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Symptom management in the older adult- 2015 Update

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Pain management

Pain is still common, and commonly undertreated

Dr. von Roenn wrote that “Pain is the most common symptom for which patients seek medical attention and is one of the most frequent complaints of older adults.” That has not changed. The good news is that, at least for cancer patients, being older is no longer associated with pain medication under-prescribing², as it was in 1994. The bad news is that moderate to severe pain is still as prevalent as it was in the 1990 despite a 10-fold increase in opioid prescribing³.

Dr. Thomas Finucane covers the important elements of pain relief elsewhere in this issue. Here, we will review some of the barriers to pain and symptom management and concentrate on non-pain symptoms – in which there has been significant progress. Recent reviews of management in older adults stress the multi-modality approach.⁴

The barriers to pain management in older adults remain much the same as in 2002. Patient barriers include at least the following:

- reluctance to complain,
- under-reporting of pain,
- interpretation of pain as other words such as “discomfort”,
- reluctance to take analgesics,
- co-morbidities that make prescribing more difficult, and
- the high cost of some pain medications, added to the cost of other medications. For instance, the price of each generic extended release oxycodone 20 mg pill is about \$5, and a 75 mg pregabalin (Lyrica®) capsule costs about \$1.50 apiece⁵.

Physician barriers remain the same as well, including reluctance to prescribe opioids (although more patients die of complications from non-steroidal anti-inflammatory drugs

than from opioids), inadequate training, fear of complications, fear of regulatory oversight, and drug interactions.

For pain: classify, classify, classify

The first principle of pain management is classification: neuropathic, and everything else. Damage to afferent nerve fibers produces neuropathic pain, at least at the start. A distinguishing characteristic of most neuropathic pain is that it becomes amplified long after the initial insult is gone. Imagine touching a hot plate with your fingers: immediate withdrawal from the heat (mediated by the fastest non-myelinated A-delta fibers), then near immediate sensation of pain (mediated by the slower myelinated C fibers), then moving away from the hot plate, then blaming your son-in-law for leaving the hot plate on. Then, imagine that pain becoming worse over the next years long after the burn healed.

Neuropathic pain

The exact mechanisms by which neuropathic pain becomes amplified and persistent is complicated and not easily explainable. At a minimum, there are increased nerve transmitter molecules and receptor sensitivity; extra nerve “channels” or amplification along the nerve pathway, which are far more plastic than imagined 20 years ago; heightened sensitivity to chronic pain that never remits; and “wind-up” of the nerve pathways in both the spinal cord and the brain⁶. Suffice it to say that nerve pain is often out of proportion to the original pathology.

The mechanism of nerve injury matters, too. For instance, chemotherapy has become a major producer of nerve pain, chemotherapy-induced peripheral neuropathy (CIPN). Drugs like bortezomib (Velcade) used in myeloma, paclitaxel (Taxol) or eribulin (Halaven) used in breast cancer, and any platinum drug such as oxaliplatin (Oxali) used in colon cancer can cause dose-limiting neuropathy in 70% of patients. In oxaliplatin CIPN, the longest nerves actually die and drop out, leading to lowered epidermal nerve fiber density⁷. In paclitaxel neuropathy, the longest nerves are damaged, with up to 25% of the damage happening in the year after the chemotherapy has stopped, but the nerves may recover. In diabetic nerve damage, the nerve death and damage appears to be nutritional rather than toxic, but the nerves are still dead or damaged.

Neuropathic pain is also easy to “score” with the 0–10 scale, just like usual pain. Remember to ask all the important questions for billing (and for patient care!): when did it start, what brings it on, what relieves it, what does it feel like, are there any associated symptoms? Neuropathic pain is typically described as sharp, burning, itching or hot, with associated numbness and tingling. If life were fair, nerves that were absent or damaged would just give numbness, but all too often numbness and tingling is associated with the worst nerve pain. There are useable, validated research scales such as the European Organization for Research and Treatment of Cancer CIPN-20 or the DN4 questionnaire, but they are not in widespread use outside of clinical trials⁸. We think it is more important to classify the pain as neuropathic, and ask “How is the pain limiting your activities?”

The physical exam is critical for neuropathic pain. First, allodynia (a painful impulse felt after normal touch, like brushing the skin), and second, because of the success of local nerve

blocks with local anesthetics such as lidocaine or bupivacaine. If the pain can be localized to a single or localized pain generator or ganglion, then it has a good chance of being blocked. Examples include occipital nerve neuropathy or pancreas cancer pain that can be treated with a local celiac or splanchnic plexus block in 75% of cases.

Neuropathic pain is treated differently from usual somatic pain: we try to quiet down the damaged nerves with anti-seizure drugs or other neuroleptics, slowly, over weeks and months. Commonly used agents include tricyclic antidepressants (desipramine, nortriptyline), anticonvulsants (pregabalin, gabapentin, carbamazepine, valproic acid), and topical agents (lidocaine, capsaicin). This is a critical teach-back moment for practitioners, as the patient must know this is a long-term strategy to allow the damaged nerve to stop “pinging” and to allow normal nerves to regrow. Neuroleptic drugs are not good pain killers by themselves, so the patient must be encouraged to give the drug at least a one-month trial even if they do not feel any relief.

The actual treatment of neuropathic pain should be relatively simple as outlined in Table 1. The largest randomized trial showed that the combination of an opioid (morphine) and a neuroleptic (gabapentin) was more effective than either alone⁹. We make the assumption that this holds true for any opioid and any neuroleptic, but evidence is scant. In fact, the Cochrane Systematic review concluded that there was no evidence that oxycodone had any sustained effect on neuropathic or fibromyalgia pain, and the usual harms¹⁰ but other expert review panels concluded there was enough evidence of benefit.¹¹

We also often hear that “Methadone is the best opioid for neuropathic pain.” but the evidence is lacking. The one largest randomized trial in cancer patients showed that morphine and methadone were equivalent in the relief of neuropathic pain, but the number of patients was too small to rule out some additional benefit¹².

Our advice is to pick a neuroleptic drug that is safe and affordable for your patient (starting with gabapentin or pregabalin as the usual first choice¹³), escalate to pain relief or the maximum tolerated dose, and convince the patient to try for at least 4 to 6 weeks.¹⁴ If not successful, start again with a different drug. Many of us do not have the experience, patience or time to do these sequential drug trials so referral to a chronic pain specialist may be helpful. Using a simple algorithm with proven drugs, neuropathic pain could be promptly and significantly reduced in nearly all cancer patients, from 5.4/10 to 2.8/10 at 12 weeks.¹⁵

Somatic pain is well described in Dr. Finucane’s article. As Dr. von Roenn describe in 2002, the “initial approach to a patient with pain begins with a comprehensive pain assessment, including a thorough history of the pain, its impact on activities, and prior therapeutic interventions and their outcomes; a complete physical examination; review of all medications; and evaluation of functional status. Older patients may present with atypical manifestations of pain, including delirium, confusion, fatigue, social withdrawal, and depression. Additionally, screening for depression and anxiety is important because either state can augment the pain response and interfere with pain control.”

The general approach to pain and associated symptoms is the same today as in 2002. We use a single question for depression screening, “Are you depressed?” or “Are you bothered by

depression?” to remind ourselves to assess this on every visit. While not perfect, single question screening has good reliability in most populations and is better than no screening tool at all^{22,23}. Delirium is also more prevalent in older patients and requires a separate screening tool.

We have sequentially modified our “rounding tool” from that used in a large multi-institutional study to the current very short form. (Table 2) The advantage is that this reminds us to ask the questions, and each question has some readily available fixes. We import this as a Smart Phrase into EPIC, and the boxes let us add the most important questions. For instance, if the patient is depressed, we will directly ask “What makes you most depressed?” and explore the topic fully. Our group has subsequently attempted to standardize responses to such patient reported outcomes – for each symptom, the practice should have a standard approach²⁴.

Nonpharmacologic techniques

Nonpharmacologic techniques can be an integral component of pain management. Even if they do not work fully, they may allow a lower opioid dose or allow the patient to have more control over the situation. We give some examples in table 3.

Pharmacologic pain management

Special considerations in older adults

Dr. Finucane outlines many of the relevant parts of the aging process and pain medications in his article. Some additional considerations, based on our experience, include the following:

- Renal function declines with each year and decade, and the risk of NSAID induced renal failure is higher. For many older adults, muscle mass is diminished so that the creatinine is artificially low.
- Liver function declines less than renal function unless there are other liver illnesses and is easier to estimate based on the liver function tests.
- Cachexia and lower fat stores means that fentanyl transdermal will not be absorbed as well. It still works, and is the least constipating of all the opioids, but a cachectic person may need almost double the expected dose³².
- For moderate or severe pain, opioids are the drugs of choice. Start low and escalate the dose over days, not hours.
- Blood levels of opioids bear almost no correlation with pain relief.
- For the person in acute pain, intravenous in-hospital titration with conversion to oral doses once stable, is faster than outpatient oral management.
- The prescribing hand that forgets to write the bowel regimen when prescribing the opioid is the hand that gets to do the disimpaction.

Nonopioids

Tramadol is available worldwide, inexpensive, and equal to low dose morphine³³. It has characteristics of both anti-depressants and opioids, and should be used in caution with SSRI/SNRI drugs at the risk of causing serotonin syndrome. However it is generally well tolerated, has some proven efficacy in neuropathic pain³⁴, and can be useful where opioids are not wanted. The starting dose is 50 mg twice a day with a maximum of 300 mg. We teach pain relief around the world in ELNEC and had to add a module for tramadol as it is uniformly available, inexpensive, and has none of the stigma of opioids. Tapentadol (Nucynta®) has a similar mechanism of action (agonist of the μ -opioid receptor and norepinephrine reuptake inhibitor) and efficacy³⁵ but is expensive at \$3–\$9 per pill.

Acetaminophen remains the drug of choice for mild pain, as it was in 2002. It works on the COX-2 receptors in the brain, and has a different mechanism of action than all the other agents, so is useful in pain management. I tell people we are building a layer cake of pain relief: we can use layers of acetaminophen, NSAIDs if safe, opioids, and nerve drugs till we get the pain down to 4 or less. Above 6, most patients will be thinking of little else than their pain; at 4 or below, the pain is tolerable. Patients should stay well below the 4 grams/day prohibition, and may need to count all their “Nyquil” and other drugs.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have changed markedly since 2002, when there was great excitement about Celecoxib (Celebrex®), rofecoxib (Vioxx®) and valdecoxib (Bextra®) as safer cyclooxygenase-2 inhibitors. Currently, only celecoxib is in common use and can be helpful for patients in whom other NSAIDs are ineffective or contra-indicated.

Corticosteroids reduce edema, and are used as adjuvant analgesics despite lack of a robust evidence base. In our own practice, we use them for liver pain, liver capsule pain, and bone pain (avoiding concurrent NSAID use). The right dose is not known for any of these indications, so we will give 4–16 mg in one daily dose in the morning to avoid late day sleeplessness.

Opioids

As in 2002, “Opioids remain the cornerstone of pain management and are the preferred agents for moderate-to-severe pain. A weak opioid is appropriate for acetaminophen-unresponsive mild pain in a patient not considered a candidate for NSAIDs. Opioids alleviate pain for most patients.” Nothing has changed since then.

We can make several generalizations:

- Geriatric patients may be reluctant to take opioids, until they find relief from them. MAKE SURE you tell people that “fuzziness” and nausea and itching are common with the first several days but wear off.
- Start with half the dose you would give a 40 year old patient, e.g. oxycodone 2.5 mg every 4 hours rather than 5. It is easier to titrate up than to convince a patient to re-try the drug that made him sleep for 3 hours.

- All the common short acting drugs work for 3–4 hours, so it makes no sense to write a prescription saying every 6 hours.
- Remember to start a bowel regimen.
- If patients are needing several daily doses, consider a long acting drug. There are no comparative studies of long acting morphine plus short acting oxycodone versus the opposite, so stick with one drug for the immediate and long acting drugs.
- That said, everyone's opioid receptors are different, and we have many patients who do well with long acting fentanyl and immediate release oxycodone. Just do not have them on 3 different long acting drugs – maximize one.
- Don't use Meperidine (Demerol®), Propoxyphene (Darvon®), or Pentazocine (Talwin®) a mixed agonist/antagonist.
- If patients are on a long acting drug, make sure they have an immediate release (“rescue”) drug available at about 10% of the daily dose of the long acting drug. For example, someone on 300 mg of daily oral long acting morphine should be on 30 mg as the short acting dose, not 10 mg.
- Use an opioid calculator to recommend dose adjustments. Some examples are <http://www.globalrph.com/narcoticonv.htm>, or <http://clincalc.com/opioids/> or others.

Methadone

- Use methadone IF you have experience using it. It is a wonderful long acting opioid, but patients show wide variability to its effects, and respiratory depression is possible.
- Start low and titrate doses no more than every 3 days unless you have experience and a highly opioid tolerant patient.
- And check an ECG to make sure the QTc interval is normal before starting. Many of the new cancer and cardiac drugs also effect the QTc interval. While torsade de pointes and ventricular fibrillation are rare, they could be preventable³⁶.

Specific pain situations common in older adults

Myofascial pain

Myofascial pain is pain due to overuse, or just use, when joints and muscles are not as young as they used to be. Since 2002 there have been substantial strides in both treatment and evidence. The data are clear that topical NSAIDs are beneficial³⁷. Derry et al focused on studies lasting longer than 8 weeks and found “Topical NSAIDs were significantly more effective than placebo for reducing pain due to chronic musculoskeletal conditions.” There was an increase in local adverse events (mostly mild skin reactions) with topical NSAIDs compared with placebo or oral NSAIDs, but no increase in serious adverse events. Gastrointestinal adverse events with topical NSAID did not differ from placebo, but were less frequent than with oral NSAIDs. Mild skin reactions were more common than with oral drugs, but there was less gastrointestinal and renal toxicity. This fits with previous research

that shows the concentration of NSAIDs in the joint fluid is substantially higher than in the blood.

Topical patches

Lidocaine 5% topical patches (Lidoderm®) also helped myofascial pain syndrome of the upper trapezius in a randomized, double-blind, placebo-controlled study – somewhat³⁸. (These may be very useful for people who have contraindications to NSAIDs. The primary endpoint, pain in the shoulder and neck, improved over 14 days compared to placebo, with less neck disability. However, at 28 days there was no difference between placebo and lidocaine patches.

Metastatic bone pain: prevention

The outlook of cancer patients has changed slowly but surely since 2002, when it comes to bone metastases. When I was in intern in 1979, the wards were full of patients with fractured femurs or hips and a calcium of 16. Now, both are half as common.

The big advance has been bone-modifying agents³⁹, first the bisphosphonates (pamidronate then zoledronic acid (Zometa®), followed by RANK-ligand inhibitors (denosumab, Xgeva®)⁴⁰. Given to patients with solid tumors and bone metastases, the risk of a “skeletal related event” (fracture, need for surgery or radiation therapy) has been cut by over half⁴¹. These drugs were initially given every month until the patient died, but recent randomized trials show that once-monthly treatment for a year, followed by every-three-month treatment is as effective. Denosumab is slightly more effective than the bisphosphonates, but the cost may be prohibitive for some patients and insurers. Denosumab is a single monthly subcutaneous injection, versus a 20 minute intravenous infusion.

The precautions with the drugs are the same. Renal failure with a creatinine over 3 is a relative contraindication, but if caused by hypercalcemia may be necessary. Osteonecrosis of the jaw has been increasingly recognized since the mid-2000's, and happens to 1 or 2 people who receive these drugs. It presents as an open non-healing ulcer down to the mandible or maxilla, often where was trauma such as radiation or a recent extraction. The exact mechanism has not been fully determined but risk is proportional to the length of time on these drugs, and the total doses.

Metastatic bone pain: treatment

Successful management of metastatic bone pain demands a multidisciplinary approach just like it did in 2002, with the same list of “systemic analgesics, bisphosphonates, radiopharmaceuticals, and external-beam radiation therapy.” It is critical that patients with bones at risk for a pathologic fracture (a long bone with 20% or more loss of the cortical bone, or over 3 cm long, or a vertebrae) be evaluated by an orthopaedic surgeon.

Pain relief is still critical to treatment, starting with NSAIDs and steroids, followed by opioids. Recognize that the pain while moving will be worse than the pain while being still, and give patients a breakthrough medication to take 15 minutes before they have to get out of bed or go to physical therapy. (See “Incident pain” below)

Radiation therapy for bone metastases has changed dramatically in the rest of the world but not so much in the U.S. All the relevant guidelines call for, if feasible, a single large dose (8 Gy) of radiation (“hypo-fractionation”) instead of the traditional 10 or more smaller fractions. This is based on numerous randomized clinical trials showing equivalent bone pain relief, and the need for 1 consultation and treatment rather than visits for consultation, simulation, and 10 treatments. In addition, the cost to society is half as much. However, the revenue to radiation oncologists is similarly cut substantially. Some radiation oncologists will argue that 1 in 8 survivors will need retreatment (meaning 7 of 8 do not), but there is now compelling data that shows a single large fraction of retreatment works just as well as longer regimens. Moghanaki et al have taken this one step further: for hospice patients, they will simulate and treat in one session for \$400 total, and had 100% relief of pain in a small series⁴². (Schuster 2014)

The use of radiopharmaceuticals has increased since 2002 but only for cancer patients. These only work for osteoblastic metastases, not osteolytic holes such as with myeloma, because the radioactive technetium is taken up by macrophages involved in inflammation. The radioactive molecule replaces calcium in the bones, and gives a radioactive particle path of less than 1 cm, so surrounding tissue is uninvolved. The marrow is radiated so anemia and thrombocytopenia are the most common side effects. The most common use is for patients with multiple bone osteoblastic metastases where pain relief can be obtained within 48 hours and last for 3 to 6 months. The most recent addition, Ra 233, actually improves the average survival by 5 months from ___ to ___ in patients with metastatic prostate cancer.

Incident pain

Mercadante has shown that “incident pain,” or pain with movement from bone metastases, is exceedingly difficult to control with any measure other than radiation. The most common dose of morphine for incident pain, rapidly titrated intravenously on day 1, was 102 mg when converted to oral doses⁴³. More recently, the same group has shown excellent response of incident pain to co-administered ketamine and switching the opioid to methadone, but the study was only 2 patients⁴⁴. (Clin J Pain. 2009 Sep;25(7):648-9) Incident pain was also relieved in one patient with a bisphosphonate infusion as part of the initial therapy⁴⁵ but this study has not been replicated.

Miscellaneous bothersome symptoms

Itching

One word: gabapentin. Gabapentin works for itching due to burns, histamine release from hematologic malignancies, cancer, uremia, and most other pruritis. (REF)

However, gabapentin does not help pruritis due to liver disease and bile cholestasis. Paroxetine (Paxil) at 10 mg a day was rapidly successfully in 3 Japanese patients (REF) and in my own practice. Sertraline (Zoloft) was highly successful in small randomized trials compared to placebo for cholestatic pruritis, and is safe and now generic.(REF)

Cough

The breakthrough clinical trial was the use of gabapentin for chronic idiopathic cough. Compared to placebo, gabapentin reduced cough intensity and frequency and the cough-quality-of-life score by half⁴⁶. (REF) Gabapentin has not been tested for the cough associated with pleural effusion, bronchiectasis, idiopathic pulmonary fibrosis, etc. but the central mechanism of action should still hold in at least some of these cases⁴⁷. The usual doses, 300 mg daily to start (100 mg in frail patients) escalating to 1800 mg, are used.

Hiccups

There are no new clinical trials and no good evidence behind any of the interventions we try. We trial baclofen, prochlorperazine or other -zine's, and benzodiazepines.

Fatigue

There are two interventions with high power randomized clinical trials to back their use: American ginseng, and dexamethasone in those near the end of life. There are several trials of psychostimulants in cancer-related fatigue that show mixed and mostly negative results.

Barton et al at the Mayo Clinic did a pilot trial, then a large randomized trial of American ginseng at 0 mg (Placebo), 2000 mg, and 4000 mg a day in patients with chemotherapy related fatigue. The side effects were the same in all three groups. There was no effect on mental fatigue, but physical fatigue improved enough to be clinically important at 4 and 8 weeks⁴⁸. The mechanism of action of ginseng is unknown but it may be anti-inflammatory and restorative. They used American ginseng from Wisconsin, purchased at the Ginseng and Herb Cooperative (<http://www.ginsengherbco-op.com/>) at about \$14 for a month supply. The evidence for other types of ginseng such as Siberian or Korean is less robust, and less robust for other conditions than cancer-related fatigue.

Bruera and colleagues at M. D. Anderson Cancer Center studied dexamethasone 4 mg twice a day versus placebo, for 2 weeks, in patients with advanced cancer. Fatigue was clinically and significantly reduced, global quality of life was improved, appetite was improved, and side effects were the same with placebo⁴⁹. This has become our "go to" drug for rapid improvement in quality of life and energy in the last 3 months of life, as long as diabetes is not a problem.

The use of psychostimulants such as methylphenidate in cancer patients has been disappointing. Promising uncontrolled trials⁵⁰ led to larger negative randomized, placebo controlled trials with methylphenidate in breast cancer patients⁵¹ or in general cancer patients except those with very high level of fatigue⁵². Similarly, modafinil that works in multiple sclerosis had no effect in advanced cancer patients⁵³ leading authorities to recognize that psychostimulants cannot overcome somatic fatigue⁵⁴. The one promising aspect of these studies has been that the response to the first day of methylphenidate is highly predictive of eventual effect⁵⁵, so a patient can be "trialed" with a 5 day supply and only continue if it works for her/him.

Respiratory symptoms

Dyspnea

Dyspnea, the uncomfortable awareness of breathing, is common in palliative care and up to 75% of patients experience it near the end of life. Dyspnea is common no matter the underlying terminal diagnosis.⁵⁶ We routinely differentiate dyspnea – trouble breathing – from hypoxia and low oxygen saturation. Some patients will have extreme dyspnea with 98% oxygen saturation, and others will be comfortable with 82%. Since oxygen represents another tether upon which to trip, and can cost \$25 to \$250 a day in the hospital or with home hospice, it should only be provided when needed.

The evidence base on which to choose therapy has expanded in the last decade. A 2008 meta-analysis of 134 cancer patients with dyspnea failed to show any benefit to oxygen therapy⁵⁷. Abernethy et al subsequently randomized 239 patients with dyspnea and PaO₂>55 mm Hg to 7 days of oxygen or room air, and found no meaningful difference in any measure; of note, dyspnea decreased with both oxygen and room air.⁵⁸

There is some variation in the usefulness of oxygen according to the underlying disease. In patients with COPD and symptomatic dyspnea but without hypoxemia, medical oxygen therapy does have beneficial effect, even in those who would not traditionally qualify for oxygen treatment.⁵⁹ The effect is in breathlessness and fatigue, with no discernible benefit on survival.⁶⁰

Opioids are still the mainstay of dyspnea treatment as they have been for 2000 years⁶¹, even though the clinical trial evidence for most situations is lacking⁶². The basic science understanding has increased with the discovery of endogenous opioids (endorphins). In an elegant experiment, investigators showed the importance of endogenous opioids by giving naloxone (Narcan®) to dyspneic patients, and worsened their dyspnea⁶³. We start patients on extremely low doses of oxycodone or morphine, 2.5 to 5 mg, every 4 hours. If patients have benefit, we will try 10mg of extended release morphine as done by Currow et al in Australia. At least a third of patients achieved clinical benefit that was long lasting, but constipation was a problem even with prophylactic senna.⁶⁴

There may be a role for benzodiazepines in the treatment of dyspnea but the evidence is slim. In one recent study, investigators added clonazepam 0.5 mg at night to extended release morphine in the morning for 15 COPD patients. the treatment was safe and appeared to have some benefit, so larger randomized trials are ongoing.⁶⁵

We and others have investigated inhaled nebulized medications for dyspnea, as they are preferred by most patients⁶⁶, but the randomized clinical trial evidence is still lacking⁶⁷. Morphine appears not to work any better than placebo. Inhaled nebulized fentanyl appeared to benefit patients in an uncontrolled study^{68,69}, so a randomized trial is ongoing.

Pulmonary secretions

Hospice and palliative medicine professionals try to prevent or treat the “Death Rattle” or secretions in the back of the throat because it is so distressing to all involved. We typically

start with a scopolamine transdermal patch every 3 days, then give scopolamine or glycopyrolate in the same doses we would give in the operating room. We, as did professionals and caregivers in the UK, often feel pressured to “do something!” even if we know it is unlikely to help.⁷⁰

However, the evidence behind any of these interventions is lacking. Mercadante reviewed 11 randomized trials and found no clearcut evidence of effectiveness of these measures as treatment modalities.⁷¹ An even more comprehensive systematic review of 99 studies found a high prevalence, but no evidence of benefit for any intervention.⁷² In addition, scopolamine 0.43 mg subcutaneously, caused significant psychomotor slowing, but no effect on cognition or memory, in elderly patients compared to 10 younger patients so it should be used with caution⁷³ – if psychomotor slowing is an issue. A more realistic approach is to reassure the family that the patient is not suffering, position the patient for maximum comfort, and offer therapeutic presence with or without drugs.⁷⁴

Neuropsychiatric symptoms

Depression

Depression remains under-diagnosed and under-treated. As discussed, we use a single question screening method, “Are you depressed?” or “Are you bothered by depression?” as a way to start the assessment. It is essential to differentiate some situations that masquerade as depression:

- fatigue (physical causes),
- sleep deprivation,
- apathy,
- sadness (for many reasons including serious illness, isolation, etc.)
- loneliness
- demoralization (loss of morale, or the will to continue, due to medical or other issues).

The fixing of each of these issues requires more than a pill and rearrangement of brain biochemistry, although treatment of depression may help each situation.

Treatment of depression in older adults is the same as in younger adults, with no significant changes in the last decade. We have listed some of the common treatments in Table 4.

Delirium

There are several decisions to make about delirium: diagnosis, evaluation, and treatment.

The diagnosis should be straightforward: delirium is an acute disturbance in consciousness, cognition, and attention. It is among the most common symptoms, and can be the most upsetting to families. We use the Confusion Assessment Method (CAM) routinely⁷⁸ (having learned from our ICU nurse colleagues) especially Feature 4, but there are other measures (Box 1).

The evaluation depends on the goals of the patient and family, the expected lifespan estimated with the palliative performance scale (very accurate when the person is bedbound⁷⁹) and our estimation that a correctable cause can be identified. We first look at all the medications especially at opioids (especially sudden discontinuation leading to withdrawal), steroids, anti-depressants, sleep aids such as quetiapine or mirtazapine, and for any benzodiazepine. It is important to let the family know that the effects of the medicines may take several days to wear off.

If we treat delirium, we start with a standardized approach:

- family or a sitter at the bedside
- orientation and re-orientation
- a well lit home-like room, with the dates and clues available (like most skilled nursing facilities do)
- haloperidol at low doses, starting the 0.25 to 0.5 mg IV or orally. The dose needed to control delirium is almost always less than 3 mg a day⁸⁰.
- alternatives to haloperidol include Quetiapine (Seroquel®), risperidone (Risperdal®) and olanzapine (Zyprexa®).
- If the patient has been on long-term opioids, remember to continue enough to prevent withdrawal.

Gastrointestinal symptoms

Constipation and fecal impaction

Constipation remains a common problem in palliative care no matter what the age but particularly so in geriatrics. The bowel itself has slower transit, and the list of medications that cause constipation continues to grow. The most common unexpected culprits we see are opioids, ondansetron and similar drugs, and calcium channel blockers.

We have a stepped approach that works for nearly all patients.

1. More fluids, till the urine is light yellow. Do this with all the other remedies.
2. First, we ask “what have you used in the past for constipation?” and start with what the person has used successfully.
3. More dietary fiber including fruit, fruit juice, bran, supplements. A good recipe is 3/4 cup of prune juice, one cup of applesauce, and one cup of coarse unprocessed wheat bran mix. This can be stored in the refrigerator. Take 1–2 large tablespoons, with at least 8 ounces of water. Some add Milk of magnesia to the mix for added effect. Do not use bulk forming agents if the person is dehydrated.
4. Senna tablets. In hospice patients, surfactants such as docusate (Colace) did not add any effect to senna, in a randomized trial.⁸¹ Give enough till the person has a bowel movement, then continue.

5. Magnesium citrate is inexpensive, readily available, and familiar. We tell people to take about 30 cc's (a shot glass) hourly until they have a bowel movement.
6. Generic polyethylene glycol 3350 (Miralax) use has become commonplace and has replaced lactulose, sorbitol, and other osmotic agents.
7. We use subcutaneous methylnaltrexone to reverse the effect of opioids on the bowel⁸², but rarely due to the success of prevention, and the high cost of the drug (at least \$45/dose.) Do not administer for ileus. There have been a few reports of opioid withdrawal after disruption of the blood-brain barrier by radiation or surgery, so use with caution in patients with recent brain surgery or radiation.

Bowel obstruction

Bowel obstruction remains a problem in advance cancer patients, especially rectal, colon, pancreas and ovarian cancer. It is often associated with carcinomatosis (peritoneal metastases) and malignant ascites, and is strongly associated with a median survival of less than 6 months⁸³.

The optimal treatment of malignant bowel obstruction has become less clearcut in the past years. As Dr. von Roenn wrote in 2002, dexamethasone at 4–8 mg a day appears to be useful although there are no randomized trials. Octreotide at standard doses has long been used to reduce small intestinal secretions to levels more manageable by an impaired large intestine, and the preponderance of evidence favors its use.⁸⁴ One large high power randomized controlled trial used all intravenous dexamethasone (8 mg/24 hours), ranitidine (200mg/24hours) (Zantac®) and octreotide (600mcg/24hours by infusion) versus dexamethasone, ranitidine, and placebo. There was no difference in the number of days free of vomiting, the primary end point. An adjusted multivariable regression showed over a 50% reduction in vomiting attributable to octreotide but with twice the incidence of colicky pain requiring treatment. And octreotide costs at least \$15 for each 100 mcg dose, typically given 3 times a day, which puts it out of reach of hospice. The authors concluded that more study was needed⁸⁵.

Nausea and vomiting

A complete review of nausea and vomiting is beyond the scope of this article, so we have summarized some points we use in our own practice.

- Try to understand the mechanism of the vomiting and nausea. Nausea due to chemotherapy requires a serotonin or neurokinin-1 blocking drug, while nausea due to constipation or opioids is more likely involving dopamine.
- Vomiting due to obstruction may or may not have nausea. Anti-nausea drugs will not help obstruction. Some patients prefer to vomit twice a day rather than have an NG tube.
- Do not use Ativan, Benadryl, Haloperidol (ABH) gel for nausea as it is not absorbed⁸⁶ and completely ineffective⁸⁷. Up to 60% of hospice patients were given a prescription for ABH or similar gels until recently, with no proof of efficacy; ABH when tested did not work.

- Haloperidol and metoclopramide are the standard drugs we use for both inpatients and outpatients, the “Cleveland Clinic” protocol⁸⁸.
- Olanzapine is now generic, \$15 for 30 tablets, and is among the best anti-nausea drugs for chemotherapy induced nausea⁸⁹ and likely for other types of nausea⁹⁰.

Summary

Symptom management continues to improve but many more improvements are needed. The evidence base behind many of our interventions is based on anecdote.

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KEY POINTS

- At least for cancer patients, being older is no longer associated with pain medication under-prescribing, however moderate to severe pain is still prevalent.
- Physician barriers include reluctance to prescribe opioids, inadequate training, fear of complications, fear of regulatory oversight, and drug interactions.
- The first principle of pain management is classification: neuropathic, and everything else
- Symptom management continues to improve but many more improvements are needed

SYNOPSIS

This article updates the 2002 Jamie von Roenn manuscript about “the palliation of commonly observed symptoms in older patients, including pain, neuropsychiatric, gastrointestinal, and respiratory symptoms.”¹ When Palliative Care was last covered in Geriatric Clinics, President George W. Bush had just signed the No Child Left Behind Act, Homeland Security was being established, Michael Jackson won the Artist of the Century Award at the American Music Awards, and gas cost \$1.61 a gallon. What has changed in the last decade and a half?

Box 1**CAM Feature 4: Disorganized Thinking**

Yes/No Questions (See training manual for alternate set of questions)

1. Will a stone float on water?
2. Are there fish in the sea?
3. Does one pound weigh more than two pounds?
4. Can you use a hammer to pound a nail?

From Ely EW. Confusion Assessment Method for the ICU (CAM-ICU): The Complete Training Manual.

Vanderbilt University. Available at: http://www.icudelirium.org/docs/CAM_ICU_training.pdf; with permission.

Table 1

treatment of neuropathic pain

Condition	Drug choices	Evidence	Comments
Diabetic neuropathy	Gabapentin or pregabalin	Randomized clinical trials	Gabapentin is much less expensive (pennies versus dollars), can cause sedation and edema, and has a ceiling effect at 2700 mg/day. Pregabalin has no upper limits of absorption, but may have more psychiatric effects.
Shingles "post herpetic pain"	Prevention (early treatment) with gabapentin ¹⁶ or pregabalin ¹⁷	Randomized clinical trials, but not in geriatric patients	The data are compelling for a single gabapentin dose of 900 mg, or pregabalin 150 mg at the outset of a shingles outbreak. I would suggest a lower dose in older adults.
Shingles "post herpetic pain"	Treatment with topical lidocaine, capsaicin, or oral gabapentin or pregabalin	Randomized clinical trials	Excellent recent review emphasized that the elderly had the most prevalence and side effects of treatment, half of patients will still have pain, and opioids are not usually effective. ¹⁸
Chemo induced peripheral neuropathy	Prevention of oxaliplatin neuropathy: venlafaxine	Randomized clinical trial	One study with 62 patients ¹⁹ showed a significant delay and/or reduction in CIPN
Chemo induced peripheral neuropathy	Treatment Only duloxetine has proven efficacy; venlafaxine, a similar generic drug, is likely to work as well	One successful RCT Multiple failed drugs	Duloxetine reduced pain scores from 6/10 to 5/10 at 6 weeks, with acceptable toxicity ²⁰ . Generic venlafaxine may have similar activity, and the clinical trial data is forthcoming. MOST of the drugs used for diabetic neuropathy do NOT work for CIPN including gabapentin, nortriptyline, lamotrigine, etc. ²¹
All others	Use an opioid if the pain is severe		The combination is better than either class of drug alone.

Data from Refs 16–21.

Table 2

An abbreviated Symptom Scale

Reported by: Patient Caregiver RN MD										
Able to respond: Yes No							Delirious: Yes No (NO BENZOS! USE HALOPERIDOL®)			
	Pain	Tiredness	Nausea	Depression	Anxiety	Drowsiness	Anorexia	Constipation	Dyspnea	Secretions
0			x	x						x
1						x				
2										
3										
4		X Exertional only		X "leaving my grandkids"	X "dying"		x	x	X exertion	
7										

Enter: 0=none, 1=a little bit, 2=somewhat, 3=quite a lot, 4=very much, 7=refused

NB. Always ask "Are you bothered by _____?"

Table 3

Nonpharmacologic techniques

Method	Indication	State of the evidence	Comment
Cognitive behavioral interventions	Pain	RCTs, not in geriatrics	Hard to find providers Hard to convince patients to go May not be reimbursed
Acupuncture	Pain	RCTs	Hard to evaluate providers May not be reimbursed
	Nausea	RCTs	
	Arthralgia associated with chemotherapy or hormonal agents	RCTs	
Trans cutaneous electrical stimulation (TENS)	Muscle pain – modestly effective		
	Cancer pain or bone pain – Ineffective	RCTs, small and underpowered	Not enough evidence to recommend ²⁵
Cold/heat			
Topical menthol for neuropathic pain ²⁶			
Promising but unproven treatments			
Scrambler Therapy for neuropathic pain	Chemotherapy induced cancer pain ^{27,28} Post-herpetic pain ²⁹ Neuropathic pain ³⁰	No RCTs yet reported >50% pain relief within days, lasting months	FDA cleared, but not reimbursed by most insurers No toxicity
High intensity light therapy	Diabetic neuropathy	RCT showed some relief of pain and dramatic return of normal function ³¹	No toxicity Not readily available

Data from Refs 26–30.

Table 4

Treatment of depression

Therapy	Usefulness	Additional considerations
Cognitive behavioral treatment	High	May be difficult to find, or be reimbursed, or convince patients to go. But well worth it.
Psychotherapy	High	
Drug treatment Anti-depressants	High- the same as with other groups of patients The side effects are the same too: energizing, sleeplessness, too much sleep, lack of sex drive/libido, and weight gain.	Try to treat other symptoms at the same time. Trazadone (Desyrel®) is useful for insomnia. Mirtazapine (Remeron®) is commonly used for nausea, insomnia, and appetite stimulation, despite a lack of randomized trials.
Psychostimulants	Variable – not well studied, but anecdotal evidence is strong ⁷⁵	Methylphenidate (Ritalin), now in long acting forms; modafinil (Provigil) Start at low doses and evaluate for tolerance.
Trans-cranial magnetic stimulation	Useful non-invasive technique that is increasingly available and effective ⁷⁶⁷⁷	

Data from Refs 75–77.