

Pain Relief Connection

The Pain Information Newsletter

Provided by MGH Cares About Pain Relief

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Clinical Focus: Pharmacologic Interventions for Pain.

NOTE: This series is intended to provide general information and context about medications for the treatment of pain. Clinical experience and judgement, individualization of treatment, and consultation with experts and standard references should guide the treatment of specific patients.

WORLD HEALTH ORGANIZATION ANALGESIC LADDER: STEP 1--NONOPIOID ANALGESICS--ACETAMINOPHEN

Acetaminophen is the most widely used analgesic and antipyretic in the United States. It is indicated for the treatment of mild to moderate pain and fever. It is available for oral or rectal administration, and is commercially available without prescription in many doses, dosage forms, and combinations. While these factors make acetaminophen relatively inexpensive, easy to get and convenient to dose, it may also cause confusion, unintended overdose when multiple medications are taken, and create an unrealistically positive perception of the safety of acetaminophen.

Step 1 of the WHO Analgesic Ladder includes both acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). It should be understood that acetaminophen does not have significant anti-inflammatory properties. Its mechanism of action is poorly understood, but recent research suggests that it acts both peripherally and centrally.

COMBINATION PRODUCTS

Acetaminophen is a frequent component of over-the-counter analgesics and cold and flu symptom remedies. It is also available by prescription in combination with the opioids propoxyphene, codeine, hydrocodone, and oxycodone. The acetaminophen dose varies fairly dramatically from product to product. The availability of combination analgesics, both opioid and non-opioid, illustrates the principle that combining analgesics with different mechanisms of action and different toxicity profiles may provide improved analgesic efficacy and decreased risk of certain toxicities. The corollary risk, however, is that suboptimal assessment, monitoring, and management of patients on combination products can paradoxically lead to increased risk of acetaminophen toxicity. The prescriber must be mindful of components and doses of all prescription and non-prescription products that the patient is taking, especially chronically, and provide education and counseling to the patient on proper use and dosing of these drugs.

DOSE:

- children < 12 yr should be dosed by age or weight--consult standard references
- children \geq 12 yr and adults may take 325 - 650mg every 4 - 6 hr; occasional use of up to 1000 mg/dose for analgesia is generally acceptable; chronic use of 1000 mg 3 - 4 daily for osteoarthritis should be undertaken with clinician supervision; the adult daily dose should not exceed 4 g
- dose limits for acetaminophen-opioid combination products are frequently determined by the total daily dose of acetaminophen

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CAUTIONS:

- extended release dosage forms should not be cut, broken, crushed, chewed, or dissolved
- liquids should be measured using an oral medication syringe or other calibrated measuring device
- the adult daily dose should not exceed 4 g
- patients may unintentionally take both acetaminophen as a single agent and acetaminophen-containing over-the-counter combination products; counsel patients to avoid combination products unless specifically instructed otherwise
- chronic use of high doses of acetaminophen is associated with analgesic nephropathy
- risk of nephropathy may be significantly increased when acetaminophen is chronically taken with other potentially nephrotoxic analgesics such as NSAIDs
- patients who drink more than 3 alcoholic beverages per day are at increased risk of acetaminophen-induced hepatotoxicity when taking acetaminophen chronically or at high doses.
- risk of hepatotoxicity is increased with prolonged use of acetaminophen-aspirin combinations
- at doses of >2600 mg/day, gastrointestinal toxicity from acetaminophen may approach that of comparable doses of NSAIDs, especially in people with a history of NSAID-induced GI problems.

DRUG INTERACTIONS:

- alcohol: significantly increases risk of hepatotoxicity
- anticonvulsants: increased risk of hepatotoxicity when standard doses of acetaminophen are exceeded
- anticoagulants: chronic concurrent use of acetaminophen and anticoagulants may require anticoagulant dose adjustment due to possible potentiation of anticoagulant effect
- isoniazid: increased risk of hepatotoxicity, especially at higher acetaminophen doses

Journal Watch: Pediatric Pain

The "Pain Control" column of the [American Journal of Nursing](#) (AJN) has just completed a 4-part series on pain assessment in infants and young children:

"Pain Assessment in Infants and Young Children: Neonates" [102(8): 61];

"Pain Assessment in Infants and Young Children: Premature Infant Pain Profile" [102(9):105];

"Pain Assessment in Infants and Young Children: The FLACC Scale: A behavioral tool to measure pain in young children" [102(10):55];

"Pain Assessment in Infants and Young Children: The Finger Span Scale" [102(11):55].

Full-text articles are accessible from MGH computers in the Ovid database via [Magic](#), but it is not possible to provide direct links from *Pain Relief Connection* to Ovid files.

The September issue of *Clinics in Perinatology*; 2002 Sep;29(3) is devoted to "Pain in Vulnerable Infants." Of note is a provocative article, "The social context of pediatric pain" by Patrick McGrath and Anita Unruh. This bound periodical is available in the journal stacks in [Treadwell Library](#).

Pain Education on the Web

The [Hospice and Palliative Nurses Association](#) web site now offers online CE based on a series of HPNA-sponsored teleconferences. [Advanced Pain Management](#) has recently been added to the site. The content is available free; if you want contact hours awarded, there is a fee.

URL notes: **Hold your cursor over the link for a second to see the URL.** If you are reading this in hard copy, this month's links are:

Center for Clinical & Professional Development course calendar: <http://tinyurl.com/23zk>

WHO Analgesic Ladder: <http://www.mcmahonmed.com/wworks/CHARTS/3step/default.html>

American Journal of Nursing: <http://www.nursingworld.org/ajn>

Magic electronic catalog at Treadwell Library: <http://magic.mgh.harvard.edu>

Treadwell Library: <http://massgeneral.org/library/default.asp>

Hospice and Palliative Nurses Association: <http://www.hpna.org>

HPNA Advanced Pain Management CE course: http://www.hpna.org/continuing_ed.asp

MGH Cares About Pain Relief web site: <http://www.massgeneral.org/painrelief>

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PAIN TOPICS

Analgesic use in the Acute Abdomen:* A History

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Thank you to Susan Stengrevics, RN, MSN, Clinical Specialist for Cardiac ICU for suggesting this month's Pain Topic. *Pain Relief Connection*, Vol 1 No. 11, November 22, 2002, p 3-6. Feedback from readers is welcome and encouraged.

"Though it may appear cruel, it is really kind to withhold morphine until one is certain or not that surgical interference is necessary, i.e. until a reasonable diagnosis has been made."¹ (unchanged in 12 revised editions over 50 years)

In 1921 Sir Zachary Cope published the first edition of his book, *Early Diagnosis of the Acute Abdomen*.² It has been so successful and influential in the training of surgeons over the intervening 80 years that there have been only a handful of competing texts. These other texts echoed the sentiment quoted above. Cope himself wrote the first 14 editions over a span of 50 years. It is currently in its 20th edition. Both Cope and his successor, William Silen of Harvard Medical School, considered the book to be a clinical reference, and therefore did not include citations or a bibliography.

In the 1987 (17th) edition, Dr. Silen began to soften the message:

"Though it may appear cruel, it is really prudent to withhold morphine until a reasonable diagnosis has been made and a plan of action formulated. This can usually be accomplished relatively quickly, within 15 - 30 minutes. . . . These comments should not be misconstrued as advocacy of a rigid policy of indefinite withholding of analgesics but rather as a proposal for the exercise of knowledgeable restraint . . ."³

In the meantime, editorials and letters had begun appearing in medical journals questioning the continued wisdom of the perceived prohibition. "We look back aghast at cruelties inflicted on patients by our predecessors, and there is no reason to suppose that our successors will not be equally appalled by some of the things we do now."⁴ The *British Medical Journal* editorialist and a letter⁵ in the same issue reflected on the history of the practice, suggesting that the relatively primitive surgery conditions and the significantly higher doses of morphine in fashion at the time of Cope's early editions constituted a very different environment than seen in the modern hospital. They further suggested that intravenous analgesia, "titrated against the pain,"⁶ may improve diagnosis because the patient would be better able to cooperate with history taking and physical examination. Even a letter contesting the new view recognized the importance of early assessment by an "experienced diagnostician"⁷ so that treatment, including analgesia, could be instituted rapidly.

Subsequently, 5 prospective randomized controlled trials,^{8,9,10,11,12} 4 of them double blind, were conducted in the 1980's and 90's to address these issues. The University of California San Francisco (UCSF)-Stanford University Evidence-based Practice Center cited the studies in a report prepared for the US Agency for Healthcare Research and Quality.¹³ The report states that "it seems inappropriate and inhumane to withhold pain medication if this practice is not supported by evidence."¹⁴ None of the five studies "found compromises in diagnosis or treatment of the acute abdomen"¹⁵ in cases in which analgesia was used. At least one study showed improvement in diagnosis when analgesia changed diffuse abdominal pain to more localized pain. The report concludes that "the appropriate use of analgesics in patients with acute abdominal pain effectively decreases pain but does not interfere with diagnosis or treatment."¹⁶

In 1991 Silen¹⁷ moved away from Cope's original prohibition in a more pronounced fashion. The change includes replacement of the assertion in 1987 that diagnosis can be made in 15 - 30 minutes with a recognition that "layers" of nurses, students, residents and attendings, interspersed with "time-consuming tests" will inevitably delay diagnosis and eventual transfer to surgery.¹⁸

*Any serious acute intra-abdominal condition attended by pain, tenderness, and muscular rigidity, and for which emergency surgery must be considered. ([Online Medical Dictionary](#))

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" . . . the suffering patient is sometimes forced to wait for many hours before any relief is offered. This cruel practice is to be condemned, but I suspect that it will take many generations to eliminate it because the rule has become so firmly ingrained in the minds of physicians." ¹⁹

Keszler's²⁰ sobering account of personal experience with the "cruel practice" puts a contemporary human face on the problem.

In other evidence-based forums, withholding of analgesia for fear of masking symptoms and interfering with diagnosis has also been found to be a fear without merit. A "Best Evidence Topic Report"²¹ (Mackway-Jones, 2000) reviewed the same studies as the UCSF-Stanford group, with the same conclusion. Concurrently, *The Western Journal of Medicine* inaugurated an ongoing series entitled "Myths and Medicine." The journal challenged readers to "evaluate critically even the most standard and widespread practices, when they are based on tradition and the weight of authority, but in the absence of, or contrary to, available evidence."²² The first "telling example"²³ of medical myth investigated was the withholding of analgesia in acute abdomen. The 5 studies previously cited were reviewed, again with the same conclusion: the studies "failed to produce any evidence that [providing analgesia] is harmful."²⁴

More recent clinical trials,^{25,26} including one that studied children with acute abdominal pain,²⁵ continue to support the finding that judicious use of opioid analgesia provides significant pain reduction without interfering with diagnosis or surgical treatment.

The most recent edition (20th) of *Cope*, marks an almost complete break with the classical approach:

"The realization, likely erroneous, that narcotics can obscure the clinical picture has given rise to the unfortunate dictum that these drugs should never be given until a diagnosis has been firmly established."²⁷

Silen reiterates his condemnation of "this cruel practice" and his fear that it will nonetheless continue. He also re-emphasizes a prior recommendation, that a "*responsible surgeon* evaluate the patient at the earliest possible time."²⁸

A more recently voiced concern about the use of analgesics in patients presenting with acute abdomen is a belief that administering opioids invalidates a patient's ability to provide informed consent for treatment, specifically surgery. Graber, et al²⁹ surveyed general surgeons in Iowa about barriers to providing analgesia to patients presenting with acute abdomen. Of 131 respondents, 53% agreed or strongly agreed that enough pain medication to allow the patient to be comfortable precluded the patient from signing a legally binding informed consent, and that 78% included this consideration in the decision about whether to order analgesics.³⁰ According to Kapp³¹ the notion that such categorical considerations (i.e., patients who receive opioids cannot give legal consent) have been "thoroughly rejected in contemporary legal and ethical mainstream thinking."³² Instead, a functional perspective (i.e., the cognitive and emotional decisional capacity of the individual patient) is the required legal standard. Brewster points out that patients who receive analgesia for acute pain are "rarely" incapacitated enough to interfere with decisional cognitive function.³³ Furthermore, severe pain may so impair a patient's judgment, as to render him/her incapable of making an informed decision. In addition, in some legal and ethical interpretations, withholding analgesia until consent is provided can be seen as coercion.³⁴

There is a subtext to this conversation that has led to a conflict of values and treatment goals. Presentation with acute abdominal pain heralds a potential life-threatening emergency. In 1921 delay in diagnosis and surgery frequently led to mortality. Cope spent 3 pages of a small volume emphasizing the need for rapid intervention. He was concerned that any delay could be fatal. Physical examination and history were the only diagnostic tools available. If the urgency to intervene was reduced (by relieving the symptom of pain), "it is possible for a patient to die happy in the belief that he is on the road to recovery, and in some cases the medical attendant may for a time be induced to share the same delusive hope."³⁵

Even today, history and physical examination remain the critical diagnostic tools, with "special complicated tests and x-ray examinations" interfering with rapid diagnosis and intervention.³⁶ Mortality has been significantly reduced because of advances in supportive care,^{36,37} but morbidity related to delay is still an issue.³⁸ Cope's

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'dictum' took on the proportion of myth and remained largely unquestioned while systems, such as emergency services, changed dramatically and the ability to titrate opioids became much more sophisticated.

To add yet another dimension, Graber et al's³⁹ survey and another by Wolfe, et al⁴⁰ suggest that even when physicians recognize that analgesia does not interfere with diagnosis and treatment of patients with abdominal pain, "the gap between understanding and practice remains large, and abdominal pain is often undertreated."⁴¹

In their essay on medical myths King and Hoffman conclude:

"Mythology in general plays to our hearts, to get us to believe things for which logic or evidence is lacking. When myths convince us to act in ways that are contrary to our own interests, or (for healers) to the interests of patients, we must first recognize them for what they are, then critically challenge their assumptions, and finally, have the courage to abandon them."²²

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