## Methadone at Therapeutic Levels Linked to SCD

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Denver — Methadone in therapeutic doses appears to be associated with increased risk of sudden cardiac death, Dr. Carmen Socoteanu reported at the annual meeting of the Heart Rhythm Society.

This observation from a prospective case-control study has important public health implications in light of how widely the drug is prescribed for chronic pain control and opioid addiction, added Dr. Socoteanu of Oregon Health and Science University, Portland.

She reported on 22 consecutive cases of sudden cardiac death (SCD) featuring therapeutic blood levels of methadone. The cases were evaluated by the state medical examiner with detailed autopsies as part of the ongoing Oregon Sudden Unexplained Death Study sponsored by the Centers for Disease Control and Prevention.

Controls comprised 106 consecutive cas-

es of SCD with no evidence of methadone on toxicology screening during the same 4-year period. Individuals with evidence of recreational drug use or any drug overdose—including a blood methadone level over 1 mg/L—were excluded.

Among controls, a specific cardiac cause of SCD was identified in 60% of cases. In contrast, a cardiac cause could be identified in only 5 of 22 methadone users, or 23%, leaving therapeutic use of methadone as the only identifiable po-

tential etiology of SCD in most cases.

A key lesson from this study is that noncardiac drugs can cause arrhythmias and cardiac death, noted Dr. John P. Di-Marco, professor of medicine and director of the electrophysiology service at the University of Virginia, Charlottesville.

Late last year, the Food and Drug Administration issued a public health advisory and ordered methadone labeling changes because of the mounting evidence of serious adverse events.



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References: 1. American Lung Association. Lung Disease Data at a Glance: Obstructive Sleep Apnea (OSA) or Sleep-Disordered Breathing, http://www.lungusa.org/site.pp.asp?c=dvLUK9O0E&b=326701. Accessed January 23, 2006. 2. Shneerson JM. The Handbook of Sleep Medicine. Malden, MA: Blackwell Science, Ltd; 2000. 3. PROVIGIL [Dackage insert] West Chester, PA: Cephalon, Inc. 2004. 4. Black JE, Hirshkowitz M. Modafinil for treatment of residual excessive sleepiness in nasal continuous positive airway pressure-treated obstructive sleep apnea/hypopnea syndrome. Sleep. 2005;284-471. S. Pack Al, Black JE, Schwartz JRI, Matheson JK. Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. Am J Respir Crit Care Med. 2001;164:1675-1681. 6. Data on file, Cephalon, Inc.