

## Is the WHO analgesic ladder still valid?

### *Twenty-four years of experience*

Grisell Vargas-Schaffer MD

Pain remains one of the main reasons for medical consultation worldwide. Numerous organizations and scientific associations have made efforts to find solutions for this problem and to facilitate the treatment of pain. In 1986 the World Health Organization (WHO) presented the analgesic ladder as a framework that physicians could use when developing treatment plans for cancer pain. This therapeutic guideline paved the way for considerable improvements in the management of cancer pain, but is it still a valid tool 24 years later?

The WHO proposed the analgesic ladder following the recommendations of an international group of experts. The document was translated into 22 different languages and has served as a catalyst for increasing awareness around the world of the importance of treating pain in cancer patients.<sup>1-6</sup> The analgesic ladder proposed the use of a limited number of relatively inexpensive medications, such as morphine, in a stepwise approach. It helped legitimize the use of opioids for treatment of cancer pain and encouraged numerous worldwide teaching campaigns on the use, benefits, and side effects of narcotics in the treatment of pain.

Both the 1986 and 1997<sup>1,2</sup> WHO treatment guides for cancer pain provide explanations of the pathophysiology of such pain, how to make adequate assessments, how to choose analgesics, and how to use the ladder. Early studies on its effectiveness demonstrated that the method proposed by the WHO offered inexpensive treatment and adequate relief for 70% to 90% of cancer patients with pain.<sup>2</sup> Today this percentage has been questioned, and the range is now thought to be 70% to 80%.<sup>7,8</sup>

### Simple advice still relevant

The cornerstone of the WHO document rests on 5 simple recommendations for the correct use of analgesics to make the prescribed treatments effective. This advice is applicable today, not only for cancer patients with pain, but also for all patients with either acute or chronic pain who require analgesics.<sup>2</sup> The 5 points for the correct use of analgesics are as follows:

**1. Oral administration of analgesics.** The oral form of medication should be privileged whenever possible.

**2. Analgesics should be given at regular intervals.** To relieve pain adequately, it is necessary to respect the duration of the medication's efficacy and to prescribe the dosage to be taken at definite intervals in accordance with the patient's level of pain. The dosage of medication should be adjusted until the patient is comfortable.

**3. Analgesics should be prescribed according to pain intensity as evaluated by a scale of intensity of pain.** This point is important because pain-relief medications should be prescribed after clinical examination and adequate assessment of the pain. The prescription must be given according to the level of the patient's pain and not according to the medical staff's perception of the pain. If the patient says that he has pain, it is important to believe him. This point makes reference to the levels of the analgesic ladder that will be explained in detail further below.

**4. Dosing of pain medication should be adapted to the individual.** There is no standardized dosage in the treatment of pain. Every patient will respond differently. The correct dosage is one that will allow adequate relief of pain. The posology should be adapted to achieve the best balance between the analgesic effect and the side effects.

**5. Analgesics should be prescribed with a constant concern for detail.** The regularity of analgesic administration is crucial for the adequate treatment of pain. Once the distribution of medication over a day is established, it is ideal to provide a written personal program to the patient. In this way the patient, his family, and medical staff will all have the necessary information about when and how to administer the medications.

The 1986 version of the WHO analgesic ladder proposes that treatment of pain should begin with a nonopioid medication (**Figure 1**).<sup>1</sup> If the pain is not properly controlled, one should then introduce a weak opioid. If the use of this medication is insufficient to treat the pain, one can begin a more powerful opioid. One should never use 2 products belonging to the same category simultaneously.<sup>1,2</sup> The analgesic ladder also includes the possibility of adding adjuvant treatments for neuropathic pain or for symptoms associated with cancer.

This article has been peer reviewed.  
*Can Fam Physician* 2010;56:514-7



La traduction en français de cet article se trouve à [www.cfp.ca](http://www.cfp.ca) dans la table des matières du numéro de juin 2010 à la page e202.

This diagram, which is very simple and clear, has been the object of numerous debates and criticisms,<sup>6,9,10</sup> owing in part to omissions as well as to the development of new techniques and medications.<sup>9,11-13</sup>

### Adapting the ladder

Several proposed modifications of the WHO diagram have been made; one of them even proposes the elimination of the second level.<sup>5,10</sup> Others recommend modifications and adaptations of the analgesic scale for other types of pain, such as acute pain and chronic noncancer pain.<sup>8,12,14,15</sup>

Despite the debate and updates to the 1986 analgesic diagram, its educational value and the benefits resulting from its worldwide dissemination are uncontested. However, the extension of its use to other types of pain has run into some roadblocks.<sup>9,16</sup> Some believe that beginning step by step is often insufficient and inefficient for controlling intense pain,<sup>16</sup> and therefore a fast-track diagram has been proposed starting directly at step 3.<sup>15-17</sup>

The adaptation of the analgesic ladder for acute pain, chronic noncancer pain, and cancer pain offered here (Figure 2) is based on the same principles as the original ladder. This revision integrates a fourth step and includes consideration of neurosurgical procedures such as brain stimulators.<sup>14,15,17</sup> Invasive techniques, such as nerve blocks and neurolysis (eg, phenolization, alcoholization, thermocoagulation, and radiofrequency<sup>6,15,16</sup>), are used at the fourth step. This adapted model has also been proposed and applied in the treatment of pediatric pain,<sup>18,19</sup> and it can be used for acute pain in emergency departments and in postoperative situations.

The new fourth step is recommended for the treatment of crises of chronic pain. Interventional pain literature suggests that there is moderate evidence for

the use of transforaminal epidural steroid injections, lumbar percutaneous adhesiolysis, and spinal endoscopy for painful lumbar radiculopathy, and limited evidence for intradiscal treatments in low back pain.<sup>20</sup> Medullar and peripheral stimulators also have been included at the fourth level.

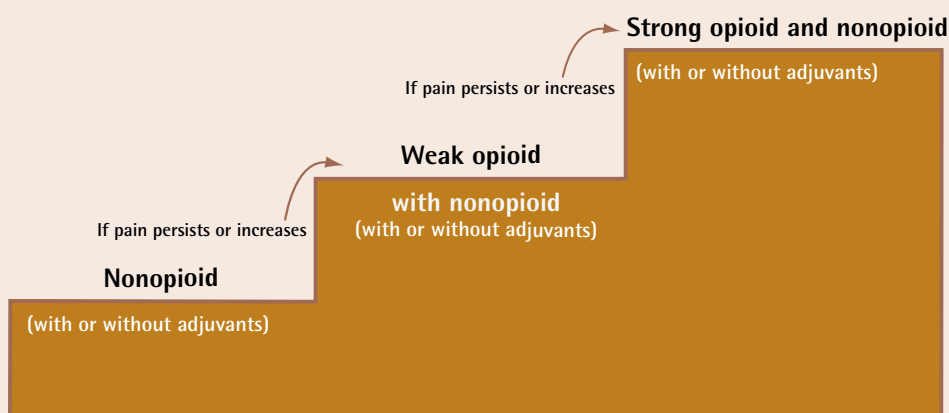
**Opioids.** This new adaptation of the analgesic ladder adds new opioids,<sup>14,15,21-26</sup> such as tramadol, oxycodone, hydromorphone, and buprenorphine, and also new ways of administering them, such as by transdermal patch, that did not exist in 1986. Opioids are classified as weak or strong, as this classification is used in daily practice by millions of physicians throughout the world with excellent results.

The use of opioids to treat chronic noncancer pain is founded on the information gleaned after the first 10 years of dissemination and worldwide use of the analgesic ladder. Since the 1990s, numerous medical articles have been published promoting opioids as a safe treatment for patients with chronic noncancer pain.<sup>20-23</sup>

Methadone, in step 3, is important because it is currently very useful in the treatment of cancer pain, chronic noncancer pain, and refractory neuropathic pain that does not respond to conventional treatment.<sup>15,24,25</sup> Methadone is also very useful in the rotation of opioids<sup>15,21-27</sup> in cancer pain.

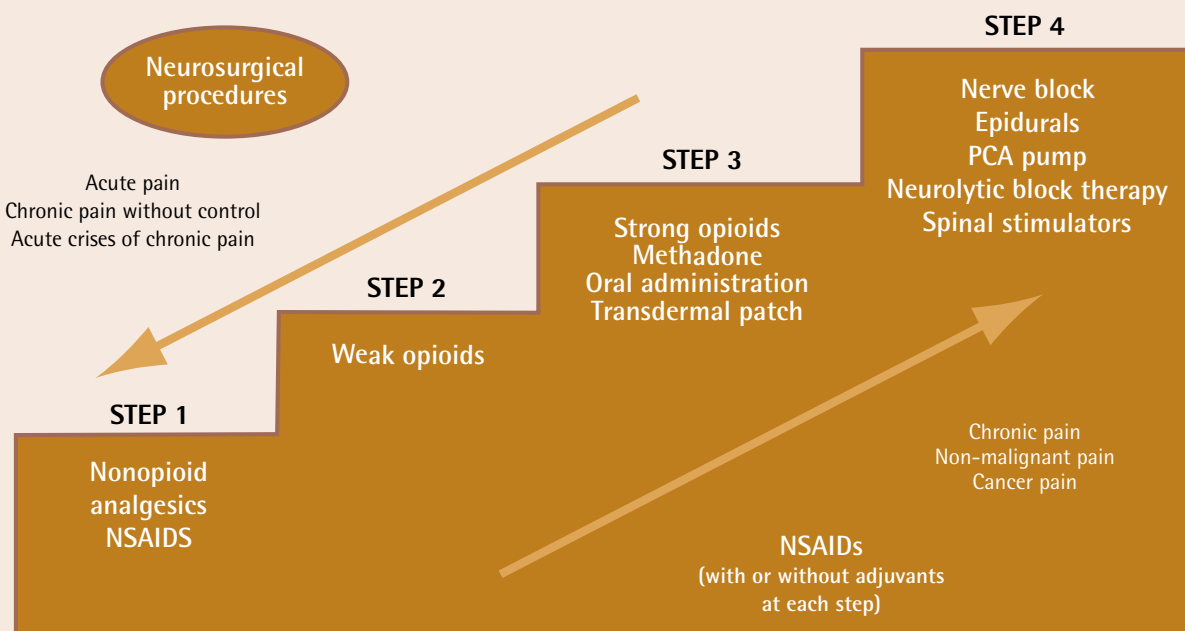
**Adjuvants.** Adjuvant medications include steroids, anxiolytics, antidepressants, hypnotics, anticonvulsants, antiepileptic-like gabapentinoids (gabapentin and pregabalin), membrane stabilizers, sodium channel blockers, and *N*-methyl-*D*-aspartate receptor antagonists for the treatment of neuropathic pain. Cannabinoids can be added to this group of adjuvant medications, not only because they hold a place as

Figure 1. The World Health Organization analgesic ladder for treating cancer pain



Adapted from the World Health Organization.<sup>1</sup>

Figure 2. New adaptation of the analgesic ladder



NSAID—nonsteroidal anti-inflammatory drug, PCA—patient-controlled analgesia.


adjuvants in the care of palliative cancer patients and patients affected by AIDS, but also because they can be used to offer a better quality of life to patients with chronic pain. They can also be used to treat chronic neuropathic pain.<sup>28-35</sup>

**Step up, step down.** This version of the analgesic ladder can be used in a bidirectional fashion: the slower upward pathway for chronic pain and cancer pain, and the faster downward direction for intense acute pain, uncontrolled chronic pain, and breakthrough pain. The advantage of this proposal is that one can ascend slowly one step at a time in the case of chronic pain and, if necessary, increase the rate of climb according to the intensity of the pain. However, one can start directly at the fourth step, in extreme cases, to control pain of high intensity, using patient-controlled analgesia pumps for continuous intravenous, epidural, or subdural administration. When the pain is controlled, one can “step down” to medications from step 3.

**Pure neuropathic pain.** This adaptation can be used for nociceptive pain and for combined nociceptive and neuropathic pain, but not for pure neuropathic pain. In neuropathic pain the treatment algorithm is completely different, and opioids should be considered adjuvant medications and not the principal drugs for the treatment of such pain. Two practice guidelines for the

treatment of neuropathic pain were published in 2007, the first by the Canadian Pain Society<sup>35</sup> and the second by the International Association for the Study of Pain.<sup>34</sup>

### Conclusion

This proposed modification of the WHO analgesic ladder is not intended to negate or advise against use of the original ladder. On the contrary, after 24 years of use the analgesic ladder has demonstrated its effectiveness and widespread usefulness; however, modifications are necessary to ensure its continued use for knowledge transfer in pain management. 

**Dr Vargas-Schaffer** is an Associate Professor in the Department of Anesthesiology at the University of Montreal in Quebec, practises pain management at the Pain Centre at Hôpital Hôtel-Dieu, and is a researcher at the Centre hospitalier de l'Université de Montréal.

**Competing interests**  
None declared

**Correspondence**  
**Grisell Vargas-Schaffer**, Hôpital Hôtel-Dieu du CHUM, Pain Clinic, 3840, rue St Urbain, pavillon Jeanne-Mance, Montreal, QC H2W 1T8; telephone 514 890-8000, extension 15126; e-mail [grisellvargas@gmail.com](mailto:grisellvargas@gmail.com)

**The opinions expressed** in commentaries are those of the authors. Publication does not imply endorsement by the College of Family Physicians of Canada.

### References

- World Health Organization. *Traitement de la douleur cancéreuse*. Geneva, Switz: World Health Organization; 1987.
- World Health Organization. *Traitement de la douleur cancéreuse*. Geneva, Switz: World Health Organization; 1997.
- Azevedo São Leão Ferreira K, Kimura M, Jacobsen-Teixeira M. The WHO analgesic ladder for cancer pain control, twenty years of use. How much pain relief does one get from using it? *Support Care Cancer* 2006;14(11):1086-93. Epub 2006 Jun 8.

4. Zernikow B, Smale H, Michel E, Hasan C, Jorch N, Andler W. Paediatric cancer pain management using the WHO analgesic ladder—results of a prospective analysis from 2265 treatment days during a quality improvement study. *Eur J Pain* 2006;10(7):587-95. Epub 2005 Oct 21.
5. Vadalouca A, Moka E, Argyra E, Sikioti P, Siafaka I. Opioid rotation in patients with cancer: a review of the literature. *J Opioid Manag* 2008;4(4):213-50.
6. Jadad AR, Browman GP. The WHO analgesic ladder for cancer pain management. Stepping up the quality of its evaluation. *JAMA* 1995;274(23):1870-3.
7. Kanpolat Y. Percutaneous destructive pain procedures on the upper spinal cord and brain stem in cancer pain: CT-guided techniques, indications and results. *Adv Tech Stand Neurosurg* 2007;32:147-73.
8. Lema MJ. Invasive procedures for cancer pain. *Pain Clin Update* 1998;6(1):1-8.
9. Krakowski I. 1986-1996: dix ans d'échelle OMS. In: Boiron M, Marty M, editors. *Eurocancer 96*. Montrouge, Fr: John Libbey Eurotext; 1996. p. 291-3.
10. Eisenberg E, Marinangeli F, Birkhahm J, Paladin A, Varrassi G. Time to modify the WHO analgesic leader? *Pain Clin Update* 2005;13(5):1-4.
11. Zech DF, Grond S, Lynch J, Hertel D, Lehmann KA. Validation of World Health Organization guidelines for cancer pain relief: a 10 year prospective study. *Pain* 1995;63(1):65-76.
12. Araujo AM, Gomez M, Pascual J, Castañeda M, Pezonaga L, Borque JL. [Treatment of pain in oncology patients.] *An Sist Sanit Navar* 2004;27(Suppl 3):63-75. [Article in Spanish].
13. Miguel R. Interventional treatment of cancer pain: the fourth step in the world Health Organization analgesic ladder? *Cancer Control* 2000;7(2):149-56.
14. Gómez-Cortéz MD, Rodríguez-Huertas F. Reevaluación del segundo escalón de la escalera analgésica de la OMS. *Rev Soc Esp Dolor* 2000;7(6):343-4.
15. Vargas-Schaffer G. Manejo y tratamiento del dolor oncológico. In: Vargas-Schaffer G, Esposito Quercía G, editors. *Dolor y cuidados paliativos en oncología. evaluación, manejo y tratamiento*. Caracas, Venezuela: Ediciones Expansión Científica G&S; 1999. p. 79-93.
16. Vargas-Schaffer G. Tratamiento del dolor oncológico y cuidados paliativos en pediatría. In: Morales Pola EA, editor. *Manual de clínica del dolor y cuidados paliativos*. Chiapas, Mexico: Universidad autónoma de Chiapas; 2002. p. 195-206.
17. Krakowski I, Falcoff H, Gestin Y, Goldberg J, Guillain H, Jaulmes F, et al. *Recommandation pour une bonne pratique dans la prise en charge de la douleur du cancer chez l'adulte et l'enfant*. Nice, Fr: Société française de la Douleur, Agency for Health Care Policy and Research; 1998. p. 11-5.
18. Torres LM, Calderon E, Pernia A, Martínez-Vasquez J, Mico JA. De la escalera al ascensor. *Rev Soc Esp Dolor* 2002;9(5):289-90.
19. Vargas-Schaffer G, Gonzalez de Mejia N, Castejon J, Fuenmayor F. Tratamiento del dolor en el paciente pediátrico. Consideraciones generales. *Arch Venez Pueric Pediatr* 2002;65(Suppl 1):S5-9.
20. Cahana A, Mavrocordatos P, Geurts JW, Groen GJ. Do minimally invasive procedures have a place in the treatment of chronic low back pain? *Expert Rev Neurother* 2004;4(3):479-90.
21. Vargas-Schaffer G. Fármacos empleados en los bloqueos anestésicos y analgésicos. In: Vargas-Schaffer G, Gonzalez de Mejia N, editors. *Manual de bloqueos anestésicos y analgésicos en pediatría*. Caracas, Venezuela: Ediciones Expansión Científica G&S; 2002. p. 41-72.
22. Jovey R., Ennis J, Gardner J, Goldman B, Hays H, Lynch M, et al. Use of opioid analgesics for the treatment of chronic noncancer pain—a consensus statement and guidelines from the Canadian Pain Society, 2002. *Pain Res Manag* 2003;8(Suppl A):3A-15A (Eng), 16A-28 (Fr).
23. Cerdá-Olmedo G, Monsalve V, Minguez A, Valiá JC, de Andrés JA. Algoritmo de decisión para el tratamiento del dolor crónico: una propuesta necesaria. *Rev Soc Esp Dolor* 2000;7(4):225-33.
24. The use of opioids for the treatment of chronic pain. A consensus statement from the American Academy of Pain Medicine and the American Pain Society. *Clin J Pain* 1997;13(1):6-8.
25. Collège des Médecins du Québec. *Treating pain: an update on the use of narcotics*. Montreal, QC: Collège des Médecins du Québec; 2002.
26. Vargas-Schaffer G. Los opioides en el tratamiento del dolor. *Rev Venez Anest* 2002;7(1):30-41.
27. Vargas-Schaffer G, Godoy D. Conceptos básicos del uso de opioides en el tratamiento del dolor oncológico. *Rev Venez Oncol* 2004;16(2):103-14.
28. Bruera E, Palmer JL, Bosnjak S, Rico MA, Moyano J, Sweeney C, et al. Methadone versus morphine as a first-line strong opioid for cancer pain: a randomized double-blind study. *J Clin Oncol* 2004;22(1):185-92.
29. Tramèr MR, Carroll D, Campbell FA, Reynolds DJ, Moore RA, McQuay HJ. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ* 2001;323(7303):16-21.
30. Clark AJ, Lynch ME, Ware M, Beaulieu P, McGilveray IJ, Gourlay D. Guidelines for the use of cannabinoid compounds in chronic pain. *Pain Res Manage* 2005;10(Suppl A):44A-6A.
31. Durán M, Capelà D. Cannabis y cannabinoides en el tratamiento del dolor neuropático. *Dolor* 2005;20:219-22.
32. Berlach DM, Shir Y, Ware MA. Experience with the synthetic cannabinoid nabilone in chronic noncancer pain. *Pain Med* 2006;7(1):25-9.
33. Frank B, Serpell MG, Huges J, Matthews JN, Kapur D. Comparison of analgesic effects and patients tolerability of nabilone and hydrocodeine for chronic neuropathic pain: randomized, crossover, double blind study. *BMJ* 2008;336:199-201. DOI: 10.1136/bmj39429.619653.80.
34. Dworkin RH, O'Connor AB, Backonja M, Farrar JT, Finnerup NB, Jensen TS, et al. Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain* 2007;132(3):237-51. Epub 2007 Oct 24. DOI: 10.1016/j.pain.2007.08.033.
35. Moulin DE, Clark AJ, Gilron I, Ware MA, Watson CP, Sessle BJ, et al. Pharmacological management of chronic neuropathic pain—consensus statement and guidelines from the Canadian Pain Society. *Pain Res Manag* 2007;12(1):13-21.

