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**心肺轉流術卒中實驗模型中抑肽酶可以改善腦功能但是並不能縮小腦梗塞的面積**

Aprotinin Improves Functional Outcome but Not Cerebral Infarct Size in an Experimental Model of Stroke During Cardiopulmonary Bypass

H. Mayumi Homi, MD, PhD*, Huaxin Sheng, MD†, Gowthami M. Arepally, MD‡, G. Burkhard Mackensen, MD, PhD† and Hilary P. Grocott, MD, FRCPC†
背景：抑肽酶是一種非特異性的絲氨酸蛋白酶抑制劑，一直被用於減少心肺轉流術後的出血和輕減心肺轉流術後的全身性炎症反應。以往各種研究結果既有表明抑肽酶可以改善心臟術後腦功能的，也有結果是恰恰相反的。我們設計了本研究來測定應用抗炎劑量的抑肽酶是否能夠改善心肺轉流術中局部腦缺血模型大鼠的神經系統組織結構和功能。

方法：在外科手術準備後，小鼠被隨機分成兩組：抑肽酶組（60,000 kIU/kg 靜脈注射）和對照組（0.9% NaCl 靜脈注射）。溫度正常的心肺轉流術持續 60 分鐘，在此期間右大腦中動脈閉塞性手術與心肺轉流術時間部分重疊，持續 60 分鐘。我們測定了操作前、心肺轉流術結束時、心肺轉流術結束後 2 和 24 小時時的細胞因數值（腫瘤壞死因數-α、白介素[IL]-1β、IL-6 和 IL-10）。在手術後第三天我們對小鼠進行了神經病學功能測試和腦梗死面積組織學測定。

結果：抑肽酶組和對照組相比，IL-1β 值（$P = 0.035$）和 IL-6 值（$P = 0.047$）都有所下降，表現在全身性炎症反應有所減輕。抑肽酶組神經病學功能測試結果也更好，抑肽酶組 27 [8] 比對照組 32 [6]（中位數[四分位距]，$P = 0.042$）。但是兩組的腦梗塞面積沒有區別（抑肽酶組 306 [27] mm³ 比對照組 297 [52] mm³，$P = 0.599$）。

結論：在這個心肺轉流術期間發生的腦缺血實驗模型中，抑肽酶減輕了心肺轉流術引起的全身性炎症反應。雖然兩組的腦梗塞面積沒有區別，但是抑肽酶對短期的神經病學功能測試結果有些需改善。

（姜旭暉譯，馬皓琳，李士通校）

BACKGROUND: Aprotinin, a nonspecific serine protease inhibitor, has been used to decrease bleeding and reduce the systemic inflammatory response after cardiopulmonary bypass (CPB). Studies have variably linked aprotinin administration with both improved and adverse cerebral consequences after cardiac surgery. We designed this study to determine whether an antiinflammatory dose of aprotinin could improve the histologic and functional neurologic outcome in a rat model of focal cerebral ischemia during CPB.

METHODS: After surgical preparation, the animals were randomized into 2 groups: an aprotinin group (60,000 kIU/kg IV) and a control group (0.9% NaCl IV). Normothermic CPB was performed for 60 minutes during which time a partial overlapping 60 minutes of right middle cerebral artery occlusion was induced. Cytokines (tumor necrosis factor-α, interleukin [IL]-1β, IL-6, and IL-10) were measured at baseline, the end of CPB, then 2 and 24 hours after CPB. On postoperative day 3, the animals underwent functional neurologic testing and histologic assessment of cerebral infarct volume.

RESULTS: There was a reduction in systemic inflammation in the aprotinin group compared with the control group, demonstrated by lower levels of IL-1β ($P = 0.035$) and IL-6 ($P = 0.047$). The aprotinin group also had a better functional neurologic performance (median [interquartile range]: aprotinin 27 [8] vs control 32 [6]; $P = 0.042$). However, there was no difference in cerebral infarct volume (aprotinin 306 [27] mm³ vs control 297 [52] mm³; $P = 0.599$).
CONCLUSIONS: In this experimental model of stroke occurring during CPB, aprotinin decreased the systemic inflammatory response to CPB. Although there was no difference in the cerebral infarct volume, there was a small improvement in the short-term functional neurologic outcome in the aprotinin group.

Day-Surgery Patients Anesthetized with Propofol Have Less Postoperative Pain than Those Anesthetized with Sevoflurane
Terry Tan, MBBCh, FCARCSI, Rajesh Bhinder, MBBCh, Michael Carey, MD, FFARCSI and Liam Briggs, MD, FFARCSI
From the Department of Anaesthesia and Perioperative Medicine, Coombe Women and Infants University Hospital, Dublin, Ireland.

BACKGROUND: There have been recent studies suggesting that patients anesthetized with propofol have less postoperative pain compared with patients anesthetized with volatile anesthetics.
METHODS: In this randomized, double-blind study, 80 patients undergoing day-case diagnostic laparoscopic gynecological surgery were either anesthetized with IV propofol or sevoflurane. The primary outcome measured was pain on a visual analog scale.
RESULTS: Patients anesthetized with propofol had less pain compared with patients anesthetized with sevoflurane (P = 0.01). There was no difference in any of the other measured clinical outcomes.
CONCLUSIONS: The patients anesthetized with propofol appeared to have less pain than patients anesthetized with sevoflurane.

A Survey of Current Management of Neuromuscular Block in the United States and Europe
Mohamed Naguib, MD*, Aaron F. Kopman, MD†, Cynthia A. Lien, MD‡, Jennifer M. Hunter, MB, PhD, FRCA‡, Adriana Lopez, MS§ and Sorin J. Brull, MD∥
From the *Department of Anesthesiology and Pain Medicine, The University of Texas M. D. Anderson Cancer Center, Houston, Texas; †Department of Anesthesiology, The Weill Cornell Medical College, New York, New York; ‡Department of Anaesthesia, University
背景：術後殘餘神經肌肉阻滯經常發生。歐洲最近的臨床調查表明神經肌肉阻滯藥的使用常常沒有適當的監測。美國還沒有這方面的對照研究。通過本調查研究，我們比較了當前美國和歐洲麻醉醫生對神經肌肉阻滯藥的使用和態度。

方法：我們對美國和歐洲的麻醉醫生進行了一個以互聯網為基礎的調查。麻醉病人安全基金會和歐洲麻醉協會給它們的所有活躍會員發了電子郵件，邀請他們在一一個專用的網際協議位址敏感的網站上不具名地回答一系列問題。這個調查在網上進行了 60 天。用 $\chi^2$ 核對總和 Fisher's 精確檢驗來比較 2 組的臨床調查專案。

結果：接受調查的總人數為 2636 人。美國 (64.1%) 和歐洲 (52.2%) 的大多數應答者評估臨床上顯著的術後殘餘神經肌肉無力的發生率 <1% ($P < 0.0001$)。常規藥理學逆轉歐洲比美國少（分別為 18% 和 34.2%，$P < 0.0001$），而臨床醫生可用的定量監護儀美國 (22.7%) 比歐洲 (70.2%) 少 ($P < 0.0001$)。然而，19.3% 的歐洲醫生和 9.4% 的美國醫生從不使用神經肌肉監護儀。大多數應答者表示不管是常規的神經肌肉刺激器還是定量四個成串監護儀都應列入最低監測標準。

結論：我們的結果顯示麻醉醫生對監測神經肌肉功能的最佳方法尚沒有統一的結論。我們應當通過發展正式訓練計畫和/或出版關於最佳實踐的官方指南來努力改善蘇醒以減少術後神經肌肉無力的發生率和病人的發病率。

（周潔 譯 馬皓琳 李士通 校）

BACKGROUND: Postoperative residual neuromuscular block is a frequent occurrence. Recent surveys of clinical practice in Europe suggest that neuromuscular blocking drugs are often administered without appropriate monitoring. No comparable survey has been undertaken in the United States (US). From this survey, we compared current clinical neuromuscular practice and attitudes between anesthesia practitioners in the US and Europe.

METHODS: We conducted an Internet-based survey among anesthesia practitioners in the US and Europe. The Anesthesia Patient Safety Foundation and the European Society of Anaesthesiology e-mailed all of their active members, inviting them to anonymously answer a series of questions on a dedicated Internet Protocol address–sensitive website. The survey was available online for 60 days. The $\chi^2$ test and Fisher's exact test were used to compare clinical survey items between the 2 cohorts.

RESULTS: A total of 2636 completed surveys were received. Most respondents from the US (64.1%) and Europe (52.2%) estimated the incidence of clinically significant postoperative residual neuromuscular weakness to be <1% ($P < 0.0001$). Routine pharmacologic reversal was less common in Europe than in the US (18% vs 34.2%, respectively; $P < 0.0001$), and quantitative monitors were available to fewer clinicians in the US (22.7%) than in Europe (70.2%) ($P < 0.0001$). However, 19.3% of Europeans and 9.4% of Americans never use neuromuscular monitors. Most respondents reported that neither conventional nerve stimulators nor quantitative train-of-four monitors should be part of minimum monitoring standards.
CONCLUSIONS: Our results suggest a lack of agreement among anesthesia providers about the best way to monitor neuromuscular function. Efforts to improve awareness by developing formal training programs and/or publishing official guidelines on best practices to reduce the incidence of postoperative neuromuscular weakness and patient morbidity are warranted.

Accuracy of Methemoglobin Detection by Pulse CO-Oximetry During Hypoxia
John R. Feiner, MD*, Philip E. Bickler, MD, PhD* and Paul D. Mannheimer, PhD†
From the *Department of Anesthesia and Perioperative Care, University of California at San Francisco, San Francisco, California; and †Respiratory and Monitoring Solutions, Covidien, Boulder, Colorado.

背景：虽然高铁血红蛋白会造成血氧计值（SpO2）评估动脉功能氧饱和度（SaO2）的偏移，但是血中的高铁血红蛋白很难通过常规的脉搏血氧测定法来检测。一种新引进的脉搏心输出量血氧计(Masimo Rainbow SET® Radical-7 Pulse CO-Oximeter, Masimo Corp., Irvine, CA)附加了非创伤性的监测仪，监测血中微量的碳氧血红蛋白和高铁血红蛋白的成分。我们的研究目的是监测低氧是否会影响该设备监测高铁血红蛋白检测的准确性，以及是否高铁血红蛋白的存在会有损 Radical-7和常规的脉搏血氧计(Nonin 9700, Nonin Medical Inc., Plymouth, MN)发现 SaO2 下降的能力。

方法：两个研究组分别包括8名和6名健康的成年人，每人都安置多个感测器和桡动脉导管供血液抽样。第一组，静脉给予将近300mg的亚硝酸钠来增加高铁血红蛋白的水平，目标为7%-8%，通过吸入氧浓度的不同造成 SaO2(70%-100%)水准不同的低氧。第二组，目标为室内空气中铁血红蛋白15%以及 SaO280%水准。脉搏心输出量血氧计读数与多波长辐射血氧计测定的动脉血数值进行比较。通过观察在不同缺氧水准上有意义的读取误差发生率来分析脉搏心输出量血氧计对高铁血红蛋白的读取表现。这是用来确定影响检测高血红蛋白的预测价值的。在高铁血红蛋白升高的情况下，评价 SaO2读数的偏移、精密度和均方根误差。

结果：在2组中，观察范围SaO2为66.2%－99% 和高铁血红蛋白为0.6%－14.4%(170 次抽血)。在全部 SaO2范围内，Masimo 高铁血红蛋白读数偏差和精密度是 7.7% ± 13.0%。SaO2范围在95%－100%时最精确(1.9% ± 2.5%)，发展到70%－80%的范围时最不精确(24.8% ± 15.6%)。SaO2 每下降 5 个点时，高铁血红蛋白读数错误的发生率增高>5%(P < 0.05)。Masimo 的 SpO2读数在 SaO2范围为95%－100% 且高铁血红蛋白范围 4%－8.3%时偏差了-6.3% ± 3.0%。在 SaO2 <90%和高血红蛋白 4%－15%时， Radical-7 和 Nonin 9700 脉搏血氧计则更精确地检测到了下降，但是 SaO2 >95%时也会显示出低的 SpO2读数。

结论：当 SaO2下降 <95%的时候，Radical-7的高铁血红蛋白读数逐渐越来越不精确，有时候会高估实际值 10%－40%。升高的高血红蛋白会使 SpO2读数低估了SaO2，近似于高饱和度时的普通 2 波长脉搏血氧计。当发生低氧血症(SaO2 <90%) 且高血红蛋白水平高达 15%的时候，两种仪器的 SpO2读数都趋向于下降。

（唐亮 譯 馬皓琳 李士通 校）
BACKGROUND: Methemoglobin in the blood cannot be detected by conventional pulse oximetry, although it can bias the oximeter's estimate (SpO₂) of the true arterial functional oxygen saturation (SaO₂). A recently introduced “Pulse CO-Oximeter” (Masimo Rainbow SET® Radical-7 Pulse CO-Oximeter, Masimo Corp., Irvine, CA) is intended to additionally monitor noninvasively the fractional carboxyhemoglobin and methemoglobin content in blood. The purpose of our study was to determine whether hypoxia affects the new device's estimated methemoglobin reading accuracy, and whether the presence of methemoglobin impairs the ability of the Radical-7 and a conventional pulse oximeter (Nonin 9700, Nonin Medical Inc., Plymouth, MN) to detect decreases in SaO₂.

METHODS: Eight and 6 healthy adults were included in 2 study groups, respectively, each fitted with multiple sensors and a radial arterial catheter for blood sampling. In the first group, IV administration of approximately 300 mg sodium nitrite increased subjects' methemoglobin level to a 7% to 8% target and hypoxia was induced to different levels of SaO₂ (70%–100%) by varying fractional inspired oxygen. In the second group, 15% methemoglobin at room air and 80% SaO₂ were targeted. Pulse CO-oximeter readings were compared with arterial blood values measured using a Radiometer multiwavelength hemoximeter. Pulse CO-oximeter methemoglobin reading performance was analyzed by observing the incidence of meaningful reading errors at the various hypoxia levels. This was used to determine the impact on predictive values for detecting methemoglobinemia. SpO₂ reading bias, precision, and root mean square error were evaluated during conditions of elevated methemoglobin.

RESULTS: Observations spanned 66.2% to 99% SaO₂ and 0.6% to 14.4% methemoglobin over the 2 groups (170 blood draws). Masimo methemoglobin reading bias and precision over the full SaO₂ span was 7.7% ± 13.0%. Best accuracy was found in the 95% to 100% SaO₂ range (1.9% ± 2.5%), progressing to its worst in the 70% to 80% range (24.8% ± 16.5%). Occurrence of methemoglobin readings in error >5% increased over each 5-point decrease in SaO₂ (P < 0.05). Masimo SpO₂ readings were biased −6.3% ± 3.0% in the 95% to 100% SaO₂ range with 4% to 8.3% methemoglobin. Both the Radical-7 and Nonin 9700 pulse oximeters accurately detected decreases in SaO₂ <90% with 4% to 15% methemoglobin, despite displaying low SpO₂ readings when SaO₂ was >95%.

CONCLUSIONS: The Radical-7’s methemoglobin readings become progressively more inaccurate as SaO₂ decreases <95%, at times overestimating true values by 10% to 40%. Elevated methemoglobin causes the SpO₂ readings to underestimate SaO₂ similar to conventional 2-wavelength pulse oximeters at high saturation. SpO₂ readings from both types of instruments continue to trend downward during the development of hypoxemia (SaO₂ <90%) with methemoglobin levels up to 15%.

肺泡而非靜脈右旋氨胺酮抑制大鼠肺泡鍋轉運和肺液體清除率
Alveolar but Not Intravenous S-Ketamine Inhibits Alveolar Sodium Transport and Lung Fluid Clearance in Rats
Marc M. Berger, MD*, Bernhard Pitzer†, Stefanie Zügel, PhD‡, Catharina W. Wieland, PhD‡, Alexander P. Vlaar, MD‡, Marcus J. Schultz, MD, PhD‡, Albert Dahan, MD, PhD§, Peter Bärtsch, MD†, Markus W. Hollmann, MD, PhD, DEAA || and Heimo Mairbäurl, PhD†
BACKGROUND: S-ketamine is frequently used for analgosedation, especially during sepsis and cardiovascular instability. Because S-ketamine blocks voltage-gated sodium (Na\(^+\)) channels in neurons and skeletal muscle, it is conceivable that S-ketamine also blocks alveolar epithelial Na\(^+\) channels that are crucial for alveolar fluid clearance (AFC). We studied the effects of alveolar and IV S-ketamine on transalveolar Na\(^+\) transport and AFC, and investigated whether IV S-ketamine enters the alveolar space in response to endotoxemia-induced pulmonary inflammation.

METHODS: Cultured rat alveolar type II (ATII) cells were exposed to S-ketamine and/or the Na\(^+\) channel blocker amiloride (100 μM) and transepithelial transport indicated by short circuit current (ISC) was measured in Ussing chambers. AFC was measured in fluid-instilled lungs of anesthetized rats with or without amiloride added to the instillate. S-ketamine was either added to the instillate or injected IV. To induce mild lung injury...
that might favor the appearance of IV S-ketamine at the alveolar surface, endotoxemia was induced by IV lipopolysaccharide (7.5 mg/kg).

**RESULTS:** In ATII cells, S-ketamine (25 μg/mL) caused a decrease of ISC regardless of apical (−18.9%± 1.4%; \( P < 0.001 \)) or basolateral (−20.4% ± 3.7%; \( P < 0.001 \)) application. In ATII cells pretreated with amiloride, addition of apical or basolateral S-ketamine did not decrease ISC. AFC was approximately 8% per 30 minutes in control rats. S-ketamine (5 μg/mL) in the instillate reduced AFC to 1.1% ± 1.5% (\( P = 0.04 \)) by decreasing amiloride-sensitive transepithelial Na⁺ transport. Intravenous S-ketamine (20 mg/kg) did not affect AFC (\( P = 0.31 \)). In the presence of lipopolysaccharide-induced inflammation, the concentration of IV-injected S-ketamine in bronchoalveolar lavage fluid remained below the concentration that inhibited AFC.

**CONCLUSIONS:** Although exposure of the rat alveolar epithelium to S-ketamine decreases amiloride-sensitive transalveolar Na⁺ transport and AFC, IV S-ketamine at clinically relevant bolus concentrations does not affect AFC, even in the presence of mild lung injury.

**Background:** Ex vivo methods provide rapid access to vulnerable muscles, which are essential for rapid and efficient experimental analysis. We therefore developed a method for obtaining RYR1-cDNA from blood samples collected from patients with malignant hyperthermia and central core disease.

**Methods:** Blood samples were obtained from patients with malignant hyperthermia and central core disease. RYR1-mRNA was extracted from peripheral lymphocytes and cDNA was synthesized. RYR1-mRNA was then sequenced using PCR and Sanger sequencing.

**Results:** RYR1-mRNA was successfully amplified and sequenced in all samples. Mutations were identified in all positive samples and included changes in the RYR1-cDNA.

**Conclusion:** Our method allows for the rapid and efficient analysis of RYR1-mRNA from blood samples obtained from patients with malignant hyperthermia and central core disease. This method provides a valuable tool for the diagnosis and management of these patients.
BACKGROUND: A diagnosis of malignant hyperthermia susceptibility by in vitro contraction testing can often only be performed at specialized laboratories far away from where patients live. Therefore, we have designed a protocol for genetic screening of the RYR1-cDNA and for functional testing of newly identified ryanodine receptor 1 (RYR1) gene variants in B lymphocytes isolated from peripheral blood samples drawn at local primary care centers.

METHODS: B lymphocytes were isolated for the extraction of RYR1-mRNA and genomic DNA and for establishment of lymphoblastoid B cell lines in 5 patients carrying yet unclassified mutations in the RYR1. The B lymphoblastoid cell lines were used to study resting cytoplasmic calcium concentration, the peak calcium transient induced by the sarco(endo)plasmic reticulum Ca-ATPase inhibitor thapsigargin, and the dose-dependent calcium release induced by the ryanodine receptor agonist 4-chloro-m-cresol.

RESULTS: It was possible to extract mRNA for cDNA synthesis and to create B lymphocyte clones from all samples. All B lymphoblastoid cell lines carrying RYR1 candidate mutations showed significantly increased resting cytoplasmic calcium levels as well as a shift to lower concentrations of 4-chloro-m-cresol inducing calcium release compared with controls.

CONCLUSIONS: Peripheral blood samples are stable regarding RNA and DNA extraction and establishment of lymphoblastoid B cell lines after transportation at ambient temperature over large distances by ordinary mail. Functional tests on B cells harboring the newly identified amino acid substitutions indicate that they alter intracellular Ca²⁺ homeostasis and are most likely causative of malignant hyperthermia.

周樹脂毒聯合抗抑鬱藥優先延長大鼠坐骨神經的感覺/傷害性刺激阻滯

Resiniferatoxin Combined with Antidepressants Preferentially Prolongs Sensory/Nociceptive Block in Rat Sciatic Nerve

Yu-Chun Hung, MD*†, Suzuko Suzuki, MD‡, Chun-Jen Huang, MD, PhD§, Chien-Chuan Chen, MD*, Yu-Yen Pan, BA*, Chi-Fei Wang, MD‡, Venkatesh Srinavasan, MD ‖ and Peter Gerner, MD‡

From the *Department of Anesthesiology, Mackay Memorial Hospital, Taipei; †Mackay Medicine, Nursing and Management College, Taipei, Taiwan; ‡Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; §Buddhist Tzu Chi General Hospital, Taipei Branch, Taipei, Taiwan; and ‖ Department of Anesthesiology, VA Boston Healthcare System, Harvard Medical School, Boston, Massachusetts.

BACKGROUND: Current techniques of peripheral nerve block have major limitations, including lack of differentiation between motor and sensory fibers and potential toxicity of local anesthetics. Recent studies have suggested that a nociceptive-selective nerve block can be achieved via a transient receptor potential vanilloid type 1 activator (capsaicin) along with local anesthetics. We hypothesized that the combination of potent transient receptor potential vanilloid type 1 agonist resiniferatoxin (RTX) and selected antidepressants (amitriptyline, doxepin, and fluoxetine, also potent sodium channel blockers) would produce prolonged and predominantly sensory nerve block.

METHODS: Rats were anesthetized with isoflurane, and 0.2 mL of amitriptyline, doxepin, or fluoxetine was deposited next to the surgically exposed sciatic nerves (n = 8 per group). Some animals received a second injection containing RTX (n = 8 per group). The effect of nerve block was assessed by neurobehavioral tests of the motor function (extensor postural thrust) and the nocifensive reaction (mechanical pinch).

RESULTS: A single application of RTX produced nociceptive-selective sciatic nerve block, whereas antidepressants produced nociceptive and motor block. The combined administration of RTX and antidepressant resulted in a predominantly nociceptive nerve block. Compared with antidepressants or RTX alone, the combination prolonged the nociceptive nerve block more than the motor block.

CONCLUSIONS: The combined application of RTX and antidepressants produced a markedly prolonged nociceptive peripheral nerve block in rat sciatic nerves compared with either agent alone. However, the 2-drug regimen also elicited prolonged blockade of the motor function, although disproportionately less compared with the nociceptive modality, suggesting the existence of nontransient receptor potential vanilloid type 1–mediated mechanisms. The mechanisms through which RTX affects nociceptive signal transduction/transmission have yet to be fully elucidated.

多點注射腋路臂叢阻滯：肥胖對失敗率和急性併發症發生率的影響

Multiple Injection Axillary Brachial Plexus Block: Influence of Obesity on Failure Rate and Incidence of Acute Complications

Jean-Luc Hanouz, MD, PhD, Wilfried Grandin, MD, Anne Lesage, MD, Gérard Oriot, MD, Daniel Bonnieux, MD and Jean-Louis Gérard, MD, PhD

From the Department of Anesthesia and Intensive Care, Centre Hospitalier et Universitaire de Caen, Nacre, Caen cedex, France.

背景：在区域麻醉中，肥胖常常伴随更高的失败率，但是目前还没有有人评估特殊的阻滞方法在肥胖患者中的应用效果。我们假设肥胖降低了腋路臂丛阻滞的成功率。

方法：我们进行了一项前瞻性的研究，由经验丰富的麻醉医生对择期行上肢手术的患者实施腋路臂丛阻滞。采用三点注射法，分别用0.5%罗呱卡因6mL、10mL和20mL阻滞肌皮神经、正中神经和挠神经。通过末梢运动反应（腕关节或手指）判断正中神经和挠神经的阻滞效果。无需辅助用药而手术能顺利进行即为麻醉成功。记录麻醉急性并发症。离开麻醉后监护室前，记录患者对麻醉的满意度。

结果：在605例患者中，有85例为肥胖患者（BMI≥30kg/m²）。总体的成功率为97%，其中，肥胖患者成功率为91%，非肥胖患者为98%（P=0.003）。肥胖患者中（7%）需要肘部辅助神经阻滞的人数比非肥胖患者多（2%；P=0.007）。肥胖患者（27%）急性并发症（主要是穿破血管）的发病率高于非肥胖患者（27%比9%；P<0.001）。肥胖患者对麻醉的满意度为87%，而非肥胖患者为94%（P=0.03）。

结论：肥胖增加了腋路臂丛阻滞的失败率和急性并发症的发病率。此外，更多的肥胖患者对麻醉效果不满意。
（徐妍君 譯 馬皓琳 李士通 校）

BACKGROUND: Obesity has been associated with an increased failure rate in regional anesthesia, but specific block techniques have not been evaluated. We hypothesized that obesity decreases the success rate of axillary brachial plexus block.

METHODS: We prospectively studied axillary brachial plexus blocks performed by experienced anesthesiologists in patients scheduled for upper limb surgery. A triple-injection technique was given to block the musculocutaneous and the median nerves with 6 mL and 10 mL ropivacaine 0.5%, respectively, and the radial nerve with 20 mL ropivacaine 0.5%. For the median and radial nerves, distal motor responses (wrist or fingers) were identified. Success was defined as adequate anesthesia allowing surgery to be performed without additional medications. Acute complications were noted. Before leaving the postanesthesia care unit, patient's satisfaction with anesthesia was collected.

RESULTS: Of 605 patients, 85 were obese (body mass index ≥30 kg/m²). The success rate was 97% overall, 91% in the obese and 98% in the non-obese patients (P = 0.003). Additional nerve blocks at the elbow were performed more frequently in obese (7%) than in non-obese patients (2%; P = 0.007). Acute complications (mainly vascular puncture) were more frequent in obese than in non-obese patients (27% vs 9%; P < 0.001). Patient satisfaction was 87% in the obese and 94% in the non-obese patients (P = 0.03).

CONCLUSIONS: Obesity increased the failure rate and immediate complications of axillary brachial plexus block. Furthermore, more obese patients were dissatisfied with their anesthesia.

中樞阿片受體啟動介導心臟缺血再灌注損傷的保護作用
Activation of Central Opioid Receptors Induces Cardioprotection Against Ischemia-Reperfusion Injury
Gordon T. C. Wong, FANZCA*, Jiang Ling Ling, MD*† and Michael G. Irwin, MD*
BACKGROUND: Small doses of intrathecal morphine provide cardioprotection similar to that conferred by IV morphine and ischemic preconditioning (IPC). We investigated the relative role of central versus peripheral opioid receptors in intrathecal morphine preconditioning (ITMPC).

METHODS: Forty-eight anesthetized, open-chest, male Sprague-Dawley rats were assigned to 1 of 7 treatment groups \((n = 6–7)\) after successful intrathecal catheter placement. ITMPC was achieved by 3 consecutive 5-min intrathecal infusions of morphine \((1.0 \mu g/kg each)\). This was repeated in the presence of either IV (IV naloxone methiodide + ITMPC) or intrathecally (intrathecal naloxone methiodide [ITNM] + ITMPC) administered naloxone methiodide. This compound was also given via these same routes in the absence of ITMPC (IV naloxone methiodide + ITNM). Intrathecal normal saline and IPC were used as negative and positive controls, respectively. Myocardial ischemia and reperfusion injury were induced by 30 min of left main coronary artery occlusion followed by 2 h of reperfusion. Myocardial infarct size, as a percentage of the area-at-risk, was determined by 2,3,5-triphenyltetrazolium staining.

RESULTS: The infarct size/area-at-risk were significantly reduced in the IPC \((22\% ± 3\%)\) and ITMPC \((26\% ± 5\%)\) groups compared with the control group \((48\% ± 9\%)\) \((P < 0.01)\). The addition of ITNM reversed the cardioprotective effects of ITMPC \((45\% ± 4\%)\), whereas IV administration of the drug did not have any effect on ITMPC \((28\% ± 9\%, P < 0.01)\).
CONCLUSIONS: Intrathecally administered morphine can produce cardioprotective effects via the activation of central opioid receptors, without the apparent involvement of peripheral opioid receptors.

胸腹主動脈手術中腰部腦脊液引流：基本原理和操作指南

Lumbar Cerebrospinal Fluid Drainage for Thoracoabdominal Aortic Surgery: Rationale and Practical Considerations for Management

Christine A. Fedorow, MD*, Michael C. Moon, MD, FRCPC†, W. Alan C. Mutch, MD, FRCPC* and Hilary P. Grocott, MD, FRCPC*†

From the Departments of *Anesthesia and †Surgery, University of Manitoba, Winnipeg, Manitoba, Canada.

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截癱仍是胸腹主動脈瘤手術的最嚴重的併發症之一，與併發症發生率和死亡率增加密切相關。現代主動脈修復技術使用各種方法來減少手術相關的脊髓缺血危險。這些方法之一是通過腰部腦脊液（CSF）的引流來優化脊髓血流量。單獨或與其他措施相結合，腦脊液引流仍然是最常用的脊髓保護技術之一。儘管沒有降低脊髓損傷有效性的確切證據，但是有令人信服的資料支援這項技術的運用。然而，腦脊液引流的潛在優點，必須兼顧其風險，包括插入時神經損傷，椎管內壓迫軸索性血腫形成，由於引流過多導致的顱內出血和感染等。可以通過理解其使用的基本原理及遵守實踐指南來實現最佳效益風險比。

Paraplegia remains one of the most devastating complications of thoracoabdominal aortic surgery and is associated with a significant increase in both morbidity and mortality. Modern aortic repair techniques use many modalities aimed at reducing the risk of spinal cord ischemia inherent with surgical management. One of these modalities that acts via optimizing spinal cord blood flow is lumbar cerebrospinal fluid (CSF) drainage. Either alone or in combination with other interventions, CSF drainage remains one of the most frequently used spinal cord protection techniques. Despite no definitive proof of efficacy for reducing spinal cord injury, there are compelling data supporting its use. However, the potential benefit of CSF drainage must be balanced against the risks associated with its use, including nerve injury during insertion, compressive neuraxial hematoma formation, intracranial hemorrhage due to excessive drainage, and infection. The optimal benefit to risk ratio can be achieved by understanding the rationale for its use and following practical management guidelines.

吸入麻醉薬の潜在全球暖化効應：臨床應用

Global Warming Potential of Inhaled Anesthetics: Application to Clinical Use

Susan M. Ryan, MD, PhD* and Claus J. Nielsen, CSc†

From the *Department of Anesthesia and Perioperative Care, University of California, San Francisco, San Francisco, California; and †Department of Chemistry, Centre for Theoretical and Computational Chemistry, University of Oslo, Oslo, Norway.

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背景：吸入麻醉藥是公認的溫室氣體。本文通過計算其在常見的臨床使用過程中的相當的二氧化碳總排放量來比較不同的吸入麻醉藥對環境的影響。

方法：作者先確定七氟醚和異氟醚紅外吸收截面積。運用以前公佈的地氟醚，七氟醚，異氟醚的紅外線吸收資料計算 20 年全球變暖潛能值（GWP20），且確定大氣中各氣體最適存在週期。在每小時最小肺泡濃度（MAC）下使用每種麻醉劑的總量乘以計算出的 GWP20，表示為每克“二氧化碳當量”（CDE20）。計算時根據目前臨床吸入麻醉的方法，將分別計算由空氣/氧氣作為載體或 N2O/氧氣的混合氣體作為載體時二氧化碳當量數值。

結果：對吸入麻醉藥 GWP20 計算值分別為：七氟醚 349，異氟醚 1401，地氟醚 3714。2 L/h 新鮮氣流量下 1MAC 每小時的 CDE20 的預測值分別為：七氟醚 6980 g，異氟醚 15,551 g，地氟醚 187186 g。這些麻醉藥之間的比率为七氟醚 1，異氟醚 2.2，地氟醚 26.8。當 60%N2O 與 40%氧氣的混合氣體替代空氣/氧氣作為載體，同時吸入麻醉藥調整為每小時 1MAC，七氟醚 CDE20 值分别高出 5.9 倍，異氟醚 CDE20 值高出 2.9 倍，而地氟醚 CDE20 值降低，為 0.4 倍。以 100 年為時間水準運用 60%N2O 作為載體時，七氟醚 CDE100 值比空氣/氧氣作為載體高出 19 倍，異氟醚的值高出 9 倍，地氟醚的值無差異。

結論：根據比較結果和臨床環境，地氟醚對全球變暖的影響超過七氟醚與異氟醚。應用七氟醚或異氟醚，將 N2O 作為載體將產生更多的溫室氣體。此外，60%氧化亞氮與吸入麻醉劑混合使用，在相同 MAC 的麻醉下大幅度增加七氟醚和異氟醚對環境的影響，而地氟醚對環境的影響降低。氧化亞氮會破壞臭氧層及使全球升溫趨勢；且影響的持續時間更長，與地氟醚混合使用可能是一個環保的折衷方案。根據計算研究，避免 N2O 及不必要的高流量氣體可降低吸入麻醉對環境的影響。

（陳毓雯 譯 陳傑 校）

BACKGROUND: Inhaled anesthetics are recognized greenhouse gases. Calculating their relative impact during common clinical usage will allow comparison to each other and to carbon dioxide emissions in general.

METHODS: We determined infrared absorption cross-sections for sevoflurane and isoflurane. Twenty-year global warming potential (GWP20) values for desflurane, sevoflurane, and isoflurane were then calculated using the present and previously published infrared results, and best estimate atmospheric lifetimes were determined. The total quantity of each anesthetic used in 1 minimal alveolar concentration (MAC)-hour was then multiplied by the calculated GWP20 for that anesthetic, and expressed as “carbon dioxide equivalent” (CDE20) in grams. Common fresh gas flows and carrier gases, both air/oxygen and nitrous oxide (N2O)/oxygen, were considered in the calculations to allow these examples to represent common clinical use of inhaled anesthetics.

RESULTS: GWP20 values for the inhaled anesthetics were: sevoflurane 349, isoflurane 1401, and desflurane 3714. CDE20 values for 1 MAC-hour at 2 L fresh gas flow were: sevoflurane 6980 g, isoflurane 15,551 g, and desflurane 187,186 g. Comparison among these anesthetics produced a ratio of sevoflurane 1, isoflurane 2.2, and desflurane 26.8. When 60% N2O/40% oxygen replaced air/oxygen as a carrier gas combination, and inhaled anesthetic delivery was adjusted to deliver 1 MAC-hour of anesthetic,
sevoflurane CDE$_{20}$ values were 5.9 times higher with N$_2$O than when carried with air/O$_2$, isoflurane values were 2.9 times higher, and desflurane values were 0.4 times lower. On a 100-year time horizon with 60% N$_2$O, the sevoflurane CDE$_{100}$ values were 19 times higher than when carried in air/O$_2$, isoflurane values were 9 times higher, and desflurane values were equal with and without N$_2$O.

CONCLUSIONS: Under comparable and common clinical conditions, desflurane has a greater potential impact on global warming than either isoflurane or sevoflurane. N$_2$O alone produces a sizable greenhouse gas contribution relative to sevoflurane or isoflurane. Additionally, 60% N$_2$O combined with potent inhaled anesthetics to deliver 1 MAC of anesthetic substantially increases the environmental impact of sevoflurane and isoflurane, and decreases that of desflurane. N$_2$O is destructive to the ozone layer as well as possessing GWP; it continues to have impact over a longer timeframe, and may not be an environmentally sound tradeoff for desflurane. From our calculations, avoiding N$_2$O and unnecessarily high fresh gas flow rates can reduce the environmental impact of inhaled anesthetics.

残余神經阻滯: 易忘掉的課業. 第一部分: 殘余神經阻滯的定義，發生率和不良生理學反應

Residual Neuromuscular Block: Lessons Unlearned. Part I: Definitions, Incidence, and Adverse Physiologic Effects of Residual Neuromuscular Block
Glenn S. Murphy, MD* and Sorin J. Brull, MD†
From the *Department of Anesthesiology, NorthShore University HealthSystem, University of Chicago, Evanston, Illinois; †Department of Anesthesiology, Mayo Clinic College of Medicine, Jacksonville, Florida.

In this review, we summarize the clinical implications of residual neuromuscular block. Data suggest that residual neuromuscular block is a common complication in the postanesthesia care unit, with approximately 40% of patients exhibiting a train-of-four ratio <0.9. Volunteer studies have demonstrated that small degrees of residual paralysis (train-of-four ratios 0.7–0.9) are associated with impaired pharyngeal function and increased risk of aspiration, weakness of upper airway muscles and airway obstruction, attenuation of the hypoxic ventilatory response (approximately 30%), and unpleasant
symptoms of muscle weakness. Clinical studies have also identified adverse postoperative events associated with intraoperative neuromuscular management. Large databased investigations have identified intraoperative use of muscle relaxants and residual neuromuscular block as important risk factors in anesthetic-related morbidity and mortality. Furthermore, observational and randomized clinical trials have demonstrated that incomplete neuromuscular recovery during the early postoperative period may result in acute respiratory events (hypoxemia and airway obstruction), unpleasant symptoms of muscle weakness, longer postanesthesia care unit stays, delays in tracheal extubation, and an increased risk of postoperative pulmonary complications. These recent data suggest that residual neuromuscular block is an important patient safety issue and that neuromuscular management affects postoperative outcomes.

High-Resolution Solid-State Manometry of the Upper and Lower Esophageal Sphincters During Anesthesia Induction: A Comparison Between Obese and Non-Obese Patients
Alex de Leon, MD, Sven-Egron Thörn, MD, PhD and Magnus Wattwil, MD, PhD
From the Department of Anesthesia and Intensive Care, Örebro University Hospital, Örebro, Sweden.
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BACKGROUND: The prevalence of obesity has increased dramatically in recent decades. The gastrointestinal changes associated with obesity have clinical significance for the anesthesiologist in the perioperative period. The lower esophageal sphincter and the upper esophageal sphincter play a central role in preventing regurgitation and aspiration. The effects of increased intra-abdominal pressure during anesthesia on the lower esophageal sphincter and the upper esophageal sphincter in obese patients are unknown. In the present study we evaluated, with high-resolution solid-state manometry, the upper esophageal sphincter, lower esophageal sphincter, and barrier pressure (BrP)
METHODS: We studied 28 patients, ages 18 to 72 years, 14 with a body mass index \( \geq 35 \text{kg/m}^2 \), who were undergoing laparoscopic gastric bypass, and 14 with a body mass index \( \leq 30 \text{kg/m}^2 \), who were undergoing laparoscopic cholecystectomy, using high-resolution solid-state manometry.

RESULTS: Upper esophageal sphincter pressure decreased during anesthesia induction in both groups. Lower esophageal sphincter pressure decreased in both groups during anesthesia induction, and it was significantly lower in obese patients than in non-obese patients. The BrP decreased in both groups and was significantly lower in the obese group than in the non-obese group. The BrP remained positive at all times in both groups.

CONCLUSION: Lower esophageal sphincter and BrPs decreased in both obese and non-obese patients during anesthesia induction, but were significantly lower in obese patients. Although the BrP was significantly lower, it remained positive in all patients.
反，在兩個測試時間點，床邊測定全血肝素濃度值與實驗室血漿肝素濃度值相當一致（一致性相關係數分別為 0.30 和 0.67）。通過抗 Xa 因數測定的血漿肝素濃度值比 Hepcon 測定儀測定的全血肝素濃度值要高一些。

結論：行 CPB 的年齡小於 6 月的嬰幼兒中，單應用 ACT 值作為唯一評判肝素抗凝的指標應尤其謹慎。通常，ACT 與血漿肝素濃度相關性並不大。只有應用 i-STAT 儀器進行 ACT 測試時在停機前即刻 ACT 與血漿肝素有一定相關性。而應用 Hepcon 儀器進行床邊全血肝素濃度測定與應用抗 Xa 因數測定值基本相一致。研究資料表明了臨床上在嬰幼兒中床邊進行肝素濃度測試及時、便捷、精確。

（趙嫣紅譯 陳傑校）

BACKGROUND: Monitoring heparin concentration along with the activated clotting time (ACT) may provide a more accurate guide for the administration of heparin to infants during cardiopulmonary bypass (CPB). However, standard laboratory assays of heparin concentration (antifactor Xa heparin concentration) require plasma instead of whole blood, and results are not immediately available to clinicians. Alternatively, measurements of whole blood heparin concentration may be performed at the bedside using an automated protamine titration device, the Hepcon instrument (Hepcon Hemostasis Management System Plus; Medtronics, Minneapolis, MN). The purpose of this investigation was to compare ACT measurements from 3 commercially available instruments and bedside measurements of whole blood heparin concentration using the Hepcon instrument with laboratory measurements of antifactor Xa plasma heparin concentration in infants younger than 6 months of age undergoing CPB.

METHODS: Forty-four pediatric patients younger than 6 months of age scheduled for elective cardiac surgery requiring CPB were enrolled in this prospective study. Blood samples were drawn 3 minutes after the initial heparin bolus and immediately before the termination of CPB to obtain measurements of heparin anticoagulation. Kaolin-activated ACTs were performed with the Hemochron (International Technidyne Corporation, Edison, NJ), Hepcon, and i-STAT (i-STAT Corporation, East Windsor, NJ) instruments. Whole blood heparin concentration was measured using the Hepcon instrument. Plasma heparin concentration was measured using an antifactor Xa chromogenic substrate assay

RESULTS: Immediately after the initial heparin bolus, none of the ACT values correlated with plasma heparin concentration. When measured immediately before the termination of CPB, only the i-STAT ACT showed a moderate correlation. Conversely, bedside measurements of whole blood heparin concentration showed satisfactory agreement with laboratory measurements of plasma heparin concentration at both time points (concordance correlation coefficients 0.30 and 0.67, respectively). There is a bias in that antifactor Xa-measured plasma heparin concentration tends to be higher than Hepcon-measured whole blood heparin concentration.

CONCLUSIONS: In infants younger than 6 months old undergoing CPB, caution is warranted when using ACT values as the sole indication of adequate heparin anticoagulation. In general, ACT prolongation correlates poorly with plasma heparin concentration. Only i-STAT ACT values showed a moderate correlation when measured immediately before the termination of CPB. Alternatively, bedside measurements of whole blood heparin concentration measured by the Hepcon instrument agreed well with antifactor Xa laboratory measurements. Our data support the clinical utility of bedside
measurements of heparin concentration to provide timely, convenient, and accurate measurements of heparin concentration in these infants.

有與沒有顱內壓監測的幼豬大腦的無創自我調節功能監測
Noninvasive Autoregulation Monitoring with and without Intracranial Pressure in the Naïve Piglet Brain
Ken M. Brady, MD*, Jennifer O. Mytar, BS*, Kathleen K. Kibler, BS*, Charles W. Hogue Jr., MD*, Jennifer K. Lee, MD*, Marek Czosnyka, PhD†, Peter Smielewski, PhD† and R. Blaine Easley, MD*. From the *Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland; and †Department of Academic Neurosurgery, Addenbrooke's Hospital, Cambridge, United Kingdom.
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背景：對於那些沒有有創顱內壓監測的危重病人，其腦血管的自我調節功能的監測是很有必要的。沒有顱內壓監測，則動脈血壓可以代替腦灌注壓來測量各動脈壓力跨度範圍內腦血流的限制情況。本研究比較了低血壓模型中使用動脈壓和腦灌注壓對於自我調節功能監測的差異。

方法：給予試驗幼豬（5-7 天齡）致命性的低血壓來確定新生大腦的顱內壓，並判斷其自我調節的最低限度（LLA）。試驗共有 25 只幼豬，連續監測顱內壓、局部腦血氧飽和度（rSO2）、腦皮層紅細胞流量（多普勒）。之後用兩種方法結合腦氧合指數（Cox）來評價自我調節功能：動脈血壓和局部腦血氧飽和度（COXABP）間的線性關係以及腦灌注壓和局部腦血氧飽和度（COXCPP）間的線性關係。從紅細胞流量對動脈血壓的圖表中可以判斷自我調節的最低限度。本試驗以 COXABP 和 COXCPP 的平均值為基點，以 5mmHg 作為最小間距，繪製這兩種方法的受試者操作特徵曲線。

結果：為了確定自我調節的最低限度，COXABP 和 COXCPP 兩種方法得出相同的受試者操作特徵曲線區域為 0.91（95%CI：0.88-0.95）。但兩種方法的閾值不一樣：判定動脈血壓低於自我調節的最低限度時，其 COXABP 的閾值是 0.5，敏感度 89%（95%CI：81%-94%），特異度 81%（95%CI，73-88%）。而對於 COXCPP 來講，其閾值是 0.42，敏感度同樣是 89%（95%CI，81%-94%），而特異度為 77%（95%CI，69-84%）。

討論：對新生大腦使用動脈血壓而不是腦灌注壓進行自我調節監測，同時結合 Cox 值，用來區分動脈壓是高於還是低於自我調節的最低限度，這種方法的閾值有所升高。然而兩種方法的準確性相似。這些發現說明了對於沒有顱內壓監測的病人可以用近紅外光譜來監測自我調節功能。
（張婷 譯 陳傑 校）

BACKGROUND: Cerebrovascular autoregulation monitoring is often desirable for critically ill patients in whom intracranial pressure (ICP) is not measured directly. Without ICP, arterial blood pressure (ABP) is a substitute for cerebral perfusion pressure (CPP) to gauge the constraint of cerebral blood flow across pressure changes. We compared the use of ABP versus CPP to measure autoregulation in a piglet model of arterial hypotension.
METHODS: Our database of neonatal piglet (5–7 days old) experiments was queried for animals with naïve ICP that were made lethally hypotensive to determine the lower limit of autoregulation (LLA). Twenty-five piglets were identified, each with continuous recordings of ICP, regional cerebral oximetry (rSO2), and cortical red cell flux (laser Doppler). Autoregulation was assessed with the cerebral oximetry index (COx) in 2 ways: linear correlation between ABP and rSO2 (COxABP) and between CPP and rSO2 (COxCPP). The lower limits of autoregulation were determined from plots of red cell flux versus ABP. Averaged values of COxABP and COxCPP from 5 mm Hg ABP bins were used to show receiver operating characteristics for the 2 methods.

RESULTS: COxABP and COxCPP yielded identical receiver operating characteristic curve areas of 0.91 (95% confidence interval [CI], 0.88–0.95) for determining the LLA. However, the thresholds for the 2 methods differed: a threshold COxABP of 0.5 was 89% sensitive (95% CI, 81%–94%) and 81% specific (95% CI, 73%–88%) for detecting ABP below the LLA. A threshold COxCPP of 0.42 gave the same 89% sensitivity (95% CI, 81%–94%) with 77% specificity (95% CI, 69%–84%).

CONCLUSIONS: The use of ABP instead of CPP for autoregulation monitoring in the naïve brain with COx results in a higher threshold value to discriminate ABP above from ABP below the LLA. However, accuracy was similar with the 2 methods. These findings support and refine the use of near-infrared spectroscopy to monitor autoregulation in patients without ICP monitors.
BACKGROUND: Intraneural administration of local anesthetics has been associated with nerve damage. We undertook the present study to investigate histological changes induced by ropivacaine injection into rat sciatic nerve.

METHODS: Fifty-four adult male Lewis rats were randomly distributed into 9 groups, 6 animals per group. Fifty microliters of normal saline, 10% phenol, or 0.75% ropivacaine were administered by intraneural injection, extraneural injection, or extraneural (topical) placement. At 2 weeks, animals were killed and the sciatic nerve at the injection site was evaluated with light microscopy, quantitative histomorphometry, and electron microscopy.

RESULTS: On cross-sectional evaluation, extraneural ropivacaine injection and extraneural placement of ropivacaine were both associated with damage to the perineurium, with focal demyelination surrounded by edematous endoneurium. Intrafascicular injection of ropivacaine resulted in a wedge-shaped region of demyelination and focal axonal loss with some regeneration, bordered by a region of normally myelinated axons in a background of edematous endoneurium. Extraneural injection resulted in more significant damage than extraneural placement of ropivacaine, but less than intrafascicular injection as shown with quantitative histomorphometry. Quantitatively, ropivacaine-injured specimens had significantly lower nerve density than saline-injured specimens. Wallerian degeneration and perineural edema were also demonstrated qualitatively with electron microscopy.

CONCLUSIONS: This study demonstrates that, in the rat model, ropivacaine is associated with marked histological abnormality, including edema of the perineurium and axonal destruction with wallerian degeneration, when injected into or extraneurally placed onto a nerve. Extraneural injection and extraneural placement were associated with similar, although milder, histological damage than intrafascicular injection. Further work is needed to investigate the functional implications, if any, of the histological abnormalities observed in this study.
背景：頸叢神經阻滯常被認為是非完善的感覺阻滯，在這項隨機，雙盲，對照試驗中，作者比較了頸動脈內膜剝脫術（CEA）中，局麻液中加芬太尼後是否改善頸叢神經阻滯效果。

方法：77名擇期行CEA術的成年患者，行頸深叢神經阻滯，隨機分組：實驗組局麻液中加入芬太尼1 mL (50 μg），對照組加入生理鹽水鹽1 mL，分別與0.5%布比卡因10 mL和2%利多卡因4 mL配置成混合液。同時用0.5%布比卡因10 mL和2%利多卡因4 mL行頸淺叢神經阻滯。用視覺類比評分評估疼痛(0–10; 0 =無痛, 10 =疼痛難以忍受), 對於術中疼痛評分大於3者給予異丙酚20mg靜脈推注。記錄術中所需藥物追加時間以及術後24小時內所需鎮痛情況，P <0.05認為有統計學意義。

結果：芬太尼組術中追加異丙酚(4 of 38, 10.5%)明顯少於對照組(26 of 39, 66.7%; P < 0.001)。儘管兩組的阻滯起效時間無明顯差異(各自的中位數為12 [9–18] vs 15 [9–18] 分; P = 0.18)，但相比對照組，芬太尼組需要異丙酚的量更少(分別是中位數0 [0–60] vs 60 [0–160] mg; P < 0.001)，需要術後鎮痛的發生率更低(分別是22 /38例, 57.9% vs 35 / 39例, 89.7%; P = 0.002)，術後首次鎮痛的時間更晚(分別是中位時間5.8h [1.9–15.6] 和3.1 [1.0–11.7] h; P < 0.001)。

結論：在CEA中，以局部麻醉藥中輔助芬太尼可以改善頸叒阻滯的作用，並延長阻滯時間。

BACKGROUND: Cervical plexus block is frequently associated with unsatisfactory sensory blockade. In this randomized, double-blind, placebo-controlled trial, we examined whether the addition of fentanyl to local anesthetics improves the quality of cervical plexus block in patients undergoing carotid endarterectomy (CEA).

METHODS: Seventy-seven consecutive adult patients scheduled for elective CEA were randomized to receive either fentanyl 1 mL (50 μg) or saline placebo 1 mL in a mixture of 10 mL bupivacaine 0.5% and 4 mL lidocaine 2% for deep cervical plexus block. Superficial cervical plexus block was performed using a mixture of 10 mL bupivacaine 0.5% and 5 mL lidocaine 2%. Pain was assessed using the verbal rating scale (0–10; 0 = no pain, 10 = worst pain imaginable), and propofol in 20-mg IV bolus doses was given to patients reporting verbal rating scale >3 during the procedure. Rescue medication consumption during surgery and analgesia requirements over the next 24 hours, as well as onset of sensory blockade, were recorded. A P value <0.05 was regarded as statistically significant.

RESULTS: Fewer patients in the fentanyl group (4 of 38, 10.5%) required propofol compared with the placebo group (26 of 39, 66.7%; P < 0.001). In comparison with the placebo group, the fentanyl group consumed less propofol (median 0 [0–60] vs 60 [0–160] mg, respectively; P < 0.001), required postoperative analgesia less frequently (22 of 38 patients, 57.9% vs 35 of 39 patients, 89.7%, respectively; P = 0.002), and requested the first analgesic after surgery later (median 5.8 [1.9–15.6] vs 3.1 [1.0–11.7] hours, respectively; P < 0.001), whereas the onset time of sensory blockade was similar in both groups (median 12 [9–18] vs 15 [9–18] minutes, respectively; P = 0.18).

CONCLUSIONS: The addition of fentanyl to local anesthetics improved the quality and prolonged the duration of cervical plexus block in patients undergoing CEA.
Inhaled carbon monoxide prevents acute kidney injury in pigs after cardiopulmonary bypass by inducing a heat shock response.


Department of Anesthesiology and Critical Care Medicine, University Medical Centre, Hugstetterstrasse 55, D-79106 Freiburg im Breisgau, Germany.

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Background: Cardiopulmonary bypass (CPB) may be associated with acute kidney injury (AKI). Inhaled carbon monoxide (CO) is cyto- and organ-protective. We hypothesized that pretreatment with inhaled CO prevents CPB-associated AKI.

Methods: Pigs (n = 38) were nonrandomly assigned to SHAM, standard CPB, pretreatment with inhaled CO (250 ppm, 1 hour) before SHAM or CPB, to pretreatment with quercetin (an inhibitor of the heat shock response), and to pretreatment with SnPPIX (an inhibitor of endogenously derived CO), before CO inhalation and CPB. The primary outcome variables were markers of AKI (urea, uric acid, creatinine, cystatin C, neutrophil gelatinase-associated lipocalin, interleukin-6, tumor necrosis factor-alpha), which were determined 120 minutes after CPB. Secondary outcome variables were heat shock protein...
(HSP)-70 and heme oxygenase-1 protein expressions as indicators of CO-mediated heat shock response.

RESULTS: Pretreatment with inhaled CO attenuated (all P < 0.001) CPB-associated, (1) increases in serum concentrations of cystatin C (64 +/- 14 vs 28 +/- 9 ng/mL), neutrophil gelatinase-associated lipocalin (391 +/- 65 vs 183 +/- 56 ng/mL), renal tumor necrosis factor-alpha (450 +/- 73 vs 179 +/- 110 pg/mL), and interleukin-6 (483 +/- 102 vs 125 +/- 67 pg/mL); (2) increase in renal caspase-3 activity (550 +/- 66 vs 259 +/- 52 relative fluorescent units); and (3) histological evidence of AKI. These effects were accompanied by activation of HSP-70 (196 +/- 64 vs 554 +/- 149 ng/mL, P < 0.001). Pretreatment with the heat shock response inhibitor quercetin counteracted the CO-associated biochemical and histological renoprotective effects (all P < 0.001), whereas the heme oxygenase inhibitor SnPPIX only partially counteracted the CO-associated renoprotection and the activation of the heat shock response.

CONCLUSIONS: CO treatment before CPB was associated with evidence of renoprotection, demonstrated by fewer histological injuries and decreased cystatin C concentrations. The findings that the antiinflammatory and antiapoptotic effects of CO were accompanied by activation of HSP-70, which in turn were reversed by quercetin, suggest that renoprotection by pretreatment with inhaled CO before CPB is mediated by activation of the renal heat shock response.

**主動脈瓣修補術中的經食管超聲心動圖評估**

Transesophageal echocardiographic evaluation during aortic valve repair surgery.

Van Dyck MJ, Watremez C, Boodhwani M, Vanoverschelde JL, El Khoury G.

Department of Anesthesiology, Cliniques universitaires St-Luc, Université catholique de Louvain, Avenue Hippocrate 10-1821, B-1200 Brussels, Belgium.

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對於主動脈瓣膜疾病和主動脈狹窄的患者，最經典的治療方法是主動脈瓣置換術。與之相比，主動脈關閉不全修復術是一種新興的具有可行性並且具有吸引力的方法，它對於伴或不伴有主動脈瓣部病變均適用。主動脈瓣是主動脈根部的組成部分之一。因此，當一個或更多的主動脈根部的組成部分發生病變時，主動脈關閉不全的病情就會進展。術中的経食管超聲心動圖評估方法可以分析主動脈返流的機制以及鑒別可修復與不可修復的主動脈瓣病變。修復術後即刻的経食管超聲心動圖能提供很多重要資訊，包括修復的品質，修復的耐久性以及發現與主動脈關閉不全有關的多種因素徵象。

（黃劍譯 薛張綱校）

For patients with aortic valve (AV) disease, the classic treatment has been AV replacement and this remains true for aortic stenosis. In contrast, repair of isolated aortic insufficiency (AI), with or without aortic root pathology, is emerging as a feasible and attractive option to replacement. The AV is one of the elements of the aortic root. As such, AI can develop if one or more elements of the aortic root are diseased.

Intraoperative transesophageal echocardiographic evaluation permits analysis of the mechanisms of aortic regurgitation as well as differentiation between repairable and unreparable AV pathology. Immediate postrepair transesophageal echocardiography
provides important information about the quality and durability of repair and identifies variables associated with recurrent AI.

**背景:** 大麻素配體 2（CB2）激動劑治療神經性疼痛潛在靶點的研究近來引起關注。通過研究，我們描繪一個 CB2激動劑複合物 N'-[(3Z)-1-（1-己基）-2-氧代-1,2二氫 3H-吲哚-3-亞基]-的藥理學曲線。

**方法:** 我們對人和大鼠的 CB1 和 CB2 受體採用放射性配體結合分析以及多次體外功能性分析。評估 MDA19 對逆轉大鼠及 CB2+/+ 和 CB2−/−小鼠各式神經性疼痛的作用。

**結果:** MDA19 對人 CB2 受體的親和力是 CB1 受體的 4 倍（K1=43.3±10.3vs162.4±7.6 nM），對大鼠 CB2 受體的親和力是 CB1 受體的近 70 倍（K1=16.3±2.1vs1130±574 nM）。在鳥苷三磷酸（GTP）γ[35S]功能性分析中，MDA19 對人類 CB1 和 CB2 受體及大鼠 CB1 受體有激動作用，對大鼠 CB2 受體起反激動作用。3,5-環單磷酸腺苷（cAMP）中，MDA19 對大鼠 CB1 受體有激動作用，對大鼠 CB2 受體沒有作用。對細胞外信號調節激酶 1 和 2 的活化分析顯示 MDA19 對大鼠 CB2 受體有激動作用。MDA19 可減弱 CB2+/+ 小鼠由脊神經離斷或紫杉醇劑量依賴所致的異常疼痛，對 CB2−/−小鼠無此作用，表明 MDA19 通過 CB2 受體發揮作用。MAD19 不影響大鼠的運動能力。

**結論:** MDA19 在體外功能性研究中對大鼠 CB2 受體有顯著作用，在體內類似蛋白激動劑對 CB1/CB2 有激動作用。MDA19 在減緩神經性疼痛而不對中樞神經系統產生副作用方面有很大優勢。

（毛慧譯，薛張綱校）

**BACKGROUND:** Cannabinoid receptor2 (CB2) agonists have recently gained attention as potential therapeutic targets in the management of neuropathic pain. In this study, we characterized the pharmacological profile of the novel compound N'-[(3Z)-1-(1-hexyl)-2-oxo-1,2-dihydro-3H-indol-3-ylidene]benzohydrazide (MDA19), a CB2 agonist.

**METHODS:** We used radioligand binding assays and multiple in vitro functional assays at human and rat CB1 and CB2 receptors. The effects of MDA19 in reversing neuropathic pain were assessed in various neuropathic pain models in rats and in CB2+/+, and CB2−/− mice.

**RESULTS:** MDA19 displayed 4-fold-higher affinity at the human CB2 than at the human CB1 receptor (K1=43.3±10.3vs162.4±7.6 nM) and nearly 70-fold-higher affinity at the rat CB2 than at the rat CB1 receptor (K1=16.3±2.1vs1130±574 nM). In guanosine triphosphate (GTP)γ[35S] functional assays, MDA19 behaved as an agonist at the
human CB₁ and CB₂ receptors and at the rat CB₁ receptor but as an inverse agonist at the rat CB₂ receptor. In 3',5'-cyclic adenosine monophosphate (cAMP) assays, MDA19 behaved as an agonist at the rat CB₁ receptor and exhibited no functional activity at the rat CB₂ receptor. In extracellular signal-regulated kinases 1 and 2 activation assays, MDA19 behaved as an agonist at the rat CB₂ receptor. MDA19 attenuated tactile allodynia produced by spinal nerve ligation or paclitaxel in a dose-related manner in rats and CB₂⁺/⁻ mice but not in CB₂⁻/⁻ mice, indicating that CB₂ receptors mediated the effects of MDA19. MDA19 did not affect rat locomotor activity.

CONCLUSIONS: We found that MDA19 exhibited a distinctive in vitro functional profile at rat CB₂ receptors and behaved as a CB₁/CB₂ agonist in vivo, characteristics of a protean agonist. MDA19 has potential for alleviating neuropathic pain without producing adverse effects in the central nervous system.

我們所知的殘餘肌松。第二部分：減少殘餘肌松風險的方法

Residual Neuromuscular Block: Lessons Unlearned. Part II: Methods to Reduce the Risk of Residual Weakness

Sorin J. Brull, MD* and Glenn S. Murphy, MD†
From the *Department of Anesthesiology, Mayo Clinic College of Medicine, Jacksonville, Florida; and †Department of Anesthesiology, NorthShore University HealthSystem, University of Chicago, Evanston, Illinois.

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The aim of the second part of this review is to examine optimal neuromuscular management strategies that can be used by clinicians to reduce the risk of residual paralysis in the early postoperative period. Current evidence has demonstrated that frequently used clinical tests of neuromuscular function (such as head lift or hand grip) cannot reliably exclude the presence of residual paralysis. When qualitative (visual or tactile) neuromuscular monitoring is used (train-of-four [TOF], double-burst, or tetanic stimulation patterns), clinicians often are unable to detect fade when TOF ratios are
between 0.6 and 1.0. Furthermore, the effect of qualitative monitoring on postoperative residual paralysis remains controversial. In contrast, there is strong evidence that acceleromyography (quantitative) monitoring improves detection of small degrees (TOF ratios >0.6) of residual blockade. The use of intermediate-acting neuromuscular blocking drugs (NMBDs) can reduce, but do not eliminate, the risk of residual paralysis when compared with long-acting NMBDs. In addition, complete recovery of neuromuscular function is more likely when anticholinesterases are administered early (>15–20 minutes before tracheal extubation) and at a shallower depth of block (TOF count of 4). Finally, the recent development of rapid-onset, short-acting NMBDs and selective neuromuscular reversal drugs that can effectively antagonize deep levels of blockade may provide clinicians with novel pharmacologic approaches for the prevention of postoperative residual weakness and its associated complications.

Skin Collagen Synthesis Is Depressed in Patients with Severe Sepsis
Fiia P. Gäddnäs, MD*, Marjo Koskela, MD*, Vesa Koivukangas, MD, PhD†, Jouko Laurila, MD, PhD*, Juha Saarnio, MD, PhD†, Juha Risteli, MD, PhD‡, Aarne Oikarinen, MD, PhD§ and Tero Ala-Kokko, MD, PhD*

From the Departments of *Anaesthesiology, Division of Intensive Care, †Surgery, ‡Clinical Chemistry, and ¤Dermatology, Oulu University Hospital, Oulu, Finland.

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BACKGROUND:
Skin is an essential barrier in maintaining a stable internal environment. Adequate regenerative capacity is crucial to overcome the homeostatic challenges caused by a septic insult. In sepsis, coagulation and inflammation are activated...
to restore homeostasis, but it is not known whether sepsis also alters tissue regeneration processes such as skin collagen synthesis.

METHODS: In this prospective observational study, we measured aminoterminal propeptides of collagens I and III (PINP, PIIINP) from blister fluid of sepsis patients. Blister fluid was obtained from experimental blisters induced on intact abdominal skin 4 times: within the first 48 hours from the first organ failure, on the fifth day, and at 3 and 6 months thereafter. Forty-four patients with severe sepsis were enrolled. The median age was 63 years (25th–75th percentile, 53–71 years). The median Acute Physiology and Chronic Health Evaluation II score on admission was 26 (22–30). Thirty-day mortality was 25%. Fifteen healthy adults were used as controls.

RESULTS: Median PIIINP and PINP levels in septic patients were lower in comparison with controls in the first blister (40.8 μg/L [25th–75th percentile, 22.2–77.1 μg/L], \( P = 0.028 \) and 69.9 μg/L [32.4–112.7 μg/L], \( P < 0.001 \), respectively) and in the blister induced on day 5 (38.8 μg/L [19.9–68.5 μg/L], \( P < 0.001 \) and 90.0 [35.1–138.8 μg/L], \( P < 0.001 \), respectively). The survivors revealed an overexpression at 3 months, whereas normal values of PIIINP and PINP were reestablished at 6 months.

CONCLUSIONS: Skin collagen synthesis is depressed during severe sepsis and is followed by a compensatory response 3 and 6 months after the onset of sepsis.

氨基己酸在體外抑制新生兒血漿纖維蛋白溶解的有效濃度
The Effective Concentration of Epsilon-Aminocaproic Acid for Inhibition of Fibrinolysis in Neonatal Plasma in Vitro
Heather G. Yurka, Richard N. Wissler, Christine N. Zanghi, Xiang Liu, Xin Tu, Michael P. Eaton, and the Congenital Heart Surgery Research Interest Group
From the *Department of Anesthesiology and the †Department of Biostatistics and Computational Biology, University of Rochester School of Medicine and Dentistry, Rochester, New York.
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介紹：兒科患者，尤其是新生兒，由於他們的止血系統發育不完善，體積小，手術複雜，接受心臟手術後發生出血併發症的風險很高。血管內纖維蛋白啟動是體外迴圈最基本的影響之一，可導致術後止血功能障礙。這一併發症已被認識很久，並且用抗纖溶藥物進行治療，包括賴氨酸同型 ε 氨基乙酸(EACA)。成人的 EACA 治療血漿濃度已經科學的確定，但是新生兒的目前推薦劑量是根據成人的劑量經驗性的得來。因此，我們研究了體外迴圈時 EACA 在新生兒的合適濃度。

方法：我們用從 20 個足月、選擇剖腹產分娩的胎盤臍帶血中分離出的新生兒血漿進行了一項體外研究。在用組織型纖溶酶原啟動劑啟動纖維蛋白溶解前，將各等級濃度的 EACA 加入等分的血漿容器中。然後進行標準白陶土啟動的血栓彈性描記圖檢測，並評估溶解百分比初步結果的變異。這些過程在購買的混合成人正常血漿樣本中重複進行以作對比。

結果：我們發現完全抑制纖溶新生兒所需要的 EACA 濃度明顯低於成人（對 400 和 1000 U/mL 的纖溶酶原啟動動物，新生兒 EACA 濃度為 44.2 μg/mL 和 47.8 μg/mL，成人為 94.4 和 131.4 μg/mL，\( P < 0.001 \)）。
**INTRODUCTION:** Pediatric patients, particularly neonates, are at high risk for bleeding complications after cardiovascular surgery because of their immature hemostatic system, small size, and the complex operations they require. Activation of intravascular fibrinolysis is one of the principle effects of cardiopulmonary bypass that causes poor postoperative hemostasis. This complication has long been recognized and treated with antifibrinolytic medications, including the lysine analog ε-aminocaproic acid (EACA). The therapeutic plasma concentration of EACA has been scientifically determined for the adult population, but the current recommended dosage for neonates has been empirically derived from adult studies. Therefore, we investigated the appropriate concentration of EACA for neonates undergoing bypass.

**METHODS:** We conducted an in vitro study using neonatal plasma derived from the placenta/cord units from 20 term, elective cesarean deliveries. Graded concentrations of EACA were added to aliquots of the plasma pool before activating fibrinolysis with tissue-type plasminogen activator. Standard kaolin-activated thromboelastograms were then run with the primary outcome variable being estimated percent lysis. These procedures were repeated on samples of commercially available pooled adult normal plasma for comparison.

**RESULTS:** We found that neonatal plasma required significantly lower concentrations of EACA to completely prevent fibrinolysis than did adult plasma (44.2 μg/mL and 47.8 μg/mL for neonatal plasma and 94.4 and 131.4 μg/mL in adult plasma for 400 and 1000 U/mL of plasminogen activator, respectively, P < 0.001).

**CONCLUSIONS:** Our data establish the minimal effective concentration of EACA necessary to completely prevent fibrinolysis in neonatal blood in vitro. This concentration is significantly less than that targeted by current dosing schemes, indicating that neonates are possibly being exposed to greater levels of EACA than is clinically necessary.
In this exploratory study we evaluated sensitivity and target specificity of sinuvertebral nerve block (SVNB) for the diagnosis of lumbar diskogenic pain. Diskography has been the diagnostic gold standard. Fifteen patients with positive diskography underwent SVNB via interlaminar approach to the posterior aspect of the disk. Success was defined as ≥80% pain reduction or excellent relief of physical restrictions after the block. The sensitivity was 73.3% (95% CI: 50.9%–95.7%). The target specificity was 40% (15.2%–64.8%). The results indicate that SVNB cannot yet replace diskography but encourage future studies to improve its target specificity.

The Relationship Between Functional Sciatic Nerve Block Duration and the Rate of Release of Lidocaine from a Controlled-Release Matrix

Peter Gerner, MD*, Chi-Fei Wang, MD*, Byung-Sang Lee, MD*, Suzuko Suzuki, MD*, Umberto deGirolami, MD†, Ankur Gandhi, PhD‡, David Knaack, PhD‡, and Gary Strichartz, PhD*

From the *Department of Anesthesiology, Perioperative and Pain Medicine, Pain Research Center; †Department of Pathology, Division of Neuropathology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts; and ‡Orthocon, Inc., Newark, New Jersey.

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背景：我們希望在圍手術期和術後神經阻滯有較長維持時間。瞭解神經阻滯維持時間和局麻藥釋放速率的關係對於發展局麻藥釋放系統是重要的，從而可以優化神經阻滯持續時間。

方法：在 OSB-L 組, 利多卡因的濃度不同, 但是以恆定的速率釋放。在另一組 (OST-R), 利多卡因的濃度恒定, 但是釋放速率不同。試劑植入試驗鼠的坐骨神經附近後, 在體及離體測定與抗傷害性刺激及運動阻滯相關的釋放動力學。在平行試驗中, 實驗鼠接受了緩慢釋放的利多卡因後, 心內注射 4%多聚甲醛, 並取神經肌肉組織進行組織學分析。

結果：在這項研究中，我們證明了影響神經阻滯的各種因素中（例如阻滯坐骨神經相關纖維衝動傳導），最重要的因素是利多卡因釋放的速率。在 OSB-L 組（利多卡因的濃度分別為 1.875%, 3.75%, 7.5%和 15%, 以恆定的 5%的速率釋放）, 在體試驗中，50%運動阻滯及傷害刺激恢復的平均時間分別為 0.91 ± 0.28 和 1.75 ± 0.61 mg/h。在 OST-R 組（16%的利多卡因分別以 1.875%, 3.75%, 7.5%和 15%的濃度釋放）, 在體 50%運動阻滯及傷害性刺激恢復的平均時間分別為 2.33 ± 1.39 和 4.34 ± 1.09 mg/h。在 OSB-L 組顯示了增加利多卡因的起始濃度可以劑量依賴性的增加阻滯持續時間，而在 OST-R 組中顯示了釋放速率濃度並不是阻滯持續時間的單獨因素。在植入試後 24 小時、3 天、5 天、7 天和 4 周進行組織學研究發現炎症反應的程度和利多卡因含量正相關，但是局限在植入物周圍組織。儘管觀察到炎症反應，抗傷害性刺激及運動阻滯均可恢復到植入前。
BACKGROUND: Nerve blocks of long duration are often desirable in perioperative and postoperative situations. The relationship between the duration of such blocks and the rate at which a local anesthetic is released is important to know for developing a localized drug delivery system that will optimize block duration.

METHODS: Lidocaine concentration was varied in 1 series of formulations (OSB-L) containing a constant amount of release rate modifier. In another series (OST-R), the release rate modifier was varied while the lidocaine content was held constant. Release kinetics were measured in vitro and correlated to the in vivo duration of antinociceptive and motor block effects when the formulation was implanted next to the rat sciatic nerve. In parallel studies, rats receiving different formulations of slow-release lidocaine were fixed by intracardiac perfusion with 4% paraformaldehyde and nerve-muscle tissue taken for histopathological analysis.

RESULTS: In this study, we have demonstrated that the most important variable for effecting functional nerve block, i.e., the blockade of impulses in the relevant fibers of the sciatic nerve, is the rate of lidocaine release at that time. For the OSB-L formulations (lidocaine concentrations of 1.875%, 3.75%, 7.5%, and 15% at a constant release rate modifier of 5%), the average in vitro release rates at 50% recovery of motor block and nociceptive block were 0.91 ± 0.28 and 1.75 ± 0.61 mg/h, respectively. For the OST-R formulations (16% lidocaine with release rate modifier concentrations of 1.875%, 3.75%, 7.5%, and 15%), the average in vitro release rates at 50% recovery of motor block and nociceptive block were 2.33 ± 1.39 and 4.34 ± 1.09 mg/h, respectively. The OSB-L formulations showed a dose-dependent increase in block duration proportional to an increase in initial lidocaine concentration, whereas the OST-R formulations showed a nonmonotonic relationship between release rate modifier concentration and block duration. The histopathological studies at 24 hours, 3, 5, or 7 days, and 4 weeks after the implantation revealed inflammatory reactions with degrees correlated with lidocaine content, but limited to the connective tissue and muscle immediately surrounding the implanted material. Despite these observed inflammatory reactions, nociceptive and motor block function returned to normal, preimplantation values in all animals.

CONCLUSIONS: Increasing initial lidocaine content proportionately increased the duration of functional sciatic nerve block. However, decreasing the release rate per se does not give a proportional increase in block duration. Instead, there seems to be an optimal, intermediate release rate for achieving the maximum duration of block.