PSNet
PATIENT SAFETY NETWORK

The Pains of Chronic Opioid Usage

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Case Objectives

- Describe the appropriate initial assessment of patients with chronic non-cancer pain.
- List the most common errors made in prescribing opioids for non-cancer pain.
- Outline appropriate monitoring for patients prescribed opioids for non-cancer pain.
- Appreciate the need to risk stratify patients on opioids for non-cancer pain.

Case & Commentary—Part 1

A 42-year-old man with a history of asthma and chronic lower back pain was admitted to the hospital with community-acquired pneumonia and an asthma exacerbation. His primary care physician (PCP) had been prescribing high doses of long-acting morphine (MS Contin), oxycodone, and gabapentin for his low back pain. He was marginally housed and often slept in shelters.

On admission to the hospital, he was treated with nebulizers, antibiotics, and prednisone. Due to some odd behavior and suspicion for substance abuse, a urine toxicology test was sent on admission and was positive for benzodiazepines, methadone, and opiates. As neither the benzodiazepines nor the methadone were prescribed medications, the hospitalist confronted the patient who admitted selling his prescribed opiates and buying diazepam and methadone on the street. He stated that they could "control [my] pain better."

The patient in this case was prescribed opioids for his low back pain. Opioids are frequently and increasingly used in managing chronic non-cancer pain. In fact, data on sales and distribution of opioids per person, per year, show an increase from 96 mg of morphine equivalents in the United States in 1997 to 710 mg in 2010—enough to supply every adult American with 5 mg of hydrocodone 3 times daily for more than 45 days.(1,2) Furthermore, US patients consume an incredible 99% of all hydrocodone and 83% of all oxycodone worldwide.(1,3,4)

Unfortunately, the dramatic rise in use of therapeutic opioids is not based on evidence of their long-term efficacy or supported by safety data in the treatment of chronic non-cancer pain.(1,5-11) Many experts

agree that the massive increase in prescribing is founded on extensive misconceptions and not based on evidence or proven safety.(1,2,5-7,10-12)

The increased prescribing of opioids to treat non-cancer pain has been widespread. In one of the earliest surveys, opioid prescribing for chronic pain in the ambulatory setting doubled from 8% in 1980 to 16% in 2000.(13) In a study from 2000 to 2005, the proportion of enrollees receiving opioids for chronic non-cancer pain grew 58% in the health insurance group and 29% in Medicaid.(14) By 2005, long-term opioid therapy was being prescribed to an estimated 10 million US adults.(1,2,15-17) Deyo and colleagues (3) showed that approximately 20% of patients in primary care settings were longtime opioid users; nearly two-thirds had received at least one course of opioids. In pain management settings, more than 90% of patients were receiving opioids on a long-term basis before presenting to interventional pain management settings.(18)

Most of this increased use likely relates to well-meaning efforts by clinicians to treat the often frustrating problem of chronic pain, as in this case. We do not have enough detail to determine whether this was necessary or appropriate. Yet, it seems from the case that the patient may have been using his prescribed opioids for non-medical purposes, which opens a window to a different side of the opiate safety problem.

Information on nonmedical use of opioids in patients with chronic non-cancer pain is not easily obtained. Nonmedical use, defined as use without prescription or outside the limits of prescription, occurs in 5% to 41% of patients.(19) Consequently, the overuse and abuse of opioids, including the escalation of the therapeutic use of opioids, can result in injury and death.(1,19) It is well known that high doses of opioids as well as the combination of multiple opioids, illicit drugs, benzodiazepines, and hypnotics may cause serious adverse effects including death.(1,19)

In 2012, the Centers for Disease Control and Prevention (CDC) (2) described the characteristics of patients who had overdosed on prescription medications and specifically reported the doses of opioids prescribed and the nature of the prescribing. Approximately 80% of the patients that were prescribed low doses (defined as less than 100 mg of morphine-equivalent dose per day by a single practitioner) accounted for an estimated 20% of all prescription overdoses. In contrast, among the remaining 20% of overdose patients, the 10% prescribed high doses (greater than 100 mg of morphine-equivalent dose per day) by a single prescriber accounted for an estimated 40% of prescription opioid overdoses.(1) The remaining 10% of patients seeing multiple doctors and typically involved in diversion of drugs for recreational purposes contributed to 40% overdoses.

The patient described here was on high doses of two different opioids, both long-acting morphine and short-acting oxycodone, which placed him at high risk for an adverse event. When prescribed in high doses, opioids are associated with an increased risk for overdose (in addition to having other adverse effects). Studies show that the majority of patients treated with traditional opioids experienced gastrointestinal- or central nervous system–related adverse events, the most common of which were constipation, nausea, and somnolence, often leading to discontinuation of opioid therapy.(1,19) Long-term opioid therapy also leads to hormonal, central nervous, respiratory, and cardiovascular complications along with tolerance, dependence, and addiction.(1,19)

Providers may make multiple errors when prescribing opioids for non-cancer pain. We find it useful to classify opioid prescribing errors into four categories: (i) inadequate screening for safe and effective opioid

use, (ii) inability to monitor adherence, (iii) improper selection of opioids, and (iv) insufficient consideration of comorbid conditions.

For the patient in this scenario, there may have been inadequate screening for safe use, potentially improper selection of opioids, and possibly insufficient consideration of his asthma. The patient was receiving high-dose long-acting morphine in addition to oxycodone for so-called breakthrough pain. Breakthrough pain may be a reality in cancer pain, but is generally not a part of non-cancer pain.(1) When a patient is prescribed long-acting opioids while continuing to take short-acting opioids, this can be a setup for fatality and death, particularly when comorbid factors are not taken into consideration.

Case & Commentary—Part 2

Given the complexity of the pain regimen and the diversion, the hospital's pain service was consulted. They changed his medications to methadone, hydromorphone, clonazepam, and venlafaxine. The morphine and oxycodone were discontinued. With this regimen, the patient had reasonable pain relief at the time of discharge. He was discharged with a prescription for a 2-week supply of medications and had a follow-up appointment with his PCP 10 days after discharge. Unfortunately, as it was a weekend the discharging hospitalist was not able to speak directly with the PCP but sent her an e-mail with the medication changes.

Five days after discharge, the patient was found unconscious at a subway station and pronounced dead at a local hospital following unsuccessful resuscitation. Based on the clinical presentation and details at the scene, the cause of death was likely from unintentional opiate/benzodiazepine overdose.

In reviewing his medications, the patient had refilled his long-acting morphine and oxycodone 1 day before admission. Unfortunately, this information was not available to the discharging hospitalist, and the patient stated that he had not gotten any recent refills of his opiates. The patient filled the new prescription for methadone, hydromorphone, and clonazepam on the day of discharge.

It is unclear from the case details whether the patient's unexpected death could have been prevented, but the scenario acts as a powerful reminder of the risks of opioid prescribing. Much can be done to prevent such events in the future. All providers should follow appropriate guidelines to provide proper prescriptions. Enhancing and updating clinical teaching and training is crucial for all providers, especially those involved in the areas of pain management. It has been suggested that pain management education for health professionals has been and continues to be insufficient. Consequently, a more comprehensive and contemporary curriculum for prescribers seems warranted.

Best practices for preventing errors and adverse outcomes when prescribing opioids are described in Figure 1. The algorithm involves a 10-step process with diagnosis, determination of medical necessity, establishment of treatment goals, informed consent, adherence monitoring, and addressing adverse effects, followed by continuation or discontinuation of opioids after initial treatment of 8 to 12 weeks.(20)

In the present case discussion, appropriate prescription practices unfortunately were not followed. The first error was prescribing both long-acting morphine and oxycodone in a patient with comorbid respiratory disorders, and who was marginally housed and lacked support systems. It might have been more appropriate to start with a single short-acting agent to determine adherence and tolerance. The second

issue refers to the hospitalist suddenly switching the patient to methadone even though the patient admitted to selling opioids and purchasing diazepam and methadone. Methadone is associated with significant variations in metabolism and cardiac toxicity including death. It would have been safer to manage with short-acting oxycodone. The combination of multiple drugs along with comorbid conditions and social instability should have been red flags.

Although screening for abuse of prescription opioids is common, there is limited evidence due to the lack of high-quality studies for the reliability and accuracy of available screening instruments. Furthermore, given the lack of long-term published quality literature, there is little evidence that screening for opioid abuse by any of the instruments will prevent abuse.(1) Prescription drug monitoring programs (statewide electronic databases) that collect data on substances dispensed in the states may help reduce risks in opioid prescribing. There is good evidence that prescription drug monitoring programs provide data on patterns of prescription drug usage, which may lead to earlier recognition of abuse. There is also fair evidence that prescription drug monitoring programs may decrease prescription drug abuse or doctor shopping.(1) However, there is only limited evidence that prescription drug monitoring programs reduce emergency room visits, drug overdoses, or deaths.(1)

Urine drug testing, as part of compliance monitoring, is crucial in managing opioid therapy. While patients may initially balk at this testing, urine drug screening for opioid misuse and abuse should be used as an exercise to strengthen the patient–physician relationship. Providers should clearly explain to patients that urine testing will build trust and allow for more effective prescribing of opioids. There is fair evidence for the diagnostic accuracy of urine drug testing and that it serves to identify patients who are noncompliant or abusing prescription or illicit drugs.(1) Moreover, there is good evidence that urine drug testing may decrease prescription drug abuse or illicit drug use when patients are in chronic pain management therapy.(1)

In the above case, inquiry of a prescription drug monitoring program including appropriate information from all the physicians and pharmacies involved could have prevented the dangerous prescription patterns. Thus, communication among health care professionals can be crucial. Urine drug testing may have helped identify some of the abuses.

Other steps can be taken to minimize the risk of harm in opioid prescribing. Pain clinics are indispensable; however, in this case the patient would have been best served with an addiction management program rather than pain clinic referral. The providers could also have engaged the patient in a formal treatment agreement (i.e., pain contract). Informed consent and a treatment agreement can be essential and should include clear descriptions of medication use and abuse, as well as consequences for violating the contract (Figure 2).

Stratification of risk for patients initiated or maintained on chronic opioid therapy is crucial to prevent misuse and abuse. Patients are generally classified as low risk, medium risk, or high risk. Patients with concurrent substance abuse and high risk for abusing the prescription opiates fall under the category of high risk. High-risk patients must be monitored frequently with repeat assessment in conjunction with prescription drug monitoring programs, random urine drug testing, and random pill counts. In addition, these patients should be placed on low-dose opioids (and not on combination opioid therapy) and should

be weaned off opioids if they develop any aberrant behaviors.

This patient had significant abuse patterns and should have been considered as high risk, and, consequently, should never have been initiated on high-dose opioid therapy, should have been appropriately monitored, and should have been weaned off opioids or referred to addiction management. This case provides a tragic lesson that can help us improve the state of opiate prescribing.

Take-Home Points

- The initial assessment in managing patients with chronic non-cancer pain should involve establishing the diagnosis, medical necessity, and treatment goals.
- The most common errors associated with opioid prescribing for non-cancer pain include the following: inadequate screening for safe and effective opioid use, inability to monitor adherence, improper selection of opioids, and insufficient consideration of comorbid conditions.
- Providers should ensure full informed consent before prescribing opioids and determine methods to monitor adherence.
- Patients who are prescribed opioids should be monitored continuously for adherence and adverse effects as well as screened for abuse; urine drug testing may be effective.
- Stratification of patients into low risk, medium risk, and high risk is an essential feature prior to embarking on initial treatment.

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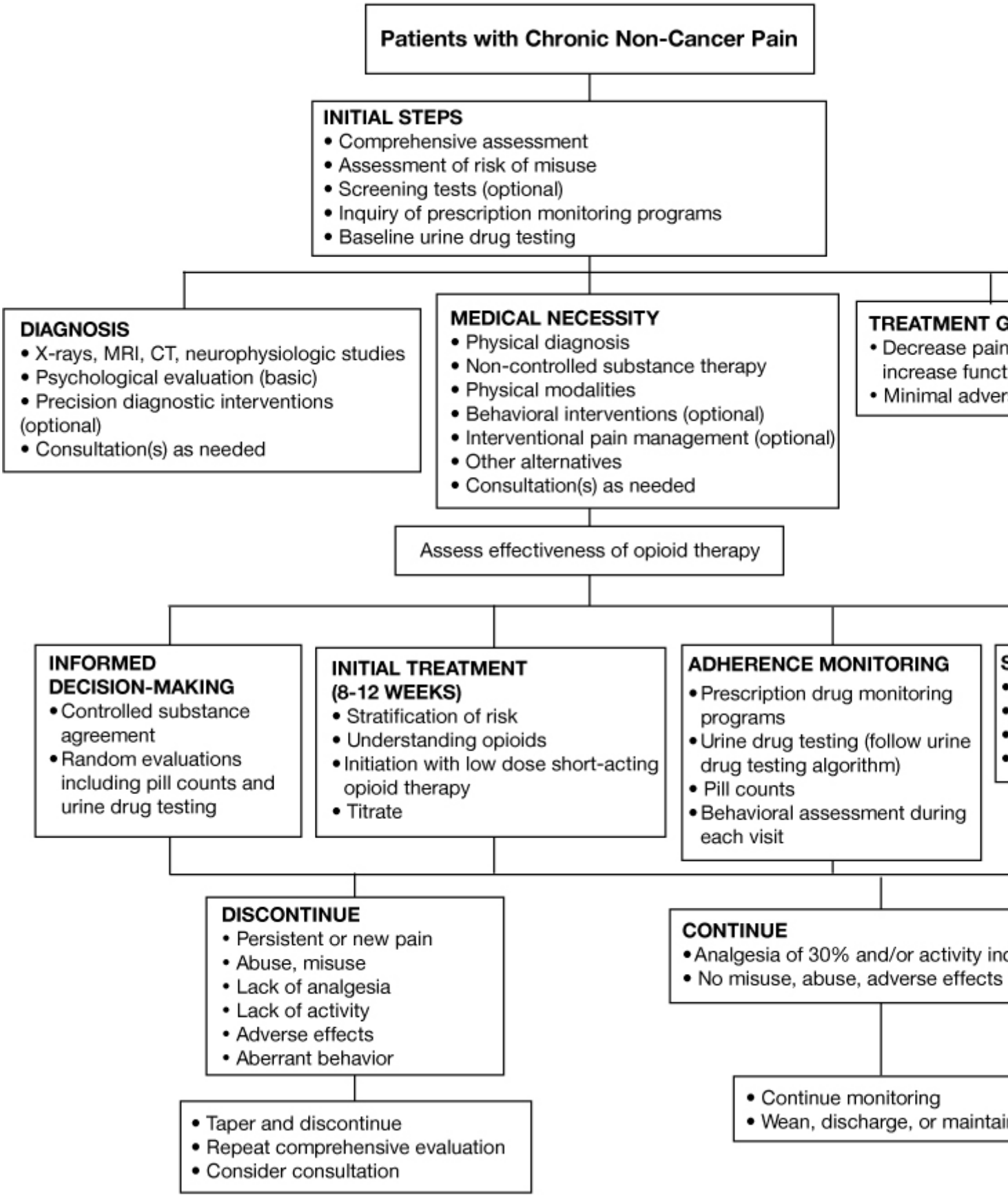
Figures

Figure 1. Guidance to opioid therapy.(1) Reprinted with permission of the American Society of Interventional Pain Physicians.



Click to enlarge.

Figure 2. Sample controlled substance agreement.

Figure 2. Sample controlled substance agreement.

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CONTROLLED SUBSTANCE AGREEMENT

We at the _____ are committed to doing all we can to treat your chronic pain condition. In some cases, controlled su
therapeutic option in the management of chronic pain and related anxiety and depression, these substances are strictly reg
federal agencies. This agreement is a tool to protect you, the _____, and your physician by establishing guidelines, w
controlled substance use. The words "we" and "our" refer to the _____, and the words "I", "you", "your", "me", or "my" re

1. i. I understand that chronic opioid therapy has been associated with not only addiction and abuse, but also multiple medica
suppression of endocrine function resulting in low hormonal levels in men and women which may affect mood, star
physical and sexual performance.
   ii. For female patients, if I plan to become pregnant or believe that I have become pregnant while taking this medication,
carry the baby to delivery while taking these medications, the baby will be physically dependent upon opioids. I
obstetrician and this office to inform them of my pregnancy. I am also aware that opioids may cause a birth defect, ev
rare.
   iii. I have been informed that long-term and/or high doses of pain medications may also cause increased levels of pain
hyperalgesia (pain medicine causing more pain) where simple touch will be felt as pain and pain gradually increases in
location is all over the body. I understand that opioid-induced hyperalgesia is a normal, expected result of using the
period of time. This is only treated with the addition of nonsteroidal anti-inflammatory drugs such as Advil, Aleve, etc., o
opioids.
   iv. I understand that physical dependence is not the same as addiction. I am aware physical dependence means that if
markedly decreased, stopped, or reversed by some of the agents mentioned above, I will experience a withdrawal synd
have any or all of the following: runny nose, yawning, large pupils, goose bumps, abdominal pain and cramping, di
throughout my body, and a flu-like feeling. I am aware that opioid withdrawal is uncomfortable, and could even result i
death.
   v. I am aware that tolerance to analgesia means that I may require more medicine to get the same amount of pain relief. I
to analgesia does not seem to be a big problem for most patients with chronic pain; however, it has been seen and
occurs, increasing doses may not always help and may cause unacceptable side effects. Tolerance or failure to resp
cause my doctor to choose another form of treatment, reduce the dose, or stop it.
2. i. All controlled substances must come from the physician whose signature appears below or during his/her absence, by
unless specific authorization is obtained for an exception.
   ii. I understand that I must tell the physician whose signature appears below or during his/her absence, the covering phys
taking, have purchased, or have obtained, even over-the-counter medications. Failure to do so may result in drug intera
could result in harm to me, including death.
   iii. I will not seek prescriptions for controlled substances from any other physician, health care provider, or dentist. I under
prescribed the same controlled medication by more than one physician at a time without each physician's knowledge.
   iv. I also understand that it is unlawful to obtain or to attempt to obtain a prescription for a controlled substance by knowingl
to a physician or his/her staff or knowingly withholding facts from a physician or his/her staff (including failure to inform th
staff of all controlled substances that I have been prescribed).
3. All controlled substances must be obtained at the same pharmacy if possible. Should the need arise to change pharmac
informed. The pharmacy that I have selected is: _____
4. i. I will not share, sell, or otherwise permit others, including my spouse or family members, to have access to any con
have been prescribed.
   ii. Early refills will not be given. I will not consume excessive amounts, I will follow prescribed instructions, and remain
of treatment. Renewals are based upon keeping scheduled appointments. Please do not call for refills after hours o
   iii. Medication changes will not be made between appointments unless medically necessary, which will be determined
5. Unannounced pill counts, random urine or serum tests, or planned drug screening may be requested from you and your
The presence of unauthorized substances in urine or serum toxicology screens may result in your discharge
_____ and its physicians and staff.
6. I will not consume excessive amounts of alcohol in conjunction with controlled substances. I will not use, purchase, or ot
legal drugs except as specifically authorized by the physician whose signature appears below or during his/her ab
physician, as set forth in Section 1 above. I will not use, purchase, or otherwise obtain any illegal drugs, including m
understand that driving while under the influence of any substance, including a prescribed controlled substance or any co
(e.g., alcohol and prescription drugs), which impairs my driving ability may result in DUI charges.
7. Medications or written prescriptions may not be replaced if they are lost, stolen, get wet, are destroyed, left on an airplan
has been stolen, it will not be replaced unless explicit proof is provided with direct evidence from authorities. A report na
authorities is not enough.
8. In the event you are arrested or incarcerated in relation to legal or illegal drugs (including alcohol), refills on controlle
given.
9. I understand that failure to adhere to these policies may result in cessation of therapy with controlled substances prescrib
other physicians at the _____ and that law enforcement officials may be contacted.
10. I also understand that the prescribing physician has permission to discuss all diagnostic and treatment details, inc
dispensing pharmacists, other professionals who provide your health care, or appropriate drug and law enforcement ag
maintaining accountability.
11. I have received the pamphlet "PAIN MEDICINE AND ANXIETY MEDICINES."
12. I affirm that I have full right and power to sign and to be bound by this agreement, that I have read it, and understand and
copy of this document has been given to me.

Patient's full name _____

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