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Hyperfibrinolysis Diagnosed by Rotational Thromboelastometry (ROTEM(R)) Is Associated with Higher Mortality in Patients with Severe Trauma.

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- Adrian Billeter, MD†, Jennifer Eismon, MD§, Burkhardt Seifert, PhD¶, Hans-Peter Simmen, MD†, Donat R. Spahn, MD, FRCA* and Werner Baulig, MD*

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此項研究旨在探究纖溶亢進及其嚴重程度與創傷或非創傷患者結局間的相互關係。2008 年 4 月至 2010 年 4 月間所有經診斷證實為纖溶亢進的急診患者均納入該項研究。根據有無軀體創傷將上述纖溶亢進患者分為創傷組（創傷纖溶亢進組）與非創傷組（非創傷纖溶亢進組）。另將 24 位無纖溶亢進的多發傷患者（創傷配對組）與創傷纖溶亢進患者相配對。採集旋轉血栓彈性測定法的測量結果、血氣分析（代謝狀態）、實驗室檢查、創傷嚴重度評分以及 30 天死亡率等相關資料以供分析。經鑒定共有 35 名患者被診斷為纖溶亢進（其中創傷患者 13 名，非創傷患者 22 名）。纖溶亢進的總體死亡率為 54%。創傷纖溶亢進組患者的死亡率（77%
We investigated whether hyperfibrinolysis and its severity was associated with outcome of traumatized and nontraumatized patients. From April 2008 to April 2010, all emergency patients with hyperfibrinolysis were enrolled in this study. Hyperfibrinolysis patients were divided into traumatized (trauma hyperfibrinolysis group) and nontraumatized (nontrauma hyperfibrinolysis group). The trauma hyperfibrinolysis group was matched with 24 polytrauma patients without hyperfibrinolysis (matched trauma group). Data from rotational thromboelastometry measurements, blood gas analysis (metabolic state), laboratory analysis, injury severity score, and 30-day mortality were collected. Thirty-five patients with hyperfibrinolysis were identified (13 traumatized, 22 nontraumatized). Overall mortality for hyperfibrinolysis was 54%. Mortality in the trauma hyperfibrinolysis group (77% ± 12%) was significantly higher than in the nontrauma hyperfibrinolysis group (41% ± 10%; P = 0.001, 95% CI 5%-67%) and the matched trauma group (33% ± 10%; P = 0.009, 95% CI 13%-74%). Hyperfibrinolysis is significantly (P = 0.017) associated with mortality in trauma patients. In the blood gas analysis representing the metabolic state, only pH (P = 0.02) and potassium (P = 0.01) were significantly lower in the trauma hyperfibrinolysis group compared to the nontrauma hyperfibrinolysis group. Mortality from hyperfibrinolysis is significantly higher in trauma compared with nontrauma patients, and hyperfibrinolysis is an independent factor predicting mortality in trauma patients. Rotational thromboelastometry provides real-time recognition of hyperfibrinolysis allowing early treatment.

Validation and insights of anesthetic action in an early vertebrate network: the isolated lamprey spinal cord
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Anesth Analg November 2011 113:1033-1042

Background: Lamprey spinal cord is a typical vertebrate network for us to understand the action of anesthetic agents. We tested a series of hypotheses regarding the clinical uses of anesthetic agents and their action sites and mechanisms.

Methods: In the isolated lamprey spinal cord, we used the effects of d-aminobutyric acid on the spinal cord, which is a critical neurotransmitter. We examined the effects of neuroactive substances on the spinal cord, such as the effects of glutamate, GABA, and glycine. We also examined the effects of nonsteroidal anti-inflammatory drugs on the spinal cord. We used this to determine the effects of anesthetic agents on the spinal cord in vitro. We also examined the effects of anesthetic agents on the spinal cord in vivo. We also examined the effects of anesthetic agents on the spinal cord in vitro. We also examined the effects of anesthetic agents on the spinal cord in vivo.
BACKGROUND: The lamprey spinal cord is a well-characterized vertebrate network that could facilitate our understanding of anesthetic action. We tested several hypotheses concerning the lamprey's clinical application to anesthesia, and the sites/mechanisms of anesthetic action.

METHODS: In isolated lamprey spinal cords, minimum immobilizing concentrations (MICs) were determined for halothane, isoflurane, sevoflurane, desflurane, propofol, or the nonimmobilizer F6 (1,2-dichlorohexafluorocyclobutane), applied during d-glutamate-induced fictive swimming or noxious tail stimulation. Isoflurane and propofol effects on fictive swimming were tested in the presence and absence of strychnine and/or picrotoxin.

RESULTS: Volatile anesthetic MICs were clinically comparable. Isoflurane MIC for fictive swimming and noxious stimulus-evoked movement were the same. F6 did not produce immobility, but decreased the amplitude and phase lag of fictive swimming. Isoflurane decreased fictive swimming cycle frequency, amplitude, autocorrelation, rostrocaudal phase lag, and coherence. Strychnine and picrotoxin elicited only disorganized motor activity under isoflurane and caused small increases in MIC. The effects of propofol differed from isoflurane for all locomotor rhythm variables except amplitude. The propofol MIC was much larger in lampreys compared with mammals. However, picrotoxin reversed propofol-induced immobility by reinitiating coordinated locomotor activity and increasing MIC >8-fold.

CONCLUSIONS: The lamprey spinal cord is a relevant and tractable vertebrate network model for anesthetic action. Isoflurane disrupts interneuronal locomotor networks. γ-Aminobutyric acid A and glycine receptors have marginal roles in isoflurane-induced immobility in lampreys. Propofol's selective γ-aminobutyric acid A receptor-mediated mechanism is conserved in lampreys. The differential immobilizing mechanisms of isoflurane versus propofol reflect those in mammals, and further suggest different network modes of immobilizing action.

Pleth variability index to predict fluid responsiveness in colorectal surgery.
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**BACKGROUND:** Goal-directed fluid therapy during major abdominal surgery may reduce postoperative morbidity. The Pleth Variability Index (PVI), derived from the pulse oximeter waveform, has been shown to be able to predict fluid responsiveness in a number of surgical circumstances. In the present study, we sought to determine whether PVI could predict fluid responsiveness in low-risk colorectal surgery patients who had fluid therapy guided by esophageal Doppler stroke volume measurements.

**METHODS:** Twenty-five low-risk patients undergoing colorectal resection under general anesthesia were studied. Baseline values for esophageal Doppler stroke volume and PVI taken from finger and ear probes were compared with final values after (a) a 500-mL fluid bolus immediately after induction (steady state) and tracheal intubation before the start of the surgery, and (b) 250-mL boluses given in response to a decrease in stroke volume of 10% during surgery as measured by esophageal Doppler (dynamic). Patients were classified into responders and nonresponders based on a stroke volume increase of >10%.

**RESULTS:** Baseline PVI at the finger was significantly higher in responders in both steady-state and intraoperative conditions. In steady state, PVI at both finger and earlobe had significant predictive ability of an increase in stroke volume: area under the curve for finger 0.96 (95% confidence interval [CI], 0.88-1.00; P = 0.011) and for earlobe 0.98 (95% CI, 0.93-1.00; P = 0.008). In dynamic intraoperative conditions, PVI at the finger predicted increases in stroke volume, area under the curve 0.71 (95% CI, 0.57-0.85; P = 0.006), but PVI at the earlobe had no predictive value.
CONCLUSIONS: PVI measured at the finger may be able to predict fluid responsiveness during surgery in ventilated patients.

A Randomized Comparison of Intraoperative PerfecTemp and Forced-Air Warming During Open Abdominal Surgery
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BACKGROUND: The PerfecTemp is an underbody resistive warming system that combines servocontrolled underbody warming with viscoelastic foam pressure relief. Clinical efficacy of the system has yet to be formally evaluated. We therefore tested the hypothesis that intraoperative distal esophageal (core) temperatures with the PerfecTemp (underbody resistive) warming system are noninferior to upper-body forced-air warming in patients undergoing major open abdominal surgery under general anesthesia.

METHODS: Adults scheduled for elective major open abdominal surgery (liver, pancreas, gynecological, and colorectal surgery) under general anesthesia were enrolled at 2 centers. Patients were randomly assigned to underbody resistive or forced-air warming. Resistive heating started when patients were transferred to the operating room table; forced-air warming started after patients were draped. The primary outcome was
noninferiority of intraoperative time-weighted average core temperature, adjusted for baseline characteristics and using a buffer of 0.5°C.

RESULTS: Thirty-six patients were randomly assigned to underbody resistive heating and 34 to forced-air warming. Baseline and surgical characteristics were generally similar. We had sufficient evidence ($P = 0.018$) to conclude that underbody resistive warming is not worse than (i.e., noninferior to) upper-body forced-air warming in the time-weighted average intraoperative temperature, with a mean difference of $-0.12°C$ [95% confidence interval (CI) $-0.37$ to $0.14$]. Core temperatures at the end of surgery averaged $36.3°C$ [95% CI $36$ to $36.5$] in the resistive warming patients and $36.6°C$ [95% CI $36.4$ to $36.8$] in those assigned to forced-air warming for a mean difference of $-0.34°C$ [95% CI $-0.69$ to $0.01$].

CONCLUSIONS: Mean intraoperative time-weighted average core temperatures were no different, and significantly noninferior, with underbody resistive heating in comparison with upper-body forced-air warming. Underbody resistive heating may be an alternative to forced-air warming.
度，FRC 平均增加了 188ml（p=0.03，95%置信区间是 18-358ml）。其他生命体征上各种体位下的比较並没有差异（p>0.16）。

结论：经过我们的研究認为，健康临產婦的 FRC 在頭上抬 30 度的體位下要比平臥位明顯要多。

（陸麗虹譯 薛張綱校）

BACKGROUND: Airway management continues to pose challenges to the obstetric anesthesiologist. Functional residual capacity (FRC), which acts as an oxygen reservoir, is reduced from the second trimester onwards and is exacerbated in the supine position. Mechanisms to increase FRC may delay the onset of hypoxemia during periods of apnea. Values for changes in FRC in term parturients in semierect positions are unknown. We hypothesized that the FRC of healthy term parturients would increase significantly in the 30° head-up position in comparison with the supine position.

METHODS: Twenty-two healthy term parturients were recruited. Initial screening spirometry was performed to exclude undiagnosed respiratory disease. FRC was measured using the helium dilution technique in the supine, 30° head-up, and sitting erect positions. Subjects were randomized to sequence of position testing order. Noninvasive systolic blood pressure, heart rate, and oxygen saturation were measured twice in each testing position.

RESULTS: Results from 20 subjects were analyzed. The spirometry results for all subjects were within predicted normal reference intervals. FRC measurements differed significantly (P < 0.001) among all positions. FRC increased by a mean of 188 mL (95% confidence interval 18 to 358 mL) from the supine to the 30° head-up position (P = 0.03). There were no significant differences in vital signs among testing positions (P > 0.16).

CONCLUSIONS: We have demonstrated that the FRC of healthy term parturients increases significantly in the 30° head-up position in comparison with supine.

综述：右旋美托嘧啶在儿童中的應用：現狀與展望

Review article: dexmedetomidine in children: current knowledge and future applications.

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摘要：關於右旋美托嘧啶在嬰兒和兒童中應用目前已有 200 多個研究和報導發表。我們回顧了其中的英文文獻，總結了實踐麻醉學家對於此藥在兒科應用目前的認識。右旋美托嘧啶對於嬰兒和兒童來說是一種有效的鎮靜劑，其幾乎不抑制呼吸系統，保持了呼吸道開放。但是右旋美托嘧啶抑制了心血管系統，特別是心動過緩、低血壓和高血壓根據兒童年齡不同程度的發生。低血壓更易發生於使用大劑量右旋美托嘧啶後的嬰兒。與其 2 小時的消除半衰期相一致，使用右旋美托嘧啶後蘇醒期較其他鎮靜藥延長。右旋美托嘧啶產生和增強鎮痛作用，並且减少了術後寒戰
Abstract: More than 200 studies and reports have been published regarding the use of dexmedetomidine in infants and children. We reviewed the English literature to summarize the current state of knowledge of this drug in children for the practicing anesthesiologist. Dexmedetomidine is an effective sedative for infants and children that only minimally depresses the respiratory system while maintaining a patent airway. However, dexmedetomidine does depress the cardiovascular system. Specifically, bradycardia, hypotension, and hypertension occur to varying degrees depending on the age of the child. Hypertension is more prevalent when larger doses of dexmedetomidine are given to infants. Consistent with its 2-hour elimination half-life, recovery after dexmedetomidine may be protracted in comparison with other sedatives. Dexmedetomidine provides and augments analgesia and diminishes shivering as well as agitation postoperatively. The safety record of dexmedetomidine suggests that it can be used effectively and safely in children, with appropriate monitoring and interventions to manage cardiovascular sequelae.

The Toxic Effects of S(+) -Ketamine on Differentiating Neurons In Vitro as a Consequence of Suppressed Neuronal Ca^{2+} Oscillations

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背景：在未成熟的大腦中，在一段高度塑型期中，神經元的 Ca^{2+} 振盪會出現，並調節神經元的分化和突觸發生。在這項研究中，我們研究了長期阻斷海馬的 Ca^{2+} 振盪，它是 NMDA 受體的重要角色，並影響了影響了 S 型氯胺酮在神經元突觸蛋白的表達。

方法：海馬的神經元被放在有特殊 NMDA 受體拮抗劑地佐環平中培養15天或者 S 型氯胺酮中培養24小時。末端去氧核苷醯酶轉移酶（TUNEL）和活化的半胱天冬酶用來檢測凋亡的神經元。給神經元染色後檢測 Ca^{2+} 振盪，並用雙波長螢光顯微鏡觀察。用 western 印跡來測量 Ca^{2+}/鈣調節蛋白激酶 II。用共焦點抗突觸蛋白免疫螢光法來鑑定突觸蛋白。

結果：用 MK801 或者 S 型氯胺酮去阻滯 NMDA 受體會引起神經元凋亡增加。MK801導致細胞溶質中 Ca^{2+}濃度顯著增加，並減少 Ca^{2+}振盪的幅度和頻率。和 MK801相似，長期使用 S 型氯胺酮可導致沖洗後24小時內細胞溶質中 Ca^{2+}濃度顯著增加。這與下調了 Ca^{2+}/鈣調節蛋白激酶 II 並降低沖洗後24小時內突觸蛋白有關係。
Background: In the immature brain, neuronal Ca\(^{2+}\) oscillations are present during a time period of high plasticity and regulate neuronal differentiation and synaptogenesis. In this study we examined the long-term blockade of hippocampal Ca\(^{2+}\) oscillations, the role of the N-methyl-d-aspartate (NMDA) receptors and the effects of S(+)-ketamine on neuronal synapsin expression.

Methods: Hippocampal neurons were incubated at day 15 in culture with the specific NMDA receptor antagonists dizocilpine (MK 801, 100 μM) or S(+)-ketamine (3 μM to 25 μM) for 24 hours. Terminal-deoxynucleotidyl-transferase (TUNEL) and activated caspase3 were used to detect apoptotic neurons. Ca\(^{2+}\) oscillations were detected after loading the neurons with the Ca\(^{2+}\)-sensitive dye fura-2AM, and dual wavelength excitation fluorescence microscopy was performed. Ca\(^{2+}\)/calmodulin kinase II (CaMKII) was measured using Western blots. Synapsin was identified with confocal antisynapsin immunofluorescence.

Results: Blocking the NMDA receptor with MK 801 or 25 μM S(+)-ketamine resulted in a significant increase in apoptotic neurons. MK 801 led to a significant increase in cytosolic Ca\(^{2+}\) concentration and reduction of the amplitude and frequency of the Ca\(^{2+}\) oscillations. Similar to MK 801, the long-term application of S(+)-ketamine resulted in a significant increase in cytosolic Ca\(^{2+}\) concentration 24 hours after washout. This was associated with a down-regulation of the CaMKII and a reduction of the synapsin 24 hours after washout.

Conclusion: Neuronal Ca\(^{2+}\) oscillations mediate neuronal differentiation and synaptogenesis via activating CaMKII. By acting via the NMDA receptor, S(+)-ketamine exerts its toxic effect through the suppression of neuronal Ca\(^{2+}\) oscillations, down-regulation of the CaMKII, and consecutively reduced synaptic integrity.
ウクレ: 38名の病人が麻醉時に過敏症を発症した。18例はIgE介導の過敏症（皮膚検査により特定の薬物を示唆）、6例は非IgE介導の過敏症（類似の蛋白の水準上昇、皮膚検査陰性）、14例は非IgE介導の過敏症（類似の蛋白の水準正常または未検出、皮膚検査陰性）であった。IgE介導の過敏症において、抗生素は最も頻繁に原因薬物と見られた（50%）、神経筋薬は11%を占めた。

結論: 抗生素はIgE介導の過敏症中最も一般的な原因薬物であったが、52.6%の過敏症では原因薬物の特定が困難であり、非IgE介導の過敏症と推定された。未特定の過敏原により、患者は同一の過敏原に再度接触することになり、必要となる薬物治療を避ける必要がある。
BACKGROUND: We conducted this study to evaluate the effects of thoracic epidural anesthesia (TEA) on inflammatory response, lipid peroxidation, and oxidative stress in a rat model of mesenteric ischemia/reperfusion (I/R).

METHOD: Rats were divided into 4 groups: sham group (n = 6; sham laparotomy), control group (n = 6; I/R), bupivacaine group (n = 6; mesenteric I/R and 20 μL/h 0.5% bupivacaine), and saline group (n = 6, mesenteric I/R and 20 μL/h 0.9% saline). I/R injury was established by occluding the superior mesenteric artery for 1 hour followed by 12 hours reperfusion. Blood gas, tumor necrosis factor-α, interleukin-6, interleukin-1β, glutathione peroxidise, superoxide dismutase, catalese, myeloperoxidase concentrations, immunohistochemical examinations (intracellular adhesion molecule-1), apoptosis determination, and wet/dry ratio of intestinal edema were determined.

RESULTS: Bupivacaine significantly decreased the cytokine, malondialdehyde, and myeloperoxidase levels and increased the antioxidant enzyme levels. Wet/dry ratio comparison showed a significant decrease in the bupivacaine (2.88 ± 0.17) group in comparison with control (5.45 ± 0.67) and saline groups. The intestinal injury score was significantly decreased in rats in the epidural bupivacaine (2 [1-2]) infusion group in comparison with rats in the control (3 [2-3]) and saline (3 [2-4]) groups. Bupivacaine (63%) caused a significant decrease in the percentage of apoptotic cells in comparison with control (85%) only. ICAM-1 levels in the bupivacaine (27.4 ± 7.1) group decreased in comparison with control (12.3 ± 7.4) and saline (24.9 ± 3.2) groups.

CONCLUSION: This study demonstrated that epidural bupivacaine attenuates the mesenteric I/R-related inflammatory response and intestinal damage.

Ketamine Activates the L-Arginine/Nitric Oxide/Cyclic Guanosine Monophosphate Pathway to Induce Peripheral Antinociception in Rats
背景：许多镇痛药物通过作用于 L-精氨酸/一氧化氮/cGMP 通路达到镇痛作用，包括 μ、κ 或 δ 阿片受体激动剂、非甾体抗炎药、胆碱能受体激动剂和 α2C 肾上腺能受体激动剂。在我们的这项研究中，我们研究了氯胺酮——一种分离性麻醉药物 NMDA 受体拮抗剂，是否也是通过 L-精氨酸/一氧化氮/cGMP 通路导致外周镇痛作用。

方法：在大鼠足底注射前列腺素 E2 诱导痛觉，并测定脚爪压力。所有的药物均局部注射入雄性 Wistar 大鼠的后爪。

结果：氯胺酮 (10, 20, 40, 80 μg/爪) 所致的局部镇痛作用可以被非选择性 NOS 抑制剂 L-NOARG (12, 18, 和 24 μg/爪) 或选择性 NOS 抑制剂 L-NPA (12, 18, 和 24 μg/爪) 拮抗。在另一项实验中，我们使用抑制剂 L-NIO 和 L-NIL (24 μg/爪) 分别选择性地抑制内皮及诱导的 NOS。这两种药物都不能有效的阻断外周使用氯胺酮的作用。此外爪均质的亚硝酸盐的水平提示外源性氯胺酮可以增加 NO 的释放。可溶性的鸟苷酰环化酶抑制剂 ODQ (25, 50 和 100 μg/爪) 可以阻断氯胺酮的作用，cGMP-磷酸二酯酶抑制剂敏喘宁 (50 μg/爪) 可以增强低剂量氯胺酮 (10 μg/爪) 的镇痛作用。

结论：我们的结果提示氯胺酮通过 NO 合酶刺激 L-精氨酸/NO/cGMP 通路，从而产生外周抗伤害性刺激的作用。

(陈珺珺译 薛张纲校)

Background: The involvement of the L-arginine/nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) pathway in antinociception has been implicated as a molecular mechanism of antinociception produced by several antinociceptive agents, including μ-, κ-, or δ-opioid receptor agonists, nonsteroidal analgesics, cholinergic agonist, and α2C adrenoeceptor agonist. In this study, we investigated whether ketamine, a dissociative anesthetic N-methyl-D-aspartate receptor antagonist, was also capable of activating the L-arginine/NO/cGMP pathway and eliciting peripheral antinociception.

Methods: The rat paw pressure test was used, with hyperalgesia induced by intraplantar injection of prostaglandin E2. All drugs were locally administered into the right hindpaw of male Wistar rats.

Results: Ketamine (10, 20, 40, 80 μg/paw) elicited a local antinociceptive effect that was antagonized by the nonselective NOS inhibitor L-NOARG (12, 18, and 24 μg/paw) and by the selective neuronal NOS inhibitor L-NPA (12, 18, and 24 μg/paw). In another experiment, we used the inhibitors L-NIO and L-NIL (24 μg/paw) to selectively inhibit endothelial and inducible NOS, respectively. These 2 drugs were ineffective at blocking the effects of the peripheral ketamine injection. In addition, the level of nitrite in the homogenized paw indicated that exogenous ketamine is able to induce NO release. The soluble guanylyl cyclase inhibitor ODQ (25, 50, and 100 μg/paw) blocked the action of ketamine, and the cGMP-phosphodiesterase inhibitor zaprinast (50 μg/paw) enhanced the antinociceptive effects of low-dose ketamine (10 μg/paw).
Conclusions: Our results suggest that ketamine stimulates the L-arginine/NO/cyclic GMP pathway via neuronal NO synthase to induce peripheral antinociceptive effects.

The Addition of Lidocaine to Bupivacaine Does Not Shorten the Duration of Spinal Anesthesia: A Randomized, Double-Blinded Study of Patients Undergoing Knee Arthroscopy

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BACKGROUND: The duration of spinal anesthesia with bupivacaine is often too long for day surgery. A recent study of patients presenting for transurethral hyperbaric bupivacaine suggested that the addition of a small amount of lidocaine to intrathecal hyperbaric bupivacaine could shorten the duration of the sensory and motor blocks. In this prospective, randomized double-blind study we investigated these findings in patients undergoing unilateral knee arthroscopy.

METHODS: Fifty patients were randomized to receive 2 mL hyperbaric 0.5% bupivacaine plus either 0.6 mL 1% lidocaine (lidocaine group) or 0.6 mL saline (control group). The sensory and motor blocks were monitored until complete regression and the patient was ready for discharge. The patients were interviewed 2 and 7 days after the operation about any side effects and any signs of transient neurologic syndrome.
RESULTS: Data on 45 patients were available for analysis (24 in the lidocaine group). There was no statistically significant difference between the groups regarding time to readiness for surgery, maximum level of sensory block, total duration of sensory, and motor blocks or time to discharge from the postoperative care unit. Two patients in the control group and 1 patient in the study group had symptoms of transient neurologic syndrome for <24 hours after the operation. One patient had voiding difficulties for 3 days. All symptoms resolved spontaneously. No patient had spinal headache or backache. CONCLUSION: We did not confirm, in patients undergoing knee arthroscopy, that the addition of a small dose of lidocaine to intrathecal hyperbaric bupivacaine could shorten the duration of sensory or motor blocks or time to readiness for discharge from the postanesthesia care unit.
result: there were 271 patients with PAC and 196 patients without PAC treated at the end of the study (21.3% vs. 15.4%; adjusted odds ratio [AOR]: 1.68; 95% confidence interval [CI], 1.24 to 2.26; P < 0.001). The PAC group had a higher mortality rate (3.5% vs 1.7% [AOR, 2.08; 95% CI, 1.11 to 3.88; P = 0.02]), and a higher rate of cerebral dysfunction (AOR, 1.58; 95% CI, 1.14 to 2.20; P = 0.007), renal dysfunction (AOR, 2.47; 95% CI, 1.68 to 3.62; P < 0.001). Patients with PAC demonstrated a higher rate of atrial fibrillation (57.8% vs. 50.0%; P < 0.001), and a larger positive IV fluid balance (3220 mL vs 3022 mL; P = 0.003), and longer times to tracheal extubation (15.40 hours [11.28/20.80] vs 13.18 hours [9.58/19.33], median plus Q1/Q3 interquartile range; P < 0.0001). Use of PAC was also associated with prolonged intensive care unit stay (14.5% vs 10.1%; AOR, 1.55; 95% CI, 1.06 to 2.27; P = 0.02).

conclusion: in this matched observational study, the use of PAC in patients undergoing OPCAB was associated with higher mortality and end-organ complications. It is important to conduct future randomized controlled trials to confirm or refute this observation.

background: the pulmonary artery catheter (PAC) is still used for monitoring of hemodynamics in patients undergoing coronary artery bypass graft (CABG) surgery despite concerns raised in other settings regarding both effectiveness and safety. Given the relative paucity of data regarding its use in CABG patients, and given entrenched practice patterns, we assessed the impact of PAC use on fatal and nonfatal CABG outcomes as practiced at a diverse set of medical centers.

methods: using a formal prospective observational study design, 5065 CABG patients from 70 centers were enrolled between November 1996 and June 2000 using a systemic sampling protocol. Propensity score matched-pair analysis was used to adjust for differences in likelihood of PAC insertion. The predefined composite endpoint was the occurrence of any of the following: death (any cause), cardiac dysfunction (myocardial infarction or congestive heart failure), cerebral dysfunction (stroke or encephalopathy), renal dysfunction (dysfunction or failure), or pulmonary dysfunction (acute respiratory distress syndrome). Secondary variables included treatment indices (inotrope use, fluid administration), duration of postoperative intubation, and intensive care unit length of stay. After categorization based on PAC and transesophageal echocardiography use (both, neither, PAC only, transesophageal echocardiography only), we performed the primary analysis contrasting PAC only and neither (total, 3321 patients), from which propensity paring yielded 1273 matched pairs.

results: the primary endpoint occurred in 271 patients with PAC versus 196 without PAC (21.3% vs 15.4%; adjusted odds ratio [AOR], 1.68; 95% confidence interval [CI], 1.24 to 2.26; P < 0.001). The PAC group had an increased risk of all-cause mortality, 3.5% vs 1.7% [AOR, 2.08; 95% CI, 1.11 to 3.88; P = 0.02] and an increased risk of cardiac (AOR, 1.58; 95% CI, 1.14 to 2.20; P = 0.007), cerebral (AOR, 2.02; 95% CI, 1.08 to 3.77; P = 0.03) and renal (AOR, 2.47; 95% CI, 1.68 to 3.62; P < 0.001) morbid outcomes. PAC patients received inotropic drugs more frequently (57.8% vs 50.0%; P < 0.001), had a larger positive IV fluid balance after surgery (3220 mL vs 3022 mL; P = 0.003), and experienced longer times to tracheal extubation (15.40 hours [11.28/20.80] versus 13.18 hours [9.58/19.33], median plus Q1/Q3 interquartile range; P < 0.0001). Use of PAC was also associated with prolonged intensive care unit stay (14.5% vs 10.1%; AOR, 1.55; 95% CI, 1.06 to 2.27; P = 0.02).
CONCLUSIONS: Use of a PAC during CABG surgery was associated with increased mortality and a higher risk of severe end-organ complications in this propensity-matched observational study. A randomized controlled trial with defined hemodynamic goals would be ideal to either confirm or refute our findings.

The Etomidate Requirement Is Decreased in Patients with Obstructive Jaundice

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BACKGROUND: Patients with obstructive jaundice have increased sensitivity to inhaled anesthetics. In rodent brain, bilirubin can enhance \( \gamma \)-aminobutyric acid A/glycinergic synaptic transmission. Etomidate is a nonbarbiturate hypnotic that induces sedation through \( \gamma \)-aminobutyric acid A receptors in the central nervous system. We tested the hypothesis that patients with obstructive jaundice have an altered sensitivity to etomidate.

METHODS: The study design was a comparison of etomidate requirements to reach a Bispectral Index of 50 in patients with obstructive jaundice versus patients with chronic cholelithiasis and normal bilirubin levels. Etomidate was infused at 30 \( \mu \)g/kg/min until this end point was reached.

RESULTS: The etomidate requirement in the obstructive jaundice group was lower than that in the control group (150 ± 46 \( \mu \)g/kg vs 206 ± 74 \( \mu \)g/kg, \( P = 0.007 \)). The average decrease in etomidate requirement was 56 \( \mu \)g/kg (95% confidence interval: 16–96 \( \mu \)g/kg). In addition, we found a significant negative correlation between serum total bilirubin and etomidate requirement with Pearson \( r \) of \(-0.545\), and 95% confidence interval for \( r \) value \((-0.791 \text{ to } -0.148)\). All subjects were hemodynamically stable during the study.
CONCLUSIONS: Etomidate requirements to reach a level of anesthesia defined by a Bispectral Index of 50 are reduced in patients with obstructive jaundice.

心臓手術後無創多波長脈搏血氧飽和度測量血紅蛋白的準確度
The Accuracy of Noninvasive Hemoglobin Measurement by Multiwavelength Pulse Oximetry After Cardiac Surgery
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BACKGROUND: In March 2008, a new multiwavelength pulse oximeter, the Radical 7 (Rad7; Masimo Corp., Irvine, CA), was developed that offers noninvasive measurement of hemoglobin concentration. Accuracy has been established in healthy adults and some surgical patients, but not in cardiac surgery intensive care patients, a group at high risk of postoperative bleeding events and anemia in whom early diagnosis could improve management.

METHODS: In this prospective, observational study conducted in a cardiovascular intensive care unit, we compared hemoglobin concentrations shown by the Rad7 with
arterial hemoglobin concentrations determined by an automated hematology analyzer, XE-2100 (Roche, Neuilly sur Seine, France). Two software versions of Rad7 (V 7.3.0.1 [42 points of comparison in 14 patients] and the updated V 7.3.1.1 [61 points of comparison in 27 patients]) were studied during two 1-week periods. Bias, defined as the difference between the 2 methods (Masimo SpHb − XE-2100 laboratory hemoglobin), was calculated. A negative bias indicated that the Masimo underestimated hemoglobin compared with the laboratory analyzer. Correlation between the perfusion index given by Rad7 and the hemoglobin bias was also studied.

RESULTS: Correlations between Rad7 and XE-2100 were weak for both software versions ($R^2 = 0.11$ for V 7.3.0.1 and $R^2 = 0.27$ for V 7.3.1.1). Mean bias was −1.3 g/dL for V 7.3.0.1 and −1.7 g/dL for V 7.3.1.1, with wide 95% prediction intervals for the bias (respectively, −4.6 to 2.1 g/dL and −5.7 to 2.3 g/dL). The absolute hemoglobin bias tended to increase when the perfusion index decreased. For the V 7.3.0.1 software, the average absolute bias was 1.9 g/dL for perfusion index <2 and 0.8 g/dL for perfusion index >2 ($P = 0.03$). For V 7.3.1.1, the mean absolute bias was 2.1 g/dL when the perfusion index was <2, and 1.6 g/dL when the perfusion index was >2 ($P = 0.26$).

CONCLUSIONS: Our study demonstrates poor correlation between hemoglobin measured noninvasively by multiwavelength pulse oximetry and a laboratory hematology analyzer. The difference was greater when the pulse oximetry perfusion index was low, as may occur in shock, hypothermia, or vasoconstriction patients. The multiwavelength pulse oximetry is not sufficiently accurate for clinical use in a cardiovascular intensive care unit.

45°特倫德倫伯格臥位下機器人協助腹腔鏡前列腺癌根治術時血流動力學的變化

Hemodynamic Perturbations During Robot-Assisted Laparoscopic Radical Prostatectomy in 45° Trendelenburg Position

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背景：機器人協助的腹腔鏡下前列腺癌根治術已被廣泛應用。然而當患者置於完全的特倫德倫伯格臥位(45°)時的血流動力學變化尚未闡明。方法：作者研究了16例平均年齡為59歲（ASA分級為I-II），擇期行機器人協助的腹腔鏡下前列腺癌根治術的患者（45°頭低位，腹腔內壓力11–12 mm Hg）。採集氣腹前以及氣腹期間、擺置特倫德倫伯格臥位時以及手術後的血流動力學參數、超聲心動圖、氣體交換以及肺通氣-灌注係數等各種資料，結果：在45°頭低位時，中心靜脈壓力較基礎值升高了3倍，平均肺動脈壓力以及肺毛細血管楔壓增加2倍 ($P < 0.01$)。平均動脈壓力增加35%。心率，每搏輸出量，心排血量以及混合靜脈血氧飽和度以及超聲心動圖下心臟大小在術中並未改變。麻醉誘導後，等容舒張期延長，在術中並未有進一步改變。減速時間是正常的並且穩定。氣腹放氣置於平臥位時，充盈壓已經平均動脈壓恢復至基礎水準。氣腹
BACKGROUND: Robot-assisted laparoscopic radical prostatectomy has gained widespread use. However, circulatory effects in patients subjected to an extreme Trendelenburg position (45°) are not well characterized.

METHODS: We studied 16 patients (ASA physical status I–II) with a mean age of 59 years scheduled for robot-assisted laparoscopic radical prostatectomy (45° head-down tilt, with an intraabdominal pressure of 11–12 mm Hg). Hemodynamics, echocardiography, gas exchange, and ventilation-perfusion distribution were investigated before and during pneumoperitoneum, in the Trendelenburg position and, in 8 of the patients, also after the conclusion of surgery.

RESULTS: In the 45° Trendelenburg position, central venous pressure increased almost 3-fold compared with the initial value, with an associated 2-fold increase in mean pulmonary artery pressure and pulmonary capillary wedge pressure (P < 0.01). Mean arterial blood pressure increased by 35%. Heart rate, stroke volume, cardiac output, and mixed venous oxygen saturation were unaffected during surgery, as were echocardiographic heart dimensions. After induction of anesthesia, isovolumic relaxation time was prolonged, with no further change during the study. Deceleration time was normal and stable. In the horizontal position after pneumoperitoneum exsufflation, filling pressures and mean arterial blood pressure returned to baseline levels. Pneumoperitoneum reduced lung compliance by 40% (P < 0.01). Addition of the Trendelenburg position caused a further decrease (P < 0.05). Arterial blood acid-base balance was normal. End-tidal carbon dioxide tension increased whereas arterial carbon dioxide was unaffected with unchanged ventilation settings. Pneumoperitoneum increased PaO₂ (P < 0.05). Ventilation-perfusion distribution, shunt, and dead space were unaltered during the study.

CONCLUSIONS: Pneumoperitoneum and 45° Trendelenburg position caused 2- to 3-fold increases in filling pressures, without effects on cardiac performance. Filling pressures were normalized immediately after surgery. Lung compliance was halved. Gas exchange was unaffected. No perioperative cardiovascular complications occurred.

Spontaneous Breathing Improves Shunt Fraction and Oxygenation in Comparison with Controlled Ventilation at a Similar Amount of Lung Collapse
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背景：在不同的急性肺损伤的模型中，机械通气(MV)时允许自主呼吸(SB)能改善氧合。然而，在机械通气不支持SB时是否能改善氧合尚不明确。因此，在猪萎陷肺的模型中，作者比较了不使用任何支持的SB与用相同的潮气量( VT )和呼吸频率(RR)不使用呼吸末正压MV的呼吸情况。

方法：在25例麻醉的猪中，通过使用负压肺萎陷模型，并随机分组至SB组或者MV组，相同的 VT (5 mL/kg; 95% 可信区间: 3.8至6.4)且RR(65每分钟[57-73])，在SB初始阶段开始记录。记录血气中的氧分压(n=15)，此外，可能的肺复张通过X线表现(n=10)。

结果：在肺萎陷后， PaO2/FIO2 下降至 90 mm Hg (76至103)。使用SB，PaO2/FIO2在15min中增加至235 mm Hg(177至93)，而MV并没有改善氧合。肺萎陷后45min，SB组中肺内分流较低(SB: 27% [24至30] vs MV: 41% [28至55]; P = 0.017)。SB和MV都不能减少减少肺萎陷的面。

结论：与相同呼吸参数下MV相比，无任何支持的SB能改善氧合，减少肺内分流。这可能有益于促进肺复张。

高解析度熔解曲線分析蘭尼堿惡性高熱致病突變基因1的篩選
Screening of the Ryanodine 1 Gene for Malignant Hyperthermia Causative Mutations by High Resolution Melt Curve Analysis

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BACKGROUND: A diagnosis of malignant hyperthermia (MH) can be determined by performing an in vitro (muscle) contracture test (IVCT) or by identifying a known MH causative mutation in the ryanodine receptor 1 gene (RYRI). Genetic diagnosis has an advantage over IVCT because it is less invasive. Direct sequencing of the very large RYRI coding region (15.117 bases) is a laborious and expensive task. In this study, we applied the High Resolution Melting (HRM) curve analysis as a tool to screen the entire coding region of the gene.

METHODS: Genomic DNA was extracted from peripheral blood samples in a cohort of 16 MH-susceptible patients diagnosed by the IVCT. The total coding region of RYRI was divided and amplified by polymerase chain reaction in 131 DNA fragments and the melting profiles were compared with those of control samples. HRM curves were evaluated by Rotor-Gene Q software and visual inspection. Fragments showing aberrant melting profiles were sequenced to identify the underlying sequence variation.

RESULTS: A subset of 520 of 2520 DNA fragments (21%) showed significantly aberrant melting profiles. Upon sequencing, 131 known polymorphisms and 17 known or
suspected mutations were found in 13 of 16 MH-susceptible patients (81%). Thus, the workload of sequencing was reduced by 79%.

**CONCLUSION:** HRM curve analysis is a sensitive and cost-effective tool for the identification of nucleotide sequence variants in complex genes such as the RYR1 gene.

GABAergic Excitotoxicity Injury of the Immature Hippocampal Pyramidal Neurons' Exposure to Isoflurane

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**Background:** Certain anesthetic agents can cause neuronal damage in immature rats but not in adults.

γ—Aminobutyric acid (GABA) is the principal inhibitory neurotransmitter in adult rats, but it excites nonmature cells through 
A-type GABA receptors and reverses the concentration gradient of chloride, causing membrane depolarization and increasing intracellular calcium. Recent studies have shown that early exposure to isoflurane can lead to neuronal cell excitotoxicity and apoptosis. A-type GABA receptors mediate the overactivation of voltage-dependent calcium channels and calcium influx involved in these neurological changes.

**Methods:** The authors used the Fluo-4 AM fluorescent imaging to monitor intracellular calcium ([Ca²⁺]i) concentration. Whole-cell patch clamp techniques were used to record the current of the voltage-dependent calcium channel (IVDCC) in primary mouse hippocampal neurons (cultured for 5 days) after exposure to isoflurane. To further explore the dose- and time-dependent effects of isoflurane on the intracellular high concentration of calcium, caspase-3 activity was assessed using western blot and quantitative real-time PCR (qRT-PCR) techniques. Statistical analysis was performed using Tukey's test.

**Results:** Under control conditions, isoflurane dose-dependently increased GABA-induced [Ca²⁺]i release. The nitroglycerin and nicardipine were effective in inhibiting this increased effect. At the same time, the calcium current in nonmature cells was enhanced by isoflurane. Different concentrations of isoflurane (0.25, 0.5, 0.75, and 1 minimum alveolar concentration [MAC]) were used to stimulate IVDCC, showing that the peak current amplitude increased to 109.11% ± 9.03%, 120.56% ± 11.46%, 141.33% ± 13.87%, and 146.78% ± 15.87%, respectively. At the protein level, isoflurane increased caspase-3 activity in a dose-dependent manner, reaching the maximum activity at 6 hours of exposure (P < 0.001). However, in mRNA levels, caspase-3 mRNA was significantly increased at 0.25 MAC6 hours later.

**Conclusion:** Isoflurane-induced GABA-evoked [Ca²⁺]i release involves membrane depolarization and subsequent IVDCC activation, which in turn causes calcium release from the intracellular stores and finally leads to apoptosis. The mechanisms of isoflurane-induced excitotoxicity in immature hippocampal neurons may serve as potential pathways for the mechanism of isoflurane neuronal toxicity.
BACKGROUND: Certain anesthetics exhibit neurotoxicity in the brains of immature but not mature animals. γ-Aminobutyric acid (GABA), the primary inhibitory neurotransmitter in the adult brain, is excitatory on immature neurons via its action at the GABA_A receptor, depolarizing the membrane potential and inducing a cytosolic Ca^{2+} increase ([Ca^{2+}]_i), because of a reversed transmembrane chloride gradient. Recent experimental data from several rodent studies have demonstrated that exposure to isoflurane during an initial phase causes neuronal excitotoxicity and apoptosis. GABA_A receptor–mediated synaptic voltage-dependent calcium channels' (VDCCs) overactivation and Ca^{2+} influx are involved in these neural changes.

METHODS: We monitored [Ca^{2+}]_i using Fluo-4 AM fluorescence imaging. Using whole-cell patch clamp techniques, I_{VDCC} (voltage-dependent calcium channel currents) were recorded from primary cultures of rat hippocampal neurons (5-day culture) exposed to isoflurane. To further investigate the neurotoxicity of high cytosolic-free calcium after isoflurane in a dose- and time-dependent manner, the possibility of increased caspase-3 levels was evaluated by Western blot and quantitative real-time polymerase chain reaction. Statistical significance was assessed using the Student t test or 1-way analysis of variance followed by the Tukey post hoc test.

RESULTS: Under control conditions, isoflurane enhanced the GABA-induced [Ca^{2+}]_i increase in a dose-dependent manner. Dantrolene and nicardipine markedly inhibited this enhancement mediated by isoflurane. Moreover, in Ca^{2+}-free media, pretreatment with isoflurane did not show any influence on the caffeine-induced increase of [Ca^{2+}]_i. Similarly, using whole-cell recording, isoflurane increased the peak amplitude of I_{VDCC} in the cultured neurons from rat hippocampus by depolarization pulses. Isoflurane (0.25, 0.5, 0.75, and 1 minimum alveolar concentration [MAC]) potentiated I_{VDCC} peak current amplitude by 109.11% ± 9.03%, 120.56% ± 11.46%, 141.33% ± 13.87%, and 146.78% ± 15.87%, respectively. To analyze variation in protein levels, the effect of treatments with isoflurane on caspase-3 activity was dose- and time-dependent, reaching a maximal caspase-3 activity after exposure to 1 MAC for 6 hours ($P < 0.001$). However, in the mRNA levels, hippocampal caspase-3 mRNA levels began to be significantly increased in isoflurane-treated developing rat hippocampal neurons after 6 hours of exposure to 0.25 MAC isoflurane ($P < 0.001$).

CONCLUSIONS: Isoflurane-mediated enhancement of GABA-triggered [Ca^{2+}]_i release results from membrane depolarization with subsequent activation of VDCCs and further Ca^{2+}-induced Ca^{2+} release from the ryanodine-sensitizing Ca^{2+} store. An increase in [Ca^{2+}]_i, caused by activation of the GABA_A receptor and opening of VDCCs, is necessary for isoflurane-induced calcium overload of immature rat hippocampal neurons, which may be involved in the mechanism of an isoflurane-induced neurotoxic effect in the developing rodent brain.

在大鼠中，遠端肢體後處理可以通過δ蛋白激酶C的活性氧調節抑制劑降低大腦再灌注損傷

Limb Remote Postconditioning Alleviates Cerebral Reperfusion Injury Through Reactive Oxygen Species-Mediated Inhibition of Delta Protein Kinase C in Rats
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背景：現在認為，遠隔缺血後處理對於腦梗死的保護有一定作用，但是其機制尚不清楚。本研究的目的是證實在大鼠腦缺血模型中活性氧和δ蛋白激酶C對於實現遠隔缺血後處理的腦保護作用以及兩者之間的聯繫。

方法：在雄性大鼠中通過夾閉大腦中動脈來建立大鼠腦缺血模型。大腦中動脈再灌注時通過反復夾閉/再灌注右側大腿股動脈來實行遠隔缺血後處理，3-10 分鐘一個週期。研究中分別只進行遠隔缺血後處理或者事先給予 N-乙醯半胱氨酸（一種活性氧的清除劑）。在各組中，再灌注開始時分別給予 TAT–δV1-1，一種δ蛋白激酶 C 的選擇性肽抑制劑。大腦缺血損傷程度由神經病學評分，梗死面積以及 TUNEL 染色來判定。在缺血半影區 δ蛋白激酶 C 被啟動，再灌注後可以被蛋白質印跡發現。

結果：遠隔缺血後處理提高了神經疾病的預後，減少梗死面積，抑制神經細胞凋亡以及再灌注後 δ蛋白激酶 C 的啓動。另外，給予 TAT–δV1-1 後可以抑制再灌注損傷，從而保護大腦。再灌注後，δ蛋白激酶 C 啟動，若事先給予 N-乙醯半胱氨酸不僅完全抑制了遠隔缺血後處理的腦保護作用，而且逆轉了遠隔缺血後處理引起的δ蛋白激酶 C 啟動的作用。

結論：結果顯示大鼠模型局部腦缺血後，通過 δ蛋白激酶 C 的活性氧調節抑制劑，遠隔缺血後處理可以減少再灌注損傷。

(張婷 譯 陳傑 校)

BACKGROUND: Remote ischemic postconditioning (RPostC) is an emerging concept for cerebral infarction protection, and its potential protective mechanisms have not been well established. We attempted to investigate the implications of reactive oxygen species (ROS) and δ protein kinase C (δPKC) in neuroprotection induced by RPostC in a rat model of focal cerebral ischemia, and also to explore a possible relationship between ROS and δPKC.

METHODS: Focal cerebral ischemia was induced by middle cerebral artery occlusion using the intraluminal filament technique in male rats. RPostC was generated by 3 10-minute cycles of femoral artery occlusion/reperfusion on the right limb at the onset of middle cerebral artery reperfusion. RPostC was performed alone or with pretreatment of N-acetylcysteine, a ROS scavenger. In separate group, TAT–δV1-1, a δPKC-selective peptide inhibitor, was administered at the onset of reperfusion. Brain ischemic injury was evaluated by neurologic scores, infarction volumes, and TUNEL staining. Moreover, the activation of δPKC in the ischemic penumbra was investigated by Western blot after reperfusion.

RESULTS: RPostC improved neurologic outcome, reduced infarct size, and inhibited neuronal apoptosis as well as suppressed the activation of δPKC after reperfusion. Moreover, systemic delivery of TAT–δV1-1 conferred neuroprotection against cerebral reperfusion injury at the onset of reperfusion. Pretreatment with N-acetylcysteine not only completely prevented all aspects of RPostC-induced neuroprotection, but also reversed RPostC-induced inhibition of δPKC activation after reperfusion.
CONCLUSION: These findings suggested that RPostC performed in one limb alleviated reperfusion injury after focal cerebral ischemia through ROS-mediated inhibition of endogenous δPKC activation signaling cascade in an in vivo rat model of focal cerebral ischemia.

A Dose-Ranging Study of the Effect of Transversus Abdominis Block on Postoperative Quality of Recovery and Analgesia After Outpatient Laparoscopy

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BACKGROUND: Postoperative pain can delay functional recovery after outpatient surgery. Multimodal analgesia can improve pain and possibly improve quality of recovery. In this study, we evaluated the dose-dependent effects of a preoperative transversus abdominis plane (TAP) block on patient recovery using the Quality of Recovery 40 (QoR-40) questionnaire after ambulatory gynecological laparoscopic surgery. Global QoR-40 scores range from 40 to 200, representing very poor to outstanding quality of recovery, respectively.
METHODS: Healthy women undergoing outpatient gynecological laparoscopy were randomly allocated to receive a preoperative TAP block using saline, ropivacaine 0.25%, or ropivacaine 0.5%. Needle placement for the TAP blocks was performed using ultrasound guidance and 15 mL of the study solution was injected bilaterally by a blinded investigator. QoR-40 score and analgesic use were assessed 24 hours postoperatively. The primary outcome was global QoR-40 score at 24 hours after surgery. Data were analyzed using the Kruskal-Wallis test. Post hoc pairwise comparisons were made using the Dunn test with P values and 95% confidence intervals Bonferroni corrected for 6 comparisons.

RESULTS: Seventy-five subjects were enrolled and 70 subjects completed the study. The median (range) for the QoR-40 score after the TAP block was 157 (127–193), 173 (133–195), and 172 (130–196) for the saline group and 0.25% and 0.5% ropivacaine groups, respectively. The median difference (99.2% confidence interval) in QoR-40 score for 0.5% bupivacaine (16 [1–30], P = 0.03) and 0.25% bupivacaine (17 [2–31], P = 0.01) was more than saline but not significantly different between ropivacaine groups (−1 [−16 to 12], P = 1.0). Increased global QoR-40 scores correlated with decreased area under the pain score time curve during postanesthesia recovery room stay (ρ = −0.56, 99.2% upper confidence limit [UCL] = −0.28), 24-hour opioid consumption (ρ = −0.61, 99.2% UCL = −0.34), pain score (0–10 scale) at 24 hours (ρ = −0.53, 99.2% UCL = −0.25), and time to discharge readiness (ρ = −0.65, 99.2% UCL = −0.42). The aforementioned variables were lower in the TAP block groups receiving ropivacaine compared with saline.

CONCLUSIONS: The TAP block is an effective adjunct in a multimodal analgesic strategy for ambulatory laparoscopic procedures. TAP blocks with ropivacaine 0.25% and 0.5% reduced pain, decreased opioid consumption, and provided earlier discharge readiness that was associated with better quality of recovery.

超前鎮痛：何去何從？

Review Article: Preventive Analgesia: Quo Vadimus?
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The classic definition of preemptive analgesia requires 2 groups of patients to receive identical treatment before or after incision or surgery. The only difference between the 2 groups is the timing of administration of the drug relative to incision. The constraint to include a postincision or postsurgical treatment group is methodologically appealing, because in the presence of a positive result, it provides a window of time within which the observed effect occurred, and thus points to possible mechanisms underlying the effect: the classic view assumes that the intraoperative nociceptive barrage contributes to a greater extent to postoperative pain than does the postoperative nociceptive barrage. However, this view is too restrictive and narrow, in part because we know that sensitization is induced by factors other than the peripheral nociceptive barrage associated with incision and subsequent noxious intraoperative events. A broader approach to the prevention of postoperative pain has evolved that aims to minimize the deleterious immediate and long-term effects of noxious perioperative afferent input. The focus of preventive analgesia is not on the relative timing of analgesic or anesthetic interventions, but on attenuating the impact of the peripheral nociceptive barrage associated with noxious preoperative, intraoperative, and/or postoperative stimuli. These stimuli induce peripheral and central sensitization, which increase postoperative pain intensity and analgesic requirements. Preventing sensitization will reduce pain and analgesic requirements. Preventive analgesia is demonstrated when postoperative pain and/or analgesic use are reduced beyond the duration of action of the target drug, which we have defined as 5.5 half-lives of the target drug. This requirement ensures that the observed effects are not direct analgesic effects. In this article, we briefly review the history of preemptive analgesia and relate it to the broader concept of preventive analgesia. We highlight clinical trial designs and examples from the literature that distinguish preventive analgesia from preemptive analgesia and conclude with suggestions for future research.
背景：關於腹腔內灌注局部麻醉藥用於腹腔鏡術後疼痛緩解治療的研究結果目前仍存在爭議。在本次隨機、雙盲研究中，作者評估了腹腔內霧化噴射局部麻醉藥對腹腔鏡膽囊切除術後疼痛的緩解作用。

方法：將接受擇期腹腔鏡膽囊切除術的患者隨機分為兩組：一組患者在氣腹後即刻在腹腔內管著0.5%羅呱卡因20ml，另一組患者在術前以及術後在腹腔內霧化噴射1%羅呱卡因各3ml。所有的患者均採用標準化的麻醉和手術方案。在術後第6、24和48小時評估患者於靜息及深呼吸時疼痛程度、肩部痛的發生率、嗎啡的消耗量、無需借助外力步行的時間以及術後噁心嘔吐的發生情况。

結果：在60位納入研究的患者中，3位因手術中轉開腹而剔除。兩組患者的疼痛評分或嗎啡消耗量沒有明顯的差異。霧化治療組的患者中無一例發生肩部痛，而灌注治療組的患者中有83%发生了肩部疼痛（絕對風險減少-83，95%置信區間-90至-90，p<0.001）。霧化治療組的患者中，有19位（70%）在術後12小時即可不借助外力步行，而灌注治療組該資料為14位（47%）（絕對風險減少-24，95%置信區間-48至1，p=0.04）。術後發生嘔吐的患者數在灌注治療組和霧化治療組分別為1位（3%）和6位（22%）。

結論：腹腔內羅呱卡因霧化療法可減少腹腔鏡膽囊切除術後肩部疼痛，並可使患者提早下床自主活動，但其術後嘔吐的發生率較高。

背景：Studies evaluating intraperitoneal local anesthetic instillation for pain relief after laparoscopic procedures have reported conflicting results. In this randomized, double-blind study we assessed the effects of intraperitoneal local anesthetic nebulization on pain relief after laparoscopic cholecystectomy.

方法：Patients undergoing elective laparoscopic cholecystectomy were randomly assigned to receive either instillation of ropivacaine 0.5%, 20 mL after induction of the pneumoperitoneum, or nebulization of ropivacaine 1%, 3 mL before and after surgery. Anesthetic and surgical techniques were standardized. Degree of pain at rest and on deep breathing, incidence of shoulder pain, morphine consumption, unassisted walking time, and postoperative nausea and vomiting were evaluated at 6, 24, and 48 hours after surgery.

結果：Of the 60 patients included, 3 exclusions occurred for conversion to open surgery. There were no differences between groups in pain scores or in morphine consumption. No patients in the nebulization group presented significant shoulder pain in comparison with 83% of patients in the instillation group (absolute risk reduction −83, 95% CI −97 to −70, P < 0.001). Nineteen (70%) patients receiving nebulization walked without assistance within 12 hours after surgery in comparison with 14 (47%) patients receiving instillation (absolute risk reduction −24, 95% CI −48 to 1, P = 0.04). One (3%) patient in the instillation group vomited in comparison with 6 (22%) patients in the nebulization group (absolute risk reduction −19%, 95% CI −36 to −2, P = 0.03).
CONCLUSIONS: Intraperitoneal ropivacaine nebulization was associated with reduced shoulder pain and unassisted walking time but with an increased incidence of postoperative vomiting after laparoscopic cholecystectomy.

在麻醉科術前評估門診使用 BATHE 法
Use of the BATHE Method in the Preanesthetic Clinic Visit
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背景：在最初的術前訪視過程中，使用 BATHE 法（詢問背景、干預措施、發現問題、解決方法、移情作用）對病人進行問診可以增加病人的滿意度。此方法是一項可以發現病人身心疾病的簡明的心理學療法。目前並沒有對 BATHE 法作為提高病人術前滿意度的一種方法進行評價。在本次研究中，我們希望瞭解麻醉醫生在術前評估病人時使用 BATHE 法是否能增加手術病人術前的滿意度。

方法：我們在一家學術性醫院的麻醉前門診訪視了 50 名心外科手術病人和 50 名普外科手術病人。所有病人隨機分到 BATHE 組和對照組，並被要求在訪視後完成一項不記名的滿意度調查。這個調查是從近期研究加工後制定的，但並未在其他研究中驗證過。與訪視過程、病人滿意度及病人對 BATHE 各項的報告相關的可能影響 BATHE 結果的相關因素我們同樣都進行了調查。

結果：研究小組訪視的病人中有 92% 自願加入本次研究中。用 BATHE 方法訪視的病人報告較對照組顯著更頻繁地被詢問所有的 BATHE 問題：t(98) = 19.10, P = 0.001 (95% 置信區間 [CI] = 2.59, 3.20)。在麻醉科術前評估門診中，BATHE 組病人較對照組滿意度更高：t(98) = 5.37, P = 0.001 (95% CI = 0.19, 0.41)。使用 BATHE 法並沒有顯著增加醫生評估病人所花的時間：t(98) = 0.110, P = 0.912 (95% CI = −1.519, 1.359)。

結論：本次初步研究顯示在學術性醫療中心的心外科和普外科麻醉前門診使用 BATHE 法進行訪視，結果是有希望的。在我們能夠令人信服地得出結論認定 BATHE 法是增加患者滿意度的有效手段之前，我們還需要更加有效和完善的的調查方法進行研究。

（劉伍 譯 馬皓琳 李士通 校）

BACKGROUND: In the primary care setting, use of the BATHE (Background, Affect, Trouble, Handling, and Empathy) method of interviewing has been shown to increase patient satisfaction. This technique is a brief psychotherapeutic method used to address patients' physical and psychosocial problems. The BATHE technique has not been evaluated in the perioperative setting as a way of improving patient satisfaction. In this study, we sought to determine whether satisfaction could be enhanced by use of the BATHE technique during the preoperative evaluation by anesthesiologists.

METHODS: Fifty cardiac and 50 general surgery patients were interviewed in the preanesthesia clinic (PAC) of an academic hospital. They were randomly enrolled in the
BATHE group or the control group and asked to complete an anonymous satisfaction survey after their visit. This survey was modified from current studies and not validated elsewhere. The relative influence of the BATHE condition was examined as it pertained to interview duration, patient satisfaction, and patient report of the BATHE items being asked.

RESULTS: Ninety-two percent of patients approached by the study group voluntarily enrolled. Patients interviewed using the BATHE method reported being asked about all BATHE questions significantly more often than control patients: \( t(98) = 19.10, P = 0.001 \) (95% confidence interval [CI] = 2.59, 3.20). Patients in the BATHE group were more satisfied with their visit to the PAC than those in the control group: \( t(98) = 5.37, P = 0.001 \) (95% CI = 0.19, 0.41). The use of the BATHE method did not significantly increase the amount of time physicians spent evaluating patients: \( t(98) = 0.110, P = 0.912 \) (95% CI = −1.519, 1.359).

CONCLUSIONS: Use of the BATHE method in an academic medical center's cardiac and general PAC showed promising results in this preliminary study. A validated and fully developed survey instrument is needed before we can convincingly conclude that the BATHE method is an effective way of improving patient satisfaction.

新型水溶性鎮靜催眠藥 JM-1232(-)對小鼠海馬 CA1 區長時程增強效應的影響

The Effect of a New Water-Soluble Sedative-Hypnotic Drug, JM-1232(−), on Long-Term Potentiation in the CA1 Region of the Mouse Hippocampus

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背景：JM-1232(−),{(−)-3-[2-(4-甲基-1-吲哚基)-2-氧代乙基]-2-苯-3,5,6,7-四氫環戊二烯並 a[f]異吲哚-1(2H)-酮}是一種對γ-氨基丁酸A受體上苯二氮卓結合位點具有親和力的新型水溶性鎮靜催眠藥物。JM-1232(−)對大腦突觸傳遞的效應還不甚明瞭。我們在本實驗中研究了JM-1232(−)對小鼠海馬切片 CA1 區樞體細胞突觸傳遞、突觸可塑性(如長時程增強效應[LTP]和成對脈衝易化)以及興奮性/抑制性突觸後電流(EPSCs/IPSCs)的影響。

方法：在小鼠海馬腦片 CA1 區，我們採用全細胞膜片鉗技術記錄了 Schaffer 側枝刺激誘發的區域興奮性突觸後電位和樞體細胞的 EPSCs 和 IPSCs。

結果：JM-1232(−)對區域興奮性突觸後電位無明顯影響。在 0 短陣快速脈衝刺激前， JM-1232(−)處理腦片 20min 能夠劑量依賴性地損傷 LTP。JM-1232(−)也損傷成對脈衝易化。苯二氮卓激動劑氟馬西尼阻斷了 JM-1232(−)對 LTP 和成對脈衝易化的抑制作用。JM-1232(−)對 Schaffer 側枝刺激誘發的 EPSCs 無影響，反而能增加 CA1 區樞體細胞中誘發的 IPSCs 的振幅，並延長其衰退。氟馬西尼阻斷 JM-1232(−)對誘發的 IPSCs 振幅和衰退的影響。JM-1232(−)抑制 0 短陣快速脈衝刺激過程中 CA1 區樞體細胞動作電位放電，且此作用可被氟馬西尼逆轉。
**BACKGROUND:**
JM-1232(−){(−)-3-[2-(4-methyl-1-piperazinyl)-2-oxoethyl]-2-phenyl-3,5,6,7-tetrahydrocyclopenta[f]isoindol-1(2H)-one} is a new water-soluble sedative-hypnotic drug with affinity for the benzodiazepine binding site on γ-aminobutyric acid A receptors. The effects of JM-1232(−) on synaptic transmission in the brain are not known. In the present study, we investigated the effects of JM-1232(−) on synaptic transmission, synaptic plasticity (i.e., long-term potentiation [LTP] and paired-pulse facilitation), and excitatory/inhibitory postsynaptic currents (EPSCs/IPSCs) of pyramidal neurons in the CA1 region of mouse hippocampal slices.

**METHODS:** We recorded Schaffer collateral–evoked field excitatory postsynaptic potentials and EPSCs and IPSCs of pyramidal neurons using whole-cell patch-clamp techniques in the CA1 region of mouse hippocampal slices.

**RESULTS:** JM-1232(−) had no significant effect on the field excitatory postsynaptic potentials. Application of JM-1232(−) for 20 minutes before theta-burst stimulation dose dependently impaired LTP. JM-1232(−) impaired paired-pulse facilitation. The benzodiazepine antagonist flumazenil abolished the inhibitory effect of JM-1232(−) on LTP and paired-pulse facilitation. JM-1232(−) had no effect on Schaffer collateral stimulation–evoked EPSCs, whereas it potentiated the amplitude and prolonged the decay of evoked IPSCs in CA1 pyramidal neurons. Flumazenil blocked the effect of JM-1232(−) on the amplitude and decay of evoked IPSCs. JM-1232(−) suppressed the action potential discharge in the CA1 pyramidal neurons during theta-burst stimulation, which was reversed by flumazenil.

**CONCLUSION:** JM-1232(−) enhances synaptic inhibition and impairs LTP and paired-pulse facilitation in area CA1 of the mouse hippocampus. These effects were mediated by benzodiazepine binding sites on γ-aminobutyric acid A receptors.
Waste anesthetic gas scavenging technology has not changed appreciably in the past 30 years. Open reservoir systems entrain high volumes of room air and dilute waste gases before emission into the atmosphere. This process requires a large vacuum pump, which is both costly to install and, although efficient, operates continuously and at near-full capacity. In an era of increasing energy costs and environmental awareness, carbon footprint reduction is a priority and a more efficient system of safely scavenging waste anesthetic gases is desirable. We tested a low-flow scavenger interface to evaluate the potential for cost and energy savings. The use of this interface in a suite of 4 operating rooms reduced scavenging flow from a constant 37 L/min to a value equal to the fresh gas flow (usually 2 L/min) for each anesthesia machine. Using the ventilator increased this flow by approximately 6 L/min because of the exhaust of ventilator drive gas into the scavenging circuit. Daytime workload of the central vacuum pump decreased from 92% to 12% (expressed as duty cycle). The new system produces energy savings and may increase vacuum pump lifespan.

Pentax-AWS 視頻喉鏡與 Macintosh 喉鏡用於病態肥胖患者的隨機對照研究
A Randomized Comparison Between the Pentax AWS Video Laryngoscope and the Macintosh Laryngoscope in Morbidly Obese Patients
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背景：Pentax-AWS 是一種新型視頻喉鏡，通過提供喉入口的間接視覺化影像以便於氣管插管。本試驗旨在比較 Pentax-AWS 喉鏡與經典的 Macintosh 喉鏡的插管成功率以及插管時間。我們還特別檢驗了以下假說：在肥胖患者中使用 Pentax-AWS 喉鏡插管比標準的 Macintosh #4 喉鏡片更快、更方便。

方法：105 名需經口氣管插管行擇期手術的肥胖患者（體重指數 30~50 kg/m²）隨機分配到 Macintosh（用#4 喉鏡片）插管或 Pentax-AWS 喉鏡插管組。由兩名經驗豐富的麻醉醫師作爲喉鏡檢查專家。記錄插管成功率、插管時間、插管難度和併發症發生率。

結果：使用 Macintosh 喉鏡和 #4 喉鏡片插管明顯快於使用 Pentax-AWS 裝置：半數使用 Macintosh #4 喉鏡片的患者成功在 26 秒內完成氣管插管，而使用 AWS 喉鏡達到同樣比例需要 38 秒。使用 Pentax-AWS 喉鏡首次嘗試的成功率為 86%，二次嘗試的成功率增加到 90%。相比之下，所有使用 Macintosh #4 喉鏡片的患者均成功完成氣管插管，首次嘗試的成功率為 92%，二次嘗試的成功率增加到 100%。

結論：使用 Pentax-AWS 喉鏡行氣管插管所需時間長於 Macintosh 喉鏡和 #4 喉鏡片。在病態肥胖患者中不應該常規用 AWS 喉鏡替代傳統的 Macintosh #4 喉鏡片。
BACKGROUND: The Pentax AWS is a novel video laryngoscope designed to facilitate tracheal intubation by providing indirect visualization of the laryngeal inlet. We sought to compare the intubation success rate and time to intubation for the Pentax AWS and the classic Macintosh laryngoscope. Specifically, we tested the hypothesis that intubation with the Pentax AWS would be easier and faster than with a standard Macintosh #4 blade in obese patients.

METHODS: One hundred five obese patients (body mass index between 30 and 50 kg/m²) requiring orotracheal intubation for elective surgery were allocated randomly to tracheal intubation with either the Macintosh (using a #4 blade) or the Pentax AWS laryngoscope. Two experienced anesthesiologists served as laryngoscopists. Intubation success rate, time to intubation, ease of intubation, and occurrence of complications were recorded.

RESULTS: Intubations using the Macintosh laryngoscope and #4 blade were significantly faster than with the Pentax AWS device: half of the patients' tracheas were intubated successfully within 26 seconds with the Macintosh #4 blade, whereas the same fraction required 38 seconds with the AWS. The first-attempt success rate with the Pentax AWS was 86%; the rate increased to 90% with a second attempt. In contrast, all patients' tracheas were intubated successfully with the Macintosh #4 blade, with a first-attempt success rate of 92%, which increased to 100% by the second attempt.

CONCLUSION: The time required for tracheal intubation using the Pentax AWS was longer than for the Macintosh laryngoscope and #4 blade. The AWS should not routinely be substituted for a conventional Macintosh #4 blade in morbidly obese patients.

Future Directions in Malignant Hyperthermia Research and Patient Care
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惡性高熱（MH）是一個複雜的肌肉代謝的遺傳性藥理學紊亂疾病。為了更進一步調查MH以及其他相關肌肉紊亂疾病的複雜性，美國惡性高熱協會（MHAUS）最近發起了一項科學會議，在會上不同學科組的專家聚集一堂，分享新資訊及新觀念。在這篇專文中，我們著重於會議提出的在MH研究及患者護理方面的關鍵概念及理論，同時還有令人欣喜的新的趨勢和挑戰。
（瞿亦楓譯 馬皓琳 李士通 校）
Malignant hyperthermia (MH) is a complex pharmacogenetic disorder of muscle metabolism. To more closely examine the complexities of MH and other related muscle disorders, the Malignant Hyperthermia Association of the United States (MHAUS) recently sponsored a scientific conference at which an interdisciplinary group of experts gathered to share new information and ideas. In this Special Article, we highlight key concepts and theories presented at the conference along with exciting new trends and challenges in MH research and patient care.

### 同胞出生群組中孩童時期早期麻醉暴露及發展和行為失常的風險

**Early Childhood Exposure to Anesthesia and Risk of Developmental and Behavioral Disorders in a Sibling Birth Cohort**

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**背景:** 在體內和體外實驗中，麻醉藥的研究已經證實對發育中的大腦有嚴重的神經毒性反應。然而，這些發現對於進行麻醉的兒童的臨床相關性尚不清晰。應用從同胞出生群組得到的資料，我們評估了低於 3 歲手術病人的麻醉暴露與發展和行為失常風險之間的關係。

**方法:** 我們組建了一個回顧性研究的佇列，包括出生於 1999 年至 2005 年之間並且登記入紐約州醫療援助計畫的 10450 名同胞兒童。暴露組為 304 名無發育和行為失常病史並在小於 3 歲時接受了外科手術的兒童。非暴露組為 10146 名在 3 歲以前沒有接受任何外科手術的兒童。暴露組患兒在手術之日進入資料分析。非暴露組在 10 月齡（暴露組進行手術的平均年齡）進入資料分析。隨訪暴露組和非暴露組兒童，直到診斷為發育或行為異常、失隨訪或 2005 年底。用比例危險度模型以及配對檢驗分析評價麻醉暴露與隨後的發育和行為失常之間的關係。

**結果:** 在暴露組群中，發育和行為失常的發生率為每 1000 人 － 年中 128.2 例診斷。而在非暴露暴露組中，為每 1000 人 － 年中 56.3 例診斷。通過調整性別和分娩相關的醫學佇列以及同胞情況的聚集，3 歲以前暴露於麻醉相關的發育和行為失常的估計危害比為 1.6 (95% 可信區隔 [CI] 爲 1.4, 1.8)。手術次數增加，危險度增加：1 次手術的危險度為 1.1（95% CI: 0.8, 1.4）,而 2 次手術的危險度為 2.9（94% CI: 2.5, 3.1），大於等於 3 次手術的危險度為 4.0 （95% CI: 3.5, 4.5）。138 對同胞之間進行配對分析，相對危險度為 0.9（95% CI: 0.6, 1.4）。

**結論:** 進入州醫療援助計畫且小於 3 歲時曾經進行手術的患兒隨後診斷為發育和行為失常的風險比未接受過外科手術的同胞兒童的相近組群風險高 60%。更為嚴謹的配對分析提示過分風險的限度歸因於麻醉或由待確定的不可測的因素介導。

(黃麗娜 譯 馬皓琳 李士通 校)

**BACKGROUND:** In vitro and in vivo studies of anesthetics have demonstrated serious neurotoxic effects on the developing brain. However, the clinical relevance of these findings to children undergoing anesthesia remains unclear. Using data from a sibling birth cohort, we assessed the association between exposure to anesthesia in the setting of
surgery in patients younger than 3 years and the risk of developmental and behavioral disorders.

METHODS: We constructed a retrospective cohort of 10,450 siblings who were born between 1999 and 2005 and who were enrolled in the New York State Medicaid program. The exposed group was 304 children without a history of developmental or behavioral disorders who underwent surgery when they were younger than 3 years. The unexposed group was 10,146 children who did not receive any surgical procedures when they were younger than 3 years. Exposed children were entered into analysis at the date of surgery. Unexposed children were entered into analysis at age 10 months (the mean age at which exposed children underwent surgery). Both exposed and unexposed children were followed until diagnosis with a developmental or behavioral disorder, loss to follow-up, or the end of 2005. The association of exposure to anesthesia with subsequent developmental and behavioral disorders was assessed with both proportional hazards modeling, and pair-matched analysis.

RESULTS: The incidence of developmental and behavioral disorders was 128.2 diagnoses per 1000 person-years for the exposed cohort and 56.3 diagnoses per 1000 person-years for the unexposed cohort. With adjustment for sex and history of birth-related medical complications, and clustering by sibling status, the estimated hazard ratio of developmental or behavioral disorders associated with any exposure to anesthesia when they were younger than 3 years was 1.6 (95% confidence interval [CI]: 1.4, 1.8). The risk increased from 1.1 (95% CI: 0.8, 1.4) for 1 operation to 2.9 (94% CI: 2.5, 3.1) for 2 operations and 4.0 (95% CI: 3.5, 4.5) for ≥3 operations. The relative risk in a matched analysis of 138 sibling pairs was 0.9 (95% CI: 0.6, 1.4).

CONCLUSION: The risk of being subsequently diagnosed with developmental and behavioral disorders in children who were enrolled in a state Medicaid program and who had surgery when they were younger than 3 years was 60% greater than that of a similar group of siblings who did not undergo surgery. More tightly matched pairwise analyses indicate that the extent to which the excess risk is causally attributable to anesthesia or mediated by unmeasured factors remains to be determined.

麻醉藥品對發育中大腦的神經毒性
Neurotoxicity of Anesthetic Drugs in the Developing Brain
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麻醉會導致嬰兒期動物（包括靈長類動物）的腦部神經元死亡，並可導致永久性和進行性神經認知水準下降。麻醉界和監管當局同樣關心人類是否也是這樣。在本綜述中，我總結了我們目前瞭解的小兒麻醉對於長期認知功能的風險。如果在人類中發現麻醉導致認知能力的下降，我們需要知道如何預防和治療。預防需要瞭解麻醉引起的認知能力下降的機制。本綜述概述了一些已經提出的麻醉引起認知能力下降的機制，並討論了可能的治療選擇。如果在人類中麻醉導致認知能力的下降，我們需要知道什麼類型麻醉和多長的麻醉是安全的，並且如果有的話，什麼是不安全的。本綜述討論了關於動物麻醉的神經毒性的比較性研究的早期結果。在我們知道
Anesthesia kills neurons in the brain of infantile animals, including primates, and causes permanent and progressive neurocognitive decline. The anesthesia community and regulatory authorities alike are concerned that is also true in humans. In this review, I summarize what we currently know about the risks of pediatric anesthesia to long-term cognitive function. If anesthesia is discovered to cause cognitive decline in humans, we need to know how to prevent and treat it. Prevention requires knowledge of the mechanisms of anesthesia-induced cognitive decline. This review gives an overview of some of the mechanisms that have been proposed for anesthesia-induced cognitive decline and discusses possible treatment options. If anesthesia induces cognitive decline in humans, we need to know what type and duration of anesthetic is safe, and which, if any, is not safe. This review discusses early results of comparative animal studies of anesthetic neurotoxicity. Until we know if and how pediatric anesthesia affects cognition in humans, a change in anesthetic practice would be premature, not guided by evidence of better alternatives, and therefore potentially dangerous. The SmartTots initiative jointly supported by the International Anesthesia Research Society and the Food and Drug Administration aims to fund research designed to shed light on these issues that are of high priority to the anesthesia community and the public alike and therefore deserves the full support of these interest groups.

A Prospective Survey of Patient-Controlled Epidural Analgesia with Bupivacaine and Clonidine After Total Hip Replacement: A Pre- and Postchange Comparison with Bupivacaine and Hydromorphone in 1,000 Patients

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背景和目的：用布比卡因和氯吗啡酮的病人自控硬膜外镇痛（PCEA）可以提供矫形外科手术后高质量的镇痛效果，但是伴随随着阿片类药物相关副作用的高发生率（15%–30%）。硬膜外可乐定有不同的副作用，但是没有记录其使用的大样本调查。我们进行了此项前瞻性调查，以评估全髋置换术后将PCEA从用布比卡因/氯吗啡酮改用布比卡因/可乐定前后的镇痛和副作用情况。

方法：五百名接受0.06%布比卡因和氯吗啡酮（10 mcg/mL）PCEA的连续患者作为之前描述的改变前的对照组。该标准镇痛方案随访性地改为0.06%布比卡因和可乐定（1 mcg/mL），PCEA设置和围术期医嘱均不变，五百名连续病人作为改变后组。前瞻性输入所有资料，然后从电子医疗记录中提取。采集的资料包括每日
口頭疼痛評分（VPS）、瘙癢、噁心、低血壓、靜脈注射液體的需要、鎮靜和呼吸抑制。測定對改變的員工滿意程度的線上調查表發給所有參與的外科醫生、麻醉醫師、理療醫生以及醫師助理。

結果：2組病人的特徵類似。大部分病人採用椎管內麻醉（99%）。術後當天，可樂定組病人靜息 VPS 評分更低（2.3 比 3.7，P < 0.001, 差值的 95% 信心區間 [CI] 爲 1.4 [1.1, 1.7]）。可樂定組噁心的發生率為 10%-11%，氨嗎啡酮組為 13%-15%。可樂定組瘙癢的發生率更低（1% 比 10%，P < 0.01, 差值的 95% 信心區間為 9% [6, 12]）。然而，可樂定組低血壓發生率（20% 比 11%，P < 0.001，差值的 95% CI 为 9% [5, 14]）以及靜脈需要注射液體的發生率較高（36 比 19%，P < 0.001, 差值的 95% 信心區間為 16 [11, 12]）。65%的員工完成了線上調查問卷，70% 認為可樂定比氨嗎啡酮差。

結論：從硬膜外氨嗎啡酮系統性地換成硬膜外可樂定產生了混合的結果，並且沒有明顯的優越性。靜息時 VPS 評分僅僅在術後當天降低，瘙癢減少了，但是低血壓增多了。根據醫務人員的偏愛，我們中止了系統性的更換藥物，並且回復到我們原本用於全髖置換術後 PCEA 的布比卡因和氨嗎啡酮的標準溶液。
（安光惠 譯 馬皓琳 李士通 校）

BACKGROUND AND OBJECTIVES: Patient-controlled epidural analgesia (PCEA) with bupivacaine and hydromorphone provides high quality analgesia after orthopedic surgery but is associated with a frequent incidence of opioid-related side effects (15%–30%). Epidural clonidine has a different side effect profile, but there are no large surveys documenting its use. We performed this prospective survey to evaluate analgesia and the side effect profile in total hip replacement patients before and after a systematic change from PCEA with bupivacaine/hydromorphone to bupivacaine/clonidine.

METHODS: Five hundred consecutive patients received PCEA with 0.06% bupivacaine and hydromorphone (10 mcg/mL) as a previously described prechange control group. The standard analgesic regimen was then systematically changed to 0.06% bupivacaine and clonidine (1 mcg/mL) without changing the PCEA settings or other aspects of perioperative care, and 500 consecutive patients were included as a postchange group. All data were prospectively entered and then abstracted from the electronic medical record. Data collection included daily verbal pain scores (VPS), pruritus, nausea, hypotension, need for IV fluid boluses, sedation, and respiratory depression. An online survey to measure staff satisfaction with the changeover was sent to all participating surgeons, anesthesiologists, physical therapists, and physician’s assistants.

RESULTS: Patient characteristics were similar between groups. Most patients received central neuraxial anesthesia (99%). The clonidine group had lower VPS at rest (2.3 vs 3.7, P < 0.001 with 95% confidence interval [CI] of difference of 1.4 [1.1, 1.7]) on POD0. The incidence of nausea was 10%–11% for clonidine and 13%–15% for hydromorphone. The incidence of pruritus was less with clonidine (1 vs 10%, P < 0.01 with 95% CI of difference of 9% [6, 12]). However, the incidence of hypotension (20 vs 11%, P < 0.001 with 95% CI of differences 9% [5, 14]) and IV fluid boluses was more frequent with clonidine (36 vs 19%, P < 0.001 with 95% CI of differences of 16 [11, 12]). Sixty-five percent of staff completed the online survey, and 70% considered clonidine worse than hydromorphone.
CONCLUSION: The systematic changeover from epidural hydromorphone to clonidine produced mixed results without obvious superiority. The VPS at rest was reduced only on postoperative day 0; pruritus was reduced, but hypotension was increased. On the basis of medical staff preference, we discontinued the systematic change and returned to our previous standard solution of bupivacaine and hydromorphone for PCEA after total hip replacement.

Does Sensory Stimulation Threshold Affect Lumbar Facet Radiofrequency Denervation Outcomes? A Prospective Clinical Correlational Study

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BACKGROUND: Radiofrequency facet denervation is one of the most frequently performed procedures for chronic low back pain. Although sensory stimulation is
generally used as a surrogate measure to denote sufficient proximity of the electrode to the nerve, no study has examined whether stimulation threshold influences outcome. **METHODS:** We prospectively recorded data in 61 consecutive patients undergoing lumbar facet radiofrequency denervation who experienced significant pain relief after medial branch blocks. For each nerve lesioned, multiple attempts were made to maximize sensory stimulation threshold (SST). Mean SST was calculated on the basis of the lowest stimulation perceived at 0.1-V increments for each medial branch. A positive outcome was defined as a ≥50% reduction in back pain coupled with a positive satisfaction score lasting ≥3 months. The relationship between mean SST and denervation outcomes was evaluated via a receiver's operating characteristic (ROC) curve, and stratifying outcomes on the basis of various cutoff values. **RESULTS:** No correlation was noted between mean SST and pain relief at rest (Pearson's r = −0.01, 95% confidence interval [CI]: −0.24 to 0.23, P = 0.97), with activity (r = −0.17, 95% CI: −0.40 to 0.07, P = 0.20), or a successful outcome. No optimal SST could be identified. **CONCLUSIONS:** There is no significant relationship between mean SST during lumbar facet radiofrequency denervation and treatment outcome, which may be due to differences in general sensory perception. Because stimulation threshold was optimized for each patient, these data cannot be interpreted to suggest that sensory testing should not be performed, or that high sensory stimulation thresholds obtained on the first attempt should be deemed acceptable.

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**大鼠神經病模型中抗抑鬱藥和脊髓刺激的疼痛緩解作用之間的相互作用**

The Interaction Between Antidepressant Drugs and the Pain-Relieving Effect of Spinal Cord Stimulation in a Rat Model of Neuropathy

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**背景**：脊髓刺激（SCS）已被證明為治療神經痛的有效方法。基於我們先前關於 SCS 作用模式的研究，鞘內注射亞效應劑量的特定藥物可增強 SCS 病人的疼痛緩解作用。目前認爲抗抑鬱藥對於神經痛有益的作用。我們進行本研究來檢驗抗抑鬱藥阿米替林（三環類抗抑鬱藥）、氟西汀（選擇性 5-羥色胺再攝取抑制劑）及米那普侖（選擇性 5-羥色胺/去甲腎上腺素再攝取抑制劑）與 SCS 潛在的協同或拮抗作用。

**方法**：我們評估了在清醒、可自由活動的大鼠在外周神經損傷後，SCS 對於機械超敏反應的作用。通過鞘內給予抗抑鬱藥。

**結果**：當 SCS 與亞效應劑量的阿米替林或米那普侖聯合應用時，SCS 對於機械超敏反應的抑制作用較單獨應用 SCS 有所增強。而氟西汀則未發現此作用。沒有發現任何藥物對 SCS 的作用有拮抗作用。

**結論**：這些發現表明 SCS 與三環類抗抑鬱藥或選擇性 5-羥色胺/去甲腎上腺素再攝取抑制劑的聯合應用在臨床上可能可應用於已證實 SCS 本身無效的病例。

（毛祖旻 譯　馬皓琳 李士通 校）
BACKGROUND: Spinal cord stimulation (SCS) has proven to be a valuable treatment in neuropathic pain. On the basis of our previous studies on the mode of action of SCS, intrathecal administration of subeffective doses of certain drugs has been shown to enhance the pain-relieving effect in patients with SCS. Antidepressants have a well-established beneficial effect in neuropathic pain. We performed the present study to examine potential synergistic or antagonistic effects on SCS of antidepressants: amitriptyline (tricyclic antidepressant), fluoxetine (selective serotonin reuptake inhibitor), and milnacipran (selective serotonin/noradrenaline reuptake inhibitor).

METHODS: In rats, the effect of SCS on mechanical hypersensitivity after peripheral nerve injury was assessed in awake, freely moving animals. Antidepressants were administered intrathecally.

RESULTS: When combining SCS with subeffective doses of amitriptyline or milnacipran, the suppressive effect of SCS on the mechanical hypersensitivity was enhanced in comparison with that obtained with SCS alone. There was no detectable effect of fluoxetine. No signs of an antagonistic effect of the drugs on the SCS effect were observed.

CONCLUSIONS: These findings suggest a possible clinical application with a combination of SCS and a tricyclic antidepressant or selective serotonin/noradrenaline reuptake inhibitor drug in cases in which SCS per se has proven inefficient.

超聲引導下以刺激型導管行股神經阻滯過程中用於監測導管-神經接觸的運動反應的敏感度

The Sensitivity of Motor Responses for Detecting Catheter-Nerve Contact During Ultrasound-Guided Femoral Nerve Blocks with Stimulating Catheters
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背景：以超聲檢查作爲參考，我們測定了確定導管-神經發生接觸時刺激型導管誘發的運動反應的敏感度。

方法：用刺激型導管在超聲掃描下與 25 例患者的股神經產生接觸。輸出電流從最小值開始增加，直到股四頭肌發生收縮。以 0.5 mA 作爲閾電流計算確定導管-神經接觸時運動反應的靈敏度。

結果：用來激發運動反應的導管刺激所需要電流範圍爲 0.18 到 2.0 mA。25 例患者中有 16 例對 0.5 mA 電流刺激產生了肌肉收縮反應。運動反應對神經刺激的敏感度爲 64%(95%可信區間：0.43, 0.82)。

結論：當刺激電流≤0.5 mA 而肌肉無反應時，並不一定代表導管-神經未發生接觸。

（瞿亦楓 譯 馬皓琳 李士通 校）

BACKGROUND: We determined the sensitivity of motor responses evoked by stimulating catheters in determining catheter-nerve contact using ultrasonography as reference.
METHODS: Femoral nerves were contacted using stimulating catheters under ultrasonography scanning in 25 patients. The output current was increased from its minimum until quadriceps muscle contraction occurred. The sensitivity of the motor response in determining catheter-nerve contact was calculated using 0.5 mA as current threshold.

RESULTS: The current required for catheter stimulation to evoke a motor response ranged between 0.18 and 2.0 mA. Muscle contraction in response to 0.5 mA occurred in 16 of 25 subjects. The sensitivity of motor response for nerve stimulation was 64% (95% confidence interval: 0.43, 0.82).

CONCLUSIONS: The absence of muscle responses at a stimulating current ≤0.5 mA does not necessarily indicate the absence of catheter-nerve contact.