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New Approaches to Pain Control in Patients with Cancer

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Pain affects most patients with malignant disease, and the prevalence of severe pain increases in the advanced stages of the condition. One in 5 patients with cancer has uncontrolled pain, even after 10 years of the use of the World Health Organization programme for cancer pain control and its 'three-step ladder' for the rational use of analgesics including morphine. Morphine has long been the 'gold standard' for the treatment of severe cancer pain. However, its side-effects, particularly sedation, cognitive impairment and myoclonus at high doses, have provoked the use of 'opioid rotation' to alternatives such as methadone and hydromorphone. The new 72-h transdermal patch for fentanyl also offers advantages of reduced side-effects and increased convenience over oral morphine. Intravenous strontium-89 and bisphosphonate therapy are effective for both short- and long-term control of metastatic bone pain. The spinal *N*-methyl-D-aspartate (NMDA) receptor is important in modulating the plasticity of the central nervous system and in aggravating chronic pain through the phenomenon of 'wind-up'. The NMDA antagonist ketamine, an anaesthetic, can be used at low doses for the management of refractory and neuropathic pains. Among adjuvant drugs, ketorolac has emerged as a potent non-steroidal anti-inflammatory drug. Palliative care is gaining acceptance as a new discipline in healthcare. Its strategic role is being reviewed as an adjunct to cancer therapy at all stages and its use is no longer confined to the terminal phase of disease after curative treatment has failed. Pain control and other aspects of symptom control are, therefore, viewed as an integral part of cancer management. © **1997 Elsevier Science Ltd.**

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IMPACT OF PAIN IN ONCOLOGY

THE CONTROL of pain has always been an important part of cancer therapy, even long before the World Health Organization (WHO) first met to discuss this problem in 1982. A crucial outcome of that meeting, however, was the birth of the WHO Cancer Pain Relief and Palliative Care programme, which led to the publication of its seminal handbook *Cancer Pain Relief* in 1986 [1]. In this document the WHO three-step analgesic ladder (Figure 1) was proposed. This had a major impact on the way in which cancer pain management was subsequently organised and delivered. However, now, 10 years later, can we assume that pain is no longer a problem for our patients with cancer? Sadly this is far from the truth; while cancer specialists, particularly those working in chronic pain clinics and in palliative care settings, implement the WHO principles, most of them are either unaware of the potential benefits of these principles or are unable to make them available for patients in their own care. One reason for this is the rapid pace of developments in pain therapies; it is easy for non-specialists to become out-of-date in this area. This paper gives an overview of modern cancer pain control methods for doctors and nurses working in the oncology field.

The prevalence of pain reported by patients with malignancy ranges from 5% in leukaemia to 20% in lymphoma, 40% in gastrointestinal cancers, 45% in lung cancer, 52% in breast cancer and 85% in primary bone cancer [2]. The picture is even more worrying in those with advanced cancer, as was revealed in a recently published international WHO study of patients receiving palliative care for incurable malignancy [3]. Data were gathered on the prevalence of 8 major symptoms in 1840 patients receiving care in seven services covering Europe (England, Finland, Scotland and Switzerland), the U.S.A. and Australia. Overall, the prevalence of pain was rated by the units as absent in 24%, mild in 24%, moderate in 30% and severe in 21% of patients. As expected, the severity of pain varied in advanced cancer according to primary site, with the lowest rate being found in stomach cancer and the highest in gynaecological primary malignancies (Table 1).

IMPACT OF PAIN ON PATIENTS

The high level of pain experienced with cancer at both early and advanced stages places a great burden on patients and their families. Pain has a significant impact on the mobility, independence, psychological state and, ultimately,

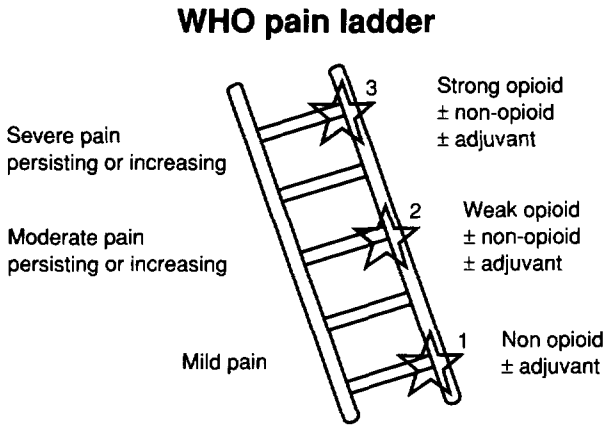

Figure 1. The WHO analgesic ladder (adapted from [1]).

quality of life of the patient. This negative impact is nearly always transferred onto the family or other informal carers; for example, lack of sleep in a patient because of nocturnal pain affects the carer, who has to wake up to give extra medication. The psychological, social and even financial and existential components of chronic uncontrolled pain have been brought together in the concept of 'total pain' [4].

The patient can be compromised not only by the pain itself but by many of the therapeutic interventions involved in pain treatment. Even when these are used in 'expert' hands they may give troublesome side-effects which often threaten quality of life. The side-effects are often physical, such as gastric intolerance from non-steroidal anti-inflammatory drugs (NSAIDs); constipation, nausea or sedation from opioids; or the well-known toxicities of so-called palliative regimens of cytotoxic chemotherapy or radiotherapy. Often, the need for attending hospital for treatment can lead to social and financial consequences for the patients' families, and the economic cost of uncontrolled pain to the clinical service must also be considered.

It is, therefore, important for oncologists to learn how to be rational and effective in both recognising pain in their patients and treating it without adding to their burden. A fully comprehensive review of all pain interventions would include the palliative chemotherapy and radiation regimens already referred to and the increasing role of hormonal manipulations for symptom control in prostate and breast cancers. However, this paper will concentrate mostly on non-oncological therapies; these are usually regarded as falling outside the scope of cancer services, though MacDonald has forcefully argued that it is obligatory for all oncologists to be mindful of their patients' symptoms and quality of life [5].

APPROACHES TO PAIN CONTROL IN CANCER

Managing bone pain

There have been a number of new developments in analgesic therapy for cancer pain (Table 2). It is not possible to cover all the surgical interventions that may be used to relieve pain, but the role of orthopaedic surgery in the management of bone fractures and metastases which threaten the stability of long bones is worth higlighting. There have been recent improvements in the techniques and fixatives used in placing endoprostheses for long bone stabilisation [6]. Orthopaedic fixation should not be seen as the sole management technique, but if pain persists after conventional analgesic therapy, oncologists and palliative care specialists should certainly consider referring patients with bone metastases from cancers such as breast, lung and kidney, which commonly cause major problems with long bone fractures or vertebral collapse.

A useful intervention for widespread bony metastases is the injection of a radioisotope, such as strontium-89. This is currently indicated for the treatment of pain from widespread bone infiltration in prostate cancer which affects 70% of patients with this disease at some stage [7]. However, because of its expense and limited availability, strontium is still seen as a second-line therapy after multiple fractions of local external beam radiation, or hemibody irradiation, have failed.

An alternative approach for the treatment of pain in bone metastases which has gained favour recently is the use of bisphosphonates. These were originally introduced into cancer treatment for the control of hypercalcaemia, and at least two agents effective for this indication—pamidronate and clodronate—are now available [8]. The use of such compounds led to the exciting observation that bone pain could be reduced by the bisphosphonate, whether the patient was hypercalcaemic or not. The degree of pain control, while being measurable and associated with reduction in the use of analgesics, is not usually sufficient in itself. Most patients, therefore, continue to need oral analgesics, but at lower doses, resulting in reduced side-effects. Furthermore, since only about half the patients respond satisfactorily to current bisphosphonates, there is a need to identify factors which will improve selection for this type of pain treatment.

More recently, evidence is accumulating that in some diseases, particularly breast cancer, the prolonged use of bisphosphonates can slow down the progression of bone metastases themselves and possibly prevent fractures [9]. In

Table 1. Pain in advanced cancer (based on a WHO international study, n = 1840). (Adapted from [3])

Site	Frequency (%)
Stomach	43
Lung	51
Oesophagus	51
Breast	52
Lymphohaematological	58
Colorectal	59
Prostate	61
Head and neck	72
Gynaecological	78

Table 2. New developments in cancer pain control

Bone pain	Orthopaedic surgery
	Strontium-89
	Bisphosphonates
Opioids	WHO cancer pain programme
	Re-evaluation of morphine side-effects
	Transdermal fentanyl
	Opioid rotation
NSAIDs	Ketorolac
NMDA blockers	Ketamine

advanced malignancies with relatively longer prognoses, such as breast cancer or myeloma, the prevention of fractures and long-term reduction of bone pain could clearly be a major advance. At present, bisphosphonates have to be given intravenously, but the newer analogues, which are several hundred times more potent, may be effective orally [8].

Opioids

The WHO three-step analgesic ladder referred to above (see Figure 1) was designed primarily to rationalise the use of opioids in cancer pain management. Current thinking recognises two classes of opioid drugs—'weak' and 'strong'. Codeine, dihydrocodeine and dextropropoxyphene are prime examples of the former, while morphine is the present 'gold standard' for the latter. Several long-established alternatives to morphine exist, many of which are several times more potent, such as hydromorphone, methadone, phenazocine, dextromoramide and fentanyl. The new agent tramadol is weaker than morphine and thus escapes the legal restrictions placed on other strong opioids in many countries. This has led to its popularity in Germany and elsewhere, but although it is said to work for moderate to severe cancer pain, most authorities would now classify it as a weak opioid. Tramadol has perhaps a theoretical advantage in that it may also work by preventing the reuptake of pain neurotransmitters. This should theoretically increase its benefit in treating neuropathic pains; however, no clinical trials have demonstrated its superiority in this respect.

The WHO ladder requires the use of weak opioids for mild to moderate pain, but severe pain needs the prescription of a strong opioid [1]. The definitions of 'mild', 'moderate' and 'severe' and the length of time that patients may stay on Step 2 with uncontrolled pain before being transferred onto a strong opioid are not rigidly laid down. This is not a problem for specialists such as anaesthesiologists, who work constantly with chronic pain, or physicians in palliative care settings, as they develop local guidelines for the transfer of patients through the steps. The recently published guidelines for the use of morphine from the European Association for Palliative Care (EAPC) include 20 such rules (see Table 3), many of which could easily be incorporated into the prescribing patterns of oncology units [10].

A review of over 2266 patients who attended the Pain Institute in Cologne from 1983 to 1992 yielded 2118 individuals with data relating to their time of first attendance and at a mean of 6, 37 and 66 days afterwards [11]. In addition, 864 were seen shortly before death. This is one of the largest data sets of patients undergoing chronic cancer pain management and it comprehensively covers many aspects of the correct use of the WHO ladder. For example, WHO Step 1 drugs were used on 11% of treatment days, Step 2 drugs on 31% and Step 3 drugs on 49% of days. The route of analgesia was enteral in 82% of patients, parenteral in 9% and spinal in 2%. Morphine itself was used in 56% of patients, in whom the dose was significantly escalated in 47%, remained stable in 40% and decreased in 15%.

A survey of opioid use in the Trent region of the North of England covered 1007 patients receiving specialist palliative care (SPC) in in-patient hospices, day hospices and through home care teams [12]. Of this sample, 970 patients had malignant disease and though the mean length of time spent with SPC was 265 days (median = 107), it is noteworthy that 43% were taking no opioids. Weak opioids were used in 10% and strong opioids in 45% of patients (39% being morphine). This is typical of British SPC, in which Step 2 of the WHO ladder is relatively underused, no doubt partly because of the ease of prescribing of strong opioids by hospital specialists and general practitioners alike. It is not advisable or necessary, however, to eliminate the second step altogether: a Canadian/U.S.A. study of slow-release codeine versus placebo in milder cancer pain showed that this was effective, provided that 'rescue' medication with codeine plus acetaminophen (paracetamol) was used [13].

The results of the U.K. survey were remarkably similar to those of the German study in that the dose of opioid was unchanged during the time in SPC in 43% of cancer patients and was reduced in 16% (and stopped altogether in 6%) [12]. These data show that the use of WHO guidelines for cancer pain should not be taken as a licence for unrestricted and inevitably escalating morphine prescription: at least in experienced hands, opioid usage can be well controlled and may often be reduced, even in progressively advancing cancer. The EAPC guidelines state that when morphine, given orally or subcutaneously by infusion, is used properly in this way, it can provide relief of cancer pain in 80% of patients [10]. However, this also means that one in five people will need other treatment modalities or alternatives to morphine to control their pain.

Morphine side-effects

One of the most important reasons for the 'failure' of morphine is its side-effect profile. It has long been recognised that morphine (and most other strong opioids) are associated with constipation, nausea and central cerebral sedative effects. Constipation is often overlooked by physicians, who may regard it is as unimportant and a nursing issue. From the patient's perspective, however, it is troublesome and may have a major impact on general comfort and living arrangements. Laxative prescription is mostly carried out by doctors who often do not understand their mode of action and the correct indications for stool softeners, bulking agents, lubricants or bowel stimulants. Until recently, little research had been carried out on opioid-induced constipation. In one study, oral naloxone was administered simultaneously with oral morphine in an attempt to block the gastrointestinal opioid receptors responsible for reduced bowel mobility [14]. The results showed that naloxone doses which were at least 20% of the 24-h morphine dose could reduce constipation; however, opioid withdrawal symptoms may occur and this approach clearly needs further study and refinement.

The central cerebral effects of morphine have also come under scrutiny. It has been shown that morphine initiation or dose escalation may be associated with measurable levels of cognitive dysfunction [15]. One treatment approach which is gaining favour is opioid rotation (OR), in which patients who are intolerant of a strong opioid (usually morphine as it is commonly used at higher doses) are transferred to an alternative strong opioid. Often the total daily dose can also be reduced at the same time without loss of pain control, indicating that the previous dose of morphine had gone beyond the therapeutic window for analgesia and into the level of toxicity. In one retrospective series, OR was practised in 80/191 patients with terminal cancer. The drugs from which patients were rotated were predominantly morphine but also hydromorphone, and most were moved onto hydromorphone or methadone. Significant improvement was noted in 29/42

Table 3. Recommendations for use of morphine for cancer pain. Reprinted with permission [10]

(1) The optimal route of administration of morphine is by mouth. Ideally, two types of formulation are required: immediate release (for dose titration) and controlled release (for maintenance treatment)
(2) The simplest method of dose titration is with a dose of immediate-release morphine given every four hours and the same dose for breakthrough pain. This rescue dose may be given as often as required (for example, every hour) and the total daily dose of morphine can be reviewed daily. The regular dose can then be adjusted according to how many rescue doses have been given
(3) If pain returns consistently before the next regular dose is due the regular dose should be increased. In general, immediate release morphine does not need to be given more often than every four hours and controlled-release morphine more often than every 12 h
(4) Several countries do not have an immediate release formulation of morphine (though such a formulation is necessary for optimal management). A different strategy is needed if treatment is started with controlled-release morphine
(5) For patients receiving immediate release morphine every four hours, a double dose at bedtime is a simple and effective way of avoiding being woken by pain
(6) Administration of controlled-release morphine every eight hours may be occasionally necessary or preferred
(7) Several controlled-release formulations are available. There is no evidence that they are substantially different in their duration of effect and relative analgesic potency
(8) If patients are unable to take drugs orally, the preferred alternative routes are rectal and subcutaneous
(9) The bioavailability of morphine by rectal and oral routes is the same and the duration of analgesia is also the same
(10) The relative potency ratio of oral morphine to rectal morphine is 1:1
(11) Controlled-release morphine tablets should not be crushed or used for rectal or vaginal administration
(12) Morphine may be given subcutaneously either as bolus injections every four hours or by continuous infusion
(13) The relative potency ratio of oral morphine to subcutaneous morphine is about 1:2
(14) There is generally no indication for giving morphine intramuscularly for chronic cancer pain because subcutaneous administration is simpler and less painful
(15) Other opioids may be preferred to morphine for parenteral use because of their greater solubility: diamorphine in Britain and hydromorphone elsewhere
(16) Subcutaneous administration of morphine may not be practical in patients:
(a) with generalised oedema
(b) who develop crythema, soreness, or sterile abscesses with subcutaneous administration
(c) with coagulation disorders
(d) with very poor peripheral circulation
In these patients intravenous administration is preferred. Intravenous administration may also be the best parenteral route in patients who, for other reasons, have an indwelling central or peripheral line
(17) The relative potency ratio of oral to intravenous morphine is about 1:3
(18) The above guidelines produce effective control of chronic cancer pain in about 80% of patients. In the remaining 20% other methods of pain control must be considered, including spinal administration of opioid analgesics alone or in combination with local anaesthetic or other drugs. There is insufficient evidence to allow recommendations about precise indications for these routes of administration
(19) The buccal, sublingual, and nebulised routes of administration of morphine are not recommended because there is presently no evidence of clinical advantage over conventional routes
(20) Sublingual or transdermal use of other opioids may be an alternative to subcutaneous injection

patients with cognitive failure and 9/9 with myoclonus; lesser, but non-significant, benefits were noted in terms of hallucinations, uncontrolled pain and nausea [16].

Workers in an Australian hospice programme observed that acute delirium associated with morphine cleared when the patient was rotated to oxycodone or fentanyl [17]. A prospective trial was therefore performed and this confirmed that mental state (impaired cognition and clouding of consciousness using the Diagnostic and Statistical Manual Third edition (DSM III) criteria) improved as well as nausea, with no deterioration in pain control, on transferring from morphine to oxycodone. In the U.K., many physicians in SPC rotate patients taking morphine onto methadone because of suspected intolerance.

It is surprising that it is not common practice to give cerebral stimulants to counteract the sedation often seen with strong opioids. Part of the reluctance to prescribe stimulants is physicians' lack of experience with, and fears of adverse effects from, these drugs. One prospective study documented the possible benefit from the psychostimulant, methylphenidate, in 43 patients taking a variety of strong opioids [18]. The results were inconclusive because of significant carry-over effects, but they suggested that methylphenidate could reduce daytime drowsiness and improve nocturnal sleep patterns. Another double-blind randomised placebo controlled crossover trial of methylphenidate in 20 patients receiving continuous infusions of opioids for cancer pain demonstrated a significant improvement both in subjective drowsiness and in objective psychomotor performance in patients taking methylphenidate [19]. There were no treatment-related side-effects reported and 13 patients chose methylphenidate blindly. There is a need for more studies to guide clinicians in their choice of which stimulants to use and how [20], but at present psychostimulants should probably not be used too freely.

A more practical approach to this problem is the more selective use of current and new strong opioids with less central adverse effects than morphine. One such agent is fentanyl. Fentanyl is the first drug in this class to be available as a transdermally active patch that can be applied every 72 h [21]. Fentanyl is an established synthetic opioid with 75–100 times the potency of morphine; it was chosen for administration via the transdermal route because of its low molecular weight and high lipophilicity. Studies and clinical experience over the past 5 years in North America and Germany have established the efficacy of Transdermal Therapeutic System fentanyl (TTS-fentanyl or TTS-fen) and raised prospects of reduced side-effects compared with morphine. A small study in the U.K. has confirmed the efficacy data, and TTS-fen showed significant improvements over 12-hourly slow-release

morphine in terms of constipation and sedation [22]. More recently, a larger U.K. randomised, crossover study involving 202 patients, in which a battery of questionnaires and a daily patient diary were used, showed that for the same degree of pain control as morphine, TTS-fen was associated with significantly less constipation, nausea and daytime drowsiness [23]. Patients on TTS-fen also reported a slightly shorter duration of sleep at night, but overall significantly more preferred the patch to oral, 12-hourly, slow-release morphine.

One problem concerning the use of 72-h patch technology is the lack of confidence that some clinicians may have in starting patients on this form of treatment and titrating the dosage to match the pain. This is understandable but unfortunate because the slow-release formulation is more convenient for some patients and may be the reason for the reduced side-effect profile compared with other agents. As other longer acting drugs, such as 24-h oral morphine formulations, become more readily available, lack of familiarity and reluctance to accept new or unfamiliar technology may become less of a practical obstacle [24, 25].

Morphine responsiveness

Evidence that some types of pain are inherently less responsive to morphine and other strong opioids is increasing. These pains are characteristically associated with neurological damage or direct infiltration (e.g. as a result of tumour growth, spinal vertebral collapse and postradiation damage), and are called 'neuropathic' pains. It is recognised that though opioids may attenuate these pains, merely increasing the drug dose may lead only to the sedation or cerebral irritation which has necessitated opioid rotation, as described above.

For treating neuropathic pain, both malignant and benign (e.g. posthepetic neuralgia) in nature, it is customary to use the adjuvant drugs included in the WHO analgesic ladder. These include corticosteroids (particularly useful for direct nerve compression and raised intracranial or spinal cord pressure), antidepressants and anticonvulsants. The mode of action of the latter agents is not entirely clear, but they are believed to work by stabilising nerve cell membranes, rather than through the primary medical use of these drugs. The use of anticonvulsants has been subjected to a recent systematic review, which confirmed their effectiveness for trigeminal neuralgia, diabetic neuropathy and migraine prophylaxis [26]. Unfortunately it has proved to be too difficult so far to conduct good clinical trials of anticonvulsants in cancer pain. Likewise, though antidepressants, such as amitriptyline and fluoxetine, have demonstrated analgesic activity better than placebo for the treatment of chronic rheumatic pain, large, randomised controlled trials have not been carried out in patients with malignant disease [27]. However, their use is still advocated, based on the large positive clinical experience of pain clinics and palliative care units.

NSAIDs

The WHO analgesic approach has always recommended the use of non-opioid drugs, both to accompany opioids in Steps 2 and 3 and alone in Step 1. One of the most common non-opioid drugs is paracetamol (acetaminophen). This is often combined in proprietary forms with the weak opioids. Analgesic doses of aspirin alone are usually associated with unacceptable gastric effects for many people, but stronger NSAIDs which cause variable degrees of gastric irritation but more potent analgesia are frequently used. As prostaglandins have a role in bone metastases, it was thought that NSAIDs had a specific role in malignant bone pain [28]. The evidence for this is still poor, but slow-release NSAIDs, often covered by H_2-antagonists or other gastric protectors, are certainly helpful in most types of cancer pain [29].

There are few controlled studies of NSAIDs in treatment of cancer pain, but a new, potent drug of this class, which has been used in palliative care as well as postoperative pain management, is ketorolac [30]. It is a strong analgesic which can be given as a continuous subcutaneous infusion, and may allow the dose of morphine to be reduced. The risk of gastrointestinal toxicity is present, as with other NSAIDs, but in experienced hands this may be contained.

N-methyl-D-aspartate (NMDA) receptors and chronic pain

NMDA receptors are found in the dorsal horn of the spinal cord and are known to be involved in the modulation of chronic pain through newly understood mechanisms of the 'plasticity' of the central nervous system. Activation of these receptors by noxious stimuli can lead to the phenomenon of increased sensitivity to further painful stimuli, known as 'wind-up'. The anaesthetic ketamine is an NMDA receptor blocker and can be used at subanaesthetic doses to provide fine control of severe and refractory pain, even of the neuropathic type which is poorly responsive to morphine [31]. Most research and clinical experience has taken place in postoperative and acute pain management, but there is increasing experience in palliative care of cancer pain [32]. No randomised controlled trials in cancer patients have been carried out so far, but several case reports and larger series have been published [33].

Ketamine is usually given as an intravenous bolus to induce immediate pain reduction and is then continued as an intravenous or subcutaneous infusion. A significant problem associated with this drug is cerebral stimulation leading to dysphoria and hallucinations, which are observed when the dose is reduced or withdrawn ('emergent phenomena'). These effects may be minimised by the concurrent administration of a small dose of benzodiazepine, such as midazolam, alongside ketamine. It remains to be seen whether this potent drug can be used routinely in cancer pain management outside the specialist pain control setting.

NEW VIEW OF PALLIATIVE CARE IN CANCER THERAPY

So far this paper has focused on the control of pain as if it were the sole symptom of cancer. This is clearly not the case and, as discussed earlier, all symptoms (including those arising as side-effects of therapy) have a wider impact on the patients' family and other carers. The recognition of broader issues regarding symptom control, family-based care and the attendance to psychological, social and existential factors in patients' distress are the key components of the new discipline of palliative care [4]. Unfortunately, palliative care is often seen by surgeons and oncologists as the stage of treatment occurring after they have finished trying to cure the patient. Indeed, the current WHO model of palliative care provision for cancer tends to emphasise this sequential model of curative treatment passing over to palliative care (Figure 2).

In recent years, oncologists have become both interested in symptom control and more sophisticated in their palliative skills. Correspondingly, the previously 'independent' hospice

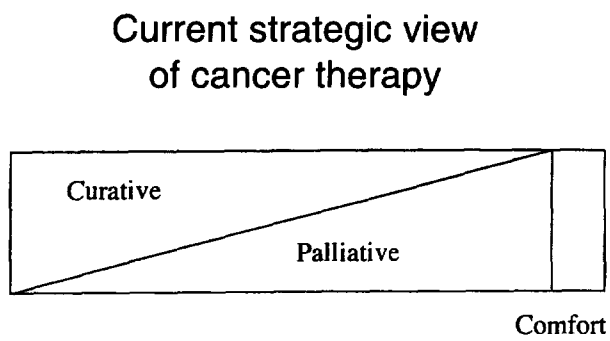

Figure 2. Current strategic view of cancer therapy.

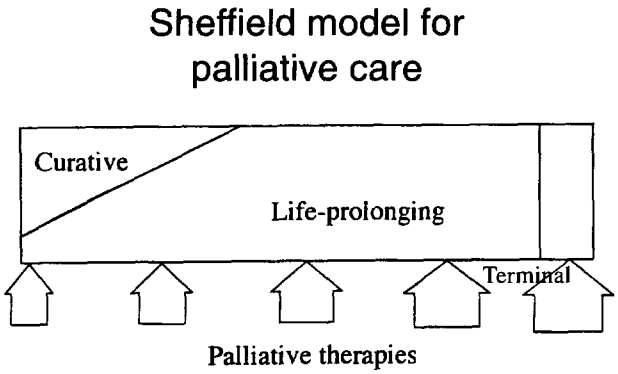

Figure 3. Sheffield model for palliative care.

movement is becoming more closely aligned to mainstream medical care—even in the U.K., where over 200 stand-alone hospices exist. (However, the medical specialty of palliative medicine is still only recognised in a few countries worldwide, currently the U.K., Ireland, Canada, Australia and Norway.) The discipline of oncology has started to embrace the concept of quality of life being an endpoint of its interventions, not only in palliative regimens but when survival rates are equivalent from different treatments and drug toxicities are high [34]. In the U.K., the government has announced a radical programme of reform of cancer services and part of this is the requirement for all centres to offer multidisciplinary palliative care at all stages of the disease [35].

This new awareness has led to a widespread reappraisal of the WHO approach to palliative care. One proposed alternative strategy is the Sheffield framework (Figure 3) [36, 37]. In this model, the *anti-cancer intention* of oncological therapy is separated from the supportive elements of care. The intention can often be seen as a transition from curative to 'life-prolonging', until death is imminent and the emphasis is then on nursing care. Alongside these cancer-directed phases, patients' symptom needs and psychosocial distress should be addressed by the simultaneous application of palliative therapies, rather than waiting until the patient is deemed 'terminal'.

Seen this way, treatments currently called 'palliative' radiotherapy, chemotherapy or hormone therapies (i.e. treatments to reduce symptoms not to prolong life) could be regarded as supportive care in the broadest sense of 'support'. Similarly, rehabilitation therapies should be offered throughout the illness trajectory to help patients and families come to terms with loss of function and role. This new way of perceiving palliative care—as an adjunct, rather than an alternative, to oncology—may be more helpful than the older WHO model for the late 1990s and the next decade. Good access to pain control should then be seen as the right of all cancer patients *at all stages* of their disease.

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