A Practical Introduction to the Use of Opioids for Chronic Pain

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With proper knowledge, safeguards, structure and record keeping in place, primary care physicians may find a personal comfort level in prescribing opioids to chronic pain patients who legitimately require them.

Despite the availability of monographs, papers, lectures, and websites to teach about opioids—and the fact that the American Geriatrics Society has written that opioids are safer than NSAIDs for geriatric patients[1]— the majority of primary care clinicians are uncomfortable prescribing them for chronic pain because they:

(1) don't understand the difference between physical dependence and addiction and assume that they will turn their patients into addicts;
(2) believe that appropriate patients for opioid analgesia are only those whose chronic pain has a cause that can be seen on imaging studies;
(3) believe they will have to endlessly increase the opioid dose as their patients develop tolerance to the pain-relieving effects of opioids;
(4) are afraid of being scammed and assume that most patients want drugs for their mood-altering effects;
(5) assume that patients who are on opioids would be constantly phoning for refills on evenings and weekends;
(6) believe that once a patient is put on opioids, it's very difficult to wean them off;
(7) tend to use only short-acting opioids (if they use opioids at all) and do not understand the benefits of prescribing sustained-release drugs for chronic pain;
(8) have heard that urine drug tests are a good idea but don't understand when and how to order them or how to interpret the results;
(9) are unfamiliar with opioid risk tools that can help them decide which patients are less or more likely to abuse prescription drugs;
(10) need instruction in efficient record keeping so as to be able to keep track of what they have prescribed and when the next refill is due; and
(11) need a framework for the appropriate elements of a follow-up visit.

The goals of this paper are to debunk the mistaken beliefs about opioid prescribing for chronic pain (items 1-6); to educate clinicians on the basic features of opioids (item 7); and to describe office procedures and tools that will make them more willing to consider using opioids for selected legitimate pain patients (items 8-11).

Basic Concepts

Chronic pain is not just acute pain that lasts beyond some arbitrary time period. It differs from acute pain in several respects. Acute pain provides a useful signal and constitutes a call or action. The primary goals of acute pain treatment are to diagnose the source and remove it. Chronic pain, on the other hand, has outlived its usefulness as a signal and is no longer beneficial. The severity and extent of chronic pain may be out of proportion to the original injury and may continue long past the period in which the damaged tissue has healed. The primary goals of of chronic pain treatment are to relieve the pain and to improve the person's function. Diagnosis is, of course, the first step but frequently the cause is either already clearly understood (e.g. osteoarthritis of the knee) or is poorly understood and unlikely to be better characterized (such as in most chronic back or pelvic pain). In either case, the pain persists and must be treated in its own right. Patients must be educated to shift their focus from the diagnosis to improving their pain and function. A reasonable goal is to reduce the level of pain by 30 to 50%.

The gold standard of assessing the level of a patient's pain is the patient's word. With chronic pain, there may be a disconnect between the patient's perception of pain and the results of imaging studies. In one study, 50% of people without back pain had abnormal CT scans of the back, with such diagnoses as herniated disks, facet degeneration, and spinal stenosis.[2] On the other hand, people with back pain often have normal imaging studies.

Once surgery has been ruled out, chronic pain is best treated with a combination of non-drug modalities (especially exercise and physical therapy) and, typically, combinations of medications which can include non-opioid analgesics such as acetaminophen and NSAIDs, opioids, muscle relaxants, and anticonvulsants such as gabapentin and pregabalin for neuropathic pain. In patients with a mixed pain pattern—such as chronic back pain along with sciatica (i.e. both somatic and neuropathic pain)—the combination of an opioid plus an anticonvulsant may be superior to either alone. Sedative-hypnotics may improve sleep, while stimulants such as modafinil and methylphenidate can counteract opioid-induced sedation. Antidepressants are helpful for the depression that frequently accompanies chronic pain. Testosterone replacement therapy is effective in treating opioid-induced testosterone deficiency, which is exceedingly common with the use of chronic opioids. This paper will focus specifically on the use of opioids, which are the least understood and most effective analgesics.

Physical Dependence Versus Addiction

Physical dependence, a property of several drug classes including opioids and corticosteroids, means that the body has adapted to the drug such that abrupt cessation results in a characteristic withdrawal syndrome. Continued use of opioids usually results in physical dependence, but uncommonly in *de novo* addiction. While addiction to some drugs (alcohol, amphetamines) is associated with physical dependence, some other drugs of abuse do not have a recognizable withdrawal syndrome (marijuana, cocaine). Physical dependence is not the same as addiction, but opioids can produce both physical dependence and addiction. Patients who have a previous history of drug or alcohol addiction or abuse are at an increased risk of addiction.

Drug addiction—which, to confuse matters is termed *drug dependence* by psychiatrists—has three elements, all of which express themselves as *behaviors*:

1. Loss of control (i.e., compulsive use): the person uses more than intended, fails in efforts to cut down, etc.
2. Continuation despite significant adverse consequences—such as disease or injury, arrest, job loss.
3. Preoccupation or obsession with obtaining, using and recovering from the effects of the drug.[3]

When prescribed opioids are effective, the patient's life improves. Their pain diminishes, their activities expand and their mood is better. On the other hand, when a person is addicted, the addiction comes to occupy an increasingly important part of a person's life. The addict's life constricts as they sacrifice activities and relationships in order to focus on their relationship with the drug (see criterion 3 above). That's why, during follow-up visits with the patient, it's important to regularly ask about what's happening in their life.

In the medical setting, the following behaviors may signal possible drug addiction or abuse:

- crushing and injecting an oral medication;
- selling prescribed drugs;
- forging or altering prescriptions;
- repeated requests for early refills; recurrent stories that the drug was lost, stolen, fell into the toilet, or was eaten by the dog;
- obtaining pain medications from multiple prescribers;
- repeatedly using up the drug before the next scheduled refill.

Pseudoaddiction

Aberrant drug-related behaviors (a term coined by Portenoy in 1996)[4] do not always indicate the presence of addiction. Rather, the patient's behaviors may be a desperate attempt to alleviate undertreated pain—a phenomenon that has been termed *pseudoaddiction*.[5] Once the analgesic dose is adjusted to more effective levels, the behaviors disappear. When evaluating a patient's bad behaviors, it is wise to consider the possibility that they resulted from undertreated pain. However, injecting oral or topical opioids or selling prescription drugs are clear signs of abuse or addiction. The goal of injecting an oral or topical opioid is to induce euphoria rather than to alleviate pain. When faced with a patient who is exhibiting aberrant behaviors, consider the following differential:

- addiction,
- pseudoaddiction (undertreated pain),
- other psychiatric diagnoses, or
- criminal intent (diversion).

Tolerance

Tolerance has been defined as "a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more o the drug's effect over time."[6] In other words, increasing doses of the drug are needed to get the same effect. Opioids have several effects on the body, so it is important to specify which effect is being discussed. It is well

recognized that within days of initiation of opioid treatment, tolerance develops to its sedative, nauseating, and euphoria-producing effects. However, tolerance does not develop to constipation, which is why it is important to discuss with the patient the need for a ongoing pre-emptive bowel program when initiating opioid therapy. This program usually needs to include a bowel stimulant to combat the slowdown in peristalsis induced by opioids.

There is controversy in the literature about whether tolerance develops to opioid analgesia, but pain specialists with extensive clinical experience in long-term opioid prescribing recognize that many patients remain on stable opioid doses for years (for example, Tennant, 2008[7]). In 2000, Scimeca et al wrote, "Extensive clinical experience has documented that the doses of [opioid] required to maintain analgesia typically stabilize in the absence of progressive disease. . . Tolerance is seldom a problem in the clinical setting. . . When a need to increase the dose does materialize, the clinician should search for worsening disease rather than assume that analgesic tolerance has occurred."[8] Considering that tolerance to other opioid effects develops within days, it is unlikely that tolerance to analgesia develops months later.

When patients are first begun on opioids, they often require upward titration. There are two reasons for this and neither is related to tolerance to pain relief. First, opioids must be initiated at low doses because of the sedation and nausea they produce. Over a few days, as these effects abate (due to tolerance), the dose is then gradually increased until adequate analgesia obtains. Second, the patient often returns after a short time reporting that the pain level has increased. At this point, the most likely reason is increased activity. As the pain level diminishes, the patient begins (hopefully!) to spend less time at rest and engages in more physical activities. The resulting increased pain level will require upward dose titration. Within weeks, however, the patient will reach an equilibrium between the improved level of functioning and the opioid dose. At this point, the dose is likely to stabilize. Published outcome studies are needed to confirm this common clinical observation.

Caveat: When titrating an opioid upwards, the clinician can expect that increased doses will produce decreased pain levels. It is then reasonable to keep increasing the dose until sufficient pain relief is obtained. But if, after several dose increases, there is no improvement in pain levels—which should be assessed at each visit using, for example, a scale of 1 to 10 or a visual analog scale—then one may reasonably conclude that this opioid is ineffective. The next step may be to switch to another opioid, as people differ genetically in their responses to different opioids. One opioid may be significantly more effective than another for a specifica patient. If this strategy is not effective, then a non-opioid approach is appropriate.

Opioid-Induced Hyperalgesia

Studies of laboratory animals, patients given intrathecal opioids or given intravenous opioids acutely during surgery, and people studied under unusual conditions (e.g., Compton et al[9]) have led to the hypothesis that some patients who take high-dose opioids develop increased pain with increased doses. This has not been confirmed in any published studies on chronic pain patients treated with oral or transdermal opioids. In clinical practice, if a patient reports an increase in pain on his opioid dose, the first step is to check for disease progression or a new pain problem rather than concluding that hyperalgesia is present and that the dose needs to be decreased.

The Safety of Opioids

In 2009, the American Geriatrics Society updated their *Guidelines to Improve Pain Management for Older Patients*. In these recent guidelines the panel recommends that NSAIDs and COX-2 inhibitors be considered rarely, with extreme caution, and only in highly selected individuals. The guidelines recommend that all patients with moderate-to-severe pain or diminished quality of life due to pain should be considered for opioid therapy, which may be safer for many patients than long term use of NSAIDs.[1] Unlike NSAIDs, opioids are not known to cause hypertension, gastrointestinal bleeding, or organ toxicity. In addition, much attention has been paid recently to the potential harm of acetaminophen on the liver. The single most common cause of liver failure in the U.S. is acetaminophen toxicity. Efforts are currently underway to limit the prescribing of short-acting opioid combinations such as Percocet and Vicodin because of their content of acetaminophen.

The side-effects of opioids—nausea and vomiting, respiratory depression, and sedation—resolve quickly with continued dosing. Residual effects can be treated. Constipation is an ongoing problem requiring maintaining a bowel regimen. Subnormal testosterone levels in men are common.[10] It's a good idea to check serum testosterone levels in all male patients who are on opioid maintenance and, unless contraindicated, consider testosterone replacement.

There is no upper limit of safety for opioid analgesic doses, and patients can differ greatly in the dose required to attain effective pain relief. Many patients on opioid maintenance believe they should not drive while taking these drugs. However, an extensive medical literature supports the conclusion that patients who are on stable doses and feel alert can drive safely.[11-13] After an opioid regimen is begun or the dose increased, patients need to avoid driving for a few days if they feel sedated.

Breakthrough Pain and the Role of Short-Acting Vs. Sustained Release Opioids

Most patients with chronic pain do not experience a uniform level of intensity over a 24-hour period. Temporarily increased pain can result from increased physical activity, weather changes, mood changes, or when their previous medication dose wears off. Breakthrough pain may be predictable or unpredictable, sudden or gradual. In a study by Portenoy et al,[14] 74% of a group of opioid-treated patients with non-cancer pain experiences two or more breakthrough pain episodes per day.

The opioids most commonly prescribed for acute pain are combinations such as hydrocodone and acetaminophen (e.g., Vicodin®, Lorcet®, Norco®), hydrococodone and aspirin (Lortab®), oxycodone and acetaminophen (Percocet®), and oxycodone and aspirin (Percodan®). These have a duration of action of 4-6 hours. Their maximal dose is limited by the non-opioid component. In fact, there is currently an effort to limit the availability of combinations containing acetaminophen because of its potential liver toxicity if daily doses of 4 grams are exceeded (and probably lower doses if used chronically). Morphine, oxycodone, and oxymorphone are also available in

immediate-release form. Tramadol (Ultram®) is a weak mu opioid agonist, which also has weak serotonin and norepinephrine reuptake inhibition. A new opioid analgesic, tapentadol (Nucynta®), also has a dual mode of action: it is both a mu-opioid agonist and also a norepinphrine reuptake inhibitor. In addition, fentanyl is available in transbuccal formulations (Actiq®, Fentora®) which provide onset of pain relief more quickly than do oral analgesics—almost as rapidly as intraveous morphine. These fentanyl formulations are FDA-approved only for cancer-related breakthrough pain but, in fact, are frequently used off-label for non-cancer pain episodes that tend to be severe at onset (e.g., headaches, office procedures, and some back pain). Other immediate-release (IR) opioid analgesics are codeine combinations, propoxyphene, and meperidine. All are weak and meperidine has the additional problem that, with repeated dosing, its metabolite, normeperidine, can produce seizures.

Among the products mentioned above, hydrocodone/APAP and the weak opioids tramadol, acetaminophen with codeine, and propoxyphene are classified by the DEA as Schedule III, meaning prescriptions can be phoned in and refills are permitted. All the other IR formulations above are Schedule II, meaning they require written prescriptions with no refills.

When prescribed for chronic pain, the IR drugs produce up-and-down blood levels, must be taken repeatedly, and usually don't last through the night. To overcome these limitations, the same opioids (except for tapentadol at present) have been formulated in time-release preparations, with a duration of action of 8-24 hours for oral morphine (Avinza®, Kadian®, Oramorph®, MSContin®, and generic), oxycodone (OxyContin®), oxymorphone (Opana®), and tramadol (Ultram ER®, Ryzolt®), and 2-3 days for transdermal fentanyl (Duragesic® and generic) patches. These single-agent formulations avoid acetaminophen or aspirin toxicity and so have no upper limit of dose. They provide smoother blood levels so more stable pain relief is attained and have a longer duration of action so fewer doses (and less clock-watching) are required.

When treating chronic pain patients with opioids, it's preferable to prescribe a combination of a sustained-release opioid for round-the-clock dosing plus a small quantity of an IR preparation to be used for breakthrough pain as needed. Selected patients can be maintained on IR opioids for long-term management.

Methadone

Methadone deserves special mention, as it requires caution in its use. The chief advantage of methadone is its much lower cost compared to other long-acting opioids. Taken once a day, methadone effectively prevents withdrawal but its analgesic effect is shorter, typically requiring 3-4 doses per day. Methadone has a long and highly variable serum half-life, in the range of 36 hours, so that it requires careful upward titration, with increases made only after several days. The FDA has reported numerous methadone-related deaths which typically occur during the first few days of methadone titration. This is a result of the accumulation of the drug in the body when the dose is increased too rapidly. Moreover, conversion to methadone from other opioids is non-linear, such that the ratio of morphine to methadone may be 1:1 for single low doses, but increases dramatically to approximately 10:1 when converting from high doses of morphine. Conversion from morphine-equivalents to methadone needs to be extremely conservative. High doses of methadone can cause a prolonged Q-T interval on the EKG, which can lead to *torsades de pointes*, a potentially lethal arrhythmia. Some pain specialists advise getting an EKG on patients who are prescribed more than 60-80mg/day of methadone to be sure that the Q-T interval is not prolonged. Methadone can be prescribed for pain by any practitioner who has a DEA license. The words "for pain" should be written on such prescriptions.

Assessment

The Federation of State Medical Boards has issued model guidelines for treatment of chronic pain with opioids[15] which describe appropriate assessment. Another valuable resource for assessment and treatment is the paper by Gourlay and Heit[16] on universal precautions in pain medicine. Initial assessment should include:

- history of the pain problem including onset and course, prior treatments—including surgery, other procedures, and medications—and current medications since detailed information about past and current medications and doses can help in deciding which analgesics and doses to use;
- request for old medical records, if the pain problem is not new;
- past and current employment history, social history, psychiatric history, and how the pain has affected the patient's functioning;
- the patient's treatment goals;
- past or present use of cigarettes, alcohol, and illicit drugs;
- some type of opioid risk assessment tool;
- physical exam; and
- urine drug test.

A treatment plan should be formulated and clearly discussed with the patient. If opioids are part of the treatment plan, the physician needs to educate the patient about opioid side effects, about physical dependence and the risk of addiction, about the withdrawal syndrome associated with opioid cessation, and the need to avoid abrupt cessation.

Urine Testing

A urine drug test (UDT) is a useful tool to assess whether the patient is taking currently prescribed opioids and whether he or she is using non-prescribed opioids or illicit substances. Current recommendations are to test the patient initially and then randomly, as well as for cause. The absence of a prescribed opioid in the urine suggests the possibility of diversion or else intermittent dosing. At the time the urine is collected, the patient should be asked specifically when the last dose of each prescribed opioid was taken and at

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what dose. For example, if the last dose of Percocet for breakthrough pain was taken more than a day or two earlier, the urine might legitimately be negative for oxycodone.

Ordering a UDT requires some knowledge of the procedures of the clinical laboratory used. The usual immunoassay (EIA, ELISA) screen for opiates tests only for the presence of natural opiates (such as morphine, codeine, and hydrocodone) and will not reliably detect semi-synthetic or synthetic opioids such as oxycodone, oxymorphone, or fentanyl. These substances may be found only on testing by gas chromatography/mass spectroscopy (GC/MS) or high-performance liquid chromatography (HPLC), which will also provide quantitative results. Immunoassays are subject to false-positive results due to cross-reaction with various other substances, so positive EIA results are routinely followed up by confirmatory GC/MS or HPLC, which will be negative in such cases. To avoid falsely accusing a patient of diverting his or her prescribed oxycodone or fentanyl when the screening test comes back negative, it is recommended that the lab slip be labeled "routine urine drug test plus oxycodone" or "plus fentanyl" if those drugs are being prescribed. Immunoassays usually have thresholds of detection, so that a therapeutic drug level in the urine will be reported as "negative" if the level falls below the test's cutoff. If a patient is taking a low dose of a prescribed opioid, a relatively high cut-off IEA test may be another explanation for a false negative result.

The opposite problem may be encountered if the urine is sent to a specialty lab (such as Dominion, Ameritox, or AIT) that routinely tests for multiple opioids. In that situation, the report may come back positive for unexpected opioids, and it is then the clinician's responsibility to find out if there is a legitimate reason for this. Patients have been unfairly discharged for unexpected results that, in fact, reflected the presence of a known metabolite of the prescribed drug. For example, a major metabolite of oxycodone (as in Percocet or OxyContin) is oxymorphone (which is now available as Opana). In a study of 86 patients prescribed oxycodone (but not oxymorphone), 93% had UDTs that were also positive for oxymorphone and often in large quantities.[17] Other well-known metabolic pathways include codeine to morphine and hydrocodone to hydromorphone (e.g., Dilaudid). The lesson here is that every unexpected finding in the urine drug test needs to be checked out with the clinical laboratory. A useful guide to urine drug testing is the paper by Heit and Gourlay.[18]

Finally, contrary to what some laboratories suggest, there is no direct relationship between dose and urine concentration. The quantity of the drug in the urine at any specific time depends on multiple factors, including the time elapsed since last dose, kidney function, and the drug's metabolism. Quantitative results of specific opioids in the urine cannot reliably indicate whether or not the patient is taking the drug as prescribed. Quantitative testing is rarely useful for compliance. It is best used as a follow-up to a false-negative screening test, when the confirmatory test may show that the patient's urine does have the prescribed drug but at a level below the EIA's cutoff.

Opioid Risk Assessment Tools

Several brief screening tests are available that assess a person's risk of abusing prescribed opioids. Two commonly used ones are:

- The Opioid Risk Tool (ORT), a brief 5-item questionnaire that asks about family history of substance abuse, personal history of substance abuse, age, history of preadolescent sexual abuse, and psychiatric disease.[19]
- Screener and Opioid Assessment for Patients in Pain (SOAPP), which has several versions of different lengths: 24, 14, or 5 items. The brief version asks about mood swings, smoking, history of taking non-prescribed medications, prior use of illicit drugs, and past legal problems or arrests.[20]

These tests are best utilized to help assess the amount of caution and structure that the patient will require rather than to exclude pain patients from opioid treatment.

Providing Structure

Once the decision has been made to initiate opioid analgesia therapy, it's advisable to have the patient sign an agreement that spells out the physician's expectations and the patient's agreement. Some elements typically include:

- Physician will educate the patient about opioids.
- Patient facilitates obtaining old records.
- Only one physician prescibes opioids.
- Patient uses only one pharmacy (of their choice).
- Patient will not change the dose without first consulting with physician.
- Physician will not give early refills (unless there is a valid reason).
- Patient agrees to consultations or physical therapy referral by physician.
- Patient does not use illegal drugs.
- Patient agrees to urine drug testing whenever requested by physician.

Breaches of the agreement are evaluated on a case-by-case basis.

If a patient cannot reliably manage his or her own medications, a plan to do so must be arranged. Otherwise, controlled substances should not be prescribed. Some problems and solutions are:

- *A patient is found to have an active addiction problem.* Refer for addiction treatment. In some cases, if the patient is actively involved in addiction treatment, it may be possible to continue prescribing opioid analgesics only by having a responsible friend or relative dispense them. Increase the frequency of urine drug screens, require continued attendance at the addiction treatment program, and request confirmation of such. Schedule more frequent office visits and ask the patient to bring in prescription bottles for pill counts.
- *A patient has dementia and can't remember when the last dose was taken*. Identify another person to dispense the medications.
- *A patient is severely depressed, possibly suicidal*. Refer for psychiatric assessment and treatment. A patient who is at risk for overdosing on medications you prescribe should not be given the opportunity to do so.

If problems influencing a patient's adherence develop during the course of treatment and it is not possible to add enough structure to provide for the patient's safety, then the patient should be tapered off the drugs (see below).

Initiating Opioid Therapy

The initial dose and the specific drug

prescribed depends on what opioid (if any) the patient is currently taking, what experience the patient has had with various opioids, and what attitudes the patient has about particular drugs.When an opioid regimen is initiated, some patients experience more sedation or nausea than others. It is wise, therefore to begin with a low dose. If side-effects result, then decrease or maintain that dose until they abate—typically a few days. The physician can then increase the dose as needed for pain relief. In opioid-naïve patients, I prefer to begin with an IR opioid so that if side effects such as severe nausea develop, they will last a shorter time than if the patient were on a sustained-release (SR) medication. Also, because IR opioids such as Vicodin or Percocet come in low doses (2.5 or 5 mg), they can be titrated up in small doses until an effective dose is reached, at which time the daily dose can be converted to a sustained-release formulation.

It is desirable to convert to an SR formulation as soon as possible. Patients who have been maintained on large doses of IR opioids for long periods of time may find it difficult to transition to equivalent SR doses. The reason is most likely based on the mechanism of euphoria. Everyone knows that smoking marijuana produces euphoria more effectively than does eating marijuana brownies. This is because the concentration of cannabinoids in the blood stream feeding the brain rises much more rapidly after inhalation than ingestion. Euphoria is related to the *rate of increase* of the drug in the brain. This is the reason that addicts crush and inject oral analgesics. It makes sense that ingesting an IR opioid will result in a more rapid increase (and subsequent more rapid decrease) of the opioid in the brain than will a SR opioid. It is likely that, for some patients, ingesting an IR opioid will produce a sense of well-being in addition to peripheral analgesia and this sense will understandably be interpreted by the person as part of the pain relief the drug gives them. Some patients report that the same daily dose of the same drug in an SR formulation just doesn't give as effective pain relief. It may be that they are, in fact, experiencing some mood alteration only with the IR version. It is best to transition patients to the SR formulations as soon as an effective dose is reached.

Follow-up Visits: Evaluating Treatment Outcomes

Chronic pain patients on opioids need to be seen regularly in follow-up—usually every one to two months. A key goal of the follow-up visit is to assess the outcome of the current treatment approach. The written plan of the previous visit should be reviewed. If imaging studies, physical therapy, urine drug test, and/or referral to a specialist had been ordered on the previous visit, the clinician should ascertain (and document) whether these recommendations were carried out and what the results were.

An easy way of remembering the key elements of each follow-up visit was described by Passik & Weinreb[21] as the "4A's" These are:

1. Analgesia: Level of pain, e.g. on a scale of 1-10.
2. Activities of daily living: What the patient is actually doing (be as specific as possible: "Now walking the dog daily for 15 minutes, about half a mile.")
3. Adverse effects: For example, ask about constipation, which can be an ongoing problem.
4. Aberrant drug-related behaviors: For example: "Ran out early because…" or "Leaving on vacation, needs early refill." Or, "UDT positive for cocaine."

Many clinicians have now added a fifth A for Affect that is indicative of the patient's mood. This is because depression and anxiety exacerbate pain and because many chronic pain patients are chronically depressed and require antidepressants. The outcome of antidepressant treatment should be assessed.

If some aberrant behavior is reported or becomes apparent, the clinician needs to address the issues that have been raised and make a plan to deal with them. The discussion and plan should be documented in the chart.

You will notice that a physical examination is not part of the "4As." This is because a physical exam is *not* required on every visit before a prescription can be given. Of course, if the patient reports a change in symptoms, then a focused physical exam is in order. But for stable patients, I believe that a formal physical exam every six months or so will most likely suffice but, of course, every visit (which for me takes place every two months if the patient is stable) provides the clinician with an opportunity to observe the patient in motion and at rest and quickly assess their level of alertness.

If a patient needs a prescription between scheduled office visits, there is no requirement that the patient be seen by a practitioner. It is acceptable for the patient to simply pick up the prescription(s). If a patient is routinely seen only every two months, the question often arises about how to write the prescription for alternate months. The current policy of the Drug Enforcement Administration (DEA) is that the physician can write more than one prescription at a time, for up to a 90-day period from the current date. Each prescription needs to be dated on the date it is actually written. The second prescription needs to say in the body of the prescription "Do not fill until. . ." and add the date, often 30 days after the present date. The pharmacist is then required to wait until the date written in the body of the prescription. Before you issue such a prescription, however, check with your state's law regarding prescribing. When state and Federal law differ, the stricter version holds. Some states, for example, allow Schedule II prescriptions to be filled only 15 days or 30 days after the date they were written (In my state of Arizona, the law permits filling for up to 60 days). For frequently updated and very useful information on medicolegal issues of prescribing controlled substances, visit the web site of attorney Jennifer Bolen, www.legalsideofpain.com.

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Record Keeping

Although documentation is important in any medical practice, it is particularly crucial in the records of patients being

treated for chronic pain with opioids. The Model Policy of the Federation of State Medical Boards[15] lists the following items that should be maintained in the records:

1. the medical history and physical examination;
2. diagnostic, therapeutic and laboratory results;
3. evaluations and consultations;
4. treatment objectives;
5. discussion of risks and benefits;
6. informed consent;
7. treatments;
8. medications (including date, type, dosage and quantity prescribed);
9. instructions and agreements; and
10. periodic reviews.

Some of these items are relevant only for the initial visit or occasionally. In addition, the record of every follow-up visit should contain the findings of the 4As (or 5As). An assessment of the patient's current status should be included, as well as a list of the plans for the patient (referrals, studies ordered, instructions to the patient regarding exercise etc) and prescriptions written (including dose, quantity, and date to be filled).

It is particularly important to create a dedicated page (or pages) in which to maintain an updated record of every prescription written for each controlled drug, including the dose, quantity and date. All prescriptions—whether written or phoned in, whether prescribed during an office visit or between visits—should be included. This record needs to be easily accessible any time the patient calls for refills or renewals, and should be consulted. This is the most efficient way to avoid inadvertent excessive prescribing.

Exit Strategy: Getting Pain Patients Off Opioids

Before starting a patient on chronic opioid treatment it is desirable to have a plan to get him or her off the drug if necessary. Reasons for deciding to stop opioid analgesia include:

- The patient may no longer need opioid analgesia, for example after recovery from back surgery or knee replacement, or because of success with other modalities.
- Unacceptable side effects.
- No convincing evidence of benefit despite attempts at optimal therapy. This may have included repeated dose increase or transition to other opioids.
- Persistent adherence problems. The patient may no longer be considered a candidate for chronic opioid analgesia.

Abrupt cessation of opioids in a patient who has been taking them for more than one to two weeks is likely to lead to a recognized withdrawal syndrome, which includes sweating, yawning, lacrimation, diarrhea, muscle aches and pains, abdominal cramps, piloerection, rhinorrhea, insomnia, and anxiety. Some patients seem much more prone to experiencing withdrawal than do others who have been on the same dose. This syndrome can be very uncomfortable but is not life-threatening. It is preventable by *tapering* or *weaning* the patient off the drug. (Do not use the term *detoxification*, as this refers to getting drug addicts off their drug of addiction; the Drug Enforcement Administration does not permit prescribers to use opioids to detoxify opioid addicts unless the prescriber has a special DEA permit to do so). Withdrawal symptoms emerge within six to twelve hours after the last dose of morphine, hydromorphone, oxycodone, oxymorphone, hydrocodone or fentanyl, but later (up to three to four days) after stopping methadone, whose serum half-life is so much longer. For patients who no longer have pain such as after recovery from hip or knee replacement, the taper can be quite rapid—for example, 25% of the dose every two days. With methadone, the taper needs to be significantly slower. An additional option would be the temporary addition of clonidine, 0.1-0.2 mg every 6 hours as needed. The chief side effect of clonidine is its tendency to cause hypotension.

For patients who have chronic pain, the rate of tapering should be driven more by the residual pain than by the need to prevent withdrawal symptoms. The taper should be more gradual to allow for time to assess the pain level as the dose is reduced. Non-opioid analgesics and the use of alternative modalities may need to be increased as the opioid dose is decreased. ■

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