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*Anesth Analg January 2013 116:247-254; published ahead of print December 7, 2012*

### **关于药物治疗在病人血液保护方面的当前状况**

#### **Current Status of Pharmacologic Therapies in Patient Blood Management**

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病人血液管理包括以病人为中心、循证医学及外科途径并同时通过应用病人自体血而非同种异体血来改善病人结局。对那些首要措施需特别注意，例如贫血治疗。强调以病人为中心，是有区别于原先输血医学（强调血制品制造，关注其风险，代价，库存方面而不是病人的预后）。病人血制品管理目标是避免输血，选择有效地替代品避免同种异体学的应用。替代措施包括自体血储存，术前自体血储备，急性等容性血液稀释，术中或术后红细胞回收洗涤和回输。这样对于贫血及血液管理应用药物措施有：

促红细胞生成素，铁剂治疗，止凝血药，人工氧载体。

(邓利兵译 薛张纲校)

Patient blood management<sup>1,2</sup> incorporates patient-centered, evidence-based medical and surgical approaches to improve patient outcomes by relying on the patient's own (autologous) blood rather than allogeneic blood. Particular attention is paid to preemptive measures such as anemia management. The emphasis on the approaches being "patient-centered" is to distinguish them from previous approaches in transfusion medicine, which have been "product-centered" and focused on blood risks, costs, and inventory concerns rather than on patient outcomes. Patient blood management<sup>3</sup> structures its goals by avoiding blood transfusion<sup>4</sup> with effective use of alternatives to allogeneic blood transfusion.<sup>5</sup> These alternatives include autologous blood procurement, preoperative autologous blood donation, acute normovolemic hemodilution, and intra/postoperative red blood cell (RBC) salvage and reinfusion. Reviewed here are the available

pharmacologic tools for anemia and blood management:erythropoiesis-stimulating agents (ESAs), iron therapy, hemostatic agents, and potentially, artificial oxygen carriers.

### 预注低剂量氯胺酮的阿片类药物节省效应为接受体外冲击波碎石术的阿片类药物滥用者中度镇静：一项随机临床实验

#### Opioid-Sparing Effect of Preemptive Bolus Low-Dose Ketamine for Moderate Sedation in Opioid Abusers Undergoing Extracorporeal Shock Wave Lithotripsy: A Randomized Clinical Trial

Babak Gharaei, MD\*, Alireza Jafari, MD\*, Homayoun Aghamohammadi, MD\*, Mohammadreza Kamranmanesh, MD\*, Mahtab Poorzamani, MD\*, Hedayatollah Elyassi, MD†, Baharak Rostamian, MD\* and Alireza Salimi, MD‡

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**背景：**氯胺酮已被用作阿片类药物滥用者接受全身麻醉的多模式镇痛机制的一部分。我们研究了氯胺酮静脉推注一个极低剂量在阿片类药物滥用者接受体外冲击波碎石术中中度镇静的阿片类药物节省效应。

**方法：**有190名阿片类药物滥用者参与了这项随机、安慰剂对照的临床试验。根据他们日常阿片类药物用量分成2组。2组随机接受0.1 mg/kg 氯胺酮静脉注射（K组）或安慰剂（P组）。在间歇静脉推注瑞芬太尼（0.2 μg/kg）减轻疼痛来中度镇静下进行体外碎石术。在这2组中比较瑞芬太尼总量（主要结果）和呼吸系统不良事件（次要结果）。

**结果：**在低剂量阿片类药物滥用者中使用瑞芬太尼 $1.6 \pm 0.4 \mu\text{g/kg}$ （P组），相较K组为 $1.0 \pm 0.2 \mu\text{g/kg}$ （95%的置信区间[CI]，0.4–0.7； $P < 0.001$ ）。高剂量阿片类药物滥用者中使用瑞芬太尼 $2.0 \pm 0.5 \mu\text{g/kg}$ （P组），相较K组为 $1.5 \pm 0.3 \mu\text{g/kg}$ （95%的置信区间，0.40–0.75； $P < 0.001$ ）。统计出在高剂量阿片类药物滥用者中接受安慰剂相较K组的准备排出时间更长（ $55 \pm 13$  分钟 vs  $44 \pm 8$ 分钟，95%置信区间，6–15； $P < 0.001$ ）。在氯胺酮组和安慰剂组中呼吸缓慢、呼吸暂停、恶心、呕吐和血流动力学变化的发生率无明显统计学意义。

**结论：**在阿片类药物滥用者中度镇静中预注低剂量氯胺酮（0.1 mg/kg）有阿片类药物节省效应。

（方昕译 薛张纲校）

**BACKGROUND:** Ketamine has been used as part of a multimodal analgesia regime in opioid abusers undergoing general anesthesia. We studied the opioid-sparing effect of a very low-dose bolus of ketamine as part of moderate sedation for opioid abuse patients undergoing extracorporeal shock wave lithotripsy.

**METHODS:** In this randomized, placebo-controlled clinical trial, 190 opioid abusers were enrolled. They were stratified into 2 blocks based on their daily opioid consumption. Both blocks were then randomized to receive 0.1 mg/kg IV ketamine (group K) or placebo (group P). Lithotripsy was performed under moderate sedation with intermittent bolus doses of remifentanyl

(0.2 µg/kg) to alleviate pain. The total remifentanyl dose (primary outcome) and respiratory adverse events (secondary outcome) were compared in the 2 groups.

**RESULTS:** Remifentanyl administration in the group with low-opioid consumers was  $1.6 \pm 0.4$  µg/kg (group P) compared with  $1.0 \pm 0.2$  µg/kg in group K (confidence interval [CI] of difference 95%, 0.4–0.7;  $P < 0.001$ ). Patients who had high-opioid consumption received  $2.0 \pm 0.5$  µg/kg (group P) vs  $1.5 \pm 0.3$  µg/kg (group K) remifentanyl (CI of difference 95%, 0.40–0.75;  $P < 0.001$ ). Ready to discharge time was statistically longer in high-consumption opioid abusers who received placebo compared with group K ( $55 \pm 13$  minutes vs  $44 \pm 8$  minutes, CI of difference 95%, 6–15;  $P < 0.001$ ). The incidences of bradypnea, apnea, nausea, vomiting, and hemodynamic changes were not statistically different between the ketamine and placebo groups.

**CONCLUSION:** Preemptive low-dose ketamine (0.1 mg/kg) as a bolus has opioid-sparing effects in opioid abusers undergoing moderate sedation.

### 多腔输液设备对于已知药物物理不相溶现象的影响：一项控制性体外研究

#### The impact of multilumen infusion devices on the occurrence of known physical drug incompatibility: a controlled in vitro study.

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**背景：**药物不相溶性如今已成为一个问题，这个问题尤其存在于ICU病人的管理中。我们设计了这项控制性体外研究用于评估多腔输液设备对于已知药物物理不相溶现象的影响。

**方法：**通过给一个单腔导管连接三种不同的输液设备进行研究：标准设备由2个分支和1个延长支组成，2组多腔设备分别是：一个3腔延长设备和一个9腔延长设备(Edelvaiss-Multiline™; Doran International, Toussieu, France)。

对于9腔延长设备，我们将3输液设备拼接进行研究。我们将速尿、咪达唑仑和盐水同时通过3组输液设备滴注，并对3种不同浓度速尿进行测试。盐水（载体）的输注速度初始设定为100ml/h，以10ml/h逐渐降低滴速直至沉淀形成。根据欧洲药典通过2项测试评估物理不溶：视觉评估和可视粒子数计数。每组设备都得到一个最低盐水输注速率，此时刚刚好无可视沉淀且无可视粒子沉淀（即通过2项测试）。

**结果：**标准组显示即使是在最高盐水流速（100ml/h）时，可见沉淀依然存在。3腔设备通过最低浓度的速尿与同其浓度一同下降的盐水滴注速率来防止沉淀。9腔设备在无论组合前两项速尿浓度为多少时只要盐水注射速度在20–60ml/h之间即能防止沉淀，但组合第三项中即使盐水滴速达到100ml/h也无法避免沉淀。

**结论：**输液设备看上去似乎会对2种药物的物理相容性产生影响。在特定条件下，9腔输液设备能防止速尿–咪达唑仑的物理不相溶性。

（郭晨跃译 薛张纲校）

**BACKGROUND:** Drug incompatibility is a problem, especially when managing patients in intensive care units. We designed the present study to assess the impact of multilumen infusion access devices on the occurrence of known physical drug incompatibility through a controlled in vitro study.

**METHODS:** Three infusion devices connected to a single-lumen catheter were studied: a standard set with 2-port manifold and 1-m extension set and 2 multilumen infusion access devices: a 3-lumen extension set and a 9-lumen extension set (Edelvaiss-Multiline™; Doran International, Toussieu, France). For the 9-lumen extension set, 3 infusion access combinations were studied. Furosemide, midazolam, and saline were infused simultaneously through 3 infusion devices. Three concentrations of furosemide were tested. The infusion rate of saline (carrier) was initially set at 100 mL/h and stepwise decreased by 10 mL/h until precipitate formation. Physical incompatibility was assessed by 2 tests: visual inspection and the subvisible particle count test according to the European Pharmacopeia. The lowest saline infusion rate to prevent visible precipitate and attain an acceptable particle count (i.e., to pass "the 2 tests") was reported for each infusion set.

**RESULTS:** The standard set revealed visible precipitate even at the highest saline flow rate (100 mL/h). The 3-lumen device prevented drug precipitation using the 2 lowest furosemide concentrations with a saline infusion rate that decreased with furosemide concentration. The 9-lumen infusion access device prevented drug precipitation whatever the furosemide concentration for 2 access combinations using saline infusion rates of between 20 and 60 mL/h but not for a third access combination, despite saline infusion rates equal to 100 mL/h.

**CONCLUSIONS:** Infusion device characteristics appear to have an impact on the physical compatibility of the 2 drugs. Under specified conditions, the 9-lumen infusion access device prevents physical furosemide-midazolam incompatibility.

### 评估琥珀胆碱引发恶性高热的风险

#### Estimate of the relative risk of succinylcholine for triggering malignant hyperthermia.

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**背景：**恶性高热MH应用丹曲林和吸入麻醉药治疗，麻醉中出现的恶性高热，应用丹曲林只需1天1个剂量即可起效；不用吸入麻醉剂，通过已注册数据和麻醉期间使用司可林的次数，估计丹曲林的需要量，以此判断司可林引起MH的几率。

**方法：**司可林引发MH的原因有两个，来自MHAUS的284名患者分别被分为2组，一组接受司可林的MH患者，另一种不给予司可林的MH患者，麻醉剂与琥珀胆碱的比例的估计，使用麻醉信息管理系统的来自一个典型的北美医院由三级手术室、产科、门诊手术中心、和内镜和放射室。

**结果：**用司可林引起MH的相对危险度比没用司可林组高19.6（低95%可信区间大于16.1）。挥发性麻醉药的相对风险为9.1（大于7.5）。两个相对风险超过1.0(P < 0.0001)。在北美，使用司可林的患者超过一半出现MH，而没使用司可林的患者出现MH的不足一半。与挥发性麻醉药相比，琥珀胆碱的发生率在院使用分别为5.8%和11.6%。

**结论：**我们的结果不能洞察的触发机制MH(即。琥珀胆碱引起MH的发病率极低,但明显增加联合挥发性麻醉药诱导时MH的风险)。需要更多的流行病学数据的收集和分析,丹曲林在琥珀胆碱引起的MH有效果,是合理的,这种做法应该保持。

(韩叙译 薛张纲校)

**BACKGROUND:** Facilities with volatile anesthetic agents stock dantrolene for the treatment of malignant hyperthermia (MH). The availability of dantrolene at these facilities satisfies cost-utility norms even for sites with as few as 1 anesthetic per workday, based on the overall incidence of MH per anesthetic. We considered the stocking of dantrolene at facilities with succinylcholine alone (i.e., where volatile anesthetics are not available), by using registry data and estimates of the frequency of administration of succinylcholine during anesthesia. We determine the magnitude of the relative risk of the administration of succinylcholine for triggering MH.

**METHODS:** The relative risk of triggering MH by succinylcholine versus volatile agents was calculated using data from 2 sources. The ratio of the number of cases of MH among patients receiving succinylcholine to number among patients not receiving succinylcholine was estimated from the previously published cohort of 284 cases of MH from the North American MH Registry of the MH Association of the United States (MHAUS). The percentage of anesthetics with succinylcholine was estimated using anesthesia information management system data from a typical North American hospital comprising tertiary operating rooms, obstetrics unit, ambulatory surgical center, and endoscopy and radiological suites.

**RESULTS:** The relative risk of MH with versus without succinylcholine was 19.6 (lower 95% confidence limit > 16.1). Limiting to cases with volatile anesthetics, the relative risk was 9.1 (>7.5). Both relative risks exceed 1.0 ( $P < 0.0001$ ). Because more than half of the reported cases of MH included the use of succinylcholine, the relative risk exceeded 1.0 provided fewer than half of anesthetics in North America included the use of succinylcholine. The incidences of succinylcholine use at the hospital were 5.8% and 11.6% for all anesthetics and for anesthetics with volatile agents, respectively.

**CONCLUSIONS:** Our results provide no insight into the triggering mechanism for MH (i.e., succinylcholine could in isolation have an extremely low incidence of inducing MH, yet markedly increase the risk when administered in combination with volatile anesthetics). Until more epidemiologic data are collected and analyzed, having dantrolene available, where succinylcholine may be used, is reasonable, and this practice should be maintained..

**使用Episure™自动检测™注射器与传统的玻璃注射器实施硬膜外技术相关的学习曲线：经验丰富的麻醉医师对产科病人实施的一个非盲，随机，对照，交叉试验。**

**The Learning Curve Associated with the Epidural Technique Using the Episure™ AutoDetect™ Versus Conventional Glass Syringe: An Open-Label, Randomized, Controlled, Crossover Trial of Experienced Anesthesiologists in Obstetric Patients.**

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Anesth Analg January 2013 116:145-154

**背景：**在2相初步研究中，我们已经观察到使用Episure™自动检测™（弹簧）注射器能成功地确定硬膜外腔。在这项研究中，我们评估经验丰富的麻醉医师使用弹簧式注射器对建立成功的硬膜外分娩镇痛（主要结果），放置硬膜外导管的时间，以及学习曲线（累计汇总分析，即CUSUM）的影响。

**方法：**14位麻醉科主治医师随机使用带弹簧式注射器或传统的玻璃注射器每人实施50个连续硬膜外麻醉技术。

10位参加者使用这两种注射器每人完成另外一个50个连续硬膜外麻醉技术。

**结果：**一共实施了1200个硬膜外技术。使用弹簧式注射器与使用传统的玻璃注射器实施硬膜外麻醉相比在获得镇痛成功方面两者成功率无显著差异，（绝对差异为1.0%，95%可信区间，CI：-8.9%至10.8%），前者硬膜外导管放置平均时间更短（比为0.92

95%CI:0.89-0.96），P =

0.003）两者有类似累积曲线相。麻醉科医生镇痛成功更常见（绝对差为34.6%，95%CI，14.9%-54.3%，P

<0.001），首选连续生理盐水阻力消失法与使用间歇空气法相比镇痛成功更常见（绝对差为33.8% 95%CI，12.6%-55.0%，P

<0.001）。我们也观察到首先使用弹簧式注射器组所用的平均时间更短（比为0.65

95%CI，0.62 - 0.67，P= 0.02）。

**结论：**在建立成功的硬膜外分娩镇痛方面，经验丰富的产科麻醉医师使用弹簧式注射器与使用常规的玻璃注射器相比有类似的整体比率，硬膜外导管插入时间更短，有类似的累积曲线，尤其是当麻醉师第一次随机使用新型注射器时。参加的麻醉师使用新型注射器时偏爱连续生理盐水阻力消失法时镇痛成功率更高。

（贺盼译 薛张纲校）

**BACKGROUND:** The Episure™ AutoDetect™ (spring-loaded) syringe has been observed to successfully identify the epidural space in 2 pilot studies. In this study we evaluated the impact of the spring-loaded syringe on the establishment of successful epidural labor analgesia (primary outcome), elapsed time for catheter placement, and learning curve (cumulative summary analysis, i.e., Cusum) of experienced anesthesiologists.

**METHODS:** Fourteen attending and fellow anesthesiologists were randomized to perform 50 consecutive epidural technique attempts using a spring-loaded or conventional glass syringe. Ten participants completed an additional 50 attempts with the alternate syringe in a crossover design.

**RESULTS:** A total of 1200 epidural placement attempts were performed. Use of the spring-loaded syringe was associated with a nonsignificant difference of estimated success rate in obtaining analgesia success (absolute difference of 1.0% 95% confidence interval, CI: -8.9% to 10.8%), shorter elapsed mean time to epidural catheter placement (ratio of 0.92 95% CI, 0.89-0.96); P = 0.003) and similar Cusum curves when compared with a conventional glass syringe. Analgesia success was more common with attending versus fellow anesthesiologists (absolute difference of 34.6% 95% CI, 14.9% to 54.3%; P < 0.001), and when the initial preferred technique was loss-of-resistance to continuous saline versus intermittent air (absolute difference of 33.8% 95% CI, 12.6% to 55.0%; P < 0.001). Shorter elapsed mean times were also observed in the group exposed to the spring-loaded syringe first (ratio of 0.65 95% CI, 0.62-0.67; P = 0.02).

**CONCLUSIONS:** When used by experienced obstetric anesthesiologists, the spring-loaded syringe was associated with a similar overall rate for establishing successful epidural labor analgesia, a shorter elapsed time to epidural catheter insertion, particularly when the

anesthesiologist was randomized to use the novel syringe first, and a similar Cusum curve when compared with a conventional glass syringe. Attending versus fellow anesthesiologists and an initial technique preference for loss-of-resistance to continuous saline were associated with greater analgesia success with the novel syringe.

### 一项关于处理产后出血的新鲜冰冻血浆与红细胞比率的观察研究

#### **An observational study of the fresh frozen plasma: red blood cell ratio in postpartum hemorrhage.**

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**背景：**产后出血是全世界产妇死亡的首要原因。最近一些关于创伤性病人和创伤后失血性休克的病人数据表明增加的新鲜冰冻血浆与红细胞比率对大量失血有利。我们解决这个问题来处理严峻的产后出血。

**方法：**我们回顾了4年间（2006-

2009）被诊断为产后出血病人的所有相关数据。在这项研究中，病人获得前列磺酮及在6小时内输血处理，根据她们对前列磺酮的反应分成2个组：出血仅需前列磺酮控制（前列磺酮组）和出血需要进一步的介入手段包括动脉血管栓塞和/或外科手术（B-Lynch缝合术，动脉结扎术或全子宫切除术；干预组）。进一步介入手段的需要与否决定该研究的终点。利用倾向评分标准来评估高的新鲜冰冻血浆与红细胞比率在控制出血方面的作用。

**结果：**在12226名被研究人员中，142（占1.1%）人并发了严重的产后出血。仅用前列磺酮控制住出血的有90位病人（占63%）。需要进一步介入手术的有52人（占37%）。41位病人同时输注了红细胞和新鲜冰冻血浆。新鲜冰冻血浆：红细胞的比例增加，在整个研究中（ $P < 0.001$ ）从最初的1:1.8到最后1:1.1。倾向评分模型（相反概率的处理），对于行进一步介入手术（比率[95%可信区间]，1.25[1.07-

1.47]； $P = 0.008$ ）而言，高的新鲜冰冻血浆：红细胞比率是不需要的。研究病例中没有死亡，重要器官功能衰竭或者其他因产后出血造成的并发症。

**结论：**在这项回顾性研究中看出，对于产后出血而进行的进一步介入手术并不需要输入高的新鲜冰冻血浆：红细胞比率的血。使用高的新鲜冰冻血浆：红细胞比率输血的益处需要通过随机对照试验来证实。

（胡晓清译 薛张纲校）

**BACKGROUND:** Postpartum hemorrhage is the leading cause of maternal death worldwide. Recent data from trauma patients and patients with hemorrhagic shock have suggested that an



increased fresh frozen plasma:red blood cell (FFP:RBC) ratio may be of benefit in massive bleeding. We addressed this issue in cases of severe postpartum hemorrhage.

**METHODS:** We reviewed data from all patients diagnosed with severe postpartum hemorrhage during a 4-year period (2006-2009). Patients who were treated with sulprostone and required transfusion within 6 hours of delivery were included in the study and were divided into 2 groups according to their response to sulprostone: bleeding controlled with sulprostone alone (sulprostone group) and bleeding requiring an additional advanced interventional procedure including arterial angiographic embolization and/or surgical procedures (arterial ligation, B-Lynch suture, or hysterectomy; intervention group). The requirement or no requirement for advanced procedures constituted the primary end point of the study. Propensity scoring was used to assess the effect of a high FFP:RBC ratio on bleeding control.

**RESULTS:** patients were transfused with both RBCs and FFP. The FFP:RBC ratio increased over the study period ( $P < 0.001$ ), from 1:1.8 at the start to 1:1.1 at the end of the study period. After propensity score modeling (inverse probability of treatment weighting), a high FFP:RBC ratio was associated with lower odds for advanced interventional procedures (odds ratio [95% confidence interval], 1.25 [1.07-1.47];  $P = 0.008$ ). There were no deaths, severe organ dysfunction, or other complications as a consequence of severe postpartum hemorrhage.

**CONCLUSIONS:** In this retrospective study, a higher FFP:RBC ratio was associated with a lower requirement for advanced interventional procedures in the setting of postpartum hemorrhage. The benefits of transfusion using a higher FFP:RBC ratio should be confirmed by randomized-controlled trials.

### 蛛网膜下腔出血和脑出血患者的复极异常：发病诱因和预后

#### Repolarization abnormalities in patients with subarachnoid and intracerebral hemorrhage: predisposing factors and association with outcome

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**背景：**颅内病变患者心电图异常十分常见。在本研究中，我们评估了复极异常的诱发因素，例如，校正的QT

(QTc)间期延长，心电图缺血样改变和复极末形态异常，并且考查了需要重症监护的蛛网膜下腔出血和脑出血患者中这些异常指标的预示价值。

**方法：**本研究在重症监护室进行，是一个前瞻性、观察性的研究。入院时记录患者的临床特征，意识水平，早期的头颅CT结果。研究分为三阶段，各两天。每个阶段均记录12导联心电图、经胸心超、电解质和肌钙蛋白I等指标，以及血管活性药物和镇静药物输注速度。复极异常比如QTc间期延长（毫秒），心电图缺血样改变，复极末形态异常（存在/缺失）等被评估和分析。格拉斯哥预后评分评估一年功能恢复。

**结果：**本研究历时两年，共108名患者参加研究。在两种出血类型中不同的复极异常均频繁发生。QTc间期延长易发生于女性( $\beta$ , 24.5;  $P = 0.010$ )和使用异丙酚者( $\beta$ , 30.5;  $P =$

0.001)。心电图缺血样改变易发生于男性(比值比[OR], 5.9; P = 0.003), 复极末形态异常易发生于动脉瘤出血(OR, 13.0; P = 0.002)。心电图缺血样改变比较常见, 占研究的87/108, 并且与一年功能恢复较差相关(OR, 4.7; 较低的95%可信区间, 1.5; P = 0.010)。

**结论:**每一种复极异常都有特有的发病诱因。心电图缺血样改变比较常见, 并且与一年功能恢复较差相关。

(郁玲玲译 薛张纲校)

**BACKGROUND:** Electrocardiographic (ECG) abnormalities are frequent in patients with intracranial insult. In this study, we evaluated the factors predisposing to the repolarization abnormalities, i.e., prolonged corrected QT (QTc) interval, ischemic-like ECG changes and morphologic end-repolarization abnormalities, and examined the prognostic value of these abnormalities in patients with subarachnoid and intracerebral hemorrhages requiring intensive care.

**METHODS:** This was a prospective, observational clinical study in a university-level intensive care unit. Clinical characteristics, the level of consciousness, and findings in primary head computed tomography were recorded on admission. The study period was divided into three 2-day sections. In each section, a 12-lead ECG, transthoracic echocardiography, the results of standard blood electrolytes and cardiac troponin I, as well as the rate of vasoactive and sedative drug infusions were recorded. Repolarization abnormalities such as prolongation of the QTc interval (millisecond), ischemic-like ECG changes, and morphologic end-repolarization abnormalities (present/absent) were evaluated and analyzed. The 1-year functional outcome was determined using the Glasgow Outcome Score.

**RESULTS:** During the 2-year study period, 108 patients were included in the study. Different repolarization abnormalities were frequent in both types of hemorrhage. Prolongation of the QTc interval was predisposed by female gender ( $\beta$ , 24.5; P = 0.010) and the use of propofol ( $\beta$ , 30.5; P = 0.001). The predisposing factor for ischemic-like ECG changes were male gender (odds ratio [OR], 5.9; P = 0.003) and for morphological end-repolarization abnormalities aneurysmatic bleeding (OR, 13.0; P = 0.002). Ischemic-like ECG changes were common, in 87/108 patients during the study period, and were associated with a poorer 1-year functional outcome (OR, 4.7; lower 95% confidence interval, 1.5; P = 0.010).

**CONCLUSIONS:** Each repolarization abnormality has characteristic predisposing factors. Ischemic-like ECG changes are common and are associated with a poorer 1-year functional outcome.

**pan-**

**caspase**抑制剂可减少患坐骨神经慢性挤压伤的大鼠的心肌细胞凋亡和神经病理性疼痛

**A pan-caspase inhibitor reduces myocyte apoptosis and neuropathic pain in rats with chronic constriction injury of the sciatic nerve.**

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**背景：**慢性压迫性损伤是一种广泛使用的用于研究神经病理性疼痛的大鼠模型。它表现出了类似人类神经病理性疼痛的症状，如自发性疼痛，痛觉过敏和异常痛觉。最近，神经病理性疼痛的大鼠中，细胞凋亡被认为可能是疼痛和运动障碍的一个启动子。我们的这项研究是要证明在此动物模型中，肌肉细胞凋亡是否会引发神经病理性疼痛。

**方法：**为了弄清这个问题，我们对患有由坐骨神经的慢性挤压伤而产生神经病理性疼痛的大鼠进行疼痛、营养灌注、肌肉组织的炎症以及心肌细胞凋亡的研究。动物接受pan-caspase抑制剂ZVAD (OMe)-fmk (N =5) 或相等剂量的赋形药 (n =6)。假手术组作为对照组 (n =6)。

**结果：**在神经结扎后第4天，各实验组没有任何灌注异常或肌肉组织炎症的迹象。然而，赋形药组出现明显的细胞凋亡，而这在用ZVA-D治疗的动物中是几乎完全阻断的。与假手术对照组的结果相比，用ZVA-D治疗的动物对由热、冷和机械性刺激引起的疼痛明显减少。

**结论：**从本次神经病理性疼痛的实验模型发现，细胞凋亡可能有助于产生温度和机械性异常痛觉。神经病理性疼痛的症状发展并不依赖于微循环紊乱或肌肉组织的炎症。

(周玲译 薛张纲校)

**BACKGROUND:** Chronic constriction injury is a widely used model for neuropathic pain in rats. It presents with symptoms resembling human neuropathic pain, such as spontaneous pain, hyperalgesia, and allodynia. Recently, myocyte apoptosis was found in neuropathic rats as a possible promoter of pain and motor dysfunction. Our aim in this study was to demonstrate whether muscle cell apoptosis contributes to neuropathic pain in this animal model.

**METHODS:** To clarify this issue, we examined pain, nutritive perfusion, and inflammation in muscle tissue as well as myocyte apoptosis in rats with neuropathic pain established by chronic constriction injury of the sciatic nerve. Animals received either the pan-caspase inhibitor zVAD (OMe)-fmk (n = 5) or equivalent volumes of vehicle (n = 6). Sham-operated rats served as controls (n = 6).

**RESULTS:** At day 4 after nerve ligation, there were no signs of perfusion failure or muscle tissue inflammation in all experimental groups. However, animals treated with the vehicle had marked myocyte apoptosis, which was found almost completely blocked in zVA-Dtreated animals. The zVA-Dtreated animals presented with a significant reduction of pain upon heat, cold, and mechanical stimulation comparable with values found in sham controls.

**CONCLUSIONS:** Myocyte apoptosis possibly contributes to thermal and mechanical allodynia in this experimental model for neuropathic pain. The development of neuropathic pain symptoms did not depend on disturbances in microcirculation or muscle tissue inflammation.

**细胞外信号调节激酶1/2/P2X3信号转导通路在慢性坐骨神经损伤的大鼠脊髓的电针影响。**

**The Effects of Electroacupuncture on the Extracellular Signal-Regulated Kinase 1/2/P2X3 Signal Pathway in the Spinal Cord of Rats with Chronic Constriction Injury.**

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**背景:**作为传统的治疗疼痛的方法，电针（EA）被广泛用于临床，但其镇痛疗效尚未确切。在本研究中，我们探讨EA对慢性疼痛的疗效以及患有慢性压迫性脊髓损伤的大鼠P2X3受体的表达。

**方法:**本研究分2部分，第1部分，将SD大鼠分成6组（n=10）：假-

CCI，CCI，LEA，CCI+2Hz，电针穴位），HEA，CCI+15Hz电针刺激穴位），NA-LEA（CCI+2Hz电针非穴位）以及NA-

LEA（CCI+15Hz电针非穴位）。4至9天CCI后电针治疗隔天一次，伤害性刺激由电子触觉测量仪和热板装置执行。印记检查测量脊髓内蛋白质和P2X3受体的mRNA以及实时聚合酶链反应。第2部分，大鼠被分成5组（n=10）：假-

CCI,CCI,EA(CCI+EA电针穴位)，NA-

EA(CCI+EA非穴位)以及U0126(CCI+鞘内注射U0126)。EA治疗和第一部分相似，给予U0126组大鼠鞘内注射5 $\mu$ gU0126和5%二甲基亚砜。十微升作为其他四组的载体在CCI治疗后4至9天每两天给一次。使用印迹法检验细胞外信号调节激酶1/2（ERK1/2）和其磷酸化。

**结果:**电针治疗具有很显著的镇痛效果，减少了CCI引起的脊髓P2X3受体蛋白和mRNA表达增加。此外，相比15Hz，2Hz电针具有较好的止痛效果，同时15Hz电针穴位的取穴比2Hz电针治疗大鼠脊髓P2X3受体在蛋白和mRNA水平的降低。无论是EA在穴位或鞘内注射U0126释然异常性疼痛和痛觉过敏和降低P2X3受体的表达和ERK1/2磷酸化的脊髓。

**结论:**本研究显示，EA能部分缓解神经性疼痛的行为，并通过ERK1/2信号通路在脊髓P2X3受体的表达减少。相比高频EA，低频EA对神经病理性疼痛有较好的止痛效果。

（杨琰译 薛张纲校）

**BACKGROUND:** Electroacupuncture (EA), as a traditional clinical method, is widely accepted in pain clinics, but the analgesic effect of EA has not been fully demonstrated. In the present study, we investigated the effect of EA on chronic pain and expression of P2X3 receptors in the spinal cord of rats with chronic constriction injury (CCI).

**METHODS:** The study was conducted in 2 parts. In part 1, Sprague Dawley rats were divided into 6 groups (n = 10): sham-CCI, CCI, LEA; CCI + 2 Hz EA at acupoints), HEA; CCI + 15 Hz EA at acupoints), NA-LEA (CCI + 2 Hz EA at nonacupoints), and NA-HEA (CCI + 15 Hz EA at nonacupoints). EA treatment was performed once a day on days 4 to 9 after CCI. Nociception was assessed using von Frey filaments and a hotplate apparatus. The protein and the messenger RNA (mRNA) levels of P2X3 receptors in the spinal cord were assayed by Western blotting and real-time polymerase chain reaction, respectively. In part 2, rats were divided into 5 groups (n = 10): sham-CCI, CCI, EA (CCI + EA at acupoints), NA-EA (CCI + EA at nonacupoints), and U0126 (CCI + intrathecal injection of U0126). EA treatment was conducted similar to part 1. Rats were given 5  $\mu$ g U0126 in the U0126 group and 5% dimethyl sulfoxide intrathecally. Ten microliters was used as a vehicle for the other 4 groups twice a day on days 4 to 9 after CCI. Extracellular signal-regulated kinase 1/2 (ERK1/2) and ERK1/2 phosphorylation in the spinal cord were also assayed by Western blotting.

**RESULTS:** EA treatment exhibited significant antinociceptive effects and reduced the CCI-induced increase of both protein and mRNA expression of P2X3 receptors in the spinal cord. Furthermore, 2 Hz EA had a better analgesic effect than 15 Hz EA, and the protein and mRNA level of P2X3 receptor in spinal cord were lower in rats treated with 2 Hz EA at acupoints than 15 Hz EA at acupoints. Either EA at acupoints or intrathecal injection of U0126 relieved allodynia and hyperalgesia and reduced the expression of P2X3 receptors and ERK1/2 phosphorylation in the spinal cord.

**CONCLUSIONS:** The data demonstrated that EA alleviates neuropathic pain behavior, at least in part, by reducing P2X3 receptor expression in spinal cord via the ERK1/2 signaling pathway. Low frequency EA has a better analgesic effect than high frequency HEA on neuropathic pain.

### 综述：现代淀粉在外科手术中应用的安全性

#### Review Article: Safety of Modern Starches Used During Surgery

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各种以增加血容量为目的的羟乙基淀粉（HES）制剂已被使用了几十年。在重症监护病房使用HES，尤其应用于感染性休克患者，可能出现不良后果是最近备受关注的话题。然而，HES制剂的药代动力学和药效学性质取决于其化学成分和原材料。因此，不同的临床条件可导致这些制剂不同的有效性和安全性。通过一项对符合纳入标准的59个已发表研究进行的正规调查，4529个对象随机接受羟乙基淀粉（2139名）和对照制剂（2390名）处理，来评估外科手术中使用低替代级羟乙基淀粉的安全性。没有证据表明手术过程中使用低替代级淀粉会引起肾脏的不良反应（这一影响使用血肌酐浓度变化或其绝对值或需要肾脏替代治疗来评估，39项实验，3389名对象），失血量增加（38项试验，3280个患者），异体红细胞输注（20项试验，2151个病人；羟乙基淀粉输注比值比为0.73，95%可信区间=0.61-0.87]p=0.0005）或死亡率增加（羟乙基淀粉死亡比值比=0.51[0.24-1.05]，p=0.079）。

（郑华容 译 陈杰 校）

Various hydroxyethyl starch (HES) preparations have been used for decades to augment blood volume. There has been concern recently regarding possible adverse outcomes when using HES in the intensive care setting, especially in patients with septic shock. However, the pharmacokinetic and pharmacodynamic properties of HES preparations depend on their chemical composition and source material. Thus, different clinical conditions could result in differing effectiveness and safety for these preparations. Consequently, we assessed the safety of tetrastarches when used during surgery, using a formal search, that yielded 59 primary full publications of studies that met a priori inclusion criteria and randomly allocated 4529 patients with 2139 patients treated with tetrastarch compared with 2390 patients treated with a comparator. There were no indications that the use of tetrastarches during surgery induces adverse renal effects as assessed by change or absolute concentrations of serum creatinine or need for renal replacement therapy (39 trials, 3389 patients), increased blood loss (38 trials, 3280 patients), allogeneic erythrocyte transfusion (20 trials, 2151 patients; odds ratio for HES transfusion 0.73 [95% confidence interval = 0.61–0.87], P = 0.0005), or increased mortality (odds ratio for HES mortality = 0.51 [0.24–1.05], P = 0.079).

## 布比卡因和罗哌卡因的心肌蓄积与线粒体逆转效应和心功能降低相关

### Myocardial Accumulation of Bupivacaine and Ropivacaine Is Associated with Reversible Effects on Mitochondria and Reduced Myocardial Function

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**背景：**局麻药引起心脏毒性的机理至今仍未完全清楚。此项研究分析了能引起临床毒性的局麻药浓度是否会影响心肌线粒体结构和氧耗。

**方法：**游离出豚鼠心脏建立Langendorff离体心脏模型，将其暴露于布比卡因(3.0 和 7.5  $\mu\text{g/mL}$ ) 和罗哌卡因(3.6 和 9.0  $\mu\text{g/mL}$ )

10min。记录心率，收缩压，左室内压变化速率，心电图和冠脉流量。给药后即刻或20 min洗脱期、60min洗脱期后测量组织的局麻药浓度。另外，使用电子显微镜观察心肌线粒体并对其结构损伤进行评分。将心肌细胞放入布比卡因液进行培养，测定氧耗率、细胞外酸化情况和PGC-1 $\alpha$ mRNA相对量（一种细胞能量代谢的调节因子）的表达。

**结果：**布比卡因和罗哌卡因引起PR间期及QRS可逆性延长，左室内压及其变化率降低。心肌组织中局麻药浓度是动脉浓度的3倍。局麻药应用后线粒体表现出显著的浓度依赖性形态肿胀。对于罗哌卡因和布比卡因，这些变化分别在进行了20min、60min洗脱期后被逆转。布比卡因在乳鼠心肌细胞培养中，降低线粒体氧耗，增加PGC-1 $\alpha$ 的表达，而脂肪酸代谢不受影响。

**结论：**布比卡因和罗哌卡因可在心肌组织中蓄积。当达到负性肌力作用的浓度时，局麻药可逆性引起线粒体肿胀。布比卡因降低细胞代谢，然而此效应可被脂肪酸逆转。与线粒体的相互作用可能是导致局麻药负性肌力作用的原因。

（诸琳婕 译 陈杰 校）

**BACKGROUND:** Mechanisms of local anesthetic cardiac toxicity are still not completely understood. In this study, we analyzed whether concentrations of local anesthetics found in clinical toxicity affect myocardial mitochondrial structure and oxygen consumption.

**METHODS:** Guinea pig isolated heart Langendorff preparations were exposed to bupivacaine (3.0 and 7.5  $\mu\text{g/mL}$ ) and ropivacaine (3.6 and 9.0  $\mu\text{g/mL}$ ) for 10 minutes. Heart rate, systolic blood pressure, the first derivative of left ventricular pressure (+dP/dt), electrocardiogram, and coronary flow were recorded. The local anesthetic tissue concentration was measured either immediately after local anesthetic exposure, or after 20- and 60-minute washout periods. In addition, electron microscopy of myocardial mitochondria was performed using a scoring system for structural damage of mitochondria. Cardiomyocyte cell culture was incubated with bupivacaine, and oxygen consumption ratio, extracellular acidification, and relative amounts of PGC-1 $\alpha$  mRNA, a regulator of cellular energy metabolism, were determined.

**RESULTS:** Bupivacaine and ropivacaine induced reversible PR interval and QRS prolongation, and left ventricular pressure and +dP/dt reduction. Myocardial tissue concentration of local anesthetics was 3-fold the arterial concentration. Mitochondria showed a significant

concentration-dependent morphological swelling after local anesthetic application. These changes were reversed by a 20-minute washout period for ropivacaine and by a 60-minute washout for bupivacaine. Bupivacaine reduced mitochondrial oxygen consumption and increased PGC-1 $\alpha$  expression in neonatal cardiomyocyte cell cultures, whereas fatty acid metabolism remained unaffected.

**CONCLUSIONS:** Bupivacaine and ropivacaine accumulate in the myocardium. Reversible local anesthetic-induced mitochondrial swelling occurs at concentrations that induce a negative inotropic effect. Bupivacaine reduces cellular metabolism, whereas this reduction is reversible by fatty acids. Interaction with mitochondria may contribute to the negative inotropic effect of local anesthetics.

### 特稿：疼痛医疗危机资源管理教育课程和案例

#### **Special Article: Curriculum and Cases for Pain Medicine Crisis Resource Management Education**

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在疼痛医疗机构可能发生的罕见紧急医疗事件需要技巧以及协作来保证病人的安全预后。环境模拟对于获得和增强这方面的知识和技能是一个理想的设施。本文中为疼痛医学专科医师以及主治医师介绍一项疼痛医疗危机资源管理教学课程，以及这项试验计划的成果。  
(瞿亦枫 译 陈杰 校)

Medical crises that may occur in the setting of a pain medicine service are rare events that require skillful action and teamwork to ensure safe patient outcome. A simulated environment is an ideal venue for both acquisition and reinforcement of this knowledge and skill set. Here, we present an educational curriculum in pain medicine crisis resource management for both pain medicine fellows and attending physicians as well as the results of a successful pilot program.

### 比较鞘内注射30mg利多卡因和45mg利多卡因试验剂量对产科人群影响的一项前瞻性随机实验

#### **A Prospective Randomized Trial of Lidocaine 30 mg Versus 45 mg for Epidural Test Dose for Intrathecal Injection in the Obstetric Population**

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**背景：**硬膜外试验剂量，用于排除意外的鞘内置管，在对患者不造成危险的前提下应产生确切的脊髓阻滞效果。大多数的麻醉医生通常会用45mg的利多卡因作为局麻试验剂量。孕妇对局麻药更为敏感，相关报道提示这个剂量在孕妇人群中更容易出现麻醉平面过高以及全脊麻现象。因此本实验假设与45mg利多卡因相比，30mg剂量可产生相同的感觉和运动阻滞作用。

**方法：**在这个前瞻性随机双盲实验中，将择期行剖宫产病人分成四组：30mg利多卡因鞘内或硬膜外给药组，或45mg利多卡因鞘内或硬膜外给药组。然后不知情的观察者对四组病人的感觉和运动阻滞的程度进行评估。比较各剂量对鞘内注射的预测能力。高于T6节段的感觉阻滞或低血压被记录为不良事件。

**结果：**鞘内注射30mg利多卡因能在3min内迅速产生主观与客观的神经阻滞症状（100%，95%可信区间CI, 分别为85%–100%

）。而45mg的利多卡因也能产生相同作用。两组中所有病人都描述了在3min后下肢发热和沉重的感觉及5min后的运动阻滞作用。基于鞘内置管发生率为1：

380，如果患者在3分钟后没有感觉的改变，则30mg和45mg利多卡因给药对于鞘内置管的阴性预测值分别为100% (95% CI, 99.95%–100%) and 100% (95% CI, 99.93%–

100%)，同时本研究未发现低剂量组的不良事件发生率降低。

**结论：**本研究结果指出这两组剂量在确认导管误置鞘内方面没有显著差异。两组的鞘内注射的阴性预测值都非常高。这两个剂量敏感度的95%可信区间太宽以至于不能明确所有误置导管来保障临床安全性。因此还需要进行大量研究来评价30mg的剂量是否具有较低的灵敏度，或者45mg的剂量能产生较高平面的运动阻滞。

（马霄雯 译 陈杰 校）

**BACKGROUND:** The epidural test dose, used to identify unintended intrathecal placement, should reliably produce a spinal block without posing a threat to the patient. Most anesthesiologists administer a dose of local anesthetic, commonly lidocaine 45 mg. Pregnant patients are more sensitive to local anesthetics; high and total spinal anesthesia have been reported in the pregnant population with this dose. We hypothesized that lidocaine 30 mg was as effective as lidocaine 45 mg in creating rapid objective evidence of a sensory or motor block. **METHODS:** In this prospective, randomized, double-blind trial, patients scheduled for cesarean delivery were assigned to 1 of 4 groups: lidocaine 30 mg in the spinal or epidural space, or lidocaine 45 mg by the same routes. A blinded observer assessed the degree of sensory and motor block. The ability to identify intrathecal injection of each dose was compared. Sensory block above T6 dermatome and hypotension were recorded as side effects.

**RESULTS:** Intrathecal administration of lidocaine 30 mg produced rapid subjective and objective signs of neuroblockade within 3 minutes (100%, 95% confidence interval CI, 85%–100% for each). Lidocaine 45 mg produced similar results. All patients in both groups described their legs as warm or heavy after 3 minutes and had a motor block by 5 minutes. On the basis of an intrathecal catheter rate of 1:380, the observed negative predictive value for intrathecal placement if the patient described no sensory changes at 3 minutes was 100% (95% CI, 99.95%–100%) for 30 mg and 100% (95% CI, 99.93%–100%) for 45 mg. We did not identify a decrease in the rate of side effects with the lower dose.

**CONCLUSIONS:** Our results suggest that there is unlikely to be a large difference in the ability of these doses to detect unintentional intrathecal catheter placement. While the negative predictive value for intrathecal injection is very high for both doses, the 95% CI for the sensitivity of either dose is too wide to demonstrate clinical safety to identify all intrathecal catheters. A much larger study is warranted to assess whether there is a lower sensitivity with the 30-mg dose, or a propensity toward high cephalad motor block levels with the 45-mg dose.

**疼痛多基因易感性的首要证据：一项儿童队列研究**

**First Evidence of a Polygenic Susceptibility to Pain in a Pediatric Cohort**



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**背景：**目前还没有证据表明儿童术后疼痛变异的遗传基础。

**方法：**本研究前瞻性地随访168名接受整形或腹部手术并在术后使用吗啡自控镇痛的儿童。将孩子及其父母有关痛觉和阿片药物代谢的基因归为6个候选基因多态性分型（单核苷酸多态性[SNPs]），分别是：ABCB1C3435T, COMTVal158Met, NTRK1His40Tyr, OPRMA118G, POMCArg236Gln和单倍型CYP2D6，术后24小时内分别进行11次静息和活动时表情疼痛评分（FPS）来评估术后疼痛。

**结果：**静息时和较小程度上在活动时，ABCB1<sub>CC</sub>基因的儿童比ABCB1<sub>CT</sub>和ABCB1<sub>TT</sub>基因的儿童在24小时内至少4个FPS峰值大于6的发生率更高（调整后风险比=4.5；95%可信区间[CI]，1.5–13.4；多重比较的校正可信区间，0.98–20.55），且OPRM<sub>GA</sub>基因的儿童比OPRM<sub>AA</sub>基因的儿童发生率更高（调整后的危险比=3.5；95%可信区间，1.1–11.2；校正可信区间：0.70–17.30）。对亲本交配型和多次比较校正后，静息时OPRM<sub>GA</sub>基因儿童术后24小时人平均FPS得分高于OPRM<sub>AA</sub>基因儿童（ $P < 0.0002$ ），在活动期NTRK1<sub>CT</sub>基因或者NTRK1<sub>TT</sub>基因比NTRK1<sub>CC</sub>基因的平均FPS值更高（ $P = 0.002$ ），而在活动时COMT<sub>GG</sub>基因比COMT<sub>AA</sub>基因和COMT<sub>GA</sub>基因平均FPS值更低（ $P = 0.005$ ）。

**结论：**ABCB1和OPRM基因型与临床意义的疼痛变异有关，而NTRK1和COMT与亚临床效应相关。首个小样本量研究为进一步探讨小儿疼痛的遗传基础提供了线索。

（孙莉荔 译 陈杰 校）

**BACKGROUND:** There is currently no evidence about the genetic bases of postoperative pain variability in children.

**METHODS:** We prospectively followed a cohort of 168 children after orthopedic or abdominal surgery, who were under morphine patient-controlled analgesia. The children and their parents were genotyped for 6 candidate-gene polymorphisms (single-nucleotide polymorphisms [SNPs]) implicated in nociception and opiate metabolism: ABCB1C3435T, COMTVal158Met, NTRK1His40Tyr, OPRMA118G, POMCArg236Gln, and a haplotype of CYP2D6. Postoperative pain was assessed using the Faces Pain Scale (FPS), at rest and during mobilization, 11 times during the first 24 postoperative hours.

**RESULTS:** At rest, and to a lesser extent, at mobilization, having at least 4 pain peaks of FPS score  $>6$  in 24 hours was more frequent in children with ABCB1<sub>CC</sub> than in children with ABCB1<sub>CT</sub> and ABCB1<sub>TT</sub> (adjusted risk ratio = 4.5; 95% confidence interval [CI], 1.5–13.4; corrected CI for multiple comparisons, 0.98–20.55) and was more frequent in children with

OPRM\_GA than those with OPRM\_AA (adjusted risk ratio = 3.5; 95% CI, 1.1–11.2; corrected CI, 0.70–17.30). After adjusting for parental mating type and correcting for multiple comparisons, mean FPS scores across the 24 postoperative hours were higher for OPRM\_GA than for OPRM\_AA at rest ( $P < 0.0002$ ), higher for NTRK1\_CT or NTRK1\_TT than NTRK1\_CC during mobilization ( $P = 0.002$ ), and lower for COMT\_GG than COMT\_AA and COMT\_GA, during mobilization ( $P = 0.005$ ).

CONCLUSIONS: ABCB1 and OPRM genotypes are associated with clinically meaningful pain variability, whereas NTRK1 and COMT are linked to subclinical effects. This first but small cohort study provides clues to further explore the genetic foundations of pediatric pain.

### 进化早期暴露于吸入麻醉药导致秀丽隐杆线虫行为学异常

#### Early Developmental Exposure to Volatile Anesthetics Causes Behavioral Defects in *Caenorhabditis elegans*

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**背景：**越来越多的动物实验证据表明生命早期暴露于麻醉药会导致发展中的神经系统凋亡，神经元的减少会引起成人阶段的功能性不良后果。临床回顾综述表明儿童时期暴露于多种麻醉药与学习能力障碍也有着紧密的关联。尽管很多人关注过这个现象，但很少人知道麻醉药引起神经细胞死亡的机理。秀丽隐杆线虫，一个非常有力的基因动物模型，具有神经系统发育和细胞凋亡路径的特征性表现，提供了一个非常好的机会来研究麻醉引起的神经毒性。本研究假设这种线虫在其生命早期暴露于吸入麻醉药下会引起神经细胞的死亡，会产生一种成年期的行为学异常。

**方法：**在同步孵化后，幼虫被暴露于95%有效浓度的吸入麻醉药中持续4小时，在出生后第四天，测试暴露和对照组幼虫的感知和向引诱物（趋化剂）移动的能力。使用标准趋化指数来测定成功趋化的比例。

**结果：**野生型线虫在暴露于异氟醚或七氟醚后在其第一幼虫期出现了趋化指数的显著异常（趋化指数：未暴露组， $85 \pm 2$ ；异氟醚组， $52 \pm 2$ ；七氟醚组， $47 \pm 2$ ；两暴露组 $P < 0.05$ ）。线粒体突变型gas-1对暴露产生更强效果（趋化性指数：未暴露组， $71 \pm 2$ ；异氟醚组， $29 \pm 12$ ；七氟醚组， $24 \pm 13$ ；两暴露组 $P <$

$0.05$ ）。相反，介导细胞死亡程序通路突变的动物（ced-3）保留其感知和向引诱物移动的能力而不产生凋亡（趋化指数：未暴露组， $76 \pm 10$ ；异氟醚组， $73 \pm 9$ ；七氟醚组， $76 \pm$

$10$ ）。另外，本研究发现线虫对麻醉药神经毒性最敏感的窗口期发生于孵化后的第一幼虫期(L1)，这与此模型种神经形成期相一致。所有数值以平均数 $\pm$ 标准差表示。

**结论：**这些数据表明，麻醉剂影响线虫的神经习性，延伸到这一门的范围，早期暴露于吸入麻醉药可导致功能上的神经学的异常。这意味着麻药相关的神经毒性通过古老的根本

的机制发生。秀丽隐杆线虫是一个易控制的生物模型用来调查整个分子基因引起的发展中的神经系统的吸入麻醉药的毒性效应。

(詹恺诞 译 陈杰 校)

**BACKGROUND:** Mounting evidence from animal studies shows that anesthetic exposure in early life leads to apoptosis in the developing nervous system. This loss of neurons has functional consequences in adulthood. Clinical retrospective reviews have suggested that multiple anesthetic exposures in early childhood are associated with learning disabilities later in life as well. Despite much concern about this phenomenon, little is known about the mechanism by which anesthetics initiate neuronal cell death. *Caenorhabditis elegans*, a powerful genetic animal model, with precisely characterized neural development and cell death pathways, affords an excellent opportunity to study anesthetic-induced neurotoxicity. We hypothesized that exposing the nematode to volatile anesthetics early in life would induce neuron cell death, producing a behavioral defect that would be manifested in adulthood.

**METHODS:** After synchronization and hatching, larval worms were exposed to volatile anesthetics at their 95% effective concentration for 4 hours. On day 4 of life, exposed and control worms were tested for their ability to sense and move to an attractant (i.e., to chemotax). We determined the rate of successful chemotaxis using a standardized chemotaxis index.

**RESULTS:** Wild-type nematodes demonstrated striking deficits in chemotaxis indices after exposure to isoflurane (ISO) or sevoflurane (SEVO) in the first larval stage (chemotaxis index: untreated,  $85 \pm 2$ ; ISO,  $52 \pm 2$ ; SEVO,  $47 \pm 2$ ;  $P < 0.05$  for both exposures). The mitochondrial mutant *gas-1* had a heightened effect from the anesthetic exposure (chemotaxis index: untreated,  $71 \pm 2$ ; ISO,  $29 \pm 12$ ; SEVO,  $24 \pm 13$ ;  $P < 0.05$  for both exposures). In contrast, animals unable to undergo apoptosis because of a mutation in the pathway that mediates programmed cell death (*ced-3*) retained their ability to sense and move toward an attractant (chemotaxis index: untreated,  $76 \pm 10$ ; ISO,  $73 \pm 9$ ; SEVO,  $76 \pm 10$ ). Furthermore, we discovered that the window of greatest susceptibility to anesthetic neurotoxicity in nematodes occurs in the first larval stage after hatching (L1). This coincides with a period of neurogenesis in this model. All values are means  $\pm$  SD.

**CONCLUSION:** These data indicate that anesthetics affect neurobehavior in nematodes, extending the range of phyla in which early exposure to volatile anesthetics has been shown to cause functional neurological deficits. This implies that anesthetic-induced neurotoxicity occurs via an ancient underlying mechanism. *C. elegans* is a tractable model organism with which to survey an entire genome for molecules that mediate the toxic effects of volatile anesthetics on the developing nervous system.

**技术交流:验证单机近红外光谱系统在心脏手术中监测脑血流自动调节的作用**

**Technical Communication: Validation of a Stand-Alone Near-Infrared Spectroscopy System for Monitoring Cerebral Autoregulation During Cardiac Surgery**

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**背景:**在体外循环(CPB)期间基于脑血流(CBF)自动调节功能监测的动脉血压 (ABP) 个体化控制, 可以提供一个比现行使用的监护标准更为有效的预防脑血流灌注不足的方法。经颅多普勒(TCD)可实时监测血流自动调节功能。之前研究证实近红外光谱(NIRS)衍生出的局部脑氧饱和度(rScO<sub>2</sub>)监测可以在临床上替代脑血流(CBF)自动调节功能的监测。本研究目的是确定单机“即插即用”血流自动调节监控的临床试用系统的准确性, 此调节监控使用市售的近红外光谱(NIRS)监测仪以及TCD方法。

**方法:**对70例病人在体外循环(CPB)期进行大脑中动脉血流速率的TCD监测和近红外光谱(NIRS)监测。通过一台基于个人电脑的系统, 和一台基于监控近红外光谱(NIRS)的监测仪, 计算血流自动调节指数。ABP的慢波和脑血流(CBF)速率 (平均速率指数[Mx]) 之间的动态的线性相关性指数, 以及ABP与局部脑氧饱和度rScO<sub>2</sub> (脑氧饱和度指数[CO<sub>x</sub>]) 之间的动态的线性相关性指数被计算出。当CBF

(脑血流)在自动调节范围, 脑血流(CBF)和ABP之间就不会有相关性; 当脑血流(CBF)失调时, 平均速率指数 (Mx) 和脑氧饱和度指数 (CO<sub>x</sub>) 接近1 (即脑血流[CBF]和ABP相关)。通过基于个人计算机的系统和脑氧饱和度指数 (CO<sub>x</sub>) 监测仪得出平均速率指数 (Mx) 和脑氧饱和度指数 (CO<sub>x</sub>) 值, 进行后两者之间的时间平均值的线性回归和方差分析。每一个病人的Mx和CO<sub>x</sub>的值都以5mmHg为单位的ABP条柱进行分类。CBF的下限自动被定义为当Mx逐步增加到大于或等于0.4时ABP。

**结果:**在Mx和原型监测仪得到的CO<sub>x</sub>之间有相关性和良好的一致性 (r=0.510, 95%的可信区间为0.414-0.595; p<0.001, 偏差在-0.07±0.19之间)。基于个人计算机的CO<sub>x</sub>值与基于原型NIRS监测仪的CO<sub>x</sub>值之间的相关性和偏差为r=0.957(95%的可信区间为0.945-0.966; p<0.001, -0.06±0.06)。在自动调节下限的ABP平均值为63±11mm Hg(95%的预测区间为52-74 mm Hg)。虽然通过原型监测仪监测到的CO<sub>x</sub>的下限-APB平均值与来自Mx测定的APB平均值 (59±9mm Hg; 95%的预测区间为50-68 mm Hg; p=0.026) 有统计学差异性, 但是这个差异性似乎不具有临床意义。

**结论:**通过研究单机NIRS监测仪和以TCD为基础的监测方法监测的CBF自动调节之间有相关性和良好的一致性。这种装置可使血流自动调节监测广泛用于CPB期间对ABP的个性化监测成为可能。

(王苑 译 陈杰 校)

**BACKGROUND:** Individualizing arterial blood pressure (ABP) targets during cardiopulmonary bypass (CPB) based on cerebral blood flow (CBF) autoregulation monitoring may provide a more effective means for preventing cerebral hypoperfusion than the current standard of care. Autoregulation can be monitored in real time with transcranial Doppler (TCD). We have previously demonstrated that near-infrared spectroscopy (NIRS)-derived regional cerebral oxygen saturation (rScO<sub>2</sub>) provides a clinically suitable surrogate of CBF for autoregulation monitoring. The purpose of this study was to determine the accuracy of a stand-alone “plug-and-play” investigational system for autoregulation monitoring that uses a commercially available NIRS monitor with TCD methods.

**METHODS:** TCD monitoring of middle cerebral artery CBF velocity and NIRS monitoring were performed in 70 patients during CPB. Indices of autoregulation were computed by both a personal computer-based system and an investigational prototype NIRS-based monitor. A moving linear correlation coefficient between slow waves of ABP and CBF velocity (mean velocity index [Mx]) and between ABP and rScO<sub>2</sub> (cerebral oximetry index [CO<sub>x</sub>]) were

calculated. When CBF is autoregulated, there is no correlation between CBF and ABP; when CBF is dysregulated, Mx and COx approach 1 (i.e., CBF and ABP are correlated). Linear regression and bias analysis were performed between time-averaged values of Mx and COx derived from the personal computer-based system and from COx measured with the prototype monitor. Values for Mx and COx were categorized in 5 mm Hg bins of ABP for each patient. The lower limit of CBF autoregulation was defined as the ABP where Mx incrementally increased to  $\geq 0.4$ .

**RESULTS:** There was correlation and good agreement between COx derived from the prototype monitor and Mx ( $r = 0.510$ ; 95% confidence interval, 0.414–0.595;  $P < 0.001$ ; bias,  $-0.07 \pm 0.19$ ). The correlation and bias between the personal computer-based COx and the COx from the prototype NIRS monitor were  $r = 0.957$  (95% confidence interval, 0.945–0.966;  $P < 0.001$  and  $0.06 \pm 0.06$ , respectively). The average ABP at the lower limit of autoregulation was  $63 \pm 11$  mm Hg (95% prediction interval, 52–74 mm Hg). Although the mean ABP at the COx-determined lower limit of autoregulation determined with the prototype monitor was statistically different from that determined by Mx ( $59 \pm 9$  mm Hg; 95% prediction interval, 50–68 mm Hg;  $P = 0.026$ ), the difference was not likely clinically meaningful.

**CONCLUSIONS:** Monitoring CBF autoregulation with an investigational stand-alone NIRS monitor is correlated and in good agreement with TCD-based methods. The availability of such a device would allow widespread autoregulation monitoring as a means of individualizing ABP targets during CPB.

通过阈值测定、条件性位置偏爱 (CPP) 图及背根神经节激活的转录因子3变化来研究顺铂诱发持续性痛觉过敏的小鼠模型中加巴喷丁、酮咯酸和依那西普的作用

**Persistent Hyperalgesia in the Cisplatin-Treated Mouse as Defined by Threshold Measures, the Conditioned Place Preference Paradigm, and Changes in Dorsal Root Ganglia Activated Transcription Factor 3: The Effects of Gabapentin, Ketorolac, and Etanercept**

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**背景：**疼痛性神经病变是一种癌症化疗中导致剂量限制的副作用。为了描述此现象，对顺铂处理的多发性神经病变小鼠模型进行疼痛行为和镇痛作用研究。

**方法：**对雄性C57BL/6小鼠每隔一日进行腹腔注射顺铂或生理盐水 (2.3mg/kg/d) 6次，持续2周，总剂量13.8mg/kg。对热逃逸潜伏期，von Frey hairs触发机械痛觉，行为/发病率以及体重进行评估。触发痛觉过敏后，检测腹腔内注射加巴喷丁(100 mg/kg)、依那西普(20 and 40 mg/kg)、酮咯酸(15 mg/kg)和吗啡(1, 3, and 10 mg/kg)各自作用。此外，采用CPP方法，研究加巴喷丁和酮咯酸对由顺铂触发的疼痛状态的影响。另外，还研究了顺铂处理小鼠的脊髓和背根神经节 (DGR)。

**结果：**顺铂而非生理盐水产生持续46天的后肢痛觉过敏，但对热逃逸现象无影响。加巴喷丁和吗啡而非依那西普或酮咯酸可产生完全但短暂 (2小时) 的痛觉过敏逆转。依那西普(40 mg/kg)

预处理使机械性痛觉过敏延迟触发。加巴喷丁而非酮咯酸用于顺铂处理小鼠，基于CPP发

现存在对药物相关治疗室的显著偏爱行为。加巴喷丁注射后，在非顺铂处理小鼠（无痛觉过敏）中没有发现位置偏爱行为。顺铂处理小鼠的免疫组织化学未显示胶质纤维酸性蛋白（星形胶质细胞）或Iba1（离子钙结合调节分子1）小胶质神经细胞激活状态的变化，但在DRG中观察到激活的转录因子3显著增加。

**结论：**与其对CPP系统中行为效应一致，顺铂处理小鼠表现痛觉过敏和DRG活化的转录因子3激活，然而加巴喷丁而非酮咯酸在顺铂引起的多发性神经病中是有积极作用的，明确了神经病变是一种负面（痛苦的）状态，且加巴喷丁可以缓解。

（黄萍 译 陈杰 校）

**BACKGROUND:** Painful neuropathy is a dose-limiting side effect in cancer chemotherapy. To characterize this phenomenon, we examined pain behavior and analgesic actions in a mouse model of cisplatin polyneuropathy.

**METHODS:** Male C57BL/6 mice received intraperitoneal cisplatin or saline (2.3 mg/kg/d) every other day 6 times over 2 weeks for a total dose of 13.8 mg/kg. Thermal escape latencies, mechanical allodynia using von Frey hairs, and observation of behavior/morbidity and body weights were assessed. After onset of allodynia, we examined the actions of intraperitoneal gabapentin (100 mg/kg), etanercept (20 and 40 mg/kg), ketorolac (15 mg/kg), and morphine (1, 3, and 10 mg/kg). Additionally, using the conditioned place preference (CPP) paradigm, we examined the effects of gabapentin and ketorolac on the presumed pain state initiated by cisplatin. Additionally, we examined the spinal cord and dorsal root ganglia (DRG) of cisplatin-treated mice.

**RESULTS:** Cisplatin, but not saline treatment, produced persistent hindpaw tactile allodynia, which persisted 46 days with no effect on thermal escape. Gabapentin and morphine, but neither etanercept nor ketorolac, produced a complete but transient (2-hour) reversal of the allodynia. Etanercept (40 mg/kg) pretreatment resulted in a delay in onset of mechanical allodynia. Using CPP, gabapentin, but not ketorolac, in cisplatin animals resulted in a significant preference for the drug-associated treatment compartment. There was no place preference in non-cisplatin-treated (nonallodynic) mice after gabapentin injection. Immunohistochemistry in cisplatin-treated mice showed no change in glial fibrillary acidic protein (astrocyte) or Iba1 (ionized calcium binding adaptor molecule 1) (microglia) activation states, but a significant increase in activated transcription factor 3 was observed in the DRG.

**CONCLUSIONS:** Cisplatin-treated mice display allodynia and an activation of DRG activated transcription factor 3, which is paralleled by its effects on behavior in the CPP system, wherein gabapentin, but not ketorolac, in the presence of the cisplatin polyneuropathy, is positively rewarding, confirming that this neuropathy is an aversive (painful) state that is ameliorated by gabapentin.

用于腋路臂丛阻滞的高低刺激电流阈值对比：一项对205名病人的前瞻随机三盲非劣效性试验

### **High- Versus Low-Stimulation Current Threshold for Axillary Plexus Blocks: A Prospective Randomized Triple-Blinded Noninferiority Trial in 205 Patients**

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**背景：**对于神经刺激器引导下的局部麻醉，麻醉医师必须在假定低成功率（使用高电流阈值）和假定增加神经损伤风险（使用低电流阈值）这二者之间做出权衡。针对神经刺激引导的臂丛神经阻滞，本研究假设使用0.9至1.1mA范围内的高电流阈值在操作和起效时间方面并不比0.3至0.5mA范围内的低电流阈值要差。

**方法：**205名计划择期手术病人被随机分为低刺激电流阈值组（0.3-0.5mA，n=103）或者高刺激电流阈值组（0.9-1.1mA，n=102），两组都使用40mL局麻药混合液（1%丙胺卡因和0.75%罗哌卡因各20mL）进行腋路臂丛神经阻滞。研究主要终点为感觉完全阻滞时间。次要结果是手术准备时间（定义为从开始阻滞至感觉完全阻滞时间）和操作时间。非劣效性边界设为5分钟并且以双边95%的自举置信区间（[CIs] 100,000次重复）均数差来评价。

**结果：**低刺激电流阈值组的感觉完全阻滞平均时间显著减少（ $17.9 \pm 12.1$ （平均值  $\pm$  标准差）对  $22.8 \pm 12.4$  分钟；95% 置信区间，1.1 至 8.6； $p = 0.012$ ）。低刺激电流阈值组的手术准备时间为  $30.3 \pm 13.8$  分钟而高刺激电流阈值组为  $31.7 \pm 12.9$  分钟（95% 置信区间，-2.7 至 5.5； $p = 0.49$ ）。高刺激电流阈值组的操作时间明显缩短（ $9.5 \pm 4.7$  对  $11.9 \pm 5.7$  分钟；95% 置信区间，-4 至 1.1； $p = 0.001$ ）。

**结论：**

次要终点都不能确认高电流阈值技术的非劣效性。但考虑到临床实践，在满足手术要求的平均花费时间方面约8.5分钟的差异是可以接受的。

（孙晓琼 译 陈杰 校）

**BACKGROUND:** For nerve stimulator-guided regional anesthesia, one has to compromise between a presumed low success rate (using a high-current threshold) and a presumed increased risk of nerve damage (using a low-current threshold). We hypothesized that high-current thresholds in the range of 0.9 to 1.1 mA are not inferior with respect to the procedural and latency times compared with low threshold currents in the range of 0.3 to 0.5 mA for nerve stimulation in brachial plexus blocks.

**METHODS:** Two hundred five patients scheduled for elective surgery were randomized to a low (0.3–0.5 mA, n = 103) or a high (0.9–1.1 mA, n = 102) stimulation current threshold for the axillary plexus block with 40 mL local anesthetic mixture (20 mL, each of prilocaine 1% and ropivacaine 0.75%). The primary end point was the time to complete sensory block. The secondary outcome measures were the time to readiness for surgery (defined as the time from the start of block procedure to complete sensory block) and the block performance time. The noninferiority margin was set at 5 minutes and was evaluated using the two-sided 95% bootstrap-confidence intervals ([CIs] 100,000 replications) for differences in means.

**RESULTS:** The mean times to complete sensory block revealed a significant decrease with the low-current group ( $17.9 \pm 12.1$  (mean  $\pm$  SD) versus  $22.8 \pm 12.4$  minutes; 95% CI, 1.1 to 8.6;  $p =$

0.012). The time to readiness for surgery was  $30.3 \pm 13.8$  minutes in the low-current group and  $31.7 \pm 12.9$  minutes in the high-current group (95% CI, -2.7 to 5.5;  $p = 0.49$ ). The performance time was significantly shorter in the high-current threshold group ( $9.5 \pm 4.7$  versus  $11.9 \pm 5.7$  minutes; 95% CI, -4 to 1.1;  $p = 0.001$ ).

**CONCLUSION:** Noninferiority for the high-current threshold technique could neither be confirmed for the primary end point nor for secondary end points. However, we consider a difference in mean times of approximately 8.5 minutes to achieve readiness for surgery acceptable for clinical practice.

### 地塞米松预防术后恶心呕吐：一项随机对照试验的最新Meta分析

#### **Dexamethasone to Prevent Postoperative Nausea and Vomiting: An Updated Meta-Analysis of Randomized Controlled Trials**

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**背景：**地塞米松确实可以减少术后恶心呕吐（PONV）的发生，然而，地塞米松用作单一或者联合预防性用药时减少PONV的最佳剂量未清楚阐明。这项研究中，我们评估了静脉内注射4-5mg和8-10mg作为单一或者联合预防用药的一部分预防PONV的应用。

**方法：**为了鉴定全身性给予地塞米松预防术后恶心和/或呕吐的随机临床试验，开展了一项广泛的研究。过把集中起来的试验分为两组来地塞米松剂量的效应：4-5mg和8-10mg。第一组是非住院麻醉学会（SAMBA）指南预防PONV的推荐地塞米松剂量，第二组是两倍的推荐剂量。SAMBA指南是根据那些检查地塞米松不同剂量的研究所发展起来的。

**结果：**入选了60个随机临床试验包含6696个受试者。和对照组比，4-5mg地塞米松剂量组降低了24小时PONV发生率(OR, 0.31; 95%可信区间, 0.23-0.41)和需要处理的病例数(NNT, 3.7; 95%可信区间, 3.0-4.7)。和另一种止吐药合用时，4-5mg地塞米松组的24小时PONV发生率也较对照组低(OR, 0.50; 95%可信区间, 0.35-0.72; NNT, 6.6; 95%可信区间, 4.3-12.8)。8-10mg地塞米松剂量组的24小时PONV发生率比对照组少(OR, 0.26; 95% CI, 0.20-0.32; NNT, 3.8; 95% CI, 3.0-4.3)。在对8-10mg剂量组的分析中发现了不对称漏斗曲线图，提示有发表偏倚的可能。和另一种止吐药合用时，8-10mg剂量组的24小时PONV的发生率也降低了(OR, 0.35; 95% CI, 0.22-0.53; NNT, 6.2; 95% CI, 4.5-10)。在两组之间直接对比的研究显示，对于术后恶心和/或呕吐的发生率，8-10mg地塞米松没有比4-5mg的剂量有临床优势。

**结论：**我们的结果表明地塞米松作为单一或者联合用药在降低PONV的发生方面，好像4-5mg与8-10mg有相似的临床效应。这些发现支持了SAMBA指南目前推荐的全身性给予4-5mg地塞米松降低PONV的发生率。

（王晓莉 译 马皓琳 李士通 校）

**BACKGROUND:** Dexamethasone has an established role in decreasing postoperative nausea and vomiting (PONV); however, the optimal dexamethasone dose for reducing PONV when it is



used as a single or combination prophylactic strategy has not been clearly defined. In this study, we evaluated the use of 4 mg to 5 mg and 8 mg to 10 mg IV doses of dexamethasone to prevent PONV when used as a single drug or as part of a combination preventive therapy.

**METHODS:** A wide search was performed to identify randomized clinical trials that evaluated systemic dexamethasone as a prophylactic drug to reduce postoperative nausea and/or vomiting. The effects of dexamethasone dose were evaluated by pooling studies into 2 groups: 4 mg to 5 mg and 8 mg to 10 mg. The first group represents the suggested dexamethasone dose to prevent PONV by the Society for Ambulatory Anesthesia (SAMBA) guidelines, and the second group represents twice the dose range recommended by the guidelines. The SAMBA guidelines were developed in response to studies, which have been performed to examine different dosages of dexamethasone.

**RESULTS:** Sixty randomized clinical trials with 6696 subjects were included. The 4-mg to 5-mg dose dexamethasone group experienced reduced 24-hour PONV compared with control, odds ratio (OR, 0.31; 95% confidence interval [CI], 0.23–0.41), and number needed to treat (NNT, 3.7; 95% CI, 3.0–4.7). When used together with a second antiemetic, the 4-mg to 5-mg dexamethasone group also experienced reduced 24-hour PONV compared with control (OR, 0.50; 95% CI, 0.35–0.72; NNT, 6.6; 95% CI, 4.3–12.8). The 8-mg to 10-mg dose dexamethasone group experienced decreased 24-hour PONV compared with control (OR, 0.26; 95% CI, 0.20–0.32; NNT, 3.8; 95% CI, 3.0–4.3). Asymmetric funnel plots were observed in the 8-mg to 10-mg dose analysis, suggesting the possibility of publication bias. When used together with a second antiemetic, the 8-mg to 10-mg dose group also experienced reduced incidence of 24-hour PONV (OR, 0.35; 95% CI, 0.22–0.53; NNT, 6.2; 95% CI, 4.5–10). In studies that provided a direct comparison between groups, there was no clinical advantage of the 8-mg to 10-mg dexamethasone dose compared with the 4-mg to 5-mg dose on the incidence of postoperative nausea and/or vomiting.

**CONCLUSIONS:** Our results showed that a 4-mg to 5-mg dose of dexamethasone seems to have similar clinical effects in the reduction of PONV as the 8-mg to 10-mg dose when dexamethasone was used as a single drug or as a combination therapy. These findings support the current recommendation of the SAMBA guidelines for PONV, which favors the 4-mg to 5-mg dose regimen of systemic dexamethasone.

### 在高血压病人麻醉诱导期间使用无创性脉搏传导时间监测每搏收缩压

#### **Beat-to-Beat Tracking of Systolic Blood Pressure Using Noninvasive Pulse Transit Time During Anesthesia Induction in Hypertensive Patients**

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**背景：**已有研究报道脉搏传导时间（PPT）在清醒的人中，与动脉血压（BP）有较好的相关性。我们测量了高血压病人麻醉诱导期间，无创每搏PPT是否与持续有创动脉血压监测有精确的相关性。

**方法：**23名择期行肾移植手术的高血压病人被选入组。同步记录桡动脉BP、心电图和指脉血氧体积描记。PTT定义为从心电图上的R波的波峰到光电容积描记的最大上升支的时

间间隔。每搏PTT和BP之间的关系用相关性和受试者工作特征（ROC）曲线分析来进行评价。

**结果：**在麻醉诱导期间，PPT的变化与BP的变化是成正比的：当BP下降时，PPT延长，反之亦然。PPT的改变与收缩压的相关性显著优于与平均动脉压( $r = 0.81 \pm 0.11$  vs  $r = 0.72 \pm 0.17$ ;  $P < 0.001$ )和舒张压( $r = 0.81 \pm 0.11$  vs  $r = 0.52 \pm 0.24$ ;  $P < 0.001$ )的相关性。PPT的改变与舒张压下降的相关性比与舒张压上升的相关性明显 ( $r = 0.83 \pm 0.12$  vs  $r = 0.68 \pm 0.20$ ;  $P = 0.001$ )。ROC曲线分析表明，在麻醉诱导期间，PTT增加15%可以发现收缩压下降 $\geq 30\%$ ，ROC曲线下面积为0.85。

**结论：**每搏PPT与有创收缩压有良好的相关性，并且可以预测麻醉诱导期间的收缩压下降。在高风险的高血压患者不可用有创血压时，每搏PPT可以作为潜在有用的收缩压无创性监测指标。

（安光惠 译 马皓琳 李士通 校）

**BACKGROUND:** Pulse transit time (PTT) has been reported to show good agreement with arterial blood pressure (BP) in awake humans. We evaluated whether noninvasive beat-to-beat PTT accurately correlated with invasively measured continuous arterial BP during anesthesia induction in hypertensive patients.

**METHODS:** Twenty-three hypertensive patients who were scheduled for kidney transplant were enrolled. Radial arterial BP, electrocardiogram, and finger pulse oximetric plethysmography were simultaneously recorded. PTT was measured as the time interval from the R-wave peak on the electrocardiogram to the maximal upslope of the photoplethysmogram. Relationships between beat-to-beat PTT and BP were evaluated by correlation and receiver operating characteristic (ROC) curve analysis.

**RESULTS:** During anesthesia induction, changes in PTT were directly proportional to changes in BP: when BP decreased, PTT lengthened, and vice versa. The inverse of PTT demonstrated significantly better correlation with systolic BP than with mean BP ( $r = 0.81 \pm 0.11$  vs  $r = 0.72 \pm 0.17$ ;  $P < 0.001$ ) or diastolic BP ( $r = 0.81 \pm 0.11$  vs  $r = 0.52 \pm 0.24$ ;  $P < 0.001$ ). The inverse of PTT was more highly correlated with decreasing than with increasing changes in systolic BP ( $r = 0.83 \pm 0.12$  vs  $r = 0.68 \pm 0.20$ ;  $P = 0.001$ ). The ROC curve analysis revealed that a 15% increase in PTT during anesthesia induction could detect a  $\geq 30\%$  decrease in systolic BP, with an area under the ROC curve of 0.85.

**CONCLUSION:** Beat-to-beat PTT was fairly well correlated with invasive systolic BP and could predict a reduction in systolic BP during anesthesia induction. Beat-to-beat PTT may show potential as a useful noninvasive index of systolic BP when invasive BP is unavailable in high-risk hypertensive patients.

### 心脏电生理学实验中心对多名患者气道损伤的研究

#### Airway Trauma in a High Patient Volume Academic Cardiac Electrophysiology Laboratory Center

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**背景：**在电生理治疗过程中实施麻醉和气道管理是有挑战的，因为其独特的设备需置于常规手术房间之外。我们报道了对于一些有气道损伤，包括舌和咽部血肿及声带麻痹的病例中我们的经验。

**方法：**我们分析了心脏电生理实验中心2009年12月至2011年1月间所有报道的气道损伤病例，并且与没有气道损伤的病例进行了比较。数据采集通过回顾医疗记录收集了来自于87例病人的数据，包括16例气道损伤病人（损伤组）和71例没有气道损伤的来自同一时期相同病人群体的病人（控制组）。

**结果：**在14个月间2434例麻醉病人中，有16例（0.7%）报道了气道损伤。所有这些病人都没有发生威胁生命的气道梗阻。我们发现对于体重指数小于30的病人诱导时不使用肌松药是气道损伤的显著风险因素（ $P=0.04$ ；比值比，10；95%可信区间，1.1-482）。在2例未使用软性咬口的心脏复律病人中发生了舌头或软组织咬伤。创伤组和控制组之间在操作前抗凝、操作期间抗凝及操作结束时逆转肝素方面均未发现统计学显著性差异。

**结论：**在我们的研究人群中，报道的气道损伤的总体发生率为0.7%。舌损伤是最常见的气道损伤。原因可能为多因素；然而，不应用肌松药的气道管理显现为一个潜在的危险因素。推荐在心脏复律前使用肌松药行气管插管和放置软咬口，并且要保证牙齿间没有软组织。

（张怡 译 马皓琳 李士通校）

**BACKGROUND:** Providing anesthesia and managing airways in the electrophysiology suite can be challenging because of its unique setting outside of the conventional operating room. We report our experience of several cases of reported airway trauma including tongue and pharyngeal hematoma and vocal cord paralysis in this setting.

**METHODS:** We analyzed all of the reported airway trauma cases between December 2009 and January 2011 in our cardiac electrophysiology laboratories and compared these cases with those without airway trauma. Data from 87 cases, including 16 cases with reported airway trauma (trauma group) and 71 cases without reported airway trauma from the same patient population pool at the same period (control group), were collected via review of medical records.

**RESULTS:** Airway trauma was reported for 16 patients (0.7%) in 14 months among 2434 anesthetic cases. None of these patients had life-threatening airway obstruction. The avoidance of muscle relaxants during induction in patients with a body mass index less than 30 was found to be a significant risk factor for airway trauma ( $P = 0.04$ ; odds ratio, 10; 95% confidence interval, 1.1–482). Tongue or soft tissue bite occurred in 2 cases where soft bite block was not used during cardioversion. No statistically significant difference was found between the trauma and the control groups for preprocedure anticoagulation, anticoagulation during the procedure, or reversal of heparin at the end of the procedure.

**CONCLUSIONS:** The overall incidence of reported airway trauma was 0.7% in our study population. Tongue injury was the most common airway trauma. The cause seems to have been multifactorial; however, airway management without muscle relaxant emerged as a potential risk factor. Intubation with muscle relaxant is recommended, as is placing a soft bite block and ensuring no soft tissue is between the teeth before cardioversion.

**间歇性硬膜外注射与连续性硬膜外输注用于分娩镇痛的比较：一项系统回顾和荟萃分析**  
**Intermittent Epidural Bolus Compared with Continuous Epidural Infusions for Labor Analgesia: A Systematic Review and Meta-Analysis**

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**背景：**目前标准硬膜外分娩镇痛方案为局麻药结合阿片类药物通过持续硬膜外输注（CEI）。使用CEI局麻药镇痛的剂量可能较大，产生深度运动阻滞，从而潜在影响器材辅助分娩发生率。在本随机对照试验（RCTs）的系统性回顾中，我们对采用硬膜外镇痛分娩的健康产妇，比较了间断硬膜外注射（IEB）和标准CEI使用或不使用患者自控硬膜外镇痛，对患者满意度、人为麻醉干预的需要、产程和分娩方式的影响。

**方法：**本研究为一项比较CEI和IEB分娩镇痛的RCTs系统性评价。这些文章进行了有效性评估，数据由作者提取，并用比值比（ORs）、平均差（MDS）和95%可信区间（CIs）进行总结。

**结果：**9项随机对照试验被纳入该系统性回顾。344名受试者接受了CEI，350名受试者接受了IEB分娩镇痛。所有9个研究被认为为低偏倚风险。IEB和CEI在剖腹产率(OR, 0.87; 95% CI, 0.56–1.35)、产程(MD, -17分; 95% CI, -42 to 7)和麻醉干预的需要(OR, 0.56; 95% CI, 0.29–1.06)均无统计学差异。IEB能轻度但统计学显著性减少局麻药使用量(MD, 每小时-1.2 mg 布比卡因; 95% CI, -2.2 到-0.3)。产妇的满意度得分（100-mm视觉模拟评分法）IEB（MD, 7.0mm; 95% CI, 6.2-7.8）较高。

**结论：**IEB是一个有研究前景的概念，目前证据表明IEB稍微降低了局部麻醉剂使用量并提高产妇的满意度。考虑到收集的很多结果中CIs较多，不能得出明确结论，但IEB仍是一个潜在改善器械助产率及麻醉干预需要的方法。需要更多研究来使理想的IEB方案概念化，并研究其对分娩镇痛和产科转归的影响。

（许辛译，马皓琳，李士通校）

**BACKGROUND:** The current standard labor epidural analgesic regimens consist of a local anesthetic in combination with an opioid delivered via continuous epidural infusion (CEI). With CEI local anesthetic, doses may be large with resulting profound motor blockade potentially affecting the incidence of instrumental deliveries. In this systematic review of randomized controlled trials (RCTs), we compared the effect of intermittent epidural bolus (IEB) to standard CEI dosing with or without patient-controlled epidural analgesia on patient satisfaction, the need for manual anesthesia interventions, labor progression, and mode of delivery in healthy women receiving labor epidural analgesia.

**METHODS:** A systematic review of RCTs that compared CEI with IEB for labor analgesia was performed. The articles were evaluated for validity, and data were extracted by the authors and summarized using odds ratios (ORs), mean differences (MDs), and 95% confidence intervals (CIs).

**RESULTS:** Nine RCTs were included in this systematic review. Three hundred forty-four subjects received CEI, whereas 350 subjects received IEB labor analgesia. All 9 studies were

deemed to be low risk of bias. There was no statistical difference detected between IEB and CEI in the rate of cesarean delivery (OR, 0.87; 95% CI, 0.56–1.35), duration of labor (MD, –17 minutes; 95% CI, –42 to 7), or the need for anesthetic intervention (OR, 0.56; 95% CI, 0.29–1.06). IEB did result in a small but statistically significant reduction in local anesthetic usage (MD, –1.2 mg bupivacaine equivalent per hour; 95% CI, –2.2 to –0.3). Maternal satisfaction score (100-mm visual analog scale) was higher with IEB (MD, 7.0 mm; 95% CI, 6.2–7.8).

**CONCLUSIONS:** IEB is an appealing concept; current evidence suggests IEB slightly reduces local anesthetic usage and improves maternal satisfaction. Given the wide CIs of the pooled results for many outcomes, definite conclusions cannot be drawn for those outcomes, but there is also a potential that IEB improves instrumental delivery rate and need of anesthesia interventions. More study is required to conceptualize the ideal IEB regimen and investigate its effect on labor analgesia and obstetric outcomes.

### 转运降低模拟孕妇心跳骤停时的心肺复苏质量

#### Transport Decreases the Quality of Cardiopulmonary Resuscitation During Simulated Maternal Cardiac Arrest

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Anesth Analg January 2013 116:162-167;

**背景：**本研究的目的是为了比较对模拟心跳骤停孕妇行心肺复苏（CPR）时转运至手术室和留在产房的复苏效果。我们假设在转运过程中心肺复苏质量恶化。

**方法：**包括两名实施者（产科医师、护士或者麻醉医师）的26人团队随机分组，分别在转运时或者原地固定对Laerdal Resusci Anne

SkillReporter™人体模型行心肺复苏。主要评测指标是正确的传递到模型的胸外按压（定义为按压频率≥100bpm，手掌按压胸骨的位置正确，按压深度≥1.5英寸即3.8厘米及适当的释放）的比例。次要指标包括按压过程的中断、转运过程中按压者相对于人体模型的位置和通气潮气量。

**结果：**在II期中正确的胸外按压率的中位数（四分间距），转运组是32%（10%-63%），固定组为93%（58%-100%）（ $P=0.002$ ,平均差异的95%可信区间是22%-58%）。

转运组的按压频率的中位数（四分间距）是124（110-140）bpm，固定组则为123（115-132）bpm（ $P=$

0.531）。在心肺复苏过程中，转运组被打断的发生率为92%，而固定组只有7%（ $P<0.001$ ,差异的95%可信区间是61%-

92%）。转运过程中，18名施救者跪在人体模型旁，2名跨坐在模型上，4名在跟着推床跑。转运组的通气潮气量的中位数（四分间距）是270（166-430）ml，固定组为390（232-513）ml（ $P=0.03$ ）。

**结论：**我们的研究结果验证了我们的假设，证实了转运对模拟孕妇心跳骤停模型的心肺复苏总体质量带来不利影响。这些结果和先前出版的有关从产房移到手术室时转运相关延迟的数据进一步加强了这样的建议：心跳骤停的产妇的剖腹产手术需在原地实施。

（方斌 译 马皓琳 李士通校）

**BACKGROUND:** The purpose of this study was to compare cardiopulmonary resuscitation (CPR) for simulated maternal cardiac arrest rendered during transport to the operating room with that rendered while stationary in the labor room. We hypothesized that the quality of CPR would deteriorate during transport.

**METHODS:** Twenty-six teams composed of 2 providers (obstetricians, nurses, or anesthesiologists) were randomized to perform CPR on the Laerdal Resusci Anne SkillReporter™ mannequin during transport or while stationary. The primary outcome measure was the percentage of correctly delivered compressions, defined as compression rate  $\geq 100$  beats per minute, correct sternal hand placement, compression depth  $\geq 1.5$  inches (3.8 cm), and proper release. Secondary outcomes included interruptions in compressions, position of providers relative to the mannequin during the transport phase, and ventilation tidal volume.

**RESULTS:** The median (interquartile range) percentage of correctly rendered compressions during phase II was 32% (10%–63%) in the transport group and 93% (58%–100%) in the stationary group ( $P = 0.002$ , 95% confidence interval of mean difference = 22%–58%). The median (interquartile range) compression rates were 124 (110–140) beats per minute in the transport group and 123 (115–132) beats per minute in the stationary group ( $P = 0.531$ ). Interruptions in CPR were observed in 92% of transport and 7% of stationary drills ( $P < 0.001$ , 95% confidence interval of difference = 61%–92%). During transport, 18 providers kneeled next to the mannequin, 2 straddled the mannequin, and 4 ran alongside the gurney. Median (interquartile range) tidal volume was 270 (166–430) mL in the transport group and 390 (232–513) mL in the stationary group ( $P = 0.03$ ).

**CONCLUSIONS:** Our data confirm our hypothesis and demonstrate that transport negatively affects the overall quality of resuscitation on a mannequin during simulated maternal arrest. These findings, together with previously published data on transport-related delays when moving from the labor room to the operating room further strengthen recommendations that perimortem cesarean delivery should be performed at the site of maternal cardiac arrest.

## 被动腿抬高和/或头低脚高位对接受手术治疗的先天性心脏病婴幼儿颈内静脉截面积的影响

### The Effect of Passive Leg Elevation and/or Trendelenburg Position on the Cross-Sectional Area of the Internal Jugular Vein in Infants and Young Children Undergoing Surgery for Congenital Heart Disease

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**背景：**在这项研究中，我们评估了被动腿抬高（LE）和头低脚高位（T）对手术治疗先天性心脏病的婴幼儿颈内静脉（IJV）截面积（CSA）的影响。另外一个目的是比较右向左（RL）和左向右（LR）分流的受试者之间颈内静脉截面积的差异。

**方法：**将90例10天—31个月大，重量1.5公斤—9.7公斤的婴儿和幼儿分配至RL组（ $n = 48$ ）或LR组（ $n = 42$ ）。在这两个群体中，使用一个二维超声传感器在以下体位时测量颈部两侧的IJV的横

截面积横径和垂直径：仰卧位、15°T位、LE 50°的仰卧位、15°T位+LE 50°（TLE）。颈内静脉的平均截面积增加超过25%被视为具有临床意义。

**结果：**在LR组，T、LE和TLE显著增加右侧IJVs的CSA（至少分别为12.3%、10.3%和18.3%，“至少”指的是95%置信度）和左侧IJVs的CSA（至少分别为15.8%、15.0%和18.9%），而在RL组中只有TLE增加双侧IJVs的CSA（右侧和左侧至少分别为8.2%和7.7%）。LR组中与T和TLE相关的右侧IJV的CSA增加比RL组显著（T至少是12.3%比1.2%，TLE至少是18.3%比8.2%）。

在LR组中TLE时右侧和左侧IJVs的CSA有临床意义的显著增加（平均分别为28.6%和26.3%）。在大部分病人中（至少为69.2%），右侧IJV的CSA比左侧显著大。

**结论：**被动LE和T体位一样能有效增加IJV的CSA，但是没有任何一种单一的方法可以使CSA有临床意义上的显著增加。只有LR分流组中T体位+被动LE体位的婴幼儿两侧IJVs的CSA有临床意义上的显著增加，但在RL组中相同年龄的婴幼儿却无此差别。

（崔晓娜 译 马皓琳 李士通 校）

**BACKGROUND:** In this study we evaluated the effect of passive leg elevation (LE) and Trendelenburg (T) position on the cross-sectional area (CSA) of the internal jugular vein (IJV) in infants and young children undergoing surgery for congenital heart disease. A secondary aim was to compare the CSA of the IJV between subjects with right-to-left (RL) shunt and left-to-right (LR) shunt.

**METHODS:** Ninety infants and small children from 10 days to 31 months old weighing from 1.5 to 9.7 kg were assigned to group RL ( $n = 48$ ) or LR ( $n = 42$ ). In both groups, the CSA, transverse, and vertical diameters of the IJV on both sides of the neck were measured using a 2-dimensional ultrasound transducer in the following positions: supine position, 15° of T position, supine position with 50° of LE, and 15° of Trendelenburg position with 50° of LE (TLE). A more than 25% increase in mean CSA of the IJV was considered clinically significant.

**RESULTS:** In group LR, T, LE, and TLE significantly increased CSA of both right (at least 12.3%, 10.3%, and 18.3%, respectively, “at least” refers to the lower 95% confidence limits) and left (at least 15.8%, 15.0%, and 18.9%, respectively) IJVs, whereas only TLE increased the CSA of both IJVs significantly in group RL (at least 8.2% and 7.7% in the right and left, respectively). The increase in the CSA of the right IJV related to T and TLE was larger in group LR than in group RL (at least 12.3% vs 1.2% for T and at least 18.3% vs 8.2% for TLE, respectively). A clinically significant increase in CSA was achieved in both right and left IJVs with TLE in group LR (mean 28.6% and 26.3%, respectively). The CSA of the right IJV was larger than that of the left IJV in most (at least 69.2%) patients.

**CONCLUSIONS:** Passive LE was as effective as T position to increase the CSA of the IJV, but there was no clinically significant increase in the CSA with any single maneuver. Only T position with passive LE achieved a clinically significant increase in the CSA of both IJVs in infants and young children with LR shunt, but not in the same age group with RL shunt.

### 鞘内注射巴氯芬对复杂性区域疼痛综合征中不同性质疼痛的功效

#### Efficacy of Intrathecal Baclofen on Different Pain Qualities in Complex Regional Pain Syndrome

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**背景：**复杂性区域疼痛综合征（CRPS）以使人严重衰弱的慢性疼痛为特点。患有CRPS的病人可能会经历各种疼痛感觉，它们很可能体现了不同的病理生理机制。本研究中，我们评估了中枢 $\gamma$ -

氨基丁酸（B）受体刺激对患有肌张力障碍的CRPS患者中不同性质疼痛的独特作用。

**方法：**在一个为期一年的开放性设计中，我们每3个月对接受滴定剂量鞘内注射巴氯芬（ITB）治疗的42名有肌张力障碍的CRPS患者评估一次10项疼痛性质的神经病理性疼痛量表、肌张力障碍程度和镇痛药物使用情况的改变。

**结果：**我们使用一个线性混合模型分析并以总体肌张力障碍程度和追加镇痛药物的使用情况作为控制手段。在最初的6个月中，我们发现总体的剧烈痛、尖锐痛、钝性痛和深部痛有显著的改善。在这个时期之后，尽管肌张力障碍进一步改善并继续提升ITB剂量但评分趋于平稳。

**结论：**ITB刺激 $\gamma$ -

氨基丁酸（B）受体对有肌张力障碍的CRPS患者特定性质的疼痛表现出独特的镇痛效果。

（唐莹 译 马皓琳 李士通 校）

**BACKGROUND:** Complex regional pain syndrome (CRPS) is characterized by severe debilitating chronic pain. Patients with CRPS may experience various pain sensations, which likely embody different pathophysiologic mechanisms. In this study, we evaluated the differential effects of central  $\gamma$ -aminobutyric acid (B) receptor stimulation on the different pain qualities in CRPS patients with dystonia.

**METHODS:** The 10 pain qualities of the neuropathic pain scale, dystonia severity, and changes in use of antinociceptive drugs were evaluated every 3 months for a period of 1 year in 42 CRPS patients with dystonia receiving titrated doses of intrathecal baclofen (ITB) treatment in an open design.

**RESULTS:** Using a linear mixed model analysis and controlling for global dystonia severity and the use of supplemental analgesics, we found a significant improvement in global intense pain, sharp pain, dull pain, and deep pain during the first 6 months. After this period, the scores leveled off despite further improvement of dystonia and continued ITB dose escalation.

**CONCLUSIONS:**  $\gamma$ -Aminobutyric acid (B) receptor stimulation by ITB exerts differential antinociceptive effects on specific pain qualities in CRPS patients with dystonia.

钾离子通道在大鼠鞘内注射吗啡所致抗外周水肿效应中的作用。

### The Involvement of Potassium Channels in the Peripheral Antiedematogenic Effect of Intrathecally Injected Morphine in Rats

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**背景：**既往研究显示鞘内注射吗啡可通过激活一氧化氮/环磷酸鸟苷酸通路减少大鼠实验性炎性水肿。这个证据支持了这样一个假设，即在这种情况下钾通道的开放在调解吗啡的效应中起重要作用。

**方法：**雄性韦氏大鼠接受鞘内注射药物（20微升）30分钟后，予角叉菜胶（150微克）刺激爪。通过记录爪体积的增加（以毫升为单位）来评估水肿情况，通过依蓝染液渗出计算血浆渗漏。通过髓过氧化物酶分析来间接评价中性粒细胞迁移情况。通过组织学检查来观察炎性细胞浸润和血管充血情况。

**结果：**与磷酸盐缓冲液相比较，吗啡（37nmol）可以抑制炎性水肿、血浆漏出及血管充血，但是对髓过氧化物酶活性及中性粒细胞数量无作用。同时注射4-氨基吡啶（10 nmol）、格列本脲（5 nmol）和地喹铵（10pmol）可逆转吗啡的作用，而尼克地尔（0.03nmol）可增强吗啡的作用。

**结论：**这些结果支持这样一个假设，即鞘内注射吗啡所致的外周抗水肿效应由钾通道的激活所介导。而且，阿片类药物不影响急性中性粒细胞迁移的抑制，但影响毛细血管募集反应的减小。

（王赞 译 马皓琳 李士通 校）

**BACKGROUND:** A previous study indicated that intrathecal administration of morphine reduces experimental inflammatory edema in rats by activating the nitric oxide/cyclic guanosine monophosphate pathway. This evidence supports the hypothesis that potassium channel opening may play an important role in mediating morphine's effect under such conditions.

**METHODS:** Male Wistar rats received intrathecal injections of drugs (20  $\mu$ L) 30 minutes before paw stimulation with carrageenan (150  $\mu$ g). Edema was measured as paw volume increase (in milliliters), and plasma leakage was measured by Evans blue dye leakage. Neutrophil migration was evaluated indirectly by myeloperoxidase assay. The inflammatory infiltration and vascular congestion were observed by histologic examination.

**RESULTS:** Morphine (37 nmol) inhibited inflammatory edema, plasma leakage, and vascular congestion but had no effect on myeloperoxidase activity or neutrophil content compared with phosphate-buffered saline. Coinjection with 4-aminopyridine (10 nmol), glibenclamide (5 nmol), and dequalinium (10 pmol) reversed, but nicorandil (0.03 nmol) enhanced the effect of morphine.

**CONCLUSIONS:** These results support the hypothesis that the peripheral antiedematogenic effect produced by intrathecal morphine is mediated by potassium channel activation. Furthermore, this opioid effect does not involve the inhibition of acute neutrophil migration but does involve a reduction in capillary recruitment.