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Upcoming Issues

**The Science of Coping
Anxiety and Grief
Opioids in Cancer Pain**

Cancer Pain Management in Developing Countries

Cancer Prevalence

Cancer, a relatively neglected disease, is steadily becoming a more important cause of pain, suffering, and premature mortality in developing countries. AIDS-related cancer, a group of cancers that are frequently diagnosed in people with HIV-AIDS, also contributes to the problem in many countries, especially in sub-Saharan Africa. By 2002 there were 10.9 million new cancer cases as documented in the global cancer statistics, 6.7 million deaths, and 24.6 million persons alive with cancer (within 3 years of diagnosis).¹ The World Health Organization (WHO) estimated that of the 9 million new cancer cases every year, more than half are in developing countries.² In China and a number of middle-income countries, cancer deaths already exceed infectious deaths. This issue of *Pain: Clinical Updates* defines “developing countries,” discusses the problems with late diagnosis of cancer, and presents strategies for adequate assessment and management of cancer pain.

Developing Countries and Cancer Pain

The term “developing countries” is based on the World Bank’s classification of economies of countries according to gross national income per capita. The groups are low income, lower middle income (subdivided into lower middle and upper middle income), and high income.³ Low- and middle-income countries are sometimes referred to as developing countries for convenience. This categorization does not necessarily reflect the development status of the following broad groups: East Asia and Pacific, Europe and Central Asia, Latin America and Caribbean, Middle East and North Africa, sub-Saharan Africa, and South Asia. More than 5 billion people (85% of the world’s population) live in developing countries, which account for only 20% of the global gross national product.⁴ Hence, the resources available in developing countries remain grossly inadequate to deal with various health problems, including cancer and cancer-related pain.

In developing countries, patients tend to present with advanced disease associated with severe pain that can become the predominant problem for the patients and their families. Even when patients present early, the disease may not be diagnosed immediately, or therapy may not be affordable or available at the appropriate time. It may be pain itself that prompts patients to seek medical advice. Reports from the developed world have shown that in general, the prevalence of pain at the time of cancer diagnosis and early in the course of disease is estimated to be approximately 50%, increasing to 75% at advanced stages. A recent meta-analysis found the prevalence of pain in cancer survivors to be 33%.⁵ Also, most patients referred for cancer-related symptom management have at least two anatomically distinct pain sites. The pain may be caused by several mechanisms, including direct tumor involvement, cancer therapy (chemotherapy, surgery, or radiation therapy), and noncancer-related problems

such as preexisting diseases. Despite the paucity of published data from developing countries, the situation is unlikely to be any better than in the developed world.

Cancer Pain Diagnosis and Assessment

The generally accepted management strategy for cancer pain involves a comprehensive evaluation with an accurate history, a full physical examination of the patient, and a review of laboratory, radiographic, and other investigations. Each type of pain must be assessed and reassessed following treatment interventions and progression of the disease. In many developing countries, there are few specialist oncologists, so cancer pain is often treated by nonspecialists. Palliative care teams are nonexistent in many centers. National cancer or palliative care policy guidelines are lacking in many countries, and little attention is given to cancer pain as a subject in nursing and medical school curricula. There are also few opportunities for continuing medical education and in-service training in cancer and pain management. Thus, only a small number of health workers are familiar with cancer pain management principles, including the WHO cancer pain management guidelines introduced in 1986. The International Association for the Study of Pain (IASP), through its Developing Countries Project, is currently supporting training activities to improve pain management in developing countries. IASP has also launched the 2008–2009 Global Year Against Cancer Pain to focus attention on the pain and suffering faced by people with cancer. Fact sheets on various aspects of cancer have been released, and a cancer pain research symposium will be held in June 2009.⁶

In many developing countries, pain is regarded as inevitable, and patients are encouraged to live with it

In many developing countries, pain is regarded as an inevitable manifestation of the cancer, and patients are encouraged to live with it. However, the need for a comprehensive medical and neurological evaluation in the treatment of cancer pain is well described in the literature. IASP has developed a classification of cancer pain consisting of a catalogue of lesions and diseases that can cause pain.⁷ Other systems have focused on pain pathophysiology, using mechanisms of cancer pain syndromes.⁸ The Edmonton Staging System attempts to classify cancer pain on the basis of seven characteristics thought to have clinical prognostic value. These characteristics are mechanism of pain (visceral, bone or soft tissue, neuropathic, mixed, unknown), incidental pain (presence or absence), daily opioid usage, cognitive function (impaired or normal), psychological distress (present or absent), tolerance (present or absent according to an average daily increase in opioid consumption of more than 5% over the first 3 weeks of follow-up), and past history of alcoholism or drug addiction (positive or negative).⁹

In general, a detailed history will reveal the location and distribution of the pain, its severity and quality, whether it is present all the time or intermittent, what factors make it worse or better, and whether it limits the patient's activity or disturbs his or her sleep. Pain severity can be measured simply by using a visual analogue scale, verbal rating scale, numerical scale, or more complex questionnaires. It is helpful for patients to describe types of pain in their own words, such as aching, burning, or stabbing. Such words may indicate the type of pain,

including whether the pain is nociceptive or neuropathic. The words could be translated into some of the local languages for ease of administration and comprehension by patients.¹⁰ Young children may be able to convey pain intensity by selecting from a set of drawings of faces, ranging from neutral or smiling to crying. Observation by caregivers is particularly helpful in children and in those with cognitive impairment. Information about functional incapacity, level of anxiety, depression, and suicidal thoughts is valuable in the evaluation of the patient's psychological state. Prompt evaluation and treatment is called for in emergencies involving pain (e.g., pathological fractures, back pain due to spinal cord compression, or headache due to raised intracranial pressure).

A detailed history and careful examination may be sufficient to determine the type and cause of the pain, and all health professionals (not just the few oncologists) in developing countries should acquire this skill. An increase in pain intensity following a stable period necessitates reevaluation of the underlying etiology and reassessment of each type of pain. Although specific investigations, such as computed tomography, magnetic resonance imaging, or nuclear imaging may be able to provide more information in some cases, these tests are expensive and often unaffordable for most patients in developing countries.

Pain Relief Methods

Cancer pain is very treatable, but success requires a holistic approach, an understanding of the type of patient and the psychosocial issues involved, the pathophysiology of the pain, and the pharmacology of the pain-relieving drugs. Drug treatment is the mainstay of pain management; between 70% and 90% of all cancer pain can be controlled with oral medication.¹¹ Adequate pain relief can be achieved in more than 75% of patients who receive optimal analgesic management using simple techniques such as opioids, non-opioid analgesics, and adjuvant medications, as suggested by the WHO analgesic ladder.¹² It is recommended that drugs should be given by mouth, by the clock, and tailored to the individual patient with attention to details. Acetaminophen (paracetamol) or nonsteroidal anti-inflammatory drugs are effective analgesics for patients with mild cancer pain and can be combined with opioids in patients with moderate to severe pain. Experience with the use of the WHO ladder has shown that the simple principle of escalating from non-opioid to strong opioid analgesics is safe and effective. Familiarity with opioid pharmacokinetics and pharmacodynamics is helpful in selecting the most appropriate analgesic strategy. However, the role of the weak opioids in the treatment of moderate cancer pain has been questioned, and some experts speculate that this second step of the ladder could be omitted.¹² These weak opioids, including codeine, dextropropoxyphene, and tramadol, are more expensive in many developing countries, where they are not manufactured. Patients started on strong opioids as a first-line analgesic require significantly fewer changes in therapy and may have better pain relief. In most patients, side effects associated with the use of opioids can easily be managed with a combination of patient education and reassurance about the transient nature of sedation and emesis, careful selection of dose and route of opioid, and the use of additional drugs such as antiemetics and laxatives.¹³

Opioid availability is severely limited in most developing countries, which constitutes a major barrier to

effective cancer pain treatment. Other barriers that interfere with adequate pain management have been broadly classified as problems related to health care professionals, to patients, and to the health care system. The WHO document “Achieving balance in national opioids control policy—guidelines for assessment”¹⁴ was used to propose balanced legislation that would facilitate modern pain management and provide adequate control of these substances while preventing the potential for abuse. The Pain and Policy Studies Group at the University of Wisconsin also has several international resources, including a recent online course on “Increasing patient access to pain medicines around the world.”¹⁵ With proactive government policy, national education programs are being implemented in many countries to improve cancer pain relief and palliative care.^{16,17}

Cancer pain is very treatable, but success requires a holistic approach

Adjuvant drugs are used for difficult pain syndromes, including neuropathic and bone pain. Among the agents frequently used to manage neuropathic pain, tricyclic antidepressants, systemic local anesthetics, and baclofen are used for dysesthetic pain, whereas anticonvulsants such as gabapentin, carbamazepine, and phenytoin are more frequently used for lancinating pain.¹⁸ The cheaper drugs such as carbamazepine and phenytoin are already being used to treat other medical conditions in developing countries, and they only require knowledge and skills by health professionals for their appropriate use in cancer pain treatment. It must also be kept in mind that many patients in developing countries, especially in Africa and Asia, go to traditional healers and take other medications concurrently with those prescribed in hospitals.

Pain can also be relieved by modification of the disease

process, when appropriate, with surgery, chemotherapy, and radiotherapy, but these therapies are expensive and inaccessible to many patients, especially in rural communities. Nondrug methods including psychological interventions, physical therapy, and complementary medicine are also employed for pain relief, sometimes by nonspecialists. With regard to complementary therapy, it is necessary to educate patients on how to distinguish between harmful and beneficial treatments and to know which therapies can be safely integrated with conventional treatments. About 10% of cancer patients may benefit from advanced treatment options that are more readily available and well-documented in developed countries. Such treatments include interventional techniques (peripheral nerve blocks, autonomic nervous system blocks, radiofrequency lesions, and neurosurgical procedures) for some pain problems as part of a multimodal, multidisciplinary approach to pain control. For pain that is not well controlled with oral medications, low doses of an opioid plus a local anesthetic can be delivered by the spinal or epidural routes to provide relief with relatively few side effects. However, resource constraints such as the availability of trained clinicians, infrastructure, materials, and money (Table I) limit the use of such treatment options in developing countries.

Palliative Care

Most of the high-tech approaches to pain management are not feasible in developing countries because there are several competing priorities for the limited resources available. It is estimated that less than 5% of cancer patients in developing countries have access to these forms of treatment. In most countries, the cost of treatment is a major constraint because there is no social security or health insurance system to cover the bills, and most treatment costs are met out-of-pocket. However, with appropriate training in palliative care,

Table I Pain treatment methods and resources required for their implementation in developing countries

Pain Treatment Methods	Resources Required		
	Clinicians	Infrastructure and Equipment	Costs
Non-opioid drugs	Trained personnel	Minimal	Cheap
Opioid analgesics	Trained nurse, doctor, pharmacist	Minimal	Relatively cheap (when available)
Surgery	Surgeon, anesthesiologist, nurses	Operating theatre, patient accommodations, anesthetics, sterile surgical equipment	Expensive
Chemotherapy	Oncologist	Chemotherapy drugs, delivery pumps, disposable catheters	Expensive
Radiotherapy	Radio-oncologist	Radiotherapy machine, special suites	Expensive
Nondrug therapy (physical and rehabilitative therapy, psychotherapy, spiritual support, social support)	Physiotherapist, psycho-oncologist, psychologist, spiritual caregiver, social worker	Specialized training and equipment	Less expensive and more affordable
Advanced therapies (intrathecal drugs, nerve blocks, radiofrequency lesions, neurosurgery)	Palliative care specialist, anesthesiologist, neurologist, physiotherapist, specialist nurses, radiologist	Specialized infusion pumps, disposable items, radiodiagnostic equipment, treatment rooms	Expensive

clinicians in developing countries should be able to control the pain in most of their cancer patients, and an interdisciplinary pain management clinic would be required in only about 15% of cases.¹⁹ Culturally appropriate and affordable palliative care is becoming a known entity in many developing countries, with an emphasis on achieving coverage at low cost, while making sure that quality of care is maintained. Palliative care emphasizes pain and symptom control and psychosocial and spiritual support, thus ensuring the best quality of life for patients and support for families. The International Association for Hospice and Palliative Care promotes hospice and palliative care worldwide and provides resources including lists of essential medications for palliative care and educational programs.²⁰

Palliative care emphasizes pain and symptom control and psychosocial and spiritual support

In many countries, including Uganda and India, models have been developed to facilitate home care, which is mostly delivered by relatives who are supported by a specially trained palliative care team, an outpatient clinic, and a day care hospice.^{19,21} In other countries such as Lebanon, where no home care system exists, patients rely on three-generation family support.²² WHO has initiated the Community Health Approach to Palliative Care for HIV/AIDS and Cancer Patients in Africa Project. The goal of this project is to improve the quality of life of patients and their families in African countries by developing home-based palliative care programs with a public health approach that will provide comprehensive care, including pain relief.^{23,24} In many developing countries with poor resources and inadequate health care infrastructure, such projects with appropriate educational activities may be the only feasible means of providing adequate access to effective cancer pain relief and improved quality of life for those with the burden of cancer.

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