Table of Contents

December 2010

Cardiovascular Anesthesiology

Ambulatory Anesthesiology

液体限制的持续时间对异丙酚诱导期低血压的影响

(唐颖译　陈杰校)

The Influence of Duration of Fluid Abstinence on Hypotension During Propofol Induction

- Andrew P. Morley,
- Bhanu P. Nalla,
- Shelley Vamadevan,
- Gustav Strandvik,
- Arun Natarajan,
- A. Toby Prevost,
- and Cathryn M. Lewis

Anesth Analg December 2010 111:1373-1377; published ahead of print September 22, 2010

门诊手术麻醉学会制定了糖尿病患者门诊手术围手术期血糖管理的共识声明

（黄剑译 薛张纲校）

Special Article: Society for Ambulatory Anesthesia Consensus Statement on Perioperative Blood Glucose Management in Diabetic Patients Undergoing Ambulatory Surgery

- Girish P. Joshi,
- Frances Chung,
- Mary Ann Vann,
- Shireen Ahmad,
- Tong J. Gan,
- Daniel T. Goulson,
- Douglas G. Merrill,
- and Rebecca Twersky

Anesth Analg December 2010 111:1378-1387; published ahead of print October 1, 2010

Anesthetic Pharmacology

苯乙胺增加 S(+)氯胺酮对淋巴瘤，神经元和神经胶质细胞的细胞毒性

(瞿亦枫译 马皓琳 李士通校)

Benzethonium Increases the Cytotoxicity of S(+)-Ketamine in Lymphoma, Neuronal, and Glial Cells

- Sebastian Braun,
- Robert Werdehausen,
- Nina Gaza,
- Henning Hermanns,
- David Kremer,
- Patrick Küry,
- Markus W. Hollmann,
- and Markus F. Stevens

Anesth Analg December 2010 111:1389-1393; published ahead of print October 1, 2010

地西泮通过两种截然不同的机制减少大脑新皮层神经元动作电位的释放

(陈灵科译　陈杰校)

Diazepam Decreases Action Potential Firing of Neocortical Neurons via Two Distinct Mechanisms

- Berthold Drexler,
- Stefan Zinser,
- Harald Hentschke,
- and Bernd Antkowiak

Anesth Analg December 2010 111:1394-1399; published ahead of print October 1, 2010

丹曲林的细胞保护机制：一种**Ryanodine**受体拮抗剂

(毛慧译 薛张刚校)

Review Article: The Cytoprotective Effects of Dantrolene: A Ryanodine Receptor Antagonist

- Saadet Inan and
- Huafeng Wei

Anesth Analg December 2010 111:1400-1410; published ahead of print September 22, 2010

简报：挥发性麻醉药调节乳腺和脑肿瘤细胞基因的表达

(张蕾译　陈杰校)

Brief Report: Volatile Anesthetics Modulate Gene Expression in Breast and Brain Tumor Cells

- Johannes M. Huitink,

- Mike Heimerikxs,
- Marja Nieuwland,
- Stephan A. Loer,
- Wim Brugman,
- Arno Velds,
- Daoud Sie,
- and Ron M. Kerkhoven

Anesth Analg December 2010 111:1411-1415; published ahead of print October 1, 2010

Technology, Computing, and Simulation

在受试者血液稀释过程中使用脉搏碳氧血氧仪持续无创监测总血红蛋白含量的准确性

(任云译 薛张刚校)

The Accuracy of Noninvasive and Continuous Total Hemoglobin Measurement by Pulse CO-Oximetry in Human Subjects Undergoing Hemodilution

- Mark R. Macknet,
- Martin Allard,
- Richard L. Applegate II,
- and James Rook

Anesth Analg December 2010 111:1424-1426; published ahead of print November 3, 2010

Critical Care, Trauma, and Resuscitation

对海地地震的一个有组织的、综合性的、安全的战略策略反应：一项由无国际性灾难应急预案的一个学术性麻醉系描述的关于前期部署准备和初步经验的叙述

(毛祖旻译 马皓琳 李士通校)

An Organized, Comprehensive, and Security-Enabled Strategic Response to the Haiti Earthquake: A Description of Pre-Deployment Readiness Preparation and Preliminary Experience from an Academic Anesthesiology Department with No Preexisting International Disaster Response Program

- Maureen McCunn,
- Michael A. Ashburn,
- Thomas F. Floyd,
- C. William Schwab,

- Paul Harrington,
- C. William Hanson III,
- Babak Sarani,
- Samir Mehta,
- Rebecca M. Speck,
- and Lee A. Fleisher

Anesth Analg December 2010 111:1438-1444; published ahead of print September 14, 2010

在海地 2010 地震后的麻醉实践

(徐妍君译， 马皓琳、李士通校)

Special Article: Anesthetic Practice in Haiti After the 2010 Earthquake

- Mark J. Rice,
- Alan Gwertzman,
- Timothy Finley,
- and Timothy E. Morey

Anesth Analg December 2010 111:1445-1449; published ahead of print October 1, 2010

Obstetric Anesthesiology

剖腹产术后伤口皮下连续灌输布比卡因相比于生理盐水可减少切口白细胞介素－10 及增加 P 物质的产生

(陈毓雯译　陈杰校)

Continuous Subcutaneous Instillation of Bupivacaine Compared to Saline Reduces Interleukin 10 and Increases Substance P in Surgical Wounds After Cesarean Delivery

- Brendan Carvalho,
- David J. Clark,
- David C. Yeomans,
- and Martin S. Angst

Anesth Analg December 2010 111:1452-1459; published ahead of print September 22, 2010

在受试者血液稀释过程中使用脉搏碳氧血氧仪持续无创监测总血红蛋白含量的准确性

(任云译 薛张刚校)

Five Unit Bolus Oxytocin at Cesarean Delivery in Women at Risk of Atony: A Randomized, Double-Blind, Controlled Trial

- Kylie J. King,
- M. Joanne Douglas,
- Waldemar Unger,
- Areta Wong,
- and Robert A. R. King

Anesth Analg December 2010 111:1460-1466; published ahead of print October 1, 2010

硬膜外镇痛分娩和产妇发热

(杨秀娟 译 马皓琳 李士通 校)

Review Article: Labor Epidural Analgesia and Maternal Fever

- Scott Segal

Anesth Analg December 2010 111:1467-1475; published ahead of print September 22, 2010

焦点回顾：产科连续脊麻和镇痛

(杨秋娟译　陈杰校)

Focused Review: Continuous Spinal Anesthesia and Analgesia in Obstetrics

- Craig M. Palmer

Anesth Analg December 2010 111:1476-1479; published ahead of print October 1, 2010

2009 年产科麻醉进展----分娩患者安全的知识更新

(姚敏敏译 薛张纲校)

Special Article: What's New in Obstetric Anesthesia in 2009? An Update on Maternal Patient Safety

- Jill M. Mhyre

Anesth Analg December 2010 111:1480-1487; published ahead of print September 22, 2010

Pediatric Anesthesiology

接受常规心导管检查的心脏移植患儿静脉快速注射右旋美托咪定后的急性血流动力学变化

(龚寅 译 马皓琳 李士通校)

Acute Hemodynamic Changes After Rapid Intravenous Bolus Dosing of Dexmedetomidine in Pediatric Heart Transplant Patients Undergoing Routine Cardiac Catheterization

- E. H. Jooste,
- W. T. Muhly,
- J. W. Ibinson,
- T. Suresh,
- D. Damian,
- A. Phadke,
- P. Callahan,
- S. Miller,
- B. Feingold,
- S. E. Lichtenstein,
- J. G. Cain,
- C. Chrysostomou,
- and P. J. Davis

Anesth Analg December 2010 111:1490-1496; published ahead of print November 8, 2010

Neuroscience in Anesthesiology and Perioperative Medicine

高热对血浆谷氨酸浓度的影响

(张婷译　陈杰校)

The Effect of Hyperthermia on Blood Glutamate Levels

- Alexander Zlotnik,
- Boris Gurevich,
- Alan A. Artru,
- Shaun E. Gruenbaum,
- Michael Dubilet,
- Akiva Leibowitz,
- Gad Shaked,
- Sharon Ohayon,
- Yoram Shapira,
- and Vivian I. Teichberg

Anesth Analg December 2010 111:1497-1504; published ahead of print November 3, 2010

颅脑外伤中肌酐清除率增长

(张玥琪译，薛张纲校)

Augmented Creatinine Clearance in Traumatic Brain Injury

- Andrew Udy,
- Robert Boots,
- Siva Senthuran,
- Janine Stuart,
- Renae Deans,
- Melissa Lassig-Smith,
- and Jeffrey Lipman

Anesth Analg December 2010 111:1505-1510; published ahead of print November 3, 2010

既往有椎管狭窄、腰椎间盘疾病或脊柱手术史的病人行椎管内阻滞：效能和神经系统并发症

(江继宏 译 马皓琳 李士通 校）

Neuraxial Blockade in Patients with Preexisting Spinal Stenosis, Lumbar Disk Disease, or Prior Spine Surgery: Efficacy and Neurologic Complications

- James R. Hebl,
- Terese T. Horlocker,
- Sandra L. Kopp,
- and Darrell R. Schroeder

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一氧化碳释放因子 2 可促进肝素或阿加曲班抗凝血浆的凝血并减少纤溶受损

Carbon Monoxide Releasing Molecule-2 Enhances Coagulation and Diminishes Fibrinolytic Vulnerability in Plasma Exposed to Heparin or Argatroban

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背景：最近的研究表明：在正常及血友病人的血浆中加入一氧化碳释放因子（三羰基二氯代钌(II) 二聚物，CORM-2）能增强凝血作用并降低纤溶损伤。作者验证了以下假说：经过肝素或者阿加曲班抗凝的血浆在暴露于 CORM-2 后能加强凝血同时减少纤溶蛋白受损。

方法：正常血浆以 0 至 0.1 U/mL 不同剂量的普通肝素或者 0 至 1 μg/mL 不同剂量的阿加曲班抗凝处理。随后将部分样本暴露于 0 至 100 μM 浓度的 CORM-2，再予组织因子激活。另外一些样本予以同样的抗凝及 CORM-2 方案处理，相应的以 100 U/mL tPA（组织型纤维蛋白溶酶原激活剂）激活，用以评估纤维蛋白的受损性。收集血栓弹性描记器的数据直至血栓的强度趋于稳定或者至血栓溶解。

结果：未加入 tPA 的样本，CORM-2 显著增加了血栓形成的速度，其中肝素组 75%，阿加曲班 40%。血栓的强度也明显增加，肝素组为 69%，阿加曲班 72%。tPA 处理组，两种抗凝剂处理的样本在暴露于 CORM-2 后血栓的形成速度与强度增加更加明显，达到 94%–731%，同时血栓溶解时间也长达 103%–200%。

结论：肝素或者阿加曲班抗凝的血浆暴露于 CORM-2 能增加血栓的形成速度，血栓强度以及寿命。对于 CORM-2 是否能降低血栓相关的出血并发症，还需要进行其他的临床前研究。

（邹巧群　译　陈杰　校）

BACKGROUND: It has been recently demonstrated that a carbon monoxide releasing molecule (tricarbonyldichlororuthenium [II] dimer; CORM-2) enhances coagulation and attenuates vulnerability to fibrinolysis in normal and hemophiliac human plasma. We tested the hypothesis that plasma anticoagulated with heparin or argatroban would demonstrate improved coagulation and decreased fibrinolytic vulnerability after exposure to CORM-2.

METHODS: Normal plasma was anticoagulated with 0 to 0.1 U/mL unfractionated heparin or 0 to 1 μg/mL argatroban. Samples were subsequently exposed to 0 or 100 μM CORM-2 and activated with tissue factor. Additional samples with the same anticoagulant and CORM-2 exposure schema were incubated with 100 U/mL tissue-type plasminogen activator (tPA) to assess fibrinolytic vulnerability. Thrombelastographic data were collected until either clot strength stabilized or clot lysis occurred as appropriate.

RESULTS: In the absence of tPA, CORM-2 significantly increased the velocity of clot growth in heparin (75%) and argatroban-exposed (40%) samples. Clot strength was also significantly increased in heparin (69%) and argatroban-exposed (72%) samples. In the presence of tPA, CORM-2–treated samples had even greater (94%–731%) increases in velocity of growth and strength after exposure to either anticoagulant and significantly increased clot lysis time (103%–200%).

CONCLUSIONS: CORM-2 exposure resulted in faster-growing, stronger, longer-lived thrombi after anticoagulation with heparin or argatroban. Additional preclinical investigation is warranted to determine whether CORM-2 administration will be useful in attenuating bleeding complications associated with thromboprophylaxis.

液体限制的持续时间对异丙酚诱导期低血压的影响

The Influence of Duration of Fluid Abstinence on Hypotension During Propofol Induction

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背景：术前长时间禁食可能加重全麻诱导期的低血压。本文的研究目的是确定是否术前液体限制的持续时间与异丙酚诱导期的动脉血压变化及药物用量有关。

方法：选取了 130 名 ASA 分级在 I 到 II、无高血压、年龄在 18 到 65 岁、择期行全身麻醉下手术的患者。应用标准的生理监测和脑电图双频指数 (BIS) 监测。静脉输注异丙酚开始时 40 mg ·kg^{-1} ·h^{-1} ，当 BIS 降至 50 时减至 8 mg ·kg^{-1} ·h^{-1} 。收集 15 分钟内的心血管数据。主要观察指标是从基础平均动脉压减少的最大的百分比（max%ΔMAP)。次要指标是 BIS 下降至 50 时的异丙酚用量（PDBIS50）。应用一元线性回归和多元线性回归用来分析空腹时间、主次观察指标的指标之间的潜在关系。

结果：平均液体限制时间是 694 min（范围：115 至 1263 min）。液体限制（分钟）对应最大值 %ΔMAP (%)和 PDBIS50 (mg)的非标准化回归系数（95%可信区间）分别是 0.003%(−0.002%至+ 0.009%) 和 0.021 mg (−0.017 mg 至+ 0.059 mg)。校正多元模型中具有显著性。其他因素并应用 2 型离差平方和检验后，相应回归系数是 −0.0001%（−0.004%至+ 0.004%，P = 0.94） 和 −0.006 mg (−0.039 mg 至+ 0.026 mg，P = 0.70）。以小时为单位的液体限制对最大 %ΔMAP 影响是 −0.01%(−0.26%至+ 0.24%) ，对 PDBIS50 的影响是−0.38 mg （−2.34 mg 至+ 1.58 mg）。

结论：小于 65 岁的健康成人异丙酚麻醉诱导迅速静脉注射时，术前液体限制的持续时间不会影响 MAP 及异丙酚的用量。

（唐颖　译　陈杰　校）

BACKGROUND: Prolonged preoperative fasting might be expected to exacerbate hypotension during the induction of general anesthesia. We aimed to establish whether

the duration of preoperative abstinence from fluids independently contributed to arterial blood pressure changes and dosage requirements during propofol induction.

METHODS: We prospectively recruited 130 ASA I or II nonhypertensive patients, ages 18 to 65 years scheduled for surgery under general anesthesia. Standard physiological and electroencephalographic bispectral index (BIS) monitoring was applied to each patient. Intravenous propofol infusion was commenced at 40 mg $\cdot kg^{-1} \cdot h^{-1}$ and reduced to 8 mg $\cdot kg^{-1} \cdot h^{-1}$ when the BIS decreased to 50. Frequent cardiovascular data were collected for 15 minutes. The primary endpoint was maximal percentage decrease from baseline mean arterial blood pressure (max%ΔMAP). The secondary endpoint was the propofol dose at which BIS decreased to 50 (PDBIS50). Univariate linear regression and then multivariate linear regression was used to analyze the associations between potential predictors, including fasting time, and these 2 endpoints.

RESULTS: Mean fluid abstinence time was 694 minutes (range: 115 to 1263 minutes). Unstandardized regression coefficients (95% confidence intervals [CIs]) for fluid abstinence (minutes) versus max%ΔMAP (%) and PDBIS50 (mg) were, respectively, 0.003% (−0.002% to + 0.009%) and 0.021 mg (−0.017 mg to + 0.059 mg). On adjusting for other, significant predictors in a multivariate model and applying type II sum of squares tests, the corresponding values were −0.0001% (−0.004% to + 0.004%, P = 0.94) and −0.006 mg (−0.039 mg to + 0.026 mg, P = 0.70). The effect of a 1-hour increase in fluid abstinence on max%ΔMAP was therefore −0.01% (−0.26% to + 0.24%) and on PDBIS50, −0.38 mg (−2.34 mg to + 1.58 mg).

CONCLUSION: When propofol is infused rapidly for induction of anesthesia in healthy adults younger than 65 years, the duration of preoperative fluid abstinence does not appear to affect MAP or propofol dose requirements.

地西泮通过两种截然不同的机制减少大脑新皮层神经元动作电位的释放

Diazepam Decreases Action Potential Firing of Neocortical Neurons via Two Distinct Mechanisms

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背景：苯二氮卓类药物广泛用于临床麻醉的术前用药和全麻诱导。最近的体外研究表明 A 型 γ-氨基丁酸受体除了含有一个经典高亲和力结合位点，还拥有另外一个非经典的苯二氮卓类药物结合位点。目前，这个新的非经典的结合位点对苯二氮卓类药物在中枢神经系统中的作用还不清楚。

方法：因为新皮层介导全麻中镇静、催眠作用，作者在新皮层培养脑片应用多细胞记录法定量记录浓度范围（从 10 nM 到 100 μM）较宽的地西泮对细胞外自发动作电位的影响。

结果：地西泮浓度从低浓度至 6.25 μM 能降低大脑神经元的活动性，接近于最大值的 20%。这种作用可被苯二氮卓类拮抗剂氟马西尼逆转。在地西泮浓度>12.5 μM，诱发另一浓度相关网状活动抑制。与低浓度作用不同，这种高浓度效应不能被氟马西尼拮抗。

结论：地西泮诱发大脑新皮层神经元自发性动作电位释放的双相抑制作用。低中浓度通过经典的结合位点产生单相的，缓和的抑制作用且能被氟马西尼拮抗。然而，高浓度地西泮的作用不受氟马西尼的影响。因此，这些发现支持苯二氮卓类药物在 A 型 γ-氨基丁酸受体上至少有两个不同的结合位点。此外，研究结果也支持以下假设：经典的高亲和力的结合位点调节低剂量的地西泮的作用，例如遗忘，抗焦虑和镇静，而另一非经典独立的结合部位则与地西泮的催眠肌松等麻醉效应有关。

（陈灵科　译　陈杰　校）

BACKGROUND: Benzodiazepines are widely used in clinical anesthesia as premedication, but also to induce general anesthesia. Recent in vitro studies suggest that γ-aminobutyric acid type A receptors, harboring a classical high-affinity benzodiazepine binding site, possess another “nonclassical” binding site for benzodiazepines. At present, it is unclear if, and to what extent, this novel nonclassical binding site is of relevance for the actions of benzodiazepines in the central nervous system.

METHODS: Because neocortex is involved in mediating the sedative and hypnotic properties of general anesthetics, we quantified the actions of diazepam over a wide range of concentrations (from 10 nM up to 100 μM) in organotypic slice cultures using extracellular multiunit recordings of spontaneous action potential activity.

RESULTS: Up to a concentration of 6.25 μM, diazepam reduced the activity of neocortical neurons, approaching a maximum of approximately 20%. This action was nullified by the benzodiazepine antagonist flumazenil. At concentrations >12.5 μM, diazepam evoked a second concentration-dependent dampening of network activity. Unlike the low concentration effect, this high concentration component was resistant to flumazenil.

CONCLUSIONS: Diazepam induced a biphasic attenuation of spontaneous action potential firing of neocortical neurons. Low to moderate concentrations caused a monotonic, mild depression that is mediated via the classical binding site as it is antagonized by flumazenil. However, the effects of diazepam observed at high concentrations were not affected by flumazenil. Hence, these findings support the concept of at least 2 different binding sites for benzodiazepines on γ-aminobutyric acid type A receptors. Furthermore, our results are consistent with the hypothesis that the classical high-affinity binding site mediates low-dose diazepam actions, such as amnesia, anxiolysis, and sedation, while a second, nonclassical and independent site contributes to the anesthetic effects of diazepam, such as hypnosis and immobility.

简报：挥发性麻醉药调节乳腺和脑肿瘤细胞基因的表达

Brief Report: Volatile Anesthetics Modulate Gene Expression in Breast and Brain Tumor Cells

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基因表达越来越多地应用于临床实践中诊断、预后判断和治疗。作者对挥发性麻醉药可以影响肿瘤细胞的基因表达这一假说进行了测试。将离体的神经细胞系 SH-SY5Y 细胞和乳腺细胞系 MCF-7细胞暴露于安氟醚，异氟醚，地氟醚，氟烷和七氟醚或笑气中。对此，应用微阵列基因表达谱进行研究。结果显示在细胞培养中，基因表达水平有显著性的差异，并且暴露于不同时间长度和不同的挥发性麻醉药，反应也不同。一些构成乳房癌预测基因指纹法的基因受挥发性麻醉药的影响。结果表明挥发性麻醉药在乳腺和脑肿瘤的细胞培养中，可以以一种独特和时间依赖式的方式对基因的表达进行调制。

（张蕾　译　陈杰　校）

Gene expression is increasingly used for diagnostic, prognostic, and therapeutic purposes in clinical practice. We tested the hypothesis that volatile anesthetics (VA) affect gene expression of tumor cells. Cells from the neuronal cell line SH-SY5Y and from the breast cell line MCF-7 were exposed ex vivo to enflurane, isoflurane, desflurane, halothane, sevoflurane, or nitrous oxide. Microarray gene expression profiles were studied. We observed significant differences in gene expression levels of cell cultures and response in time when exposed to different VA. Some genes used for predictive genetic fingerprints for breast cancer were affected by VA. Our findings suggest that VA modulate gene expression in breast and brain tumor cell cultures in a unique and time-dependent manner.

剖腹产术后伤口皮下连续灌输布比卡因相比于生理盐水可减少切口白细胞介素－10 及增加 P 物质的产生

Continuous Subcutaneous Instillation of Bupivacaine Compared to Saline Reduces Interleukin 10 and Increases Substance P in Surgical Wounds After Cesarean Delivery

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背景：最新的证据表明，局部麻醉药局部给药可能对局部组织产生影响，如关节内注射后软骨组织溶解。炎症反应的改变为局部麻醉诱导组织毒性的可能机制之一。这项研究中，作者测试了连续局部浸润麻醉对炎症介质的释放及对剖宫产术后伤口皮肤的影响。

方法：腰麻下剖宫产术的 38 名健康妇女参与了这项研究，随机分为两组，一组产妇术后 24 小时给予布比卡因 5mg/mL 手术伤口皮下浸润，另一组给予 2 mL/h 生理盐水。术后 1, 3, 5, 7 及 24 小时采用皮下伤口引流技术收集伤口渗出液。采用多重 Bio-Plex®（Bio-Rad, Hercules, CA）和酶联免疫吸附法测定细胞因子，趋化因子，P 物质，前列腺素 E2 和神经生长因子。

结果：手术伤口布比卡因皮下浸润与生理盐水浸润相比，白细胞介素 10 明显降低，P 物质明显增加（24 小时浓度时间曲线；P<0.001）。其他细胞因子，神经生长因子，前列腺素 E2 无显着差异。

结论：这项研究表明，术后伤口连续输注临床常用剂量的布比卡因会影响局部炎症介质成份。白细胞介素 10 减少意味着抗炎机制受损。在皮肤愈合过程中这一变化伴随这促炎介质如 P 物质的释放是否导致手术伤口炎症反应加剧需更多的研究来证实。

（陈毓雯　译　陈杰　校）

BACKGROUND: Recent evidence suggests that locally delivered local anesthetics may exert tissue-damaging effects such as chondrolysis after intraarticular injection. Alteration of the inflammatory response is a potential mechanism for local anesthetic-induced tissue toxicity. In this study, we tested the effects of continuous local anesthetic infiltration on the release of inflammatory and nociceptive mediators in skin wounds after cesarean delivery.

METHODS: Thirty-eight healthy women undergoing cesarean delivery with spinal anesthesia were enrolled in this study, and were randomized to receive subcutaneous surgical wound infiltration with bupivacaine 5 mg/mL or saline at 2 mL/h for 24 hours

after cesarean delivery. Wound exudate was sampled at 1, 3, 5, 7, and 24 hours after cesarean delivery using a subcutaneous wound drain technique. Cytokines, chemokines, substance P, prostaglandin E_2, and nerve growth factor were assayed using multiplex Bio-Plex® (Bio-Rad, Hercules, CA) and enzyme-linked immunosorbent assays.

RESULTS: Bupivacaine wound infusion resulted in a significant decrease of interleukin 10 and increase of substance P in wounds compared with saline infusion (area under the 24-hour concentration-time curve; $P < 0.001$). No statistically significant differences were detected for other cytokines, nerve growth factor, and prostaglandin E_2.

CONCLUSIONS: This study demonstrates that the continuous administration of clinically used doses of bupivacaine into wounds affects the local composition of wound mediators. Observed changes in interleukin 10 are compatible with a disruption of antiinflammatory mechanisms. Whether such modulation combined with the release of the proinflammatory mediator substance P results in an overall proinflammatory wound response will require future studies of wound healing

焦点回顾：产科连续脊麻和镇痛

Focused Review: Continuous Spinal Anesthesia and Analgesia in Obstetrics

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本文重述连续脊麻技术在产科人群中的应用。探讨连续脊麻的利弊，目前常用的导管和配件。同时讨论了连续脊麻在无痛分娩和手术麻醉中的管理策略。连续脊麻在一些特殊临床情况下可能有独特的价值。

（杨秋娟　译　陈杰　校）

The development of the technique of continuous spinal anesthesia as it relates to the obstetric population is recounted. The advantages and disadvantages of continuous spinal anesthesia are examined, currently available catheters and kits are reviewed, and strategies for the management of continuous spinal techniques for labor analgesia and

surgical anesthesia are discussed. Continuous spinal anesthesia may have particular value over other regional techniques in several specific clinical circumstances.

高热对血浆谷氨酸浓度的影响

The Effect of Hyperthermia on Blood Glutamate Levels

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前言：谷氨酸的神经毒性是由谷氨酸在脑内合成和过度后释放入血这两者之间的平衡所决定。血浆中谷氨酸浓度降低会增加谷氨酸经血脑屏障滤过的量。而有关高热对于降低血液中谷氨酸浓度的机制及其有效性的报道尚不完全。虽然有假设认为高热可能是通过激活应激机制来降低血浆谷氨酸浓度的，但是阻滞β受体后可以减弱这种应激反应从而防止血浆谷氨酸浓度的降低。此外，处于高热状态的同时，谷氨酸也会从肌肉释放到血液中，这又造成了血液中谷氨酸浓度的增加。因而本研究旨在探讨高热对血液中谷氨酸浓度的影响以及β受体阻滞剂-心得安对应激引起的谷氨酸浓度改变的作用。本试验同时还研究了血浆谷氨酸清除剂草酰乙酸盐对于改善高热引起的谷氨酸浓度增加的有效性。

材料方法：24 只小鼠随机分成 3 组。小鼠的体温每隔 40min 升高 1℃，从 37℃一直升高到 42℃。第一组给予 1ml/100g 的等张生理盐水（对照）。当体温升至 39℃后，第二组给予 ml/100g 的 1M 草酰乙酸盐。而第三组在加热前给予 10mg/kg 的心得安。

结果：将小鼠的体温从 37℃升高到 39℃，对照组和草酰乙酸盐治疗组的血浆谷氨酸浓度都有显著下降（分别 P<0.01 vs P<0.0001），但是从 40℃继续升高到 42℃

则会增加血浆谷氨酸的浓度（分别 P<0.01 vs P<0.0001）。用心得安预处理的小鼠可以防止轻微体温升高导致的血浆谷氨酸浓度降低，但是心得安不影响 41℃ 和 42℃ 高热时引起的血浆谷氨酸浓度的增加（P<0.005）。

讨论：本研究的结果证明高热会降低血浆中谷氨酸浓度，其可能的机制是刺激了交感神经系统。之前报道草酰乙酸盐在 37℃ 时能减少血浆谷氨酸的浓度，但是在 40℃ 是无效的。给予心得安预处理后能减弱血浆谷氨酸浓度减少的程度，而心得安的这种效应在对照组和治疗组是没有差异的。从而可以理解在高热时血浆中谷氨酸浓度改变的基本机制，以及在治疗神经退行性疾病时应激具有重要的临床意义。（张婷　译　陈杰　校）

INTRODUCTION: Glutamate neurotoxicity is determined by the balance between glutamate release within the brain and efflux of excess glutamate from the brain. Brain-to-blood efflux of glutamate is increased by decreasing the concentration of glutamate in blood. Little is known about the effect of hyperthermia on blood glutamate concentrations, and the effectiveness of blood glutamate–decreasing mechanisms in these conditions. Although hyperthermia is hypothesized to decrease blood glutamate concentrations by activation of stress mechanisms, blunting the stress response by blocking β-adrenergic receptors should prevent this decrease. Furthermore, during hyperthermia there should be a concurrent process of leakage of glutamate from muscle tissue into blood, resulting in a contradictory increase of blood glutamate concentrations. In this study we investigated the effects of hyperthermia on blood glutamate levels and studied the effects of the β-adrenergic receptor antagonist propranolol on stress-induced changes in glutamate levels. We then studied the effectiveness of the blood glutamate scavenger oxaloacetate on hyperthermia-induced increases of glutamate levels.

MATERIALS AND METHODS: Twenty-four rats were randomly divided into 3 groups. Rats' body temperatures were increased (by 1℃ every 40 minutes) from 37℃ to 42℃. The first group received 1 mL per 100 g of isotonic saline (control). The second group received 1 mL per 100 g of 1M oxaloacetate when the temperature reached 39℃. The third group received 10 mg/kg of propranolol before initiation of the warming.

RESULTS: Warming the rats from 37℃ to 39℃ decreased the blood glutamate levels in the control group ($P < 0.01$) and oxaloacetate treatment group ($P < 0.0001$), whereas further increases in temperature from 40℃ to 42℃ increased the blood glutamate levels ($P < 0.01$ and $P < 0.0001$, respectively). Pretreatment with propranolol prevented the decrease in blood glutamate concentrations seen in mild hyperthermia and did not affect the increase in blood glutamate levels seen at temperatures of 41℃ and 42℃ ($P < 0.005$).

DISCUSSION: The results of this study demonstrated that hyperthermia leads to decreases in glutamate levels in the blood, presumably by activation of the sympathetic nervous system. Oxaloacetate, previously reported to reduce blood glutamate levels at 37℃, was ineffective at temperatures over 40℃. Propranolol pretreatment blunted the initial decrease in blood glutamate, and thereafter had no effect when compared with control and treatment groups. Understanding the mechanisms underlying glutamate regulation in the blood during states of hyperthermia and stress has important clinical implications in treating neurodegenerative conditions.

心脏再同步疗法治疗心脏衰竭

Cardiac Resynchronization Therapy for Treatment of Heart Failure

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传导异常，通常可见于收缩期心衰，因为没有正常传导组织的帮助电脉冲传播缓慢导致心机激活延迟。心室收缩不同步的结果是机械性效力较少，收缩功能减退和舒张期充盈受损。左右心室同时起搏（即两心室起搏）可以减少心室不同步收缩，可以克服传导延迟的这些后果。使用可植入性节律管理装置进行心脏再同步疗法的一个重要作用就是在心力衰竭中使得心室功能最佳化。在病人预后中其远期好处已被充分确认。随着使用的增多，对心脏再同步治疗装置及其治疗原理的理解对医生处理围手术期间和重症监护中的心衰病人很重要。
（周洁 译 马皓琳 李士通 校）

Conduction abnormalities, commonly seen in systolic heart failure, lead to delayed activation of the myocardium as the electrical impulse spreads slowly without the aid of healthy conduction tissue. The resulting dyssynchronous ventricular contraction is mechanically less efficient, reducing systolic function and impairing diastolic filling. Simultaneous pacing of the right and left ventricles (i.e., biventricular pacing) reduces ventricular dyssynchronous contraction, overcoming these consequences of conduction delay. An important role for implantable rhythm-management devices providing cardiac

resynchronization therapy has emerged in the optimization of ventricular function in heart failure. Long-term benefits in patient outcomes have been well established. With increasing use, understanding of cardiac resynchronization therapy devices and the principles behind the therapy are important for physicians providing perioperative and intensive care for patients with heart failure.

苯乙胺增加 S(+)氯胺酮对淋巴瘤，神经元和神经胶质细胞的细胞毒性

Benzethonium Increases the Cytotoxicity of S(+)-Ketamine in Lymphoma, Neuronal, and Glial Cells

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背景：已有研究表明氯胺酮在动物及人体有神经毒性。已归咎于氯胺酮中添加的防腐剂诱导了这种神经毒性。因此，我们体外研究了使用最广的氯胺酮防腐剂——氯化苄乙铵——是否会增加 S(+)-氯胺酮在淋巴瘤、成神经瘤细胞及初级星形胶质细胞中的毒性
方法：将人外周血白血病 T 淋巴瘤细胞和成神经瘤细胞（SHEP）与通过商业途径可获得的含有苯乙胺的 S-氯胺酮、纯 S-氯胺酮和纯氯化苄乙铵中孵育 24 小时。用流式细胞仪评价早期和晚期细胞凋亡率。第二步，通过对成神经瘤细胞以及小鼠初级星形胶质细胞进行线粒体活性测定（XTT）来研究苯乙胺与氯胺酮的混合毒性。用等辐射分析法来评估毒性的相加效应。
结果：在人外周血白血病 T 淋巴瘤细胞和成神经瘤细胞中，苯乙胺增加了氯胺酮的毒性，细胞坏死率分别从 32%增加到 80%及从 64%增加到 84%。从等效线图解法中可以看出，成神经瘤细胞和小鼠初级星形胶质细胞中测的的混合毒性在计算得出的纯净物毒性之和的置信区间内。
结论：我们的结论是苯乙胺以相加的方式增加了氯胺酮对造血、神经元和神经胶质起源细胞的局部毒性。因此，建议当使用含有防腐剂的 S-氯胺酮作为长时程椎管内镇痛治疗的添加药物时应特别予以谨慎。
（瞿亦枫 译 马皓琳 李士通校）

INTRODUCTION: Ketamine has been demonstrated to be neurotoxic in animals as well as in patients. Preservatives added to ketamine have been accused to induce this neurotoxicity. Therefore, we investigated whether the most widely used preservative of ketamine–benzethonium chloride–enhances the toxicity of S(+)-ketamine in vitro in lymphoma, neuroblastoma cells and primary astrocytes.
METHODS: Human Jurkat T-lymphoma- and neuroblastoma cells (SHEP) were incubated for 24 hours with commercially available S-ketamine containing benzethonium, pure S-ketamine and pure benzethonium chloride. The rate of early- and late-apoptotic cells was evaluated by flowcytometry. In a second step the combined toxicity of

benzethonium and ketamine was investigated in neuroblastoma cells and primary rat astrocytes in a mitochondrial activity assay (XTT). The additivity of the toxicities was evaluated by employing isobolographic analysis.
RESULTS: In Jurkat T-lymphoma and neuroblastoma cells benzethonium increased the toxicity of ketamine from 32% to 80% and from 64% to 84% cell deaths, respectively. In neuroblastoma cells as well as in primary rat astrocytes the measured combined toxicity was within the confidence interval of the calculated pure additive toxicity as seen in the isobolograms.
CONCLUSIONS: We conclude that benzethonium increases the local toxicity of ketamine in cells of hematopoetic, neuronal and glial origin in an additive manner. Therefore, caution is recommended especially when using preservative containing S-ketamine as an additive for long-term neuraxial analgesia.

对海地地震的一个有组织的、综合性的、安全的战略策略反应：一项由无国际性灾难应急预案的一个学术性麻醉系描述的关于前期部署准备和初步经验的叙述

An Organized, Comprehensive, and Security-Enabled Strategic Response to the Haiti Earthquake: A Description of Pre-Deployment Readiness Preparation and Preliminary Experience from an Academic Anesthesiology Department with No Preexisting International Disaster Response Program

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背景：海地当地时间 2010 年 1 月 12 日（星期二）16 时 53 分发生了里氏 7.0 级地震。全球人道主义组织对此的反应是迅速的，但是薄弱的基础设施和对紧急事件的准备限制了很多艰难的尝试。对于大型灾难人员伤亡应急有经验的组织能快速成功地对紧急事件医疗处理团队进行部署。有应急意向但无准备的医疗团队对紧急事件也做出了反应。在本次报道中，我们描述了一个无国际性灾难应急预案的学术大学麻醉系在接到海地的一个美国非政府组织寻求医疗支援的电话后所做出的准备和规划过程。本文的焦点是前期部署准备的过程，而不是描述在海地当地提供医疗处理的后期部署报道。
方法：我们对宾夕法尼亚大学附属医院与海地地震有关的通讯和措施进行了一项实时的定性评估和系统回顾。回顾并摘要了直到部署当天的关于计划、决策支持、设备获取的团队会议、电话会议和电子邮件通讯及行动和步骤。我们编译了重要事件的计时并发展了此过程的反应时间线。我们组织了回国的麻醉成员的访谈。

结果：海地地震后 4 天，一个在海地以马塞诸塞州波士顿为基地的名为“健康”的非营利、非政府组织里有超过 20 年医疗工作经验的成员与宾夕法尼亚大学健康机构取得联系，要求提供医疗团队的支持。麻醉科、外科、整形外科和护理部回应了该请求，并进行了志愿者的选择、疫苗接种以及装备清单的系统化研究。用世界卫生组织和疾病控制中心指南、美国麻醉协会创伤和急症准备委员会、发表的文章及国内的讨论交流来指导准备过程。
结论：对于国际性自然灾害紧急事件后的医疗需求而做出的有组织的战略应答可以由一个有医疗系统支持但无先前已建立应急系统的学术性麻醉系在 6 到 12 天内安全有效地完成。在今后的研究中，该应答的价值和时机有待确定。当与灾难当地已有支持基础的医护机构以有组织的方式互相合作时，在将应急医疗团队投放到该区域方面经验有限的机构可迅速地做出该应答。
（毛祖旻 译 马皓琳 李士通 校）

BACKGROUND: On Tuesday, January 12, 2010 at 16:53 local time, a magnitude 7.0 M_w earthquake struck Haiti. The global humanitarian attempt to respond was swift, but poor infrastructure and emergency preparedness limited many efforts. Rapid, successful deployment of emergency medical care teams was accomplished by organizations with experience in mass disaster casualty response. Well-intentioned, but unprepared, medical teams also responded. In this report, we describe the preparation and planning process used at an academic university department of anesthesiology with no preexisting international disaster response program, after a call from an American-based nongovernmental organization operating in Haiti requested medical support. The focus of this article is the pre-deployment readiness process, and is not a post-deployment report describing the medical care provided in Haiti.
METHODS: A real-time qualitative assessment and systematic review of the Hospital of the University of Pennsylvania's communications and actions relevant to the Haiti earthquake were performed. Team meetings, conference calls, and electronic mail communication pertaining to planning, decision support, equipment procurement, and actions and steps up to the day of deployment were reviewed and abstracted. Timing of key events was compiled and a response timeline for this process was developed. Interviews with returning anesthesiology members were conducted.
RESULTS: Four days after the Haiti earthquake, Partners in Health, a nonprofit, nongovernmental organization based in Boston, Massachusetts, with >20 years of experience providing medical care in Haiti contacted the University of Pennsylvania Health System to request medical team support. The departments of anesthesiology, surgery, orthopedics, and nursing responded to this request with a volunteer selection process, vaccination program, and systematic development of equipment lists. World Health Organization and Centers for Disease Control guidelines, the American Society of Anesthesiology Committee on Trauma and Emergency Preparedness, published articles, and in-country contacts were used to guide the preparatory process.
CONCLUSION: An organized strategic response to medical needs after an international natural disaster emergency can be accomplished safely and effectively within 6 to 12 days by an academic anesthesiology department, with medical system support, in a center with no previously established response system. The value and timeliness of this response will be determined with further study. Institutions with limited experience in putting an

emergency medical team into the field may be able to quickly do so when such efforts are executed in a systematic manner in coordination with a health care organization that already has support infrastructure at the site of the disaster.

在海地 2010 地震后的麻醉实践

Anesthetic Practice in Haiti After the 2010 Earthquake

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2010 年 1 月 12 日，里氏 7 级地震袭击了海地——一个医疗资源极其匮乏、西半球最贫穷的国家。我们来到了米洛（位于太子港以北）的圣心医院照顾那些受伤的患者，圣心医院是海地地震中幸存的一所医院，拥有 74 张床位和 2 个手术房间。由直升机从受震地区送来的大量病患使该医院规模扩充到 400 张床位和 6 个手术房间。如同 2005 年克什米尔和 2008 年中国的地震一样，大多数受灾者都遭受着极度的创伤的折磨，包括挤压伤、撕裂伤、骨折和截肢，并伴有脱水和贫血。术前评估包括询问一些基本的问题，如空腹状态、过敏症及已有疾病情况等，但是由于语言问题的限制而需要一名翻译。目标包括适当的麻醉深度，但避免窒息/气道操作。这些目标使我们频繁地使用了咪达唑仑和氯胺酮或区域麻醉。虽然我们有各种名称及各种浓度的很多药物，但是中央供气的缺乏仍然带来了不少麻烦。有破伤风、糖尿病酮症酸中毒、吸入性肺炎、由挤压导致的急性肾衰、严重贫血、脓毒血症以及其他一些疾病的患者需要的术后监护，由于麻醉后监护室/重症监护室只有 8 张床位而受到限制。我们这次工作的其他一些重要方面还包括有卫生保健专业人员区分患者治疗的轻重缓急，适应有限的实验室和影像学辅助装置，并合理安排现场物资供应。虽然各方面都存在很大的挑战，但是这次的经历让我们在感情上充实了自我，并回忆起当初之所以选择医学和麻醉作为专业的最根本原因。
（徐妍君 译， 马皓琳、李士通 校）

On January 12, 2010, a 7.0 M_L earthquake devastated Haiti, the most impoverished nation in the Western hemisphere with extremely limited health care resources. We traveled to Milot, Haiti situated north of Port-au-Prince, to care for injured patients at Hôpital Sacré Coeur, an undamaged hospital with 74 beds and 2 operating rooms. The massive influx of patients brought by helicopter from the earthquake zone transformed the hospital to >400 beds and 6 operating rooms. As with the 2005 Kashmir and 2008 China earthquake, most victims suffered from extremity injuries, encompassing crush injuries, lacerations, fractures, and amputations with associated dehydration and anemia. Preoperative evaluation was limited by language issues requiring a translator and included basic questions of fasting status, allergies, and coexisting conditions. Goals included adequate depth of anesthesia, while avoiding apnea/airway manipulation. These goals led to frequent use of midazolam and ketamine or regional anesthesia. Although many medications were present under various names and concentrations, the absence of a central gas supply proved troublesome. Postoperative care was limited to an 8-bed

postanesthesia care unit/intensive care unit caring for patients with tetanus, diabetic ketoacidosis, pulmonary aspiration, acute renal failure due to crush, extreme anemia, sepsis, and other illnesses. Other important aspects of this journey included the professionalism of the health care personnel who prioritized patient care, adaptation to limited laboratory and radiological services, and provision of living arrangements. Although challenging from many perspectives, the experience was emotionally enriching and recalls the fundamental reasons why we selected medicine and anesthesiology as a profession.

硬膜外镇痛分娩和产妇发热

Labor Epidural Analgesia and Maternal Fever

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接受硬膜外镇痛的分娩妇女更有可能经历高热和明显的临床发热。在行硬膜外镇痛分娩的妇女中观察到的逐步发展的中度发热在那些选择行其他镇痛方法或没有做镇痛治疗的分娩妇女中都没有见到。临床发热在行硬膜外镇痛分娩的妇女中也是大大地更多见。观察到的平均体温的缓慢上升也许是一小部分最终发热的妇女和更多的在分娩过程中无发热的妇女的体温曲线平均的假象。选择偏差混淆了硬膜外镇痛和发热之间的关系，因为存在发热风险（由于经受更长时间的羊膜破裂、更长时间的分娩期、接受更频繁的子宫颈检查和更多其他干扰）的妇女也更可能选择硬膜外镇痛。然而，即使随机实验已经证实接受硬膜外镇痛的妇女发热的发生率较高，并提示其因果关系，但硬膜外相关性发热的机制仍然不能完全被理解。未接受硬膜外镇痛的妇女体温调节的改变和阿片类药物的解热作用也许能部分解释这种现象，但更可能的原因是炎症，且最常见于胎盘和羊膜（绒毛膜羊膜炎）。产妇发热的后果是多种多样的。产科医生更可能对发热的分娩妇女进行手术干预，而新生儿科医生更可能去评估患有败血症的发热妇女的新生儿状况。更严重的是，产妇炎症性高热与新生儿脑部损伤有关，表现为脑瘫、脑病以及儿童期后期中的学习障碍。现在，还没有能安全有效抑制硬膜外相关发热的方法。将来的研究应该确定这种发热的病因，并且寻找安全有效的干预措施，以预防这种发热和抑制其对新生儿脑部的潜在危害作用。

(杨秀娟 译 马皓琳 李士通 校)

Women in labor who receive epidural analgesia are more likely to experience hyperthermia and overt clinical fever. The gradual development of modest hyperthermia observed in laboring women with epidural analgesia is not seen in those electing other forms of analgesia or unmedicated labor. Clinical fever is also far more likely in women laboring with epidural analgesia. It is possible that the observed slow increase in mean temperature is an artifact of averaging the temperature curves of a small group of women who eventually develop fever with a larger group who remain afebrile throughout labor. Selection bias confounds the association between epidural analgesia and fever, because women at risk for fever—due to longer duration of ruptured membranes, longer labor,

more frequent cervical examinations, and other interventions—are also more likely to select epidural analgesia. However, even randomized trials have confirmed a higher incidence of fever in epidural-exposed women, suggesting a causal relationship. The mechanisms of epidural-associated fever remain incompletely understood. Altered thermoregulation and an antipyretic effect of opioids given to women without epidural analgesia may explain part of the phenomenon, but the most likely etiology is inflammation, most commonly in the placenta and membranes (chorioamnionitis). The consequences of maternal fever are diverse. Obstetricians are more likely to intervene surgically in laboring women with fever, and neonatologists are more likely to evaluate neonates of febrile women for sepsis. More ominously, maternal inflammatory fever is associated with neonatal brain injury, manifest as cerebral palsy, encephalopathy, and learning deficits in later childhood. At present, there are no safe and effective means to inhibit epidural-associated fever. Future research should define the etiology of this fever and search for safe and effective interventions to prevent it and to inhibit its potential adverse effects on the neonatal brain.

接受常规心导管检查的心脏移植患儿静脉快速注射右旋美托咪定后的急性血流动力学变化

Acute Hemodynamic Changes After Rapid Intravenous Bolus Dosing of Dexmedetomidine in Pediatric Heart Transplant Patients Undergoing Routine Cardiac Catheterization

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背景：右美托咪定是一种高选择性的 α_2-肾上腺素能受体激动剂，具有镇静、抗焦虑以及镇痛功能，并且对呼吸动力影响较小。其镇静以及降压作用经由中枢 α_{2A} 以及 1 型咪唑啉受体调节，而外周 α_{2B}-肾上腺素受体活化则导致动脉血压以及外周血管阻力增加。在这项随机、前瞻性的临床研究中，我们尝试去量化在心脏移植的患儿中快速静脉注射右美托咪定的短期的血流动力学作用。
方法：12 例年龄小于或者等于十岁，体重小于等于 40kg，在心脏移植术后行左心和右心导管插入术的常规监测的患儿被纳入本项研究。在吸入或者静脉诱导后，进行气管插管，麻醉维持以 1MAC 的异氟醚混合空气吸入、芬太尼(1 μg/kg)和罗库溴铵(1 mg/kg)。在计划的心导管插入术结束时，吸入 100%纯氧。记录一系列的基础值包括心率（HR）、收缩压、舒张压、中心静脉压、肺动脉收缩压、肺动脉舒张压、肺毛细血管楔压以及热稀释心输出量后，在 5 秒内快速静脉推注右美托咪定 0.25 或 0.5 μg/kg。在 1 分钟以及 5 分钟后再次测量血流动力学指标。
结果：每组有六位患者。研究显示在快速静脉注射两种剂量的右美托咪定 1 分钟后收缩压、舒张压、肺动脉收缩压、肺动脉舒张压、肺毛细血管楔压以及全身血管阻

力均增高，并且在 5 分钟后均显著下降至接近基础值。这种压力的短暂上升在全身系统较肺系更为明显。在全身系统中，舒张压的上升百分率较收缩压大。心输出量、中心静脉压以及肺血管阻力并无明显变化。心率在两组不同剂量推注后 1 分钟时均下降，并且是 0.5 μg/kg 组中注射后 5 分钟时唯一一个与基础值仍然有差异的血流动力学指标。

结论：这组小样本的已行心脏移植的患儿接受快速静脉注射右美托咪定在临床上完全能耐受，虽然其导致了短暂并且显著的全身和肺动脉压力升高以及心率的减慢。在全身系统，舒张压上升比率较舒张压大，而且这些短暂的压力升高在全身系统较肺系更为明显。

（龚寅 译 马皓琳 李士通校）

BACKGROUND: Dexmedetomidine is a highly selective α_2-adrenoceptor agonist with sedative, anxiolytic, and analgesic properties that has minimal effects on respiratory drive. Its sedative and hypotensive effects are mediated via central α_{2A} and imidazoline type 1 receptors while activation of peripheral α_{2B}-adrenoceptors result in an increase in arterial blood pressure and systemic vascular resistance. In this randomized, prospective, clinical study, we attempted to quantify the short-term hemodynamic effects resulting from a rapid IV bolus administration of dexmedetomidine in pediatric cardiac transplant patients.
METHODS: Twelve patients, aged 10 years or younger, weighing ≤40 kg, presenting for routine surveillance of right and left heart cardiac catheterization after cardiac transplantation were enrolled. After an inhaled or IV induction, the tracheas were intubated and anesthesia was maintained with 1 minimum alveolar concentration of isoflurane in room air, fentanyl (1 μg/kg), and rocuronium (1 mg/kg). At the completion of the planned cardiac catheterization, 100% oxygen was administered. After recording a set of baseline values that included heart rate (HR), systolic blood pressure, diastolic blood pressure, central venous pressure, systolic pulmonary artery pressure, diastolic pulmonary artery pressure, pulmonary artery wedge pressure, and thermodilution-based cardiac output, a rapid IV dexmedetomidine bolus of either 0.25 or 0.5 μg/kg was administered over 5 seconds. The hemodynamic measurements were repeated at 1 minute and 5 minutes.
RESULTS: There were 6 patients in each group. Investigation suggested that systolic blood pressure, diastolic blood pressure, systolic pulmonary artery pressure, diastolic pulmonary artery pressure, pulmonary artery wedge pressure, and systemic vascular resistance all increased at 1 minute after rapid IV bolus for both doses and decreased significantly to near baseline for both doses by 5 minutes. The transient increase in pressures was more pronounced in the systemic system than in the pulmonary system. In the systemic system, there was a larger percent increase in the diastolic pressures than the systolic pressures. Cardiac output, central venous pressure, and pulmonary vascular resistance did not change significantly. HR decreased at 1 minute for both doses and was, within the 0.5 μg/kg group, the only hemodynamic variable still changed from baseline at the 5-minute time point.
CONCLUSION: Rapid IV bolus administration of dexmedetomidine in this small sample of children having undergone heart transplants was clinically well tolerated, although it resulted in a transient but significant increase in systemic and pulmonary pressure and a decrease in HR. In the systemic system, there is a larger percent increase

in the diastolic pressures than the systolic pressures and, furthermore, these transient increases in pressures were more pronounced in the systemic system than in the pulmonary system.

既往有椎管狭窄、腰椎间盘疾病或脊柱手术史的病人行椎管内阻滞：效能和神经系统并发症

Neuraxial Blockade in Patients with Preexisting Spinal Stenosis, Lumbar Disk Disease, or Prior Spine Surgery: Efficacy and Neurologic Complications

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背景：有椎管病变（包括椎管狭窄和腰椎间盘病变）的病人，通常避免行椎管内阻滞，因为有已存在的神经系统病变恶化或发展为新的神经系统功能障碍的风险。相反，既往脊柱手术史被认为会增加椎管内阻滞的困难和失败率。我们在本回顾性研究中调查了既往存在椎管病变伴或无脊柱手术史的病人行椎管内麻醉后的神经系统并发症的风险和阻滞效能。
方法：以 15 年内具有椎管狭窄或腰神经根疾病史且行椎管阻滞的所有病例为研究对象。记录病人人口统计、术前神经病学诊断和手术／椎管内阻滞时的神经系统发现、椎管内阻滞细节（腰麻比硬膜外麻醉，单次注射比.持续输注）、注射剂、操作并发症（诱发感觉异常、进针或置管见血、无法置管、硬膜意外穿破）和阻滞成功率。识别新的或进行性的神经系统病变。所有病人随访至症状缓解或评估的最后日期。
结果：共纳入 937 位病例，其中 207 例(22%)曾接受脊柱手术。椎管狭窄病人 187 例（20%），腰神经根病变者 570 例（61%），周围神经病变 210 例（22%）；180 位病人（19%）存在多种神经病学诊断。大多数病人手术时有活动的但稳定的神经系统症状。总阻滞成功率为 92.7%。脊柱手术史不影响阻滞成功率和穿刺操作并发症的发生率。10 位病人(1.1%; 95% 可信区间[CI] 0.5%–2.0%)出现新的神经系统缺陷或现有症状恶化。3 例（1.4%）并发症发生于有脊柱手术史的病人，余下 7 例（1.0%）并发症发生于无手术减压或固定术史的病人(P = NS)。尽管畸形矫正术不是一个危险因子，6 位单侧下肢手术的病人中有 5 位术后并发症出现于手术侧。同样地，由于发展为双侧缺陷而行双侧畸形矫正的病人，在先前受累一侧的预后较差。假定 10 位病人中 4 位（40%）并发症的主要原因是手术操作。余下 6 位病人（60%）并发症的主要原因经鉴定为非手术原因（包括麻醉相关因素）。术前存在压迫性神经根病变的诊断(P = 0.0495)或具有多种神经病学诊断(P = 0.005)增加了术后神经系统并发症的风险。
结论：我们推断，既往存在椎管病变的病人比不存在这些基础病变的病人在椎管阻滞后神经系统并发症发生率较高(1.1%; 95% CI 0.5%–2.0%)。然而，在缺乏具有相似解剖病变并行全身麻醉的手术病人作为对照组的情况下，我们无法确定这种较

高的神经系统损伤发生率是否是继发于手术操作、麻醉方法、脊柱病变的自然病程或者是这些相关因素的复合效应以及每个因素的相对作用。
(江继宏 译 马皓琳 李士通 校）

BACKGROUND: Patients with spinal canal pathology, including spinal stenosis and lumbar disk disease, are often not considered candidates for neuraxial blockade because of the risk of exacerbating preexisting neurologic deficits or developing new neurologic dysfunction. In contrast, a history of spine surgery is thought to increase the likelihood of difficult or unsuccessful block. In this retrospective study we investigated the risk of neurologic complications and block efficacy in patients with preexisting spinal canal pathology, with or without a history of spine surgery, after neuraxial anesthesia.
METHODS: During the 15-year study period, all patients with a history of spinal stenosis or lumbar radiculopathy undergoing a neuraxial technique were studied. Patient demographics, preoperative neurologic diagnoses and neurologic findings at the time of surgery/neuraxial block, details of the neuraxial block including technique (spinal vs. epidural, single injection vs. continuous), injectate, technical complications (paresthesia elicitation, bloody needle/catheter placement, inability to advance catheter, accidental dural puncture), and block success were noted. New or progressive neurologic deficits were identified. All patients were followed until resolution or last date of evaluation.
RESULTS: There were 937 patients included, 207 (22%) of whom had undergone spinal surgery. A history of spinal stenosis was present in 187 (20%), lumbar radiculopathy in 570 (61%), and peripheral neuropathy in 210 (22%) patients; 180 patients (19%) had multiple neurologic diagnoses. A majority of patients had active but stable neurologic symptoms at the time of surgery. Overall block success was 97.2%. A history of spine surgery did not affect the success rate or frequency of technical complications. Ten (1.1%; 95% confidence interval [CI] 0.5%–2.0%) patients experienced new deficits or worsening of existing symptoms. Three (1.4%) complications occurred in patients with a history of spinal surgery, and the remaining 7 (1.0%) in patients without prior surgical decompression or stabilization (P = NS). Although an orthopedic procedure was not a risk factor, in 5 of the 6 patients in which the surgery was a unilateral lower extremity procedure, the postoperative deficit involved the operative side. Likewise, in both patients undergoing bilateral orthopedic procedures who developed bilateral deficits, the outcome was worse on the previously affected side. A surgical cause was presumed to be the primary etiology in 4 (40%) of 10 patients. The primary etiology of the remaining 6 (60%) complications was judged to be nonsurgical (including anesthetic-related factors). The presence of a preoperative diagnosis of compressive radiculopathy (P = 0.0495) or multiple neurologic diagnoses (P = 0.005) increased the risk of neurologic complications postoperatively.
CONCLUSIONS: We conclude that patients with preexisting spinal canal pathology have a higher incidence of neurologic complications after neuraxial blockade (1.1%; 95% CI 0.5%–2.0%) than that previously reported for patients without such underlying pathology. However, in the absence of a control group of surgical patients with similar anatomic pathology undergoing general anesthesia, we cannot determine whether the higher incidence of neurologic injury is secondary to the surgical procedure, the anesthetic technique, the natural history of spinal pathology, or a combination of factors and the relative contributions of each.

人血中右旋布洛芬、布洛芬及氟比洛芬抗血小板差异的体外研究

Differences in the in vitro antiplatelet effect of dexibuprofen, Ibuprofen, and flurbiprofen in human blood.

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背景：此项研究旨在通过比较体外环境下右旋布洛芬、布洛芬及氟比洛芬的药效学特性，明确其各自抗血小板效应间的相互差异。
方法：此项研究的全血标本来源于健康志愿者。此项研究须在乙酰水杨酸、右旋布洛芬、布洛芬及氟比洛芬浓度增加的前后，分别检测全血标本中二磷酸腺苷、胶原及花生四烯酸介导的血小板聚集功能，血小板血栓烷 B（2）（TxB（2））、脂多糖介导的前列腺素 E（2）、白细胞 6-酮-前列腺素 F（1a）（PGF（1a））及构成和诱导两种途径介导的一氧化氮的生成。每抑制（IC（50））或增加 50%时的药物浓度则被要求计算。
结果：所有这 3 种药物均剂量依赖性地抑制血小板聚集、抑制 TxB（2）、前列腺素 E（2）及 6-酮-PGF（1a）合成，增加钙离子介导的一氧化氮生成。与布洛芬和氟比洛芬相比，右旋布洛芬展现出更强的抗血小板效应，其药效学特征与阿司匹林更为近似。例如，右旋布洛芬对于花生四烯酸介导的血小板聚集功能的 IC（50）值为 0.85 ± 0.06 uM，布洛芬为 14.76 ± 1.22 uM，氟比洛芬为 6.39 ± 0.51 uM，阿司匹林为 0.38 ± 0.03 uM。所有这 3 种药物均可抑制血栓烷与前列腺素合成，但右旋布洛芬其抗- TxB（2）的 IC（50）值与其抗-6-酮-PGF（1a）的 IC（50）值之比为 0.21 ± 0.03，布洛芬为 1.05 ± 0.08，氟比洛芬为 0.79 ± 0.11，阿司匹林为 0.46 ± 0.06。所有这 3 种药物均可增加钙离子依赖的一氧化氮生成。
结论：芳香基丙酸衍生物右旋布洛芬是最强效的抗血小板药物，其药理学特性与阿司匹林相似。
（范羽译 薛张纲校）

BACKGROUND: In this study, we compared the in vitro pharmacodynamic profile of dexibuprofen, ibuprofen, and flurbiprofen to identify possible differences in antiplatelet activity.
METHODS: In whole blood samples from healthy volunteers, we measured platelet aggregation induced by adenosine diphosphate, collagen and arachidonic acid, platelet thromboxane B(2) (TxB(2)), lipopolysaccharide-induced prostaglandin E(2), leukocyte 6-keto-prostaglandin F(1a) (PGF(1a)), and nitric oxide induced by both constitutive and inducible pathways before and after incubation with increasing concentrations of acetylsalicylic acid, dexibuprofen, ibuprofen, or flurbiprofen. The concentration that inhibited (IC(50)) or increased each variable by 50% was calculated.
RESULTS: All 3 drugs inhibited platelet aggregation in a dose-dependent manner, TxB(2), prostaglandin E(2), and 6-keto-PGF(1a), and increased calcium-induced nitric oxide production. Dexibuprofen showed greater antiplatelet potency than ibuprofen and

flurbiprofen, and its profile was similar to that of aspirin. For example, IC(50) values for arachidonic acid-induced platelet aggregation were 0.85 ± 0.06 uM for dexibuprofen, 14.76 ± 1.22 uM for ibuprofen, 6.39 ± 0.51 uM for flurbiprofen, and 0.38 ± 0.03 uM for aspirin. All drugs inhibited both thromboxane and prostacyclin synthesis, but the IC(50) anti-TxB(2)/IC(50) anti-6-keto-PGF(1a) ratio was 0.21 ± 0.03 for dexibuprofen, 1.05 ± 0.08 for ibuprofen, 0.79 ± 0.11 for flurbiprofen, and 0.46 ± 0.06 for aspirin. All drugs increased calcium-dependent nitric oxide production.
CONCLUSIONS: The aryl propionic acid derivative dexibuprofen was the most potent antiplatelet drug, and its pharmacodynamic profile is similar to aspirin.

门诊手术麻醉学会制定了糖尿病患者门诊手术围手术期血糖管理的共识声明

Special article: society for ambulatory anesthesia consensus statement on perioperative blood glucose management in diabetic patients undergoing ambulatory surgery.

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Anesth Analg. 2010 Dec;111(6):1378-87.

关于门诊手术患者的围手术期血糖控制的最佳方案仍然存在着争议。因此，门诊手术麻醉学会制定了一个门诊手术患者围手术期血糖管理的共识声明，并且根据Cochrane协作网推荐的方法对文献进行了系统性回顾。共识小组对于这些建议分别给予了推荐等级、评估、发展和评价分级系统。据透露，并没有足够的证据显示这能够为临床问题提出有力的建议。由于缺乏高质量的证据，提出这些建议是基于糖尿病患者血糖控制的一般原则、药物的药理学、住院手术病人的人群数据以及临床经验和判断。此外，也确定了在这一区域未来需要更进一步的研究。
（黄剑译 薛张纲校）

Optimal evidence-based perioperative blood glucose control in patients undergoing ambulatory surgical procedures remains controversial. Therefore, the Society for Ambulatory Anesthesia has developed a consensus statement on perioperative glycemic management in patients undergoing ambulatory surgery. A systematic review of the literature was conducted according the protocol recommended by the Cochrane Collaboration. The consensus panel used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system for providing suggestions. It was revealed that there is insufficient evidence to provide strong recommendations for the

posed clinical questions. In the absence of high-quality evidence, recommendations were based on general principles of blood glucose control in diabetics, drug pharmacology, and data from inpatient surgical population, as well as clinical experience and judgment. In addition, areas of further research were also identified.

丹曲林的细胞保护机制：一种Ryanodine受体拮抗剂

The Cytoprotective Effects of Dantrolene:A Ryanodine Receptor Antagonist

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钙，作为一个第二信使，在众多细胞功能中有很重要的作用。然而，细胞内钙失衡会引起细胞毒性甚至细胞死亡。细胞内储存的钙离子过度释放，钙离子通道ryanodine受体激活都会促成细胞损伤。钙失衡引起的机能障碍已在组织培养和缺血、缺氧、损伤、麻醉及神经变性疾病动物模型中得以确定。丹曲林，作为治疗恶性高热的首选药物，是ryanodine受体拮抗剂。丹曲林抑制细胞内主要的钙库-肌浆网内钙离子的异常释放。丹曲林在不同的组织培养和动物疾病模型中对抗由细胞内钙失衡介导的细胞毒性 引起的细胞损伤可能的细胞保护机制已被广泛研究。在这篇综述中，我们总结了细胞内钙失衡在细胞死亡中的作用，丹曲林的药理学和药代动力学，以及丹曲林在众多应激及疾病模型中抑制细胞损伤的细胞保护机制及潜在的应用价值。
（毛慧译 薛张刚校）

Calcium, as a second messenger, has an important role in a variety of cellular functions.However, disruption of intracellular calcium homeostasis leads to cytotoxicity and cell death.Excessive calcium release from intracellular stores, via the calcium channel ryanodine receptor, contributes to cell damage. Dysfunction of calcium homeostasis is established in tissue culture and animal models of ischemia, hypoxia, seizure, trauma, anesthesia, and neurodegenerative diseases. Dantrolene, the primary drug to treat malignant hyperthermia, is a ryanodine receptor antagonist. Dantrolene inhibits abnormal calcium release from the sarco-endoplasmic reticulum, which is the primary intracellular calcium store. Dantrolene has been investigated widely for its possible cytoprotective effects against cell damage in different tissue culture or animal models of diseases involving cytotoxicity induced by disruption of intracellular calcium homeostasis in pathogenesis. In this review, we summarize the role of the disruption of intracellular calcium homeostasis on cell death, the pharmacologic and pharmacokinetic features of dantrolene, and the cytoprotective effects and potential application of dantrolene for the inhibition of cell damage in a wide variety of models of stress and disease. (Anesth Analg 2010;111:1400–10)

在受试者血液稀释过程中使用脉搏碳氧血氧仪持续无创监测总血红蛋白含量的准确性

The Accuracy of Noninvasive and Continuous Total Hemoglobin Measurement by Pulse CO-Oximetry in Human Subjects Undergoing Hemodilution

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背景：总血红蛋白含量测定(tHb)是最常用的实验室检查之一。脉搏碳氧血氧仪可通过多波长分光光度计测量方法持续无创监测血红蛋白含量(SpHb)。本研究中，我们通过测量血液稀释的 20 例健康志愿者总血红蛋白含量，并与实验室检查对照，评估了 SpHb 的准确性。
方法：受试者入选试验后，约 500ml 血液被经静脉或动脉导管导出。随后他们都接受了静脉快速输晶体液以代偿减少的血容量，这同时降低了血红蛋白浓度。补液量最多为 30ml/kg。过程中持续监测记录 SpHb，并采集了一系列的动脉血样。把动脉血样测得的 tHb 与 SpHb 配对并进行分析以检测的 SpHb 准确性。同时计算了偏倚、精确度和平均标准误。
结果：实验共收集了 165 个 tHb 结果。在失血和血液稀释后 tHb 平均减少了(2.4±0.8)g/dL (均值±标准差)。在 335 对测量数据中，SpHb 与 tHb 的平均差异是-0.15g/dL，差异的 1 个单位标准差是 0.92g/dL，平均均方根差异是 0.94g/dL。对于 97%的测量数据，SpHb 与 tHb 的差异小于 2.0 g/dL。在 tHb 小于 10 g/dL 的情况下，对于 97%的测量数据，SpHb 与 tHb 的差异小于 1.5g/dL。
结论：在受试者血液稀释过程中，以脉搏碳氧血氧仪为基础的 SpHb 测量与实验室碳氧血氧仪测量值相差在 1 g/dL (1 个标准差)内。
（任云译 薛张刚校）
BACKGROUND: Total hemoglobin (tHb) is one the most frequently ordered laboratory measurements. Pulse CO-Oximetry™ (Masimo Corp., Irvine, CA) is a multi-wavelength spectrophotometric method for noninvasive and continuous hemoglobin monitoring (SpHb). In this study, we evaluated the accuracy of SpHb compared with laboratory CO-Oximeter measurement of tHb from arterial blood samples in 20 healthy volunteer subjects undergoing hemodilution.
METHODS: After enrollment, approximately 500 mL of blood was drawn from subjects through an arterial or venous catheter. Each subject then rapidly received crystalloid IV fluid to compensate for the decrease in intravascular volume and reduce the hemoglobin concentration. Subjects received a maximum of 30 mL/kg IV fluid. SpHb was continuously monitored and recorded, and serial arterial blood samples were taken during the procedure. SpHb accuracy was analyzed by pairing SpHb and tHb measurements after the arterial blood draw with the resulting tHb test result. Bias, precision, and the average root-mean-square error were calculated.
RESULTS: One hundred sixty-five tHb measurements were collected. The average decrease in tHb during the blood removal and hemodilution procedure was 2.4 ± 0.8 g/dL (mean ± SD). The average difference between 335 paired measurements of SpHb and tHb was -0.15 g/dL, 1 SD of the difference was 0.92 g/dL, and the average root-mean-square difference was 0.94 g/dL. The difference between SpHb and tHb was <2.0 g/dL for 97% of the measurements. The difference was <1.5 g/dL for 97% of the measurements when tHb was <10 g/dL.

CONCLUSIONS: Pulse CO-Oximetry-based SpHb measurement is accurate within 1.0 g/dL (1 SD) compared with laboratory CO-Oximeter tHb measurement in subjects undergoing hemodilution.

一项随机双盲多对照实验：剖宫产术后子宫收缩乏力的病人单次给予 5 个单位剂量的催产素

Five Unit Bolus Oxytocin at Cesarean Delivery in Women at Risk of Atony: A Randomized, Double-Blind, Controlled Trial

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背景：静脉内常规使用催产素可以预防剖宫产术后出血。它会引起血流动力学的不良反应也是人们所熟知的，所以导致了最近的剂量从 10 个单位减少到了 5 个单位。是否这 5 个单位的催产素比持续输注更有优势，我们不是很清楚。所以我们提出了我们的假设：是否剖宫产后子宫收缩乏力的病人在给予催产素持续输注前单次给予 5 个单位的催产素能减少产后 24 小时内对其他子宫收缩药物的需求量，将这组病人与持续输注催产素组相比。
方法：一项随机双盲对照实验在 143 名剖宫产后有子宫收缩乏力的病人中进行。病人在脐带血流夹闭 30 秒后静脉内分别给予 5 个单位的催产素或者生理盐水。之后所有的病人给予 40 个单位的催产素加入 500 毫升的生理盐水持续输注 30 分钟，然后给予 20 个单位的催产素加入 1 升的生理盐水持续输注 8 个小时。我们主要目的是比较患者在产后 24 小时内对其他子宫收缩药物的需求量。同时还要观察子宫的收缩力（由妇产科医生来评估，0 分=松软，4 分=像石头一样坚硬），失血量，静脉一次注射后的不良反应，静脉一次输注后到胎盘娩出所需的时间。
结果：两组病人在产后 24 小时内对其它子宫收缩药物的需求量是没有差异的。但两组在胎盘娩出后子宫收缩力有显著性差异（P＜0.01 ，催产素组是 2.8，95%可信区间 2.6-3.0；生理盐水组是 2.2，95%可信区间 1.8-2.5），5 分钟后这种差异消失。两组之间能观察到的和被报道的不良反应没有差异。
结论：我们发现在给予持续输注催产素前静脉内先单次给予 5 个单位的催产输并不能治疗和预防剖宫产术后病人子宫收缩乏力，减少对其它子宫收缩药物的需求量，但是催产素组可引起子宫在最初时更强烈的收缩。我们的研究中两组的不良反应没有显著差异。这个研究可能意味着持续输注催产素的量已经很充足，没有必要单次注射，即使是高危病人。
（翁梅琳译 薛张刚校）

Background: IV bolus oxytocin is used routinely during cesarean delivery to prevent postpartum hemorrhage. Its adverse hemodynamic effects are well known, resulting in a recent change in dose from 10 IU to 5. Whether a 5 IU bolus has any advantages over

infusion alone is unclear. We tested the hypothesis that a 5 IU IV bolus of oxytocin before the initiation of a continuous infusion decreases the need for additional uterotonic drugs in the first 24 hours after delivery in women with risk factors for uterine atony undergoing cesarean delivery, compared with infusion alone.

Methods: A prospective, randomized, double-blind, controlled trial was conducted in 143 subjects undergoing cesarean delivery with at least 1 risk factor for uterine atony. Subjects received 5 IU bolus of oxytocin or normal saline IV over 30 seconds after umbilical cord clamping. All subjects received an infusion of 40 IU oxytocin in 500 mL normal saline over 30 minutes, followed by 20 IU in 1 L over 8 hours. The primary outcome was the need for additional uterotonics in the first 24 hours after delivery. Secondary outcomes included uterine tone as assessed by the surgeon (5-point Likert scale: 0 = “floppy,” 4 = “rock hard”), estimated blood loss, side effects of bolus administration, and the oxytocin bolus–placental delivery interval.

Results: There was no difference in the need for additional uterotonic drugs in the first 24 hours between groups. There was a significant difference in uterine tone immediately after placental delivery ($P < 0.01$) (2.8 in the oxytocin group [95% confidence interval 2.6–3.0] vs 2.2 in the saline group [95% confidence interval 1.8–2.5]), which disappeared after 5 minutes. There were no differences in observed or reported side effects between groups.

Conclusions: We found that a 5 IU IV bolus of oxytocin added to an infusion did not alter the need for additional uterotonic drugs to prevent or treat postpartum hemorrhage in the first 24 hours in women undergoing cesarean delivery with risk factors for uterine atony, despite causing an initial stronger uterine contraction. Our study was not powered to find a difference in side effects between groups. These results suggest that an oxytocin infusion may be adequate without the need for a bolus, even in high-risk patients.

2009 年产科麻醉进展----分娩患者安全的知识更新

What's New in Obstetric Anesthesia in 2009? An Update on Maternal Patient Safety

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每年,产科麻醉学会和围生医学会都会推荐一个人对前一年的文献进行调查找出对产科麻醉科学和临床实践最重要的文章.本文回顾了 2009 年针对分娩病人安全的文献,并且主张产科麻醉医师不但是围术期而且是围产期的内科医师.回顾了三个特别的话题:产科麻醉的并发症,全身性产科并发症和围产期质控和安全.

(姚敏敏译 薛张纲校)

Every year, the Society of Obstetric Anesthesia and Perinatology nominates 1 individual to survey the prior year's literature and to identify the most notable articles for the science and practice of obstetric anesthesiology. This article reviews the 2009 literature, focusing on the theme of maternal patient safety, and advancing the notion of the obstetric anesthesiologist as both a perioperative and a peripartum physician. Three specific topics are reviewed: complications of obstetric anesthesia, general obstetric complications, and quality and safety in peripartum care.

颅脑外伤中肌酐清除率增长

Augmented Creatinine Clearance in Traumatic Brain Injury

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背景：输注高张生理盐水和/或去甲肾上腺素在处理颅脑外伤时被常规用来获得理想的脑灌注压。我们假定肌酐清除率在这种情况下会显著增高。
方法：这是个对 16 岁以上的拥有正常血肌酐并需要维持脑灌注压的颅脑外伤病人进行的队列观察研究。在积极处理开始和结束时收集 8 小时尿肌酐清除率。在研究过程中记录人口数据、血管活性药的使用情况、液体平衡、营养治疗和血流动力学变化。肌酐清除率升高定义为女性>150 mL/min/1.73 m(2)，男性>160 mL/min/1.73 m(2)。
结果：20 名患者入组，17 名发现肌酐清除率升高（85%）。接受脑灌注压治疗的患者平均最高肌酐清除率为 179 mL/min/1.73 m(2)（95%置信区间 159-198），而该数据在离开重症监护室后则回到了 111 mL/min/1.73 m(2) (95% CI, 91-131; P < 0.001)。没有接受脑灌注压治疗的患者平均最高肌酐清除率为 150 mL/min/1.73 m(2)（95%置信区间 134-167; P = 0.03）。接受积极治疗的患者肌酐清除率达到峰值的平均时间是 4.7 天(95% CI, 3.0-6.4)。在一个多元分析中，去甲肾上腺素的应用、盐水负荷、平均动脉压和中心静脉压与肌酐清除率升高相关。
结论：颅脑外伤病人接受积极地脑灌注压治疗后肌酐清除率通常升高并持续至治疗结束。进一步的工作需要展开来明晰这种情况下该治疗对肾脏清除药物的影响。
（张玥琪译，薛张纲校）

Background: Hypertonic saline and/or norepinephrine infusion are routinely used to achieve a desired cerebral perfusion pressure (CPP) in the management of traumatic brain injury (TBI). We hypothesized that creatinine clearances (CrCls) would be significantly augmented in this setting.
Methods: This was an observational cohort study in TBI patients older than 16 years with normal serum creatinine concentrations, requiring maintenance of CPP. Eight-hour urinary CrCl collections were performed while on and off active management. Demographic data, use of vasoactive medications, fluid balance, feeding regimen, and hemodynamic variables were recorded throughout the study period. Augmented CrCl was defined as >150 mL/min/1.73 m(2) in women and >160 mL/min/1.73 m(2) in men.
Results: Twenty patients were enrolled, and augmented clearances were demonstrated in 17 (85%). The mean maximum CrCl was 179 mL/min/1.73 m(2) while receiving CPP therapy (95% confidence interval [CI], 159-198), returning to a mean of 111 mL/min/1.73 m(2) (95% CI, 91-131; P < 0.001) when measured after discharge from the intensive care unit. The mean CrCl in the intensive care unit while not receiving CPP

therapy was 150 mL/min/1.73 m(2) (95% CI, 134-167; P = 0.03). The mean time to reach peak CrCl while receiving active treatment was 4.7 days (95% CI, 3.0-6.4). In a multivariate analysis, norepinephrine use, saline loading, mean arterial blood pressure, and central venous pressure were associated with augmented CrCl on the day of measurement.

Conclusions: Augmented CrCls are common in TBI patients receiving active management of CPP and persist even after discontinuation of such therapy. Further work is needed to clarify the impact of such clearances on renally excreted drugs in this setting.