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**心肺转流术卒中实验模型中抑肽酶可以改善脑功能但是并不能缩小脑梗塞的面积
Aprotinin Improves Functional Outcome but Not Cerebral Infarct Size in an
Experimental Model of Stroke During Cardiopulmonary Bypass**

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Anesth Analg 2010;111(1):38-45

背景：抑肽酶是一种非特异性的丝氨酸蛋白酶抑制剂，一直被用于减少心肺转流术后的出血和减轻心肺转流术后的全身性炎症反应。以往各种研究结果既有表明抑肽酶可以改善心脏术后脑功能的，也有结果是恰恰相反的。我们设计了本研究来测定应用抗炎剂量的抑肽酶是否能够改善心肺转流术中局部脑缺血模型大鼠的神经系统组织结构和功能。

方法：在外科手术准备后，小鼠被随机分成两组：抑肽酶组（60,000 kIU/kg 静脉注射）和对照组（0.9% NaCl 静脉注射）。温度正常的心肺转流术持续 60 分钟，在此期间右大脑中动脉闭塞手术与心肺转流术时间部分重叠，持续 60 分钟。我们测定了操作前、心肺转流术结束时、心肺转流术结束后 2 和 24 小时时的细胞因子值（肿瘤坏死因子- α 、白介素[IL]-1 β 、IL-6 和 IL-10）。在手术后第三天我们对小鼠进行了神经病学功能测试和脑梗死面积组织学测定。

结果：抑肽酶组和对照组相比，IL-1 β 值 ($P = 0.035$) 和 IL-6 值 ($P = 0.047$) 都有所下降，表明了全身性炎症反应有所减轻。抑肽酶组神经病学功能测试结果也更好，抑肽酶组 27 [8] 比对照组 32 [6]（中位数[四分位距]， $P = 0.042$ ）。但是两组的脑梗塞面积没有区别（抑肽酶组 306 [27] mm³ 比对照组 297 [52] mm³， $P = 0.599$ ）。

结论：在这个心肺转流术期间发生的脑缺血实验模型中，抑肽酶减轻了心肺转流术引起的全身性炎症反应。虽然两组的脑梗塞面积没有区别，但是抑肽酶对短期的神经病学功能测试结果有些需改善。

（姜旭晖译，马皓琳，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 as well as 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]-1 β , 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-1 β ($P = 0.035$) 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.

使用异丙酚麻醉与七氟醚麻醉相比减轻日间手术病人的术后疼痛

Day-Surgery Patients Anesthetized with Propofol Have Less Postoperative Pain than Those Anesthetized with Sevoflurane

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背景：近期有研究发现使用异丙酚麻醉与吸入麻醉药麻醉相比可以减轻病人的术后疼痛。

方法：在本次随机双盲研究中，80位接受日间妇科诊断性腹腔镜手术的病人静脉给予异丙酚或吸入七氟醚实施麻醉。主要的测量内容是用视觉模拟评分（VAS）测量疼痛程度。

结果：接受异丙酚麻醉的病人与吸入七氟醚麻醉的病人相比疼痛较轻（ $P=0.01$ ），其他测量的临床指标之间无显著差异。

结论：使用异丙酚麻醉与吸入麻醉药麻醉相比病人的术后疼痛较轻。

（刘伍译 马皓琳 李士通校）

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.

美国和欧洲神经肌肉阻滞管理的现状调查

A Survey of Current Management of Neuromuscular Block in the United States and Europe

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背景：术后残余神经肌肉阻滞经常发生。欧洲最近的临床调查表明神经肌肉阻滞药的使用常常没有适当的监测。美国还没有这方面的对照研究。通过本调查研究，我们比较了当前美国和欧洲麻醉医生对神经肌肉阻滞药的使用和态度。

方法：我们对美国和欧洲的麻醉医生进行了一个以互联网为基础的调查。麻醉病人安全基金会和欧洲麻醉协会给它们的所有活跃会员发了电子邮件，邀请他们在一个专用的网际协议地址敏感的网站上不具名地回答一系列问题。这个调查在网上进行了60天。用 χ^2 检验和Fisher's精确检验来比较2组的临床调查项目。

结果：接受调查的总人数为2636人。美国(64.1%)和欧洲(52.2%)的大多数应答者评估临床上显著的术后残余神经肌肉无力的发生率 $<1\%$ ($P < 0.0001$)。常规药理学逆转欧洲比美国少(分别为18%和34.2%， $P < 0.0001$)，而临床医生可用的定量监护仪美国(22.7%)比欧洲(70.2%)少($P < 0.0001$)。然而，19.3%的欧洲医生和9.4%的美国医生从不使用神经肌肉监护仪。大多数应答者表示不管是常规的神经肌肉刺激器还是定量四个成串监护仪都应列入最低监测标准。

结论：我们的结果显示麻醉医生对监测神经肌肉功能的最佳方法尚没有统一的结论。我们应当通过发展正式训练计划和/或出版关于最佳实践的官方指南来努力改善苏醒以减少术后神经肌肉无力的发生率和病人的发病率。

(周洁译 马皓琳 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 χ^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.

在低氧血症中通过脉搏心输出量—血氧测定法检测高铁血红蛋白的准确性

Accuracy of Methemoglobin Detection by Pulse CO-Oximetry During Hypoxia

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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读取的准确性，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，每个人安置多个传感器和桡动脉导管供血液采样。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%)水平不同的低氧。第二组，目标为室内空气中高铁血红蛋白 15% 以及 SaO₂80% 水平。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平上有意义的读取错误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。这是用来确定影响测定高铁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确度是 7.7% ± 13.0%。SaO₂ 范围在 95%—100% 时最准确(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% 和高铁血红蛋白 4%—15% 时，Radical-7 和 Nonin 9700 脉搏血氧计都精确地检测到了下降，但是 SaO₂ >95% 时也会显示低的 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准确，有时候会高估实际值 10%—40%。升高的高铁血红蛋白会使 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%) 且高铁血红蛋白水平高达 15% 的时候，两种仪器的 SpO₂ 读数都趋向于下降。

(唐亮译 马皓琳 李士通校)

BACKGROUND: Methemoglobin in the blood cannot be detected by conventional pulse oximetry, although it can bias the oximeter's estimate (SpO_2) of the true arterial functional oxygen saturation (SaO_2). 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 SaO_2 .

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 SaO_2 (70%–100%) by varying fractional inspired oxygen. In the second group, 15% methemoglobin at room air and 80% SaO_2 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. SpO_2 reading bias, precision, and root mean square error were evaluated during conditions of elevated methemoglobin.

RESULTS: Observations spanned 66.2% to 99% SaO_2 and 0.6% to 14.4% methemoglobin over the 2 groups (170 blood draws). Masimo methemoglobin reading bias and precision over the full SaO_2 span was $7.7\% \pm 13.0\%$. Best accuracy was found in the 95% to 100% SaO_2 range ($1.9\% \pm 2.5\%$), progressing to its worst in the 70% to 80% range ($24.8\% \pm 15.6\%$). Occurrence of methemoglobin readings in error $>5\%$ increased over each 5-point decrease in SaO_2 ($P < 0.05$). Masimo SpO_2 readings were biased $-6.3\% \pm 3.0\%$ in the 95% to 100% SaO_2 range with 4% to 8.3% methemoglobin. Both the Radical-7 and Nonin 9700 pulse oximeters accurately detected decreases in $SaO_2 < 90\%$ with 4% to 15% methemoglobin, despite displaying low SpO_2 readings when SaO_2 was $>95\%$.

CONCLUSIONS: The Radical-7's methemoglobin readings become progressively more inaccurate as SaO_2 decreases $<95\%$, at times overestimating true values by 10% to 40%. Elevated methemoglobin causes the SpO_2 readings to underestimate SaO_2 similar to conventional 2-wavelength pulse oximeters at high saturation. SpO_2 readings from both types of instruments continue to trend downward during the development of hypoxemia ($SaO_2 < 90\%$) with methemoglobin levels up to 15%.

肺泡而非静脉右旋氯胺酮抑制大鼠肺泡钠转运和肺液体清除率

Alveolar but Not Intravenous S-Ketamine Inhibits Alveolar Sodium Transport and Lung Fluid Clearance in Rats

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背景：右旋氯胺酮(S-ketamine)常用于镇痛镇静，特别是败血症和心血管不稳定情况下。由于右旋氯胺酮阻断神经元和骨骼肌电压门控钠离子(Na⁺)通道，因此可以推测右旋氯胺酮也能阻断决定肺泡液体清除率(AFC)的肺泡上皮钠通道。我们研究了经肺泡和经静脉给予右旋氯胺酮对跨肺泡膜 Na⁺转运和 AFC 的影响，并观察右旋氯胺酮静脉注射是否会因为内毒素血症引起的肺炎而进入肺泡腔。

方法：在培养的大鼠肺泡 II 型 (ATII) 细胞中加入右旋氯胺酮和/或 Na⁺通道阻滞剂阿米洛利(100 μM)，并在体外扩散池(Ussing chambers)中通过测量短路电流 (ISC) 反映跨上皮转运率。在采用含有或不含有阿米洛利的灌流液缓慢灌注的麻醉大鼠肺中测量肺泡液体清除率(AFC)。右旋氯胺酮静脉注射或加入灌注液中。采用静脉注射脂多糖(7.5 mg/kg)诱导内毒素血症所致轻度肺损伤模型，该模型或许使静脉注射的右旋氯胺酮易于到达肺泡表面。

结果：不管肺顶端(-18.9%± 1.4%; *P* < 0.001) 还是底外侧(-20.4% ± 3.7%; *P* < 0.001) 给药，右旋氯胺酮(25 μg/mL)均能降低 ATII 细胞的 ISC。对于阿米洛利预处理的 ATII 细胞，顶端或者底外侧给予右旋氯胺酮均不能降低 ISC。对照组大鼠每 30 min 的 AFC 大约为 8%。灌注液中的右旋氯胺酮(5 μg/mL)则通过降低阿米洛利敏感性跨上皮钠转运，而使得 AFC 降低至 1.1% ± 1.5% (*P* = 0.04)。静脉注射右旋氯胺酮(20 mg/kg)不影响 AFC(*P* = 0.31)。在脂多糖诱导的炎症情况下，静脉注射右旋氯胺酮后支气管肺泡灌洗液中的右旋氯胺酮浓度仍低于抑制 AFC 的浓度。

结论：尽管右旋氯胺酮处理大鼠肺泡上皮降低了阿米洛利敏感性跨肺泡的 Na⁺转运和 AFC，但是，即使在轻度肺损伤的情况下，静脉注射临床剂量右旋氯胺酮也不影响 AFC。

(江继宏 译 马皓琳 李士通 校)

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 $\mu\text{g}/\text{mL}$) caused a decrease of ISC regardless of apical ($-18.9\% \pm 1.4\%$; $P < 0.001$) or basolateral ($-20.4\% \pm 3.7\%$; $P < 0.001$) 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 $\mu\text{g}/\text{mL}$) in the instillate reduced AFC to $1.1\% \pm 1.5\%$ ($P = 0.04$) 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.

患有恶性高热和中央轴空病的瑞典患者中 RYR1 突变基因的功能特性

Functional Properties of RYR1 Mutations Identified in Swedish Patients with Malignant Hyperthermia and Central Core Disease

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背景：经体外收缩测试得到的恶性高热易感性诊断往往只是在远离患者生活的专科实验室里完成的。因此，我们设计了一个方案用于得到 RYR1-cDNA 的基因筛选和从当地初级医疗中心收集到外周血标本分离的 B 淋巴细胞中新确定的兰尼碱受体-1 (RYR1) 基因变种的功能性测试。

方法：分离 B 淋巴细胞用于提取 RYR1-mRNA 和基因组 DNA，并用于在 5 名携带未分类 RYR1 突变的患者体内建立类 B 淋巴母细胞系。用类 B 淋巴母细胞系来研究静态胞质钙浓度、来自胞质网状组织 Ca-ATP 酶抑制剂毒胡萝卜素诱发的钙瞬变高峰以及兰尼碱受体激动剂 4-氯间甲酚诱发的剂量依赖性的钙释放。

结果：通过提取 mRNA 用于合成 cDNA, 以及在所有的标本中建立 B 淋巴细胞株都是可能的。和对照组相比，所有携带 RYR1 潜在突变基因的 B 淋巴细胞系与对照相比较，都显示了静息期胞浆钙浓度的明显增高及引起钙释放的 4-氯间甲酚浓度的下降。

结论：常温下通过长途平信运送的用于提取 DNA 和 RNA 以及建立 B 类 B 淋巴母细胞系的外周血标本是稳定的。隐藏有新确定的氨基酸取代基的 B 细胞功能的测试表明，他们改变细胞内钙离子的内稳态，并且是恶性高热发生的最可能因素。

(杨秀娟 译 马皓琳 李士通校)

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.

周树脂毒联合抗抑郁药优先延长大鼠坐骨神经的感觉/伤害性刺激阻滞

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

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背景：当前外周神经阻滞技术具有较大的限制，包括运动纤维和感觉纤维之间缺乏分化以及局麻药的潜在毒性。最近的研究提示通过一个短暂受体潜在的类香草精1型活化剂（辣椒辣素）以及局麻药得到感受伤害选择性神经阻滞。我们假设结合强效短暂的受体潜在的类香草精1型活化剂周树脂毒（RTX）以及选择性抗抑郁药（阿米替林、多虑平、氟西汀和强效钠离子通道阻滞剂）可以延长并优先感觉神经阻滞。

方法：异氟醚麻醉大鼠，0.2ml 阿米替林、多虑平或者氟西汀注射于仅靠外科暴露的坐骨神经（每组 $n=8$ ）。一些动物接受包括 RTX 的第二次注射（每组 $n=8$ ）。

通过运动功能的神经行为学测试（伸肌突伸）以及疼痛反射（机械性回缩）评价神经阻滞的效果。

结果：单纯运用 RTX 产生疼痛选择性坐骨神经阻滞，而抗抑郁药物产生感受伤害以及运动阻滞。联合运用 RTX 以及抗抑郁药可得到主要为疼痛神经的阻滞。对比单用抗抑郁药或 RTX，联合使用可延长疼痛神经阻滞并优于运动阻滞。

讨论：联合运用 RTX 以及抗抑郁药物较各自单用可显著延长大鼠坐骨神经中的外周疼痛阻滞。然而，两种药物给药法也诱出延长运动功能的阻滞，但其效果小于疼痛感觉阻滞，提示了存在非短暂的受体潜在的类香草精 1 型活化剂的机制。RTX 影响疼痛信号传导/传递的机制并没有得到完全解释。

（龚寅 译 马皓琳、李士通 校）

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 nociceptive 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.

多点注射腋路臂丛阻滞：肥胖对失败率和急性并发症发生率的影响

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

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背景: 在区域麻醉中, 肥胖常常伴随着更高的失败率, 但是目前还没有人评估过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% 罗哌卡因 6mL、10mL 和 20mL 阻滞肌皮神经、正中神经和桡神经。通过末梢运动反应(腕关节或手指)判断正中神经和桡神经的阻滞效果。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 ($BMI \geq 30 \text{ kg/m}^2$)。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) 的发生率高于非肥胖患者 (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生率。此外, 更多的肥胖患者对麻醉效果不满意。

(徐妍君 译 马皓琳 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 $\geq 30 \text{ kg/m}^2$). 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.

中枢阿片受体激活介导心脏缺血再灌注损伤的保护作用

Activation of Central Opioid Receptors Induces Cardioprotection Against Ischemia-Reperfusion Injury

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背景：鞘内注射小剂量吗啡可以产生类似于静脉注射吗啡合并缺血预处理的心脏保护作用。作者研究了鞘内注射吗啡预处理（ITMPC）时中枢和外周阿片受体的相对作用。

方法：48只开胸后麻醉中的SD雄性大鼠，成功放置鞘内导管后，被分配到7个治疗组中的一组（每组6-7个）。ITMPC通过连续3次鞘内注射吗啡预处理5分钟（每次1.0 μg/kg）获得。结合静脉（静脉注射碘化纳络酮+ITMPC）或者鞘内（鞘内注射碘化纳络酮+ITMPC）注射碘化纳络酮，重复应用预处理。另外，在不用鞘内注射吗啡预处理下，采用相同的方法注射化合物（静脉+鞘内注射碘化纳络酮）。鞘内注射生理盐水和缺血预处理分别作为阴性和阳性对照。心肌缺血再灌注损伤通过阻断左冠状动脉30min后再灌注2h获得。由2,3,5-三苯基四唑染色来确定缺血危险区比例，即心肌梗死面积。

结果：与对照组(48% ± 9%)相比，缺血预处理组(22% ± 3%)和鞘内吗啡预处理组(26% ± 5%)的梗死面积/危险区域(22% ± 3%)明显降低($P < 0.01$)。此外鞘内注射碘化纳络酮还逆转了鞘内注射吗啡预处理的心脏保护作用(45% ± 4%)，而静脉用药对鞘内注射吗啡预处理没有任何影响(28% ± 9%, $P < 0.01$)。

结论：鞘内注射吗啡预处理可以通过激活中枢阿片受体来产生心脏保护作用，外周阿片受体没有明显的作用。

（黄丹 译 陈杰 校）

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 μg/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.

胸腹主动脉手术中腰部脑脊液引流：基本原理和操作指南

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

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截瘫仍是胸腹主动脉瘤手术的最严重的并发症之一，与并发症发生率和死亡率增加密切相关。现代主动脉修复技术使用各种方法来减少手术相关的脊髓缺血危险。这些方法之一是通过腰部脑脊液（CSF）的引流来优化脊髓血流量。单独或与其他措施相结合，脑脊液引流仍然是最常用的脊髓保护技术之一。尽管没有降低脊髓损伤有效性的确切证据，但是有令人信服的数据支持这项技术的运用。然而，脑脊液引流的潜在优点，必须兼顾其风险，包括插入时神经损伤，椎管内压迫轴索性血肿形成，由于引流过多导致的颅内出血和感染等。可以通过了解其使用的基本原理及遵守实践指南来实现最佳效益风险比。

（陈毓雯 译 陈杰 校）

Paraplegia remains one of the most devastating 灾难性 complications of thoracoabdominal aortic surgery and is associated with a significant increase in both morbidity and mortality. Modern aortic repair techniques use many modalities 方式 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 有说服力的 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.

吸入麻醉药的潜在全球变暖效应：临床应用

Global Warming Potential of Inhaled Anesthetics: Application to Clinical Use

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背景：吸入麻醉药是公认的温室气体。本文通过计算其在常见的临床使用过程中的相当的二氧化碳总排放量来比较不同的吸入麻醉药对环境的影响。

方法：作者先确定七氟醚和异氟醚红外吸收截面积。运用以前公布的地氟醚，七氟醚，异氟醚的红外线吸收数据计算 20 年全球变暖潜能值（GWP₂₀），且确定大气中各气体最适存在周期。在每小时最小肺泡浓度（MAC）下使用每种麻醉剂的总量乘以计算出的 GWP₂₀，表示为每克“二氧化碳当量”（CDE₂₀）。计算时根据目前临床吸入麻醉的方法，将分别计算由空气/氧气作为载体或 N₂O/氧气的混合气体作为载体时二氧化碳当量数值。

结果：对吸入麻醉药 GWP₂₀ 计算值分别为：七氟醚 349，异氟醚 1401，地氟醚 3714。2 L/h 新鲜气流量下 1MAC 每小时的 CDE₂₀ 的预测值分别为：七氟醚 6980 g，异氟醚 15,551 g，地氟醚 187186g。这些麻醉药之间的比率为七氟醚 1，异氟醚 2.2，地氟醚 26.8。当 60%N₂O 与 40%氧气的混合气体替代空气/氧气作为载体，同时吸入麻醉药调整为每小时 1MAC，七氟醚 CDE₂₀ 值分别高出 5.9 倍，异氟醚 CDE₂₀ 值高出 2.9 倍，而地氟醚 CDE₂₀ 值降低，为 0.4 倍。以 100 年为时间水平运用 60%N₂O 作为载体时，七氟醚 CDE₁₀₀ 值比空气/氧气作为载体高出 19 倍，异氟醚的值高出 9 倍，地氟醚的值无差异。

结论：根据比较结果和临床环境，地氟醚对全球变暖的影响超过七氟醚与异氟醚。应用七氟醚或异氟醚，将 N₂O 作为载体将产生更多的温室气体。此外，60% 氧化亚氮与吸入麻醉剂混合使用，在相同 MAC 的麻醉下大幅度增加七氟醚和异氟醚对环境的影响，而地氟醚对环境的影响降低。氧化亚氮会破坏臭氧层及使全球升温趋势；且影响的持续时间更长，与地氟醚混合使用可能不是一个环保的折衷方案。根据计算研究，避免 N₂O 及不必要的高流量气体可降低吸入麻醉对环境的影响。

（陈毓雯 译 陈杰 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 CDE₂₀ values were 5.9 times higher with N₂O than when carried with air/O₂, isoflurane values were 2.9 times higher, and desflurane values were 0.4 times lower. On a 100-year time horizon with 60% N₂O, the sevoflurane CDE₁₀₀ values were 19 times higher than when carried in air/O₂, isoflurane values were 9 times higher, and desflurane values were equal with and without N₂O.

CONCLUSIONS: Under comparable and common clinical conditions, desflurane has a greater potential impact on global warming than either isoflurane or sevoflurane. N₂O alone produces a sizable greenhouse gas contribution relative to sevoflurane or isoflurane. Additionally, 60% N₂O 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. N₂O 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 N₂O and unnecessarily high fresh gas flow rates can reduce the environmental impact of inhaled anesthetics.

残余神经阻滞:易忘掉的课业.第一部分:残余神经阻滞的定义,发生率和不良生理学反应

Residual Neuromuscular Block: Lessons Unlearned. Part I: Definitions, Incidence, and Adverse Physiologic Effects of Residual Neuromuscular Block

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在这篇综述中,作者总结了残余神经阻滞的临床并发症。数据表明,残余神经阻滞在麻醉后监护室是一个常见的并发症,将近 40% 的患者出现了一次 TOF<0.9。志愿者研究表明,低程度的残余麻痹 (TOF 0.7–0.9) 与咽反射受损,误吸风险增加,上呼吸道肌无力,气道阻塞,低氧通气反应 (将近 30%), 以及肌肉无力的不愉快症状相关。临床研究已经证实术中神经肌肉管理与术后不良事件相关。大型数据库调查发现,术中神经肌肉阻滞剂的应用和残余神经神经肌肉阻滞是麻醉相关发病率和死亡率的重要危险因素。此外,观察和随机临床试验表明,术后早期不完全的神经肌肉功能的恢复可能导致急性呼吸症状 (低氧血症和气道阻塞), 肌肉无力引起的不愉快症状,麻醉后监护室停留时间延长,气管拔管延迟,以及术后肺部并发症风险增加。这些近期的数据表明,残余神经肌肉阻滞是一个有关患者安全的重要问题,且神经肌肉阻滞的管理影响手术预后。

(怀晓蓉 译 陈杰 校)

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.

麻醉诱导期间采用高分辨率固体测压计测定食管上、下括约肌压力：肥胖和非肥胖病人间的比较

High-Resolution Solid-State Manometry of the Upper and Lower Esophageal Sphincters During Anesthesia Induction: A Comparison Between Obese and Non-Obese Patients

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背景：近几十年肥胖发生率有了显著增长。肥胖相关的围术期胃肠道变化对于麻醉医师有重要的临床意义。食管下、上括约肌在防止反流和误吸中起主要作用。麻醉过程中增加的腹内压对肥胖病人的食管上下括约肌的影响尚未明确。此研究采用高分辨率固体测压计评估麻醉诱导过程中肥胖和非肥胖病人的食管上括约肌、食管下括约肌和屏障压（BrP）（食管下端压力－胃内压）。

方法：使用高分辨率固态食管测压计研究 28 名 18—72 岁的患者。14 名进行腹腔镜胃旁路手术的病人 BMI 指数大等于 35 kg/m²，另 14 名进行腹腔镜胆囊切除术的病人 BMI 指数小等于 30kg/m²。

结果：两组食管上括约肌压力在麻醉诱导时均有下降。两组食管下括约肌压力在麻醉诱导时也均下降，且肥胖组较非肥胖组病人下降更为明显。两组屏障压也下降，且肥胖组较非肥胖组下降更为明显。但两组所有时刻屏障压为正值。

结论：两组麻醉诱导时食管下括约肌和屏障压均下降，但肥胖组下降更显著。尽管屏障压有明显下降，但所有病人的压力值均为正值。

（於章杰 译 陈杰 校）

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)

(lower esophageal pressure – gastric pressure) in obese patients during anesthesia induction and compared them with pressures in non-obese patients.

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.

行心肺转流术的婴幼儿中活化凝血时间值与肝素浓度测定值的关系

Correlations Between Activated Clotting Time Values and Heparin Concentration Measurements in Young Infants Undergoing Cardiopulmonary Bypass

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背景：在婴幼儿行心肺转流术（CPB）时检测活化凝血时间（ACT）的同时检测肝素浓度可以给我们肝素的应用提供一个更为精确的指导。然而，肝素的标准实验室测定法（即抗 Xa 因子浓度测定）需要测定的是血浆而不是全血，且医生并不能马上得到其测定结果。另外，应用一种自动鱼精蛋白滴定仪器——Hepcon 测试仪（即 Hepcon 完整式凝血测试系统支持；美国美敦力公司提供，美国明尼苏达州明尼阿波利斯市，MN）能在床边进行全血肝素浓度测试。本次研究的目的是为在年龄小于 6 月的行 CPB 的婴幼儿中，将三种不同商家的仪器测试出的 ACT 及床边运用 Hepcon 测试出的全血肝素浓度和实验室抗 Xa 因子血浆肝素浓度测定法的结果进行比较。

方法：本次研究的入组患者为年龄小于 6 月择期行 CPB 下心脏手术的婴幼儿 44 例。抽取注射肝素首次剂量后 3 分钟以及 CPB 停机前即刻的血样作为肝素抗凝指标的检测样本。高岭土-激活活化凝血时间 ACTs 应用 Hemochron 测定仪（由美国国际诊断技术公司提供，Edison, NJ），Hepcon 测定仪，及 i-STAT 测定仪（由 i-STAT 公司提供，东温莎，NJ）三种仪器进行测试。全血肝素浓度应用 Hepcon 测定仪进行测试。血浆肝素浓度应用实验室抗 Xa 因子发色底物法测定。

结果：在肝素首次剂量后即刻的测量值中，三组 ACT 值均与血浆肝素浓度不相关。在 CPB 停机前即刻，只有 i-STAT 仪器测定的 ACT 值与其有一定相关性。相

反，在两个测试时间点，床边测定全血肝素浓度值与实验室血浆肝素浓度值相当一致（一致性相关系数分别为 0.30 和 0.67）。通过抗 Xa 因子测定的血浆肝素浓度值比 Hepcon 测定仪测定的全血肝素浓度值要高一些。

结论：行 CPB 的年龄小于 6 月的婴幼儿中，单应用 ACT 值作为唯一评判肝素抗凝的指征应尤为谨慎。通常，ACT 与血浆肝素浓度相关性并不大。只有应用 i-STAT 仪器进行 ACT 测试时在停机前即刻 ACT 与血浆肝素有一定相关性。而应用 Hepcon 仪器进行床边全血肝素浓度测定与应用抗 Xa 因子测定值基本相一致。研究数据表明了临床上在婴幼儿中床边进行肝素浓度测试及时、便捷、精确。

（赵嫣红 译 陈杰 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 发色底物法

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 恰当 when using ACT values as the sole 单独的 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.

有与没有颅内压监测的幼猪大脑的无创自我调节功能监测

Noninvasive Autoregulation Monitoring with and without Intracranial Pressure in the Naïve Piglet Brain

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背景：对于那些没有有创颅内压监测的危重病人，其脑血管的自我调节功能的监测是很有必要的。没有颅内压监测，则动脉血压可以代替脑灌注压来测量各动脉压力跨度范围内脑血流的限制情况。本研究比较了低血压模型中使用动脉压和脑灌注压对于自我调节功能监测的差异。

方法：给予试验幼猪(5-7天龄)致命性的低血压来确定新生大脑的颅内压，并判断其自我调节的最低限度(LLA)。试验共有 25 只幼猪，连续监测颅内压、局部脑血氧饱和度 (rSO₂)、脑皮层红细胞流量 (多普勒)。之后用两种方法结合脑氧合指数 (Cox) 来评价自我调节功能：动脉血压和局部脑血氧饱和度 (COX_{ABP}) 间的线性关系以及脑灌注压和局部脑血氧饱和度 (COX_{CPP}) 间的线性关系。从红细胞流量对动脉血压的图表中可以判断自我调节的最低限度。本试验以 COX_{ABP} 和 COX_{CPP} 的平均值为基点，以 5mmHg 作为最小间距，绘制这两种方法的受试者操作特征曲线。

结果：为了确定自我调节的最低限度，COX_{ABP} 和 COX_{CPP} 两种方法得出相同的受试者操作特征曲线区域为 0.91 (95% CI : 0.88-0.95)。但两种方法的阈值不一样：判定动脉血压低于自我调节的最低限度时，其 COX_{ABP} 的阈值是 0.5，敏感度 89% (95% CI, 81%-94%)，特异度 81% (95% CI, 73-88%)。而对于 COX_{CPP} 来说，其阈值是 0.42，敏感度同样是 89% (95% CI, 81%-94%)，而特异度为 77% (95% CI, 69-84%)。

讨论：对新生大脑使用动脉血压而不是脑灌注压进行自我调节监测，同时结合 Cox 值，用来区分动脉压是高于还是低于自我调节的最低限度，这种方法的阈值有所升高。然而两种方法的准确性相似。这些发现说明了对于没有颅内压监测的病人可以用近红外光谱来监测自我调节功能。

(张婷 译 陈杰 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 (CO_xABP) and between CPP and rSO₂ (CO_xCPP). The lower limits of autoregulation were determined from plots 作图 of red cell flux versus ABP. Averaged values of CO_xABP and CO_xCPP from 5 mm Hg ABP bins 箱? were used to show receiver operating characteristics for the 2 methods.

RESULTS: CO_xABP and CO_xCPP yielded 生产 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 CO_xABP 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 CO_xCPP 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 近红外光谱 to monitor autoregulation in patients without ICP monitors.

啮齿类动物模型中罗哌卡因外周神经注射伤

Ropivacaine-Induced Peripheral Nerve Injection Injury in the Rodent Model

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背景：神经内注射局麻药总是与神经损伤相关。作者本研究的目的是探索罗哌卡因神经内注射所引起的大鼠坐骨神经的组织学改变。

方法：54只雄性成年 Lewis 大鼠随机分成9组，每组6只。将50微升生理盐水或10%苯酚或0.75%罗哌卡因分别进行神经束内、神经束外或者神经外（局部）注射。2周后将动物处死，分别用光学显微镜、定量组织学检查和电子显微镜评估注射部位的坐骨神经。

结果：横断面评估发现，神经束外及神经外注射罗哌卡因均可引起神经束膜的损伤，并伴随着神经组织中心脱髓鞘，外周环绕着水肿的神经内膜。神经束内注射罗哌卡因引起的脱髓鞘改变呈楔形，中央轴突消失，并伴有一些再生组织，边缘是正常有髓鞘区域，它们的周围是水肿的神经内膜。定量组织学检查显示，神经束外注射引起的神经损伤较神经外注射严重得多，但仍轻于神经束内注射者。从数量上来说，注射罗哌卡因的标本较注射生理盐水的标本其神经密度低得多。从电镜下还可以发现神经组织呈华勒样变性，以及神经周围水肿。

结论：本次研究表明，向大鼠模型以神经束内或神经束外的方式注射罗哌卡因后，可引起严重的组织学异常，包括神经束膜水肿和华勒样变性后发生的轴突的破坏。神经束外和神经外注射引起的损伤是相似的，尽管比神经束内注射的组织学损伤轻微。如果本次研究中观察到的组织学异常真实存在，那么将来还需进一步的工作以研究其对功能的影响。

(周姝婧 译 陈杰 校)

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 intrafascicular injection, extrafascicular 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, extrafascicular 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. Extrafascicular 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. Extrafascicular 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.

颈丛神经阻滞局麻液中辅以芬太尼对局麻时效的影响：一项随机、对照研究

The Addition of Fentanyl to Local Anesthetics Affects the Quality and Duration of Cervical Plexus Block: A Randomized, Controlled Trial

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背景：颈丛神经阻滞常被认为是非完善的感觉阻滞，在这项随机，双盲，对照试验中，作者比较了颈动脉内膜剥脱术（CEA）中，局麻液中加入芬太尼后是否改善颈丛神经阻滞效果。

方法：77名择期行CEA术的成年患者，行颈深丛神经阻滞，随机分组：实验组局麻液中加入芬太尼1 mL (50 μg)，对照组加入生理盐水1 mL，分别与0.5%布比卡因10 mL和2%利多卡因4 mL配置成混合液。同时用0.5%布比卡因10 mL和2%利多卡因4 mL行颈浅丛阻滞。用视觉模拟评分评估疼痛(0–10; 0 = 无痛, 10 = 疼痛难以忍受), 对于术中疼痛评分大于3者给予异丙酚20mg静脉推注。记录术中所需药物追加时间以及从术后24小时内所需镇痛情况, $P < 0.05$ 认为有统计学意义。

结果：芬太尼组术中追加异丙酚(4 of 38, 10.5%)明显少于对照组(26 of 39, 66.7%; $P < 0.001$)。尽管两组的阻滞起效时间无明显差异(各自的中位数为12 [9–18] vs 15 [9–18] 分; $P = 0.18$)。但相比对照组, 芬太尼组需要异丙酚的量更少(分别是中位数0 [0–60] vs 60 [0–160] mg; $P < 0.001$), 需要术后镇痛的发生率更低(分别是22 / 38例, 57.9% vs 35 / 39例, 89.7%; $P = 0.002$), 术后首次镇痛的时间更晚(分别是中位时间5.8h [1.9–15.6] 和3.1 [1.0–11.7] h; $P < 0.001$)。

结论：在CEA中, 以局部麻醉药中辅助芬太尼可以改善颈丛阻滞的作用, 并延长阻滞时间。

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.

吸入一氧化碳可通过介导热休克反应预防猪体外循环术后急性肾损伤的发生

Inhaled carbon monoxide prevents acute kidney injury in pigs after cardiopulmonary bypass by inducing a heat shock response.

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背景：体外循环术（CPB）与急性肾损伤（AKI）之间可能存有一定联系。而吸入一氧化碳（CO）具有细胞及器官的保护作用。此研究拟通过以吸入CO为预处理措施预防体外循环相关性急性肾损伤的发生。

方法：将试验用猪（n=38）非随机地分配至假CPB组、标准CPB组、假或标准CPB前CO预处理组（250ppm、1小时）、吸入CO和进行CPB前槲皮素（热休克反应抑制剂）或肾小管间质性原卟啉-IX（SnPPIX、内源性CO衍生抑制剂）预处理组。初步的试验数据为AKI的相关指标（包括尿素、尿酸、肌酐、半胱氨酸蛋白酶抑制剂C、中性粒细胞明胶酶相关脂质运载蛋白、白介素-6、肿瘤坏死因子- α 等），其均取CPB后120分钟时予以检测。进一步的检测数据为热休克蛋白（HSP）-70及血红素氧化酶-1蛋白的表达量，其可作为CO介导的热休克反应的指示剂。

结果：CO预处理减轻了体外循环相关性急性肾损伤的发生（P均<0.001），主要表现在（1）血清中半胱氨酸蛋白酶抑制剂C（64±14对28±9 ng/mL）、中性粒细胞明胶酶相关脂质运载蛋白（391±65对183±56 ng/mL）、肾肿瘤坏死因子- α （450±73对179±110 pg/mL）、及白介素-6（483±102对125±67 pg/mL）的浓度均明显提高；（2）肾脏天冬氨酸特异性半胱氨酸蛋白酶-3活性（550±66对259±52相对荧光单位）显著增加及（3）急性肾损伤的组织学证据。上述效应均伴随有HSP-70的激活（196±64对554±149 ng/mL，P<0.001）。热休克反应抑制剂槲皮素预处理可消除CO相关的生化和组织学肾保护效应（P均<0.001），而血红素氧化酶抑制剂SnPPIX仅能部分抵抗CO相关的肾保护作用及阻碍热休克反应激活。

结论：组织学受损表现的减少及半胱氨酸蛋白酶抑制剂C浓度的下降证实CPB前行CO预处理具有明确的肾保护依据。研究发现，CO的抗炎及抗细胞凋亡效应与HSP-70的受激活相伴产生，而槲皮素对其效应的逆转作用提示CPB前行CO预处理的肾保护措施是通过激活肾脏的热休克反应而介导的。

（范羽译 薛张纲校）

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- α (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.

主动脉瓣修补术中的经食管超声心动图评估

Transesophageal echocardiographic evaluation during aortic valve repair surgery.

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对于主动脉瓣膜疾病和主动脉狭窄的患者，最经典的治疗方法是主动脉瓣置换术。与之相比，主动脉关闭不全修复术是一种新兴的具有可行性并且具有吸引力的方法，它对于伴或不伴有主动脉根部病变均适用。主动脉瓣是主动脉根部的组成部分之一。因此，当一个或更多的主动脉根部的组成部分发生病变时，主动脉关闭不全的病情就会进展。术中的经食管超声心动图评估方法可以分析主动脉返流的机制以及鉴别可修复与不可修复的主动脉瓣病变。修复术后即刻的经食管超声心动图能提供很多重要信息，包括修复的质量，修复的耐久性以及发现与主动脉关闭不全有关的多种因素征象。

(黄剑译 薛张纲校)

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.

大麻素配体 MDA19 治疗神经性疼痛的药理特性

Pharmacological Characterization of a Novel Cannabinoid Ligand, MDA19, for Treatment of Neuropathic Pain

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背景：大麻素受体 2 (CB₂) 激动剂治疗神经性疼痛潜在靶点的研究近来引起关注。通过研究，我们描绘一个 CB₂ 激动剂复合物 N'-[(3Z)-1-(1-己基)-2-氧代-1,2-二氢-3H-吲哚-3-亚基]的药理学曲线。

方法：我们对人和大鼠的 CB₁ 和 CB₂ 受体采用放射性配体结合分析以及多次体外功能性分析。评估 MDA19 对逆转大鼠及 CB₂^{+/+} 和 CB₂^{-/-} 小鼠各式神经性疼痛的作用。

结果：MDA19 对人 CB₂ 受体的亲和力是 CB₁ 受体的 4 倍

(K₁=43.3±10.3vs162.4±7.6 nM)，对大鼠 CB₂ 受体的亲和力是 CB₁ 受体的近 70 倍 (K₁=16.3±2.1vs1130±574nM)。在鸟苷三磷酸 (GTP) γ[³⁵S]功能性分析中，MDA19 对人类 CB₁ 和 CB₂ 受体及大鼠 CB₁ 受体有激动作用，对大鼠 CB₂ 受体起反激动作用。3,5-环单磷酸腺苷 (cAMP) 中，MDA19 对大鼠 CB₁ 受体有激动作用，对大鼠 CB₂ 受体没有作用。对细胞外信号调节激酶 1 和 2 的活化分析显示 MDA19 对大鼠 CB₂ 受体有激动作用。MDA19 可减弱 CB₂^{+/+} 小鼠由脊神经离断或紫杉醇剂量依赖所致的异常疼痛，对 CB₂^{-/-} 小鼠无此作用，表明 MDA19 通过 CB₂ 受体发挥作用。MDA19 不影响大鼠的运动能力。

结论：MDA19 在体外功能性研究中对大鼠 CB₂ 受体有显著作用，在体内类似蛋白激动剂对 CB₁/CB₂ 有激动作用。MDA19 在减缓神经性疼痛而不对中枢神经系统产生副作用方面有很大优势。

(毛慧译，薛张纲校)

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±574nM). 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.

我们所知的残余肌松。第二部分：减少残余肌松风险的方法

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

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本综述第二部分的目的是观察可在术后早期供临床医生运用的最优的神经肌肉管理策略。现代观点认为临床频繁使用的判断神经肌肉功能的测试如抬头或握拳不能可靠的排除残余肌松的存在。当使用定性（视和触）的神经肌肉监测如四个成串刺激，双重爆发刺激或强直刺激，四个成串刺激比值为0.6至1.0之间视临床医生常常不能发现衰减。而且定性监测在术后残余肌松方面的作用意见仍不一。然而，强有力的证据显示加速度法监测（定量法）能更好的检测较少的残余肌松（四个成串刺激比值>0.6）。中效的神经肌肉阻滞剂与长效神经肌肉阻滞剂相比能减少但不能消除残余肌松的风险。而且，抗胆碱酯酶药物应用早（拔管前15-20分钟）、神经阻滞较浅时（四个成串刺激比值为4）更有可能使神经肌肉功能完全恢复。最后，新近发明的起效快、作用时程短的神经肌肉阻滞药物和有效拮抗较深程度神经肌肉阻滞的选择性的神经肌肉逆转药物可能在预防术后残余肌松及其并发症方面为临床医生提供新的选择。

(姚敏敏译 薛张纲校)

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.

严重败血症患者的皮肤胶原蛋白合成降低

Skin Collagen Synthesis Is Depressed in Patients with Severe Sepsis

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背景：皮肤是保持内环境稳定的重要屏障。足够的再生能力对于克服污染菌侵袭所带来的对内稳态的挑战是非常重要的。已知在发生败血症时凝血功能和炎症被激活来恢复内稳态，但不知道败血症是否也影响组织再生如皮肤胶原蛋白的合成。

方法：在这项前瞻性观察研究中，我们测量败血症患者水疱液中胶原蛋白 1 和胶原蛋白 3 的氨基酸多肽的合成。水疱液来自于腹部皮肤实验诱导所得的水疱的四个时相：第一个器官功能衰竭内的 48 小时、第 5 天以及 3 个月和 6 个月后。44 个重度脓毒症患者收入组内。年龄中位数为 63 岁（四分之一位数和四分之三位数为 53 岁和 71 岁）。入选者的急性生理学和慢性健康评估得分的中位数为 26（22-30）。30 天的死亡率为 25%。15 名健康成人入选对照组。

结果：与对照组相比，胶原蛋白 1 和胶原蛋白 3 的中位数水平在败血症患者的水疱第一时相降低（分别为 40.8 μg/L [P1/4 和 P3/4, 22.2–77.1 μg/L], $P = 0.028$ 和 69.9 μg/L [32.4–112.7 μg/L], $P < 0.001$ ），第二时相也相对对照组降低（分别为 38.8 μg/L [19.9–68.5 μg/L], $P < 0.001$ 和 90.0 [35.1–138.8 μg/L], $P < 0.001$ ）。幸存者显示胶原蛋白 1 和胶原蛋白 3 在三个月后超表达，在六个月后正常表达。

结论：严重败血症时皮肤胶原蛋白合成抑制，并在发病后的三个月和六个月发生代偿反应。

（张玥琪译，薛张纲校）

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 $\mu\text{g/L}$ [25th–75th percentile, 22.2–77.1 $\mu\text{g/L}$], $P = 0.028$ and 69.9 $\mu\text{g/L}$ [32.4–112.7 $\mu\text{g/L}$], $P < 0.001$, respectively) and in the blister induced on day 5 (38.8 $\mu\text{g/L}$ [19.9–68.5 $\mu\text{g/L}$], $P < 0.001$ and 90.0 [35.1–138.8 $\mu\text{g/L}$], $P < 0.001$, 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.

氨基己酸在体外抑制新生儿血浆纤维蛋白溶解的有效浓度

The Effective Concentration of Epsilon-Aminocaproic Acid for Inhibition of Fibrinolysis in Neonatal Plasma in Vitro

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介绍: 儿科患者, 尤其是新生儿, 由于他们的止血系统发育不完善, 体积小, 手术复杂, 接受心脏手术后发生出血并发症的风险很高。血管内纤维蛋白激活是体外循环最基本的影响之一, 可导致术后止血功能障碍。这一并发症已被认识很久, 并且用抗纤溶药物进行治疗, 包括赖氨酸同型 ϵ -氨基乙酸(EACA)。成人的 EACA 治疗血浆浓度已经科学的确定, 但是新生儿的目前推荐剂量是根据成人的剂量经验性的得来。因此, 我们研究了体外循环时 EACA 在新生儿的合适浓度。

方法: 我们用从 20 个足月、选择剖腹产分娩的胎盘脐带血中分离出的新生儿血浆进行了一项体外研究。在用组织型纤溶酶原激活剂激活纤维蛋白溶解前, 将各等级浓度的 EACA 加入等分的血浆容器中。然后进行标准白陶土激活的血栓弹性描记图检测, 并评估溶解百分比初步结果的变异。这些过程在购买的混合成人正常血浆样本中重复进行以作对比。

结果: 我们发现完全抑制纤溶新生儿所需要的 EACA 浓度明显低于成人 (对 400 和 1000 U/mL 的纤溶酶原激活物, 新生儿 EACA 浓度为 44.2 $\mu\text{g/mL}$ 和 47.8 $\mu\text{g/mL}$, 成人为 94.4 和 131.4 $\mu\text{g/mL}$, $P < 0.001$)。

结论：我们的数据确定了 EACA 在体外新生儿血中完全抑制纤维蛋白溶解所必需的最低有效浓度。这一浓度显著低于目前的定量规则确定的浓度值，表明新生儿可能暴露于较临床所必需的更高水平的 EACA。

（朱兰芳译，薛张纲校）

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 $\mu\text{g}/\text{mL}$ and 47.8 $\mu\text{g}/\text{mL}$ for neonatal plasma and 94.4 and 131.4 $\mu\text{g}/\text{mL}$ 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.

窦椎神经阻滞应用于腰段椎间盘来源疼痛的诊断：一项探索性研究

Blockade of the Sinuvertebral Nerve for the Diagnosis of Lumbar Diskogenic Pain: An Exploratory Study

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在这个探索性研究中，我们评估了窦椎神经阻滞（SVNB）用于诊断腰段椎间盘来源疼痛的敏感性和特异性。椎间盘造影是诊断该类疾病的金标准。15名椎间盘造影阳性的患者经后路行SVNB。阻滞成功的定义为 $\geq 80\%$ 的疼痛缓解或身体限制缓解。SVNB的灵敏度为73.3%（95%置信区间为50.9%-95.7%）。特异性为40%

(15.2%-64.8%)。结果表明，SVNB 还不能取代椎间盘造影，但鼓励进一步研究来提高其特异性。

(陈珺珺译 薛张纲校)

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 $\geq 80\%$ 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.

在一项对照研究中研究坐骨神经阻滞持续时间和利多卡因释放速率的关系

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

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背景：我们希望在围手术期和术后神经阻滞有较长维持时间。了解神经阻滞维持时间和局麻药释放速率的关系对于发展局麻药释放系统是重要的，从而可以优化神经阻滞持续时间。

方法：在 OSB-L 组，利多卡因的浓度不同，但是以恒定的速率释放。在另一组 (OST-R),利多卡因的浓度恒定，但是释放速率不同。试剂植入试验鼠的坐骨神经附近后，在体及离体测定与抗伤害性刺激及运动阻滞相关的释放动力学。在平行试验中，实验鼠接受了缓慢释放的利多卡因后，心内注射 4% 多聚甲醛，并取神经肌肉组织进行组织学分析。

结果：在这项研究中，我们证明了影响神经阻滞的各种因素中（例如阻滞坐骨神经相关纤维冲动传导），最重要的因素是利多卡因释放的速率。在 OSB-L 组（利多卡因的浓度分别为 1.875%, 3.75%, 7.5% 和 15% ，以恒定的 5% 的速率释放），在体试验中，50% 运动阻滞及伤害刺激恢复的平均时间分别为 0.91 ± 0.28 和 1.75 ± 0.61 mg/h。在 OST-R 组（16% 的利多卡因分别以 1.875%, 3.75%, 7.5% 和 15% 的浓度释放），在体 50% 运动阻滞及伤害性刺激恢复的平均时间分别为 2.33 ± 1.39 和 4.34 ± 1.09 mg/h。在 OSB-L 组显示了增加利多卡因的起始浓度可以剂量依赖性的增加阻滞持续时间，而在 OST-R 组中显示了释放速率浓度并不是阻滞持续时间的单独因素。在植入试剂后 24 小时、3 天、5 天、7 天和 4 周进行组织学研究发现炎症反应的程度和利多卡因含量正相关，但是局限在植入物周围组织。尽管观察到炎症反应，抗伤害性刺激及运动阻滞均可以恢复到植入前。

结论：增加利多卡因的起始浓度可以成比例地延长坐骨神经阻滞时间。然而降低每次释放地速率并不能成比例地延长阻滞时间。相反，间断给药可以最大程度延长阻滞持续时间，是优化的方案。

（陈珺珺译 薛张纲校）

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.