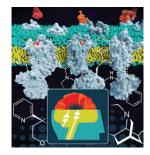
# ANESTHESIOLOGY





#### ON THE COVER:

New scientific discoveries are emerging in the field of opioid pharmacology at the same time the United States is responding to a surge in prescription opioid misuse. "Frontiers in Opioid Pharmacology," the 2017 ANESTHESIOLOGY Journal Symposium held during the American Society of Anesthesiologists Annual Meeting, highlighted many of these new scientific discoveries. In this issue of ANESTHESIOLOGY, readers will find articles describing new original laboratory and clinical research, retrospective and population studies with practice and policy implications, and reviews on a number of topics related to the pharmacology and clinical use of opioid analgesics. Many of these are written by anesthesiologists that are leading clinician-scientists in our field. We invite you to read and learn more from the Frontiers in Opioid Pharmacology. Cover illustration by Sara Jarret, C.M.I.; opioid receptor illustration ©ThinkStock; Journal Symposium logo by Annemarie Johnson, Vivo Visuals.

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SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

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Frontiers in Opioid Pharmacotherapy Symposium

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	Association of Multimodal Pain Management Strategies with Perioperative Outcomes and Resource Utilization: A Population-based Study S. G. Memtsoudis, J. Poeran, N. Zubizarreta, C. Cozowicz, E. E. Mörwald, E. R. Mariano, and M. Mazumdar	89
	Using a Premier Perspective database of total hip and knee arthroplasties, patients were grouped into "opioids only" and 1, 2, or more than 2 additional modalities. There was a stepwise modality number-associated decrease in opioid patient-controlled analgesia use, opioid prescriptions, and some opioid-related side effects, but not cost of hospitalization. The strongest association was for cyclooxygenase-2 inhibitors and nonsteroidal antiinflammatory drugs. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT	
◆ ●	Effects of Ambient Temperature and Forced-air Warming on Intraoperative Core Temperature: A Factorial Randomized Trial L. Pei, Y. Huang, Y. Xu, Y. Zheng, X. Sang, X. Zhou, S. Li, G. Mao, E. J. Mascha, and D. I. Sessler	90
	Ambient operating room temperature has a negligible effect on core temperature for forced-air warmed patients, and only a small effect on unwarmed patients. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT	

#### **BASIC SCIENCE**



# 🔰 🌐 Influence of Cardiac Output on the Pharmacokinetics of Sufentanil in Anesthetized Pigs

912

T. Birkholz, C. Leuthold, J. Schmidt, H. Ihmsen, J. Schüttler, and C. Jeleazcov

In 20 anesthetized pigs randomly assigned to have the pharmacokinetics of intravenously administered sufentanil studied under low, high, or normal cardiac output conditions, sufentanil intercompartmental clearance, compartmental volumes, and elimination clearance increased with cardiac output. As a result of cardiac output-related changes in pharmacokinetics, simulated sufentanil doses required to maintain a target plasma concentration increased with increasing cardiac output, as did its context-sensitive half-times. SUPPLEMENTAL DIGITAL CONTENT IS AVAILABLE IN THE TEXT

# Dexmedetomidine Prevents Cognitive Decline by Enhancing Resolution of High Mobility Group Box 1 Protein-induced Inflammation through a Vagomimetic Action in Mice

921

J. Hu, S. Vacas, X. Feng, D. Lutrin, Y. Uchida, I. K. Lai, and M. Maze

In a preclinical model, dexmedetomidine prevented cognitive deficits resulting from administration of high molecular group box 1 protein via both vagomimetic and humoral pathways. The results are consistent with the notion that the cognitive deficits noted after surgery or medical illness may be prevented by the administration of dexmedetomidine.

### ■ PAIN MEDICINE

#### **CLINICAL SCIENCE**



### Senefit versus Severe Side Effects of Opioid Analgesia: Novel Utility Functions of Probability of Analgesia and Respiratory Depression

932

M. Roozekrans, R. van der Schrier, L. Aarts, E. Sarton, M. van Velzen, M. Niesters, A. Dahan, and E. Olofsen

The concept of the utility function was further developed for alfentanil by calculating the probabilities of adequate analgesia with or without respiratory depression and the probabilities of inadequate analgesia with or without respiratory depression using data from three studies of 48 patients. A 50% decrease in minute ventilation was taken as the threshold for severe respiratory depression and both 25% and 50% increases in tolerated electrical current were thresholds for analgesia. The probabilities of the four conditions varied with alfentanil effect-site concentrations.



## Pharmacokinetic Properties of a Sufentanil Sublingual Tablet Intended to Treat Acute Pain D. M. Fisher, P. Chang, D. R. Wada, A. Dahan, and P. P. Palmer

943

With sublingual administration of a newly developed 30-µg sufentanil tablet, the time to maximum plasma concentration was approximately 1 h, but the analgesic threshold was typically reached at or before 30 min, which is consistent with the onset of analgesia observed in clinical trials of the 30-µg product. The time for the plasma concentrations to decrease below the analgesic threshold after a single 30-µg dose was approximately 3 h, which is consistent with the duration of analgesia in those published clinical trials.



## 👁 🜣 New Opioid Analgesic Approvals and Outpatient Utilization of Opioid Analgesics in the United States, 1997 through 2015

953

G. Chai, J. Xu, J. Osterhout, M. A. Liberatore, K. L. Miller, C. Wolff, M. Cruz, P. Lurie, and G. Dal Pan

Data on new brand and generic opioid analgesic product approvals, and on retail dispensed prescription claims, were used to evaluate the opioid product space. Opioid prescriptions dispensed and amount per prescription nearly doubled, and total morphine milligram equivalents more than tripled, from 1997 to the peak in 2010, and partially declined thereafter. Generic products accounted for 68% of total opioid prescriptions in 1997 and 96% in 2015. Approval of new branded opioid products alone does not appear to be a primary driver of increased opioid prescribing.

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Neurologic Considerations and Complications Related to Liver Transplantation

S. S. Kumar, G. A. Mashour, and P. Picton

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