

Chapter 4

Pain Management***Overview***

In Africa, where antiretroviral therapy (ART) is not yet freely available, pain in HIV/AIDS is still a significant problem. In two South African studies on rural and urban patients with AIDS, the incidence of pain ranged from 91–98% of patients (Norval, 2004). Even in areas where ART is available, pain control and palliative care will still be a very important part of care.

In the developed world, the advent of ART has not diminished the need for palliative care for people living with HIV/AIDS. In fact, because of new treatments, fewer patients are dying from HIV/AIDS in the U.S. and the total number of people living with HIV/AIDS is increasing. New treatments, particularly ART, are also responsible for additional symptoms and complications, including pain that must be understood and managed.

This chapter describes the types and prevalence of pain syndromes encountered in adult patients with HIV disease and outlines the principles of pain management. We will review the psychological and functional impact of pain as well as the barriers to adequate pain treatment in this population, including ‘opiophobia’, or fear of opioids. Refer to other chapters in Part 2 (Clinical Supportive Care) for additional management of specific symptoms (e.g., Chapter 8: Mouth Care). See Chapter 27 for more on pain management in children and for paediatric doses.

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Occurrence of Pain in HIV/AIDS

Common Pain Syndromes

Several studies have documented that people with HIV infection or AIDS suffer from pain (Breitbart, 1996a; Breitbart, 1996b; Breitbart, 1996c; Breitbart, 1997; Frich, 2000; Hewitt, 1997; Larue, 1997; Lebovits, 1989; McCormack, 1993; O'Neill, 1993; Rosenfeld, 1996; Singer, 1993).

The characteristics of HIV-related pain are:

- Highly prevalent, diverse, and varied in syndromal presentation
- Associated with significant psychological and functional morbidity
- Alarming under-treated

Pain syndromes encountered in AIDS are diverse in nature and etiology (see Table 4.1: Pain Syndromes). The most common pain syndromes reported in studies to date include painful sensory peripheral neuropathy, pain due to extensive Kaposi's sarcoma, headache, oral and pharyngeal pain, abdominal pain, chest pain, arthralgias and myalgias, and painful dermatological conditions.

Moreover, pain has a profound negative impact both on physical and psychological functioning and on overall quality of life. It is important, therefore, that pain management be more integrated into the total care of patients with HIV disease.

Table 4.1: Pain Syndromes

Pain Type	N	% Patients (n=151)
Somatic pain	107	71
Neuropathic pain	69	46
Visceral pain	44	29
Headache	69	46

Source: Hewitt, 1997. Reprinted with permission.

Issues of Pain in Women in Africa

A number of factors contribute to women in Africa being more likely to suffer from pain than men or than women in other parts of the world. One study has suggested that women with HIV disease experience pain more frequently than men with HIV disease and report somewhat higher levels of pain intensity (Hewitt, 1997). This may in part reflect the fact that women with AIDS-related pain are twice as likely as men to be under-treated for their pain (Breitbart, 1996b). In addition, women with AIDS in Africa have been shown to have higher levels of anxiety than men (Norval, 2004). Anxiety is known to exacerbate and contribute to total pain in people with HIV/AIDS.

Women with HIV disease have unique pain syndromes of a gynaecologic nature specifically related to opportunistic infections (OIs) and cancers of the pelvis and genitourinary tract, and in one survey women with AIDS were significantly more likely to be diagnosed with radiculopathy and headache (Hewitt, 1997; Lobb, 1995; Marte, 1991). In Africa, women with HIV/AIDS are vulnerable to OIs of the genital tract, and carcinoma of the cervix is highly prevalent.

African women with HIV are often young with babies and young children. The fact that some of their children will also test positive for HIV or be ill with AIDS adds emotional, social, and spiritual suffering to their physical pain. It is therefore essential when providing care to women to be sensitive to all aspects of pain and to provide effective pain management.

Issues of Pain in Children

Children with HIV infection also experience pain (Strafford, 1991). Pain in children is often related to medical procedures and severe and/or chronic bacterial viral and parasitic infections (see Chapter 27: Management of Clinical Conditions). HIV-related conditions in children that are observed to cause pain include:

- Meningitis and sinusitis (headaches)
- Otitis media
- Shingles
- Cellulitis and abscesses
- Severe candida dermatitis and oral and oesophageal candidiasis
- Dental caries
- Chronic diarrhoea and intestinal infections, such as *Mycobacterium avium* intracellulare (MAI) and cryptosporidium
- Diffuse lymphadenopathy
- Hepatosplenomegaly
- Spasticity associated with encephalopathy that causes painful muscle spasms
- Neuropathy

Defining Pain

'Pain is a more terrible lord of mankind than even death itself.'

Albert Schweitzer

Definition

Pain, one of the most common symptoms in palliative care, is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage (IASP, 1994). It is frequently inadequately treated, resulting in unnecessary suffering. The aim of palliative care is to allow patients to be pain free or for the pain to be sufficiently controlled that it does not interfere with their ability to function or their quality of life.

The Concept of Total Pain

The concept of total pain was introduced by Dame Cecily Saunders, who described the overlapping components of pain as physical, emotional, social, and spiritual (see Figure 4.1: The Concept of Total Pain). Pain is always subjective, and the perception of pain may be modified by problems or influences related to any or all of the potential causes of suffering. The relationship of pain and suffering is complicated by the interdependence and inter-relationships between the different causes of suffering (Woodruff, 2004).

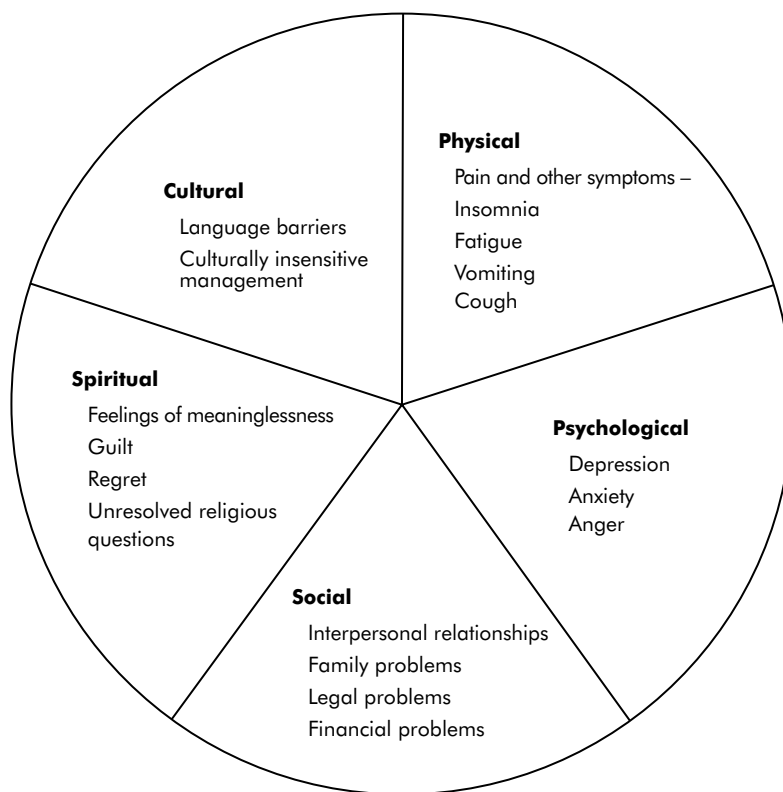
Physical pain must be controlled before other problems can be addressed and treated. Pain can be caused by or aggravated by psychosocial concerns which must also be addressed before optimal pain control can be achieved.

Types of Pain

Good pain control requires accurate and detailed assessment of every different pain experienced. Many patients with terminal illness have more than one pain, and each pain requires accurate assessment. Pain control requires knowledge of the different types of pain. In palliative care, where a lot of pain is chronic in nature, a different therapeutic approach is followed compared to the control of acute pain (see Table 4.2: Acute vs. Chronic Pain).

Determining the type of pain is important as different types of pain respond to different treatments. Pain can be classified according to whether intact nerves are stimulated, nerve cells have been damaged, or the basis is purely psychological (see Figure 4.2):

Figure 4.1: The Concept of Total Pain

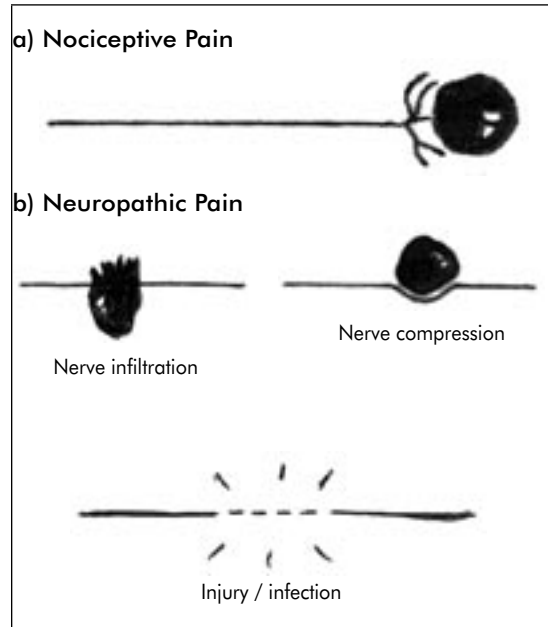


Source: Adapted to the South African setting from Cecily Saunders' concept of total pain (Saunders, 1984).

Table 4.2: Acute vs. Chronic Pain

Acute Pain	Chronic Pain
Usually due to definable acute injury or illness	Results from a chronic pathological process
Well defined onset	Gradual or ill-defined onset
Duration limited to days/weeks. Transient and foreseeable end or clear means of relief. Predictable.	Continues unabated for months/years and may become progressively more severe. Unpredictable.
Accompanied by clinical signs of sympathetic over-activity, e.g. <ul style="list-style-type: none"> - sweating - tachycardia - tachypnoea - pupil dilation 'obviously in pain'	No sympathetic over-activity, patients frequently labelled as 'not looking like somebody in pain'
Accompanied by anxiety	Patient depressed, withdrawn, and other psychological changes
Treatment is directed at the acute illness or injury, with or without the use of short-term analgesics. 'PRN' (as required) or once off analgesia is acceptable. Analgesia often administered intra-muscularly or intravenously.	Treatment of underlying disease where possible. Regular use of analgesics to suppress pain and prevent recurrence. Psychosocial supportive care. 'PRN' medications are ineffective. Oral analgesia is the route of choice.
A 'positive' pain in that it has meaning, draws attention to injury or illness, is protective	Has no meaning, serves no useful purpose and so a patient should never be allowed to suffer with chronic pain

Figure 4.2: Sources of Pain



Source: Debbie Norval.

Nociceptive Pain

- Nociceptive pain is produced by stimulation of specific sensory receptors called nociceptors (or pain receptors) in the tissues. In nociceptive pain, the nerve pathways are normal and intact. Nociceptors are found in the viscera and somatic structures.
- Nociceptive pain may be well-localised (common in somatic pain, from skin, tendons, or ligaments) or more diffuse (common in visceral pain, e.g., cardiac or liver capsule pain), and may be sharp, dull, aching, gnawing, throbbing, constant, or spasmodic, with varying intensity. Visceral pain may be referred to cutaneous sites.
- Nociceptive pain responds well to opioid analgesics.

Neuropathic Pain

- Neuropathic pain is caused by damage to the central or peripheral nervous system. Neuropathic pain can be caused by injury or compression or infiltration of a nerve; examples include post herpetic neuralgia or sciatic pain. Injured nerves react abnormally to stimuli or discharge spontaneously. They become hyperexcitable.
- Often neuropathic pain is described as a burning, tingling, or stinging sensation or a shooting electric shock-like sensation — ‘pins and needles’.
- Neuropathic pain is less sensitive to the opioid analgesics and will require adjuvant treatment in addition to analgesics.

Psychogenic Pain

- This is pain for which there is no physical basis. There is also evidence of psychopathology. Psychogenic pain will not respond to analgesics.

Physical Causes of Pain in Palliative Care

In palliative care there are many different possible causes of pain. It is important to establish the cause of pain, as therapy should be directed at the cause wherever possible (see Table 4.3).

Table 4.3: Physical Causes of Pain

	Cause	Example
1.	Pain due to HIV itself	HIV encephalopathy HIV neuropathy HIV myelopathy HIV myopathy
2.	Pain related to the consequences of immunosuppression, opportunistic infections, and tumours	Oral pain caused by Kaposi's sarcoma Genital pain caused by herpes infection Headache caused by cryptococcal meningitis Aphthous ulceration
3.	Pain related to treatment	Antiretrovirals Antivirals Antifungals PCP prophylaxis Chemotherapy (vincristine) Radiation Surgery Procedures (bronchoscopy, biopsies)
4.	Pain related to general debilitating disease	Pressure sores Constipation causing abdominal cramps Immobility causing muscle and joint pain Diffuse skin pain
5.	Pain caused by concurrent disorder	Arthritis Ischaemic heart disease

Assessment

Pain Assessment

A comprehensive clinical assessment is fundamental to successful pain management.

How questions are asked is important:

Ask the patient to describe the pain in his or her own words.

Assess each pain separately. Many patients have two to three different pains.

Assess the impact of the pain on sleep, mobility, and function.

Supplement this information by specific questions to define the exact nature of the pain.

Ask what the pain means to the patient.

Pain is always subjective, so believe the patient!

Pain is what the patient says hurts.

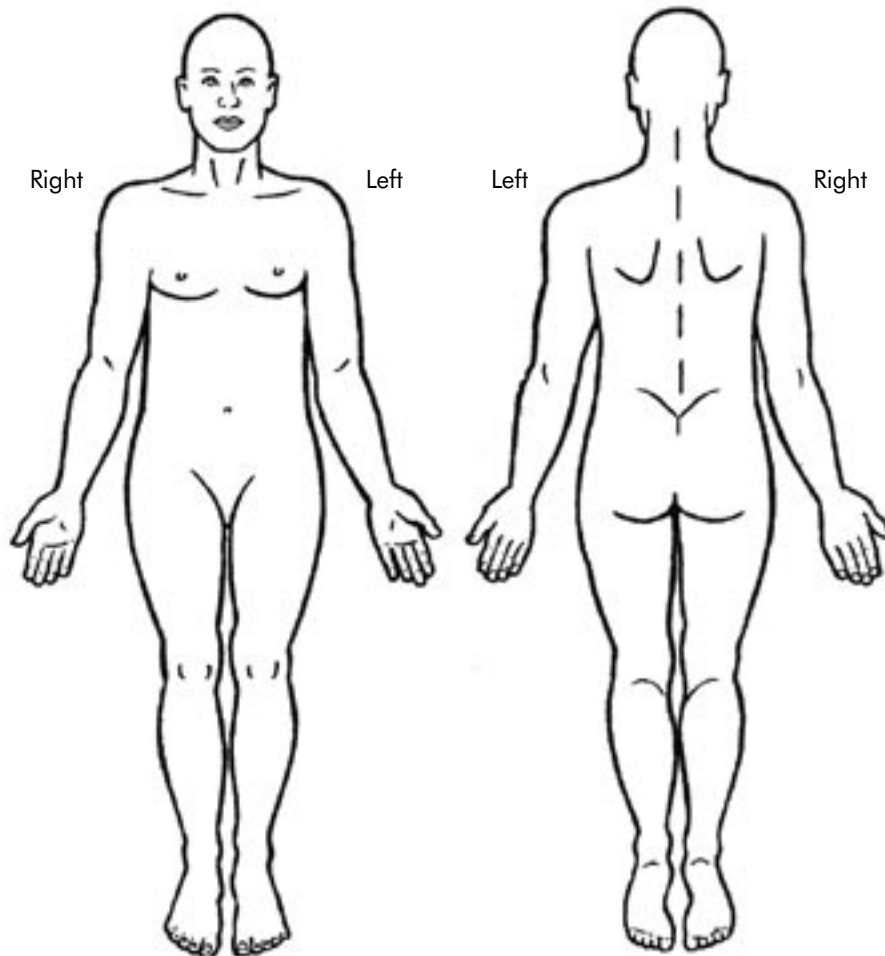
The *PQRST of Pain* is a good tool for organising an assessment (see Table 4.4).

Table 4.4: The 'P Q R S T' of Pain

P	Precipitating and palliating (relieving) factors
Q	Quality of pain (e.g. 'burning, stabbing, throbbing, aching, stinging')
R	Radiation of pain
S	Site (document on body diagram) Severity (document on pain assessment scale)
T	Timing (periodicity) Treatment (the effect of current and previous medications)

To document the site of pain it is helpful to draw the pain on a body diagram (see Figure 4.3: The Body Diagram).

Figure 4.3: The Body Diagram



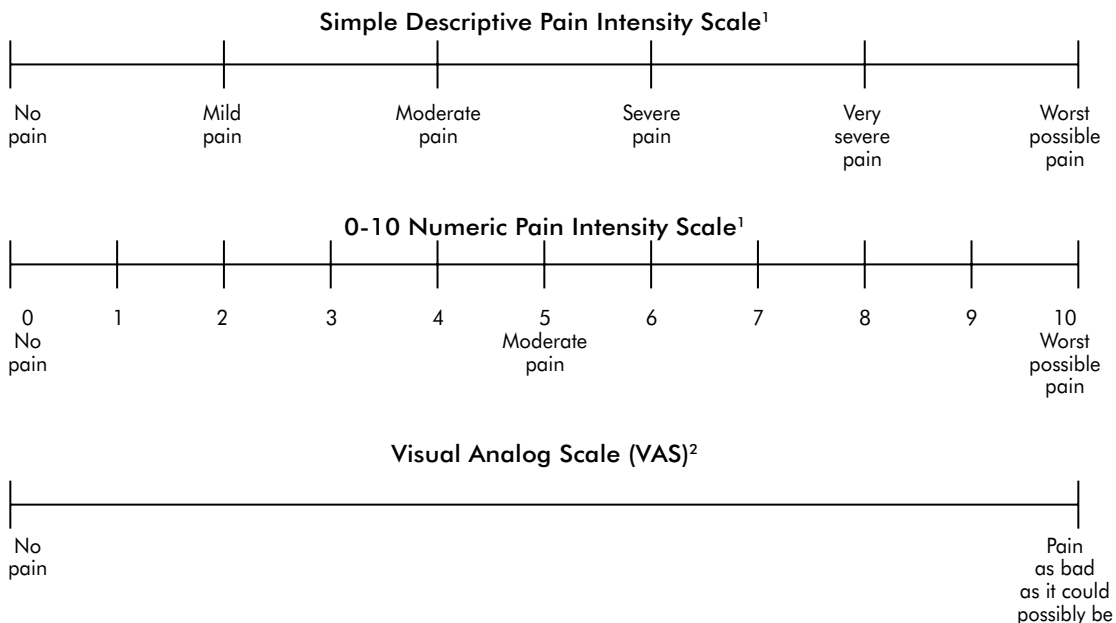
Pain Measurement

Because pain is subjective, an objective measurement of pain is not possible. However, pain rating scales are simple techniques to follow the course of a patient's pain and the effect of treatment and are particularly useful in managing difficult pain.

The most commonly used pain rating scales are the Visual analogue scale and the Numerical rating scale (see Figure 4.4) as well as the Wong-Baker Faces for Children Scale (see Figure 4.5).

Pain rating scales are the most useful tools to determine the patient's response to treatment and are an effective and practical way for HCWs to demonstrate concern about a patient's pain.

Figure 4.4: Pain Intensity Scales
Visual Analogue and Numerical Pain Rating Scales



¹ If used as a graphic rating scale, a 10-cm baseline is recommended.

² A 10-cm baseline is recommended for VAS scales.

Source: AHCPR, 1992.

Figure 4.5: Pain Faces Scale
Wong-Baker FACES Pain Rating Scale



Explain to the person that each face is for a person who feels happy because he has no pain (hurt) or sad because he has some or a lot of pain. Face 0 is very happy because he doesn't hurt at all. Face 2 hurts just a little bit. Face 4 hurts a little more. Face 6 hurts even more. Face 10 hurts as much as you can imagine, although you don't have to be crying to feel this bad. Ask the person to choose the face that best describes how he is feeling.

Rating scale is recommended for persons age 3 and older.

Source: Wong DL, Hockenberry-Eaton M, Wilson D, Winkelstein ML, Schwartz P. *Wong's Essentials of Paediatric Nursing, 6th ed.* St. Louis: Mosby, Inc., 2001. Copyrighted by Mosby, Inc. Reprinted by permission.

Management

Treating Reversible Causes

Pain is often reduced or eliminated when opportunistic infections are treated and when ART is initiated in patients with low CD4 counts.

Non-Pharmacological Pain Management

Psychological and social and spiritual factors can play an important role in the aggravation or relief of pain. Assessing psychosocial and spiritual issues in a patient with chronic pain requires the approach of an interdisciplinary team.

Psychological Distress

Psychological distress related to chronic pain often manifests as depression or anxiety. However distress associated with chronic pain may present as anger, frustration, hopelessness, helplessness, denial, grief, sadness, or withdrawal. Management should be directed at facilitating the patient's adaptive and coping mechanisms (see Chapter 14: Communicating with Patients and Their Families, Chapter 16: Spiritual and Cultural Care, 17: Loss, Grief, and Bereavement; and 18: Complementary Care).

Psychosocial support of a patient with chronic pain could have a profound effect on pain control and on the patient's quality of life (Doyle, 2004).

Psychological therapy for pain includes:

- Psychosocial support and counselling
- Support groups
- Relaxation therapy
- Distraction therapy
- Meditation
- Coping skills training

If available, consider the following:

- Hypnosis
- Psychotherapy or cognitive behavioural therapy

The rationale for explaining the pain to the patient is that there is often a significant emotional component to the patient's distress. Patients struggle with chronic pain as it is difficult to understand and accept, is seen as a useless, meaningless pain, and often hasn't responded well to treatment thus far.

- Understanding the cause of the pain will help build the patient's confidence.
- Provide realistic expectations (e.g., pain relief will be gradual) in steps, starting with a good night's sleep. This will build trust and avoid disappointment and later noncompliance.
- For patients with neuropathic pain, explain that pain, especially nerve pain, is difficult to treat and may need several different analgesic strategies, and that full response to treatment may take several days or weeks.
- Describe the different drugs and why they are used. Patients need to know why they are taking 'epilepsy' and 'depression' medication for pain!

Social Factors

Unresolved social problems can aggravate pain, whereas recognition and management of social issues can greatly facilitate pain control. This includes supportive counselling, practical assistance such as the provision of aids for daily living, and accessing community resources and services. Financial and legal problems should be sensitively managed (see Chapter 24: Financial and Legal Issues).

Sensitivity to the different cultural and ethnic backgrounds will help facilitate pain control. Patients of differing cultural backgrounds vary greatly in their response to pain, and HCWs should be nonjudgemental in their assessment of pain. Language barriers should be overcome as far as possible with the use of interpreters. A sensitive approach to culture, ethnicity, and language will prevent aggravation of pain and will help reduce emotional distress.

Spiritual and Religious Concerns

Spiritual and existential distress, which may manifest in physical problems, are an important source of clinical suffering and can aggravate and even cause pain. Recognition and successful management of spiritual problems is an important part of pain control (see Chapter 16: Spiritual and Cultural Care). Pain unresponsive to appropriate therapy should alert the palliative care professional to the possibility of unrecognised spiritual or existential problems (Doyle, 2004).

Mechanical Therapies

Therapies that support or manipulate the body can assist in the prevention or management of pain. These include:

- Massage (see Chapter 18: Complementary Care)
- Exercise (active and passive)

If available, consider the following:

- Manipulation (e.g., by chiropractors and physiotherapists)
- Orthopaedic devices (braces and supporting devices)
- Mobility aids (e.g., crutches, walking frames)
- Immobilisation

Other Non-Pharmacological Measures

A wide range of other interventions can alleviate or manage pain.

If available, consider the following:

- Trans-cutaneous electrical nerve stimulation (TENS)
- Acupuncture
- Topical counter-irritants
- Heat therapy, including ultrasound
- Surgery (e.g., for orthopaedic complications and visceral obstruction)
- Radiotherapy: Local pain due to tumour infiltration usually responds to local radiotherapy, irrespective of the histological type, tissue origin of tumour, or whether the tumour is termed radio-resistant. Palliative radiotherapy should employ the minimum dose of radiotherapy required to achieve the desired result given in the minimum number of treatment fractions. The doses used for the palliation of pain in patients with advanced disease are usually much less than the doses used to treat the cancer, and small but effective doses can often be delivered, even in previously treated areas.

Pharmacological Pain Management

General Principles of Treatment for Chronic Pain

The aims of treatment for chronic pain are:

- Prompt relief of pain
- Prevention of recurrence

It is important to discourage the acceptance of pain by HCWs as well as by patients and family members.

The WHO Pain Ladder (see Box 4.1), while not yet validated in AIDS, has been recommended by clinical authorities in the fields of pain management and AIDS (Schofferman, 1990; Griffin, 1994). In addition, clinical reports have appeared in recent literature describing successful application of the WHO Analgesic Ladder principles to pain management in AIDS, with particular emphasis on the use of opioids (Anand, 1994; Kimball, 1996; Newshan, 2001; Patt, 1993).

Chapter 4: Pain Management

The WHO guidelines for pain management include principles guiding route, timing, and dose: By the mouth, By the clock, and By the ladder.

By the mouth

- The oral route is best for the management of chronic pain. Oral medications should only be abandoned if the patient is unable to take or retain them.
- The intramuscular and intravenous routes are seldom used for long-term pain control. There are many other less invasive alternatives when a patient is no longer able to take oral medication such as the subcutaneous, buccal, sublingual, transdermal, and rectal routes.

By the clock

- Analgesics should be given according to the clock (i.e., at regular intervals).
- Analgesics are given according to a strict schedule determined by the duration of action, in order to prevent recurrence of pain.
- Analgesics for chronic pain should never be given 'PRN' (as required).
- It is important to give the next dose before recurrence of pain.
- If pain is allowed to resurface, higher doses of analgesics will be needed to suppress the pain and it will subsequently be more difficult to control.
- A patient on a strict regular schedule of analgesia will also need to have available a breakthrough dose for any episodes of breakthrough pain.

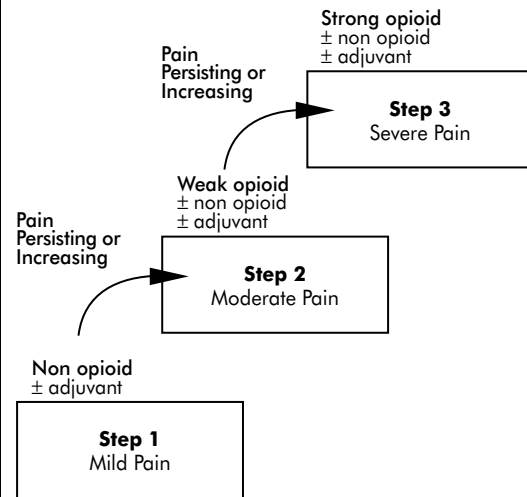
By the ladder

- The choice of analgesic should be guided by the WHO three-step analgesic ladder.
- The three steps of the ladder represent mild, moderate, and severe pain.
- Patients are usually commenced on Step 1 analgesics. If the Step 1 drugs do not produce adequate analgesia, treatment is escalated in an orderly manner to Step 2 and then to Step 3. If a weak opioid ceases to be effective it is important not to switch to another weak opioid on Step 2: switch to Step 3.

- A combination of a non-opioid and an opioid drug is effective in that the different drugs have different mechanisms of action and they potentiate each other's actions. It is often necessary and beneficial to continue with Step 1 analgesics even when a patient is on Step 3.
- Do not use Step 2 and Step 3 analgesics together. Weak opioids should not be combined with strong opioids. These drugs bind to the same receptors and Step 2 opioids will interfere with the efficacy of Step 3 opioids.

Box 4.1:

The WHO Pain Ladder



The WHO Three-Step Analgesic Ladder

- Step 1** Non opioid (e.g., paracetamol, aspirin) ± adjuvant (e.g., antidepressant)
 If pain is not controlled on Step 1 analgesics, move to Step 2 by adding a weak opioid:
- Step 2** Opioid for mild to moderate pain (e.g., codeine) ± non opioid ± adjuvant
 If an opioid for mild to moderate pain has been used to a maximum dose and the patient still has pain, then move to Step 3 by changing to a strong opioid:
- Step 3** Strong opioid (e.g., morphine) ± non opioid ± adjuvant

Source: WHO, 1986. Reprinted with permission.

Other considerations in analgesic use

- Give medication in the dose that is required for the individual patient.
- The correct dose is the dose that gives relief of pain.
- There is a maximum dose for most commonly used analgesics. However, morphine has no ceiling dose. Starting with a low dose, it is prescribed incrementally, until pain relief is obtained. The correct dose of morphine is, therefore, the dose that relieves pain.
- The choice of analgesic is determined by the severity, site, and type of pain:
 - Step 1: paracetamol
aspirin
 - Step 2: codeine
paracetamol-codeine combinations
If available: dextropropoxyphene
 - Step 3: morphine
morphine sulphate injectable
mist morphine
If available: slow release morphine or fentanyl (patches)

Morphine Administration*Guidelines for starting morphine*

Start with quick-acting oral morphine solution and give orally as long as possible.

- Starting dose: Always consider patient's age and general condition.
 - Usual adult starting dose: 10–20 mg, 4 hourly
 - Starting dose for elderly or cachexic patients: 2.5–5 mg, 4 hourly
- Give regularly: 4 hourly (e.g., 06.00, 10.00, 14.00, 18.00, 22.00, 02.00 [if patient wakes]).
- Titrate dose of oral morphine solution against analgesic response, e.g., 5 mg → 10 mg → 15 mg → 20 mg → 30 mg → 45 mg → 60 mg → 90/100 mg → 120/160 mg given as 4-hourly doses.
- Titrate in 30–50% dose increments. Increments of less than 33% are not effective.
- Explain the side effects that the patient may experience.
 - Co-prescribe laxatives and give a prescription for an antiemetic for 1 week (40% of patients will experience nausea which will wear off within a week).
 - Explain that drowsiness will wear off in a few days.
 - Ongoing drowsiness is a sign that the dose is too high.
- Address breakthrough pain, prescribing a breakthrough dose at this time (see below).

Managing Breakthrough Pain

Breakthrough pain is that which is experienced before the next dose of morphine is due to be taken.

- Always give instructions for dealing with breakthrough pain and ensure that a qualified person can be contacted to give ongoing support.
- Manage breakthrough pain by allowing an additional *half to full* dose as needed *in addition* to regular four-hourly dose of oral morphine solution.
- Give the regular prescribed dose at the normal time even if this is one hr after a full breakthrough dose.
- If breakthrough pain is frequent, the current four-hourly dose of oral morphine solution should be increased by adding the total milligrams required in 24 hours, and dividing this by six to establish a new four-hourly requirement.
- Having breakthrough doses of oral morphine solution available is reassuring for the patient. It helps the patient feel in control and avoids despair if the analgesic programme is ineffective.
- If a patient is taking slow-release morphine and develops breakthrough pain, use morphine oral solution as a breakthrough dose to bring the pain under control. Use 50% to 100% of the dose of oral morphine solution being taken before converting to the slow release tablets.

Side Effects of Morphine

The common side effects of morphine need to be anticipated and prevented.

Constipation is a long-lasting side effect of the opioid drugs and needs to be prevented by the use of stool softeners and ongoing laxatives. Always prescribe a laxative concurrently (except in a patient with AIDS who has persistent diarrhoea). Examples: lactulose 20 mL once or twice daily plus senna 1–2 tablets daily.

Nausea is a transient side effect lasting 7 to 10 days. Prevent with concomitant administration of an antiemetic for approximately one week, e.g. haloperidol 2.5–5 mg PO noctè (before the very first dose of morphine give 2.5–5 mg haloperidol PO stat).

Drowsiness is also transient and resolves after a few days. Explain to patients and their carers that the drowsiness will wear off. Continued sedation is uncommon in patients with moderate to severe pain because pain is the natural antagonist to the opioids. Many patients will have experienced significant insomnia for a long time due to their pain. It may be useful to negotiate a ‘catch-up’ period of drowsiness with the expectation of effective pain control and clear cognitive function within 3–4 days.

Sedation: Patients on a stable dose of morphine should have normal cognitive function. If a patient continues to be over-sedated, reduce the dose of morphine and consider the adjuvant analgesics.

If available, slow-release morphine

Slow-release morphine should be used only once pain is controlled.

- Where available, consider changing to slow-release morphine for convenient twice-daily administration. Divide total 24-hour oral morphine solution dose by two.

For example: Mrs. Smith is on a dose of morphine syrup 10 mg 4 hourly. She would like to convert to slow-release morphine tablets. Calculation: Total daily dose of oral morphine solution would be

$$\begin{aligned} 10 \text{ mg} \times 6 &= 60 \text{ mg} \\ 60 \text{ mg} \div 2 &= 30 \text{ mg} \\ \text{therefore give slow-release morphine} \\ 30 \text{ mg } 2 \text{ times/day} \end{aligned}$$

- If prescribing fentanyl patches, these should be started once a patient’s pain is under control on morphine, and once a patient’s morphine requirement is well known
- Double Dose at Bedtime: It can be suggested that taking a double dose at bedtime (i.e., 22.00 hours) may allow the patient to sleep through the night undisturbed by pain. If the patient wakes in the early hours anyway, it is permissible to take a dose of morphine syrup (left measured at the bedside).

Box 4.2:**Myths About Morphine**

Ignorance surrounding the use of morphine results in patients suffering unnecessarily; effective analgesia is often withheld because of misconceptions. The myths about morphine include that it is addictive, leads to morphine tolerance and drowsiness, causes respiratory depression, and hastens death.

Fear of Addiction

Differentiate addiction (or psychological dependence) from physical dependence, which is a normal physiological response to chronic opioid therapy.

Physical dependence: Physical dependence is a normal physiological response to chronic opioid therapy which causes withdrawal symptoms if the drug is abruptly stopped or an antagonist administered. Physical dependence is not unique to opioid drugs and occurs with many other medications such as corticosteroids, antidepressants, and certain benzodiazepines. Unlike with addiction, patients can be easily taken off drugs on which they become physically dependent.

- Patients whose pain has been relieved by ART or other treatment should have their opioid reduced by about 25% per day.
- Reassure patients that physical dependence does not prevent withdrawal of the medication if their pain has been relieved by other means, providing they are weaned from the drug slowly.

Psychological dependence and addiction: Addiction to a drug describes a condition characterised by abnormal behavioural and other responses, which always include a compulsion to take the drug to experience its psychic effects.

- Psychological drug dependence is a pathological, psychological response and not physiological.
- Several large studies of patients with cancer and pain have shown that with the exception of a few patients with a past history of psychiatric disturbance or drug dependence, these patients do not become psychologically dependent.

Tolerance

Tolerance, the need for increasing doses of morphine over time, is uncommon and usually relates to disease progression, as shown through experience in cancer patients with chronic pain. Misinformed concern about tolerance is not a reason for 'saving up' the use of opioids until the terminal phase.

- Reassure patients that there is adequate scope to treat more severe pain if it occurs.
- There is no maximum dose of morphine!

Respiratory Depression

Respiratory depression is very uncommon except in opioid-naïve patients commenced on parenteral therapy. Respiratory depression will not occur if the right drug is given, at the right time, by the right route; and it usually only occurs in overdose. If used properly, morphine should not cause respiratory depression.

- Many patients are managed on high doses of morphine to control their pain without compromise of respiratory function.
- In palliative care, low doses of morphine can safely be used in patients with end-stage chronic obstructive pulmonary disease (COPD), lung cancer, and in patients with severe dyspnoea.

Fear of Hastening of Death

Morphine can be used for many months or years, and if correctly used is compatible with a normal lifestyle.

Morphine can only result in death through respiratory depression, which does not occur if it is given correctly (i.e., orally if possible), regularly, at the correct dose for control of an individual patient's pain, and using the principles of the WHO analgesic ladder.

The Adjuvant Analgesics

The adjuvant analgesics are not analgesics in the true pharmacological sense, but may contribute significantly to pain relief whether used alone or in combination with the analgesics on the WHO 3-Step Analgesic Pain Ladder.

Adjuvant analgesics are of particular use in pain that is only partially sensitive to opioids.

- Neuropathic pain, bone pain, and pain associated with inflammation and sepsis are less sensitive to opioids.
- Pain associated with smooth or skeletal muscle spasm does not respond to opioids.
- Pain related to anxiety also benefits from adjuvant analgesics.

Adjuvant analgesics are important in the management of HIV-related pain (see Table 4.5). Adjuvant analgesic drugs are used to enhance the analgesic effects of opioids, treat concurrent symptoms that exacerbate pain, and provide independent analgesia.

Table 4.5: Examples of Adjuvant Analgesics

Adjuvant Analgesics	Example	Use
Corticosteroids	Dexamethasone Prednisolone	Bone pain Neuropathic pain Headache due to raised intracranial pressure Pain associated with oedema and inflammation
Antidepressants	Amitriptyline	Neuropathic pain
Anticonvulsants	Carbamazepine Gabapentin	Neuropathic pain
Antispasmodics	Hyoscine butylbromide	Smooth muscle spasm (e.g., colicky abdominal pain, renal colic)
Muscle relaxants	Benzodiazepine, (e.g., Diazepam)	Skeletal muscle spasm Tension headache
Anxiolytics	Benzodiazepine (e.g., Diazepam, Alprazolam)	Anxiety-related pain
Bisphosphonates	Disodium pamidronate Zoledronic acid	Bone pain
NMDA receptor antagonist	Ketamine	Severe neuropathic pain or other pain unresponsive to morphine and other standard therapies

Non-steroidal Anti-inflammatory Drugs (NSAIDs)

Using NSAIDs in patients with AIDS requires monitoring for toxicity and adverse effects, especially in people who are cachectic, wasted and hypoalbuminaemic. Patients with HIV/AIDS are frequently hypovolaemic, on concurrent nephrotoxic drugs, and experiencing HIV nephropathy, and so are at increased risk for renal toxicity related to NSAIDs. The antipyretic effects of the NSAIDs may also interfere with early detection of infection in patients with AIDS.

Major adverse effects associated with NSAIDs include the following:

- Gastric ulceration
- Renal failure
- Hepatic dysfunction
- Bleeding

Patients using the NSAIDs should be informed about these side effects and taught to check their stool weekly.

Antidepressants

Antidepressants with mixed actions (both serotonergic and noradrenergic) are most effective in the control of nerve pain. For example:

Amitriptyline 10–150 mg nocté (start with low dose and slowly increase to maximum doses)

Tricyclic antidepressants block the re-uptake of monoamines (serotonin and noradrenalin) thereby increasing activity in endogenous pain-modulating pathways. These pathways descend from the brain stem, use noradrenaline and serotonin as neurotransmitters, and have an inhibitory effect on the dorsal horn. This pain is modulated in the spinal cord.

When tricyclics are used together with an opioid, the resultant interaction leads to higher opioid concentrations and enhancement of opioid analgesia. The analgesic effect of tricyclics is independent of mood alteration as they have a separate analgesic action; however, effective treatment of concurrent depression will also contribute to total pain control.

If an opioid alone is not effective, it is appropriate to have a trial of antidepressant therapy. In obvious cases of neuropathic pain (e.g., post-herpetic neuralgia), prescribe an antidepressant before using opioids (see section on management of neuropathic pain below).

Anticonvulsant Drugs

All anticonvulsants work in different ways but the basic rationale for their use is to stabilise neuronal membranes. This diminishes abnormal neuronal hyper-excitability and suppresses spontaneous and paroxysmal discharges.

The most commonly used are carbamazepine, gabapentin, and sodium valproate. Phenytoin may also be used in the absence of the above medications.

carbamazepine start 100 mg 2 times/day,
increase to 1,600 mg/day

valproate 200–1,200 mg/day

phenytoin 100 mg 2 or 3 times/day

If available, consider the following:

gabapentin 100 mg 3 times/day, increase
up to 3,600 mg daily

A trial of anticonvulsant usually starts with low doses which are slowly titrated upwards.

Anticonvulsants are used as co-analgesics with morphine and are usually added after a trial of tricyclic therapy has not sufficiently relieved pain or if there is residual stabbing pain.

Although mostly used as a second line drug after tricyclics, anticonvulsants may also be started as a first line co-analgesic with morphine. Phenytoin and carbamazepine should be used with caution as they cause liver enzyme induction and rapid metabolism of other drugs metabolised in the liver.

Corticosteroids

Corticosteroid drugs have analgesic potential in a variety of chronic pain syndromes, including neuropathic pains and pain syndromes resulting from inflammatory processes (Portenoy, 1998). Like other adjuvant analgesics, corticosteroids are usually added to an opioid regimen.

There is understandable concern about the use of corticosteroids in a patient with HIV due to potential acceleration of OIs in an immunocompromised patient (for more discussion on this, see Box 5.1 in Chapter 5: Constitutional Symptoms). However, there is value in the use of steroids in the palliative management of:

- Severe aphthous ulceration
- Neuropathic pain
- Musculoskeletal pain
- Headache from raised intracranial pressure

Patients with *Pneumocystis carinii* pneumonia who are hypoxic and patients with TB meningitis or TB pericarditis respond to steroids.

In patients with advanced disease, these drugs may also improve appetite, decrease nausea and malaise, and improve the overall quality of life. Adverse effects include neuropsychiatric syndromes, gastrointestinal disturbances, and immunosuppression.

To treat raised intracranial pressure, start with a large dose:

dexamethasone 24 mg/day
reduce by 2 mg daily to lowest
effective maintenance dose

In other situations, doses are often in the low range and have minimal, if any, adverse effects:

dexamethasone 2–4 mg/day

Patients often need a combination of a non-opioid with an opioid (weak or strong) and an adjuvant analgesic. Adjuvant analgesics may be used alone or in combination with any step of the 3-step ladder.

NMDA Receptor Blockers

The NMDA receptor is involved in the sensitisation of central neurons following injury. This results in the development of the ‘wind-up’ phenomenon: central nervous system changes that underlie chronic neuropathic pain. NMDA receptor inhibition therefore results in a ‘wind down’ phenomenon and control of neuropathic pain.

There is also synergistic effect between ketamine and opiates, as ketamine restores the opioid sensitivity of relatively opioid-resistant pain. Ketamine has been shown to have analgesic effects at low doses. A trial of ketamine is appropriate in patients with severe refractory neuropathic pain.

Special Issues

Managing Neuropathic Pain

Neuropathic pain results from dysfunction or damage to the peripheral or central nervous system. It may also be associated with over-activity of the sympathetic nervous system.

Nerve pains are often complex and difficult to treat and involve a wide range of different approaches. See Box 4.3: Summary of Treatment of Neuropathic Pain.

Box 4.3:

Summary of Treatment of Neuropathic Pain

Management of neuropathic pain requires analgesic plus 2–3 adjuvant analgesics:

- WHO step 1/2/3 analgesic
- + Antidepressant (amitriptyline starting at 10–25 mg nocté) or Anticonvulsant (carbamazepine 100 mg 2 times/day or gabapentin 100 mg 3 times/day)
- Vitamin Bco
- NSAID for 5–10 day trial

Treating Reversible Causes

If available, consider the following:

ART: When appropriate, ART will improve the pain of peripheral neuropathy, although some ARV drugs may cause neuropathy.

Radiotherapy is effective in treating Kaposi's sarcoma.

Pharmacological Symptom Management

WHO Step 1, 2, or 3 analgesics

Opioid sensitivity is a spectrum. Nociceptive pains are more fully opioid sensitive, whereas neuropathic pains tend to be less opioid sensitive. However, nerve pains respond partially if not fully to opioids and opioids should always be the first step in the management of nerve pain.

Early nerve injury pain is initially transmitted in the normal pain nerve pathways and this might explain the response to opioids.

Nerve compression pain is due to stimulation of the nervi nervorum which is nociceptive and thus responds to opioids.

Adjuvant Analgesics

Antidepressants and anticonvulsants are useful in neuropathic pain (see above for drugs and doses). NSAIDs may also be helpful (try ibuprofen 400 mg 3 times/day for a 5-day trial). A second- or third-line choice would be an NMDA receptor Blocker such as ketamine.

Managing Pain in People With Substance Abuse Problems

As in any patient, effective pain management in the substance-using patient involves multiple modalities and usually requires contributions from all members of the palliative care team (O'Neill, 2003). See Chapter 23: Special Populations for more on caring for people with substance abuse problems.

HCWs must be aware, however, that in a patient who has developed tolerance to opioids, strong opioids (Step 3) may be needed sooner, at greater frequency, and at higher doses, than would otherwise be expected.

Provider experience: It is better for HCWs to work and be comfortable with one or two drugs in each class (doses, pharmacokinetics, conversions, side effects, interactions etc.) than to have only a superficial knowledge of all of them. As a general rule, it is best to push lower level treatment to the maximum before advancing to the next level. In cases of moderate to severe pain, therapy can rightly begin at step two.

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Suggested Resources

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