MAYO CLINIC

Cancer Pain Management

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CME Activity

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Abstract

Safe, effective, and evidence-based management of cancer-related pain is a cornerstone of comprehensive cancer care. Despite increasing interest in and efforts to improve its management, pain remains poorly controlled in nearly half of all patients with cancer, with little change in the past 20 years. Limited training in pain assessment and management, overestimation of providers' own skills to treat pain, and failure to refer patients to pain specialists can result in suboptimal pain management with devastating effects on quality of life, physical functioning, and increased psychological distress. From a thorough assessment of cancer-related pain to appropriate treatments that may include opiates, adjuvant medications, nerve blocks, and nondrug interventions, this article is intended as a brief overview of the mechanisms and types of pain as well as a review of current, new, and promising approaches to its management.

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In 2015, 14.5 million Americans are living with a recent or remote history of cancer.[1,2] Worldwide, those estimates were 32.6 million in 2012.[3] Pain is among the most distressing and disabling sequelae of cancer and its related treatments and remains poorly managed across the globe. The prevalence of cancer-related pain has ranged from 14% to 100% in surveys.[4] The incidence of pain is surprisingly similar across stages of disease, with 64% of those with advanced disease reporting pain vs 53% of patients with all stages of disease. Pain persists in 33% of those who have completed curative treatments.[5] We see this in our own practice as previously healthy people can be hobbled with poor quality of life after curative treatments leave them with neuropathic pain.[6,7]

Safe, effective, and evidence-based management of cancer-related pain is a cornerstone of comprehensive cancer care. Despite increasing interest in and efforts to improve

its management, pain remains poorly controlled in nearly half of all patients with cancer.[8] The consequences of suboptimal pain management on quality of life, physical functioning, and psychological distress can be devastating. Two-thirds of patients report that pain interferes with their activities of daily living, and half believe that their providers do not prioritize quality of life in their overall plan of care.[9]

These figures stand in stark contrast with oncologists' perceptions of their ability to manage pain. Oncologists rated their training in pain management as a score of 3 (on a scale of 0 to 10) in medical school and 5 in residency but gave themselves a 7 for cancer pain expertise. Oncologists performed worse than pain specialists on pain vignettes, with 60% and 87% giving answers that would be unacceptable to pain specialists on 2 challenging cases.[10] A recent update with 8 vignettes was more concerning when oncologists were compared with pain management specialists and palliative medicine specialists.[11] Oncologists did worse than either group in selection of an opioid, management of opioid adverse effects, management of a pain crisis, use of a coanalgesic to treat neuropathic pain, and use of interventions such as nerve blocks. Despite their lower scores on these vignettes, oncologists rated their own skills at 7 of 10, while pain specialists rated their skills at 6. Contemporary oncology practice results indicate less than optimal management as well. Even in practices that were being self-monitored for pain management, one-third of patients with cancer pain had inadequate prescriptions for pain, despite 20 years of emphasis on cancer pain relief.[12] Minority patients had twice as much difficulty: in this national study of 6 academic and 32 community practices, the chances of a white patient getting inadequate pain prescription was half that of a minority patient (odds ratio, 0.51; 95% CI, 0.37-0.70; P=.002). Of 2700 patients followed up for symptoms, one-third had improvement after consultation with the oncologist, but one-fifth had worsening of their pain.[13] A persistent theme has been our failure to properly assess pain, especially neuropathic pain, as part of the management process and failure to get help. Even today, 8% of oncologists never and 21% rarely refer patients to a pain specialist.[11]

We can and should do better, whatever our branch of medicine or nursing. We present a brief overview of the mechanisms and types of pain as well as current and new approaches to its management.

MECHANISMS AND TYPES OF CANCER PAIN

Cancer pain is the result of complex interactions among cancer cells, the peripheral and central nervous systems, and the immune system.[14,15] Cancer cells and the local immune cells produce a wide range of substances that mediate or interact with pain receptors (nociceptors). As more is understood about the functioning of these molecules in the pain signal transduction process, they have emerged as important targets for novel analgesic interventions.[16] Additionally, in animals, and likely in humans, peripheral nociceptors appear to become activated, sensitized, or injured in the presence of certain cancers.[17]

Once pain receptors are stimulated, impulses are transmitted first by afferent A-delta (thinly myelinated) fibers and then by separate slower (nonmyelinated) C fibers. These fibers end in cell bodies in the dorsal root or trigeminal ganglion, which then interact with neurons in the central nervous system cells in the spinal cord. These cells synapse to the contralateral thalamus from which impulses are transmitted to regions of the cortex via somatosensory pathways. Interactions at the cortical level are highly complex, involving the somatosensory cortex, frontal cortex, and limbic system. Each transmission implies some chance to block the pain signal at that point.

The observation that perceptions of pain can vary depending on factors (anxiety, depression, distraction) that have no direct relationship to nociceptors or the painful stimulus indicates the presence of additional mechanisms that modulate transduction and response.[18] These mechanisms include inhibition at the spinal level by nonpainful input (the gate control theory[19]) and descending inhibition from midbrain and higher regions that contain high concentrations of opioid receptors. Visceral pain arising from nociceptors in internal organs is mostly transmitted by C fibers. Often less well localized and less sharp than somatic pain, visceral pain is triggered by direct irritation from the tumor, distention

or contraction of an organ, ischemia, necrosis, or inflammatory mediators.

Neuropathic pain arises from injury to nerve tissue in either the central or peripheral nervous system. It differs from nociceptive pain in several important ways. First, the inciting stimulus may be gone, so there is nothing to "fix" at the nociceptor. Second, the pain stimulus can arise at any place along the pathway, eg, peripheral, spinal cord, or even central areas. Finally, chronic neuropathic pain may serve no protective purpose. These mechanisms are discussed in an excellent review by Cohen and Mao.[20] Such pain is less likely to respond to standard opioid or nonsteroidal anti-inflammatory drug (NSAID)—based therapy.[20] Neuropathic pain is also complicated by the "wind-up" phenomena[21]: repetitive stimulation of the C fibers leads to biochemical and physical genetic changes in the central nervous system.[22] In fact, the damaged nerves and their undamaged counterparts may both be giving pain signals by cross talk mediated by gap junctions,[23] reinforcing the pain stimulus.

In patients with cancer, such injury often arises as a result of treatment (chemotherapy, surgical procedure, or radiotherapy) but can also be caused by infection, direct action of the tumor, ischemia, or a combination of these factors. Unlike somatic or visceral pain, the quality of neuropathic pain is often described as burning, numbness, or tingling and may be further diagnosed as allodynic (caused by stimuli that do not normally trigger pain) or hyperalgesic (pain perception that is much greater than would be expected). The distinction between nociceptive pain (somatic and visceral) and neuropathic pain is clinically important because different therapeutic approaches are often needed to achieve relief.

Cancer pain can be readily categorized on the basis of the mechanism of nerve damage or type of sensation, but most pain is actually mixed (Table 1). In our own study of refractory cancer pain in 5 countries, 60% of patients had mixed pain.[55] It is important to try to discern the cause of the pain—the "pain generator"—because consequences and treatment options vary tremendously. For instance, local pain from a T12 vertebral metastatic tumor should mandate concern about an epidural mass causing spinal cord compression. In addition, the pain may be well controlled with injections of a local anesthetic or, if mostly neuropathic, from a combination of opioids and neuropathic drugs.

THE FIRST STEP: ASSESSMENT OF PAIN

An editorial commenting on an article in the *Journal of Clinical Oncology* that reported no progress in pain management in the past 20 years called for "ensuring that every consultation includes the patient's rating of pain, that the oncologist pays attention to the answer, and that there is an agreed-upon plan to increase analgesia when it is inadequate."[56] We agree but believe that a pain rating alone is insufficient. Table 2 listed the common questions that we use

TABLE 1. Types of Commonly Encountered Cancer Pain

Type of pain	Cause	Characteristics	Examples
Nociceptive	Pressure on nerves	Deep, dull, aching, constant, and worsening with time	Pancreas cancer, deep boring, and epigastric
Visceral	Distention of a hollow viscus	Cramping, bloating pain, intermittent	Intestinal obstruction, renal colic
Neuropathic	Direct damage to the nerves from cancer, treatment, or both[24]	Local pain, sharp shooting, burning, stabbing, often with allodynia (painful sensation with normal touch) or hyperalgesia	Diffuse, constant, stabbing pain in bilateral mastectomy scars, "Like wearing a bra made of barbed wire"
	Chemotherapy-induced neuropathic pain; direct damage to the longest nerves with damaged receptors and even loss of nerve fiber density	Numbness, tingling, and pain together; longest nerves affected most, giving a stocking-glove neuropathy	Increasingly common and dose limiting, occurring in 40%-70% of patients receiving modern treatments[25]; duloxetine is the only proven medication. See Table 3
Incident or movement pain	Pathologic fractures, bone damage from cancer, residual damage left after cancer	Minimal pain at rest but excruciating pain with movement "bone on bone"	Very difficult to control. See Table 3

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in our pain assessment, modified to be practical and usable.

THE SECOND STEP: MANAGEMENT OF THE PAIN

Once pain is assessed, treatment may begin. The World Health Organization's cancer pain ladder for adults[59] recognizes 3 fundamental categories of analgesics—nonopioids (aspirin, acetaminophen, paracetamol, or NSAIDs), "weak" opioids (codeine), and strong opioids (morphine, hydromorphone, and others)—and 3 levels of pain (mild, mild-moderate, and moderate-severe). Mild pain is treated with nonopioids, mild-moderate pain with "weak" opioids with or without a nonopioid, and moderate-severe pain with strong opioids with or without nonopioids. Adjuvant medications are recommended on an ad hoc basis. The World Health Organization's cancer pain ladder for adults recommends around-the-clock dosing of analgesics with provision for

TABLE 2. Questions for Pain Assessment in Adults With Cancer Pain

Question	Searching for	What to do with the response
Describe your pain to me	Get the patient's own words, rather than presuming some mechanism	Successful pain management requires a trusting relationship with a health care professional. In a recent study, trust in the physician, higher education level, and white race were all strongly correlated with better knowledge about how to control cancer pain[57]
When did it start?	Searching for the cause of the pain	Determine if it started before or after the surgery, radiation, chemotherapy, or shingles
Where is it?	Searching for the cause Symmetry? Nerve, plexus, root or cord?	Try to isolate the pain origin to control it with nerve blocks, local treatments
What does it feel like?	Dull, aching (nociceptive) or sharp and stabbing associated with tingling (neuropathic)	Neuropathic pain requires nerve medications. We describe it to patients as being like treating seizures: we are trying to quiet down the nerve over some weeks
How long does it last?	Searching for pain generators	Pain that lasts seconds, only with bone movement, indicates bone instability or damage
What makes it better or worse?	Searching for pain generators and mechanism	If heat, cold, or massage works, then local treatments may help
Does touching the skin hurt?	Allodynia—pain on normal touch—indicates neuropathic pain	Treat with neuropathic drugs and look for a spot to administer a local nerve block or try topical treatments
Is there associated numbness and tingling?	Indicates nerve damage such as a plexopathy or chemotherapy-induced peripheral neuropathy	Patients may not tell you about these symptoms unless you ask
What has worked or not before?	Make a list of potential things to try; do not include things that the patient has tried that were not effective	It is very hard to convince a patient with a serious adverse reaction to a drug, eg, delirium or urinary hesitancy, to try it again
What adverse effects have you experienced with pain medications?	Sedation, constipation, delirium, pruritus, nausea	Understanding predictable adverse effects allows for better teaching
What impact has it had on your life?	Does the pain restrict activity? The pain may be less because the person never goes outside or tries to walk	Do they think it means the cancer is growing and so will not report it? Is their pain controlled but they never go outside anymore?
Please rate your pain on a scale of 0 to 10	A number. Every patient can at least say if the pain is well controlled or not well controlled	Even though this is the fifth vital sign, the score is less important than the mechanism. Getting the pain score down to 0 is often impossible, but patients function well if the pain score is ≤ 4
Are there major risks of respiratory or organ dysfunction that limit choice?	Liver disease, kidney disease, allergies, high doses of serotonin drugs	Influences prescribing and may need consultation with a pain or palliative care expert and pharmacist
Are there red flags for potential abuse?	Prior drug addiction or misuse, multiple prescribers, pain out of keeping with the known anatomy and physiology	Every prescriber should be able to use their available prescription drug monitoring plan. A full review of their use is beyond the scope of this review

Modified from questions used by Judith Paice, RN, MSN, PhD, Northwestern University. Data from UpToDate.[58]

TABLE 3. Standard Ways of Relieving Cancer Pain With Drugs

Method	Current uses	Effectiveness	Comments
Opioids	Somatic pain Neuropathic pain Mixed pain	For morphine, 63% of patients have "treatment success" (very satisfied, very good, or excellent patient reports)[26]	All the available drugs (morphine, oxycodone, hydrocodone, hydromorphone and oxymorphone) have efficacy with no randomized trial evidence of superiority. In the one randomized trial, methadone had no more effect than morphine in neuropathic pain, but the study was underpowered to detect small improvements[27]
Mixed-mechanism drugs (bind to μ-opioid receptor and some blockade of serotonin and norepinephrine)	Most of the world has inexpensive tramadol when opiates are not available. Tapentadol is new drug that has proven efficacy with fewer gastrointestinal adverse effects than morphine[28]	Moderately effective against pain and some cancer-related neuropathic pain	Conversion ratio of tramadol to morphine is 10:1 but variable[29] Use with caution because these drugs lower seizure threshold and can cause serotonin syndrome Tapentadol is substantially more expensive ($132) vs oxycodone ($27)[30]
Adjuvant drugs Antidepressants Neuroleptics/seizure medications Corticosteroids	Somatic pain, neuropathic pain, mixed pain	One systematic review reported that a reduction in cancer pain intensity of >1 point was unlikely.[31] Pain relief occurred in 4-8 d, if it occurred	All have some efficacy, but sequential trials may be required.[20] New drugs are needed because the number needed to treat is often equal to the number who are harmed with adverse effects[32]
Bone strengtheners	Bisphosphonates	50%-70% of patients report benefit.[33] Six of 11 randomized trials reported benefit[34]	Patients with cancer who have lytic bone metastases should receive these drugs routinely.[35] Whether added doses provide benefit is unknown
	Denosumab	Delays onset of bone pain 4 mo longer than bisphosphonates[36]	Substantially more expensive than bisphosphonates ($2500 per dose vs $600)
	Calcitonin	Reduced pain from acute osteoporotic compression fractures by 3 points at 1 wk and by 6 points at 4 wk. No effect on chronic pain.[37] Reduced pain associated with aromatase inhibitors more than placebo, from 5 to 2[38]	Does not work for chronic metastatic bone pain[39]
	Corticosteroids in addition to other pain drugs	Methylprednisolone 32-mg/d did not improve pain compared with placebo in patients with cancer but did improve fatigue, nausea, and well-being.[40] A Cochrane systematic review found a mean difference in reduction in pain of 0.84 at 1 week[41]	If you use a corticosteroid, use for 1 wk and reevaluate. There may be good reasons to use corticosteroids to treat fatigue and improve quality of life.[42] Use 8 mg of dexamethasone before any stereotactic bone radiation to prevent a pain flare[43]
	Acetaminophen in addition to opioids	There are conflicting data. A small (N=22) randomized trial of paracetamol added to strong opioids found no benefit.[44] A slightly larger (N=30) trial found some benefit to adding paracetamol vs placebo, a 0.6-point change in pain with a 0.7-point improvement in well-being[45]	If you add acetaminophen, evaluate at 48 h for benefit. Do not expect much change

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TABLE 3. Continued

Method	Current uses	Effectiveness	Comments
Bone strengtheners, continued			
	NSAIDs in addition to opioids	The majority of trials report some additional benefit[46,47]	Getting an 15% additional pain relief may be welcomed and possible, given different mechanisms of action
Special situation: incident pain (pain on movement of bones)	Opioids, NSAIDs	Opioids are only partially effective, at the cost of oversedation)[48]	A few patients have been treated with opioid switching and "burst" ketamine at 100 mg/d[49]
Topical drugs	Menthol 1% twice daily	Effective in one large nonrandomized study and nontoxic, with 82% of patients reporting clinically significant relief and better mood[50]	Randomized trials are ongoing. Do **not** use 10% menthol creams like Bengay or Tiger Balm—dilute to 1%
	Baclofen-amitriptyline-ketamine gel twice daily	In RCTs, improvements in pain and sensation; worked better on hands[51]	Works best on the hands, not the feet. Trials of higher concentrations are needed
	Gabapentin	There are no randomized trials. Relieves pain of vulvodynia, postherpetic neuropathy, and other local pain problems. In a recent series, 20 of 23 patients benefited with pain scores falling from 8.2 to 5.6 at 1 mo, and 11 of 23 achieved a clinically meaningful 30% reduction in pain[52]	Most centers use 6% gabapentin, compounded, applied 3 times daily. It does affect local nociception,[53] so there is rationale for it working
	Lidocaine 5% patch	Limited randomized trials. A recent study reported a reduction in pain of 0.3 points compared with placebo for peripheral neuropathic pain[54]	Expensive—$10 per patch generic. Try for 1 d and evaluate before commitment

NSAID = nonsteroidal anti-inflammatory drug; RCT = randomized controlled trial.

break-through or rescue doses, adaption of regimens based on individual needs, patient education, and administration via the oral route when possible. We commonly use some modifications to these recommendations. These modifications include the use of low doses of strong opioids for mild-moderate pain (elimination of step 2 on the ladder, especially the use of codeine, because 10% of patients do not metabolize these medications to the active component, as now recommended by the National Comprehensive Cancer Network[60]), concerns about long-term use of NSAIDs on renal and cardiac health, validation of various routes of administration, the addition of a fourth step of interventions for severe and intractable pain, and specific recognition of neuropathic pain requiring a different approach.[61,62] Some available modalities of treatment are provided in Tables 3 and 4.

At least 15% of patients will not experience pain relief with pain medication or will have severe adverse effects. In these patients, nerve blocks or other interventional procedures are needed (Table 5). In our experience, many health care professionals have little experience with the power of nerve blocks. We describe a splanchnic nerve block to our patients in simple terms: "Remember when the dentist put some Novocain into your cheek and your teeth suddenly stopped feeling pain? Same principle. You will know if it works right away, and if it does, you will ask why we did not do this months ago."

Some common practices in pain management that should be avoided are presented in Table 6.

STEP 3: PREVENTION AND MANAGEMENT OF ADVERSE EFFECTS

There are important opiate-induced adverse effects to anticipate, prevent, and educate patients and families about. Some are predictable and expected such as constipation, fuzzy-headedness, and mild nausea. Most patients

TABLE 4. Nondrug Pain Treatments

Method	Current uses	Effectiveness	Comments
Radiation therapy	Bone pain	60% or more patients experience pain relief in days[63] that may last months	Important to emphasize that pain relief will not occur in just 1 day but takes several days to kill enough cancer cells to relieve pain. Single-fraction radiation is strongly recommended if possible for convenience, efficacy, and cost[64]
Surgical procedure	Obstruction, abdominal pain	Very little actual data because many patients die before reevaluation[65] May be used more for obstruction	The disease situation carries a high mortality, so this should be an automatic hospice or palliative referral "trigger"
Nerve blocks	Celiac and other plexus blocks, local injections	In general, about a 75% chance of success, with the ability to repeat in the future if needed	See Table 5
Acupuncture	Cancer pain	There is good evidence for benefit in nausea/vomiting but less for cancer pain because of the high risk of bias in studies or underpowered trials[79]	Pain is the most common cancer symptom for which acupuncture is used. Nine of 11 trials of acupuncture reported positive results but had a high risk of bias. Because the risks are low, acupuncture is worth a trial for most patients
Advanced locoregional pain techniques	Spinal cord stimulation	Over half of patients experience significant benefit[80]	Pain relief can be instantaneous and dramatic, without opioid and drug side effects, but requires a referral to a pain specialist
	Peripheral nerve stimulation	Appears similar to spinal cord stimulation but with no randomized trials	Insertion of sterile electrodes around the painful area, with stimulation across the area of pain. Not widely available
	Intrathecal infusion	Randomized trial found better pain control, less drug toxicity, and longer survival compared with conventional best pain management[55]	Preservative-free morphine is the only FDA-approved drug, but fentanyl, hydromorphone, bupivacaine, and clonidine are commonly added
	Scrambler therapy	One randomized trial and 16 uncontrolled trials found some relief of pain with minimal adverse effects (Mathia et al 2015; unpublished data)	Better designed placebo-controlled trials are needed to reduce risk of bias
Integrative therapies	Music therapy, massage, and healing touch have definable benefit	An excellent review documented no harm and modest evidence of improvement[81]	Widely available, but not usually require out of pocket payment. Welcomed by patients as no side effects and gives a sense of control

FDA = US Food and Drug Administration.
Modified from Springer-Verlag.[82]

with pain will need a stool stimulant or softener; however, for hospice patients, there is no advantage to using a stool softener.[93] If opioid induced, constipation refractory to an aggressive bowel regimen can also be managed with the use of methylnaltrexone, a modification of naltrexone that does not cross the blood-brain barrier and therefore will not reverse analgesia. In the most recent placebo-controlled trial, 63% of patients achieved a bowel movement with use of methylnaltrexone compared with just 9% in those receiving placebo.[94] The primary adverse effect of methylnaltrexone is the expense.

The management of nausea and vomiting associated with opioid use is based on practical experience and nonrandomized trials. The available evidence suggests that dopamine antagonists such as prochlorperazine or metoclopramide may be the most effective, available, and inexpensive; serotonin-blocking ondansetron can be effective but is much more expensive and can be constipating.[95]

UNRESOLVED CLINICAL QUESTIONS AND FUTURE DIRECTIONS

The biggest unresolved issue in pain management is neuropathic pain because of relatively ineffective drugs, some placebo response, publication bias, and no major "winners."[96] Long after the stimulus is gone, the nerve is still sending a danger signal that can be disabling.

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TABLE 5. Summary of Evidence for Intra-abdominal and Ganglion Nerve Blocks[a]

Type of block	Indication	Effect on pain	Adverse effects
Celiac plexus[b]	Deep visceral pain especially from the pancreas or nearby organs	70%-96% success in pancreas cancer,[66] often lasting months May be very successful in pancreatitis[67]	Hypotension, diarrhea (usually a good sign that the right area was reached and blocked)
Superior hypogastric plexus block[b]	Pelvic pain from recurrent rectal, bladder, uterine, cervical cancer	If diagnostic block is successful, long-lasting pain relief occurs in 72% of patients[66] whether done early or late in the disease course[68]	Hypotension, diarrhea
Splanchnic nerve block[b]	Deep visceral pain for more diffuse metastases or sites of disease	Good to excellent success[69]	The splanchnic nerves are "upstream" of the celiac plexus, and block may cover more of the entire upper abdomen
Stellate ganglion block	Menopausal hot flashes, upper extremity pain, PHN, angina, Raynaud disease, angina pectoris, phantom limb pain, CRPS	Safe, with 64% reduction in hot flashes.[70] Safe and effective but few randomized or large trials[8]	Paresthesias, anesthesias
Ganglion impar block, anterior to the sacrococcygeal junction	Perineal pain	Good to excellent relief for perineal and coccyx pain, 90% response with >50% reduction in pain[71]	Can treat pain including pelvic, genital, perineal, anal pain, and visceral pain in these areas
Brachial plexus block or infusion	Chronic pain from cancer, scar, radiation, accidents	Few large series but small reports detail excellent pain relief[72]	Thoracic ganglion blocks may also be highly effective in similar patients[73]
Lumbar sympathetic block	Lower extremity cancer pain, phantom limb pain, CRPS, PHN, pelvic/urogenic pain, vertebral fracture pain	Few large series. In a recent randomized trial, L2 block for osteoporosis/fracture pain helped for 2 wk but not beyond that time[74]	Can relieve lower back or leg pain, especially if due to the abnormal vascular tone of complex regional pain syndrome
Peroneal or popliteal nerve	Chronic ischemia-related or cancer-related pain	Good results in chronic ischemia with either local anesthetic or combined with morphine[75]	Few to no trials in chronic pain. IV ketamine may be a better choice for ischemic pain based on small single-arm trials, either as a single infusion[76] or low-dose continuous infusion[77]

[a]CRPS = complex regional pain syndrome; IV = intravenous; PHN = postherpetic neuralgia.
[b]Only visceral pain responds, not bone or muscle pain from the same region.
Modified from *Ann Oncol*.[78]

We and others have had good clinical success with a novel method of cutaneous electrical stimulation. The machine synthesizes 16 different electrical currents, assembles them into packages, and transmits them to the existing nerves using modified electrocardiogram pads for 30 minutes a day. In the largest review, Mayo Clinic researchers included 16 clinical trials (Mathia et al 2015; unpublished data) with some positive effect ranging from 25% pain relief in low back pain, 50% to 60% relief of refractory chemotherapy-induced peripheral neuropathy,[97,98] and 95% pain relief in postherpetic neuralgia, failed back syndrome, and spinal cord stenosis[99] with no toxicity. However, randomized trials are still needed. High-intensity light treatments (photon therapy that penetrated 4 cm into the tissue with no adverse effects) has been reported to improve quality of life and sensation in patients with diabetic neuropathy while not affecting pain significantly[100]; further trials in patients with cancer are ongoing and demonstrate how much we still have to learn about nerves.

An unexplored but highly promising field is mindfulness-based stress reduction and cognitive therapy, which had positive effects on stress and on mental and some physical functioning in multiple randomized trials.[101] Recent data reveal that mindfulness-based stress reduction is effective for cancer-related fatigue and chemotherapy-induced cognitive dysfunction,[102] but effects on pain have been nonsignificant[103]; we are not aware

TABLE 6. Common Mistakes in Cancer Pain Management

Mistake	Remedy	Evidence
Not assessing for neuropathic pain and treating everything with opioids without trying gabapentin first	Always do a full assessment including for neuropathic pain	Opioids alone help neuropathic pain as does gabapentin, but the combination is more effective than either alone[83]
Treating chemotherapy-induced peripheral neuropathy (CIPN) like any other type of neuropathic pain such as diabetic neuropathy	**Do** use duloxetine. **Do not** use gabapentin or other drugs for CIPN until proven beneficial in randomized trials[84]	The only drug to date with significant activity in CIPN is duloxetine, which reduced pain scores from 6 to 5 in 6 wk.[85] Do not use acetyl-L-carnitine, which looked promising in phase 2 trials but is actually harmful[86]
Not sending patients with pancreas cancer or other serious pain for consultation with a pain specialist	**Do** refer patients to a pain specialist early. Develop a working relationship with a pain management team, just like with radiation oncology	Pain relief from splanchnic block is often immediate (minutes to hours), is long-lasting (months), and can be repeated if needed. The initial randomized trial found that patients who underwent chemical splanchnicectomy had longer survival,[87] but a modern trial reported only markedly better pain relief with neurolytic block vs opioids, with 16% vs 6% of patients alive at 2 years[88]
Not performing single-fraction radiation for painful bone metastases	Instruct radiation therapists to give single-fraction radiation whenever possible	It works just as well as 10 fractions in most people, with 60% of patients having pain relief and 25% being pain free.[63] One in 8 patients may need retreatment, but repeated single-fraction radiation is also effective and has less toxicity than multiple-fraction radiation.[89] Single-fraction radiation is recommended by all national guidelines, works quickly, is much easier to perform, and is less costly for families
Putting a lidocaine patch on anything that hurts	Lidocaine patches work slightly better than placebo for myofascial pain[90] at 7 d but not at 1 mo. They may help with postthoracotomy or mastectomy pain or for local recurrences,[91] but randomized trials are lacking, and a Cochrane database review found no convincing evidence for efficacy[92]	Even generic patches are $10 each, and because they often are not covered by insurance, they can be a financial burden. If you must use them, try one to see if it works before committing your patient to the expense

of any trial with cancer pain as a primary end point.

CONCLUSION

Cancer pain remains an unresolved problem 20 years after initiation of a campaign to make pain the fifth vital sign. The primary barriers for effective pain management include (1) inadequate pain assessment and management training (lack of awareness of one's own knowledge deficits), (2) failure to refer patients to pain management specialists, (3) patient reluctance and poor adherence (not covered in this review), and (4) poor reimbursement for nonprocedural pain management (not covered in this review). These barriers are in addition to the complexities of pain itself.

Specific actions that providers can take are to always do a thorough pain assessment, learn to use both opioids and adjunctive medications, tailor neuropathic pain treatments to the cause of the pain, and refer patients to pain specialists earlier and more often.

Abbreviations and Acronyms: **NSAID** = nonsteroidal anti-inflammatory drug

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The Symposium on Pain Medicine will continue in an upcoming issue.

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