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馬克.阿.魏, 麗安.菲茨查理斯, 劳倫斯.約瑟夫, 羅亞馬.柴

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啟動大鼠脊髓α2 腎上腺受體而非μ-阿片受體，降低鞘內注射N-甲基-D-天冬氨酸（NMDA）所致脊髓NR1 亞單位磷酸化增加和感受傷害行為學改變
(江繼宏 譯 馬皓琳 李士通 校)

Activation of Spinal α-2 Adrenoceptors, but Not μ-Opioid Receptors, Reduces the Intrathecal N-Methyl-d-Aspartate-Induced Increase in Spinal NR1 Subunit Phosphorylation and Nociceptive Behaviors in the Rat

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Seo-Yeon Yoon,
Sunok Song,
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Alvin J. Beitz,
and Jang-Hern Lee


REGIONAL ANESTHESIA
Serum Ropivacaine Concentrations and Systemic Local Anesthetic Toxicity in Trauma Patients Receiving Long-Term Continuous Peripheral Nerve Block Catheters

- Lisa L. Bleckner,
- Saiid Bina,
- Kyung H. Kwon,
- Geselle McKnight,
- Anthony Dragovich,
- and Chester C. Buckenmaier III


- Michael J. Buys,
- Christopher D. Arndt,
- Firoz Vagh,
- Anna Hoard,
- and Neal Gerstein


Hemofiltration During Cardiopulmonary Bypass Does Not Decrease the Incidence of Atrial Fibrillation After Cardiac Surgery
BACKGROUND: Atrial fibrillation (AF) occurs in 20%–50% of patients after cardiac surgery and is associated with increased morbidity and mortality. Corticosteroids are reported to decrease the incidence of postoperative AF, presumably by attenuating inflammation caused by surgery and cardiopulmonary bypass (CPB). We hypothesized that hemofiltration during CPB, which may attenuate inflammation, might decrease the incidence of AF after cardiac surgery.

METHODS: This was a retrospective review of patients previously enrolled in a double-blind, placebo-controlled trial evaluating the effects of perioperative steroid therapy and hemofiltration during CPB on duration of postoperative mechanical ventilation. In that study, 192 patients undergoing cardiac surgery were randomized to 1 of 3 groups: controls (placebo), hemofiltration during CPB, or perioperative steroid therapy. Patient records were reviewed to determine the incidence of new onset AF defined as any electrocardiogram evidence of AF or AF diagnosed by the patients' clinicians.

RESULTS: Of the 192 enrolled patients, 3 were excluded for protocol violations and 4 were excluded for history of chronic AF. Data from 185 patients from the original study were available for review. Sixty patients (32%) had new onset AF after cardiac surgery. There was no difference among groups in the incidence of AF (control group, 21%; steroid group, 41%; hemofiltration group, 36%; \( P = 0.057 \) among groups). The only risk factor for the development of AF was age (mean age of patients with AF, 65.4 ± 10.1 yr vs patients without AF, 61.4 ± 11.5 yr; \( P = 0.024 \)). When age, procedure type, and presence or absence of chronic obstructive pulmonary disease were controlled for in multivariate analysis, the difference among study groups remained nonsignificant (\( P = 0.108 \)).
CONCLUSIONS: Perioperative corticosteroids or the use of hemofiltration during CPB did not decrease the incidence of AF after cardiac surgery. Further studies evaluating the efficacy and safety of perioperative corticosteroids for prevention of postoperative AF are warranted before their routine use can be recommended.

心臟手術病人，大劑量氨甲環酸與臨床非缺血性癲癇發作有關
High-Dose Tranexamic Acid Is Associated with Nonischemic Clinical Seizures in Cardiac Surgical Patients
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BACKGROUND: In 2 separate centers, we observed a notable increase in the incidence of postoperative convulsive seizures from 1.3% to 3.8% in patients having undergone major cardiac surgical procedures. These events were temporally coincident with the initial use of high-dose tranexamic acid (TXA) therapy after withdrawal of aprotinin from general clinical usage. The purpose of this review was to perform a retrospective analysis to examine whether there was a relation between TXA usage and seizures after cardiac surgery.

METHODS: An in-depth chart review was undertaken in all 24 patients who developed perioperative seizures. Electroencephalographic activity was recorded in 11 of these patients, and all patients had a formal neurological evaluation and brain imaging studies.

RESULTS: Twenty-one of the 24 patients did not have evidence of new cerebral ischemic injury, but seizures were likely due to ischemic brain injury in 3 patients. All patients with seizures did not have permanent neurological abnormalities. All 24 patients with seizures received high doses of TXA intraoperatively ranging from 61 to 259 mg/kg, had a mean age of 69.9 years, and 21 of
24 had undergone open chamber rather than coronary bypass procedures. All but one patient were managed using cardiopulmonary bypass. No evidence of brain ischemic, metabolic, or hyperthermia-induced causes for their seizures was apparent.

CONCLUSION: Our results suggest that use of high-dose TXA in older patients in conjunction with cardiopulmonary bypass and open-chamber cardiac surgery is associated with clinical seizures in susceptible patients.

Intraosseous Infusions: A Review for the Anesthesiologist with a Focus on Pediatric Use

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Intraosseous (IO) access is used most frequently for emergency care of critically ill infants and children when IV access cannot be rapidly achieved. Despite its efficacy in such situations, applications outside of the emergency room or resuscitation scenario have been limited. Furthermore, although the technique is emphasized in the teaching of those caring for critically ill infants and children in the emergency room or critical care setting, there is limited emphasis on its potential use in the perioperative setting. When peripheral venous access cannot be achieved in the operating room, alternative means of securing vascular access such as central line placement or surgical cutdown are generally successful; however, these techniques may be time consuming. Anyone providing anesthesia care for infants and children may want to become facile with the use of IO infusions for selected indications. We present the history of IO infusions, review the anatomy of the bone marrow space, discuss the potential role of IO infusions in the perioperative period, and analyze its adverse effect profile.

Anesthesia and the Old Brain

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The perioperative period may have long-term consequences on cognitive function in the elderly patient. In this special article, we summarize the rationale and evidence that the anesthetic per se is a contributor. The evidence at this point is considered suggestive and further research is needed, especially in humans.

**Transgenic Alzheimer Mice Have a Larger Minimum Alveolar Anesthetic Concentration of Isoflurane than Their Nontransgenic Littermates**

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**BACKGROUND:** More than 12% of all people older than 65 yr have Alzheimer's disease. Because nothing is known about changes in demand of volatile anesthetics in this disease, we determined minimum alveolar anesthetic concentration (MAC) values of isoflurane in young and aged transgenic mice at risk of developing Alzheimer's disease (heterozygote APP23 with Swedish double mutation). To differentiate between unspecific effects of the transgenic model and specific Alzheimer effects, we additionally evaluated MAC values in mice with the same genetic construct but without the Alzheimer's disease-causing Swedish double mutation (heterozygote APP51/16 mice).

**METHODS:** MAC was determined in 60 mice (10 per group): heterozygote APP23 mice and their wild type littermates at the age of 4 and 18 mo, respectively, and heterozygote APP51/16 mice.
mice and their wild type littermates at the age of 18 mo. Anesthesia was induced with isoflurane in oxygen/air. The concentration of inhaled isoflurane varied between 1.0 and 2.0 Vol%, and the motor reaction to toeclamping was recorded. Means of the MAC values were compared with an unpaired *t*-test.

**RESULTS:** The MAC of 18-mo-old heterozygote APP23 mice was 1.67 ± 0.09, i.e., 9% larger than the MAC of their wild type littermates (1.53 ± 0.14; *P* = 0.020). Heterozygote APP51/16 mice had a lower MAC than their wild type littermates (1.32 ± 0.14 vs 1.48 ± 0.13; *P* = 0.037). All wild type groups and young heterozygote APP23 mice had comparable MAC values.

**CONCLUSIONS:** The increased MAC value in aged heterozygote APP23 mice seems to be attributable to changes related to Alzheimer's disease.

**Inhibition of Human α4β2 Neuronal Nicotinic Acetylcholine Receptors by Volatile Aromatic Anesthetics Depends on Drug Hydrophobicity**

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anesthetics are useful pharmacological tools for probing the relationship between chemical structure and drug activity at putative general anesthetic targets. Neuronal nicotinic acetylcholine (nACh) receptors are ligand-gated ion channels widely expressed in the brain, which are thought to play important roles in learning and memory. In this study, we tested the hypothesis that aromatic anesthetics reversibly inhibit α4β2 neuronal nACh receptor function and sought to determine the structural correlates of receptor inhibition.

**METHODS:** Electrophysiological techniques were used to quantify the effects of 8 volatile aromatic anesthetics on currents elicited by 1 mM ACh and mediated by human α4β2 nACh receptors expressed in *Xenopus* oocytes.

**RESULTS:** All of the volatile aromatic anesthetics used in this study reversibly inhibited α4β2 nACh receptors with IC50 values ranging from 0.00091 atm for 1,2-difluorobenzene to 0.045 atm for hexafluorobenzene. With the exception of hexafluorobenzene, all of the compounds had IC50 values less than minimum alveolar concentration. Inhibitory potency correlated poorly with the cation-π binding energies of the compounds (r² = 0.48, P = 0.059). However, there was a good correlation between inhibitory potency and the octanol/gas partition coefficient (r² = 0.87, P = 0.0008).

**CONCLUSIONS:** Volatile aromatic anesthetics potently and reversibly inhibit human α4β2 neuronal nACh receptors. This inhibition may play a role in producing amnesia. In contrast to N-methyl-d-aspartate receptors, the inhibitory potencies of aromatic anesthetics for α4β2 neuronal nACh receptors seem to be dependent on drug hydrophobicity rather than electrostatic properties. This implies that the volatile aromatic anesthetic binding site in the α4β2 neuronal nACh receptor is hydrophobic in character and differs from the nature of the binding site in N-methyl-d-aspartate receptors.

**圍術期血糖調控的原則與臨床意義**

**Scientific Principles and Clinical Implications of Perioperative Glucose Regulation and Control**

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大手術後高血糖非常普遍，並由多因素調控。常見因素包括圍術期代謝狀態、術中病人管理及手術引起的神經內分泌瀉應反應。急性胰島素抵抗也會引起圍術期高血糖，並且起到很大作用。高血糖與危重病人及手術病人的不良預後具有相關性。經調查多數“高血糖”的診斷過於隨便，而且其初始治療閾值也大相逕異。曾有研究表明接受強化血糖控制（IGC,目標血糖濃度<110 mg/dL）的危重及手術病人預後得以改善。這些結果被其他臨床領域借鑒，並且圍術期也廣泛採用強化血糖控制。然而，很少有研究證實圍術期血糖控制的意義。此外，因沒有（確定）適當的血糖治療目標值，也沒有闡明圍術期血糖控制的真正效能，最近這些前瞻性實驗並不能體現IGC的益處。執業醫師們需理解不同血糖測量技術的臨床意義。IGC 顯著增加高血糖的危險性，而這在危重病人並無相關性。最新收集資料表明：圍術期血糖應慎重地控制在<180 mg/dL，同時血糖控制應基於密切的血糖監測。

(鄒巧群 譯 陳傑 校)
Development of hyperglycemia after major operations is very common and is modulated by many factors. These factors include perioperative metabolic state, intraoperative management of the patient, and neuroendocrine stress response to surgery. Acute insulin resistance also develops perioperatively and contributes significantly to hyperglycemia. Hyperglycemia is associated with poor outcomes in critically ill and postsurgical patients. A majority of the investigations use the term "hyperglycemia" very loosely and use varying thresholds for initiating treatment. Initial studies demonstrated improved outcomes in critically ill, postsurgical patients who received intensive glycemic control (IGC) (target serum glucose <110 mg/dL). These results were quickly extrapolated to other clinical areas, and IGC was enthusiastically recommended in the perioperative period. However, there are few studies investigating the value of intraoperative glycemic control. Moreover, recent prospective trials have not been able to show the benefit of IGC; neither an appropriate therapeutic glycemic target nor the true efficacy of perioperative glycemic control has been fully determined. Practitioners should also appreciate technical nuances of various glucose measurement techniques. IGC increases the risk of hypoglycemia significantly, which is not inconsequential in critically ill patients. Until further specific data are accumulated, it is prudent to maintain glucose levels <180 mg/dL in the perioperative period, and glycemic control should always be accompanied by close glucose monitoring.

Anesthetic Management of Patients with Huntington Disease
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BACKGROUND: Huntington disease (HD) is a rare autosomal dominant disease with symptoms of chorea, dystonia, incoordination, cognitive decline, and behavioral difficulties. Abnormal responses to anesthesia have been reported in case reports and raised concerns regarding the safety of anesthesia in this patient population.
METHODS: We performed a computerized search of the Mayo Clinic medical records database searching for patients with HD who underwent general anesthesia. Medical records were reviewed for anesthetic technique, medications used, and postoperative complications. RESULTS: We identified 11 patients with genetically confirmed HD who underwent 17 general anesthetics. Psychiatric medication use was common, with 6 patients using antipsychotics, 7 patients using antidepressants, and 3 patients using benzodiazepines. Succinylcholine was used in 7 anesthetics, and nondepolarizing neuromuscular blocking drugs in 11 anesthetics, all without adverse effects. Patients had normal responses to induction and maintenance of anesthesia without adverse effects. Serious postoperative complications did not occur. CONCLUSION: Contrary to previous case reports, we found that patients with HD have normal responses to general anesthesia. However, the anesthesiologist should be aware of interactions between anesthetics and psychiatric medications frequently used by these patients. Measures should also be taken to minimize the risk of pulmonary aspiration because bulbar dysfunction may be a manifestation of this disease.

血管活性藥物對內毒素血症的大鼠腸道功能性毛細血管密度（FCD）的影響：活體顯微視頻分析

The Effects of Vasoactive Drugs on Intestinal Functional Capillary Density in Endotoxemic Rats: Intravital Video-Microscopy Analysis

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BACKGROUND: The use of vasoactive drugs to restore arterial blood pressure in patients with septic shock remains a cornerstone of intensive care medicine. However, vasopressors can accentuate the hypoperfusion of the gut during septic shock, allowing bacterial translocation and endotoxemia. In this study, we compared the effects of different vasoactive drugs on intestinal microcirculation and tissue oxygenation, independent of the effects of fluid therapy, in a rat model of endotoxemic shock.

METHODS: Pentobarbital-anesthetized Wistar Kyoto rats were submitted to endotoxemic shock induced by *Escherichia coli* lipopolysaccharide (2 mg/kg IV). Arterial blood pressure was normalized by a continuous infusion of different vasoactive drugs, including epinephrine, norepinephrine, phenylephrine, dopamine, dobutamine, or a combination of dobutamine and norepinephrine. The functional capillary density (FCD) of the muscular layer of the small intestine was evaluated by intravital video-microscopy. Mesenteric venous blood gases and lactate concentrations were also analyzed.

RESULTS: FCD decreased by approximately 25% to 60% after the IV infusion of epinephrine, norepinephrine, and phenylephrine. Administration of dopamine, dobutamine, and the combination of dobutamine and norepinephrine did not induce significant alterations in gut FCD. In addition, the mesenteric venous lactate concentration increased in the presence of phenylephrine and showed a tendency to increase after the administration of epinephrine and norepinephrine, whereas there was no observable increase after the administration of dopamine, dobutamine, and the combination of dobutamine with norepinephrine.

CONCLUSION: This study confirms dissociation of the systemic hemodynamic and microvascular alterations in an experimental model of septic shock. Moreover, the results indicate that the use of dopamine, dobutamine, and dobutamine in combination with norepinephrine yields a protective effect on the microcirculation of the intestinal muscular layer in endotoxemic rats.

Meta 分析比較地氟醚和七氟醚拔管平均時間和變異率

Statistical Modeling of Average and Variability of Time to Extubation for Meta-Analysis Comparing Desflurane to Sevoflurane

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背景：理想的麻醉藥和麻醉方法是復蘇快（例如：從手術結束到拔管平均 5min）且變異度小（例如：總是 4-7min）。作者用 AIMS 資料研究如何模仿從手術結束到拔管的時間。應用 meta 分析測試那些資訊，比較使用地氟醚和七氟醚後的拔管時間。

方法：AIMS data 研究由 95 位外科醫生實施的 32,792 例手術，包括在手術室的氣管插管和拔管，以及使用麻醉揮發氣體。Meta 分析通過 2008 年 29 個隨機對照研究來比較應用七氟醚和地氟醚的拔管時間。方法和標準差百分比的不同應用隨機 meta 分析和 Bayesian 法來研究。

結果：拔管的時間用威布林分佈分析較正態分佈分析更適合。藥物選擇對平均值和標準差的影響幾乎一致，正像變異係數未變一樣（29 個研究中 26 個研究 \( P > 0.10 \)）及差值變異係數變化無意義（七氟醚－地氟醚 = –1%，95% 可信區間 [CI] –3% to 1%，\( P = 0.22 \)）。地氟
BACKGROUND: The recovery profile of an ideal anesthetic or technique would be fast (e.g., mean of 5 min from end of surgery to extubation) with little variability (e.g., always 4–7 min). We used anesthesia information management system (AIMS) data to learn how to model the time from end of surgery to extubation. We applied that knowledge for meta-analyses of trials comparing extubation times after use of desflurane and sevoflurane.

METHODS: AIMS data studied were 32,792 cases performed by 95 surgeons that included tracheal intubation and extubation in the operating room (OR) and use of volatile anesthetic(s). Meta-analysis included the 29 randomized controlled trials through 2008 comparing extubation times with desflurane and sevoflurane. Percentage differences in means and standard deviations were studied using random effects meta-analysis and a Bayesian method.

RESULTS: Times to extubation were better fit by (skewed) Weibull distributions than by (symmetric) normal distributions. Drug choice had nearly equally proportional effects on the means and standard deviations of extubation times, as shown by unchanged coefficients of variation (P > 0.10 for 26 of 29 studies) and nonsignificant pooled difference in the coefficient of variation (sevoflurane – desflurane = –1%, 95% confidence interval [CI] –3% to 1%, P = 0.22). Applying these findings, desflurane reduced the mean extubation time by 25% (95% CI 17%–32%, P < 0.0001) and standard deviation by 21% (95% CI 16%–26%). To value the intangible costs (e.g., frustrated waiting surgeons) of prolonged extubation times, we considered the 15% of AIMS cases with times >15 min. These cases averaged 4.9 min longer times from out of the OR to the start of surgery of the surgeon's next case (95% CI 2.7–7.1 min, P < 0.0001). Reduction in the means and standard deviations by 20%–25% would likely reduce incidences of these prolonged extubation times by 71%–82% (95% CI 68%–84%).

CONCLUSIONS: Desflurane reduces the average extubation time and the variability of extubation time by 20%–25% relative to sevoflurane. The principal economic value of these end points is their reductions of direct (labor) costs of OR time. However, reductions in intangible costs of prolonged extubation are real, being associated with subsequent delays. Reductions in the average and variance of times to extubation can be interpreted and monitored in terms of corresponding expected 75% reductions in the incidences of prolonged extubation times by using desflurane relative to sevoflurane.
背景：睡眠障碍会对许多有慢性疼痛的病人造成影响。曾有报告称，印度大麻可帮助病人入睡。以广泛的慢性疼痛和失眠为主要特征的纤维肌痛症也会引起睡眠障碍，因而本文主要讨论研究了一种合成的大麻素，即大麻隆，在治疗这种睡眠障碍过程中的安全性和有效性。

方法：作者应用随机、双盲、主动对照及交叉试验的方法比较了大麻隆（睡前0.5–1.0mg）和阿米替林（睡前10–20mg）对于有慢性失眠症的纤维肌痛病人的不同作用。受试者各服用大麻隆和阿米替林两种药物两个星期，之后各有两个星期的药物洗脱期。主要的评价结果是睡眠品质，用失眠严重指数以及里兹睡眠评估问卷来测试。次要的评价结果包括疼痛、情绪、生活品质和副反应。

结果：31个受试者加入了这个实验，其中29个完成了这项实验（26个女性，平均年龄49.5岁）。尽管大麻隆和阿米替林都能帮助睡眠，但是大麻隆比阿米替林的作用效果更好（失眠严重指数相差3.2，95%CI=1.2–5.3）。大麻隆可以帮助病人好好地休息，在这方面的效果比阿米替林稍稍优越（里兹睡眠评估问卷差值=0.5（0.0–1.0）），然而对于不眠症，大麻隆和阿米替林相比没有多大差别（差值=0.3（-0.2–0.8））。我们没有发现两种药物对于疼痛、情绪和生活品质的影响。但是有轻到中度的副反应，而且大麻隆的副作用较阿米替林更频繁。大麻隆最常见的副作用是头昏眼花、恶心和口干。

结论：大麻隆可有效提高纤维肌痛病人的睡眠品质，且耐受性好。作者认为，大麻隆比阿米替林更优，而不选择阿米替林。还需进行更多的试验来明确大麻隆这种药物使用的持续时间以及长期使用这种药物的安全性问题。

张婷 谭 陈杰 校

BACKGROUND: Sleep disorders affect many patients with chronic pain conditions. Cannabis has been reported by several patient populations to help sleep. We evaluated the safety and efficacy of nabilone, a synthetic cannabinoid, on sleep disturbance in fibromyalgia (FM), a disease characterized by widespread chronic pain and insomnia.

METHODS: We conducted a randomized, double-blind, active-control, equivalency crossover trial to compare nabilone (0.5–1.0 mg before bedtime) to amitriptyline (10–20 mg before bedtime) in patients with FM with chronic insomnia. Subjects received each drug for 2 wk with a 2-wk washout period. The primary outcome was sleep quality, measured by the Insomnia Severity Index and the Leeds Sleep Evaluation Questionnaire. Secondary outcomes included pain, mood, quality of life, and adverse events (AEs).

RESULTS: Thirty-one subjects were enrolled and 29 completed the trial (26 women, mean age 49.5 yr). Although sleep was improved by both amitriptyline and nabilone, nabilone was superior to amitriptyline (Insomnia Severity Index difference = 3.2; 95% confidence interval = 1.2–5.3). Nabilone was marginally better on the restfulness (Leeds Sleep Evaluation Questionnaire difference = 0.5 [0.0–1.0]) but not on wakefulness (difference = 0.3 [-0.2 to 0.8]). No effects on pain, mood, or quality of life were observed. AEs were mostly mild to moderate and were more frequent with nabilone. The most common AEs for nabilone were dizziness, nausea, and dry mouth.
CONCLUSIONS: Nabilone is effective in improving sleep in patients with FM and is well tolerated. Low-dose nabilone given once daily at bedtime may be considered as an alternative to amitriptyline. Longer trials are needed to determine the duration of effect and to characterize long-term safety.

Serum ropivacaine concentrations and systemic local anesthetic toxicity in trauma patients receiving long-term continuous peripheral nerve block catheters

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背景：羅呱卡因是一種長效局麻藥，常用于外周神經阻滯及連續外周神經阻滯導管中。在 Walter Reed 部隊醫療中心，戰爭創傷患者疼痛治療方案的一部分就是接受連續外周神經阻滯導管。這些導管通常在原處留置數日至數周不等。在本次研究中，作者通過檢測患者血清中结合的和非結合的局麻藥的濃度，以評估隨著時間的推移，創傷患者羅呱卡因的血藥濃度水準。同時，還檢測了長時間接受羅呱卡因輸注患者的血清 α-酸糖蛋白的濃度。

方法：本次研究共有 15 位患者入組，其中 2 位因僅獲取到一個羅呱卡因濃度而被排除。在其中 13 位患者中，2 位在入組時放置了外周神經阻滯導管，另外 11 位在入組前即已放置，且這些患者在首次測試局麻藥水準之前，已接受輸注 0.2% 羅呱卡因 18-126 小時。0.2% 羅呱卡因的輸注速度為 6-14ml/h，導管內單次給藥時羅呱卡因的濃度為 0.5%。在第 1、3、5、7 和 10 日及此後每 3 日一次測量局麻藥的血藥濃度，直到拔除所有導管，但患者並未全部接受所有檢測。

結果：在研究入組的 13 位患者中，共獲取了 59 個血樣本。為了控制急性疼痛，導管在原處留置的平均時間為 7 日（範圍：6-27 日）。患者入組後當管留置在原處的平均時間為 7 日（範圍：4-25 日）。每位患者平均獲取到 4 個血樣本（範圍：2-10 個樣本）。2 位患者的血清遊離羅呱卡因濃度異常升高並超出之前認為的毒性範圍，且沒有明顯的下降的跡象。這兩位患者在抽取該血樣本之前約 24 小時內接受 0.5% 羅呱卡因的單次給藥共 300mg。研究整個過程中羅呱卡因的平均濃度為 0.11mg/l（範圍：測不到至 0.63mg/l）。在研究開始後的第一周內，每位患者的血清羅呱卡因濃度的平均變化值為 0.00mg/l（範圍：-0.35-0.47mg/l）。

結論：儘管 2 位患者的血清遊離羅呱卡因濃度異常升高並超出之前認為的毒性範圍，但是 Walter Reed 部隊醫療中心所使用的連續外周神經阻滯導管及其給予的局麻藥劑量並未在臨床上導致明顯的全身毒性。除了 1 位在入組前已接受羅呱卡因輸注外，其餘患者的羅呱卡因濃度和 α-酸糖蛋白的濃度之間沒有相關性。儘管如此，局麻藥輸注的總時間似乎並不影響藥物的遊離濃度。
BACKGROUND: Ropivacaine is a long-acting local anesthetic used frequently for peripheral nerve blocks and continuous peripheral nerve block catheters. Combat trauma patients at Walter Reed Army Medical Center often receive continuous peripheral nerve block catheters as part of their pain regimen. These catheters remain in situ for several days to weeks. In this study, we evaluated the free ropivacaine drug levels over time in trauma patients by measuring the serum concentration of bound and unbound local anesthetic. The corresponding α1-acid glycoprotein concentration in patients with prolonged ropivacaine infusions was also measured.

METHODS: Fifteen patients were enrolled in the study; 2 patients were excluded because only a single ropivacaine level was obtained. Of the remaining 13 patients in the study, 2 had peripheral nerve catheters placed at the time of enrollment; the remaining 11 patients had catheters placed before enrollment. These patients were already receiving 0.2% ropivacaine infusions for a period of 18–126 h before the first assessment of local anesthetic level. Catheters infused 0.2% ropivacaine at a rate of 6–14 mL/h; catheter boluses were administered with 0.5% ropivacaine. Local anesthetic blood concentrations were scheduled to be measured on Days 1, 3, 5, 7, and 10 and every 3 days thereafter until all catheters were removed, although not all patients underwent each assessment. Specimens were assayed using high-performance liquid chromatography for total and free serum ropivacaine concentrations. α1-Acid glycoprotein was also measured.

RESULTS: Thirteen patients remained in the study, for a total of 59 blood samples. The median number of days catheters remained in situ for the duration of acute pain therapy was 7 days (range: 6–27 days). The median number of days catheters remained in situ after enrollment into the study was 7 days (range: 4–25 days). The median number of blood samples collected per patient was 4 (range: 2–10 samples). Two patients had isolated increased concentrations of free ropivacaine into a previously identified toxic range with no obvious mitigating factors; both patients had received a 300-mg bolus of 0.5% ropivacaine approximately 24 h before that blood collection. The median ropivacaine concentration over the length of the study was 0.11 mg/L (range: undetectable to 0.63 mg/L). During the first week of the study, the median change in ropivacaine concentration per patient was 0.00 mg/L (range: –0.35 to 0.47 mg/L).

CONCLUSION: Although 2 patients demonstrated isolated serum ropivacaine concentration spikes into a previously identified toxic range, continuous peripheral nerve block catheter management and local anesthetic doses as practiced at Walter Reed Army Medical Center did not result in clinically evident systemic ropivacaine toxicity. There was no correlation between free ropivacaine concentration and α1-acid glycoprotein concentration except in patients who had already been receiving ropivacaine infusions before entering the study. Despite this lack of correlation, the total duration of local anesthetic infusion did not seem to influence the free concentration of the drug.

低溫體外迴圈複溫過程中的腦血流自動調節功能受損及其與中風的潛在聯繫
Impaired Autoregulation of Cerebral Blood Flow During Rewarming from Hypothermic Cardiopulmonary Bypass and Its Potential Association with Stroke
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BACKGROUND: Patient rewarming after hypothermic cardiopulmonary bypass (CPB) has been linked to brain injury after cardiac surgery. In this study, we evaluated whether cooling and then rewarming of body temperature during CPB in adult patients is associated with alterations in cerebral blood flow (CBF)–blood pressure autoregulation.

METHODS: One hundred twenty-seven adult patients undergoing CPB during cardiac surgery had transcranial Doppler monitoring of the right and left middle cerebral artery blood flow velocity. Eleven patients undergoing CPB who had arterial inflow maintained at >35°C served as controls. The mean velocity index (Mx) was calculated as a moving, linear correlation coefficient between slow waves of middle cerebral artery blood flow velocity and mean arterial blood pressure. Intact CBF–blood pressure autoregulation is associated with an Mx that approaches 0. Impaired autoregulation results in an increasing Mx approaching 1.0. Comparisons of time-averaged Mx values were made between the following periods: before CPB (baseline), during the cooling and rewarming phases of CPB, and after CPB. The number of patients in each phase of CPB with an Mx >4.0, indicative of impaired CBF autoregulation, was determined.
RESULTS: During cooling, Mx (left, 0.29 ± 0.18; right, 0.28 ± 0.18 [mean ± sd]) was greater than that at baseline (left, 0.17 ± 0.21; right, 0.17 ± 0.20; P ≤ 0.0001). Mx increased during the rewarming phase of CPB (left, 0.40 ± 0.19; right, 0.39 ± 0.19) compared with baseline (P ≤ 0.001) and the cooling phase (P ≤ 0.0001), indicating impaired CBF autoregulation. After CPB, Mx (left, 0.27 ± 0.20; right, 0.28 ± 0.21) was higher than at baseline (left, P = 0.0004; right, P = 0.0003), no different than during the cooling phase, but lower than during rewarming (left, P ≤ 0.0001; right, P ≤ 0.0005). Forty-three patients (34%) had an Mx ≥ 0.4 during the cooling phase of CPB and 68 (53%) had an average Mx ≥ 0.4 during rewarming. Nine of the 11 warm controls had an average Mx ≥ 0.4 during the entire CPB period. There were 7 strokes and 1 TIA after surgery. All strokes were in patients with Mx ≥ 0.4 during rewarming (P = 0.015). The unadjusted odds ratio for any neurologic event (stroke or transient ischemic attack) for patients with Mx ≥ 0.4 during rewarming was 6.57 (95% confidence interval, 0.79 to 55.0, P < 0.08).

CONCLUSIONS: Hypothermic CPB is associated with abnormal CBF–blood pressure autoregulation that is worsened with rewarming. We found a high rate of strokes in patients with evidence of impaired CBF autoregulation. Whether a pressure-passive CBF state during rewarming is associated with risk for ischemic brain injury requires further investigation.

左布比卡因對離體大鼠主動脈的直接影響與脂氧酶通道啟動和內皮源性一氧化氮釋放有關

The Direct Effect of Levobupivacaine in Isolated Rat Aorta Involves Lipoxygenase Pathway Activation and Endothelial Nitric Oxide Release

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背景: 左布比卡因是一種長效局部麻醉藥,它臨床特點與消旋布比卡因類似, 但是它有較大的安全範圍。在活體上, 左布比卡因能產生劑量依賴性的血管收縮。本篇離體研究中, 我們的目的是: 研究花生四烯酸代謝通路在左布比卡因導致離體大鼠主動脈收縮中的作用及探討哪種內皮源性血管舒張劑調節左布比卡因誘導血管收縮。

方法: 分離大鼠胸主動脈環並懸吊, 用於記錄等長張力。在 10-6 到 3 x 10-4 M 濃度範圍內, 在以下三組實驗繫製等積左布比卡因濃度反應曲線: 1）無藥物預處理的主動脈環組; 2）內皮剝除的主動脈環組, 預處理用二氫腰挫木酸 (NDGA) (脂氧合酶抑制劑: 10-5、3 x 10-5 M)、消炎痛 (非特異環氧合酶抑制劑: 10-5 M)、AA-861 (5-脂氧合酶抑制劑: 10-5、5 x 10-5 M)、氟康唑 (細胞色素 P450 環氧化酶抑制劑: 10-5 M)、維拉帕米 (10-5 M) 或無鈣溶液; 3）內皮完整的主動脈環組, 預處理用 Nω-硝基-L 精氨酸甲酯 (L-NAME) (一氧化氮合成酶抑制劑: 5 x 10-5 M)、消炎痛、或氟康唑。在內皮剝除主動脈環組，評
BACKGROUND: Levobupivacaine is a long-acting local anesthetic with a clinical profile similar to that of racemic bupivacaine but with a greater margin of safety. Levobupivacaine produces dose-dependent vasoconstriction in vivo. Our goal in this in vitro study was to investigate the role of pathways involved in arachidonic acid metabolism in the levobupivacaine-induced contraction of isolated rat aorta and to determine which endothelium-derived vasodilators are involved in the modulation of levobupivacaine-induced contraction.

METHODS: Rat thoracic aortic rings were isolated and suspended for isometric tension recording. Cumulative levobupivacaine dose-response curves over a range of $10^{-6}$ to $3 \times 10^{-4}$ M were constructed in 1) aortic rings with no drug pretreatment; 2) endothelium-denuded rings pretreated with quinacrine dihydrochloride (nonspecific phospholipase A$_2$ inhibitor: $2 \times 10^{-5}$, $4 \times 10^{-5}$ M), nordihydroguaiaretic acid (NDGA) (lipoxygenase inhibitor: $10^{-5}$, $3 \times 10^{-5}$ M), indomethacin (nonspecific cyclooxygenase inhibitor: $10^{-5}$ M), AA-861 (5-lipoxygenase inhibitor: $10^{-5}$, $5 \times 10^{-5}$ M), fluconazole (cytochrome P450 epoxygenase inhibitor: $10^{-5}$ M), verapamil ($10^{-5}$ M), or calcium-free solution; and 3) endothelium-intact rings pretreated with $N^\omega$-nitro-l-arginine methyl ester (L-NAME) (nitric oxide synthase inhibitor: $5 \times 10^{-5}$ M), indomethacin, or fluconazole. Levobupivacaine-induced contractile response at each concentration ($10^{-4}$, $3 \times 10^{-4}$ M) was assessed in endothelium-denuded rings. Dose-response curves for potassium chloride in endothelium-denuded rings were generated in the presence or absence of NDGA and AA-861. Intracellular $Ca^{2+}$ levels were monitored by $Ca^{2+}$ image analysis using Fluo-4 fluorescence in vascular smooth muscle cells treated with levobupivacaine alone or AA-861 plus levobupivacaine.

RESULTS: Levobupivacaine produced a tonic contraction in isolated rat aorta rings; this response was maximal at $10^{-4}$ M levobupivacaine and gradually attenuated at $3 \times 10^{-4}$ M levobupivacaine. Levobupivacaine-induced contractions of endothelium-denuded rings were larger than those of endothelium-intact rings. Levobupivacaine-induced contraction of endothelium-denuded rings was attenuated by quinacrine dihydrochloride, NDGA, AA-861, verapamil, and calcium-free solution and, to a lesser extent, by indomethacin. L-NAME enhanced levobupivacaine-induced contraction of endothelium-intact rings and indomethacin slightly attenuated this contraction. NDGA and AA-861 attenuated the potassium chloride-
induced contraction. AA-861 attenuated the levobupivacaine-induced intracellular calcium increase in vascular smooth muscle cells.

**CONCLUSIONS:** Our data indicate that levobupivacaine-induced contraction of rat aortic smooth muscle is mediated mainly by activation of the lipoxygenase pathway and in part by activation of the cyclooxygenase pathway. In addition, activation of the lipoxygenase pathway seems to facilitate calcium influx via L-type calcium channels. Endothelial nitric oxide attenuates levobupivacaine-induced contraction.

**Perioperative Crystalloid and Colloid Fluid Management in Children: Where Are We and How Did We Get Here?**

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Anesth Analg 2010; 110:375-390

Holliday and Segar in their landmark article (Pediatrics 1957; 19:823–32) proposed the rate and composition of parenteral maintenance fluids for hospitalized children. Much of our perioperative fluid administration is based on this article. The glucose, electrolyte, and intravascular volume requirements of the pediatric surgical patient may be quite different than the original population described, and consequently, use of traditional hypotonic fluids proposed by Holliday and Segar may cause complications, such as hyperglycemia and hyponatremia, in the postoperative surgical patient. There is significant controversy regarding the choice of isotonic versus hypotonic fluids in the postoperative period. We discuss the origins of perioperative fluid management in children, review the current options for crystalloid fluid management, and present information on colloid use in pediatric patients.
A Comparison of Propofol and Dexmedetomidine for Intravenous Sedation: A Randomized, Crossover Study of the Effects on the Central and Autonomic Nervous Systems
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Anesth Analg 2010; 110:415-418

We compared, in volunteers, the effect of propofol (PROP) and dexmedetomidine (DEX) sedation on autonomic nervous activities and subjective feelings during psychological stresses. In a crossover design, 25 subjects received PROP and DEX titrated to a bispectral index value of 75 to 85. Heart rate, heart rate variability, and salivary α-amylase (objective indices) and a faces anxiety scale (subjective index) were assessed. Subjects were asked their preference between 2 sedatives. Objective indices showed similar changes in both groups. The faces anxiety scale decreased only in the PROP group and subjects preferred PROP. Propofol more effectively suppressed anxious feelings compared with DEX during sedation.

Beyond Anesthetic Properties: The Effects of Isoflurane on Brain Cell Death, Neurogenesis, and Long-Term Neurocognitive Function
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Anesth Analg 2010; 110:431-437

Weakened ability to induce brain cell death and long-term cognitive function impairment. Recently, human data also show that early life anesthesia can induce cognitive dysfunction. Brain cell death and neurocognitive dysfunction can be induced by exposure to isoflurane. In this study, we examined whether exposure to isoflurane can cause brain cell death and neurocognitive dysfunction. In a series of experiments, we demonstrated that exposure to isoflurane can induce brain cell death and neurocognitive dysfunction in the developing brain.

Propofol and dexmedetomidine were compared for their effects on autonomic nervous activities and subjective feelings during psychological stresses. In a crossover design, 25 subjects received propofol (PROP) and dexmedetomidine (DEX) titrated to a bispectral index value of 75 to 85. Heart rate, heart rate variability, and salivary α-amylase (objective indices) and a faces anxiety scale (subjective index) were assessed. Subjects were asked their preference between the two sedatives. Objective indices showed similar changes in both groups. The faces anxiety scale decreased only in the PROP group and subjects preferred PROP. Propofol more effectively suppressed anxious feelings compared with DEX during sedation.
Anesthetic drugs cause brain cell death and long-term neurocognitive dysfunction in neonatal rats. Recently, human data also suggest that anesthesia early in life may cause cognitive impairment. The connection between cell death and neurocognitive decline is uncertain. It is conceivable that mechanisms other than brain cell death contribute to neurocognitive outcomes of neonatal anesthesia. In a series of experiments, we demonstrate that isoflurane exposure causes significant hypercarbia in postnatal day 7 rats and that exposure to isoflurane or carbon dioxide for 4 h provoked brain cell death. However, 1 h of isoflurane exposure was not sufficient to cause brain cell death. Moreover, only 4 h of isoflurane exposure, but not 1 or 2 h of exposure or 4 h of carbon dioxide, led to impaired hippocampal function, questioning the association between anesthesia-induced brain cell death and neurocognitive dysfunction. Neurogenesis both in the developing and adult dentate gyrus is important for hippocampal function, specifically learning and memory. γ-Amino butyric acid regulates proliferation and neuronal differentiation both in the developing and the adult brain. Inhaled anesthetics are γ-aminobutyric acid-ergic and may therefore affect neurogenesis, which could be an alternative mechanism mediating anesthesia-induced neurocognitive decline in immature rats. Understanding the mechanism will help guide clinical trials aiming to define the scope of the problem in humans and may lead to preventive and therapeutic strategies.

The Effect of Aminophylline on Loss of Consciousness, Bispectral Index, Propofol Requirement, and Minimum Alveolar Concentration of Desflurane in Volunteers

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Anesth Analg 2010; 110:449-454

背景：腺苷是催眠類的神經遞質，而在臨床上作為支氣管擴張劑的氨茶鹼，能在中樞神經系統對抗腺苷此作用。因此，我們檢驗了此假說，即氨茶鹼延遲了丙泊酚麻醉患者的意識喪失（LOC）同時加快了意識恢復（ROC），並且增加了地氟醚的最低有效肺泡濃度（MAC）值。

方法：在這個雙盲交叉研究中，志願者在不同日期裡被隨機分到氨茶鹼組或鹽水對照組中。在研究日，先予 6 mg/kg 氨茶鹼靜脈推注，然後以 1.5 mg· kg⁻¹· h⁻¹ 速度泵入維持 24 小時。在泵入氨茶鹼或鹽水 1 小時後，以 20 mg/min 的速度給予丙泊酚 200mg。持續監測
BIS 值及達到 LOC 和 ROC 的時間。當志願者從異丙酚麻醉中恢復後，以七氟醚全麻誘導，並以地氟醚維持麻醉。用 Dixon 的“上下”法來測定在反復的強直電刺激後每個志願者的 MAC 值。

結果：八名志願者均完成了兩組研究。氨茶鹼組達到 LOC 所需時間較鹽水組延長（均值 ± 標準差）（7.7 ± 2.03 min 比 5.1 ± 0.75 min，P = 0.011）。氨茶鹼組達到 LOC 的總異丙酚用量更大（2.2 ± 0.9 比 1.4 ± 0.4 mg/kg，P = 0.01），而達到 ROC 所需時間更短（6.18 ± 3.96 比 12.2 ± 4.73 min，P = 0.035）。最低 BIS 值氨茶鹼組更大（51 ± 15 比 38 ± 9，P = 0.034），而兩組 MAC 值無明顯差異。

結論：氨茶鹼削弱了異丙酚的鎮靜作用，但對強直電刺激法檢測的地氟醚 MAC 值無影響。

BACKGROUND: Adenosine is a soporific neuromodulator; aminophylline, which is clinically used as a bronchodilator, antagonizes the action of adenosine in the central nervous system. Thus, we tested the hypothesis that aminophylline delays loss of consciousness (LOC) and speeds recovery of consciousness (ROC) with propofol anesthesia, and that aminophylline increases the minimum alveolar concentration (MAC) of desflurane.

METHODS: In this double-blind crossover study, volunteers were randomized to either aminophylline or saline on different days. Aminophylline 6 mg/kg was given IV, followed by 1.5 mg · kg⁻¹ · h⁻¹ throughout the study day. After 1 h of aminophylline or saline administration, propofol 200 mg was given at a rate of 20 mg/min. The bispectral index was continuously monitored, as were times to LOC and ROC. After recovery from propofol, general anesthesia was induced with sevoflurane and subsequently maintained with desflurane. The Dixon "up-and-down" method was used to determine MAC in each volunteer after repeated tetanic electrical stimulation.

RESULTS: Eight volunteers completed both study days. Time to LOC was prolonged by aminophylline compared with saline (mean ± sd) (7.7 ± 2.03 min vs 5.1 ± 0.75 s, respectively, P = 0.011). The total propofol dose at LOC was larger with aminophylline (2.2 ± 0.9 vs 1.4 ± 0.4 mg/kg, P = 0.01), and the time to ROC was shorter (6.18 ± 3.96 vs 12.2 ± 4.73 min, P = 0.035). The minimum bispectral index was greater with aminophylline (51 ± 15 vs 38 ± 9, P = 0.034). There was no difference in MAC.

CONCLUSION: Aminophylline decreases the sedative effects of propofol but does not affect MAC of desflurane as determined by tetanic electrical stimulation.
Background: Indocyanine green plasma disappearance rate (ICG-PDR) is used to evaluate hepatic function. Although hepatic failure is generally said to occur with an ICG-PDR <18%/min, ICG disappearance rate is poorly defined in the healthy population, and a clear cutoff value of ICG-PDR that discriminates between normal hepatic function and hepatic failure has not yet been described. We therefore defined the ICG disappearance rate in an otherwise healthy patient population. In addition, we evaluated the noninvasive measurement of ICG-PDR (transcutaneously by pulse dye densitometry [PDD] at the finger and the nose) and compared these with the simultaneously performed invasive measurements of ICG-PDR (in arterial blood).

Methods: In patients without signs of liver disease, scheduled for elective nonhepatic surgery, 10 mg ICG was administered IV and ICG-PDR measured by PDD (DDG-2001, Nihon Kohden, Tokyo, Japan). In a subset of patients, arterial blood samples were gathered to compare PDD with invasive ICG measurements. Methods were compared using Bland-Altman analysis. The results of our study and reported studies on discriminative use of ICG-PDR in assessing liver failure were used to construct receiver operating characteristic curves.

Results: Forty-one patients were studied: 33 using the finger probe and 8 using the nose probe. The mean ± sd noninvasive ICG-PDR in this patient population is 23.1% ± 7.9%/min (n = 41) with a range of 9.7% to 43.2%/min. Bias (±2 sd, limits of agreement) for ICG-PDR measured by PDD compared with those measured in arterial blood were 1.6%/min (−5.2% to 8.3%/min) for the finger probe and −6.0%/min (−15.5% to 3.4%/min) for the nose probe.

Conclusion: ICG-PDR values in a population without liver failure ranged well below 18%/min, cited as the cutoff value for hepatic failure. This cutoff value needs reconsideration. In addition, we conclude that the ICG concentration is adequately determined noninvasively by PDD.

無纖維支氣管鏡輔助下的 Univent 管置管
Placement of the Univent Tube Without Fiberoptic Bronchoscope Assistance
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Anesth Analg 2010; 110:508-514

BACKGROUND: In this study, we evaluated the feasibility and accuracy of Univent tube (Fuji
Systems, Tokyo, Japan) placement with the aid of auscultation (AUS) or as guided by a lighted
stylet (LS) compared with placement guided by the fiberoptic bronchoscope (FOB) or the blind
intubation technique as recommended by the manufacturer's guidelines.

METHODS: Eighty ASA physical status I–II adult patients requiring single-lung ventilation for
elective thoracic surgery were randomly allocated into 4 groups according to the method used for
Univent tube positioning: manufacturer-recommended (MR) group (n = 20); FOB group (n = 20);
AUS group (n = 20); and LS group (n = 20). Tracheal placement of the Univent tube was
accomplished with direct rigid laryngoscopy after anesthetic induction and was positioned by the
same anesthesiologist using 1 of the above-described methods. Its position was then checked by
another anesthesiologist with an FOB. The number of attempts required for successful tube
positioning, the volume of air needed for blocker cuff inflation, and intubation times were
recorded, as were the times for single-lung ventilation and the potential for bronchial injury.
RESULTS: The intubation time was 182 ± 42 s in the AUS group and 176 ± 50 s in the LS group, shorter than that in the FOB (278 ± 111 s) and MR (266 ± 127 s) \((P < 0.05)\) groups. The success rate of bronchial blocker insertion into the left bronchus on the first attempt was 100% in the AUS group, 79% in the LS group, and 25% in the MR group. The number of blocker insertion attempts and the volume of air in the blocker cuff in the MR group were significantly higher than those in the AUS and LS \((P < 0.05)\) groups. In the supine position, the number of acceptable bronchial blocker placements was 14 of 20 attempts (70%) in the MR group, significantly fewer than that in the FOB group (18 of 20, 90%) \((P < 0.05)\). In the AUS and LS groups, the number of acceptable bronchial blocker placements was 19 of 20 (95%) and 16 of 20 (80%), respectively. After patients were turned to the lateral decubitus position, the number of acceptable bronchial blocker placements was 10 of 18 (56%) in the MR group, significantly fewer than that in the FOB group (17 of 19, 89.5%) \((P < 0.05)\). In the AUS and LS groups, the number of acceptable bronchial blocker placements was 15 of 20 (75%) and 15 of 19 (79%), respectively.

CONCLUSIONS: The placement of the Univent tube with the aid of AUS or an LS is feasible, and both techniques require less time than placement aided by an FOB or as recommended by the manufacturer.

灌注壓對實驗性胃管模型的胃組織血流量的影響
The Effect of Perfusion Pressure on Gastric Tissue Blood Flow in an Experimental Gastric Tube Model
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Anesth Analg 2010; 110:541-546

背景: 吻合口瘻及狹窄的形成仍然是食管癌患者行食管切除術及胃管重建術後嚴重併發症。由於在胃管近端的吻合口灌注完全取決於微循環，使之容易出現灌注不足。我們推測，增加灌注壓可以改善胃管吻合口處的血流量。

方法: 9 頭豬行胃管重建術。通過鐳射散斑成像和溫度記錄成像分別測量胃管基部、中間部、近吻合口處以及頂部的血流量和溫度。取平均動脈壓（MAP）50-110 毫米汞柱作為分段測量點。

結果: 除了 MAP，實驗中血流動力學總體沒有改變。在每一個相同水準 MAP，胃管頂部血流量明顯低於基部和中間部。升高 MAP 並未對胃管任何位置的血流量造成顯著影響。溫度分佈與不同部位流量分佈相似。升高 MAP 沒有改變胃管任何位置的溫度。

結論: 胃管上部的血流量相比更近端的部位有所下降。胃組織血流量不隨灌注壓增加而上升。因此，不建議通過升高 MAP 到超常水準來增加吻合口組織血流量以及減少術後併發症。

(宋村笛 譯 馬皓琳 李士通校)
the microcirculation, making it susceptible to hypoperfusion. We hypothesized that increasing the perfusion pressure would improve blood flow at the anastomotic site of the gastric tube.

**METHODS:** A gastric tube was reconstructed in 9 pigs. Laser speckle imaging and thermographic imaging were used to measure blood flow and temperature, respectively, at the base, medial part, future anastomotic site, and top of the gastric tube. Measurements were repeated at every stepwise increase of mean arterial blood pressure (MAP) from 50 to 110 mm Hg.

**RESULTS:** Besides MAP, global hemodynamics did not change throughout the experiment. The blood flow in the top of the gastric tube was significantly lower than the flow in the base and medial part of the gastric tube at all levels of MAP. Increasing MAP did not have a significant effect on blood flow at any location in the gastric tube. Distribution of temperature was similar to distribution of flow for the different locations. Increases in MAP did not change temperature values at any location of the gastric tube.

**CONCLUSION:** Blood flow in the upper part of the gastric tube is decreased compared with more proximal sites. Gastric tissue blood flow does not increase with increased perfusion pressure. Therefore, it is not recommended to increase MAP to supranormal levels to increase anastomotic tissue blood flow and reduce postoperative complications.

**What's New in Obstetric Anesthesia: The 2009 Gerard W. Ostheimer Lecture**

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Anesth Analg 2010; 110:564-569

This article summarizes the most relevant publications in obstetric anesthesiology from 2008. Forty-two articles were selected from a pool of several thousand in >70 English-language journals that were deemed as having the most impact on the practice of obstetric anesthesia.

**Airway Management in Patients Who Develop Neck Hematomas After Carotid Endarterectomy**

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Anesth Analg 2010; 110:588-593

Background: Neck hematomas after carotid surgery are a significant complication and can lead to airway compromise. Identification of a patient at risk and development of strategies to manage these patients effectively is critical. The authors report their experience in the management of patients who developed neck hematomas postoperatively and review the current literature on this topic.
方法：我們回顧分析了明尼蘇達州羅切斯特市梅奧診所十年來在頸動脈內膜剝脫術後 72 小時內需要進行氣道管理用於頸部探查的病人。
結果：在十年裡我們的醫療機構中共有 3225 名患者進行了頸動脈內膜剝脫手術。44 名患者（1.4%）由於頸部血腫需要進行頸部探查術，其中有 42 名需要在頸部探查術前立即進行氣道管理（另外 2 名病人在頸動脈內膜剝脫術後氣道導管尚未拔除）。從 CEA 完成到重回手術室進行血腫清除的平均時間是 6.0 ± 6.0 小時(平均值± 標準差; 範圍, <1-32 小時)。在麻醉誘導前進行纖維支氣管鏡插管的 20 名患者中有 15 名（75%）成功，剩下的 5 名患者纖維支氣管鏡插管失敗後改用直接喉鏡法插管也成功了（3 名患者在麻醉誘導前完成了插管，2 名在誘導後完成了插管）。其餘 22 名患者首先用直接喉鏡作為氣道管理方法，而未嘗試用纖維支氣管鏡。在未進行麻醉誘導的情況下直接喉鏡法插管的成功率是 5/7（71%），而進行全麻誘導後直接喉鏡法插管的成功率是 13/15（87%）。血腫減壓使 4 名直接喉鏡下氣管插管失敗的患者中的 3 名直接喉鏡下插管成功，剩下的 1 名患者則做了氣管切開。用於血腫清除的喉鏡插管過程中未遇到困難的患者中有 36%發現有動脈出血點，而發生困難插管的患者概率為 6%（P = 0.03）。44 名患者中有 36 名（82%）在頸部探查術後 24 小時內就拔除了氣管導管。沒有氣道管理相關併發症發生。血腫清除術後 2 周沒有患者死亡。
結論：在全麻誘導前後我們可以採用多種方法成功地進行氣道控制。既可以選用可視纖維支氣管鏡插管也可以選用直接喉鏡。在聲門暴露困難的情況下，通過外科切開使氣道減壓可方便插管。
(薑旭暉 譯 馬皓琳 李士通 校)

BACKGROUND: Progressive airway compromise from neck hematoma and edema is a feared complication of carotid endarterectomy (CEA). Despite this, the relationship of airway management technique to patient outcome has not been systematically studied in this population. We report the rate of successful airway management using various techniques in post-CEA patients.

METHODS: A 10-year retrospective analysis was conducted to identify patients requiring airway management for neck exploration within 72 hours after CEA at Mayo Clinic, Rochester, MN.

RESULTS: Three thousand two hundred twenty-five patients underwent CEA over a 10-year period at our institution. Forty-four (1.4%) required neck exploration for hematoma, and 42 of these required airway management immediately before neck exploration surgery. (The tracheal tube had not been removed after CEA in the remaining 2 patients.) The average interval between the completion of CEA and return to the operating room for hematoma evacuation was 6.0 ± 6.0 hours (mean ± sd; range, <1-32 hours). Fiberoptic airway management, performed before the induction of anesthesia, was successful in 15 of 20 patients (75%) and, in patients in whom fiberoptic tracheal intubation failed, direct laryngoscopy (DL) was successful in all 5 (3 before and 2 after the induction of general anesthesia). In the remaining 22 patients, DL was used as the initial management technique without a trial of fiberoptic intubation. DL was successful in 5 of 7 patients (71%) when performed before induction of general anesthesia and was successful in 13 of 15 patients (87%) when performed after induction of general anesthesia. Hematoma decompression facilitated DL in 3 of 4 failures of DL; tracheostomy was performed in the remaining patient. An arterial site of bleeding was subsequently identified in 36% of patients in whom no difficulty was encountered during laryngoscopy for hematoma evacuation versus 6% in whom difficulty was noted (P = 0.03). In 36 of 44 patients (82%), the tracheal tube was removed...
within 24 hours of surgery for neck exploration. No adverse events related to airway management were noted. There were no deaths at 2 weeks after hematoma evacuation.

CONCLUSIONS: Multiple techniques resulted in successful airway control both before and after the induction of general anesthesia. Tracheal intubation was accomplished with both fiberoptic visualization and DL. In instances of poor direct visualization of the glottis, decompression of the airway by opening of the surgical incision may facilitate intubation of the trachea.

Activation of Spinal α-2 Adrenoceptors, but Not μ-Opioid Receptors, Reduces the Intrathecal N-Methyl-d-Aspartate-Induced Increase in Spinal NR1 Subunit Phosphorylation and Nociceptive Behaviors in the Rat

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Anesth Analg 2010; 110:622-629

BACKGROUND: A previous study from our laboratories showed that a significant reduction in spinal N-methyl-d-aspartate (NMDA) receptor NR1 subunit phosphorylation (pNR1) is associated with the antiallodynic effect produced by intrathecal (IT) injection of the α-2

啟動大鼠脊髓α-2 腎上腺受體而非 μ-阿片受體，降低鞘內注射 N-甲基-D-天冬氨酸（NMDA）所致脊髓NR1亞單位磷酸化增加和感受傷害行為學改變
adrenoceptor agonist, clonidine, in neuropathic rats. In this study, we determined whether the spontaneous pain and increased pNR1 expression induced by NMDA injection are reduced by IT injection of either clonidine or the µ-opioid receptor agonist, [d-Ala2, NMe-Phe4, Gly-ol5]-enkephalin (DAMGO).

**METHODS:** We examined the effect of clonidine (20 µg/rat) or DAMGO (1 µg/rat) injection on IT NMDA-induced spontaneous nociceptive behavior and pNR1 expression in the spinal dorsal horn. We also determined whether the effect of clonidine is mediated by α-2A or α-2C adrenoceptors. Finally, rat spinal cords were immunohistochemically processed for double staining of pNR1 and α-2A or α-2C adrenoceptors or µ-opioid receptors.

**RESULTS:** The NMDA-induced increase in both pNR1 expression and nociceptive behavior was significantly reduced by IT clonidine but not DAMGO. This analgesic effect of clonidine was blocked by administration of either an α-2A (BRL44408, 30 µg/rat) or an α-2C (JP-1302, 50 µg/rat) adrenoceptor antagonist. In addition, immunocytochemistry revealed that spinal pNR1 immunoreactive cells co-contain α-2A and α-2C adrenoceptors.

**CONCLUSIONS:** These results demonstrate that the IT NMDA-induced increase in pNR1 expression and nociceptive behavior is significantly reduced by activation of α-2 adrenoceptors, but not µ-opioid receptors, in the spinal cord dorsal horn. Furthermore, these findings suggest that the modulation of spinal NR1 phosphorylation is linked to the effect of IT clonidine on postsynaptic neuronal activity.

**心肺動脈分流手術對小鼠全身白細胞介素-6 釋放，腦核因數-κB 表達和神經認知功能的影響**

The Impact of Cardiopulmonary Bypass on Systemic Interleukin-6 Release, Cerebral Nuclear Factor-kappa B Expression, and Neurocognitive Outcome in Rats
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**背景**: 行心肺動脈分流手術（CPB）的心臟手術後出現神經認知功能障礙一直以來都影響著患者的生存品質，炎症反應可能是造成這一後果的原因之一。我們設計這個實驗就是為了研究小鼠在心肺動脈分流手術後圍手術期全身白細胞介素-6 (IL-6) 的濃度，腦核因數-κB (NF-κB) 的表達以及神經認知功能的狀況。氧合器大小對這些結果的影響也一起被監測研究。

**方法**: 小鼠被隨機分為四組：控制對照組（7例，未行麻醉）；偽手術組（10例，行麻醉，插套管，但未行心肺動脈分流手術）；兩組手術組，一組（10例）行麻醉，插套管，並用一台小容量的小鼠氧合器進行 90 分鐘的心肺動脈分流手術；另一組（10例）行麻醉，插套管，並用一台新生兒氧合器進行 90 分鐘的心肺動脈分流手術。分別於心肺動脈分流手術前、終止時以及兩小時後（或相同時間點）監測全身白細胞介素-6。用免疫組化法於術後 21 天測海馬腦核因數-κB 的表達值。以術前模擬洞板實驗測試結果作為神經認知功能的基礎值，於術後 21 天複測。
BACKGROUND: Neurocognitive deficits after cardiac surgery with cardiopulmonary bypass (CPB) continue to affect patients’ quality of life, and an inflammatory reaction may be one of the contributors. We designed this experiment to study perioperative systemic interleukin-6 (IL-6) concentrations, cerebral expression of nuclear factor-kappa B (NF-κB), and neurocognitive outcome after CPB in young rats. The impact of oxygenator size on these outcomes was also assessed.

METHODS: Rats were randomly assigned to 1 of 4 groups: control (n = 7, nonanesthetized), sham-operated rats (n = 10, anesthetized, cannulated, and not connected to CPB), and 2 CPB groups, anesthetized, cannulated, and subjected to 90 min of CPB, using either a small-volume rat oxygenator (CPB/rat oxygenator, n = 10) or a neonate oxygenator (CPB/neonate oxygenator, n = 10). Systemic IL-6 was determined before, at the end of, and 2 h after CPB or at equivalent times. Hippocampal NF-κB expression was assessed on postoperative day 21 using immunohistochemistry. Neurocognitive performance was assessed with the modified hole-board test at baseline and for 21 postoperative days.

RESULTS: Both CPB groups had increased systemic IL-6 levels compared with sham, with the neonate oxygenator causing a substantially larger increase at 2 h after CPB compared with the rat oxygenator group (CPB/rat oxygenator: 220 pg/mL [16-415]; CPB/neonate oxygenator: 1400 pg/mL [592-5812]) (P < 0.05). Hippocampal NF-κB was increased in experimental groups compared with controls (10 +/- 4). CPB resulted in more NF-κB-positive neurons (271 +/- 57 CPB/neonate oxygenator and 269 +/- 72 CPB/rat oxygenator) compared with sham operation (173 +/- 24). Neurocognitive and behavioral performances were unaltered and comparable among all groups.

CONCLUSIONS: Pronounced systemic inflammatory responses to experimental CPB associated with increased hippocampal expression of NF-κB were not accompanied by neurocognitive impairment. This suggests that other factors beyond CPB and inflammatory responses might contribute to adverse neurocognitive outcomes after cardiac surgery.
背景：縱向研究資料顯示脈壓差增寬往往是罹患冠心病及死亡的重要預知因素，但目前仍不清楚其是否會降低冠心病患者冠脈搭橋術後的長期生存率。因此，此項研究旨在評價脈壓差增寬患者在行冠狀動脈搭橋術後的長期生存狀況。

方法：選取 1993 年 1 月至 2004 年 7 月間行冠狀動脈搭橋手術的患者為該項回顧性觀察研究的研究物件，對其中 973 名患者行長期生存狀況評估。將麻醉誘導前自動記錄保存系統中前 3 次血壓測量結果的中間值定為患者的基礎動脈血壓。運用 Cox 比例風險回歸模型評估基礎脈壓差對患者術後生存狀況的影響，同時將所測得的基礎平均動脈壓、收縮壓、舒張壓及是否合併糖尿病、Hannan 風險指數、抑肽酶使用情況、體外迴圈持續時間等作為協同變數一併引入進行分析。

結果：隨訪期間共有 220 例（22.9%）患者死亡（中位數：7.3 年[第一四分位數：5 年，第三四分位數：10 年]），其中 94 例為心腦血管原因。基礎脈壓差增寬是預測患者術後長期生存率下降的重要因素，具有顯著的統計學差異（P<0.001）；此外，Hannan 風險指數（P<0.001）、體外迴圈持續時間（P<0.001）、是否合併糖尿病（P<0.001）等也是具有顯著統計學意義的重要預知因數。基礎動脈收縮壓（P=0.40）、舒張壓（P=0.38）及平均動脈壓（P=0.78）與患者術後長期生存狀況無關。脈壓差的危險比（已對模型中的其它變數進行校正）為每升高 10mmHg1.11(1.05-1.18)。

結論：冠狀動脈搭橋術後患者長期生存狀況不佳與圍手術期脈壓差增寬密切相關。回顧先前所報導的脈壓差與住院患者致命或非致命血管併發症間的聯繫，應考慮將脈壓差修訂並納入已制定的手術危險評估、患者諮詢及治療指南中。

Background: Data from longitudinal studies reveal that widened pulse pressure (PP) is a major predictor of coronary heart disease and mortality, but it is unknown whether PP similarly decreases survival after coronary artery bypass graft (CABG) surgery for coronary heart disease. We therefore assessed long-term survival in patients with increased PP at the time of presentation for CABG surgery.

Methods: In this retrospective observational study of patients undergoing CABG surgery between January 1993 and July 2004, 973 subjects were included for assessment of long-term survival. Baseline arterial blood pressure (BP) measurements were defined as the median of the first 3 measurements recorded by the automated record keeping system before induction of anesthesia. The effect of baseline PP on survival after surgery was evaluated using a Cox proportional hazards regression model and bootstrap resampling with baseline mean arterial BP, systolic BP, diastolic BP, diabetes, Hannan risk index, aprotinin use, and cardiopulmonary bypass time as covariates.

Results: There were 220 deaths (22.9%) during the follow-up period (median, 7.3 yr [Q1: 5, Q3: 10 yr]) including 94 deaths from cardiovascular causes. Increased baseline PP was a significant predictor of reduced long-term survival (P < 0.001) along with Hannan risk index (P < 0.001), duration of cardiopulmonary bypass (P < 0.001), and diabetes (P < 0.001). Baseline systolic (P = 0.40), diastolic (P = 0.38), and mean arterial BPs (P = 0.78) were not associated with long-term survival. The hazard ratio for PP (adjusted for other covariates in the model) was 1.11 (1.05-1.18) per 10-mm Hg increase.

Conclusions: An increase in perioperative PP is associated with poor long-term survival after CABG surgery. Together with our previous report linking PP to in-hospital fatal and nonfatal vascular complications, the established models for surgical risk assessment, patient counseling, and treatment should be revised to include PP.
A multidisciplinary panel consisting of experts chosen by the 2 chairs of the group representing experts in anesthesiology, blood banking, hematology, critical care medicine, and various surgical disciplines (trauma, cardiac, pediatric, neurologic, obstetrics, and vascular) convened in January 2008 to discuss hemostasis and management of the bleeding patient across different clinical settings, with a focus on perioperative considerations. Although there are many ways to define hemostasis, one clinical definition would be control of bleeding without the occurrence of pathologic thrombotic events (i.e., when balance among procoagulant, anticoagulant, fibrinolytic, and antifibrinolytic activities is achieved). There are common hemostatic challenges that include lack of scientific evidence and standardized guidelines for the use of therapeutic drugs, need for reliable and rapid laboratory tools for measuring hemostasis, and individual variability. Clinically meaningful and accurate real-time laboratory data reflecting a patient's hemostatic status are needed to guide treatment decisions. Current available routine laboratory tests of hemostasis (e.g., platelet count, prothrombin time/international normalized ratio, and activated partial thromboplastin time) do not reflect the complexity of in vivo hemostasis and can mislead the clinician. Although point-of-care coagulation monitoring tests including measures of
thromboelastography/elastometry provide insight into overall hemostatic status, they are time-consuming to perform, complex to interpret, and require trained personnel. There is a particular need to develop laboratory tests that can measure the effects of anticoagulant and antiplatelet agents for individual patients, predict bleeding complications, and guide therapy when and if treatment with blood products or pharmacologic drugs is required. Formation of an organization comprised of specialists who treat bleeding patients will foster multidisciplinary collaborations and promote discussions of the current state of hemostasis treatment and future priorities for hemostasis research. Controlled trials with clinically meaningful end points and suitable study populations, as well as observational studies, investigator-initiated studies, and large registry and database studies are essential to answer questions in hemostasis. Because of the complexities of maintaining hemostatic balance, advances in hemostasis research and continuing communication across specialties are required to improve patient care and outcomes.

手術解剖學分級對於術後蘇醒室內應用止吐藥物的影響

The Effect of an Anatomically Classified Procedure on Antiemetic Administration in the Postanesthesia Care Unit.

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背景：關於不同手術類型對術後噁心嘔吐（PONV）的影響一直存在著爭議。我們希望通過這個回顧性的資料分析研究來分析不同手術類型（根據解剖學定義來劃分和比較）在術後蘇醒室觀察的2小時內對應用止吐治療情況的影響。

方法：我們所使用的腫瘤手術（樣本量n=18,109）回顧性分析的資料來自於我們的自動化麻醉資訊系統資料庫。我們將手術類型按解剖學定義分為七大類，並將體表肌肉骨骼及淺表手術作為對照組。我們也就另九大噁心嘔吐危險因素對每位患者進行了分析，這九大危險因素為：性別，吸煙狀況，噁心嘔吐史或運動障礙，麻醉時間，預防性止吐藥物的應用，術中阿片類藥物、非甾體類抗炎藥物、硬膜外的應用，以及術後阿片類藥物的應用。在調整平衡其他危險因素的同時，就不同手術類型在術後蘇醒室觀察的2小時內對應用止吐治療情況的影響應用多項變異邏輯性回歸的方法進行評估分析。

結果：相較於體表肌肉骨骼及淺表手術，接受神經外科手術（P<0.0001），頭頸部手術（P<0.0001），和腹部手術（P<0.0001）的患者在蘇醒室明顯需要應用更多的止吐藥物，而接受胸外科手術（P=0.02）的患者在蘇醒室所需接受的止吐藥物則明顯較少。乳房或腋窩手術（P=0.74）以及內窩手術（P=0.28）使用止吐藥物的情況與對照組並無明顯差異。以下幾大因素與術後蘇醒室早期應用止吐藥物明顯相關：女性，不吸煙者，有噁心嘔吐史或運動障礙史，麻醉時間，以及術中或術後應用過阿片類藥物。

結論：通過使用我們的自動化麻醉資訊系統資料庫研究分析，我們發現，就人群而言，根據解剖學定義所劃分的不同類型的手術與術後蘇醒室早期應用止吐藥物的頻率增多有關。

(李瑩譯 薛張綱校)
BACKGROUND: The effect of the type of surgical procedure on postoperative nausea and vomiting (PONV) rate has been debated in the literature. Our goal in this retrospective database study was to investigate the effect the type of surgical procedure (categorized and compared anatomically) has on antiemetic therapy within 2 h of admission to the postanesthesia care unit (PACU).

METHODS: We retrospectively analyzed data for oncology surgeries (n = 18,109), from our automated anesthesia information system database. We classified the types of surgical procedures anatomically into seven categories, with the integumentary musculoskeletal and the superficial surgeries chosen as the referent group. Our analysis included nine other risk factors for each patient, such as gender, smoking status, history of PONV or motion sickness, duration of anesthesia, number of prophylactic antiemetics administered, intraoperative opioids, ketorolac, epidural use, and postoperative opioids. Multivariate logistic regression was used to assess the effect of the type of surgery on antiemetic administration within the first 2 h of PACU admission, while adjusting for the other risk factors.

RESULTS: Compared with integumentary musculoskeletal and superficial surgeries, patients undergoing neurological (P < 0.0001), head or neck (P < 0.0001), and abdominal (P < 0.0001) surgeries were administered PACU antiemetic significantly more often, whereas patients undergoing thoracic surgeries were administered PACU antiemetic significantly less often (P = 0.02). Breast or axilla (P = 0.74) and endoscopic (P = 0.28) procedures did not differ from the referent category. Female, nonsmoker, history of PONV or motion sickness, anesthesia duration, and intraoperative and postoperative opioid administration were significantly associated with antiemetic administration during early PACU admission.

CONCLUSIONS: Using our automated anesthesia information system database, we found that the type of surgery, when categorized anatomically, was associated with an increased frequency of early PACU antiemetic administration in our population.

Inhaled Anesthetic Potency in Aged Alzheimer

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背景：隨著人口老齡化，需要手術治療的明顯或初期阿茨海默症老年人數量在增加。全麻可能加重阿茨海默症的症狀和病理改變，所以減少麻醉暴露可能很重要。我們需要知道阿茨海默症持續性的病理改變是否會改變麻醉藥效能。

方法：在 12 至 14 月齡的三重轉基因阿茨海默症(3xTgAD)小鼠為實驗組和以野生型C57BL6小鼠為對照組的研究中，用 MAC 來觀察以翻正反射消失為終點時異氟醚、氟
BACKGROUND: The number of elderly patients with frank or incipient Alzheimer's disease (AD) requiring surgery is growing as the population ages. General anesthesia may exacerbate symptoms of and the pathology underlying AD, so minimizing anesthetic exposure may be important. This requires knowledge of whether the continuing AD pathogenesis alters anesthetic potency.

METHODS: We determined the induction potency and emergence time for isoflurane, halothane, and sevoflurane using the minimum alveolar anesthetic concentration for loss of righting reflex as an end point in 12- to 14-mo-old triple transgenic Alzheimer (3xTgAD) mice and wild type C57BL6 controls. 3xTgAD mice model AD by harboring three distinct mutations: the APPsw, Tau, and PS1 human transgenes, each of which has been associated with familial forms of human AD.

RESULTS: The 3xTgAD mice exhibited mild resistance (from 8% to 30%) to volatile anesthetics but displayed indistinguishable emergence patterns from all three inhaled anesthetics.

CONCLUSIONS: These results show that the genetic vulnerabilities and neuropathology associated with AD produce a small but significant decrease in sensitivity to the hypnotic actions of three inhaled anesthetics. Emergence times were not altered.

麻酔薬による神経元凋亡と対策

The Young: Neuroapoptosis Induced by Anesthetics and What to Do About It
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在父親及全世界每年有數以百萬計的胎兒、嬰兒、和兒童暴露于麻醉薬。在神經發育的關鍵階段應用麻醉藥物被認為是安全的，且沒有長期不良結果。然而，近期的報導提供的很多證據顯示在快速突觸形成期，即大腦生長突增期，未成熟動物大腦暴露於麻醉藥會引起廣泛神經元退化凋亡，抑制神經發生，導致嚴重的長期神經認知功能損害。在這裡，我們總結了現有麻醉薬導致的大腦病理改變及相關的長期神經認知缺陷方面的證據，討論如何保証麻醉薬物有益作用同時制定保護大腦避免潛在損害的有用方法。

(姚敏敏譯 薛張綱校)
period, triggers widespread apoptotic neurodegeneration, inhibits neurogenesis, and causes significant long-term neurocognitive impairment. Herein, we summarize currently available evidence for anesthesia-induced pathological changes in the brain and associated long-term neurocognitive deficits and discuss promising strategies for protecting the developing brain from the potentially injurious effects of anesthetic drugs while allowing the beneficial actions of these drugs to be realized.

Reduced Immobilizing Properties of Isoflurane and Nitrous Oxide in Mutant Mice Lacking the N-Methyl-d-Aspartate Receptor GluR1 Subunit Are Caused by the Secondary Effects of Gene Knockout
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Anesth Analg 2010 110: 461-465

BACKGROUND: Until recently, the N-methyl-d-aspartate (NMDA) receptor was considered to possibly mediate the immobility produced by inhaled anesthetics such as isoflurane and nitrous oxide. However, new evidence suggests that the role of this receptor in abolition of the movement response may be less important than previously thought. To provide further evidence supporting or challenging this view, we examined the anesthetic potencies of isoflurane and
nitrous oxide in genetically modified animals with established NMDA receptor dysfunction caused by GluR 1 subunit knockout.

METHODS: The immobilizing properties of inhaled anesthetics in mice quantitated by the minimum alveolar anesthetic concentration (MAC) were evaluated using the classic tail clamp method.

RESULTS: Compared with wild-type controls, NMDA receptor GluR 1 subunit knockout mice displayed larger isoflurane MAC values indicating a resistance to the immobilizing action of isoflurane. Knockout mice were previously shown to have enhanced monoaminergic tone as a result of genetic manipulation, and this increase in MAC could be abolished in our experiments by pretreatment with the serotonin 5-hydroxytryptamine type 2A receptor antagonist ketanserin or with the dopamine D2 receptor antagonist droperidol at doses that did not affect MAC values in wild-type animals. Mutant mice also displayed resistance to the isoflurane MAC-sparing effect of nitrous oxide, but this resistance was similarly abolished by ketanserin and droperidol. Thus, resistance to the immobilizing action of inhaled anesthetics in knockout mice seems to be secondary to increased monoaminergic activation after knockout rather than a direct result of impaired NMDA receptor function.

CONCLUSIONS: Our results confirm recent findings indicating no critical contribution of NMDA receptors to the immobility induced by isoflurane and nitrous oxide. In addition, they demonstrate the ability of changes secondary to genetic manipulation to affect the results obtained in global knockout studies.
BACKGROUND: We analyzed cases of malignant hyperthermia (MH) reported to the North American MH Registry for clinical characteristics, treatment, and complications.

METHODS: Our inclusion criteria were as follows: AMRA (adverse metabolic/musculoskeletal reaction to anesthesia) reports between January 1, 1987 and December 31, 2006; "very likely" or "almost certain" MH as ranked by the clinical grading scale; United States or Canadian location; and more than one anesthetic drug given. An exclusion criterion was pathology other than MH; for complication analysis, patients with unknown status or minor complications attributable to dantrolene were excluded. Wilcoxon rank sum and Pearson exact $\chi^2$ tests were applied. A multivariable model of the risk of complications from MH was created through stepwise selection with fit judged by the Hosmer-Lemeshow statistic.

RESULTS: Young males (74.8%) dominated in 286 episodes. A total of 6.5% had an MH family history; 77 of 152 patients with MH reported ≥2 prior unremarkable general anesthetics. In 10 cases, skin liquid crystal temperature did not trend. Frequent initial MH signs were hypercarbia, sinus tachycardia, or masseter spasm. In 63.5%, temperature abnormality (median maximum, 39.1°C) was the first to third sign. Whereas 78.6% presented with both muscular abnormalities and respiratory acidosis, only 26.0% had metabolic acidosis. The median total dantrolene dose was 5.9 mg/kg (first quartile, 3.0 mg/kg; third quartile, 10.0 mg/kg), although 22 patients received no dantrolene and survived. A total of 53.9% received bicarbonate therapy. Complications not including recrudescence, cardiac arrest, or death occurred in 63 of 181 patients (34.8%) with MH. Twenty-one experienced hematologic and/or neurologic complications with a temperature <41.6°C (human critical thermal maximum). The likelihood of any complication increased 2.9 times per 2°C increase in maximum temperature and 1.6 times per 30-minute delay in dantrolene use.

CONCLUSION: Elevated temperature may be an early MH sign. Although increased temperature occurs frequently, metabolic acidosis occurs one-third as often. Accurate temperature monitoring during general anesthetics and early dantrolene administration may decrease the 35% MH morbidity rate.

The effect of hydroxyethyl starches (HES 130/0.42 and HES 200/0.5) on activated renal tubular epithelial cells.
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背景：急性腎功能衰竭是敗血症的一個常見併發症。羥乙基澱粉(HES)廣泛應用於此類患者。然而，敗血症時應用 HES 對患者腎功能的影響仍有爭論。我們建立了腫瘤壞死因數
α（TNF-a）引導的人類近端小管上皮細胞（HK-2）的離體模型，來確定 HES 130/0.42 和 HES 200/0.5 對這些活化細胞的效果。

方法：在有 HES 130/0.42 或 200/0.5 的環境下應用 TNF-a 刺激 HK-2 細胞，同時設立空白對照。經過 4，10 和 18 小時的培養後，測定單核細胞趨化蛋白－1(MCP-1)，該蛋白是中性粒細胞和巨噬細胞的重要化學趨化因子。同時進行細胞活性和毒性測定。

結果：在 TNF-a 的刺激下 MCP-1 雙倍表達。在持續 10 小時和 18 小時的刺激期間應用含 2% 和 4% HES 200/0.5 液體，MCP-1 的濃度可下降 26% 和 56%（P < 0.05）。TNF-a 的刺激導致細胞活性顯著下降了 53%-63%，而應用 HES 130/0.42 聯合培養，細胞活性僅下降 32%-40%（P < 0.005）。應用 HES 200/0.5 聯合培養後細胞活性受 TNF-a 的影響更少（P < 0.001）。TNF-α 引導的細胞凋亡率因 HES 200/0.5 的應用而減少（P < 0.05）。

結論：這項離體研究顯示兩種羥乙基澱粉產品均可通過炎性刺激調節細胞損傷。HES 200/0.5 較 HES 130/0.42 的效果更顯著，意味著不同類型的羥乙基澱粉之間可能存在不同的生物學效應。

(張釗譯 薛張綱校)

BACKGROUND: Acute renal failure is a frequent complication of sepsis. Hydroxyethyl starch (HES) is widely used in the treatment of such patients. However, the effect of HES on renal function during sepsis remains controversial. We established an in vitro model of tumor necrosis factor-alpha (TNF-alpha)-stimulated human proximal tubular epithelial (HK-2) cells to assess the possible effects of HES 130/0.42 and HES 200/0.5 on these activated cells.

METHODS: HK-2 cells were stimulated with TNF-alpha in the presence or absence of HES 130/0.42 or 200/0.5. After 4, 10, and 18 h of incubation, monocyte chemoattractant protein-1 (MCP-1), a key chemoattractant for neutrophils and macrophages, was measured. In addition, viability and cytotoxicity assays were performed.

RESULTS: MCP-1 expression was doubled upon TNF-alpha exposure. In the presence of 2% and 4% HES 200/0.5 in 98% (96%) medium over a stimulation time period of 10 h and 18 h, the MCP-1 concentration was decreased between 26% and 56%（P < 0.05）。TNF-alpha stimulation resulted in a significant decrease of viability by 53%-63%，whereas viability decreased by only 32%-40% in coincubation with HES 130/0.42（P < 0.005）and remained even less affected by TNF-alpha in the presence of HES 200/0.5（P < 0.001）。The TNF-alpha-induced cell death rate was attenuated in the presence of HES 200/0.5（P < 0.05）.

CONCLUSIONS: This in vitro study shows that both HES products modulate cell injury upon inflammatory stimulation. The effect was more pronounced in the HES 200/0.5 group than for HES 130/0.42, suggesting a possible biological difference between the HES types.
Background: Randomized trials comparing air to saline for loss of resistance (LOR) for identification of the epidural space have suggested the superiority of saline. We hypothesized that, in actual clinical practice, anesthesiologists using their preferred technique would produce similar analgesic outcomes with either air or saline.

Methods: The labor analgesia records for 929 parturients requesting neuraxial analgesia were reviewed with respect to technique (epidural or combined spinal-epidural; air or saline for LOR), analgesic outcomes (initial comfort, asymmetry of the block, need for physician top-up during patient-controlled epidural analgesia, and catheter replacement), and complications (paresthesia, IV or intrathecal catheter placement, and unintentional dural puncture).

Results: Of 929 labor analgesics analyzed, 52.6% were performed with LOR to air and 47.4% to saline. Among anesthesiologists who performed at least 10 blocks, 82% used 1 medium at least 70% of the time. There were no differences between the air and saline groups in patient characteristics, analgesic technique, or block success. Among operators with a preference for 1 medium, use of the preferred technique was associated with fewer attempts (1.3 ± 0.7 vs 1.6 ± 0.8, P = 0.001), fewer paresthesias (8.7% vs 18.5%, odds ratio = 0.42, P = 0.007), and fewer unintentional dural punctures (1.0% vs 4.4%, odds ratio = 0.23, P = 0.03).

Conclusions: When used at the anesthesiologist's discretion, there is no significant difference in block success between air and saline for localization of the epidural space by LOR.
BACKGROUND: Ten to fifteen percent of awake patients develop neurological deficits secondary to cerebral hypoperfusion after carotid artery cross-clamping. The reversal of such deficits by increasing the inspired oxygen fraction (Fio2) has been demonstrated, and regional cerebral oxygenation (rSO2) has been shown to improve during carotid cross-clamping in awake patients by increasing Fio2. Paradoxical improvements in cerebral blood flow during carotid endarterectomy (CEA) at the time of cross-clamping and normalization of post–cross-clamp electroencephalographic abnormalities have been induced by hypocapnia. We performed this study to determine the influence of Fio2 and end-tidal carbon dioxide (Petco2) on rSO2 in patients undergoing CEA with general anesthesia during carotid cross-clamping.

METHODS: Twenty patients were recruited. Ten underwent elective shunting. Patients received standardized general anesthesia. rSO2 was measured using the INVOS 5100B monitor (Somanetics Corporation, Troy, MI). After carotid cross-clamping, Fio2 and minute ventilation were sequentially adjusted: 1) Fio2 30%, Petco2 30–35 mm Hg; 2) Fio2 100%, Petco2 30–35 mm Hg; and 3) Fio2 100%, Petco2 40–45 mm Hg. At each point, rSO2 was recorded from both operative and nonoperative sides, and arterial blood gas analysis was performed.

RESULTS: Results from shunted and unshunted patients were analyzed separately. Increasing Fio2: Administration of 100% oxygen while maintaining Petco2 in the range 30–35 mm Hg in unshunted patients resulted in an 8% increase (P = 0.008) in rSO2 on the operative side and a 6%
increase ($P = 0.011$) on the nonoperative side compared with an Fio2 of 30%. In shunted patients, administration of 100% oxygen while maintaining the Petco2 in the range 30–35 mm Hg resulted in a 4% increase in rSO2 on both the operative side ($P = 0.008$) and the nonoperative side ($P = 0.011$) compared with an Fio2 of 30%. Increasing Petco2: In unshunted patients, there was a 6% ($P = 0.008$) increase in rSO2 on the operative side and a 5% increase ($P = 0.024$) on the nonoperative side at Petco2 40–45 mm Hg compared with Petco2 30–35 mm Hg maintaining Fio2 at 100%. In shunted patients, there was a 3% increase ($P = 0.018$) in rSO2 on the operative side and a 4% increase ($P = 0.007$) on the nonoperative side at Petco2 40–45 mm Hg compared with Petco2 30–35 mm Hg maintaining Fio2 at 100%.

**CONCLUSION:** rSO2 is reliably improved during carotid cross-clamping by increasing Fio2 in patients undergoing CEA with general anesthesia. Additional improvement in rSO2 may be gained by increasing Petco2.

甘氨酸轉運體-2抑制剤ALX1393在大鼠急性疼痛模型中的抗傷害的作用

The Antinociceptive Effect of Intrathecal Administration of Glycine Transporter-2 Inhibitor ALX1393 in a Rat Acute Pain Model

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**BACKGROUND:** Glycinergic neurons in the spinal dorsal horn have been implicated in the inhibition of spinal pain processing in peripheral inflammation and chronic pain states. Neuronal isoform glycine transporter-2 (GlyT2) reuptakes presynaptically released glycine and regulates
the glycinergic neurotransmission. In this study, we examined whether a selective GlyT2 inhibitor, ALX1393, elicits an antinociceptive effect in a rat acute pain model. 

**METHODS:** Male Sprague-Dawley rats were implanted with a catheter intrathecally. The effects of intrathecal administration of ALX1393 (4, 20, or 40 µg) on thermal, mechanical, and chemical nociception were evaluated by tail flick, hot plate, paw pressure, and formalin tests. Furthermore, to explore whether ALX1393 affects motor function, a rotarod test was performed.

**RESULTS:** ALX1393 exhibited antinociceptive effects on the thermal and mechanical stimulations in a dose-dependent manner. The maximal effect of ALX1393 was observed at 15 min after administration, and a significant effect lasted for about 60 min. These antinociceptive effects were reversed completely by strychnine injected immediately after the administration of ALX1393. In the formalin test, ALX1393 inhibited pain behaviors in a dose-dependent manner, both in the early and late phases, although the influence was greater in the late phase. In contrast to antinociceptive action, ALX1393 did not affect motor function up to 40 µg.

**CONCLUSIONS:** This study demonstrates the antinociceptive action of ALX1393 on acute pain. These findings suggest that the inhibitory neurotransmitter transporters are promising targets for the treatment of acute pain and that the selective inhibitor of GlyT2 could be a novel therapeutic drug.
METHODS: Seventy-six patients undergoing foot or ankle surgery received a sciatic nerve block either proximal or distal to the point of bifurcation. A mixture of 28 mL 1.5% mepivacaine with 100 µg clonidine and 1 mL 8.4% sodium bicarbonate for a total of 30 mL was used. Ultrasound was used to guide needle adjustments to achieve circumferential spread. Block success was defined as a loss of sensation to pinprick in both nerve distributions within 46 minutes.

RESULTS: Patients in the tibial-peroneal group had significantly faster time to complete block than the sciatic group (19.2 vs 26.1 minutes; \( P = 0.006 \)).

CONCLUSIONS: Blocking the tibial and common peroneal nerves in the popliteal fossa separately provides for a faster onset than a prebifurcation sciatic block.