 2009. 23(4): p. 309-16.
47. Hechler, T., et al., *Parents' perspective on symptoms, quality of life, characteristics of death and end-of-life decisions for children dying from cancer*. Klin Padiatr, 2008. 220(3): p. 166-74.
48. Camfield, P.R., *Buccal midazolam and rectal diazepam for treatment of prolonged seizures in childhood and adolescence: a randomised trial*. J Pediatr, 1999. 135(3): p. 398-9.
49. Filin, A., S. Treisman, and A. Peles Bortz, *Radiation therapy preparation by a multidisciplinary team for childhood cancer patients aged 31/2 to 6 years*. J Pediatr Oncol Nurs, 2009. 26(2): p. 81-5.
50. Holmes, G.L. and J.J. Riviello, Jr., *Midazolam and pentobarbital for refractory status epilepticus*. Pediatr Neurol, 1999. 20(4): p. 259-64.
51. Jennings, P.D., *Providing pediatric palliative care through a pediatric supportive care team*. Pediatr Nurs, 2005. 31(3): p. 195-200.
52. Mitchell, W.G., *Status epilepticus and acute repetitive seizures in children, adolescents, and young adults: etiology, outcome, and treatment*. Epilepsia, 1996. 37 Suppl 1: p. S74-80.
53. Mpimbaza, A., et al., *Comparison of buccal midazolam with rectal diazepam in the treatment of prolonged seizures in Ugandan children: a randomized clinical trial*. Pediatrics, 2008. 121(1): p. e58-64.
54. O'Dell, C., et al., *Emergency management of seizures in the school setting*. J Sch Nurs, 2007. 23(3): p. 158-65.
55. Quest, T.E., C.A. Marco, and A.R. Derse, *Hospice and Palliative Medicine: New Subspecialty, New Opportunities*. Ann Emerg Med, 2009.
56. Vats, T.S. and P.D. Reynolds, *Pediatric hospital dying trajectories: what we learned and can share*. Pediatr Nurs, 2006. 32(4): p. 386-92.

57. Weissman, D.E., *Decision making at a time of crisis near the end of life*. Jama, 2004. 292(14): p. 1738-43.
58. Amery, J., *Children's Palliative Care in Africa*, ed. J. Amery. 2009: Oxford University Press.
59. Together for Short Lives, *A Guide to End of Life Care* available from: www.togetherforshortlives.org.uk/professionals/resources.
60. GSF. *HOLISTIC PATIENT ASSESSMENT – PEPSI COLA AIDE MEMOIRE*. Available from: www.goldstandardsframework.nhs.uk.
61. Luscombe, M.D., B.D. Owens, and D. Burke, *Weight estimation in paediatrics: a comparison of the APLS formula and the formula 'Weight=3(age)+7'*. Emerg Med J.
62. Varghese, A., et al., *Do the length-based (Broselow) Tape, APLS, Argall and Nelson's formulae accurately estimate weight of Indian children?* Indian Pediatr, 2006. 43(10): p. 889-94.
63. APLS, *The Pediatric Emergency Medicine Resource*. 4th ed.: Jones and Bartlett Publishers.
64. Bais, J.E., et al., *Surgical treatment for recurrent gastro-oesophageal reflux disease after failed antireflux surgery*. Br J Surg, 2000. 87(2): p. 243-249X.
65. Button, B.M., et al., *Chest physiotherapy, gastro-oesophageal reflux, and arousal in infants with cystic fibrosis*. Arch. Dis. Child., 2004. 89(5): p. 435-439.
66. Ceriati, E., et al., *Surgery in disabled children: general gastroenterological aspects*. Acta Paediatr Suppl, 2006. 95(452): p. 34-7.
67. Craig, W.R., et al., *Metoclopramide, thickened feedings, and positioning for gastro-oesophageal reflux in children under two years*. The Cochrane Database of Systematic Reviews, 2004. 2004(3.).
68. Gold, B.D., *Review article: epidemiology and management of gastro-oesophageal reflux in children*. Aliment Pharmacol Ther, 2004. 19 Suppl 1: p. 22-7.
69. Keady, S., *Update on drugs for gastro-oesophageal reflux disease*. Arch Dis Child Educ Pract Ed, 2007. 92(4): p. ep114-8.
70. Lehwald, N., et al., *Sandifer syndrome – a multidisciplinary diagnostic and therapeutic challenge*. Eur J Pediatr Surg, 2007. 17(3): p. 203-6.
71. Pritchard, D.S., N. Baber, and T. Stephenson, *Should domperidone be used for the treatment of gastro-oesophageal reflux in children? Systematic review of randomized controlled trials in children aged 1 month to 11 years old*. Br J Clin Pharmacol, 2005. 59(6): p. 725-9.
72. Salvatore, S., B. Hauser, and Y. Vandenplas, *The natural course of gastro-oesophageal reflux*. Acta Paediatr, 2004. 93(8): p. 1063-9.
73. Salvatore, S. and Y. Vandenplas, *Gastro-oesophageal reflux disease and motility disorders*. Best Pract Res Clin Gastroenterol, 2003. 17(2): p. 163-79.
74. Tolia, V. and Y. Vandenplas, *Systematic review: the extra-oesophageal symptoms of gastro-oesophageal reflux disease in children*. Aliment Pharmacol Ther, 2009. 29(3): p. 258-72.
75. Beckwith, R.A., *Nursing responsibilities to percutaneous endoscopic gastrostomy patients*. Gastroenterol Nurs, 2009. 32(2): p. 127.
76. Brant, C.Q., P. Stanich, and A.P. Ferrari, Jr., *Improvement of children's nutritional status after enteral feeding by PEG: an interim report*. Gastrointest Endosc, 1999. 50(2): p. 183-8.
77. Burd, A. and R.S. Burd, *Guide for home gastrostomy tube care*. Adv Neonatal Care, 2003. 3(4): p. 206-7.
78. Craig, G.M. and G. Scambler, *Negotiating mothering against the odds: gastrostomy tube feeding, stigma, governmentality and disabled children*. Soc Sci Med, 2006. 62(5): p. 1115-25.
79. Hazel, R., *The psychosocial impact on parents of tube feeding their child*. Paediatr Nurs, 2006. 18(4): p. 19-22.
80. Hirsch, B.Z., *Nutrition via gastrostomy tube in children with cancer*. J Pediatr, 1996. 128(1): p. 164.
81. Marin, O.E., et al., *Safety and efficacy of percutaneous endoscopic gastrostomy in children*. Am J Gastroenterol, 1994. 89(3): p. 357-61.
82. Mathus-Vliegen, L.M. and H. Koning, *Percutaneous endoscopic gastrostomy and gastrojejunostomy: a critical reappraisal of patient selection, tube function and the feasibility of nutritional support during extended follow-up*. Gastrointest Endosc, 1999. 50(6): p. 746-54.
83. Puntis, J.W., *Nutritional support at home and in the community*. Arch Dis Child, 2001. 84(4): p. 295-8.
84. Reading, R., *Gastrostomy tube feeding in children with cerebral palsy: a prospective, longitudinal study*. Child: Care, Health and Development, 2005. 31(4): p. 491-492.
85. Samuel, M. and K. Holmes, *Quantitative and qualitative analysis of gastroesophageal reflux after percutaneous endoscopic gastrostomy*. J Pediatr Surg, 2002. 37(2): p. 256-61.
86. Sullivan, P.B., et al., *Impact of gastrostomy tube feeding on the quality of life of carers of children with cerebral palsy*. Dev Med Child Neurol, 2004. 46(12): p. 796-800.

87. Sullivan, P.B., et al., *Prevalence and severity of feeding and nutritional problems in children with neurological impairment: Oxford Feeding Study*. Dev Med Child Neurol, 2000. 42(10): p. 674-80.
88. Tilton, A.H., M.D. Miller, and V. Khoshoo, *Nutrition and swallowing in pediatric neuromuscular patients*. Semin Pediatr Neurol, 1998. 5(2): p. 106-15.
89. Friedman, N.L., *Hiccups: a treatment review*. Pharmacotherapy, 1996. 16(6): p. 986-95.
90. Launois, S., et al., *Hiccup in adults: an overview*. Eur Respir J, 1993. 6(4): p. 563-75.
91. Lewis, J.H., *Hiccups: causes and cures*. J Clin Gastroenterol, 1985. 7(6): p. 539-52.
92. Lipsky, M.S., *Chronic hiccups*. Am Fam Physician, 1986. 34(5): p. 173-7.
93. Madanagopolan, N., *Metoclopramide in hiccup*. Curr Med Res Opin, 1975. 3(6): p. 371-4.
94. Williamson, B.W. and I.M. MacIntyre, *Management of intractable hiccup*. Br Med J, 1977. 2(6085): p. 501-3.
95. Tindyebwa, K., Musoke et al (Eds)., *African Network For Care Of Children Affected By HIV/AIDS (ANECCA) Handbook On Paediatric AIDS In Africa*. 2006. Revised Edition; Available from: www.anecca.org.
96. (DFID), D.F.I.D. *Child mortality factsheet*. Available from: www.dfid.gov.uk/mdg/childmortalityfactsheet.
97. (DFID), D.F.I.D., *WHO World Health Report 2003 – Shaping The Future*. 2003, WHO Geneva.
98. WHO, G. *WHO: Antiretroviral therapy of HIV infection in infants and children: towards universal access*. 2006.
99. Strafford M, C.C., Schwartz T, Et Al., *'Recognition And Treatment Of Pain In Pediatric Children With AIDS'*. J Pain Symptom Manage 1991. 6: p. 146.
100. Hewitt D, M.M., Portenoy R, Et Al., *'Pain Syndromes And Etiologies In Ambulatory AIDS Children'*. Pain, 1997. 70: p. 117-23.
101. (MACS), T.M.A.C.S., *Is an ongoing prospective study of the natural and treated histories of HIV-1 infection in homosexual and bisexual men conducted since 1984 by sites located in Baltimore, Chicago, Pittsburgh and Los Angeles. Data from the MACS have been the basis of more than 780 publications in peer reviewed journals*. 1984.
102. Larue F, B.L., Musseault P, Et Al. , *'Pain And Symptoms In HIV Disease: A National Survey In France.'*.
103. *Abstract: Third Congress Of The European Association For Palliative Care*. J Palliat Care, 1994. 10:: p. 95.
104. Foley, F., *AIDS Palliative Care'. Abstract: 10th International Congress On The Care Of The Terminally Ill*. J Palliat Care, 1994. 10: p. 132.
105. Moss, V., *Palliative care in advanced HIV disease: presentation, problems and palliation*. AIDS, 1990. 4 Suppl 1: p. S235-42.
106. Fontaine, A., F. Larue, and J.M. Lassauniere, *Physicians' recognition of the symptoms experienced by HIV patients: how reliable?* J Pain Symptom Manage, 1999. 18(4): p. 263-70.
107. Breitbart, W., et al., *Fatigue in ambulatory AIDS patients*. J Pain Symptom Manage, 1998. 15(3): p. 159-67.
108. Mathews, W.C., et al., *National estimates of HIV-related symptom prevalence from the HIV Cost and Services Utilization Study*. Med Care, 2000. 38(7): p. 750-62.
109. Amery, J., *Children's Palliative Care in Africa*. 2009, Oxford: OUP.
110. Republic of South Africa *"Conditions Suggestive Of Less Than Six Months Prognosis In Children With AIDS" Recommendations For Managing Hiv Infection In Children*. D.o. Health, Editor. October 2001.
111. Gwyther, M., Mpanga Sebuyira, Schietinger, *Management Of Clinical Conditions In Children. Foundation For Hospices In Sub-Saharan Africa.*, in *A Clinical Guide To Supportive And Palliative Care For HIV/AIDS In Sub-Saharan Africa*, 2006.
112. Chen, C.F., et al., *Assessment of chemotherapy-induced oral complications in children with cancer*. J Pediatr Oncol Nurs, 2004. 21(1): p. 33-9.
113. Botteron, S., et al., *Orofacial dysfunction in Duchenne muscular dystrophy*. Arch Oral Biol, 2009. 54(1): p. 26-31.
114. Coulson, S., *Mouth care in children with cancer*. Paediatr Nurs, 2007. 19(4): p. 18.
115. Gibson, F., *Best practice in oral care for children and young people being treated for cancer: can we achieve consensus?* Eur J Cancer, 2004. 40(8): p. 1109-10.
116. Glenny, A.M., et al., *A survey of current practice with regard to oral care for children being treated for cancer*. Eur J Cancer, 2004. 40(8): p. 1217-24.
117. Williams, P.D., et al., *Symptom monitoring and dependent care during cancer treatment in children: pilot study*. Cancer Nurs, 2006. 29(3): p. 188-97.
118. *Domperidone: an alternative to metoclopramide*. Drug Ther Bull, 1988. 26(15): p. 59-60.
119. *5HT3-receptor antagonists as antiemetics in cancer*. Drug Ther Bull, 2005. 43(8): p. 57-62.
120. Cinquetti, M., P. Bonetti, and P. Bertamini, *[Current role of antidopaminergic drugs in pediatrics]*. Pediatr Med Chir, 2000. 22(1): p. 1-7.

121. Culy, C.R., N. Bhana, and G.L. Plosker, *Ondansetron: a review of its use as an antiemetic in children.* Paediatr Drugs, 2001. 3(6): p. 441-79.
122. Gibson, F. and S. Hopkins, *Feeling sick is horrible, and being sick is very frightening...say Jasper and Polly* (Pearman, 1998). Eur J Oncol Nurs, 2005. 9(1): p. 6-7.
123. Graham-Pole, J., et al., *Antiemetics in children receiving cancer chemotherapy: a double-blind prospective randomized study comparing metoclopramide with chlorpromazine.* J Clin Oncol, 1986. 4(7): p. 1110-3.
124. Kennett, A., et al., *An open study of methotrimeprazine in the management of nausea and vomiting in patients with advanced cancer.* Support Care Cancer, 2005. 13(9): p. 715-21.
125. Markowitz, A.J. and M.W. Rabow, *Management of intractable nausea and vomiting in patients at the end of life: "I was feeling nauseous all of the time . . . nothing was working".* Jama, 2008. 299(15): p. 1826.
126. Roila, F., M. Aapro, and A. Stewart, *Optimal selection of antiemetics in children receiving cancer chemotherapy.* Support Care Cancer, 1998. 6(3): p. 215-20.
127. Skinner, J. and A. Skinner, *Levomepromazine for nausea and vomiting in advanced cancer.* Hosp Med, 1999. 60(8): p. 568-70.
128. BNF, *British National Formulary for Children,* ed. R. BMA, RCPCH, NPPG. 2010, London: BMJ Publishing Group, RPS Publishing, and RCPCH Publications.
129. NNF5, *Neonatal Formulary 5.* BMJ Books, ed. E. Hey. 2007: Blackwell Publishing.
130. Dickman, A., J. Schneider, and J. Varga, *The Syringe Driver. Continuous Infusions in Palliative Care.* 2005: Oxford University Press.
131. Guys, S.T.L.H., *Paediatric Formulary,*. 7th edition ed. 2005.
132. Rudd, N., *A guide for prescribing for patients with advanced malignancy.* 1998: Leicestershire Cancer Centre.
133. Shinnar, S. and J.M. Pellock, *Update on the epidemiology and prognosis of pediatric epilepsy.* J Child Neurol, 2002. 17 Suppl 1: p. S4-17.
134. Murphy, J.V. and F. Dehkharghani, *Diagnosis of childhood seizure disorders.* Epilepsia, 1994. 35 Suppl 2: p. S7-17.
135. Dunn, D.W., *Neuropsychiatric aspects of epilepsy in children.* Epilepsy Behav, 2003. 4(2): p. 101-6.
136. Holmes, G.L., et al., *[Consequences of recurrent seizures during development].* Rev Neurol, 1997. 25(141): p. 749-53.
137. Anderson, G.D., *Children versus adults: pharmacokinetic and adverse-effect differences.* Epilepsia, 2002. 43 Suppl 3: p. 53-9.
138. Blume, W.T., *Uncontrolled epilepsy in children.* Epilepsy Res Suppl, 1992. 5: p. 19-24.
139. Camfield, P.R. and C.S. Camfield, *Antiepileptic drug therapy: when is epilepsy truly intractable?* Epilepsia, 1996. 37 Suppl 1: p. S60-5.
140. Holmes, G.L., *Seizure disorders in children.* Curr Opin Pediatr, 1993. 5(6): p. 653-9.
141. Iinuma, K., *[General principles of treatment and effects of childhood intractable epilepsy].* Rinsho Shinkeigaku, 1999. 39(1): p. 75-6.
142. Steinborn, B., *[Intractable epilepsy of childhood and its treatment].* Neurol Neurochir Pol, 2000. 33 Suppl 1: p. 37-48.
143. Grimshaw, D., et al., *Subcutaneous midazolam, diamorphine and hyoscine infusion in palliative care of a child with neurodegenerative disease.* Child Care Health Dev, 1995. 21(6): p. 377-81.
144. Scott, R.C., F.M. Besag, and B.G. Neville, *Buccal midazolam and rectal diazepam for treatment of prolonged seizures in childhood and adolescence: a randomised trial.* Lancet, 1999. 353(9153): p. 623-6.
145. Gormley, M.E., Jr., L.E. Krach, and L. Piccini, *Spasticity management in the child with spastic quadriplegia.* Eur J Neurol, 2001. 8 Suppl 5: p. 127-35.
146. Koman, L.A., B. Paterson Smith, and R. Balkrishnan, *Spasticity associated with cerebral palsy in children: guidelines for the use of botulinum A toxin.* Paediatr Drugs, 2003. 5(1): p. 11-23.
147. Krach, L.E., *Pharmacotherapy of spasticity: oral medications and intrathecal baclofen.* J Child Neurol, 2001. 16(1): p. 31-6.
148. Schlaggar, B.L. and J.W. Mink, *Movement disorders in children.* Pediatr Rev, 2003. 24(2): p. 39-51.
149. Twycross, R., *Palliative Care Formulary,* A.W. R. Twycross, S. Charlesworth, and A. Dickman, Editor. 2002, Radcliffe Medical Press: Oxon. p. 339.
150. Back, I.N., et al., *A study comparing hyoscine hydrobromide and glycopyrrolate in the treatment of death rattle.* Palliat Med, 2001. 15(4): p. 329-36.
151. Bennett, M., et al., *Using anti-muscarinic drugs in the management of death rattle: evidence-based guidelines for palliative care.* Palliat Med, 2002. 16(5): p. 369-74.

152. Wee, B. and R. Hillier, *Interventions for noisy breathing in patients near to death.* Cochrane Database Syst Rev, 2008(1): p. CD005177.
153. Benini, F., et al., *Evaluating pain induced by venipuncture in pediatric patients with developmental delay.* Clin J Pain, 2004. 20(3): p. 156-63.
154. Chambers, C.T., et al., *Faces scales for the measurement of postoperative pain intensity in children following minor surgery.* Clin J Pain, 2005. 21(3): p. 277-85.
155. Chambliss, C.R., et al., *The assessment and management of chronic pain in children.* Paediatr Drugs, 2002. 4(11): p. 737-46.
156. Duivenvoorden, H.J., et al., *Pain assessment in profound cognitive impaired children using the Checklist Pain Behavior; is item reduction valid?* Pain, 2006. 126(1-3): p. 147-54.
157. Hadden, K.L. and C.L. von Baeyer, *Global and specific behavioral measures of pain in children with cerebral palsy.* Clin J Pain, 2005. 21(2): p. 140-6.
158. Hamunen, K., E.L. Maunuksela, and K.T. Olkkola, *Interpretation of the large red-and-white visual analog scale by children compared with adults.* J Pediatr Nurs, 2008. 23(2): p. 142-4.
159. Hermann, C., et al., *The impact of chronic pain in children and adolescents: Development and initial validation of a child and parent version of the Pain Experience Questionnaire.* Pain, 2008. 135(3): p. 251-61.
160. Holsti, L., et al., *Is it painful or not? Discriminant validity of the Behavioral Indicators of Infant Pain (BIIP) scale.* Clin J Pain, 2008. 24(1): p. 83-8.
161. Hunt, A., et al., *Clinical validation of the paediatric pain profile.* Dev Med Child Neurol, 2004. 46(1): p. 9-18.
162. Hunt, A., et al., *Not knowing – the problem of pain in children with severe neurological impairment.* Int J Nurs Stud, 2003. 40(2): p. 171-83.
163. Hunt, A., 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): p. 276-89.
164. Malviya, S., et al., *The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment.* Paediatr Anaesth, 2006. 16(3): p. 258-65.
165. Manworren, R.C. and L.S. Hynan, *Clinical validation of FLACC: preverbal patient pain scale.* Pediatr Nurs, 2003. 29(2): p. 140-6.
166. Peden, V., I. Choonara, and M. Vater, *Validating the Derbyshire Children's Hospital Pain Tool in children aged 6-12 years.* J Child Health Care, 2005. 9(1): p. 59-71.
167. Solodiuk, J. and M.A. Curley, *Pain assessment in nonverbal children with severe cognitive impairments: the Individualized Numeric Rating Scale (INRS).* J Pediatr Nurs, 2003. 18(4): p. 295-9.
168. Stinson, J.N., et al., *Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents.* Pain, 2006. 125(1-2): p. 143-57.
169. van Dijk, M., et al., *Observational visual analog scale in pediatric pain assessment: useful tool or good riddance?* Clin J Pain, 2002. 18(5): p. 310-6.
170. Voepel-Lewis, T., S. Malviya, and A.R. Tait, *Validity of parent ratings as proxy measures of pain in children with cognitive impairment.* Pain Manag Nurs, 2005. 6(4): p. 168-74.
171. Willis, M.H., et al., *FLACC Behavioral Pain Assessment Scale: a comparison with the child's self-report.* Pediatr Nurs, 2003. 29(3): p. 195-8.
172. von Baeyer, C.L. and L.J. Spagrud, *Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years.* Pain, 2007. 127(1-2): p. 140-50.
173. Hain, R.D., *Pain scales in children: a review.* Palliat Med, 1997. 11(5): p. 341-50.
174. Fridlund, A.J., *The new ethology of human facial expression, in The Psychology of Facial Expression,* J.A. Russell and J.M. Fernandez-Dols, Editors. 1997, Cambridge University Press: Cambridge. p. 103-129.
175. Wolfe, J., et al., *Symptoms and suffering at the end of life in children with cancer.* New England Journal of Medicine, 2000. 342(5): p. 326-333.
176. Hechler, T., et al., *Parents' perspective on symptoms, quality of life, characteristics of death and end-of-life decisions for children dying from cancer.* Klinische Padiatrie, 2008. 220(3): p. 166-174.
177. Schechter, N.L., C.B. Berde, and M. Yaster, *Pain in infants, children, and adolescents: An overview.* Pain in Infants, Children, and Adolescents, 1993: p. 3-9.
178. McGrath, P., *Pain Control,* in *Oxford Textbook of Palliative Medicine,* G.H. D Doyle, NI Cherny, K Calman, Editor. 1998, Oxford University Press: Oxford. p. 775-789.

179. McGrath, P.A., *Children - not simply "Little adults"*. The Path of Pain 1975-2005, 2005: p. 433-446.
180. Kuttner, L., *A child in pain. How to help, what to do*. 1996: Hartley & Marks Publishing Inc.
181. McGrath, P.A., *Commentary: Psychological interventions for controlling children's pain: Challenges for evidence-based medicine*. Journal of Pediatric Psychology, 1999. 24(2): p. 172-174.
182. Palermo, T.M., D. Harrison, and J.L. Koh, *Effect of disease-related pain on the health-related quality of life of children and adolescents with cystic fibrosis*. Clinical Journal of Pain, 2006. 22(6): p. 532-537.
183. Palermo, T.M. and C.T. Chambers, *Parent and family factors in pediatric chronic pain and disability: An integrative approach*. Pain, 2005. 119(1-3): p. 1-4.
184. *WHO Guidelines on the Pharmacological Treatment of Persisting Pain in Children with Medical Illness*. 2012, World Health Organisation Press.
185. Kuttner, L., *Pain: an integrative approach*, in *Oxford Textbook of Palliative Care for Children*, H.R. Goldman A, Liben S, Editor. 2012, Oxford University Press: Oxford. p. 261-270.
186. Treede, R.D., et al., *Neuropathic pain: Redefinition and a grading system for clinical and research purposes*. Neurology, 2008. 70(18): p. 1630-5.
187. Treede, R.D., et al., *Neuropathic pain: Redefinition and a grading system for clinical and research purposes*. Neurology, 2008. 70(18): p. 1630-1635.
188. Walco, G.A., et al., *Neuropathic pain in children: Special considerations*. Mayo Clinic Proceedings, 2010. 85(3 SUPPL.).
189. Hauer, J., *Identifying and managing sources of pain and distress in children with neurological impairment*. Pediatric Annals, 2010. 39(4): p. 198-205.
190. Hain, R.a.D., H, *Neurological Symptoms. Textbook of Interdisciplinary Pediatric Palliative Care*, ed. J.W.a.P.S. Hinds. 2010, Cambridge: Elsevier.
191. Klick, J.C. and J. Hauer, *Pediatric palliative care*. Current Problems in Pediatric and Adolescent Health Care, 2010. 40(6): p. 120-151.
192. Houlihan, C.M., et al., *Bodily pain and health-related quality of life in children with cerebral palsy*. Developmental Medicine and Child Neurology, 2004. 46(5): p. 305-310.
193. Kiman, R., A.C. Wuiloud, and M.L. Requena, *End of life care sedation for children*. Curr Opin Support Palliat Care, 2011. 5(3): p. 285-90.
194. Emslie, G.J., et al., *Fluoxetine Versus Placebo in Preventing Relapse of Major Depression in Children and Adolescents*. Am J Psychiatry, 2008.
195. Jones, D.P. and E.A. Jones, *Drugs for Insomnia*. Can Med Assoc J, 1963. 89: p. 1331.
196. Ashton, H., *Guidelines for the rational use of benzodiazepines. When and what to use*. Drugs, 1994. 48(1): p. 25-40.
197. Breitbart, W., et al., *A double-blind trial of haloperidol, chlorpromazine, and lorazepam in the treatment of delirium in hospitalized AIDS patients*. Am J Psychiatry, 1996. 153(2): p. 231-7.
198. Breitbart, W. and D. Strout, *Delirium in the terminally ill*. Clin Geriatr Med, 2000. 16(2): p. 357-72.
199. Dumortier, G., et al., *[Prescription of psychotropic drugs in paediatry: approved indications and therapeutic perspectives]*. Encephale, 2005. 31(4 Pt 1): p. 477-89.
200. O'Neill, J. and A. Fountain, *Levomepromazine (methotrimeprazine) and the last 48 hours*. Hosp Med, 1999. 60(8): p. 564-7.
201. *Triclofos sodium (Triclos) for insomnia*. Med Lett Drugs Ther, 1972. 14(21): p. 78-80.
202. Birmaher, B., et al., *Fluoxetine for the treatment of childhood anxiety disorders*. J Am Acad Child Adolesc Psychiatry, 2003. 42(4): p. 415-23.
203. Hetrick, S., et al., *Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents*. Cochrane Database Syst Rev, 2007(3): p. CD004851.
204. Jick, H., J.A. Kaye, and S.S. Jick, *Antidepressants and the risk of suicidal behaviors*. Jama, 2004. 292(3): p. 338-43.
205. Roth, D., et al., *Depressing research*. Lancet, 2004. 363(9426): p. 2087.
206. Whittington, C.J., et al., *Selective serotonin reuptake inhibitors in childhood depression: systematic review of published versus unpublished data*. Lancet, 2004. 363(9418): p. 1341-5.
207. Herd, L., *Ventilation via tracheostomy*. 2007 March.
208. Hewitt-Taylor, J., *Children who require long-term ventilation: staff education and training*. Intensive Crit Care Nurs, 2004. 20(2): p. 93-102.
209. Hewitt-Taylor, J., *Long-term mechanical ventilation part 1: ethical dilemmas and decisions*. British Journal of Health Care Assistants. Vol. 02 No 08.

210. Hewitt-Taylor, J., *Long-term mechanical ventilation part 2: principles*. British Journal of Health Care Assistants. Vol. 2 No 09.
211. Markstrom, A., *Non-invasive Ventilation in Children*. European Respiratory Disease, 2007: p. pg 28-30.
212. Selby A., *Paediatric long-term ventilation: a new challenge for adult intensive care?* The Intensive Care Society, 2008. July Vol. 9 (No. 2).
213. Simonds, A., *Making breathing easier*, in *Muscular Dystrophy Campaign*. Fact Sheets Medical Issues. 2007, August.
214. Pallija, G., M. Mondozzi, and A.A. Webb, *Skin care of the pediatric patient*. J Pediatr Nurs, 1999. 14(2): p. 80-7.
215. Quigley, S.M. and M.A. Curley, *Skin integrity in the pediatric population: preventing and managing pressure ulcers*. J Soc Pediatr Nurs, 1996. 1(1): p. 7-18.
216. Willock, J., et al., *Identifying the characteristics of children with pressure ulcers*. Nurs Times, 2005. 101(11): p. 40-3.
217. Twycross, A.W.a.R., *Symptom management in advanced cancer*. Third ed. 2001: Radcliffe medical Press.
218. BNF, *British National Formulary*, ed. R. BMA. 2010, London: BMJ Publishing Group, RPS Publishing,.
219. WHO, *WHO guidelines on the pharmacological treatment of persisting pain in children with medical illnesses*. 2012.
220. Twycross R, W.A., *Palliative Care Formulary (PCF 4)*. 4th Ed ed. 2012: Palliativedrugs.com Ltd.
221. RCPCH, N., *'Medicines for Children'*. 2nd ed. ed. 2003: RCPCH Publications limited.
222. Von Heijne, M., et al., *Propofol or propofol – alfentanil anesthesia for painful procedures in the pediatric oncology ward*. Paediatr Anaesth, 2004. 14(8): p. 670-5.
223. Twycross R, W.A., *Palliative Care Formulary (PCF 3)*. 3rd Ed ed. 2007: Palliativedrugs.com Ltd.
224. Duncan, A., *The use of fentanyl and alfentanil sprays for episodic pain*. Palliat Med, 2002. 16(6): p. 550.
225. Hershey, A.D., et al., *Effectiveness of amitriptyline in the prophylactic management of childhood headaches*. Headache, 2000. 40(7): p. 539-49.
226. Heiligenstein, E. and B.L. Steif, *Tricyclics for pain*. J Am Acad Child Adolesc Psychiatry, 1989. 28(5): p. 804-5.
227. Dachy, B. and B. Dan, *Electrophysiological assessment of the effect of intrathecal baclofen in dystonic children*. Clin Neurophysiol, 2004. 115(4): p. 774-8.
228. Campistol, J., *[Orally administered drugs in the treatment of spasticity]*. Rev Neurol, 2003. 37(1): p. 70-4.
229. Delgado, M.R., 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. 74(4): p. 336-43.
230. Hansel, D.E., et al., *Oral baclofen in cerebral palsy: possible seizure potentiation?* Pediatric Neurology, 2003. 29(3 SU -): p. 203-206.
231. Jones, R.F. and J.W. Lance, *Bacloffen (Lioresal) in the long-term management of spasticity*. Med J Aust, 1976. 1(18): p. 654-7.
232. Pascual-Pascual, S.I., *[The study and treatment of dystonias in childhood]*. Rev Neurol, 2006. 43 Suppl 1: p. S161-8.
233. Patel, D.R. and O. Soyode, *Pharmacologic interventions for reducing spasticity in cerebral palsy*. Indian J Pediatr, 2005. 72(10): p. 869-72.
234. Drugs.com, *http://www.drugs.com/dosage/bethanechol.html*. 2010.
235. Attina, G., et al., *Transdermal buprenorphine in children with cancer-related pain*. Pediatr Blood Cancer, 2009. 52(1): p. 125-7.
236. Zernikow, B., et al., *Pediatric palliative care: use of opioids for the management of pain*. Paediatr Drugs, 2009. 11(2): p. 129-51.
237. Colvin, L. and M. Fallon, *Challenges in cancer pain management – bone pain*. Eur J Cancer, 2008. 44(8): p. 1083-90.
238. Kienast, H.W. and L.D. Boshes, *Clinical trials of carbamazepine in suppressing pain*. Headache, 1968. 8(1): p. 1-5.
239. Klepstad, P., et al., *Pain and pain treatments in European palliative care units. A cross sectional survey from the European Association for Palliative Care Research Network*. Palliat Med, 2005. 19(6): p. 477-84.
240. Swerdlow, M., *The treatment of "shooting" pain*. Postgrad Med J, 1980. 56(653): p. 159-61.
241. Lynch, P.M., et al., *The safety and efficacy of celecoxib in children with familial adenomatous polyposis*. Am J Gastroenterol. 105(6): p. 1437-43.

242. Foeldvari, I., et al., *A prospective study comparing celecoxib with naproxen in children with juvenile rheumatoid arthritis.* J Rheumatol, 2009. 36(1): p. 174-82.
243. Stempak, D., et al., *Single-dose and steady-state pharmacokinetics of celecoxib in children.* Clin Pharmacol Ther, 2002. 72(5): p. 490-7.
244. Pandolfini, C. and M. Bonati, *A literature review on off-label drug use in children.* Eur J Pediatr, 2005. 164(9): p. 552-8.
245. Weiss, S., *Sedation of pediatric patients for nuclear medicine procedures.* Semin Nucl Med, 1993. 23(3): p. 190-8.
246. Jassal, S., ed., *Basic Symptom Control in Paediatric Palliative Care.* 7th ed. Rainbow's Hospice Symptom Control Manual, ed. S. Jassal. 2008.
247. MartindaleOnline, *The Complete Drug Reference,* S.C. Sweetman, Editor., Pharmaceutical Press.
248. Smith, H.S., *Opioid metabolism.* Mayo Clin Proc, 2009. 84(7): p. 613-24.
249. Williams, D.G., A. Patel, and R.F. Howard, *Pharmacogenetics of codeine metabolism in an urban population of children and its implications for analgesic reliability.* Br J Anaesth, 2002. 89(6): p. 839-45.
250. Drake, R., et al., *Impact of an antiemetic protocol on postoperative nausea and vomiting in children.* Paediatr Anaesth, 2001. 11(1): p. 85-91.
251. Pinder, R.M., et al., *Dantrolene sodium: a review of its pharmacological properties and therapeutic efficacy in spasticity.* Drugs, 1977. 13(1): p. 3-23.
252. Dupuis, L.L., R. Lau, and M.L. Greenberg, *Delayed nausea and vomiting in children receiving antineoplastics.* Med Pediatr Oncol, 2001. 37(2): p. 115-21.
253. de Vries, M.A., et al., *Effect of dexamethasone on quality of life in children with acute lymphoblastic leukaemia: a prospective observational study.* Health Qual Life Outcomes, 2008. 6(1): p. 103.
254. Tramer, M.R., *[Prevention and treatment of postoperative nausea and vomiting in children. An evidence-based approach].* Ann Fr Anesth Reanim, 2007. 26(6): p. 529-34.
255. Hewitt, M., et al., *Opioid use in palliative care of children and young people with cancer.* J Pediatr, 2008. 152(1): p. 39-44.
256. Mathew, A., et al., *The efficacy of diazepam in enhancing motor function in children with spastic cerebral palsy.* J Trop Pediatr, 2005. 51(2): p. 109-13.
257. O'Dell, C. and K. O'Hara, *School nurses' experience with administration of rectal diazepam gel for seizures.* J Sch Nurs, 2007. 23(3): p. 166-9.
258. Srivastava, M. and D. Walsh, *Diazepam as an adjuvant analgesic to morphine for pain due to skeletal muscle spasm.* Support Care Cancer, 2003. 11(1): p. 66-9.
259. Gubbay, A. and K. Langdon, *'Effectiveness of sedation using nitrous oxide compared with enteral midazolam for botulinum toxin A injections in children'.* Dev Med Child Neurol, 2009. 51(6): p. 491-2; author reply 492.
260. Novak, P.H., et al., *Acute drug prescribing to children on chronic antiepilepsy therapy and the potential for adverse drug interactions in primary care.* Br J Clin Pharmacol, 2005. 59(6): p. 712-7.
261. Grape, S., et al., *Formulations of fentanyl for the management of pain.* Drugs. 70(1): p. 57-72.
262. Cappelli, C., et al., *[Transdermal Fentanyl: news in oncology].* Clin Ter, 2008. 159(4): p. 257-260.
263. Borland, M., et al., *A randomized controlled trial comparing intranasal fentanyl to intravenous morphine for managing acute pain in children in the emergency department.* Ann Emerg Med, 2007. 49(3): p. 335-40.
264. Borland, M.L., I. Jacobs, and G. Geelhoed, *Intranasal fentanyl reduces acute pain in children in the emergency department: a safety and efficacy study.* Emerg Med (Fremantle), 2002. 14(3): p. 275-80.
265. Drake, R., J. Longworth, and J.J. Collins, *Opioid rotation in children with cancer.* J Palliat Med, 2004. 7(3): p. 419-22.
266. Friedrichsdorf, S.J. and T.I. Kang, *The management of pain in children with life-limiting illnesses.* Pediatr Clin North Am, 2007. 54(5): p. 645-72, x.
267. Hunt, A., et al., *Transdermal fentanyl for pain relief in a paediatric palliative care population.* Palliat Med, 2001. 15(5): p. 405-12.
268. Kanowitz, A., et al., *Safety and effectiveness of fentanyl administration for prehospital pain management.* Prehosp Emerg Care, 2006. 10(1): p. 1-7.
269. Mercadante, S., et al., *Transmucosal fentanyl vs intravenous morphine in doses proportional to basal opioid regimen for episodic-breakthrough pain.* Br J Cancer, 2007. 96(12): p. 1828-33.
270. Noyes, M. and H. Irving, *The use of transdermal fentanyl in pediatric oncology palliative care.* Am J Hosp Palliat Care, 2001. 18(6): p. 411-6.

271. Weschules, D.J., et al., *Are newer, more expensive pharmacotherapy options associated with superior symptom control compared to less costly agents used in a collaborative practice setting?* Am J Hosp Palliat Care, 2006. 23(2): p. 135-49.
272. Pienaar, E.D., T. Young, and H. Holmes, *Interventions for the prevention and management of oropharyngeal candidiasis associated with HIV infection in adults and children.* Cochrane Database Syst Rev, 2006. 3: p. CD003940.
273. Millet, B., et al., *Obsessive-compulsive disorder: evaluation of clinical and biological circadian parameters during fluoxetine treatment.* Psychopharmacology (Berl), 1999. 146(3): p. 268-74.
274. Monteleone, P., et al., *Plasma melatonin and cortisol circadian patterns in patients with obsessive-compulsive disorder before and after fluoxetine treatment.* Psychoneuroendocrinology, 1995. 20(7): p. 763-70.
275. Caraceni, A., et al., *Gabapentin for neuropathic cancer pain: a randomized controlled trial from the Gabapentin Cancer Pain Study Group.* J Clin Oncol, 2004. 22(14): p. 2909-17.
276. Butkovic, D., S. Toljan, and B. Mihovilovic-Novak, *Experience with gabapentin for neuropathic pain in adolescents: report of five cases.* Paediatr Anaesth, 2006. 16(3): p. 325-9.
277. Negro, S., et al., *Physical compatibility and in vivo evaluation of drug mixtures for subcutaneous infusion to cancer patients in palliative care.* Support Care Cancer, 2002. 10(1): p. 65-70.
278. Saito, T. and S. Shinno, *[How we have treated and cared patients with Duchenne muscular dystrophy and severe congestive heart failure].* No To Hattatsu, 2005. 37(4): p. 281-6.
279. Bell, R.F., et al., *Controlled clinical trials in cancer pain. How controlled should they be? A qualitative systematic review.* Br J Cancer, 2006.
280. Quigley, C. and P. Wiffen, *A systematic review of hydromorphone in acute and chronic pain.* J Pain Symptom Manage, 2003. 25(2): p. 169-78.
281. Titchen, T., N. Cranswick, and S. Beggs, *Adverse drug reactions to nonsteroidal anti-inflammatory drugs, COX-2 inhibitors and paracetamol in a paediatric hospital.* Br J Clin Pharmacol, 2005. 59(6): p. 718-23.
282. Anderson, B.J. and G.M. Palmer, *Recent developments in the pharmacological management of pain in children.* Curr Opin Anaesthesiol, 2006. 19(3): p. 285-92.
283. Anghelescu, D.L. and L.L. Oakes, *Ketamine use for reduction of opioid tolerance in a 5-year-old girl with end-stage abdominal neuroblastoma.* J Pain Symptom Manage, 2005. 30(1): p. 1-3.
284. Campbell-Fleming, J.M. and A. Williams, *The use of ketamine as adjuvant therapy to control severe pain.* Clin J Oncol Nurs, 2008. 12(1): p. 102-7.
285. Legge, J., N. Ball, and D.P. Elliott, *The potential role of ketamine in hospice analgesia: a literature review.* Consult Pharm, 2006. 21(1): p. 51-7.
286. Tsui, B.C., et al., *Intravenous ketamine infusion as an adjuvant to morphine in a 2-year-old with severe cancer pain from metastatic neuroblastoma.* J Pediatr Hematol Oncol, 2004. 26(10): p. 678-80.
287. Fitzgibbon, E.J., et al., *Low dose ketamine as an analgesic adjuvant in difficult pain syndromes: a strategy for conversion from parenteral to oral ketamine.* J Pain Symptom Manage, 2002. 23(2): p. 165-70.
288. Bell, R., C. Eccleston, and E. Kalso, *Ketamine as an adjuvant to opioids for cancer pain.* Cochrane Database Syst Rev, 2003(1): p. CD003351.
289. Klepstad, P., et al., *Long-term treatment with ketamine in a 12-year-old girl with severe neuropathic pain caused by a cervical spinal tumor.* J Pediatr Hematol Oncol, 2001. 23(9): p. 616-9.
290. Hans, G., et al., *Management of neuropathic pain after surgical and non-surgical trauma with lidocaine 5% patches: study of 40 consecutive cases.* Curr Med Res Opin, 2009. 25(11): p. 2737-43.
291. Garnock-Jones, K.P. and G.M. Keating, *Lidocaine 5% medicated plaster: a review of its use in postherpetic neuralgia.* Drugs, 2009. 69(15): p. 2149-65.
292. *Lidocaine plasters for postherpetic neuralgia?* Drug Ther Bull, 2008. 46(2): p. 14-6.
293. Li, S.T., D.C. Grossman, and P. Cummings, *Loperamide therapy for acute diarrhea in children: systematic review and meta-analysis.* PLoS Med, 2007. 4(3): p. e98.
294. Kaplan, M.A., et al., *A multicenter randomized controlled trial of a liquid loperamide product versus placebo in the treatment of acute diarrhea in children.* Clin Pediatr (Phila), 1999. 38(10): p. 579-91.
295. Burtles, R. and B. Astley, *Lorazepam in children. A double-blind trial comparing lorazepam, diazepam, trimeprazine and placebo.* Br J Anaesth, 1983. 55(4): p. 275-9.
296. Braam, W., et al., *Melatonin treatment in individuals with intellectual disability and chronic insomnia: a randomized placebo-controlled study.* J Intellect Disabil Res, 2008. 52(Pt 3): p. 256-64.

297. Andersen, I.M., et al., *Melatonin for insomnia in children with autism spectrum disorders*. J Child Neurol, 2008. 23(5): p. 482-5.
298. Guerrero, J.M., et al., *Impairment of the melatonin rhythm in children with Sanfilippo syndrome*. J Pineal Res, 2006. 40(2): p. 192-3.
299. Gupta, R. and J. Hutchins, *Melatonin: a panacea for desperate parents? (Hype or truth)*. Arch Dis Child, 2005. 90(9): p. 986-7.
300. Ivanenko, A., et al., *Melatonin in children and adolescents with insomnia: a retrospective study*. Clin Pediatr (Phila), 2003. 42(1): p. 51-8.
301. Mariotti, P., et al., *Sleep disorders in Sanfilippo syndrome: a polygraphic study*. Clin Electroencephalogr, 2003. 34(1): p. 18-22.
302. Masters, K.J., *Melatonin for sleep problems*. J Am Acad Child Adolesc Psychiatry, 1996. 35(6): p. 704.
303. Owens, J.A., C.L. Rosen, and J.A. Mindell, *Medication use in the treatment of pediatric insomnia: results of a survey of community-based pediatricians*. Pediatrics, 2003. 111(5 Pt 1): p. e628-35.
304. Paavonen, E.J., et al., *Effectiveness of melatonin in the treatment of sleep disturbances in children with Asperger disorder*. J Child Adolesc Psychopharmacol, 2003. 13(1): p. 83-95.
305. Smits, M.G., et al., *Melatonin for chronic sleep onset insomnia in children: a randomized placebo-controlled trial*. J Child Neurol, 2001. 16(2): p. 86-92.
306. Smits, M.G., et al., *Melatonin improves health status and sleep in children with idiopathic chronic sleep-onset insomnia: a randomized placebo-controlled trial*. J Am Acad Child Adolesc Psychiatry, 2003. 42(11): p. 1286-93.
307. van der Heijden, K.B., et al., *Prediction of melatonin efficacy by pretreatment dim light melatonin onset in children with idiopathic chronic sleep onset insomnia*. J Sleep Res, 2005. 14(2): p. 187-94.
308. Van der Heijden, K.B., et al., *Effect of melatonin on sleep, behavior, and cognition in ADHD and chronic sleep-onset insomnia*. J Am Acad Child Adolesc Psychiatry, 2007. 46(2): p. 233-41.
309. Wasdell, M.B., et al., *A randomized, placebo-controlled trial of controlled release melatonin treatment of delayed sleep phase syndrome and impaired sleep maintenance in children with neurodevelopmental disabilities*. J Pineal Res, 2008. 44(1): p. 57-64.
310. Zhdanova, I.V., *Melatonin as a hypnotic: pro*. Sleep Med Rev, 2005. 9(1): p. 51-65.
311. Zucconi, M. and O. Bruni, *Sleep disorders in children with neurologic diseases*. Semin Pediatr Neurol, 2001. 8(4): p. 258-75.
312. Dickman, A. and J. Schneider, *The Syringe Driver. Continuous Infusions in Palliative Care*. 3rd ed. 2011: Oxford University Press.
313. Benitez-Rosario, M.A., et al., *Morphine-methadone opioid rotation in cancer patients: analysis of dose ratio predicting factors*. J Pain Symptom Manage, 2009. 37(6): p. 1061-8.
314. Bruera, E., et al., *Methadone versus morphine as a first-line strong opioid for cancer pain: a randomized, double-blind study*. J Clin Oncol, 2004. 22(1): p. 185-92.
315. Berens, R.J., et al., *A prospective evaluation of opioid weaning in opioid-dependent pediatric critical care patients*. Anesth Analg, 2006. 102(4): p. 1045-50.
316. Colvin, L., K. Forbes, and M. Fallon, *Difficult pain*. Bmj, 2006. 332(7549): p. 1081-3.
317. Dale, O., P. Sheffels, and E.D. Kharasch, *Bioavailabilities of rectal and oral methadone in healthy subjects*. Br J Clin Pharmacol, 2004. 58(2): p. 156-62.
318. Davies, D., D. DeVlaming, and C. Haines, *Methadone analgesia for children with advanced cancer*. Pediatr Blood Cancer, 2008. 51(3): p. 393-7.
319. Ripamonti, C. and M. Bianchi, *The use of methadone for cancer pain*. Hematol Oncol Clin North Am, 2002. 16(3): p. 543-55.
320. Weschules, D.J. and K.T. Bain, *A systematic review of opioid conversion ratios used with methadone for the treatment of pain*. Pain Med, 2008. 9(5): p. 595-612.
321. Weschules, D.J., et al., *Methadone and the hospice patient: prescribing trends in the home-care setting*. Pain Med, 2003. 4(3): p. 269-76.
322. Heppe, D.B., M.C. Haigney, and M.J. Krantz, *The effect of oral methadone on the QTc interval in advanced cancer patients: a prospective pilot study*. J Palliat Med. 13(6): p. 638-9.
323. Mercadante, S., P. Ferrera, and E. Arcuri, *The use of fentanyl buccal tablets as breakthrough medication in patients receiving chronic methadone therapy: an open label preliminary study*. Support Care Cancer.
324. www.palliativedrugs.com, *Methylnaltrexone*. 2010.

325. Alhashimi, D., H. Alhashimi, and Z. Fedorowicz, *Antiemetics for reducing vomiting related to acute gastroenteritis in children and adolescents.* Cochrane Database Syst Rev, 2006. 3: p. CD005506.
326. Yis, U., et al., *Metoclopramide induced dystonia in children: two case reports.* Eur J Emerg Med, 2005. 12(3): p. 117-9.
327. Castro Conde, J.R., et al., *Midazolam in neonatal seizures with no response to phenobarbital.* Neurology, 2005. 64(5): p. 876-9.
328. Harte, G.J., et al., *Haemodynamic responses and population pharmacokinetics of midazolam following administration to ventilated, preterm neonates.* J Paediatr Child Health, 1997. 33(4): p. 335-8.
329. Lee, T.C., et al., *Population pharmacokinetic modeling in very premature infants receiving midazolam during mechanical ventilation: midazolam neonatal pharmacokinetics.* Anesthesiology, 1999. 90(2): p. 451-7.
330. Hu, K.C., et al., *Continuous midazolam infusion in the treatment of uncontrollable neonatal seizures.* Acta Paediatr Taiwan, 2003. 44(5): p. 279-81.
331. Berde, C.B. and N.F. Sethna, *Drug therapy – Analgesics for the treatment of pain in children.* New England Journal of Medicine, 2002. 347(14): p. 1094-1103.
332. Boyle, E.M., et al., *Assessment of persistent pain or distress and adequacy of analgesia in preterm ventilated infants.* Pain, 2006. 124(1-2): p. 87-91.
333. Cohen, S.P. and T.C. Dawson, *Nebulized morphine as a treatment for dyspnea in a child with cystic fibrosis.* Pediatrics, 2002. 110(3): p. e38.
334. Dougherty, M. and M.R. DeBaun, *Rapid increase of morphine and benzodiazepine usage in the last three days of life in children with cancer is related to neuropathic pain.* J Pediatr, 2003. 142(4): p. 373-6.
335. Flogegard, H. and G. Ljungman, *Characteristics and adequacy of intravenous morphine infusions in children in a paediatric oncology setting.* Med Pediatr Oncol, 2003. 40(4): p. 233-8.
336. Hain, R.D., et al., *Strong opioids in pediatric palliative medicine.* Paediatr Drugs, 2005. 7(1): p. 1-9.
337. Hall, R.W., et al., *Morphine, Hypotension, and Adverse Outcomes Among Preterm Neonates: Who's to Blame? Secondary Results From the NEOPAIN Trial.* Pediatrics, 2005. 115(5): p. 1351-1359.
338. Lundeberg, S., et al., *Perception of pain following rectal administration of morphine in children: a comparison of a gel and a solution.* Paediatr Anaesth, 2006. 16(2): p. 164-9.
339. Miser, A.W., et al., *Continuous subcutaneous infusion of morphine in children with cancer.* Am J Dis Child, 1983. 137(4): p. 383-5.
340. Nahata, M.C., et al., *Analgesic plasma concentrations of morphine in children with terminal malignancy receiving a continuous subcutaneous infusion of morphine sulfate to control severe pain.* Pain, 1984. 18(2): p. 109-14.
341. Sittl, R. and R. Richter, *[Cancer pain therapy in children and adolescents using morphine].* Anaesthesist, 1991. 40(2): p. 96-9.
342. Van Hulle Vincent, C. and M.J. Denyes, *Relieving children's pain: nurses' abilities and analgesic administration practices.* J Pediatr Nurs, 2004. 19(1): p. 40-50.
343. Viola, R., et al., *The management of dyspnea in cancer patients: a systematic review.* Support Care Cancer, 2008.
344. Wiffen, P.J. and H.J. McQuay, *Oral morphine for cancer pain.* Cochrane Database Syst Rev, 2007(4): p. CD003868.
345. Zeppetella, G., J. Paul, and M.D. Ribeiro, *Analgesic efficacy of morphine applied topically to painful ulcers.* J Pain Symptom Manage, 2003. 25(6): p. 555-8.
346. Zernikow, B. and G. Lindena, *Long-acting morphine for pain control in paediatric oncology.* Medical & Pediatric Oncology, 2001. 36(4): p. 451-458.
347. Zernikow, B., et al., *Paediatric cancer pain management using the WHO analgesic ladder – results of a prospective analysis from 2265 treatment days during a quality improvement study.* Eur J Pain, 2006. 10(7): p. 587-95.
348. Liu, M. and E. Wittbrodt, *Low-dose oral naloxone reverses opioid-induced constipation and analgesia.* J Pain Symptom Manage, 2002. 23(1): p. 48-53.
349. Litalien, C., Y. Theoret, and C. Faure, *Pharmacokinetics of proton pump inhibitors in children.* Clin Pharmacokinet, 2005. 44(5): p. 441-66.
350. Simpson, T. and J. Ivey, *Pediatric management problems.* GERD. Pediatr Nurs, 2005. 31(3): p. 214-5.
351. Kyriakides, K., S.K. Hussain, and G.J. Hobbs, *Management of opioid-induced pruritus: a role for 5-HT3 antagonists?* Br J Anaesth, 1999. 82(3): p. 439-41.

352. Kokki, H., et al., *Comparison of oxycodone pharmacokinetics after buccal and sublingual administration in children.* Clin Pharmacokinet, 2006. 45(7): p. 745-54.
353. Kokki, H., et al., *Pharmacokinetics of oxycodone after intravenous, buccal, intramuscular and gastric administration in children.* Clin Pharmacokinet, 2004. 43(9): p. 613-22.
354. Zin, C.S., et al., *A randomized, controlled trial of oxycodone versus placebo in patients with postherpetic neuralgia and painful diabetic neuropathy treated with pregabalin.* J Pain. 11(5): p. 462-71.
355. Zin, C.S., et al., *An update on the pharmacological management of post-herpetic neuralgia and painful diabetic neuropathy.* CNS Drugs, 2008. 22(5): p. 417-42.
356. Czarnecki, M.L., et al., *Controlled-release oxycodone for the management of pediatric postoperative pain.* J Pain Symptom Manage, 2004. 27(4): p. 379-86.
357. Villa, M.P., et al., *Nocturnal oximetry in infants with cystic fibrosis.* Arch Dis Child, 2001. 84(1): p. 50-54.
358. Balfour-Lynn, I.M., *Domiciliary oxygen for children.* Pediatr Clin North Am, 2009. 56(1): p. 275-96, xiii.
359. Saugstad, O.D., *Chronic lung disease: oxygen dogma revisited.* Acta Paediatr, 2001. 90(2): p. 113-5.
360. Ross, J.R., et al., *A systematic review of the role of bisphosphonates in metastatic disease.* Health Technol Assess, 2004. 8(4): p. 1-176.
361. Rowland, A.G., et al., *Review of the efficacy of rectal paraldehyde in the management of acute and prolonged tonic-clonic convulsions.* Arch Dis Child, 2009. 94(9): p. 720-3.
362. www.palliativedrugs.com, *Phenobarbital.* 2010.
363. Osorio, I., R.C. Reed, and J.N. Peltzer, *Refractory idiopathic absence status epilepticus: A probable paradoxical effect of phenytoin and carbamazepine.* Epilepsia, 2000. 41(7): p. 887-94.
364. Bell, S.G., *Gastroesophageal reflux and histamine2 antagonists.* Neonatal Netw, 2003. 22(2): p. 53-7.
365. Palazon Garcia, R., A. Benavente Valdepenas, and O. Arroyo Riano, *[Protocol for tizanidine use in infantile cerebral palsy].* An Pediatr (Barc), 2008. 68(5): p. 511-5.
366. Henney, H.R., 3rd and M. Chez, *Pediatric safety of tizanidine: clinical adverse event database and retrospective chart assessment.* Paediatr Drugs, 2009. 11(6): p. 397-406.
367. Vasquez-Briceno, A., et al., *[The usefulness of tizanidine. A one-year follow-up of the treatment of spasticity in infantile cerebral palsy].* Rev Neurol, 2006. 43(3): p. 132-6.
368. Spiller, H.A., G.M. Bosse, and L.A. Adamson, *Retrospective review of Tizanidine (Zanaflex) overdose.* J Toxicol Clin Toxicol, 2004. 42(5): p. 593-6.
369. Chauhan, S., et al., *Tranexamic acid in paediatric cardiac surgery.* Indian J Med Res, 2003. 118: p. 86-9.
370. Graff, G.R., *Treatment of recurrent severe hemoptysis in cystic fibrosis with tranexamic acid.* Respiration, 2001. 68(1): p. 91-4.
371. Mehta, R. and A.D. Shapiro, *Plasminogen deficiency.* Haemophilia, 2008. 14(6): p. 1261-8.
372. Brook L, V.J., Osborne C., *Paediatric palliative care drug boxes; facilitating safe & effective symptom management at home at end of life.* Archives of Disease in Childhood, 2007. 92 (Suppl I): A58.

Basic Symptom Control in Paediatric Palliative Care

Basic Symptom Control in Paediatric Palliative Care is a key clinical tool used by children's palliative care doctors and nurses across the world. It is the only resource of its kind that provides comprehensive guidelines for treating a wide range of symptoms experienced by children with life-limiting or complex health conditions. *Basic Symptom Control in Paediatric Palliative Care*, now in its ninth edition, has become known as the symptom control 'industry bible' for professionals working in the field.

Basic Symptom Control in Paediatric Palliative Care has been developed and edited by Dr Satbir Singh Jassal, GP and Medical Director at Rainbows Children's Hospice, with contributions and peer reviews from 29 leading paediatric and palliative care specialists. It provides doctors and nursing staff with an 'all in one' reference tool for symptom management and children's palliative care medicines. It's been designed to provide both practical support and hands on clinical information in the acute setting. It's also been written in language that parents can easily understand, as doctors and nursing staff who care for children in the community often leave a copy in the family home so it is on hand for reference.

Basic Symptom Control in Paediatric Palliative Care is packed with information about how to appropriately treat a wide range of symptoms including: infections, nausea and vomiting, seizures and muscle spasm, as well as pain management. The new updated edition reflects the changes and developments in children's palliative care, as well as seeking to address gaps in guidance on key topics. There is a new chapter on end of life management – responding to the key concern of how to manage the final stages of a child's life. There are also major rewrites to the pain and gastrostomy sections. It also includes a comprehensive prescribing formulary, adapted from the Association of Paediatric Palliative Medicine's master formulary (second edition), to support those prescribing in children's palliative medicine.

Basic Symptom Control in Paediatric Palliative Care has international appeal and is essential reading for all doctors and nursing staff who are involved in delivering palliative care to babies, children and young people.

Together for Short Lives
4th Floor, Bridge House, 48-52 Baldwin Street,
Bristol BS1 1QB

T: 0117 989 7820
F: 0117 929 1999
E: info@togetherforshortlives.org.uk

www.togetherforshortlives.org.uk

Together for Short Lives is a registered charity in England and Wales (1144022) and Scotland (SC044139) and is a company limited by guarantee (7783702)