

# Table of Contents

## February, 2015

### Cardiovascular Anesthesiology

Research Report

[异氟醚通过保护线粒体呼吸与超分子构造而避免心肌缺血性损伤](#)

(柳韶华 译 陈杰 校)

**Isoflurane Protects the Myocardium Against Ischemic Injury via the Preservation of Mitochondrial Respiration and Its Supramolecular Organization**

- Lotz, Christopher;
- Zhang, Jun;
- Fang, Caiyun;
- Liem, David;
- Ping, Peipei

*Anesthesia & Analgesia. 120(2):265-274, February 2015.*

Review Article

[肾素血管紧张素在心血管稳态中作用更新](#)

(吕越昌译 薛张纲校)

**An Update of the Role of Renin Angiotensin in Cardiovascular Homeostasis**

- Farag, Ehab;
- Maheshwari, Kamal;
- Morgan, Joseph;
- Sakr Esa, Wael Ali;
- Doyle, D. John

*Anesthesia & Analgesia. 120(2):275-292, February 2015.*

### Ambulatory Anesthesiology and Perioperative Management

Research Report

[呼气末正压通气在外科领域条件下对功能性内窥镜鼻窦手术的影响](#)

(王晓莉译 李士通审校)

## **The Influence of Positive End-Expiratory Pressure on Surgical Field Conditions During Functional Endoscopic Sinus Surgery**

- DeMaria, Samuel;
- Govindaraj, Satish;
- Huang, Alice;
- Hyman, Jaime;
- McCormick, Patrick;
- Lin, Hung Mo;
- Levine, Adam

*Anesthesia & Analgesia. 120(2):305-310, February 2015.*

## **Anesthetic Pharmacology**

Research Report

### [2-脱氧-D-葡萄糖增强小鼠麻醉作用](#)

(池晓颖 译 陈杰 校)

#### **2-Deoxy-D-Glucose Enhances Anesthetic Effects in Mice**

- Wang, Hui;
- Xu, Zhipeng;
- Wu, Anshi;
- Dong, Yuanlin;
- Zhang, Yiyang;
- Yue, Yun;
- Xie, Zhongcong

*Anesthesia & Analgesia. 120(2):312-319, February 2015.*

### [氯胺酮急性损伤大鼠脑内线粒体功能并增强超氧化物歧化酶活性](#)

(江凌慧译 薛张纲校)

#### **Acute Ketamine Impairs Mitochondrial Function and Promotes Superoxide Dismutase Activity in the Rat Brain**

- Venâncio, Carlos;
- Félix, Lu ís;
- Almeida, Vanessa;
- Coutinho, João;
- Antunes, Lu ís;
- Peixoto, Francisco;
- Summavielle, Teresa

*Anesthesia & Analgesia*. 120(2):320-328, February 2015.

[丙泊酚（得普利麻）和脂肪乳通过削弱 GLUT4 的转运增强 2 型糖尿病病人心脏的胰岛抵抗](#)

(王晓莉译 李士通审校)

**Propofol (Diprivan®) and Intralipid® Exacerbate Insulin Resistance in Type-2 Diabetic Hearts by Impairing GLUT4 Trafficking**

- Lou, Phing-How;
- Lucchinetti, Eliana;
- Zhang, Liyan;
- Affolter, Andreas;
- Gandhi, Manoj;
- Zhakupova, Assem;
- Hersberger, Martin;
- Hornemann, Thorsten;
- Clanachan, Alexander S.;
- Zaugg, Michael

*Anesthesia & Analgesia*. 120(2):329-340, February 2015.

## Technology, Computing, and Simulation

Research Report

[氧供的有效性和二氧化碳波形的可靠性：4 种鼻导管的交叉比较](#)

(王筱婧译 陈杰校)

**The Effectiveness of Oxygen Delivery and Reliability of Carbon Dioxide Waveforms: A Crossover Comparison of 4 Nasal Cannulae**

- Ebert, Thomas J.;
- Novalija, Jutta;
- Uhrich, Toni D.;
- Barney, Jill A.

*Anesthesia & Analgesia*. 120(2):342-348, February 2015.

## Technical Communication

[使用拉曼光谱学原理的方法检测表明在儿童腹腔镜手术的气腹中有空气的存在](#)

(王飞译 薛张纲校)

## **Gas Analysis Using Raman Spectroscopy Demonstrates the Presence of Intraperitoneal Air (Nitrogen and Oxygen) in a Cohort of Children Undergoing Pediatric Laparoscopic Surgery**

- Taylor, Susan P.;
- Sato, Thomas T.;
- Balcom, Anthony H.;
- Groth, Travis;
- Hoffman, George M.

*Anesthesia & Analgesia*. 120(2):349-354, February 2015.

### **Brief Report**

[在一系列体外的实验中发现硬质和软质气管交换导管所造成的明显的肺损伤](#)

(李蔚文译 李士通审校)

## **Macroscopic Barotrauma Caused by Stiff and Soft-Tipped Airway Exchange Catheters: An In Vitro Case Series**

- Axe, Robert;
- Middleditch, Alex;
- Kelly, Fiona E.;
- Batchelor, Tim J.;
- Cook, Tim M.

*Anesthesia & Analgesia*. 120(2):355-361, February 2015.

## **Patient Safety**

### **Research Report**

[在国家麻醉临床预后登记中观察到的围术期心脏骤停发生率和危险因素](#)

(徐欢译 陈杰校)

## **The Incidence and Risk Factors for Perioperative Cardiac Arrest Observed in the National Anesthesia Clinical Outcomes Registry**

- Nunnally, Mark E.;
- O'Connor, Michael F.;
- Kordylewski, Hubert;
- Westlake, Benjamin;
- Dutton, Richard P.

*Anesthesia & Analgesia*. 120(2):364-370, February 2015.

## **Critical Care, Trauma, and Resuscitation**

Research Report

[通过测定一氧化碳弥散率和肺泡表面活性物质 B 型蛋白来评估麻醉、肌松和机械通气对肺功能的影响](#)

(潘艳译 薛张纲校)

**The Effects of Anesthesia, Muscle Paralysis, and Ventilation on the Lung Evaluated by Lung Diffusion for Carbon Monoxide and Pulmonary Surfactant Protein B**

- Di Marco, Fabiano;
- Bonacina, Daniele;
- Vassena, Emanuele;
- Arisi, Erik;
- Apostolo, Anna;
- Banfi, Cristina;
- Centanni, Stefano;
- Agostoni, Piergiuseppe;
- Fumagalli, Roberto

*Anesthesia & Analgesia. 120(2):373-380, February 2015.*

[外源性表面活性物质的治疗对于二次损伤的小鼠肺模型的影响](#)

(李蔚文译 李士通审校)

**The Effects of Exogenous Surfactant Treatment in a Murine Model of Two-Hit Lung Injury**

- Zambelli, Vanessa;
- Bellani, Giacomo;
- Amigoni, Maria;
- Grassi, Alice;
- Scanziani, Margherita;
- Farina, Francesca;
- Latini, Roberto;
- Pesenti, Antonio

*Anesthesia & Analgesia. 120(2):381-388, February 2015.*

[晶体液和胶体液：通过系统回顾和 meta 回归分析探索两者在液体需求中的差异](#)

(林雨轩译 陈杰校)

**Crystalloids Versus Colloids: Exploring Differences in Fluid Requirements by Systematic Review and Meta-Regression**

- Orbegozo Cortés, Diego;
- Gamarano Barros, Teresa;

- Njimi, Hassane;
- Vincent, Jean-Louis

*Anesthesia & Analgesia*. 120(2):389-402, February 2015.

## **Pediatric Anesthesiology**

Research Report

[新生儿心肺转流术后过量出血以及预后](#)

(杜芳译 薛张纲校)

### **Excessive Postoperative Bleeding and Outcomes in Neonates Undergoing Cardiopulmonary Bypass**

- Guzzetta, Nina A.;
- Allen, Nadine N.;
- Wilson, Elizabeth C.;
- Foster, Gregory S.;
- Ehrlich, Alexandra C.;
- Miller, Bruce E.

*Anesthesia & Analgesia*. 120(2):405-410, February 2015.

[由于小儿围手术期呼吸事件产生的医院额外费用和住院时间](#)

(田园译 李士通审校)

### **Excess Costs and Length of Hospital Stay Attributable to Perioperative Respiratory Events in Children**

- Oofuvong, Maliwan;
- Geater, Alan Frederick;
- Chongsuvivatwong, Virasakdi;
- Chanchayanon, Thavat;
- Sriyanaluk, Bussarin;
- Saefung, Boonthida;
- Nuanjun, Kanjana

*Anesthesia & Analgesia*. 120(2):411-419, February 2015.

[靶向治疗对儿科肺动脉高压患者围术期发病率和死亡率影响](#)

(张帆译 陈杰校)

### **The Impact of Targeted Therapies for Pulmonary Hypertension on Pediatric Intraoperative Morbidity or Mortality**

- Taylor, Katherine;

- Moulton, Dagmar;
- Zhao, Xiu Yan;
- Laussen, Peter

*Anesthesia & Analgesia*. 120(2):420-426, February 2015.

[超声用于评估儿科患者喉罩放置位置的一项观察性研究](#)

(黄文惠译 薛张纲校)

### **An Ultrasound Evaluation of Laryngeal Mask Airway Position in Pediatric Patients: An Observational Study**

- Kim, Jeongmin;
- Kim, Ji Young;
- Kim, Won Oak;
- Kil, Hae Keum

*Anesthesia & Analgesia*. 120(2):427-432, February 2015.

## **Neuroscience in Anesthesiology and Perioperative Medicine**

Research Report

[异丙酚诱导新生大鼠脑电图发作：糖皮质激素和  \$\gamma\$ -氨基丁酸 A 型受体介导的激励作用](#)

(田园译 李士通审校)

### **Propofol-Induced Electroencephalographic Seizures in Neonatal Rats: The Role of Corticosteroids and $\gamma$ -Aminobutyric Acid Type A Receptor-Mediated Excitation**

- Willis, Jesse;
- Zhu, Wanting;
- Perez-Downes, Julio;
- Tan, Sijie; Xu, Changqing;
- Seubert, Christoph;
- Gravenstein, Nikolaus;
- Martynyuk, Anatoly

*Anesthesia & Analgesia*. 120(2):433-439, February 2015.

## **Pain and Analgesic Mechanisms**

Research Report

[在神经病理性疼痛的大鼠模型中鞘内给予安非他酮，一种多巴胺和去甲肾上腺素再摄取抑制剂的抗痛觉过敏效应](#)

(秦懿译 陈杰校)

## **The Antihyperalgesic Effects of Intrathecal Bupropion, a Dopamine and Noradrenaline Reuptake Inhibitor, in a Rat Model of Neuropathic Pain**

- Hoshino, Hajime;
- Obata, Hideaki;
- Nakajima, Kunie;
- Mieda, Rie;
- Saito, Shigeru

*Anesthesia & Analgesia*. 120(2):460-466, February 2015.

## [刺激性挥发麻醉剂通过 TRPA1 和 TRPV1 通道导致离体小鼠气管神经性炎症](#)

(盖晓冬译 薛张纲校)

## **Irritant Volatile Anesthetics Induce Neurogenic Inflammation Through TRPA1 and TRPV1 Channels in the Isolated Mouse Trachea**

- Kichko, Tatjana I.;
- Niedermirtl, Florian;
- Leffler, Andreas;
- Reeh, Peter W.

*Anesthesia & Analgesia*. 120(2):467-471, February 2015.

## [大鼠急性术后疼痛模型中自发痛行为比机械诱发疼痛对吗啡或丁丙诺啡更敏感](#)

(田园译 李士通审校)

## **Spontaneous Pain-Like Behaviors Are More Sensitive to Morphine and Buprenorphine Than Mechanically Evoked Behaviors in a Rat Model of Acute Postoperative Pain**

- Kabadi, Rajiv;
- Kouya, Francois;
- Cohen, Hillel W.;
- Banik, Ratan K.

*Anesthesia & Analgesia*. 120(2):472-478, February 2015.

## **Regional Anesthesia**

Research Report

## [一项关于脊麻复合静脉镇静下行全膝置换术时鼻持续正压通气对动脉二氧化碳分压影响的初步研究](#)

(李慧 译 陈杰 校)

## **A Pilot Study on the Effect of Nasal Continuous Positive Airway Pressure on Arterial Partial Pressure of Carbon Dioxide During Spinal Anesthesia with Intravenous Sedation for Total Knee Arthroplasty**

- Smith, Stephen B.;
- Carr, Shawn;
- Psikula, Stacey;
- Das, Anita;
- Grichnik, Katherine

*Anesthesia & Analgesia*. 120(2):479-483, February 2015.

### 肾素血管紧张素在心血管稳态中作用更新

#### **An Update of the Role of Renin Angiotensin in Cardiovascular Homeostasis**

Farag, Ehab MD, FRCA\*†,§; Maheshwari, Kamal MD\*†; Morgan, Joseph MD‡; Sakr Esa, Wael Ali MD, PhD\*; Doyle, D. John MD, PhD§

*Anesthesia & Analgesia* 2015 120 275–292

肾素血管紧张素系统（RAS）是人体内主要的血管收缩相关的系统，通过血管紧张素 II 与血管紧张素 I 受体之间的相互作用来发挥生理作用（即经典的 RAS 模型）。尽管如此，随着七肽血管紧张素 1-7 的发现和 RAS 系统的概念的变化，我们所理解的可以降低动脉血压的 RAS 生理系统也发生了巨大的改变。在这篇综述中，我们聚焦在最新发现的 RAS 系统的功能上，特别是这些最新发现的潜在临床意义，尤其是在治疗心血管疾病最新的药理学领域。

（吕越昌译 薛张纲校）

The renin angiotensin system (RAS) is thought to be the body's main vasoconstrictor system, with physiological effects mediated via the interaction of angiotensin II with angiotensin I receptors (the "classic" RAS model). However, since the discovery of the heptapeptide angiotensin 1-7 and the development of the concept of the "alternate" RAS system, with its ability to reduce arterial blood pressure, our understanding of this physiologic system has changed dramatically. In this review, we focus on the newly discovered functions of the RAS, particularly the potential clinical significance of these developments, especially in the realm of new pharmacologic interventions for treating cardiovascular disease.

### 氯胺酮急性损伤大鼠脑内线粒体功能并增强超氧化物歧化酶活性

#### **Acute Ketamine Impairs Mitochondrial Function and Promotes Superoxide Dismutase Activity in the Rat Brain**

Venâncio, Carlos DVM, PhD\*†; Félix, Luís MSc†; Almeida, Vanessa MSc\*; Coutinho, João PhD‡; Antunes, Luís DVM, PhD†; Peixoto, Francisco PhD\*; Summavielle, Teresa PhD§

*Anesthesia & Analgesia* 2015 120 320–328

**背景：**氯胺酮常常与改变线粒体功能和氧化应激有关。然而，氯胺酮在体内对线粒体生物能量和氧化还原状态的作用研究甚少。越来越多的证据支持一氧化氮（NO）可能为氯胺酮副作用的调节介质。本文我们研究了 NO 在氯胺酮麻醉中对脑线粒体功能和氧化还原状态的调节机制。

**方法：**成年雄性大鼠分别给予腹腔注射单剂量氯胺酮（50 mg/kg、100 mg/kg、150mg/kg）或氯胺酮联合 N-硝基-L-精氨酸（3mg/kg），6 小时后将动物处死。采集脑组织和血标本进行 NO 测定和线粒体分离，并运用多个变量来评价脑线粒体的功能。

**结果：**氯胺酮可干扰复合物 I 功能，增加耗氧量，使谷氨酸-苹果酸基质氧化磷酸化的效率受损，降低 NADH 泛醌氧化还原酶活性。此外，在给予 50mg/kg 和 100mg/kg 的剂量后，线粒体一氧化氮合酶（mtNOS）活性和血浆 NO 水平有所增加。氯胺酮增加过氧化氢的产生并触发超氧化物歧化酶作用。mtNOS 抑制剂可以通过 N-硝基-L-精氨酸来部分或完全阻止这些效果产生。

**结论：**氯胺酮急性给药会损害线粒体复合物 I 的作用，增强 mtNOS 活性，增加过氧化氢和 NO 的产生，从而触发超氧化物歧化酶的作用并增强抗氧化活性。本研究结果阐明在氯胺酮麻醉中 NO 的调制作用，为临床作用机制提供依据。

（江凌慧译 薛张纲校）

**BACKGROUND:** Ketamine is often associated with altered mitochondrial function and oxidative stress. Nevertheless, limited data are still available regarding the in vivo action of ketamine in mitochondrial bioenergetics and redox state. Accumulating evidence supports a role for nitric oxide (NO) as a possible modulator of ketamine's side effects. In the present study, we investigated the role of NO modulation on ketamine anesthesia at the level of brain mitochondrial function and redox status.

**METHODS:** Adult male rats received a single dose of ketamine (50, 100, or 150 mg/kg IP) or a combination of ketamine and N-nitro-L-arginine (3 mg/kg IP). Animals were killed 6 hours after treatment. Brain and blood samples were collected for plasma NO determination and mitochondria isolation. Several variables of brain mitochondrial function were evaluated.

**RESULTS:** Ketamine interfered with complex I function, revealing increased oxygen consumption in state 4, impaired oxidative phosphorylation efficiency of glutamate-malate substrate, and decreased NADH-ubiquinone oxidoreductase activity. In addition, mitochondrial NO synthase (mtNOS) activity and NO plasma levels were increased for the 50 and 100 mg/kg doses. Ketamine administration increased hydrogen peroxide generation and triggered superoxide dismutase activity. All these effects could totally or partially be prevented by mtNOS inhibition through N-nitro-L-arginine.

**CONCLUSIONS:** Acute ketamine administration impaired the function of mitochondrial complex I leading to increased mtNOS activity, increased generation of hydrogen peroxide and NO, resulting in superoxide dismutase triggering, and improved antioxidant activity. The present findings clarify the role of NO modulation in ketamine anesthesia, providing new data on a relevant clinical mechanism.

使用拉曼光谱学原理的方法检测表明在儿童腹腔镜手术的气腹中有空气的存在

### Gas Analysis Using Raman Spectroscopy Demonstrates the Presence of Intraperitoneal Air (Nitrogen and Oxygen) in a Cohort of Children Undergoing Pediatric Laparoscopic Surgery

Taylor, Susan P. MD, MPH\*; Sato, Thomas T. MD†; Balcom, Anthony H. MD‡; Groth, Travis MD‡; Hoffman, George M. MD§

Anesthesia & Analgesia 2015 120 349–354

临床上，在腹腔镜手术中发生的严重的气体栓塞事件虽然罕见但却是灾难性的。病例报告显示，腹腔中除了充入腹腔的气体外，空气也存在。我们研究了在实验及常规儿童手术中，应用不同的设备及充气方法后气腹中空气的成分。在一种模拟的腹腔镜手术中，我们应用拉曼光谱的方法检测了充入模拟气腹和从气腹中回收的气体中氮气、氧气及二氧化碳

的含量。我们随后分析了在常规的腹腔镜手术中应用二氧化碳充入及抽出管道中进入和回收气体中的组成，发现其中有 10% 的空气含量存在。体外实验中，在充入 0.2L 以下气体的情况下，在充入气体管道的末端是检测不到二氧化碳的。但在 0.4L 以下时，氮气是持续存在的，从模拟气腹回收的气体中大约有  $40\% \pm 8\%$  的氮气含量。在临床试验中，预充气体能将氮气的含量从原来的  $78\% \pm 0.5\%$  降到  $23\% \pm 15\%$ ，但不管应用什么充气技术，在随后的检测样本中均有超过 10% 的空气存在。腹腔镜实践中常规允许一定量的空气充入腹腔中。在设备中预充二氧化碳虽然能减少气腹中空气的含量但却不能完全排除空气，因此，当血管破损发生后，栓塞的气体中含有不同量的氮气、氧气和二氧化碳。在儿童患者中，当气腹的充气空间充满后，氮气的含量接近未充气系统中室内空气的含量。小的充气量中含有高浓度的氮气可造成新生儿及小儿灾难性的空气栓塞。

(王飞译 薛张纲校)

Clinically significant gas embolism during laparoscopy is a rare but potentially catastrophic event. Case reports suggest that air, in addition to the insufflation gas, may be present. We studied the effects of equipment design and flushing techniques on the composition of gas present under experimental and routine pediatric surgical conditions. Concentrations of nitrogen (N<sub>2</sub>), oxygen (O<sub>2</sub>), and carbon dioxide (CO<sub>2</sub>) were measured by Raman spectroscopy in gas delivered to and retrieved from a mock peritoneum during simulated laparoscopy. We then analyzed the composition of insufflated and recovered gases during elective laparoscopic procedures conducted with CO<sub>2</sub>-preflushed and unflushed tubing to determine the presence of significant (10%) quantities of air. In vitro, CO<sub>2</sub> was not detected at the distal end of insufflator tubing until after delivery of approximately 0.2 L of gas, and N<sub>2</sub> persisted until >0.4 L was delivered, with  $40\% \pm 8\%$  (mean  $\pm$  SD, range 33%–49%) recovered from the mock peritoneum at the termination of initial insufflation. In clinical studies, preflushing reduced the initial concentration of N<sub>2</sub> from  $78\% \pm 0.5\%$  to  $23\% \pm 15\%$ , but >10% air was detected in all subsequent samples, regardless of insufflation technique. Laparoscopic equipment and practice routinely permit delivery of air to the insufflated cavity. Purging the equipment with CO<sub>2</sub> reduces but does not eliminate air (N<sub>2</sub>, O<sub>2</sub>) within the peritoneal cavity during laparoscopy. Thus, when vascular injury occurs, embolized gases will contain variable quantities of N<sub>2</sub>, O<sub>2</sub>, and CO<sub>2</sub>. As the initial insufflation volume diminishes and approaches the volume of the insufflation tubing, which occurs in infants and young pediatric patients, the concentration of N<sub>2</sub> will approximate that of room air in an unflushed system. Small insufflation volumes containing high N<sub>2</sub> concentrations can contribute to catastrophic air emboli in neonates and small pediatric patients.

通过测定一氧化碳弥散率和肺泡表面活性物质 B 型蛋白来评估麻醉、肌松和机械通气对肺功能的影响

### The Effects of Anesthesia, Muscle Paralysis, and Ventilation on the Lung Evaluated by Lung Diffusion for Carbon Monoxide and Pulmonary Surfactant Protein B

Di Marco, Fabiano MD, PhD\*; Bonacina, Daniele MD†; Vassena, Emanuele MD†; Arisi, Erik MD†; Apostolo, Anna MD‡; Banfi, Cristina PhD‡; Centanni, Stefano MD, PhD\*; Agostoni, Piergiuseppe MD, PhD§ ||; Fumagalli, Roberto MD, PhD†¶

Anesthesia & Analgesia 2015 120 373–380

**背景：**麻醉患者的肺泡-动脉氧分压差通常会增加。本研究旨在评估麻醉，肌松以及短期机械通气对肺功能的影响。

**方法：**我们选取 45 名接受非胸部手术并且无肺部疾病的病人，测定他们的一氧化碳弥散率（DLCO），包括肺毛细血管血容量（Vc），肺泡-毛细血管屏障的导电性以及肺泡表面活性物质 B 型蛋白（肺泡损伤的标志）

**结果：**麻醉、肌松以及机械通气都会导致肺泡气体交换受损，伴随着 DM 和 Vc 的下降，麻醉诱导后 DLCO 值也立即下降。然而，DM 的下降是由于肺容量的下降，Vc 的变化并非如此，而是由于 Vc/肺泡容积比值的显著下降。尽管 DLCO 和它的各组成成分在麻醉诱导后立即下降，但在接下来的 1 到 3 小时内它们的数值并没有进一步下降。而表面活性物质 B 型蛋白在麻醉诱导后并没有立即改变，但在诱导后 1 小时后有所增加，而诱导 3 小时后则进一步增加。肺泡损伤的程度与肺灌注和肺顺应性的下降有关（即潮气量与呼末肺容量之比）。

**结论：**短时间麻醉及控制通气将会带来：（1）与肺顺应性和肺灌注下降相关的肺泡损伤（2）主要与肺容量下降相关的气体交换障碍，同时也与肺灌注下降有关。

（潘艳译 薛张纲校）

**BACKGROUND:** An increased alveolar-arterial oxygen tension difference is frequent in anesthetized patients. In this study, we evaluated the effect on the lung of anesthesia, muscle paralysis, and a brief course of mechanical ventilation.

**METHODS:** Lung diffusion for carbon monoxide (DLCO), including pulmonary capillary blood volume (Vc) and conductance of the alveolar-capillary membrane (DM), and pulmonary surfactant protein type B (a marker of alveolar damage) were measured in 45 patients without pulmonary disease undergoing extrathoracic surgery.

**RESULTS:** Anesthesia, muscle paralysis, and mechanical ventilation led to impairment of gas exchange, with a reduction of DLCO values immediately after anesthetic induction due to a concomitant reduction of both DM and Vc. While changes in DM were due to the reduction of lung volume, changes in Vc were not limited to volume loss, since the Vc/alveolar volume ratio decreased significantly. Although DLCO and its components decreased immediately after induction, none of the values decreased further at 1 and 3 hours. Surfactant protein type B, however, was unchanged immediately after anesthesia but increased at 1 hour after induction and further increased after 3 hours of anesthesia. The level of alveolar damage correlated with the reduction of lung perfusion and lung dynamic strain (i.e., ratio between tidal volume and end-expiratory lung volume).

**CONCLUSIONS:** A brief course of anesthesia and controlled ventilation leads to: (1) alveolar damage, which is correlated with lung strain and perfusion, and (2) impaired gas exchange mainly due to volume loss but also to reduced aerated lung perfusion.

### 新生儿心肺转流术后过量出血以及预后

#### Excessive Postoperative Bleeding and Outcomes in Neonates Undergoing Cardiopulmonary Bypass

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**背景：**进行心脏手术的新生儿特别易于发生与心肺转流（CPB）相关的凝血功能异常，CPB 后出血的风险增高。不成熟的凝血系统，CPB 预充时严重的血液稀释，CPB 时间长时的低体温，过多的缝合增加了新生儿 CPB 后出血的风险以及术后严重并发症的发生。

**方法：**我们回顾性分析了在 2010 年 1 月至 2011 年 12 月 31 日之间在 CPB 下行复杂先天性心脏病手术的 169 名新生儿的病史资料。收集并分析了围术期患者的资料，通过测定术后 24h 的胸腔引流量（CTO），CPB 术后输血的需要量以及严重的术后并发症，包括肾功能不全、血液透析、血栓、体外膜肺以及住院死亡率，从而重点分析了 CPB 后的出血量。我们使用 Spearman 相关性分析来确定多个围术期的变量和 24hCTO 及术后血制品需

要量之间的关系。此外，我们使用 logistic 回归分析来确定过量出血（定义为 24h CTO 大于第 75 百分位数）及术后重大并发症之间的关系。

**结果：**24h CTO 和术后输血需要量与先天性心脏病手术风险评分（RACHS-1），CPB 时间及低体温之间显著相关。Logistic 回归分析发现 CPB 后过量出血使术后血透（相对危险度[RR] 12.0；可信区间，1.50–54.69；P=0.02）以及 ECMO（RR 9.95；可信区间，3.07–28.47；P=0.0008）的独立预测因素。RACHS-1 评分是住院死亡率的有意义的预测因素（P=0.03）。

**结论：**新生儿 CPB 术后过量出血与术后不良事件的增加独立相关，尤其是术后血透以及 ECMO 支持。我们在新生儿中研究的结果与近期一致：在儿童 CPB 后增加的输血需要量与术后重大并发症的发生独立相关。我们的研究结果可以帮助临床医生预测新生儿心肺转流术后潜在的并发症的发生以及分配资源以处理这些不良事件。

（杜芳译 薛张纲校）

**BACKGROUND:** Neonates undergoing cardiac surgery are especially prone to the hemostatic alterations of cardiopulmonary bypass (CPB) and are at high risk for post-CPB bleeding. An immature coagulation system, significant hemodilution from the CPB prime, long CPB times at low temperatures, and extensive suture lines increase neonates' susceptibility to bleeding after CPB. In this study, we examined the relationship between excessive bleeding in neonates after CPB and major postoperative adverse events.

**METHODS:** We retrospectively reviewed the medical records of 169 neonates who underwent complex congenital heart surgery with CPB between January 1, 2010, and December 31, 2011. Perioperative data were collected and analyzed with specific focus on post-CPB bleeding as measured by 24-hour postoperative chest tube output (CTO), post-CPB transfusion requirements, and major postoperative adverse events, including renal dysfunction, dialysis, thrombosis, extracorporeal membrane oxygenation (ECMO), and in-hospital mortality. We used Spearman correlation to determine correlations between multiple perioperative variables and 24-hour CTO and postoperative blood product requirements. Also, we used logistic regression analysis to determine the association between excessive bleeding (defined as 24-hour CTO >75th percentile) and major postoperative adverse events.

**RESULTS:** Significant correlations were found between 24-hour CTO and postoperative blood product transfusion with weight, Risk Adjustment for Congenital Heart Surgery (RACHS-1) score, CPB time, and lowest temperature. Logistic regression found that excessive bleeding after CPB was an independent predictor of postoperative dialysis (relative risk [RR] 12.0; confidence interval, 1.50–54.69; P = 0.02) and ECMO (RR 9.95; confidence interval, 3.07–28.47; P = 0.0008). RACHS-1 score was a significant predictor of in-hospital mortality (P = 0.03).

**CONCLUSIONS:** Excessive postoperative bleeding in neonates after CPB is independently associated with increased adverse events, specifically the need for postoperative dialysis and ECMO support. Our findings in neonates are congruent with other recent research that also has found increasing transfusion requirements after pediatric CPB to be independently associated with an increase in major postoperative adverse events. Our results may aid clinicians in anticipating potential adverse events after neonatal bypass and in allocating the resources necessary to manage these events.

### 超声用于评估儿科患者喉罩放置位置的一项观察性研究

#### An Ultrasound Evaluation of Laryngeal Mask Airway Position in Pediatric Patients: An Observational Study

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**背景：**对于儿科患者，喉罩（LMA）经常在咽喉处移位而需要重新定位。当 LMA 的顶端放置在食管入口时，杓状软骨向前侧移位。当 LMA 时旋转或倾斜时，杓状软骨的腹侧运动可能导致杓状软骨的不对称，这一现象可被超声检测到。在本研究中，我们试图用超评估儿科患者 LMA 移位的发生率。主要研究终点是使用超声和支气管镜检查（FOB）评估喉罩移位的发生率。次要终点是测定使用超声和支气管镜用于发现喉罩移位间的关系，并且归纳出超声诊断 LMA 移位的影像表现。

**方法：**在这项观察研究包括有 100 名儿童。麻醉诱导后，我们分别在喉罩置入前后将超声探头置于患者颈前得到声门处图像用以评估。纤维支气管镜用于评估喉罩位置（纤支镜喉罩分级及喉罩旋转分级）。放置好喉罩后，可以通过超声就杓状软骨的对称性进行评估。基于声门中线来评估杓状软骨的不对称性，并且相对的杓状软骨被分为 0 到 3 级（超声杓状软骨分级）。我们对超声杓状软骨分级、纤支镜喉罩分级及喉罩旋转分级之间相互关系进行分析。

**结果：**不对称的杓状软骨的发生率为 50%（95%可信区间(CI)，40% - 60%）。对于纤支镜，喉罩移位的发生率为 78%（95%可信区间，69% - 86%），喉罩旋转分级为 43%（95%可信区间，33% - 53%）。纤支镜检查喉罩移位的发生率较高（ $P < 0.0001$ ），但旋转的发生率是相似的（ $P = 0.395$ ）。超声杓状软骨分级与纤支镜喉罩分级无相关性（ $P = 0.611$ ），但与喉罩旋转分级呈显著相关（ $P < 0.0001$ ，95%可信区间，60% - 83%）。用于检测喉罩旋转，超声灵敏度为 93%（95%可信区间，81% - 98%），特异度为 82%（95%可信区间，70% - 91%）。阳性和阴性预测值分别为 80%（95%可信区间，66% - 90%）和 94%（95%可信区间，83% - 99%），准确度为 87%（95%可信区间，79% - 93%）。

**结论：**虽然超声无法检测喉罩放置的最适宜深度，但我们可以认为超声是一种精确检测喉罩旋转移位的工具。

（黄文惠译 薛张纲校）

**BACKGROUND:** In children, the laryngeal mask airway (LMA) is frequently displaced within the hypopharynx, resulting in repositioning of the device. When the tip of the LMA is placed in the esophageal inlet, the arytenoids are moved ventrally. When the LMA is rotated or deviated, the ventral movement of the arytenoids may result in asymmetric elevation of an arytenoid cartilage, which can be detected with ultrasound (US). In this study, we sought to estimate the incidence of LMA malposition detected with US in pediatric patients. The primary end point was to compare the incidence of LMA malposition between US and fiber optic bronchoscopy (FOB). The secondary end points were to find the interrelationship between US-detected and FOB-detected malposition of the LMA and to locate the diagnostic performance of US in detecting LMA malposition.

**METHODS:** In this observational study, 100 consecutive children were included. After anesthetic induction, US evaluation was performed before and after LMA insertion to obtain the glottic image on the anterior neck. FOB was performed to assess LMA position (FOB LMA grade and LMA rotation grade). With a post-LMA US image, the symmetry of the arytenoid cartilages was evaluated. Asymmetrical elevation of an arytenoid cartilage in reference to the glottic midline and the opposite arytenoid cartilage was graded as 0 to 3 (US arytenoid grade). The interrelationships between US arytenoid grade and FOB LMA grade or LMA rotation grade were assessed.

**RESULTS:** The incidence of asymmetrical elevation of an arytenoid was 50% (95% confidence interval [CI], 40%–60%). On FOB, the incidence of LMA malposition was 78% (95% CI, 69%–86%), and that of LMA rotation was 43% (95% CI, 33%–53%). The incidence of LMA malposition was higher with FOB ( $P < 0.0001$ ), but the incidence of rotation was similar ( $P = 0.395$ ). US arytenoid grade did not correlate with FOB LMA grade ( $P = 0.611$ ) but showed a significant correlation with LMA rotation grade ( $P < 0.0001$ ; 95% CI, 60%–83%). To detect a rotated LMA, US had a sensitivity of 93% (95% CI, 81%–98%) and a specificity of 82% (95%

CI, 70%–91%). The positive and negative predictive values were 80% (95% CI, 66%–90%) and 94% (95% CI, 83%–99%), respectively. The accuracy was 87% (95% CI, 79%–93%).

**CONCLUSIONS:** Although US could not detect the suboptimal depth of an LMA, US has promise of being an accurate tool in detecting a rotated LMA.

### 刺激性挥发麻醉剂通过 TRPA1 和 TRPV1 通道导致离体小鼠气管神经性炎症

#### Irritant Volatile Anesthetics Induce Neurogenic Inflammation Through TRPA1 and TRPV1 Channels in the Isolated Mouse Trachea

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**背景：**挥发性全身麻醉剂对气管神经末梢的刺激作用导致气道痉挛的分子机制还不甚清楚。神经肽的释放和神经性炎症有明确作用。

**方法：**我们分析液体浇注的离体小鼠气管释放降钙素基因相关肽（CGRP）的基础释放量及受刺激后的释放量，用于指示感觉神经元的激活，其中使用刺激性挥发麻醉剂（地氟烷和异氟烷）及非刺激性挥发麻醉剂（七氟烷）作为刺激物。在 38 摄氏度条件下，在不同的气体浓度（0.5 倍, 1 倍, 或 2 倍最小肺泡浓度 [MAC]）和不同的氧浓度中给予气管刺激。用辣椒素受体 TRPV1 和化学受体 TRPA1 的无变异的以及两基因均被敲除的小鼠作为组织供体。

**结果：**地氟烷以及异氟烷导致浓度相关的气管 CGRP 的释放，两者均在 1MAC（人）时达到饱和，也就是分别为 6% 和 1.25% 的浓度。地氟烷组，氧气浓度（25% 或者 94%）的差异对结果没有影响。七氟烷 1MAC 浓度不会导致气管 CGRP 的释放。TRPV1 小鼠的地氟烷反应降低 75%，而 TRPA1 和双敲除变异体完全没有反应。

**结论：**我们的结果证实了临床经验所显示的：在相同的麻醉气体浓度下，地氟烷较异氟烷更具刺激性，而七氟烷不会刺激气管支气管感觉神经释放神经肽或者导致神经性炎症。就两个刺激受体通道而言，TRPA1 较 TRPV1 更多地与介导不良反应有关，甚至可以延伸导致全身促炎反应后遗症。

（盖晓冬译 薛张纲校）

**BACKGROUND:** Irritating effects of volatile general anesthetics on tracheal nerve endings and resulting spastic reflexes in the airways are not completely understood with respect to molecular mechanisms. Neuropeptide release and neurogenic inflammation play an established role.

**METHODS:** The basal and stimulated calcitonin gene-related peptide (CGRP) release from the isolated superfused mouse trachea was analyzed as an index of sensory neuron activation, applying irritant (desflurane and isoflurane) and nonirritant (sevoflurane) volatile anesthetics as stimuli. Various gas concentrations (0.5-, 1-, or 2-fold minimum alveolar concentration [MAC]) and different O<sub>2</sub> atmospheres were used for tracheal stimulation at 38°C. Null mutants of the capsaicin receptor TRPV1 and of the chemoreceptor TRPA1, as well as double knockout mice, were used as tissue donors.

**RESULTS:** Desflurane and, less so, isoflurane caused a concentration-dependent tracheal CGRP release, both saturating at 1 MAC (human), that is, 6% and 1.25%, respectively. With desflurane, the O<sub>2</sub> concentration (25% or 94%) did not make a difference. Sevoflurane 1 MAC did not activate tracheal CGRP release. TRPV1 mice showed 75% reduced desflurane responses, and TRPA1 and double-null mutants showed no responses at all.

**CONCLUSIONS:** Our results confirm the clinical experience that desflurane is more irritating than isoflurane at equal anesthetic gas concentration, whereas sevoflurane does not activate

tracheobronchial sensory nerves to release neuropeptides and induce neurogenic inflammation. Both irritant receptor channels, TRPA1 more than TRPV1, are involved in mediating the adverse effects that may even extend to systemic proinflammatory sequelae

### 异氟醚通过保护线粒体呼吸与超分子构造而避免心肌缺血性损伤

#### Isoflurane Protects the Myocardium Against Ischemic Injury via the Preservation of Mitochondrial Respiration and Its Supramolecular Organization

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**背景：**异氟醚已被证明可限制心肌缺血性损伤。此效应推测部分通过影响线粒体而介导。本研究考察这一假设，即异氟醚维持线粒体呼吸链功能，从而限制心肌缺血损伤期间的线粒体损伤和线粒体膜解体。

**方法：**小鼠（9-12 周龄）暴露于（1.0MAC）异氟醚 36 h 后给予 30 min 的冠状动脉血管钳夹，随后进行 24 h 再灌注。再灌注每 4h 分离心肌线粒体。2、3、5-氯化三苯基四氮唑染色用于确定心肌梗塞大小。应用蓝绿温和聚丙烯酰胺凝胶电泳及特定的生化分析，研究线粒体呼吸链功能。通过丙二醛形成量化线粒体脂质过氧化反应；通过钙离子诱导肿胀评估线粒体膜的完整性。通过液相色谱质谱法和质谱法确认蛋白。

**结果：**共 31 只小鼠纳入研究。暴露于异氟醚的小鼠心肌梗死面积更少（ $P=0.0011$ ，与缺血/再灌注[I/R]组相比），且线粒体呼吸复合物 III 损伤更小（ $P=0.0008$ ，与 I/R 组相比）。异氟醚稳定了由复杂 III/IV 低聚物组成的线粒体超复合体（ $P=0.0086$ ，与 I/R 组相比）。丙二醛形成减少（ $P=0.0019$ ，与 I/R 组相比）以及对钙离子诱导肿胀敏感性降低（ $P=0.0010$ ，与 I/R 组相比）进一步证实了经异氟醚处理后线粒体损伤可减轻。

**结论：**本研究结果支持异氟醚维持线粒体呼吸链在体功能使心脏免受缺血性损伤的假设。这些效应可能部分由于对线粒体超分子组织和最小化氧化损伤的保护，避免了线粒体膜完整性缺失。

（柳韶华 译 陈杰 校）

**BACKGROUND:** Isoflurane has been demonstrated to limit myocardial ischemic injury. This effect is hypothesized to be mediated in part via effects on mitochondria. We investigated the hypothesis that isoflurane maintains mitochondrial respiratory chain functionality, in turn limiting mitochondrial damage and mitochondrial membrane disintegration during myocardial ischemic injury.

**METHODS:** Mice (9–12 weeks of age) received isoflurane (1.0 minimum alveolar concentration) 36 hours before a 30-minute coronary artery occlusion that was followed by 24 hours of reperfusion. Cardiac mitochondria were isolated at a time point corresponding to 4 hours of reperfusion. 2,3,5-Triphenyltetrazoliumchloride staining was used to determine myocardial infarct size. Mitochondrial respiratory chain functionality was investigated using blue native polyacrylamide gel electrophoresis, as well as specific biochemical assays. Mitochondrial lipid peroxidation was quantified via the formation of malondialdehyde; mitochondrial membrane integrity was assessed by  $Ca^{2+}$ -induced swelling. Protein identification was achieved via liquid chromatography mass spectrometry/mass spectrometry.

**RESULTS:** Thirty-one mice were studied. Mice receiving isoflurane displayed a reduced myocardial infarct size ( $P=0.0011$  versus ischemia/reperfusion [I/R]), accompanied by a preserved activity of respiratory complex III ( $P=0.0008$  versus I/R). Isoflurane stabilized mitochondrial supercomplexes consisting of oligomers from complex III/IV ( $P=0.0086$  versus I/R). Alleviation of mitochondrial damage after isoflurane treatment was further demonstrated as

decreased malondialdehyde formation ( $P = 0.0019$  versus I/R) as well as a diminished susceptibility to  $Ca^{2+}$ -induced swelling ( $P = 0.0010$  versus I/R).

**CONCLUSIONS:** Our findings support the hypothesis that isoflurane protects the heart from ischemic injury by maintaining the in vivo functionality of the mitochondrial respiratory chain. These effects may result in part from the preservation of mitochondrial supramolecular organization and minimized oxidative damage, circumventing the loss of mitochondrial membrane integrity.

## 2-脱氧-D-葡萄糖增强小鼠麻醉作用

### 2-Deoxy-D-Glucose Enhances Anesthetic Effects in Mice

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**背景：**挥发性药物的全身麻醉机制仍知之甚少。有研究认为能量水平上线粒体功能障碍和降低与全身麻醉效应相关。2-脱氧-D-葡萄糖（2-DG），一种葡萄糖的类似物，可以抑制己糖激酶和减少细胞三磷酸腺苷（ATP）水平。3-硝基丙酸是另外一种可消耗 ATP 水平的化合物。与此相反，艾地苯醌和左旋肉碱可挽救能量不足。因此本研究试图确定 2-DG 和/或 3-硝基丙酸是否可以增强异氟醚的麻醉作用，而艾地苯醌和左旋肉碱是否能够逆转 2-DG 的作用。

**方法：**C57BL/6J（8月龄）小鼠暴露于不同浓度的异氟醚，同时给予或不给予 2-DG、3-硝基丙酸、艾地苯醌和左旋肉碱处理。观察实验小鼠异氟醚诱导的翻正反射（LORR）消失。处理后评估 H4 人类神经胶质瘤细胞的 ATP 水平。最后，通过 <sup>31</sup>P-磁共振光谱来确定异氟醚对小鼠大脑 ATP 水平的影响。

**结果：**2-DG 增强异氟醚引起的 LORR ( $P = 0.002$ ,  $N = 15$ )。3-硝基丙酸可以增强异氟醚的麻醉作用 ( $P = 0.005$ ,  $N = 15$ )。艾地苯醌（艾地苯醌+生理盐水与艾地苯醌+2-DG 比较： $P = 0.165$ ,  $N = 15$ ），而非左旋肉碱（左旋肉碱+生理盐水与左旋肉碱+2-DG： $P < 0.0001$ ,  $N = 15$ ）可以抑制 2-DG 对小鼠异氟醚诱导的 LORR 的增强作用，同时证实 2-DG 无法增强艾地苯醌预处理小鼠异氟醚诱导的 LORR 作用。艾地苯醌（艾地苯醌+生理盐水与艾地苯醌+2-DG 相比： $P = 0.177$ ,  $N = 6$ ），而非左旋肉碱（左旋肉碱+生理盐水与左旋肉碱+2-DG 相比： $P = 0.029$ ,  $N = 6$ ）可以缓和 2-DG 减少细胞内 ATP 水平的作用，同时证实 2-DG 无法减少艾地苯醌预处理细胞的 ATP 水平。最后，异氟醚可以减少培养细胞和小鼠大脑细胞中 ATP 水平（ $\beta$ -ATP： $P = 0.003$ ,  $N = 10$ ； $\beta$ -ATP/磷酸： $P = 0.006$ ,  $N = 10$ ； $\beta$ -ATP/无机磷酸盐： $P = 0.001$ ,  $N = 10$ ）。

**结论：**初步研究中得出的这些结果建立了一个体系并产生假设，即 2-DG 通过降低能耗水平增强麻醉作用。这些结果促进对麻醉机制的进一步探讨。

（池晓颖 译 陈杰 校）

**BACKGROUND:** The mechanisms of general anesthesia by volatile drugs remain largely unknown. Mitochondrial dysfunction and reduction in energy levels have been suggested to be associated with general anesthesia status. 2-Deoxy-D-glucose (2-DG), an analog of glucose, inhibits hexokinase and reduces cellular levels of adenosine triphosphate (ATP). 3-Nitropropionic acid is another compound which can deplete ATP levels. In contrast, idebenone and L-carnitine could rescue deficits of energy. We therefore sought to determine whether 2-DG and/or 3-nitropropionic acid can enhance the anesthetic effects of isoflurane, and whether idebenone and L-carnitine can reverse the actions of 2-DG.

**METHODS:** C57BL/6J mice (8 months old) received different concentrations of isoflurane with and without the treatments of 2-DG, 3-nitropropionic acid, idebenone, and L-carnitine.

Isoflurane-induced loss of righting reflex (LORR) was determined in the mice. ATP levels in H4 human neuroglioma cells were assessed after these treatments. Finally, <sup>31</sup>P-magnetic resonance spectroscopy was used to determine the effects of isoflurane on brain ATP levels in the mice.

**RESULTS:** 2-DG enhanced isoflurane-induced LORR ( $P = 0.002$ ,  $N = 15$ ). 3-Nitropropionic acid also enhanced the anesthetic effects of isoflurane ( $P = 0.005$ ,  $N = 15$ ). Idebenone (idebenone + saline versus idebenone + 2-DG:  $P = 0.165$ ,  $N = 15$ ), but not L-carnitine (L-carnitine + saline versus L-carnitine + 2-DG:  $P < 0.0001$ ,  $N = 15$ ), inhibited the effects of 2-DG on enhancing isoflurane-induced LORR in the mice, as evidenced by 2-DG not enhancing isoflurane-induced LORR in the mice pretreated with idebenone. Idebenone (idebenone + saline versus idebenone + 2-DG:  $P = 0.177$ ,  $N = 6$ ), but not L-carnitine (L-carnitine + saline versus L-carnitine + 2-DG:  $P = 0.029$ ,  $N = 6$ ), also mitigated the effects of 2-DG on reducing ATP levels in cells, as evidenced by 2-DG not decreasing ATP levels in the cells pretreated with idebenone. Finally, isoflurane decreased ATP levels in both cultured cells and mouse brains ( $\beta$ -ATP:  $P = 0.003$ ,  $N = 10$ ;  $\beta$ -ATP/phosphocreatine:  $P = 0.006$ ,  $N = 10$ ;  $\beta$ -ATP/inorganic phosphate:  $P = 0.001$ ,  $N = 10$ ).

**CONCLUSIONS:** These results from our pilot studies have established a system and generated a hypothesis that 2-DG enhances anesthetic effects via reducing energy levels. These findings should promote further studies to investigate anesthesia mechanisms.

### 氧供的有效性和二氧化碳波形的可靠性：4种鼻导管的交叉比较

#### The Effectiveness of Oxygen Delivery and Reliability of Carbon Dioxide Waveforms: A Crossover Comparison of 4 Nasal Cannulae

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**背景：**有效氧输送和准确的呼气末 CO<sub>2</sub> (ETCO<sub>2</sub>) 采样是对呼吸功能受损患者鼻导管 (NCs) 吸氧基本要求。本实验研究了 4 种 NC 设计：分叉鼻塞 (NPs) 供氧同时在两侧均有 CO<sub>2</sub> 传感器 (Hudson), 独立的 O<sub>2</sub>/CO<sub>2</sub> NPs (Salter), CO<sub>2</sub> 传感器位于 NPs 上, 在 NPs 外通过多喷口 (Oridion) 和双喷口 (Medline) 进行氧供。本研究假设 NCs 之间设计的差异会影响氧供和 ETCO<sub>2</sub> 检测。

**方法：**45 名 18 至 35 岁的健康志愿者参与了这项无限制、随机、区组设计试验, 每个受试者在一个试验阶段按照他们的意愿控制 4 种 NCs 的 4 个交叉研究周期。监测包括心电图, 由 Hauge 气道的后咽 O<sub>2</sub> 抽样 (Sharn 麻醉产品, Tampa, 佛罗里达州) 和 NC ETCO<sub>2</sub>。在 11 名志愿者中, 桡动脉血液采样用于检测 O<sub>2</sub> 和 CO<sub>2</sub> 分压 (PaO<sub>2</sub> 和 PaCO<sub>2</sub>)。在吸入空气和 2、4、6 Lpm 的新鲜氧气 (FGFs) 期间, 依照随机化原则, 提供每种 NC, 收集每 2 分钟数据 (ETCO<sub>2</sub>, 咽后 O<sub>2</sub>, PaO<sub>2</sub> 和 PaCO<sub>2</sub>)。统计分析采用 SAS 分析软件, 9.3 版本及 JMP 统计软件, 11 版本 (SAS Institute Inc., Cary, NC),  $P < 0.05$  为统计学差异。

**结果：**血气分析表明每次实验期间 PaCO<sub>2</sub> 稳态值与基线值无差异。不同 NC 间, 在基线和 2 Lpm O<sub>2</sub> 时 PaO<sub>2</sub> 没有差异。吸氧 4 Lpm 时, 独立 NPs 和分叉 NCs 的 PaO<sub>2</sub> 显著高于多喷口 NC。吸氧 2、4、6 Lpm 时, 独立 NPs 的咽后 O<sub>2</sub> 显著高于应用多喷口和双喷口 NCs。吸氧 2 Lpm 时, 分叉 NPs 的咽后 O<sub>2</sub> 显著高于应用多喷口 NC; 并在吸氧 4、6 Lpm 时显著高于喷口 NC。分叉 NPs 的 ETCO<sub>2</sub> 显著低于其他 3 种 NCs, 这与在较高 FGF 时难以追踪 CO<sub>2</sub> 相一致。

**结论：**NCs 为肺功能受损患者提供了额外的 O<sub>2</sub> 吸入。ETCO<sub>2</sub> 准确测定有利于评估呼吸频率并确定在肺换气不足时是否发生 CO<sub>2</sub> 潴留。这些发现表明应用分叉鼻塞 (NPs) 的鼻导管 (NC) 在氧供时是最有效的, 并且在较高 FGFs 时提供最可靠且稳定的 CO<sub>2</sub> 波形。

(王筱婧译 陈杰校)

**BACKGROUND:** Effective O<sub>2</sub> delivery and accurate end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>) sampling are essential features of nasal cannulae (NCs) in patients with compromised respiratory status. We studied 4 NC designs: bifurcated nasal prongs (NPs) with O<sub>2</sub> delivery and CO<sub>2</sub> sensing in both NPs (Hudson), separate O<sub>2</sub>/CO<sub>2</sub> NPs (Salter), and CO<sub>2</sub> sensing in NPs with cloud O<sub>2</sub> delivery outside the NPs via multi vents (Oridion) and dual vents (Medline). We hypothesized that design differences between NCs would influence O<sub>2</sub> delivery and ETCO<sub>2</sub> detection.

**METHODS:** Forty-five healthy volunteers, 18 to 35 years, participated in an unrestricted, randomized block design, each subject serving as their own control in a 4-period crossover study design of 4 NCs during one session. Monitoring included electrocardiogram, posterior pharynx O<sub>2</sub> sampling from a Hauge Airway (Sharn Anesthesia Products, Tampa, FL), and NC ETCO<sub>2</sub>. In 11 volunteers, radial artery blood was sampled from a catheter for partial pressures of O<sub>2</sub> and carbon dioxide (PaO<sub>2</sub> and PaCO<sub>2</sub>) determination. Per randomization, each NC was positioned, and data were collected over 2 minutes (ETCO<sub>2</sub>, pharyngeal O<sub>2</sub>, PaO<sub>2</sub>, and PaCO<sub>2</sub>) during room air and during O<sub>2</sub> fresh gas flows (FGFs) of 2, 4, and 6 Lpm. Statistical analyses were performed with SAS Analytics Pro, Version 9.3, and JMP Statistical Software, Version 11 (SAS Institute Inc., Cary, NC), significance at P < 0.05.

**RESULTS:** Blood gas analyses indicated PaCO<sub>2</sub> during steady state at each experimental time period remained unchanged from physiologic baseline. PaO<sub>2</sub> did not differ between NC devices at baseline or 2 Lpm O<sub>2</sub>. The PaO<sub>2</sub> at 4 Lpm from the separate NPs and bifurcated NCs was significantly higher than the multi-vented NC. Pharyngeal O<sub>2</sub> with the NC with separate NPs was significantly higher than multivented and dual-vented cloud delivery NCs at 2, 4, and 6 Lpm FGF. Pharyngeal O<sub>2</sub> with the NC with bifurcated NPs was significantly higher than the multi-vented NC at 2 Lpm, and higher than cloud delivery NCs at 4 and 6 Lpm FGF. ETCO<sub>2</sub> was significantly lower with the NC with bifurcated NPs compared to the other 3 NCs, consistent with errant CO<sub>2</sub> tracings at higher FGF.

**CONCLUSIONS:** NCs provide supplemental inspired O<sub>2</sub> concentrations for patients with impaired pulmonary function. Accurate measures of ETCO<sub>2</sub> are helpful in assessing respiratory rate and determining whether CO<sub>2</sub> retention is occurring from hypoventilation. These findings suggest the NC with separate NPs was the most effective in delivering O<sub>2</sub> and the most consistent at providing reliable CO<sub>2</sub> waveforms at higher FGFs.

### 在国家麻醉临床预后登记中观察到的围术期心脏骤停发生率和危险因素

#### The Incidence and Risk Factors for Perioperative Cardiac Arrest Observed in the National Anesthesia Clinical Outcomes Registry

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**背景：**在手术室和复苏室里，对于经严密监测的手术患者，心脏骤停是一个罕见但重要的事件。近期发表文献报道了后续住院期间而非围术期手术患者心脏骤停的发生率。本文假设在此期间（围术期和复苏期）心脏骤停发生率较报道的住院期间发生率更低。

**方法：**抽取 2010 年至 2013 年国家麻醉临床预后登记的所有心脏骤停和急性围手术期死亡的数据并且分析麻醉相关危险因素。比较其与发表的术后住院期间心脏骤停发生率差异性。

**结果：**总体而言，心脏骤停的风险为 5.6/10000 例，低于先前报道的手术患者住院期间总体死亡率，且心脏停跳相关死亡率为 58.4%。心脏骤停的发生率随着年龄和 ASA 分级增加而增加。男性心脏骤停率发生率和死亡率更高。

**结论：**国家麻醉临床预后登记是检验围手术期和麻醉相关预后的一种新兴资源。心脏骤停在手术期间比在住院期间发生率更低，大部分发生于 ASA III–V 级的患者。难以解释男性死亡风险较高的现象，故需要进一步研究。

（徐欢 译 陈杰 校）

**BACKGROUND:** Cardiac arrest is a rare but important event in the operating room and postanesthesia care unit, when surgical patients are most intensively monitored. Several recent publications have reported the rate of cardiac arrest in surgical patients during the subsequent hospital stay but have not uniquely identified the immediate perioperative period. We hypothesized that cardiac arrest during this time (intraprocedure and postanesthesia care) would occur at a lower frequency than that described for inpatient hospital care in the available literature.

**METHODS:** We extracted data from all cardiac arrests and immediate perioperative deaths reported to the National Anesthesia Clinical Outcomes Registry for the period from 2010 to 2013 and analyzed for anesthesia-related risk factors. We compared these data to published rates of in-hospital cardiac arrest after surgery.

**RESULTS:** Overall, the risk of cardiac arrest was 5.6 per 10,000 cases, which is less than in previous reports of in-hospital arrests in surgical patients overall, with an associated mortality from the arrest of 58.4%. The rate of cardiac arrest increased with age and ASA physical status. The rate of cardiac arrest was significantly higher for males, as was the mortality.

**CONCLUSIONS:** The National Anesthesia Clinical Outcomes Registry is an emerging resource for examination of perioperative and anesthesia-related outcomes. Cardiac arrest is less frequent in the periprocedural setting than later in the hospital course, with most arrests predictably occurring in patients with ASA physical status III–V. The finding of increased risk of mortality in male patients cannot be readily explained and should prompt future research attention.

## 晶液体和胶液体：通过系统回顾和 meta 回归分析探索两者在液体需求中的差异

### Crystalloids Versus Colloids: Exploring Differences in Fluid Requirements by Systematic Review and Meta-Regression

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**背景：**液体正平衡与较差的预后相关。关于不同类型不同量的液体如何达到相同终点的临床意义重大。大分子比小分子在血管内持续更长时间，与晶体相比，较少的胶体可能达到相同的血流动力学终点。然而，最近的临床数据挑战了这个生理概念，研究者报告了在不同人群低于预期的晶体/胶体比率。

**方法：**截止至 2013 年 12 月 18 日，在 MEDLINE、EMBASE 和 CENTRAL 上检索所有关于在各种患者中比较胶体和晶体的研究来进行此项系统检索。计算每个研究的晶体/胶体比值。对所有研究进行了描述性分析，并对那些有输注液体量完整数据的研究（均值和标准差）进行 meta 分析。根据研究和人口学特征进行分组。然后通过 meta 回归分析评估晶体/胶体比值差异的一些可能原因。

**结果：**在 976 项研究中，48 项在最后分析中被保留；24 项研究有足够数据进行 meta 分析。在所有这些包括 meta 分析的研究中，晶体/胶体比例为 1.5(95%置信区间, 1.36 - 1.65)，存在显著的非均质性( $I^2 = 94%$ )。从 meta 回归分析，近十年的出版文献( $P = 0.001$ )和白蛋白亚组研究( $P = 0.001$ )的浓度（张力）与晶体/胶体比例管理相关。meta 分析所有出版物的异质性下降是最小的，且纳入的近十年出版物显示下降幅度最大( $R^2 = 12%$ )。

**结论:**与胶体相比,要达到同样的目标需要更大的晶体容量,比值约为 1.5(1.36 - 1.65),但研究中有明显异质性。晶体/胶体比率近年来似乎有所下降,比值的差异与白蛋白的浓度相关。然而研究的高异质性的主要原因尚不清楚。

(林雨轩 译 陈杰 校)

**BACKGROUND:** Positive fluid balance has been associated with worse outcomes, and knowledge of differences in the amounts of different types of fluid needed to achieve the same end points may have important clinical implications. Large molecules persist longer in the blood vessels than smaller molecules, such that less IV colloid may be needed to achieve similar hemodynamic end points compared with crystalloid. Recent clinical data have, however, challenged this physiological concept, with investigators reporting lower-than-expected crystalloid/colloid ratios in various populations.

**METHODS:** We performed a systematic search in MEDLINE, EMBASE, and CENTRAL up to December 18, 2013, to retrieve all studies comparing (any) crystalloid with (any) colloid in all types of patients. The crystalloid/colloid ratio was calculated for each study. Descriptive analysis was performed for all studies, and a meta-analysis was performed in those studies reporting full data (in terms of means and standard deviations) of infused fluid volumes. Studies were grouped according to study and population characteristics. A meta-regression analysis was then performed to evaluate some of the possible reasons for differences in crystalloid/colloid ratios across studies.

**RESULTS:** From 976 studies, 48 were retained for the final analysis; 24 of the studies had sufficient data for meta-analysis. The crystalloid/colloid ratio across all the studies included in the meta-analysis was 1.5 (95% confidence interval, 1.36–1.65) with marked heterogeneity among studies ( $I^2 = 94\%$ ). From the meta-regression analysis, decade of publication across all publications ( $P = 0.001$ ) and concentration (tonicity) in the subgroup of albumin studies ( $P = 0.001$ ) were associated with the administered crystalloid/colloid ratio. The reduction in heterogeneity among studies for all publications in the meta-regression was minimal, with the maximal decrease obtained when decade of publication was considered ( $R^2 = 12\%$ ).

**CONCLUSIONS:** Greater fluid volumes are required to meet the same targets with crystalloids than with colloids, with an estimated ratio of 1.5 (1.36–1.65), but there is marked heterogeneity among studies. The crystalloid/colloid ratio seems to have decreased over the years, and differences in ratios are correlated with the concentration of albumin solutions; however, the main reasons behind the high heterogeneity among studies remain unclear.

### 靶向治疗对儿科肺动脉高压患者围术期发病率和死亡率影响

#### **The Impact of Targeted Therapies for Pulmonary Hypertension on Pediatric Intraoperative Morbidity or Mortality**

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**背景:**肺动脉高压(PHT)是麻醉期间主要不良事件的重要风险因素,据报道其发生率为5%至7%,并可继发急性肺动脉高压危象或右心室缺血。PHT新型治疗方法已可减少死亡率。在此次单中心研究中,研究者统计了在当前治疗PHT的策略下麻醉期间主要和次要事件发生率。

**方法:**研究者回顾了2008年至2012年间PHT患儿进行非心肺转流手术的记录。研究者记录了麻醉前的临床主要症状,体征和研究数据,并收集了围术期并发症和死亡(至术后7天)的发生率及类型。

**结果：**数据来自于 122 位患者进行的 284 例手术。次要（3.9%）和主要（3.2%）并发症的发生率和先前的报道没有发生变化。PHT 的病因和并发症无显著相关性（ $P=0.14$ ）。疾病导向的治疗和并发症减少无相关性：治疗组 4.1%，未治疗组 8.6%（组间比  $P$  值均大于 0.14）。接受家庭氧疗的患儿有更多的并发症（ $P=0.02$ ）。多因素 Logistic 回归分析发现年龄和 PHT 分级是并发症的有效预测因素（ $P$  值均小于等于 0.03）。

**结论：**尽管使用了最新的以疾病为导向的治疗措施，麻醉期间 PHT 患儿的不良事件风险依然很高。并发症的危险因素包括年龄和 PHT 的严重程度。

（张帆 译 陈杰 校）

**BACKGROUND:** Pulmonary hypertension (PHT) is a significant risk factor for major adverse events during anesthesia, with a reported incidence of 5% to 7%, secondary to acute pulmonary hypertensive crises or right ventricular ischemia. Newer therapies for treating PHT have reduced mortality. In this single-center study, we investigated the frequency of major and minor events during anesthesia under the current strategies to manage PHT.

**METHODS:** We reviewed the records of children with PHT who underwent noncardiopulmonary bypass procedures from 2008 to 2012. Clinically important symptoms, physical signs, and results of investigations present before anesthesia were recorded. The incidence and type of intraoperative complications and death (up to 7 days) were collected.

**RESULTS:** Data were collected for 122 patients undergoing 284 procedures. Minor (3.9%) and major (3.2%) complication rates were unchanged from previous publications. The etiology of PHT was not significant for complications ( $P = 0.14$ ). Disease-modifying agents were not associated with reduced complications: 4.1% in treated versus 8.6% untreated (all  $P > 0.14$ ). Patients receiving home oxygen had more complications ( $P = 0.02$ ). Multiple logistic regression identified age and degree of PHT as significant predictors of complications (all  $P \leq 0.03$ ).

**CONCLUSIONS:** The risk for adverse events during anesthesia in patients with PHT remains high, despite newer disease-modifying treatments. Risk factors for complications include age and severity of PHT.

在神经病理性疼痛的大鼠模型中鞘内给予安非他酮，一种多巴胺和去甲肾上腺素再摄取抑制剂的抗痛觉过敏效应

### The Antihyperalgesic Effects of Intrathecal Bupropion, a Dopamine and Noradrenaline Reuptake Inhibitor, in a Rat Model of Neuropathic Pain

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**背景：**抗抑郁药物通常用于治疗神经病理性疼痛，通过增加脊髓的去甲肾上腺素和 5-羟色胺水平达到镇痛效果。临床研究也表明：作为一种多巴胺和去甲肾上腺素再摄取抑制剂，安非他酮的对治疗神经病理性疼痛具有很强疗效，然而，脊髓多巴胺在神经病理性疼痛方面的作用机制尚不清楚。本文假设安非他酮通过增加脊髓的去甲肾上腺素和多巴胺水平抑制神经病理性疼痛。此项研究考察了对神经病理性疼痛的大鼠模型鞘内注射安非他酮，其有效性及潜在机制。

**方法：**雄性 SD 大鼠麻醉后，右侧 L5 脊神经进行结扎(SNL)以生产后足机械性痛觉过敏。在有或没有鞘内注射  $\alpha_2$  肾上腺素受体和多巴胺 D2 受体拮抗剂条件下，在鞘内注射安非他酮前后测量退缩阈值以完成爪压测试。鞘内注射安非他酮后对在体腰髓灰质后角的微量透析可以测量去甲肾上腺素和多巴胺的浓度。同时也测量了正常大鼠和 SNL 后 2、3、4 周大鼠同侧腰髓后角中去甲肾上腺素和多巴胺含量。

**结果:**鞘内注射安非他酮产生剂量依赖性抗痛觉过敏效应 (3、10、30 和 100 ug,  $P < 0.001$ )。使用(安非他酮注射前 15 分钟) $\alpha_2$ -肾上腺素受体拮抗剂咪唑克生(3、10 和 30 ug,  $P < 0.001$ )和 D2 受体拮抗剂舒必利(3、10 和 30 ug,  $P < 0.001$ )进行鞘内预处理可剂量依赖性地逆转此效应 (30ug 组)。微量透析表明在鞘内注射安非他酮(30 ug)后脊髓背角去甲肾上腺素和多巴胺浓度增加 (分别  $P < 0.001, P = 0.001$ )。此外脊髓背角去甲肾上腺素和多巴胺含量在 SNL 2 周后增加(分别  $P < 0.001, P = 0.044$ ),然后逐渐下降。

**结论:**这些研究结果表明,下行抑制通路,如去甲肾上腺素和多巴胺系统,其适应性与神经病理性疼痛的维持相关,脊髓去甲肾上腺素和多巴胺在神经病理性疼痛中起到抑制作用。

(秦懿译 陈杰校)

**BACKGROUND:** Antidepressants are often used for the treatment of neuropathic pain, and their analgesic effects rely on increased noradrenaline and serotonin levels in the spinal cord. Clinical studies have also shown that bupropion, a dopamine and noradrenaline reuptake inhibitor, has strong efficacy in neuropathic pain; however, the role of spinal cord dopamine in neuropathic pain is unknown. We hypothesized that bupropion inhibits neuropathic pain by increasing noradrenaline and dopamine in the spinal cord. In the present study, we determined the efficacy and underlying mechanisms of intrathecal administration of bupropion in a rat model of neuropathic pain.

**METHODS:** Male Sprague-Dawley rats were anesthetized, and right L5 spinal nerve ligation (SNL) was performed to produce mechanical hyperalgesia of the hindpaw. Withdrawal threshold to a paw pressure test was measured before and after intrathecal administration of bupropion, without or with intrathecal antagonists for  $\alpha_2$ -adrenoceptors and dopamine D2 receptors. In vivo microdialysis was performed in the dorsal horn of the lumbar spinal cord to measure noradrenaline and dopamine concentrations after intrathecal injection of bupropion. We also measured the noradrenaline and dopamine contents in the ipsilateral dorsal lumbar spinal cord in normal rats and in rats 2, 3, and 4 weeks after SNL.

**RESULTS:** Intrathecal injection of bupropion produced a dose-dependent antihyperalgesic effect (3, 10, 30, and 100 ug,  $P < 0.001$ ). The effect (30 ug) was dose-dependently reversed by intrathecal pretreatment (15 minutes before bupropion injection) with the  $\alpha_2$ -adrenoceptor antagonist idazoxan (3, 10, and 30 ug,  $P < 0.001$ ) and D2 receptor antagonist sulpiride (3, 10, and 30 ug,  $P < 0.001$ ). Microdialysis revealed that noradrenaline and dopamine concentrations in the spinal dorsal horn were increased after intrathecal injection of bupropion (30 ug,  $P < 0.001$  and  $P = 0.001$ , respectively). Furthermore, the noradrenaline and dopamine contents in the spinal dorsal horn were increased 2 weeks after SNL ( $P < 0.001$  and  $P = 0.044$ , respectively) and then decreased gradually.

**CONCLUSIONS:** These findings suggest that plasticity of descending inhibitory pathways such as the noradrenaline and dopamine systems contributes to the maintenance of neuropathic pain and that spinal cord noradrenaline and dopamine both play an inhibitory role in neuropathic pain.

**一项关于脊麻复合静脉镇静下行全膝置换术时鼻持续正压通气对动脉二氧化碳分压影响的初步研究**

**A Pilot Study on the Effect of Nasal Continuous Positive Airway Pressure on Arterial Partial Pressure of Carbon Dioxide During Spinal Anesthesia with Intravenous Sedation for Total Knee Arthroplasty**

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**背景：**尽管高碳酸血症程度很少被量化，手术患者的深度镇静可能与低通气、气道塌陷和高碳酸血症相关。这项前瞻、随机、对照临床初步研究评估了对脊麻（SAB）复合深度镇静下行全膝置换术（TKA）保持自主呼吸的患者进行鼻持续性正压通气（nCPAP）与标准气道管理的差异。

**方法：**纳入 40 名 ASA 分级 I-III、SAB 下行 TKA 患者，术中给予异丙酚使患者深镇静程度达到改良观察者评估警觉性/镇静评分（MOAA/SS）2 级。由麻醉团队自行决定鼻腔或口腔通气装置的放置，但不能与 nCPAP 同时使用。当 MOAA/SS 达到 2 级时，进行动脉血气分析（ABG-1）。之后患者被随机分配接受 nCPAP（nCPAP 组，N=20）或标准气道管理（对照组，N=20）处理。30 分钟后进行第二次 ABG（ABG-2）以评估 nCPAP 对 PaCO<sub>2</sub> 的影响。主要疗效终点是从基线至第 30 分钟时 PaCO<sub>2</sub> 的改变。

**结果：**nCPAP 与对照组基础 PaCO<sub>2</sub> 值相似，分别为 54.5 和 56.1 mmHg。而与对照组（中位数 0.95 mm Hg [10% 至 90% 四分位间距为 -4.75 至 9.85]）相比，nCPAP 组的 PaCO<sub>2</sub> 明显下降（中位数 -4.6 mm Hg [四分位间距为 -14.75 至 9.85]）（P = 0.015；95% 可信区间 [CI] 为 -9.5-9.5）。对照组 PaCO<sub>2</sub> 从 ABG-1 至 ABG-2 是相似的（中位数 [10% 至 90% 四分位间距] 为 56.1 mm Hg [47.2-67.0] 与 56.6 mm Hg [46-68.8] 相比；P = 0.52；中位数的 95% 可信区间为 -3.4 to 3.4）。40% 患者在 ABG1 之前都接受了一种通气装置。这些患者的基线 PaCO<sub>2</sub> 值与非气道装置患者相似。

**结论：**对在 SAB 下行 TKA 的患者进行深度镇静可导致中度高碳酸血症（平均值和中位数 PaCO<sub>2</sub>=55 mmHg）。实验表明与接受标准气道管理的患者相比，接受 nCPAP 处理的患者有减少 PaCO<sub>2</sub> 趋势。然而估计处理间差异的范围较大，从 1.4 至 12.6 mmHg 不等。接受深度镇静的对照组患者，基线 PaCO<sub>2</sub> 类似于持续深镇静后 30min 的 PaCO<sub>2</sub>。最后事先给予或不给予气道装置的深镇静患者，其基线 PaCO<sub>2</sub> 并无差异。

（李慧译 陈杰校）

**BACKGROUND:** Deep sedation of surgical patients may be associated with hypoventilation, airway collapse, and hypercarbia, although the extent of hypercarbia is rarely quantified. In this prospective, randomized, controlled clinical pilot study, we assessed the efficacy of nasal continuous positive airway pressure (nCPAP) for reducing arterial partial pressure of carbon dioxide (PaCO<sub>2</sub>) among deeply sedated, spontaneously ventilated patients undergoing total knee arthroplasty (TKA) under subarachnoid block (SAB), versus standard airway management in a control group.

**METHODS:** Forty ASA status I-III patients underwent deep sedation with propofol to level 2 on the Modified Observers Assessment of Alertness/Sedation Scale during TKA performed under SAB. Nasal or oral airways were placed at the discretion of the anesthesia team, but they were not used in conjunction with nCPAP. Baseline arterial blood gas analysis (ABG-1) was performed after Modified Observers Assessment of Alertness/Sedation Scale level 2 was reached. Patients were then randomized to receive nCPAP (nCPAP group, N = 20) or standard oxygen mask management (control group, N = 20). A second ABG (ABG-2) was performed 30 minutes later to assess the effect of nCPAP on PaCO<sub>2</sub>. The primary efficacy end point was change in PaCO<sub>2</sub> from baseline to the 30-minute time point.

**RESULTS:** Baseline (ABG-1) PaCO<sub>2</sub> values were similar between nCPAP and control groups with median values of 54.5 and 56.1 mm Hg, respectively. There was a significant decline in PaCO<sub>2</sub> in the nCPAP group (median of -4.6 mm Hg [10th-90th quantile, -14.55 to 3.85]) as compared with the control group (median of 0.95 mm Hg [-4.75 to 9.85]; P = 0.015; 95% confidence interval [CI] for location shift = -9.5 to -1.3). Within the control group, PaCO<sub>2</sub> was similar from ABG-1 to ABG-2 (median [10th-90th quantile] = 56.1 mm Hg [47.2-67.0] vs 56.6 mm Hg [46-68.8]; P = 0.52; 95% CI for the median = -3.4 to 3.4). Forty percent of all patients received an airway before ABG-1. The baseline PaCO<sub>2</sub> value of patients receiving an airway was not different from that of patients without an airway (median [10th-90th quantile] = 56.0 mm Hg [46.0-68.4] vs 54.1 mm Hg [45.6-65.6], respectively; P = 0.33; 95% CI for location shift = -2.30 to 7.20).

**CONCLUSIONS:** Deep sedation of TKA patients during SAB resulted in moderate hypercarbia (mean and median PaCO<sub>2</sub> = 55). There was a trend showing that nCPAP treatment reduced PaCO<sub>2</sub> versus treatment for control group patients receiving standard airway management; however, estimated treatment difference varied widely, from 1.4 to 12.6 mm Hg. Among control group patients, the initial PaCO<sub>2</sub> during deep sedation was similar to the PaCO<sub>2</sub> when measured after a 30-minute period of continued deep sedation. Finally, baseline PaCO<sub>2</sub> among deeply sedated patients who received an airway was not different from that of patients who did not receive an airway.

### 呼气末正压通气在外科领域条件下对功能性内窥镜鼻窦手术的影响

#### **The influence of positive end-expiratory pressure on surgical field conditions during functional endoscopic sinus surgery.**

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**背景：**功能性内窥镜鼻窦手术（FESS）是鼻腔鼻窦疾病外科治疗中的中流砥柱。这个手术也有一定的风险。大部分风险与手术的质量有关。因此，研究这种能提高手术质量的机制很重要。我们试图确定呼气末正压通气（PEEP）是否对急诊手术患者的术野质量产生有害的影响。

**方法：**407例患者随机采用5 cm H<sub>2</sub>O PEEP或零PEEP通气策略。手术野的质量每15分钟用一个有效的手术评分方法进行测量。

**结果：**PEEP的加入没有对术后质量发生任何可衡量的效果（比值比[OR]（95%置信区间[CI]）= 1.06，P = 0.895（0.44-2.58）侧面1；或（95% CI）= 0.56，P = 0.356（0.16-1.93）侧面2）。吸气峰压确实影响手术成绩。每增加1 cm H<sub>2</sub>O的压力，超过15 cm H<sub>2</sub>O的总压力将贡献于增加更高的手术得分率。每增加1 cm H<sub>2</sub>O的吸气压，将有超过15 cm H<sub>2</sub>O用于增加手术得分。

**结论：**在鼻内镜手术中通过增加平均吸气压力低于15cm H<sub>2</sub>O的PEEP，可以避免手术野的模糊程度。

（王晓莉译 李士通审校）

**BACKGROUND:** Functional endoscopic sinus surgery (FESS) is the mainstay of surgical treatment for sinonasal disease. This surgery carries certain risks. Most of these risks relate to the quality of the surgical field. Thus, mechanisms by which the surgical field can be improved are important to study. We sought to determine whether positive end-expiratory pressure (PEEP) had a deleterious effect on the quality of the surgical field in patients undergoing primary FESS.

**METHODS:** Forty-seven patients were randomized to a ventilation strategy using either 5 cm H<sub>2</sub>O of PEEP or zero added PEEP. The quality of the surgical field was measured every 15 minutes using a validated surgical scoring method.

**RESULTS:** The addition of PEEP did not have any measurable effect on the surgical field scores after onset of surgery (odds ratio [OR] (95% confidence interval [CI]) = 1.06 (0.44-2.58), P = 0.895 for side 1; OR (95% CI) = 0.56 (0.16-1.93), P = 0.356 for side 2). The peak inspiratory pressure did have an effect on surgical grades. Every cm H<sub>2</sub>O of added pressure over 15 cm H<sub>2</sub>O total pressure contributing to increased odds of higher surgical field score. For each cm H<sub>2</sub>O increase in inspiratory pressure above 15cm H<sub>2</sub>O increased the surgical field score (OR [95% CI] 1.13 [1.04-1.22], P = 0.002).

**CONCLUSIONS:** During FESS surgery if PEEP is added, it is important to keep the mean inspiratory pressure below 15cm H<sub>2</sub>O to avoid worsening surgical field conditions.

## 丙泊酚（得普利麻）和脂肪乳通过削弱 GLUT4 的转运增强 2 型糖尿病病人心脏的胰岛素抵抗

### Propofol (Diprivan®) and Intralipid® Exacerbate Insulin Resistance in Type-2 Diabetic Hearts by Impairing GLUT4 Trafficking.

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**背景：**当静脉麻醉药——丙泊酚作为脂肪乳剂基制剂给药（得普利麻）时，能促进胰岛素抵抗，但丙泊酚和它的溶剂，脂肪乳，对心脏胰岛素抵抗的直接影响是未知的。

**方法：**健康和 2 型糖尿病大鼠的心脏（果糖喂养产生）的进行 10μM 异丙酚或相同浓度的溶剂脂肪乳剂（25μM）±胰岛素（100U·L）有氧灌注 60 分钟。葡萄糖摄取，糖酵解和糖原代谢用葡萄糖测定。Akt 和 GSK3β，AMPK，ERK1 / 2，p38MAPK 和 S6K1，JNK，蛋白激酶 Cθ（PKCθ），以及蛋白激酶 CCβII（PKCβII）的活化，用免疫印迹测定。GLUT4 和胰岛素受体底物-1（IRS-1）的 Ser307（H312），Ser1100（H1101）的磷酸化物，和 Tyr608（hTyr612）进行了测定。质谱用于测定酰基肉碱，磷脂和鞘脂。

**结果：**得普利麻和脂肪乳降低胰岛素诱导葡萄糖的摄取和重定向葡萄糖糖原储备糖尿病。降低葡萄糖的摄取，伴随着较低的 GLUT4 转运肌膜。得普利麻和脂肪乳灭活 GSK3β 但糖尿病心活化 AMPK 和 ERK1 / 2。得普利麻只增加 Akt 磷酸化（的 Ser473 / Thr308）和易位 PKCθ 和 PKCβII 的在健康的心脏肌膜，而它在糖尿病的心激活 S6K1 以及 p38 和易位 PKCβII。此外，只有得普利麻在健康和糖尿病心脏磷酸 IRS-1 在 Ser1100（H1101）。JNK 表达，磷酸化的 IRS-1 Ser307（H312），并 PKCθ 表达和转位的增加，而 GLUT4 表达减少胰岛素治疗的糖尿病心。磷脂酰甘油，磷脂，和 C18-鞘脂积累得普利麻灌注和脂肪乳灌注糖尿病心。

**结论：**丙泊酚和脂肪乳主要是促进 2 型糖尿病患者的的心脏胰岛素抵抗。

（王晓莉译 李士通审校）

**BACKGROUND:** The IV anesthetic, propofol, when administered as fat emulsion-based formulation (Diprivan) promotes insulin resistance, but the direct effects of propofol and its solvent, Intralipid, on cardiac insulin resistance are unknown.

**METHODS:** Hearts of healthy and type-2 diabetic rats (generated by fructose feeding) were aerobically perfused for 60 minutes with 10 μM propofol in the formulation of Diprivan or an equivalent concentration of its solvent Intralipid (25 μM) ± insulin (100 mU·L). Glucose uptake, glycolysis, and glycogen metabolism were measured using [<sup>3</sup>H]glucose. Activation of Akt, GSK3β, AMPK, ERK1/2, p38MAPK, S6K1, JNK, protein kinase Cθ (PKCθ), and protein kinase CCβII (PKCβII) was determined using immunoblotting. GLUT4 trafficking and phosphorylations of insulin receptor substrate-1 (IRS-1) at Ser307(h312), Ser1100(h1101), and Tyr608(hTyr612) were measured. Mass spectrometry was used to determine acylcarnitines, phospholipids, and sphingolipids.

**RESULTS:** Diprivan and Intralipid reduced insulin-induced glucose uptake and redirected glucose to glycogen stores in diabetic hearts. Reduced glucose uptake was accompanied by lower GLUT4 trafficking to the sarcolemma. Diprivan and Intralipid inactivated GSK3β but activated AMPK and ERK1/2 in diabetic hearts. Only Diprivan increased phosphorylation of Akt(Ser473/Thr308) and translocated PKCθ and PKCβII to the sarcolemma in healthy hearts, whereas it activated S6K1 and p38MAPK and translocated PKCβII in diabetic hearts.

Furthermore, only Diprivan phosphorylated IRS-1 at Ser1100(h1101) in healthy and diabetic hearts. JNK expression, phosphorylation of Ser307(h312) of IRS-1, and PKC $\theta$  expression and translocation were increased, whereas GLUT4 expression was reduced in insulin-treated diabetic hearts. Phosphatidylglycerol, phosphatidylethanolamine, and C18-sphingolipids accumulated in Diprivan-perfused and Intralipid-perfused diabetic hearts.

**CONCLUSIONS:** Propofol and Intralipid promote insulin resistance predominantly in type-2 diabetic hearts

在一系列体外的实验中发现硬质和软质气管交换导管所造成的明显的肺损伤

### Macroscopic Barotrauma Caused by Stiff and Soft-Tipped Airway Exchange Catheters: An In Vitro Case Series

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**背景：**许多呼吸道管理指南包括气道交换导管都有所报道，但是在使用过程中，不论是导管位置异常还是通过气道交换导管给氧都会导致气道压伤。

**方法：**我们运用离体猪肺模型来观察 2 种不同的气道交换导管，一种为标准导管，而另一种是软导管，分别通过他们给予高压源下的 4 种不同流速的氧气。在实验过程中，导管位置可以在隆突上方也可以在其下方，最重要的就是对抗其阻力，保持位置固定。这项实验选择了 32 例样本。

**结果：**我们发现，置于隆突上方的气道交换导管在给氧后没有造成明显的肺损伤。但是导管位置在隆突下方的案例中，给氧后我们发现，不论氧气的流速是多少，都会造成明显的肺损伤，而氧流速越大，造成的肺损伤越快而且越广泛。通过使用 2.5 或 4 条的“注射器”将会立即导致肺组织损伤，而且气道交换导管会导致损伤的进一步加剧。同时我们发现两种不同的气道交换导管的结果造成的损伤都是一样的。

**结论：**我们的实验结果和以往关于放置于隆突下方的气道交换导管造成的肺损伤的报道是相同的，并且证明了放置于隆突下方的气道交换导管给氧的风险。一种新的气道交换导管，在制造时设计为放置于牙齿水平，将会减少原来置于隆突水平的气道交换导管所造成的损伤，并且增加使用这种导管的安全性。

（李蔚文译 李士通审校）

**BACKGROUND:** Many airway management guidelines include the use of airway exchange catheters (AECs). There are reports, however, of harm from their use, from both malpositioning and in particular from the administration of oxygen via an AEC leading to barotrauma.

**METHODS:** We used an in vitro pig lung model to investigate the safety of administering oxygen at 4 different flow rates from a high-pressure source via 2 different AECs: a standard catheter and a soft-tipped catheter. Experiments were performed with the catheters positioned either above the carina or below it at the first point of resistance to advancement (hold-up). The experiments were then repeated to produce a series of 32 cases.

**RESULTS:** With an AEC positioned above the carina, we did not observe macroscopic lung damage after the administration of oxygen. The administration of oxygen through an AEC positioned below the carina resulted in macroscopic barotrauma regardless of the rate of oxygen delivery. Increasing speed of oxygen flow led to faster and more extensive damage. Use of an “injector” at 2.5 or 4 bar led to instantaneous macroscopic lung damage and advancement of the AEC through the lung tissue. Our observations were the same when both types of AECs were used.

**CONCLUSIONS:** Our results are consistent with reports of harm during the use of AECs and demonstrate the risk of administering oxygen through these devices when they are positioned below the carina. An indicator, ideally made on an AEC at the time of manufacture and designed to lie at the same level as the teeth, may be useful in preventing the insertion of that AEC beyond the level of the carina and improve the safety of using such devices.

### 外源性表面活性物质的治疗对于二次损伤的小鼠肺模型的影响

#### The Effects of Exogenous Surfactant Treatment in a Murine Model of Two-Hit Lung Injury

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**背景：**在急性呼吸窘迫综合征的患者中，我们发现肺内源性表面活性物质生成发生了改变，而肺表面活性物质的替代剂的使用将会改变临床结果。然而，一些试验中的肺表面活性物质已经造成了混乱的结果。我们设计了动物右肺损伤的模型来研究外源性表面活性物质对于已经损伤以及未损伤的肺所造成的炎症方面的影响。

**方法：**我们将盐酸（1.5mL/kg）灌入小鼠的右侧支气管，并且延长机械通气（25mL/kg）时间（7h）。在3小时后，实验组的小鼠右肺给予1mL/kg的外源性表面活性物质，而盐水组小鼠右肺给予0.9%的氯化钠，另外对照组小鼠没有给予任何处理（包括盐酸灌注和呼吸机损伤）。我们从气体交换、肺顺应性和支气管肺泡炎症（包括细胞、蛋白和细胞因子）这几方面来评价实验结果。我们运用显著的方差分析和Tukey事后检验进行系统分析。

**结果：**每组的小鼠中至少十分之八存在评估的变量可以分析。表面活性物质处理后明显增加了吸入的氧分压后的动脉血氧张力，并且明显提高了呼吸系统静态顺应性（分别为实验组  $P=0.027$ ，盐水组  $P=0.007$ ）。表面活性物质明显增强了支气管肺泡炎症反应，炎症细胞：实验组为 685（602-733），盐水组为 216（125-305）\*1000/mL ( $P<0.001$ )；在肺泡灌洗液中的蛋白，实验组为  $1442\pm 588$ ，盐水组为  $743\pm 647\mu\text{g/mL}$  ( $P=0.027$ )。然而这些差异在对侧健肺中并没有被发现 ( $P=0.96$ ,  $P=0.54$ ，炎症细胞 131（78-195）和 119（87-149）\*1000/mL，蛋白  $135\pm 100$  和  $173\pm 115\mu\text{g/mL}$ )。

**结论：**外源性表面活性物质用于盐酸灌注损伤的右肺，将会增加肺的气体交换和整个呼吸系统的顺应性。但是，损伤的右肺中炎症反应标志物也会增加，尽管这些在左侧健肺中没有被发现。这些数据表明肺表面活性物质对于损伤和未损伤的肺泡都有增强其功能的作用。

（李蔚文译 李士通审校）

**BACKGROUND:** Because pulmonary endogenous surfactant is altered during acute respiratory distress syndrome, surfactant replacement may improve clinical outcomes. However, trials of surfactant use have had mixed results. We designed this animal model of unilateral (right) lung injury to explore the effect of exogenous surfactant administered to the injured lung on inflammation in the injured and noninjured lung.

**METHODS:** Mice underwent hydrochloric acid instillation (1.5 mL/kg) into the right bronchus and prolonged (7 hours) mechanical ventilation (25 mL/kg). After 3 hours, mice were treated with 1 mL/kg exogenous surfactant (Curosurf®) (surf group) or sterile saline (NaCl 0.9%) (vehicle group) in the injured (right) lung or did not receive any treatment (hydrochloric acid, ventilator-induced lung injury). Gas exchange, lung compliance, and bronchoalveolar

inflammation (cells, albumin, and cytokines) were evaluated. After a significant analysis of variance (ANOVA) test, Tukey post hoc test was used for statistical analysis.

**RESULTS:** At least 8 to 10 mice in each group were analyzed for each evaluated variable. Surfactant treatment significantly increased both the arterial oxygen tension to fraction of inspired oxygen ratio and respiratory system static compliance ( $P = 0.027$  and  $P = 0.007$ , respectively, for surf group versus vehicle). Surfactant therapy increased indices of inflammation in the acid-injured lung compared with vehicle: inflammatory cells (685 [602–773] and 216 [125–305]  $\times 1000/\text{mL}$ , respectively;  $P < 0.001$ ) and albumin in bronchoalveolar lavage (BAL) ( $1442 \pm 588$  and  $743 \pm 647 \mu\text{g}/\text{mL}$ , respectively;  $P = 0.027$ ). These differences were not found ( $P = 0.96$  and  $P = 0.54$ ) in the contralateral (uninjured) lung (inflammatory cells 131 [78–195] and  $119 [87\text{--}149] \times 1000/\text{mL}$  and albumin  $135 \pm 100$  and  $173 \pm 115 \mu\text{g}/\text{mL}$ ).

**CONCLUSIONS:** Exogenous surfactant administration to an acid-injured right lung improved gas exchange and whole respiratory system compliance. However, markers of inflammation increased in the right (injured) lung, although this result was not found in the left (uninjured) lung. These data suggest that the mechanism by which surfactant improves lung function may involve both uninjured and injured alveoli.

### 由于小儿围手术期呼吸事件产生的医院额外费用和住院时间

#### Excess Costs and Length of Hospital Stay Attributable to Perioperative Respiratory Events in Children

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**背景：**由于围手术期呼吸事件导致多余的住院费用和住院时间的认知在医院规划是有用的。在这项研究中，我们在泰国南部的一家三级医院，比较小儿有围手术期呼吸事件和没有该事件成本（多余的住院费用和间接费用）和住院长度。

**方法：**对 2012 十一月到 2013 十二月在 songklanagarind 儿童医院年龄 < 15 岁患者，全麻儿童进行前瞻性队列研究。孩子们没有孩子前预匹配 (1:1) 使用一个随机选择的程序对门诊/住院，手术类型，手术费（泰铢），ASA 分级，年龄 < 9 岁，和不同的手术 < 6 个月的时间进行分组。主要终点是术后多余的住院费用和住院天数。手术后住院天数，多余的住院费用和间接费用，组与组之间的父母的收入损失进行比较采用 Wilcoxon 符号秩检验。术后住院天数比较采用 McNemary 检测。障碍模型被用来预测术后住院天数和住院天数。多个混合效应线性回归被用来确定预测的调整多余的住院费用和间接费用

**结论：**研究共包括 430 名儿童（215 配对）。更多的呼吸事件的孩子需要术后住院（81% vs 72%， $P = 0.004$ ），并且有较长的住院天数手术后（中位数[四分位数]：1 [ 1 ] 1 [ 0 VS 3.5—2 ]； $P < 0.001$ ）和产生较高的超额成本（ $P < 0.001$ ）而不是间接成本（ $P = 0.23$ ）。在多变量分析中，围手术期呼吸事件是一个重要的预测因子，预测手术后住院时长（优势比，2.56；95%置信区间，）成本（成本比 1.30 [ 1.12, 1.53 ]）和间接成本（成本比 1.58 [ 1.20, 2.08 ]），可以调整病人的麻醉特点。普遍覆盖（74%）与 35%和 64%更高的超额成本与审计总署相比较（17%）和自付（7%），分别为（ $P = 0.003$ ）。

（田园译 李士通审校）

**BACKGROUND:** Knowledge of the excess hospital costs and prolonged length of stay attributable to perioperative respiratory event (PRE) in pediatric anesthesia is useful for hospital planning. In this study, we compared costs (excess hospital costs and indirect costs) and length

of hospital stay between children who had PRE and did not have PRE for noncardiac surgery at a tertiary care hospital in southern Thailand.

**METHODS:** A prospective matched cohort study was conducted in children aged <15 years who underwent general anesthesia between November 2012 and December 2013 at Songklanagarind Hospital. PRE children were matched with no PRE children (1:1) using a random selection procedure on outpatients/inpatients, type of surgery, surgical charge (baht), ASA physical status, age difference <9 years, and difference in time of surgery <6 months. Primary end points were excess hospital costs and number of days hospitalized after surgery. Number of days hospitalized after surgery, excess hospital costs and indirect costs regarding transportation, and income loss of parents between groups were compared using Wilcoxon signed rank test. Any hospital stay after surgery between groups was compared using McNemar  $\chi^2$  test. A hurdle model was used to predict any hospital stay and number of days hospitalized after surgery. Multiple mixed-effects linear regression was used to identify predictors of adjusted excess hospital costs and indirect costs.

**RESULTS:** A total 430 children were included (215 matched pairs). More PRE children required hospital stay after surgery (81% vs 72%,  $P = 0.004$ ), and PRE children had a longer number of days hospitalized after surgery (median [interquartile ranges]: 1 [1–3.5] vs 1 [0–2];  $P < 0.001$ ) and incurred higher excess costs ( $P < 0.001$ ) but not indirect costs ( $P = 0.23$ ). In multivariate analysis, PRE was a significant predictor for hospital stay after surgery (odds ratio, 2.56; 95% confidence interval, 1.23–5.31), longer hospitalization (count ratio, 2.10 [1.31–3.35]), higher excess costs (cost ratio, 1.30 [1.12–1.53]), and indirect cost (cost ratio, 1.58 [1.20–2.08]) after adjusting for patient and anesthesia characteristics. Universal coverage (74%) was associated with 35% and 64% higher excess cost compared with the Comptroller General's Department (17%) and self-pay (7%), respectively ( $P = 0.003$ ).

**CONCLUSIONS:** The effects of PRE in pediatric anesthesia were hospital stay after surgery, 2 times longer hospitalization, 30% higher excess hospital costs, and 58% higher indirect cost among outpatients. Hospital policy to efficiently manage hospital beds and compensatory budget should be developed.

### 异丙酚诱导新生大鼠脑电图发作：糖皮质激素和 $\gamma$ -氨基丁酸 A 型受体介导的激励作用

#### **Propofol-Induced Electroencephalographic Seizures in Neonatal Rats: The Role of Corticosteroids and $\gamma$ -Aminobutyric Acid Type A Receptor-Mediated Excitation**

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**背景：**中枢神经系统兴奋和抑制之间的不平衡可能会导致病理结果。我们研究麻醉剂异丙酚通过内分泌活性物质和  $\gamma$ -氨基丁酸 A 型受体 (GABAAR) 介导的选择性激发 GABAAR 对新生大鼠脑电图癫痫发作作用机理

**方法：**出生 4 天的 SD 大鼠 6，接受小手术植入电极，腹腔注射异丙酚 (40 毫克公斤<sup>-1</sup>) 前 1 小时和 1 小时后观察脑电活动 (40 毫克公斤<sup>-1</sup>)。各种治疗前给予丙泊酚 15 分钟。

**结论：**异丙酚麻醉时发生的脑电图癫痫发作样持续低幅度尖峰。血清多种皮质酮增加 (T (10) = -5.062;  $P = 0.0005$ ) 醛固酮 (T (10) = -5.069;  $P = 0.0005$ ) 增加，在动物身上进行的实验操作相同，见于研究脑电活动丙泊酚给药后 1 小时。预处理与布美他尼，Na<sup>+</sup>K<sup>+</sup>-2Cl<sup>-</sup>共转运体抑制剂，从而减少 GABAAR 介导的激励，消除异丙酚引起发作尖峰脑电活动。盐皮质激素和糖皮质激素受体拮抗剂 RU486，RU 28318 和抑郁症脑电图癫痫发

作，但不影响丙泊酚的尖峰脑电图的影响。依托咪酯，在剂量足以引起翻正反射，弱增加血清皮质醇水平和诱发脑电图癫痫发作。

(田园译 李士通审校)

**BACKGROUND:** An imbalance between excitation and inhibition in the developing central nervous system may result in a pathophysiological outcome. We investigated the mechanistic roles of endocrine activity and  $\gamma$ -aminobutyric acid type A receptor (GABAAR)-mediated excitation in electroencephalographic seizures caused by the GABAAR-selective anesthetic propofol in neonatal rats.

**METHODS:** Postnatal day 4–6 Sprague Dawley rats underwent a minor surgical procedure to implant electrodes to measure electroencephalographic activity for 1 hour before and 1 hour after intraperitoneal administration of propofol (40 mg·kg<sup>-1</sup>). Various treatments were administered 15 minutes before administration of propofol.

**RESULTS:** Episodes of electroencephalographic seizures and persistent low-amplitude spikes occurred during propofol anesthesia. Multifold increases in serum levels of corticosterone ( $t(10) = -5.062$ ;  $P = 0.0005$ ) and aldosterone ( $t(10) = -5.069$ ;  $P = 0.0005$ ) were detected 1 hour after propofol administration in animals that underwent experimental manipulations identical to those used to study electroencephalographic activity. Pretreatment with bumetanide, the Na<sup>+</sup>–K<sup>+</sup>–2Cl<sup>-</sup> cotransporter inhibitor, which diminishes GABAAR-mediated excitation, eliminated both seizure and spike electroencephalographic activities caused by propofol. Mineralocorticoid and glucocorticoid receptor antagonists, RU 28318 and RU486, depressed electroencephalographic seizures but did not affect the spike electroencephalographic effects of propofol. Etomidate, at a dose sufficient to induce loss of righting reflex, was weak at increasing serum corticosteroid levels and eliciting electroencephalographic seizures. Etomidate given to corticosterone-pretreated rat pups further increased the total duration of electroencephalographic seizures caused by administration of exogenous corticosterone ( $t(21) = -2.512$ ,  $P = 0.0203$ ).

**CONCLUSIONS:** Propofol increases systemic corticosteroid levels in neonatal rats, which along with GABAAR-mediated excitation appear to be required for propofol-induced neonatal electroencephalographic seizures. Enhancement of GABAAR activity alone may not be sufficient to elicit neonatal electroencephalographic seizures.

### 大鼠急性术后疼痛模型中自发痛行为比机械诱发疼痛对吗啡或丁丙诺啡更敏感

#### Spontaneous Pain-Like Behaviors Are More Sensitive to Morphine and Buprenorphine Than Mechanically Evoked Behaviors in a Rat Model of Acute Postoperative Pain

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**背景：** nonevoked 自发性疼痛是术后最棘手的问题。医师通常利用人类视觉模拟评分或口头的数字评定量表评估这种形式的疼痛。最近的研究提出，自发抬足（SFL）的行为是一种动物脊髓神经损伤后表达自发性疼痛的行为。在目前的研究中，我们系统的描述了大鼠急性术后疼痛行为，其中包括比较镇痛治疗诱发的行为

**方法：** 对四系手动 5 分钟的时间用 10 分钟的时间间隔记录每个测试结果。随后用电子 Von Frey 计测定缩爪阈值。年龄的影响进行评估，大鼠在不同年龄组的测试：2，7，和大于 26 个月。丁丙诺啡和吗啡的作用在单独的一组动物进行了测试，测试前腹腔注射生理盐水，吗啡（0.01，0.1，1，或 2 毫克/公斤），或丁丙诺啡（0.001，0.01，或 0.1 毫克/公斤）

**结果：**SFL 行为在切开后的第三或第四天显著恢复 3 小时内达到高峰 ( $P < 0.0001$ )。这些行为的表现不同的动物年龄 (2, 7, 和 26 个月;  $P = 0.30$  并没有显著不同。机械性痛觉过敏逆转药物的半数有效剂量 (0.0452 毫克/公斤; 95% CI, 0.0259–0.0787) 显著大于反转快速 (0.0027 毫克/公斤; 95% CI, 0.0009–0.0083;  $P < 0.0001$ ) 和长期 (0.0004 毫克/公斤, 95% CI, 0, 0.0035;  $P = 0.001$ ) 切开后。同样, 在术后 3 小时, 对于机械超敏反应行为逆转吗啡的半数有效剂量 (2.901 毫克/公斤; 95% CI, 1.132–7.436) 大于 SFL 计数 (0.4044 毫克/公斤; 95% CI, 0.1048–1.561;  $P = 0.0103$ ) 和功能的持续时间 (0.0309 毫克/公斤; 95% CI, 0.0095–0.0998;  $P < 0.0001$ )。

**结论：**本研究表明, 与机械诱发的行为相比, 诱导大鼠后肢足底切口 SFL 的行为对镇痛吗啡与丁丙诺啡有较高的检测灵敏度

(田园译 李士通审校)

**BACKGROUND:** Nonevoked spontaneous pain is most problematic for postoperative patients. Physicians assess this form of pain using the human visual analog scale or verbal numeric rating scale. Recent studies have proposed that spontaneous foot-lifting (SFL) behaviors are an expression of spontaneous pain in animals after spinal nerve injury or adjuvant-induced inflammation. In the current study, we characterize SFL behaviors in a rat model of acute postoperative pain, which includes comparisons with evoked behaviors to analgesic treatments.

**METHODS:** SFL was manually recorded over four 5-minute periods with 10-minute intervals between each testing session. Paw-withdrawal thresholds were subsequently measured with an electronic von Frey esthesiometer. To evaluate the effects of age, rats were tested in different age groups: 2, 7, and >26 months. The effects of buprenorphine and morphine were tested in a separate group of animals, which received intraperitoneal injections of saline, morphine (0.01, 0.1, 1, or 2 mg/kg), or buprenorphine (0.001, 0.01, or 0.1 mg/kg) before testing.

**RESULTS:** SFL behaviors peaked at 3 hours after incision and significantly recovered by the 3rd or 4th postoperative day ( $P < 0.0001$ ). The presentation of these behaviors did not significantly vary with animal age (2, 7, and >26 months old;  $P = 0.30$ ). SFL behaviors, with the exception of rapid SFL at 3 hours after incision, did not show significant correlation with paw-withdrawal threshold behaviors. The median effective dose of buprenorphine for reversal of mechanical hyperalgesia (0.0452 mg/kg; 95% CI, 0.0259–0.0787) was significantly larger than for reversing rapid (0.0027 mg/kg; 95% CI, 0.0009–0.0083;  $P < 0.0001$ ) and prolonged (0.0004 mg/kg, 95% CI, 0.0000, 0.0035;  $P = 0.001$ ) SFL at 3 hours after incision. Similarly, the median effective dose of morphine for reversal of mechanical hypersensitivity behaviors (2.901 mg/kg; 95% CI, 1.132–7.436) was larger than for SFL count (0.4044 mg/kg; 95% CI, 0.1048–1.561;  $P = 0.0103$ ) and SFL duration (0.0309 mg/kg; 95% CI, 0.0095–0.0998;  $P < 0.0001$ ) at 3 hours after incision.

**CONCLUSIONS:** The present study demonstrates that a hindpaw plantar incision induces SFL behaviors in rats and that these behaviors have higher bioassay sensitivity to analgesic interventions with morphine and buprenorphine compared with mechanically evoked behaviors.