USING MORPHINE TO MANAGE HIV/AIDS PAIN: A FACT BOOK FOR ZAMBIA

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August 2008 (printed)

This publication was produced for review by the United States Agency for International Development. It was prepared by the SHARe project.

SHARe
Support to the HIV/AIDS response in Zambia

Recommended Citation: SHARe Project. January 2008. *Using Morphine to Manage HIV/AIDS Pain: A Fact Book for Zambia.* Bethesda, MD: SHARe project, Abt Associates Inc.

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Contract/Project No.: 690-A00-04-00250-00

Submitted to: Ngaitila Phiri, CTO
United States Agency for International Development/Zambia

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CONTENTS

ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
APCA	African Palliative Care Association
CMS	Central Medical Store
DDA	Dangerous Drugs Act
DEC	Drug Enforcement Commission
HIV	Human Immunodeficiency Virus
INCB	International Narcotics Control Board
MST	Morphine Sustained-release Tablets
NAC	National AIDS Council
NDP	National Drug Policy
NSAID	Non-steroidal Anti-inflammatory Drug
PCAZ	Palliative Care Association of Zambia
PRA	Pharmaceutical Regulatory Authority
RN	Registered Nurse
SHARe	Support to the HIV/AIDS Response in Zambia
UTH	University Teaching Hospital
WHO	World Health Organisation

DEFINITIONS

Addiction (psychological dependence): Pattern of compulsive drug use characterised by a continued craving for an opioid, such as morphine, and the need to use the opioid for effects other than pain relief. The World Health Organisation (WHO) no longer uses the term; the preferred terminology is "dependence syndrome".

Adjuvant analgesic drug: A drug that is not a primary analgesic but that research has shown to have independent or additive analgesic properties.

Breakthrough pain: Transitory exacerbation of pain experienced by a patient who has relatively stable and adequately controlled baseline pain.

Epidural: Situated within the spinal canal, on or outside the dura mater (tough membrane surrounding the spinal cord); synonyms are "extradural" and "peridural".

Iatrogenic: Induced inadvertently by the medical treatment or procedures of a physician.

Lancinating: Type of pain characterised by piercing or stabbing sensations.

Music therapy: Music is used to alleviate pain in conjunction with pain medication, to elevate moods, sedate to allow sleep, and to lessen muscle tension for the purpose of relaxation, all of which improve patients' quality of life (American Music Theory Association, 2007).

Neuropathic pain: Type of pain experienced where there is a disturbance of function or pathologic change in a nerve, i.e. the pain pathway is not intact; in one nerve mononeuropathy; in several nerves, if diffuse and bilateral, polyneuropathy.

Nociceptive pain: The process of pain transmission; usually relating to a receptive neuron for painful sensations. Nociceptive pain occurs in an intact pain pathway. It may be somatic, i.e., arising from musculo-skeletal tissues, or visceral, i.e. from internal organs such as intestines.

NSAID (non-steroidal anti- inflammatory drugs): These are aspirin-like drugs that reduce inflammation (and hence pain) arising from injured tissue, e.g. ibuprofen, diclophenac.

Opiate: A term used to describe drugs (natural or semi-synthetic) derived from the juice of the opium poppy plant.

Opiate receptor: Opiate-binding sites found throughout primary afferents and the neuraxis.

Opioid: A general term that includes natural/semi-synthetic and synthetic drugs, such as morphine, which produce their effects by attaching to opioid receptors in the central nervous system.

Opioid partial agonist: A compound that has an affinity for and stimulates physiologic activity at the same cell receptors as opioid agonists but that produces only a partial (i.e. submaximal) bodily response.

Pain: A subjective, unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

Physical dependence: Physiologic adaptation of the body to the presence of an opioid is required to maintain the same level of analgesia.

Pseudoaddiction: Pattern of drug-seeking behaviour of pain patients receiving inadequate pain management that can be mistaken for addiction.

Psychological dependence (addiction): Pattern of compulsive drug use characterised by a continued craving for an opioid and the need to use the opioid for effects other than pain relief.

Relaxation: A state of relative freedom from both anxiety and skeletal muscle tension.

Suffering: A state of severe distress associated with events that threaten the intactness of the person.

Tolerance: A common physiologic result of chronic opioid use; it means that a larger dose of the opioid is required to maintain the same level of analgesia.

TENS (transcutaneous electrical nerve simulator): An electronic device used to relieve pain (especially nerve pain) through production of electrical signals that stimulate nerves through unbroken skin.

FOREWORD

Pain management is central to palliative care, a branch of medicine that deals with the care of chronically ill patients such as those suffering from incurable illnesses like HIV and cancer. According to the World Health Organisation (WHO), palliative care is "... an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual." (WHO, 2002)

There are a number of potent and tested drugs that are used in the management of chronic pain. Morphine has, nevertheless, proved to be a drug of choice in pain management. It would, however, appear that the procurement, distribution, prescription, and dispensation of morphine are heavily controlled by both domestic and international laws. The result is that access to morphine by patients experiencing chronic pain is severely limited. Consequently, many patients needlessly endure chronic pain when this could be avoided if access to Morphine were not unduly restricted. Given the restricted nature of morphine, there are widespread fears of arrest by drug enforcement authorities, myths, misconceptions, including plain ignorance of accruable benefits from rational use of drug.

In order to contribute to addressing these and other related constraints, NAC has been working with its partners with a view to contributing to the creation of an enabling policy and regulatory environment for facilitated access to morphine for chronic pain management in HIV and AIDS and related life-threatening illnesses. These include Pharmaceutical Regulatory Authority (PRA), Medical

Council of Zambia (MCA), the USAID-funded Support to the HIV/AIDS response in Zambia (SHARe), Palliative Care Association of Zambia (PCAZ) and the African Palliative Care Association (APCA). This Fact Book on Morphine is one of the key outputs of the collaboration and work by NAC with these partners.

The Fact Book is meant to be a user-friendly pocket-size publication with the capacity to address facts, myths and misconceptions about morphine, what the law says about morphine and who can prescribe and/or dispense morphine. It is also meant to provide information in regard to how health providers can access morphine for their patients, which health facilities may access it, including its security, storage and logistics.

I wish to recommend this Fact Book to all authorized health facilities, legally-prescribed health providers and duly registered pharmacies in government and private health facilities.

Brig. Gen. Dr Brian Chituwo (Rtd) GCDS, MP
Minister of Health

ACKNOWLEDGEMENT

The compilation of this Fact Book on Morphine involved tireless and committed work several partners who brought to the table their skills and experiences in chronic pain management. The Support to the HIV/AIDS response in Zambia (SHARe) is highly indebted to all of them and particularly to the Ministry of Health (MoH), National AIDS Council (NAC), Pharmaceutical Regulatory Authority (PRA), Medical Council of Zambia (MCZ), Zambia Nurses Association (ZNA), Palliative Care Association of Zambia (PCAZ), and the African Palliative Care Association (APCA) who reviewed and printed this document..

Mukachilima Chikuba, MD, MPH
Chief of Party
Support to the HIV/AIDS Response in Zambia

1. INTRODUCTION

This Fact Book is a user-friendly reference on the role of morphine and other opioid analgesics in the management of severe pain. Pain management is central to palliative care, a branch of medicine that deals with the care of chronically ill people such as those suffering from incurable illnesses like HIV/AIDS and cancer. It is applicable beginning early in the course of illness, in conjunction with other therapies intended to prolong life (antiretroviral treatment, chemoradiation) and investigations needed to better understand and manage distressing clinical complications, through to the terminal stages of the illness.

Palliative Care

The World Health Organization defines palliative care as "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual."

(http://www.who/int/cancer/palliative/definition/en/)

In Zambia, physicians often prescribe weaker, less-controlled analgesics due in part to strict regulatory control of morphine but also because of the exaggerated fears and concerns about morphine addiction. As a result, pain in people living with HIV/AIDS (PLWHA) and cancer usually is not adequately controlled. Children suffer pain even more often than adults, because reluctance to give them morphine is greater.

The Fact Book collects into a readily accessible document the most relevant information from various sources. It is intended for use by a variety of people involved in the care of persons suffering from chronic pain:

- Health professionals – doctors, medical students, nurses, clinical officers, and pharmacists;
- Authorised health facility managers in government and private hospitals, clinics, and hospices;
- Members of the general public who are involved in patient care; and
- Policymakers who make policy and regulations for health care.

The Fact Book comprises both this longer guide and a pocket sheet on dosing and side effects of morphine that health professionals can carry for easy reference during rounds and consultations.

The rest of the guide contains chapters on what international and Zambian law says about prescribing and dispensing morphine, as well as institutional challenges to accessing morphine in Zambia; myths and misconceptions surrounding the use of morphine and its side effects; pain and steps to take in treating it; and procuring morphine. Annexes contain information on assessing pain; treating pain, in particular, with morphine; managing side effects of morphine; preparing morphine syrup; and additional pain control measures.

2. BACKGROUND

There are an estimated 1.6 million PLWHA in Zambia. The HIV prevalence rate is 16% among those in their most productive years (ages 15–49) (Joint United Nations Programme on HIV/AIDS, 2006), who have the potential to contribute to the country's development.

PLWHA experience pain with different causes and levels of severity from the point of diagnosis of HIV until death. It is estimated that 80% of PLWHA have severe pain toward the end of life.

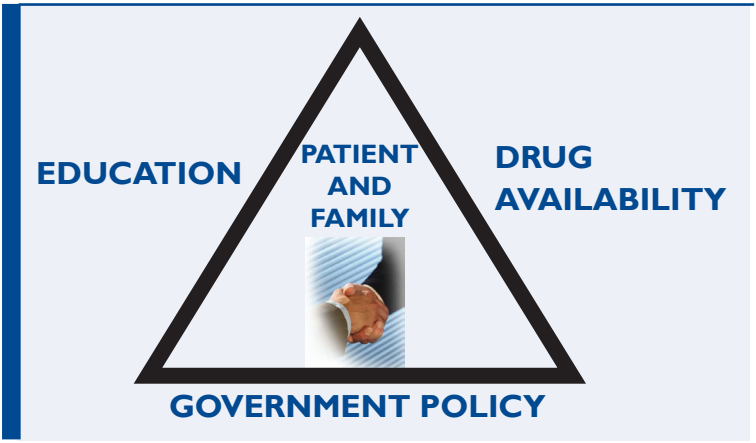
The World Health Organisation (WHO) advocates effective pain management, with palliative care, as "an essential component of a comprehensive HIV care package because of the variety of symptoms they (PLWHA) can experience such as pain, diarrhea, coughing, and shortness of breath, nausea, weakness, fatigue, fever, and confusion. Palliative care is an important means of relieving symptoms, including pain that results in undue suffering and frequent visits to the hospital or clinic, and improves an individual's ability to continue his or her activities of daily life" (www.euro.who.int/document/SHA/e90840_cahpter_3.pdf).

Palliative care services focus on the patient and the patient's family. Zambia has a three-part strategy to improve the pain management aspect of palliative care (Figure 1). The strategy's three components, as well as needs for each, are the following:

- Government policy: Review and harmonise existing laws and regulations to make pain relief a high priority in the health care system.

- Drug availability: Ensure the availability of morphine and other palliative care drugs.
- Education and training: Sensitise the public, policymakers, and regulators on pain relief and train health care professionals to manage pain using the WHO three-step analgesic ladder (see chapter 6).

FIGURE. 1. ZAMBIA'S THREE-PART STRATEGY TO IMPROVE PAIN MANAGEMENT



Source: Adapted from WHO, 1996.

3. POLICY AND REGULATORY ENVIRONMENT

3.1 INTERNATIONAL TREATIES AND CONVENTIONS ON CONTROLLED SUBSTANCES

Most countries have replaced legislation regarding "dangerous drugs", a term implying "poison", with legislation regarding "controlled substances" – narcotic drugs and psychotropic substances under international control.

Trade in and use of these drugs/substances is under the control of the International Narcotic Control Board (INCB), an independent quasi-judicial entity that implements United Nations drug conventions. The INCB works to ensure that identified drugs are available for medical and scientific uses and that their diversion from licit sources to illicit channels does not occur. To achieve this, countries are expected to act in accordance with the provisions of the 1961 Single Convention on Narcotic Drugs and the 1971 Convention on Psychotropic Drugs as amended by the 1988 protocol.

3.2 POLICY IN ZAMBIA

LEGISLATION AND POLICY

Each country or region that is party to the major international drug control treaties develops the domestic legislation and policy needed to effectively implement the treaties.

In Zambia, two pieces of legislation deal with licit and illicit trade in, and use of narcotic drugs and psychotropic substances:

- The Dangerous Drug Act (DDA) Chapter 95 (of 1967), implemented by the Pharmaceutical Regulatory Agency (PRA), which ensures that these drugs are available for legal, medical and scientific uses; and
- The Narcotic Drugs and Psychotropic Substances Act Chapter 96 (of 1993), administered by the Drug Enforcement Commission (DEC) to control illicit dealing in these drugs.
- The Government has additional policies regarding morphine:
- The National Drug Policy (NDP) recognises that morphine is crucial to manage pain in chronically and seriously ill patients.
- The NDP establishes that the Government must ensure the availability of morphine.
- The PRA is responsible for all aspects of licensing and registration, doing statistical reporting of morphine use and estimating future needs.
- There is no policy restricting the amount of morphine that a physician can prescribe or the duration of treatment although, in practice, morphine is usually dispensed for periods of two weeks, once the health care provider and patient have determined the appropriate dose.

REPORTING ON MORPHINE USE, ESTIMATING NEEDS

As noted in the preceding section, the PRA is responsible for reporting on morphine use. All permit holders and user institutions send quarterly reports on morphine and other opioid consumption to the PRA, which uses the statistics to prepare annual reports on usage and to estimate future drug needs. The PRA submits these reports and estimates to the INCB on behalf of the Ministry of Health. Based on these estimates, Zambia is granted a drug import allocation for the following year. If medical need exceeds the estimated amount in the course of the year, the Government can send a supplementary estimate of drug need to the INCB.

3.3 MAJOR CHALLENGES

Major challenges to the use of morphine for pain management in chronically ill patients can be grouped according to the three components of the palliative care strategy:

GOVERNMENT POLICY

- Application of the two laws relating to the use of morphine needs to be better coordinated.
- Specific regulation is needed to improve access to oral morphine for medical use.
- Health professionals must be made more cognizant of the legislation on the use of morphine and other opioid analgesics.

ADMINISTRATIVE AND LOGISTICAL ISSUES OF MORPHINE AVAILABILITY AND USE

Health facility level:

- Some facilities restrict prescribing of morphine to consulting physicians, although the law allows for any doctor to prescribe them.
- Bureaucratic procedures make some nurses reluctant to administer morphine, even when it is prescribed by doctors, for the following reasons:
  - Hospitals lock ward stocks of morphine in the DDA cupboard and it is difficult to access the drug – only the sister-in-charge has the keys to the cupboard. When she will be absent, she can delegate responsibility for the keys (and drug access) only to a registered nurse (RN).
  - The sister-in-charge/RN can open the DDA cupboard only in the presence of two other nurses, who must sign the DDA book as witnesses.

Who Can Prescribe and Dispense Morphine in Zambia?

Who can prescribe morphine?
Medical practitioner, dental surgeon, or veterinary surgeon.

Who can dispense or supply morphine?
Medical practitioner, dental surgeon, veterinary surgeon, pharmacist, government analyst, appointed inspector, midwife, nurse in charge of ward, surgical theatre or outpatient department, laboratory in-charge for research/instruction/education or any other person appointed at the discretion of the Permanent Secretary of the Ministry of Health.

(Zambia Dangerous Drug Act, Chapter 95)

- Used ampoules and empty medicine bottles (in the case of tablets) of DDA drugs must be accounted for and returned to the pharmacy with the necessary documentation by the responsible RN before the pharmacist can issue drugs to re-stock the ward.

- Drug procurement and availability is poorly coordinated:
  - Facilities fail to anticipate stock-outs.
  - Existing stocks of drugs are not consumed. Hospital morphine consumption records often show adequate amounts of morphine are available for medical needs, but patients who need morphine are not adequately supplied. Meanwhile morphine powder at the Central Medical Stores expires because there are few requisitions/prescriptions for its use.
  - Communication between user departments and pharmacies is poor; for example, the pharmacy may not issue timely updates on the types of opioid drugs available at any given time.
  - Very few facilities have health professionals who prepare and dispense morphine suspension/syrup.
- Most hospices are unaware of the procedures for accessing and dispensing opioids.

Government level:

- Lack of coordination among the various government agencies dealing with morphine procurement and use (DEC, PRA, customs, police, health facilities) limits the availability of the drug.

- Some opioid substances (for example, morphine powder) are currently packaged in lots that are too big for efficient use by smaller facilities such as hospices; the PRA should source the substances in smaller units.

EDUCATION AND TRAINING

Health care providers and administrators in Zambia need additional education and training in matters of morphine availability and use. Currently, there is:

- Lack of training in procurement procedures;
- Lack of emphasis on pain management in the training of health professionals; and
- Lack of awareness of the role of morphine in palliative care.

4. DISPELLING MYTHS AND MISCONCEPTIONS ABOUT MORPHINE USE

In Zambia, health care providers and patients alike have misconceptions about pain. They accept pain a part of illness that must be endured, and do not see it as a symptom that can and should be controlled with treatment. There also are misconceptions about the legality of prescribing morphine and side effects and other results of its use. These perceptions need to be changed – it is important for all to know that providing pain relief is possible, compassionate, and an important element of care.

Following are myths about the use of morphine that should be dispelled.

MYTH – IT IS ILLEGAL IN ZAMBIA TO PRESCRIBE MORPHINE FOR MEDICAL USE.

As seen in the preceding chapter, prescribing morphine to manage pain in patients with chronic and/or terminal conditions is legal in Zambia, regulated both by international conventions and domestic legislation and policy.

MYTH – MORPHINE IS GIVEN TO PATIENTS ONLY WHEN DEATH IS IMMINENT.

It is not the stage of an illness, but the degree of pain that dictates which medicine to use at which time. Morphine should be prescribed when a patient needs it. Some patients never need morphine, while other will require it starting relatively early in the disease progression and will use if for a protracted period.

MYTH – PEOPLE WHO TAKE MORPHINE BECOME ADDICTED TO IT.

Patients with chronic pain usually do not develop compulsive drug-seeking behaviour – they do not crave more morphine than the dose prescribed to control their pain. When a patient takes morphine on a regular basis, the body does become physically dependent on the drug, and sudden withdrawal of it will produce side effects. (Morphine should therefore not be stopped suddenly.) This is not addiction.

Doctors concerned about abuse can prescribe limited amounts of morphine (e.g. a two-week supply), so that the patient will return often for monitoring and, if needed, an additional prescription. If a patient's pain is caused by an opportunistic infection, the pain should ameliorate – and need for morphine decrease – as the infection improves under treatment.

MYTH – PEOPLE ON MORPHINE ARE TOO SLEEPY TO FUNCTION.

Patients may experience drowsiness when they start to take morphine. However, this sedative effect is temporary, usually of a few days duration. If drowsiness persists, and the pain is controlled, the dosage should be lowered. To help the patient sleep well at night, a double dose may be administered at bedtime.

If drowsiness persists and the pain in not controlled, then there is need to reassess the pain – it could be a type of pain that responds poorly to morphine, e.g., nerve pain. Long-term drowsiness also is a clinical indicator of central nervous system toxicity.

MYTH – PEOPLE ON MORPHINE DIE SOONER BECAUSE THEIR BREATHING IS IMPAIRED.

Fortunately, patients quickly adjust to any effect that morphine may have on their breathing. So rarely do breathing problems occur, they are usually not even listed as side effects. In fact, morphine is a drug of choice for respiratory distress in people with end-stage heart failure or lung disease, as it eases laboured breathing.

Should a patient present with signs of morphine toxicity, Naloxone is used to counter the effects; specifically, the drug counteracts life-threatening depression of the central nervous system and respiratory system.

MYTH - STRANGE FEELINGS AFTER STARTING MORPHINE MAY BE DUE TO ALLERGIC REACTIONS.

Few allergic reactions are attributable to morphine.

MYTH – PATIENTS NEED INCREASINGLY HIGH DOSES OF MORPHINE BECAUSE TOLERANCE TO THE DRUG DEVELOPS RAPIDLY.

Tolerance is not an inevitable consequence of prolonged morphine therapy. The same dose may provide a patient pain relief for weeks or even months. Usually the need for an increased dose means that the disease is progressing or that the pain was not inadequately controlled in the first place.

Oral morphine has no fixed upper dosage limit because there is no analgesic "ceiling" effect. The right dose is the dose that provides satisfactory relief of pain to the individual patient.

Dispelling Myths about Morphine

Proper prescribing of morphine is legal.

Morphine is safe and effective – more than 90% of severe pain cases can be well-controlled – if used according to recommended guidelines.

There is a difference between morphine addiction and tolerance. Patients rarely become addicted. Doctors concerned about abuse can prescribe limited amounts, so that the patient will return often for monitoring.

There is no such thing as too much pain medication for a patient in pain. Morphine has no upper limit as long as a patient can tolerate any side effects caused by the medicine.

With careful use of morphine, side effects are usually minimal and can be anticipated and mitigated.

5. TOTAL PAIN

Pain has always been part of the human condition, but today we have affordable ways to provide effective pain relief to people who need it. No patient should have to live with chronic pain, or reach the end of life in pain. Nor should the patient's caregivers, family, and community suffer as they watch a loved one in pain.

WHO uses the term "total pain" to describe the encompassing nature of pain (Saunders, 1978). Total pain has four elements (Figure 2):

TOTAL PAIN

Pain is experienced not only by nerve endings but also by sick people, and their families and communities.

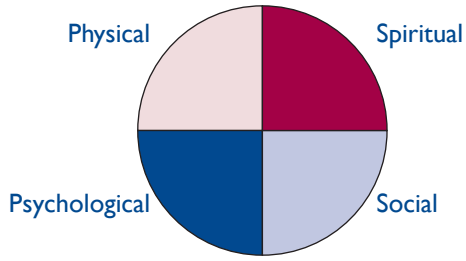
- *Physical pain*, which presents as discomfort to the patient;
- *Social pain,* which occurs when the patient's illness causes difficulties in relationships with family and significant others;
- *Emotional and psychological pain*, which occurs when the patient's illness causes distress. It includes feelings of fear, guilt, anger, frustration, anxiety, and depression; and
- *Spiritual pain*, which is the suffering experienced when one loses or questions their spirituality, the valuing of non-material aspects of life and feeling connected to other people, the earth, the universe, and God, though it is not always expressed as religious belief.

Pain

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.

International Association for the Study of Pain

FIGURE 2. TOTAL PAIN



Cultural context of the patient and the family

Source: Adapted from Wilson et al. 2007.

Patients Should Not Suffer Unnecessary Pain

Pain is what the patient says it is – not what the caregiver thinks it is.

Pain is not a normal part of the ageing or other natural process.

Relief of pain improves quality of life.

Unrelieved pain impairs all aspects of a person's life, including:

- Mood
- Appetite
- Self-esteem
- Relationships
- Physical activities of daily life

6. PAIN MANAGEMENT

Despite the availability of morphine and other methods of pain relief, too many patients endure unnecessary pain because pain management is neglected. The failure to adequately manage the severe pain that is common in advanced stages of HIV/AIDS and other illnesses is due to a variety of factors such as:

Goals of Quality Pain Management

Control pain

Prevent or minimise side effects

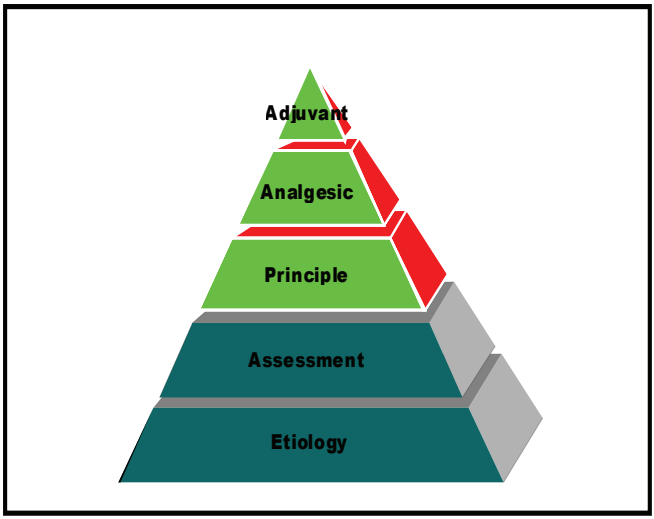
Enhance quality of life

- Inadequate training of some health professionals;
- Health professionals' fear that patients will become addicted to pain medications such as morphine;
- Lack of general awareness that pain can be controlled; and
- Unavailability of suitable drugs.

Effective pain control delivered by health care professionals is a five-step process (Fig. 3), which starts with establishing the etiology (cause) of the pain and then carefully assesses the type of pain that the patient is experiencing. The next step is to treat any underlying condition(s) and to apply the principles of pain management as provided by WHO guidelines (Saunders, 1978) for the use of analgesics by taking a holistic approach that incorporates the "total pain" concept. Finally, it involves the use, if necessary, of adjuvant drugs – drugs that are not primary analgesics but that may have

pain-relieving effects, especially when taken together with analgesics, for example, anti-depressants, corticosteroids, and muscle relaxants.

FIGURE. 3. THE FIVE-STEP PROCESS FOR BUILDING EFFECTIVE PAIN CONTROL

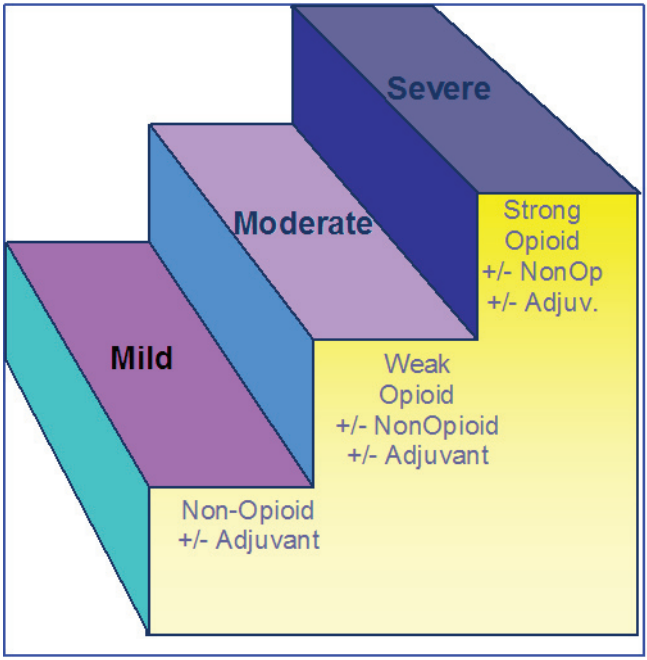


Source: Adapted from African Palliative Care Association (APCA) presentation

The health care provider should administer analgesic drugs in an appropriate dosage in the order of the WHO three-step "ladder" (Fig. 4) for effective pain relief, until the patient is free of pain. The three steps are:

- Non-opioids (e.g. aspirin and paracetamol);
- Then, as necessary, weak opioids (e.g. codeine);
- Then, morphine or other strong opioid.

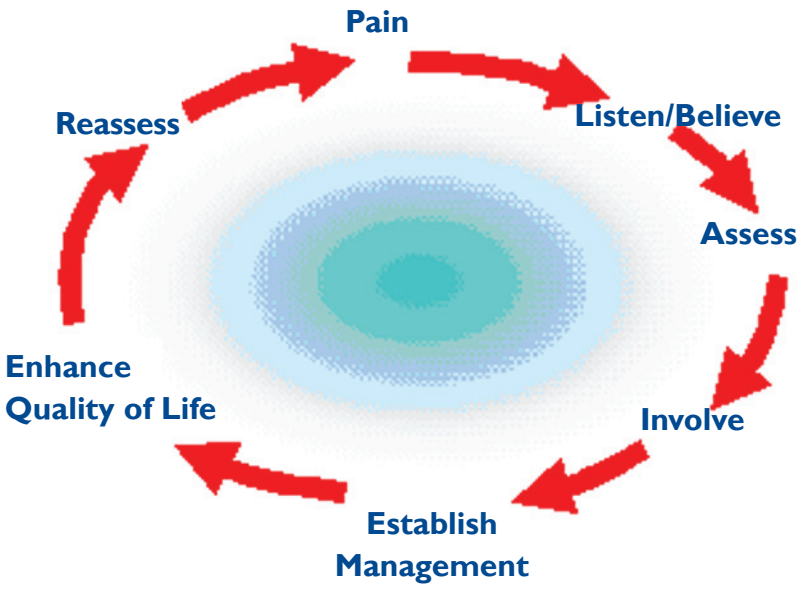
FIGURE. 4. THE WHO ANALGESIC LADDER



Source: http://www.who.int/cancer/palliative/painladder/en/

When prescribing pain (and other) medication, the provider must clearly explain to the patient and caregiver(s) the reason for treatment and potential side effects, and take into account the patient's preferences. Thereafter, the provider must reassess and evaluate the patient's response to the pain treatment and manage any side effects. There may be new problems that the provider must investigate and respond to. This pain management cycle (Fig. 5) is the process by which effective pain control is achieved.

FIGURE. 5. THE PAIN MANAGEMENT CYCLE



Source: Adapted from APCA presentation

Annexes 1-4 provide details on how a health care provider should assess and treat a patient for pain, in particular, with morphine but also with adjuvant drugs and other methods, and how to manage side effects.

7. PROCURING MORPHINE

7.1 OBTAINING MORPHINE FOR INPATIENTS

Recently, there has been some improvement in the availability of morphine and other opioids for inpatient use in Zambia's major hospitals. Public sector facilities most commonly use morphine syrup, private facilities morphine tablets. Morphine is usually available for emergencies, that is, patients with acute breakthrough pain, particularly in injectable form.

Prescribing and Dispensing Morphine at University Teaching Hospital

Prescribing

- A UTH prescription can come from any doctor.
- A record of the prescription is placed in the patient's file.
- The prescription must show:
- Patient's name and address
- Patient's diagnosis
- Concentration/volume of morphine
- No. of days written in words and in figures

Dispensing

- Details are recorded in the DDA book, and signed for by the person collecting the drug from the main pharmacy.
- The pharmacist provides detailed instructions for taking the morphine.

7.2 OBTAINING MORPHINE FOR OUTPATIENTS

FROM THE UTH

- The University Teaching Hospital (UTH) makes its own morphine syrup (Annex 5). Private health care facilities can purchase morphine from the UTH pharmacy for specific patients with authority from the UTH managing director.

- Doctors from non-UTH facilities liaise with the UTH to get their prescription written onto a UTH prescription form and countersigned by a UTH doctor. The procedure is then as per UTH prescription.

- The UTH pharmacy manager costs the morphine.

FROM OTHER HEALTH CARE PROVIDERS

- Home-based caregivers can obtain morphine through hospices, local clinics or the district health management team.

7.3 OBTAINING MORPHINE FROM AUTHORISED DEALERS

Currently five local companies are PRA-registered to import and manufacture morphine. It is not difficult for physicians, pharmacists, hospitals, private hospices and other care-giving facilities to purchase morphine from an authorised dealer, assuming that they obtain the necessary forms and other relevant documentation. An authorised person from a facility wishing to purchase morphine can do so according to the following steps:

- The buyer completes an application form, obtainable from the PRA.

- If the PRA approves the application, the buyer takes the approved form to an authorised dealer of controlled substances.

- The dealer enters the transaction in a DDA register, obtainable from Government Printers.

- User departments in the hospital or other facility maintain records of all used and unused controlled substances in their reconciliation registers or books.

- Reconciliation registers/books and DDA registers are submitted to the PRA for scrutiny and accountability when another requisition for controlled substances is made.

The Central Medical Stores (CMS) orders morphine powder in one-kilogram packages. While this amount is suitable for large facilities such as the UTH, which makes its own morphine syrup in five-litre batches, they are not convenient for distribution to institutions such as hospices, where consumption rates are much smaller than those of large hospitals. The CMS and PRA should source morphine in smaller units, preferably of 10, 25, 50 and 100 grams. This will increase access to morphine and ensure better distribution and use. In addition, to increase availability of morphine, the CMS should purchase and import morphine in tablet form.

ANNEX 1. ASSESSING THE PATIENT'S PAIN

When taking a holistic history from the patient, the health care provider must listen to and believe what the patient says, do a thorough physical examination and then carry out a pain assessment that involves the family and other health care providers. It is important to establish the cause, severity, and type of pain and determine how to manage it with a view to improving the patient's quality of life.

The health care provider begins assessing the cause of the patient's pain (new pain and/or change in existing pain) by taking a history, asking questions such as the following:

- Where is the pain?
- What type of pain is it? Describe it.
- How severe is it?
- What makes it better or worse?
- What are you taking now for the pain?

The provider may need to get or confirm information with the patient's family or caregivers and/or other professional providers who have provided care.

The provider then does a physical examination of the patient to determine the following:

- Confirm the location, type and severity of the pain that the patient described in the history. For example, is it a common pain such as bone or mouth pain, or a special pain such as shooting nerve pain, zoster, colic or muscle spasms?
- Is there an opportunistic infection or other problem that is causing the pain and that can be treated? Prompt diagnosis and treatment of the underlying cause is important for pain control.
- Does the provider observe a psychological or spiritual component to the patient's pain?

The pain should be graded with an appropriate pain scale and the findings recorded.

ANNEX 2. TREATING THE PATIENT'S PAIN

If through the medical history and physical examination the health care provider determines that the patient's pain is caused by an opportunistic infection or other underlying condition for which treatment is available, the provider should promptly begin treatment of the condition. The provider should also attend to the patient's pain. In addition, adjuvant drugs should be used to calm the patient's fears and anxiety. The provider should discuss treatment options with the patient and/or the patient's caregiver to the extent possible, and make clear to them the treatment process.

Three Steps to Pain Relief

The three-part approach to inexpensive and effective pain relief

1. Administer the right drug,

2. In the right dose,

3. At the right time.

To keep the patient free of pain, drugs (depending on their pharmacokinetics) should be given "by the clock", that is, every 3-6 hours, rather than "on demand". This three-part approach – administering the right drug in the right dose at the right time – is inexpensive and 80-90% effective (http://www.who.int/cancer/palliative/painladder/en/).

CHOOSE THE MOST EFFECTIVE PAIN RELIEF METHOD

In addition to prescribing the right medication to treat any underlying condition, the health care provider and patient must select the most appropriate medication for the patient's pain. In doing so, they should follow the WHO Analgesic Step Ladder (see chapter 6 in this Fact Book) (http://www.who.int/cancer/palliative/painladder/en/)

- Non-opioid analgesic (e.g. aspirin and paracetamol);
- Then, as needed, weak opioid analgesic (e.g. codeine);
- Then, morphine or other strong opioid analgesic.

If drugs are not wholly effective, surgical intervention on appropriate nerves may provide further pain relief.

Non-opioid/Weak Opioid Analgesics Available in Public Sector Facilities in Zambia

The following medicines, except codeine, are in the group NSAID.

- Paracetamol: mild analgesic with other properties (lowers fever).
- Aspirin (acetylsalicylic acid): an anti-inflammatory and anti-pyretic. Avoid or stop use if there is epigastric pain, indigestion, black stools, or bleeding. Do not give to children under 12 years.
- Ibuprofen (brufen): an anti-inflammatory, good for bone pain. It can be given together with morphine to relieve moderate pain.
- Diclofenac: a strong anti-inflammatory analgesic good for musculo-skeletal (nociceptive) pain.
- Indomethacin (indocid): an anti-inflammatory with properties similar to ibuprofen.
- Codeine: weak opioid for moderate to severe pain (if not available, consider alternating aspirin and paracetamol). It is always given with a laxative to avoid constipation unless the patient has diarrhoea.

Morphine and Other Opioid Analgesics Available in Zambia

Morphine

- Morphine powder for reconstitution as suspension is available only at UTH (see Annex 5).
- Morphine tablets are not readily available in Zambia in great part because the tablets are four times more expensive than injectable morphine.
- Injectable morphine is readily available for acute pain.

Other opioid analgesics:

- Injectable Pethidine is readily available in most health facilities. It is a partial opioid analgesic and is not suitable for chronic pain as its effect is of short duration and it cannot be used for long periods.
- Codeine Phosphate (tablet and in cough preparations).
- Dihydrocodeine (tartrate salt in tablet form).
- Fentanyl patches are sometimes available in the private sector.

CHOOSE THE BEST MORPHINE DELIVERY METHOD

Morphine can be administered in various ways.

- Orally, by syrup or tablet;
- Rectally; and
- By injection.

If possible, morphine should be given orally. The easiest way for the patient to take it is by tablet, to avoid the bitter taste of the syrup. However, tablets are usually available only in the private sector in Zambia; syrup is more common in public sector facilities.

Basics of morphine use

- Morphine is the opioid drug of choice for moderate to severe pain in chronically ill people.
- It is usually administered orally (by syrup or tablet) but also can be given rectally (by syringe).
- The dose can be increased by half (1.5 dose) or doubled after 24 hours if pain persists, according to the need of the patient and breathing – there is no ceiling dose.
- Morphine is always given with a laxative to avoid constipation unless the patient has diarrhoea.
- The morphine dose should be reduced when the cause of pain is controlled (common with HIV/AIDS pain as a patient's opportunistic infection improves): 1) If used for only a short time, stop or rapidly reduce.2.)

Morphine syrup (liquid)

Oral morphine syrup is a strong painkiller. It is commonly available in Zambia's hospitals.

A pharmacist must mix the morphine syrup. To administer to patients, a small amount of the morphine syrup is poured into a cup. The dose is drawn into a syringe. The liquid is then dropped from the syringe into the patient's mouth. (A needle should not be used!) The remaining morphine should be poured back into the bottle. The syrup should be given to the patient:

- By mouth.
- By the clock, i.e. regularly, every 4 hours during the day with a double dose at bedtime.
- An extra dose should be administered if pain returns before next dose is due, i.e. if breakthrough pain occurs.

Morphine syrup may be more suitable than tablets when starting treatment because it can easily be titrated to the amount of pain. For the same reason, it is better than slow-release tablets for acute pain and breakthrough pain.

Morphine tablets

Morphine in tablet form is not readily available in Zambia's public hospitals, but it can be found in the private sector.

Morphine tablets come in:

- Immediate-release morphine tablets, given every 4 hours like the syrup; or
- Sustained-release morphine tablets (MST). These long-acting tablets come in a range of different strengths (10mg, 15 mg, 30 mg, 60 mg, 100 mg and sometimes even 200 mg tablets depending on the country of origin) and usually are given twice a day (every 12 hours).

Most patients, providers and pharmacists prefer tablets to syrup:

- They are a much more convenient means to because they need no preparation.
- Because they come in multiple strengths, they allow for more flexibility of dosage.
- They are more palatable than the bitter-tasting syrup.
- Because patients can carry tablets around easily, without spillage, they encourage better patient compliance and adherence.

Side effects and toxicity of the tablet form of morphine are similar to those of the syrup.

Other methods of administering morphine

- Morphine (syrup) can also be given rectally through a syringe or as a suppository especially where the patient is unable to swallow or has uncontrollable vomiting.
- In rare cases, for acute pain, it is injected as epidural anaesthetic by a trained anaesthetist.

CHOOSE THE RIGHT DOSAGE

Regular dosing

Start with a small dose, then titrate dose against the patient's pain until the patient is comfortable. The usual starting dose for the immediate-release preparations of morphine is:

- For adult patients who are not too wasted: 5mgs 4 hourly and 10 mgs at night
- For elderly or wasted patient: 2.5mgs 4 to 6 hourly and 5 mgs at night.
- For child: according to body weight starting at 0.15-0.3mg per kg.
- The dose should be given every 4 hours.

Adjusting the dose

The dose is adjusted daily, whether the patient is an inpatient or outpatient, until the physician and patient are satisfied that the dose is appropriate. It is adjusted as follows:

- For mild to moderate pain: increase by 25%–50% daily.
- For severe pain: increase by 50%–100%.
- Adjust more quickly for severe uncontrolled pain.

Breakthrough dosing

- Use immediate-release morphine (syrup).
- Give an extra 4 hourly dose or calculate 5%–15% of the total 24-hour dose.
- The slow-release tablets should not be used for breakthrough pain as they are absorbed slowly. If the liquid or immediate release tablets are not available, the patient should chew the slow-release tablets to improve their absorption.

Night dosing

It is normal practice to administer a double dose of morphine at night to cover for the period that the patient is asleep.

PRN dosing

PRN means giving the patient medication only as and when necessary. As this Fact Book states repeatedly, PRN dosing should not be used for pain medication; one should not wait until the patient complains of pain before administering the next dose of pain medication. Morphine syrup should be given every 4 hours, MST tablets every 12 hours.

ADMINISTER MORPHINE "BY THE CLOCK"

As noted in the dosing section, morphine should be administered on a regular schedule, and the prescribing physician should make sure that the patient and caregiver thoroughly understand when and how to administer it.

Administer by the clock

- Give pain medication at fixed time intervals (by clock or radio or sun).
- Next dose should be taken before effect of previous dose wears off.
- For breakthrough pain, give an extra "rescue" dose (same dosing of the 4-hourly dose) in addition to the regular schedule.

Administer by the individual

- Link first and last dose with waking and sleeping times. In practice, this often corresponds with the 4-hourly dosage recommended above, because patients wake when pain returns.
- Write out drug regimen in full or present in a drawing.
- Teach its use.
- Check to be sure patient and family understand it.
- Ensure that pain does not return and the patient is as alert as possible.

ANNEX 3. MANAGING SIDE EFFECTS OF MORPHINE

Most side effects of morphine and other opioid analgesics occur at the start of treatment or when the dose is increased. (They also can occur at the end of life, with renal failure.) The side effects usually resolve within a few days. If side effects persist, the dose of morphine should be reduced – up to half – or the time between doses increased. The caregiver should allow for time with less analgesia if the patient wants to be more fully alert to make important decisions.

Side effects of morphine include the following:

- *Constipation:* increase fluids and bulk. Give laxatives, stool softener (Dulcolax) or stimulant like senna at time of prescribing, unless the patient has diarrhoea.
- *Nausea and vomiting:* rare, but if it occurs give an anti-emetic (metoclopromide, haloperidol or chlorpromazine). Usually resolves in several days.
- *Confusion, drowsiness and decreased alertness, twitching (myoclonus):* if due to high dose of morphine, consider reducing dose or changing opioid. Reassess the pain and its treatment.
- *Somnolence (excessive sleepiness):* extended sleep can be from exhaustion due to pain. If it persists for more than two days after starting morphine, reduce dose by half.
- *Itching:* if present for more than a few days and hard for patient to tolerate, give chlorpheniramine or phenergan.

- *Urinary retention:* treat by passing a urinary catheter in and out, since retention usually does not recur.

- *Tolerance: r*arely seen in clinical practice. If the patient continues to request a higher dose of morphine, most likely their disease is progressing or their pain was inadequately controlled in the first place.

- *Psychological addiction:* not seen when the patient is in pain. Psuedo-addiction, where a patient asks for more morphine because they are still in pain, is quite common and due to inadequate pain control.

- *Respiratory depression:* rare when oral morphine is increased gradually for pain. If severe, consider withholding the next morphine dose, then halving the following doses.

- *Opioid toxicity:* should not occur with careful titration of morphine dose. Pin-point pupils, a sign of toxicity, is rarely seen when a patient is in pain.

ANNEX 4. PREPARING MORPHINE SYRUP AT UTH

The University Teaching Hospital (UTH) prepares morphine syrup for its own patients, and dispenses it to other facilities.

Because morphine powder is very bitter, liquid morphine solution uses a sugar syrup as an agent to make the morphine more palatable. The UTH pharmacy prepares a single strength of morphine syrup in five-litre amounts, according to the following steps:

- Five litres of distilled water is added to 6.7 kg sugar.
- Five grams of morphine powder is mixed with a small amount of water to make a primary solution. This is added to the sugar solution (syrup).
- Ethanol is added as a preservative and co-solvent. (Parabene is the recommended preservative.)
- The solution is stirred until well mixed.
- No colourant is added, as only a single strength is prepared. (Morphine may also be prepared in different strengths or concentrations, which are identified by the addition of different colourants.) The sugar makes the final solution brownish; the morphine itself is colourless.
- The solution is transferred to an appropriately labeled 5-litre container, and stored in the dark.
- Morphine records are updated to reflect preparation of the syrup.

ANNEX 5. TAKING ADDITIONAL PAIN CONTROL MEASURES

The following methods of pain control may also help patients, and are available in Zambia.

ADJUVANT PAIN DRUGS

Adjuvant drugs may be appropriate as co-analgesic drugs, e.g., antidepressants, anticonvulsants and sedatives to control a patient's anxiety and drugs that treat side effects, such as laxatives for constipation and anti-emetics for nausea and vomiting. Specific drugs are listed below.

- Analgesics like NSAIDs;
- Anti-depressants like amitryptaline, for insomnia and anxiety;
- Anti-convulsants like phenobarbital, for neuropathic pain;
- Steroids like dexamethasone, for appetite, energy; and
- Muscle relaxants like valium.

OTHER COMMONLY USED DRUGS AND THEIR INDICATIONS

Common drugs can have some uncommon uses in palliative care, and providing relief from some of the symptoms and side effects of drugs usually taken by HIV/AIDS patients.

- Morphine for dyspnea and codeine for cough;

- Haloperidol and other major tranquilizers for vomiting, delirium;
- Metoclopramide for nausea/vomiting;
- Metronidazole for malodorous wounds;
- Dexamethasone for appetite, energy;
- Amitryptaline for insomnia, anxiety;
- Diazepam (valium) as a muscle relaxant; and
- Carbamezapine (tegretol) for neuropathic pain.

NON-PHARMACEUTICAL METHODS OF PAIN CONTROL

These should be combined with pain medications if the patient agrees:

- Emotional support and counseling;
- Physical methods
    - Touch, stroking, massage, rocking, vibration
    - Ice or heat compress
    - Deep breathing techniques;
- Cognitive methods
    - Distraction, e.g. listening to the radio
    - Music therapy
    - Visualisation, e.g. imagining a pleasant scene;

- Acupuncture;
- Reflexology;
- Transcutaneous electrical nerve simulator (TENS);
- Hypnosis;
- Prayer; and
- Well-established traditional practices which are helpful and not harmful to the patient.

REFERENCES

American Music Theory Association. Frequently Asked Questions about Music Therapy: How is music therapy used in hospitals? Silver Spring, MD. http://www.musictherapy.org/faqs.html#HOW_UTILIZED_IN_HOSPITALS Accessed January 2008.

Joint United Nations Programme on HIV/AIDS (UNAIDS). May 2006. 2006 Report on the global AIDS epidemic. http://www.unaidsrstesa.org/countries/Zambia/zambia.html Accessed January 2008.

Saunders, C.M. 1978. The Management of Terminal Disease. Arnold. In Sugden, Chris. 2001. Scottish Journal of Chaplaincy 4(2): 2-7. http://www.sach.org.uk/journal/0402p02_sugden.pdf Accessed January 2008.

World Health Organisaton. 2007. WHO's Pain Ladder. http://www.who.int/cancer/palliative/painladder/en/ Accessed January 2008.

World Health Organisaton. 2007. WHO Definition of Palliative Care. http://www.who.int/cancer/palliative/definition/en/ Accessed January 2008.

World Health Organisaton. 1996. Cancer Pain Relief, Second Edition, with a guide to opioid availability.

World Health Organisaton. N.d. Palliative Care for People Living with HIV: Clinical Protocol for the WHO European Region. http://www.euro.who.int/document/SHA/e90840_chapter_3.pdf.

Wilson, Keith G., Harvey Max Chochinov, Christine J. McPherson, Katerine LeMay, Pierre Allard, Srini Chary, Pierre R. Gagnon, Karen Macmillan, Marina De Luca, Fiona O'Shea, David Kuhl and Robin L. Fainsinger. 2007. Suffering with Advanced Cancer. Journal of Clinical Oncology 25(3, May 1, 2007):1691-97.

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