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- Ott, Helmut;
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- Loacker, Lorin;
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- Velik-Salchner, Corinna

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Anesthesia & Analgesia. 120(4):737-748, April 2015.

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Anesthesia & Analgesia. 120(4):749-769, April 2015.

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Loftus, Randy W.;
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Transmission Dynamics of Gram-Negative Bacterial Pathogens in the Anesthesia Work Area

Loftus, Randy W.; Brown, Jeremiah R.; Patel, Hetal M.; Koff, Matthew D.; Jensen, Jens T.; Reddy, Sundara; Ruoff, Kathryn L.; Heard, Stephen O.; Dodds, Thomas M.; Beach, Michael L.; Yeager, Mark P.

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Loftus, Randy W.; Koff, Matthew D.; Brown, Jeremiah R.; Patel, Hetal M.;
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Cole, Devon C.; Baslanti, Tezcan Ozrazgat; Gravenstein, Nikolaus L.; Gravenstein, Nikolaus

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Birnbach, David J.; Rosen, Lisa F.; Fitzpatrick, Maureen; Carling, Philip; Munoz-Price, L. Silvia

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The Dynamics and Implications of Bacterial Transmission Events Arising from the Anesthesia Work Area

Loftus, Randy W.; Koff, Matthew D.; Birnbach, David J.

Research Report

**应用呼气相辅助通气的方法通过一根小口径的气管导管对严重低氧血症猪的急救性通气**
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*Anesthesia & Analgesia. 120(4):890-894, April 2015.*

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*Anesthesia & Analgesia. 120(4):895-902, April 2015.*

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- Fortier, Michelle A.;
- Chorney, Jill MacLaren;
- Mayes, Linda

*Anesthesia & Analgesia. 120(4):905-914, April 2015.*
Research Report

Web-Based Tailored Intervention for Preparation of Parents and Children for Outpatient Surgery (WebTIPS): Formative Evaluation and Randomized Controlled Trial

- Fortier, Michelle A.;
- Bunzli, Elizabeth;
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- Olshansky, Ellen;
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Pain Medicine

Research Report

COMT Gene Haplotypes Are Closely Associated with Postoperative Fentanyl Dose in Patients

- Zhang, Fan;
- Tong, Jianbin;
- Hu, Jie;
- Zhang, Hao;
- Ouyang, Wen;
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Research Report

**EN3427**: 一种新型阳离子氨基茚型长效局部麻醉药的性能
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**室性心动过速消融：一项给予麻醉医生的系统综述**

**Ventricular Tachycardia Ablation: A Comprehensive Review for Anesthesiologists**
Mittnacht, Alexander J. C. MD*; Dukkipati, Srinivas MD†; Mahajan, Aman MD, PhD‡

Anesthesia & Analgesia 2015 120 737–748

经皮导管消融术越来越多运用于药物治疗无效的反复发作室性心动过速（ventricular tachycardia, VT）的患者。对于此类患者最佳的管理包括谨慎考虑潜在心脏疾病的严重程度，麻醉药物相互作用以及在 VT 标测和消融过程中的技术问题。目标在于选择一种致心律失常性最小的麻醉技术，这样可以使得在电生理操作室内 VT 的发生具有可重复性。麻醉药可以直接通过对于离子通道和缝隙连接作用，或间接通过对于自主神经系统作用改变动作电位和心室去极化过程。此外，在操作过程中维持血流动力学稳定以及监测终末器官灌注是另一项挑战。本综述全面地更新了当今 VT 消融的实施过程中的麻醉处理方法。

（俞芳 译 陈杰 校）

Percutaneous catheter ablation is being increasingly performed in patients with recurrent ventricular tachycardia (VT) unresponsive to medical treatment. Optimal management of patients requires careful consideration of the severity of the underlying cardiac disease, the anesthetic drug interactions, and the procedural technique during VT mapping and ablation. The goal is to choose an anesthetic technique that has the least effect on arrhythmogenicity, allowing reproducibility of the VT in the electrophysiology laboratory. Anesthetics can alter action potential and ventricular depolarization directly through their effects on ion channels and gap junctions, as well as indirectly via their effects on the autonomic nervous system. Furthermore, maintaining hemodynamic stability and monitoring for adequate end-organ perfusion are additional challenges. In this review, we provide a comprehensive update on the currently performed VT ablation procedures and their anesthetic considerations.

**丙泊酚对于高糖诱导的人脐静脉内皮细胞凋亡和功能障碍的保护作用**

**Propofol Protects Against High Glucose–Induced Endothelial Apoptosis and Dysfunction in Human Umbilical Vein Endothelial Cells**
背景：围术期高血糖症是临床上常见的一种代谢紊乱疾病。高血糖诱导内皮细胞凋亡和功能障碍。丙泊酚是一种临床上广泛使用的静脉麻醉药物。本研究检测丙泊酚是否及如何减轻高糖诱导的人脐静脉内皮细胞 (HUVECs) 凋亡和功能障碍。

方法：用不同浓度（5, 10, 15 和 25 mM）的血糖体外培养 HUVEC，时间分别是 4, 8, 12 和 24 小时。为了研究丙泊酚的效应，用不同浓度（0.2, 1, 5 和 25 μM）的丙泊酚孵育 2 小时。在平行实验中，细胞在 5 mM 葡萄糖中孵育作为对照。用硝酸还原酶法测定产生的一氧化氮（NO）。用细胞计数试剂盒-8 测定细胞活性。用 Western blot 法检测 caspase 3、细胞色素 C、内皮型一氧化氮合酶（eNOS）、p-eNOS-Thr495、p66Shc、蛋白激酶 C βII（PKCβII）和 p-PKCβII-Ser660。用亚铁细胞色素 c 减少法测定超氧阴离子（O2−）累积。用末端脱氧核苷酸转移酶介导 dUTP 缺口末端标记染色法测定细胞凋亡。

结果：与对照组相比，高糖减少 HUVEC 的 NO 产生 (P < 0.0001)，降低细胞活性 (P < 0.0001)。与高糖处理相比，丙泊酚预处理细胞 (5 μM, 2 h) 减少了高浓度葡萄糖诱导的抑制性 p-eNOS-Thr495 磷酸化 (P < 0.0001)，增加了 NO 的产生 (P = 0.0007)，降低高血糖诱导的 p66Shc 的表达 (P < 0.0001) 和 p66Shc 线粒体转位 (P < 0.0001)，线粒体细胞色素 C 释放 (P < 0.0001)，活化 Caspase 3 的表达 (P < 0.0001) 和增强内皮细胞活性 (P < 0.0001)。此外，丙泊酚抑制高糖诱导的 PKCβII 的表达 (P = 0.0002) 和 p-PKCβII-ser660 磷酸化 (P < 0.0001)。丙泊酚的保护作用与 PKCβII 抑制剂十分相似。

结论：丙泊酚通过降低高糖诱导 PKCβII 的表达和 p-PKCβII-ser660 磷酸的机制，抑制高糖诱导的 p66Shc 线粒体转位。因此保护人脐静脉内皮细胞免受高糖诱导的内皮细胞功能障碍和细胞凋亡。

（徐欢 译 陈杰 校）

BACKGROUND: Perioperative hyperglycemia is a common clinical metabolic disorder. Hyperglycemia could induce endothelial apoptosis and dysfunction. Propofol is a widely used IV anesthetic drug in clinical settings. In the present study, we examined whether and how propofol reduced high glucose-induced endothelial apoptosis and dysfunction in human umbilical vein endothelial cells (HUVECs).

METHODS: HUVECs were cultured with different concentrations (5, 10, 15, and 25 mM) of glucose for different times (4, 8, 12, and 24 hours). To study the effect of propofol, cells were incubated with different concentrations (0.2, 1, 5, and 25 μM) of propofol for 2 hours. In parallel experiments, cells were incubated in 5 mM glucose as control. Nitric oxide (NO) production was measured with a nitrate reductase assay. Cell viability was determined with a Cell Counting Kit-8. Protein expression of active caspase 3, cytochrome c, endothelial NO synthase (eNOS), p-eNOS-Thr495, p66Shc, protein kinase C βII (PKCβII), and p-PKCβII-Ser660 was measured by Western blot analysis. Accumulation of superoxide anion (O2−) was measured with the reduction of ferricytochrome c. Cell apoptosis was determined with terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling staining.

RESULTS: Compared with control, high glucose decreased NO production (P < 0.0001) and reduced cells viability (P < 0.0001) in HUVECs. Compared with high glucose treatment, pretreatment of cells with propofol (5 μM, 2 hours) reduced high glucose–induced inhibitory p-eNOS-Thr495 phosphorylation (P < 0.0001), increasing NO production (P = 0.0007), decreased high glucose–induced p66Shc expression (P < 0.0001) and p66Shc mitochondrial translocation (P < 0.0001), O2− accumulation (P < 0.0001), mitochondrial cytochrome c release (P < 0.0001), active caspase 3 expression (P < 0.0001), and enhancing endothelial viability (P < 0.0001). Furthermore, propofol inhibited high glucose–induced PKCβII expression (P = 0.0002) and p-
PKCβII-Ser660 phosphorylation (P < 0.0001). Moreover, the observed protective effect of propofol was quite similar to that of PKCβII inhibitor.

CONCLUSIONS: Propofol, by a mechanism of decreasing high glucose–induced PKCβII expression and p-PKCβII-Ser660 phosphorylation, inhibits high glucose–induced p66Shc mitochondrial translocation, therefore protecting HUVECs from high glucose–induced endothelial dysfunction and apoptosis.

The Epidemiology of Staphylococcus aureus Transmission in the Anesthesia Work Area

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BACKGROUND: Little is known regarding the epidemiology of intraoperative Staphylococcus aureus transmission. The primary aim of this study was to examine the mode of transmission, reservoir of origin, transmission locations, and antibiotic susceptibility for frequently encountered S aureus strains (phenotypes) in the anesthesia work area. Our secondary aims were to examine phenotypic associations with 30-day postoperative patient cultures, phenotypic growth rates, and risk factors for phenotypic isolation.

METHODS: S aureus isolates previously identified as possible intraoperative bacterial transmission events by class of pathogen, temporal association, and analytical profile indexing...
were subjected to antibiotic disk diffusion sensitivity. The combination of these techniques was then used to confirm S aureus transmission events and to classify them as occurring within or between operative cases (mode). The origin of S aureus transmission events was determined via use of a previously validated experimental model and links to 30-day postoperative patient cultures confirmed via pulsed-field gel electrophoresis. Growth rates were assessed via time-to-positivity analysis, and risk factors for isolation were characterized via logistic regression.

RESULTS: One hundred seventy S aureus isolates previously implicated as possible intraoperative transmission events were further subdivided by analytical profile indexing phenotype. Two phenotypes, phenotype P (patients) and phenotype H (hands), accounted for 65% of isolates. Phenotype P and phenotype H contributed to at least 1 confirmed transmission event in 39% and 28% of cases, respectively. Patient skin surfaces (odds ratio [OR], 8.40; 95% confidence interval [CI], 2.30–30.73) and environmental (OR, 10.89; 95% CI, 1.29–92.13) samples were more likely than provider hands (referent) to have phenotype P positivity. Phenotype P was more likely than phenotype H to be resistant to methicillin (OR, 4.38; 95% CI, 1.59–12.06; P = 0.004) and to be linked to 30-day postoperative patient cultures (risk ratio, 36.63 [risk difference, 0.174; 95% CI, 0.019–0.328]; P < 0.001). Phenotype P exhibited a faster growth rate for methicillin resistant and for methicillin susceptible than phenotype H (phenotype P: median, 10.32H; interquartile range, 10.08–10.56; phenotype H: median, 10.56H; interquartile range, 10.32–10.8; P = 0.012). Risk factors for isolation of phenotype P included age (OR, 14.11; 95% CI, 1.12–174; 95% CI, 5.30–318.78; P < 0.001).

CONCLUSIONS: Two S aureus phenotypes are frequently transmitted in the anesthesia work area. A patient and environmentally derived phenotype is associated with increased risk of antibiotic resistance and links to 30-day postoperative patient cultures as compared with a provider hand-derived phenotype. Future work should be directed toward improved screening and decolonization of patients entering the perioperative arena and improved intraoperative environmental cleaning to attenuate postoperative health care–associated infections.

麻醉医生的手卫生学知识和观念

Hand Hygiene Knowledge and Perceptions Among Anesthesia Providers

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与减少不完全知识相关，包括在接触环境后积极响应洗手（比值比[OR] 0.23，0.14–0.37, P < 0.001），在对病人护理中消毒环境（比值比 0.54，0.35–0.82, P = 0.004），相信他们可以影响同事（比值比 0.43，0.27–0.68, P < 0.001），并打算坚持准则（比值比 0.56，0.36–0.86, P = 0.008）。这些协变量与受试者特征曲线下面积相关性为 0.79（95% 置信区间，0.74–0.83）。结论：麻醉医生在手卫生准则方面的知识缺乏频繁发生，往往由于没有认识到手卫生在于与污染的病人接触和环境接触后。术中手卫生改进方案应解决这些知识缺陷。本研究证实的不完备知识的相关预测因素应在未来的研究中进一步验证。
Health care–associated infections are a hospital-wide concern associated with a significant increase in patient morbidity, mortality, and health care costs. Bacterial transmission in the anesthesia work area of the operating room environment is a root cause of 30-day postoperative infections affecting as many as 16% of patients undergoing surgery. A better understanding of anesthesia-related bacterial transmission dynamics may help to generate improvements in intraoperative infection control and improve patient safety.

**Haloperidol Suppresses Murine Dendritic Cell Maturation and Priming of the T Helper 1–Type Immune Response**

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**BACKGROUND:** Haloperidol has immunomodulatory effects when used to treat patients with schizophrenia and also is used to sedate critically ill patients in the intensive care unit. Although the mechanism by which haloperidol affects immune function is unclear, one possibility is that it alters dendritic cell (DC) function. DCs are potent antigen-presenting cells that influence the activation and maturation of T lymphocytes. In this study, we investigated the in vitro and in vivo immunomodulatory effects of haloperidol on DC-mediated immune responses.
METHODS: Using bone marrow–derived DCs in cell culture, we evaluated the effect of haloperidol on expression of costimulatory molecules (CD80 and CD86), major histocompatibility complex class II molecules, and the DC maturation marker CD83. DC culture supernatants also were evaluated for interleukin-12 p40 levels. In addition, we analyzed the effect of haloperidol on a mixed cell culture containing DCs and lymphocytes and measured the secretion of interferon-γ in the culture supernatants. We also assessed the in vivo effects of haloperidol on hapten-induced contact hypersensitivity responses.

RESULTS: Haloperidol inhibited the expression of CD80, CD86, major histocompatibility complex class II, and CD83 molecules on DCs and the secretion of interleukin-12p40 in DC culture supernatants. In mixed cell cultures containing both T cells (CD4+ and CD8α+) and DCs, haloperidol-treated DCs suppressed the proliferation of allogeneic T cells and effectively inhibited the production of interferon-γ. In vivo, haloperidol reduced hapten-induced contact hypersensitivity responses. Furthermore, an antagonist to D2-like receptor suppressed the maturation of DCs in a manner similar to haloperidol.

CONCLUSIONS: The results of our study suggest that haloperidol suppresses the functional maturation of DCs and plays an important role in the inhibition of DC-induced T helper 1 immune responses in the whole animal. Furthermore, the effect of haloperidol on DCs may be mediated by dopamine D2–like receptors. Together, these results demonstrate that administration of haloperidol suppresses DC-mediated immune responses.

BACKGROUND: Fentanyl’s analgesic efficacy varies widely among individuals. The single-nucleotide polymorphisms (SNPs) of catechol-O-methyltransferase (COMT) modulate
sensitivity to pain. It remains unclear, however, whether COMT genetic variability affects postoperative fentanyl analgesia in patients undergoing radical gastrectomy.

METHODS: One hundred fifteen patients, ASA physical status I–III, who were scheduled for radical gastrectomy under general anesthesia, were enrolled in this study. Patient-controlled IV analgesia with fentanyl was administered during the first 48 hours after surgery. Visual analog scale score for patients’ pain was maintained at ≤30 mm. The amount of fentanyl consumed and side effects were recorded for the first 24 and 48 hours postoperatively. The SNPs of COMT (rs6269, rs4633, rs4818, and rs4680) of all patients were screened by DNA sequence analysis of polymerase chain reaction–amplified DNA or polymerase chain reaction-restriction fragment length polymorphism.

RESULTS: There were no significant differences in the doses of fentanyl used among patients possessing different SNPs of COMT rs6269, rs4633, rs4818, and rs4680 at 24 (all P > 0.207) and 48 (all P > 0.148) hours after surgery. COMT gene haplotypes combined by COMT rs6269, rs4633, rs4818, and rs4680, however, significantly affected fentanyl consumption at 24 (P = 0.029) and 48 (P = 0.032) hours after surgery. Among the haplotypes of COMT gene, patients with haplotype ACCG consumed more fentanyl than GCGG and ATCA haplotypes during the first 24 and 48 hours (all P < 0.042) after surgery. No significant differences were found in the incidence of nausea, vomiting, and dizziness among the 4 SNPs of COMT gene (all P > 0.079) and their haplotypes (all P > 0.482).

CONCLUSIONS: COMT gene haplotype constructed by rs6269, rs4633, rs4818, and rs4680 contributes to the individual variation of postoperative analgesia with fentanyl. Patients carrying the COMT gene haplotype ACCG consumed the most drug during the first 24 and 48 hours postoperatively.

体外膜式氧合引起高分子量血管性血友病因子多聚体短暂缺失

Extracorporeal Membrane Oxygenation Induces Short-Term Loss of High-Molecular-Weight von Willebrand Factor Multimers

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背景：高分子量（HMW）血管性血友病因子（vWF）多聚体在初期的止血过程中起重要作用。心室辅助装置带来的剪切力增加导致 HMW vWF 多聚体过早降解。但是体外膜式氧合（ECMO）条件下是否同样存在 vWF 多聚体的降解仍然是疑问。

方法：我们在顽固性心功能不全伴/不伴肺功能衰竭并且需要 ECMO 治疗的患者进行了一项观察性研究。观察主要节点是在 ECMO 前，ECMO 中和 ECMO 后的 HMW vWF 的质量和数量。为了进一步研究初期止血的改变，针对入组的 38 例患者，在患者接受 ECMO 前（基础值），经行 ECMO 24 小时和 48 小时后，以及 ECMO 治疗后 24h，我们同时检测 vWF 抗原（vWF-Ag），vWF 瑞斯托茵素辅因子（vWF-RCo）和 VIII 因子的水平。

结果：与基础水平相比，经过 24h ECMO 治疗后，vWF-Ag 和 vWF-RCo 水平明显下降（平均数±标准差，vWF-Ag，307%±152%到261%±138%，P = 0.002; vWF-RCo 282%±145%到157%±103%，P < 0.0001）。同样在后续治疗过程中 vWF-Ag 和 vWF-RCo 水平亦明显下降（vWF-Ag 265%±128%，P = 0.025; vWF-RCo 163%±94%，P < 0.0001）。在终止 ECMO 治疗后，vWF-Ag 高于基础水平（359%±131%，P = 0.004），而 vWF-RCo 与基础水平持平（338%±142%，P = 0.046）。与基础值相比，vWF-RCo/vWF-Ag 比值在 24h ECMO 治疗后明显下降（0.96 ± 0.23 到 0.61 ± 0.17，P ≤ 0.0001），在 48h ECMO 治疗后该比值亦明显下降（0.63 ± 0.18，P ≤ 0.0001）。在终止治疗后，该比值迅速与基础值持平（0.94 ± 0.19，P = 0.437）。HMW vWF 多聚体的数量在 24h（21 ± 1.4 至 14
BACKGROUND: High-molecular-weight (HMW) von Willebrand factor (vWF) multimers are crucial for primary hemostasis. Increased shear stress from ventricular assist devices can provoke premature degradation of HMW vWF multimers. Whether similar loss of vWF multimers occurs during extracorporeal membrane oxygenation (ECMO) is not clear.

METHODS: We conducted a prospective observational study in a clinical cohort of patients who required ECMO for intractable cardiac and/or respiratory failure. The primary end point was the quantity and quality of HMW vWF multimer bands before, during, and after ECMO support. To investigate further changes in primary hemostasis, we also measured vWF antigen activity (vWF:Ag), vWF ristocetin cofactor activity (vWF:RCo), and factor VIII in 38 patients who required ECMO support before initiation of ECMO (baseline), after 24 and 48 hours on ECMO, and 24 hours after termination of ECMO therapy.

RESULTS: Compared with baseline, vWF:Ag and vWF:RCo decreased after 24 hours of ECMO (mean ± SD, vWF:Ag, 307% ± 152% to 261% ± 138%, P = 0.002; vWF:RCo 282% ± 145% to 157% ± 103%, P < 0.0001) and remained lower during ongoing support (vWF:Ag 265% ± 128%, P = 0.025; vWF:RCo 163% ± 94%, P < 0.0001). After termination of ECMO, vWF:Ag was greater than baseline (359% ± 131%, P = 0.004) and vWF:RCo was similar to baseline levels (338% ± 142%, P = 0.046). Compared with baseline, the calculated vWF:RCo/vWF:Ag ratio decreased after 24 hours on support (0.96 ± 0.23 to 0.61 ± 0.17, P ≤ 0.0001) and remained lower during 48 hours on ECMO (0.63 ± 0.18, P ≤ 0.0001). After termination of ECMO support (0.94 ± 0.19, P = 0.437), values rapidly returned to baseline. The number of HMW vWF multimers (n) decreased from baseline after 24 hours on ECMO (21 ± 1.4 to 14 ± 1.8, P ≤ 0.0001) and after 48 hours on ECMO (21 ± 1.4, P ≤ 0.0001). Twenty-four hours after termination of ECMO support, HMW vWF multimeric pattern had returned to baseline values (21 ± 1.8, P = 0.551).

CONCLUSIONS: Loss of HMW vWF multimer bands occurred in patients undergoing ECMO support and resolved after the termination of ECMO. Although not detectable with coagulation screening tests, a vWF:RCo/vWF:Ag ratio <0.7 during ECMO was highly indicative for loss of HMW vWF multimers. Our findings may at least in part explain increased bleeding tendency during ECMO therapy. Administration of vWF concentrates may support restoration of primary hemostasis in patients with relevant bleeding during ECMO support.
方法：病人按计划行诊断性上消化道内镜检查，随机、双盲给予 3 种剂量中的 1 种的 remimazolam 或者咪达唑仑，每组 25 位病人。给予单次的药物镇静满意后，病人性胃镜检查。我们评价检查的成功与否、镇静效果、苏醒和安全性。

结果：低剂量组 (0.10mg/kg)、中剂量组 (0.15mg/kg) 和高剂量组 (0.20mg/kg) 给予单次剂量 remimazolam 后的胃镜检查成功率分别是 32%、56%、64%，咪达唑仑组 (0.075mg/kg) 的成功率是 44%。Remimazolam 组的镇静起效时间是 1.5-2.5 分钟，而咪达唑仑组是 5 分钟。因为这项研究是给予单次剂量，必要时给予咪达唑仑或丙泊酚以维持镇静状态完成检查。所有治疗组病人镇静后的苏醒都非常迅速，但受单次剂量后选择的追加药物的影响。在 remimazolam 和咪达唑仑的安全性上没有明显的不同。

结论：这项剂量探索性研究表明在诊断性上消化道内镜检查中给予病人单次剂量 remimazolam (0.10-0.20mg/kg) 能够快速镇静和快速苏醒。Remimazolam 的安全性良好，与咪达唑仑相似，保证了这个起效迅速的药物的进一步发展。

（吕越昌 译 薛张纲 校）

BACKGROUND: This exploratory study was the first study of remimazolam in patients to assess the safety and efficacy of different single doses for procedural sedation.

METHODS: Patients scheduled to undergo a diagnostic upper gastrointestinal endoscopy were randomized to receive 1 of 3 doses of remimazolam or midazolam (25 per group) in a double-blind manner. After a single dose of study drug to achieve sedation, patients underwent gastroscopy. We assessed the success of the procedure, sedation levels, recovery from sedation, and safety.

RESULTS: A single dose of remimazolam resulted in a successful procedure in 32%, 56%, and 64% of patients in the low (0.10), middle (0.15), and high (0.20 mg/kg) dose groups compared with 44% of patients in the midazolam (0.075 mg/kg) dose group. The onset of sedation was 1.5 to 2.5 minutes in the mimazolam dose groups compared with 5 minutes for midazolam. Because this was a single administration study, sedation could be maintained for as long as necessary to complete the procedure, using rescue midazolam or propofol. Recovery from sedation was rapid for all treatment groups but was influenced by the choice of rescue medication. There were no obvious differences in the safety profiles of remimazolam and midazolam.

CONCLUSIONS: This exploratory dose-finding study showed that a single administration of remimazolam (0.10-0.20 mg/kg) was capable of inducing rapid sedation with a quick recovery profile in patients undergoing a diagnostic upper gastrointestinal endoscopy. The safety profile was favorable and appeared to be similar to that of midazolam, warranting further development of this short-acting compound.
Although needleless connectors (NC) are frequently used in the perioperative setting, the potential of modern NCs to slow delivery of IV fluids has not been thoroughly studied. We examined flow characteristics of 5 NC models during pressurized delivery of crystalloid and banked red blood cells from a Level 1 warmer through various IV catheters. Crystalloid flow rates were reduced by 29% to 85% from control in catheters >18 gauge, while red blood cell flow reductions ranged from 22% to 76% in these catheters (all P < 0.0050). We suggest that practitioners consider eliminating NCs when large IV catheters are inserted for rapid fluid administration.

The Dynamics of Enterococcus Transmission from Bacterial Reservoirs Commonly Encountered by Anesthesia Providers

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BACKGROUND: Enterococci, the second leading cause of health care-associated infections, have evolved from commensal and harmless organisms to multidrug-resistant bacteria associated with a significant increase in patient morbidity and mortality. Prevention of ongoing spread of this organism within and between hospitals is important. In this study, we characterized Enterococcus transmission dynamics for bacterial reservoirs commonly encountered by anesthesia providers during the routine administration of general anesthesia.

METHODS: Enterococcus isolates previously obtained from bacterial reservoirs frequently encountered by anesthesiologists (patient nasopharynx and axilla, anesthesia provider hands, and the adjustable pressure-limiting valve and agent dial of the anesthesia machine) at 3 major academic medical centers were identified as possible intraoperative bacterial transmission events by class of pathogen, temporal association, and phenotypic analysis (analytical profile indexing).
They were then subjected to antibiotic disk diffusion sensitivity for transmission event confirmation. Isolates involved in confirmed transmission events were further analyzed to characterize the frequency, mode, origin, location of transmission events, and antibiotic susceptibility of transmitted pathogens.

RESULTS: Three hundred eighty-nine anesthesia reservoir isolates were previously identified by gross morphology and simple rapid tests as Enterococcus. The combination of further analytical profile indexing analysis and temporal association implicated 43% (166/389) of those isolates in possible intraoperative bacterial transmission events. Approximately, 30% (49/166) of possible transmission events were confirmed by additional antibiotic disk diffusion analysis. Two phenotypes, E5 and E7, explained 80% (39/49) of confirmed transmission events. For both phenotypes, provider hands were a common reservoir of origin proximal to the transmission event (96% [72/75] hand origin for E7 and 89% [50/56] hand origin for E5) and site of transmission (94% [16/17] hand transmission location for E7 and 86% [19/22] hand transmission location for E5).

CONCLUSIONS: Anesthesia provider hand contamination is a common proximal source and transmission location for Enterococcus transmission events in the anesthesia work area. Future work should evaluate the impact of intraoperative hand hygiene improvement strategies on the dynamics of intraoperative Enterococcus transmission.

在静脉通路中留下的不只是你的指纹：一项关于异丙酚麻醉和可能存在三通污染的前瞻性研究

Leaving More Than Your Fingerprint on the Intravenous Line: A Prospective Study on Propofol Anesthesia and Implications of Stopcock Contamination

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BACKGROUND: Acute care handling of IV stopcocks during anesthesia and surgery may result in contaminated IV tubing sets. In the context of widespread propofol use, a nutrient-rich hypnotic drug, we hypothesized that propofol anesthesia increases bacterial contamination of IV stopcocks.
stopcocks and may compromise safety of IV tubing sets when continued to be used after propofol anesthesia.

METHODS: We conducted an in vitro trial by collecting IV tubing sets at the time of patient discharge from same-day ambulatory procedures performed with and without propofol anesthesia. These extension sets were then held at room temperature for 6, 24, or 48 hours. We cultured 50 samples at each interval for both cohorts. Quantitative cultures were done by aspirating the IV stopcock dead space and plating the aspirate on blood agar for colony count and speciation.

RESULTS: Positive bacterial counts were recovered from 17.3% of propofol anesthesia stopcocks (26/150) and 18.6% of nonpropofol stopcocks (28/150). At 6 hours, the average bacterial counts from stopcocks with visible residual propofol was 44 colony forming units (CFU)/mL, compared with 41 CFU/mL with no visible residual propofol and 37 CFU/mL in nonpropofol anesthesia stopcocks. There was a 100-fold increase in bacterial number in contaminated stopcock dead spaces at 48 hours after propofol anesthesia. This difference remained significant when comparing positive counts from stopcocks with no visible residual propofol and nonpropofol anesthesia (P = 0.034).

CONCLUSIONS: There is a covert incidence and degree of IV stopcock bacterial contamination during anesthesia which is aggravated by propofol anesthetic. Propofol anesthesia may increase risk for postoperative infection because of bacterial growth in IV stopcock dead spaces.
背景：抽吸产生的呼气相辅助通气（EVA）的方法使得通过一根小口径的气管导管进行双向通气成为可能。本研究中我们通过急性低氧血症猪的模型来研究 EVA 在恢复氧和以及通气的效率。

方法：对六只体重在 61-76kg 的猪进行麻醉，利用带套囊的气管导管进行间断性正压通气。接好监测后，将这些猪置入一根长 75mm，内径 2mm 的气管导管。记录好基础生命体征后，断开呼吸机。缺氧 2 分钟后，通过采用辅助呼气相通气的方法进行再氧合并且持续 15 分钟，这期间气管导管都是封闭的。本研究中的第二阶段，我们将气管导管半开半闭或者完全开放重复上述实验过程。实验中我们实时监测气道压力，血流动力学参数及动脉血气，并进行描述性统计学分析。

结果：在上呼吸道完全或部分梗阻的动物模型中，应用呼气相辅助通气的方法能使所有的动物在 20 秒内恢复氧合。在完全梗阻的气道中，二氧化碳的分压在 15 分钟内能保持稳定。在气道梗阻程度稍轻的情况下，再氧合的时间被延迟。在气道完全开放的情况下，这一方法的有效性很有限，其中的 2 只猪在 15 分钟的通气后动脉氧分压依然低于 85mmHg，并且二氧化碳分压上升到 90mmHg。

结论：在严重低氧血症猪的模型中，在气道完全封闭及部分封闭情况下通过辅助呼气相通气的方法能使氧快速恢复，而在上呼吸道完全开放的情况下，这种方法在恢复氧合和辅助通气方面就显得无能为力。
BACKGROUND: The purpose of this 2-phase project was to conduct a formative evaluation and to test the preliminary efficacy of a newly developed Web-based Tailored Intervention for Preparation of parents and children undergoing Surgery (WebTIPS).

METHODS: Phase 1 enrolled 13 children 2 to 7 years of age undergoing outpatient elective surgery and their parents for formative evaluation of WebTIPS. Parent participation focus groups are common in qualitative research and are a method of asking research participants about their perceptions and attitudes regarding a product or concept. In phase 2, children 2 to 7 years of age in 2 medical centers were assigned randomly to receive the WebTIPS program (n = 38) compared with children receiving the standard of care (n = 44). The primary outcome of phase II was child and parent preoperative anxiety.

RESULTS: In phase 2, parents reported WebTIPS to be both helpful (P < 0.001) and easy to use (P < 0.001). In phase 2, children in the WebTIPS group (36.2 ± 14.1) were less anxious than children in the standard of care group (46.0 ± 19.0) at entrance to the operating room (P = 0.02; Cohen d = 0.59) and introduction of the anesthesia mask (43.5 ± 21.7 vs 57.0 ± 21.2, respectively, P = 0.01; Cohen d = 0.63). Parents in the WebTIPS group (32.1 ± 7.4) also experienced less anxiety compared with parents in the control group (36.8 ± 7.1) in the preoperative holding area (P = 0.004; Cohen d = 0.65).

CONCLUSIONS: WebTIPS was well received by parents and children and led to reductions in preoperative anxiety.

体外循环期间的麻醉管理：一项系统回顾
Anesthetic Management During Cardiopulmonary Bypass: A Systematic Review
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心脏手术期间所必需的体外循环目前对于麻醉医生的特殊挑战主要在于以下几个方面：麻醉、镇痛和肌松。

在体外循环期间特殊的病理生理变化会导致药代动力学的改变，这一改变则会影响静脉麻醉药的血清和组织中的浓度。简而言之，体外循环期间引起药效学的改变将会影响麻醉效果。
Cardiopulmonary bypass (CPB) required for cardiac surgery presents unique challenges to the cardiac anesthesiologist responsible for providing the 3 most basic facets of any anesthetic: amnesia, analgesia, and muscle relaxation. Unique pathophysiologic changes during CPB result in pharmacokinetic alterations that impact the serum and tissue concentrations of IV and volatile anesthetics. Similarly, CPB causes pharmacodynamic alterations that impact anesthetic efficacy. The clinical significance of these alterations represents a “moving target” as practice evolves and the technology of CPB circuitry advances. In addition, perfusionists choose, modify, and maintain the CPB circuitry and membrane oxygenator. Thus, their significance may not be fully appreciated by the anesthesiologist. These issues have a profound impact on the anesthetic state of the patient. The delivery and maintenance of anesthesia during CPB present unique challenges. The perfusionist may be directly responsible for the delivery of anesthetic during CPB, a situation unique to the cardiac suite. In addition, monitors of anesthetic depth—assessment of clinical signs, hemodynamic indicators, the bispectral index monitor, end-tidal anesthetic concentration, or twitch monitoring—are often absent, unreliable, or directly impacted by the unique pathophysiology associated with CPB. The magnitude of these challenges is reflected in the higher incidence of intraoperative awareness during cardiac surgery. Further complicating matters are the lack of specific clinical guidelines and varying international policies regarding medical device specifications that add further layers of complexity and introduce practice variability both within institutions and among nations. We performed a systematic survey of the literature to identify where anesthetic practice during CPB is evidence based (or not), identify gaps in the literature to guide future investigations, and explore the implications of evolving surgical practice, perfusion techniques, and national policies that impact amnesia, analgesia, and muscle relaxation during CPB.

曲马多及其代谢产物M1会选择性的抑制瞬态电压感受器阳离子通道受体1（TRPV1）的活性，而不是瞬态受体电位香草酸受体1（TRPA1）

Tramadol and Its Metabolite M1 Selectively Suppress Transient Receptor Potential Ankyrin 1 Activity, but Not Transient Receptor Potential Vanilloid 1 Activity

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BACKGROUND: The transient receptor potential vanilloid 1 (TRPV1) and the transient receptor potential ankyrin 1 (TRPA1), which are expressed in sensory neurons, are polymodal nonselective cation channels that sense noxious stimuli. Recent reports showed that these channels play important roles in inflammatory, neuropathic, or cancer pain, suggesting that they may serve as attractive analgesic pharmacological targets. Tramadol is an effective analgesic that is widely used in clinical practice. Reportedly, tramadol and its metabolite (M1) bind to μ-opioid receptors and/or inhibit reuptake of monoamines in the central nervous system, resulting in the activation of the descending inhibitory system. However, the fundamental mechanisms of tramadol in pain control remain unclear. TRPV1 and TRPA1 may be targets of tramadol; however, they have not been studied extensively.

METHODS: We examined whether and how tramadol and M1 act on human embryonic kidney 293 (HEK293) cells expressing human TRPV1 (hTRPV1) or hTRPA1 by using a Ca\(^{2+}\) imaging assay and whole-cell patch-clamp recording.

RESULTS: Tramadol and M1 (0.01–10 μM) alone did not increase in intracellular Ca\(^{2+}\) concentration ([Ca\(^{2+}\)]\(_i\)) in HEK293 cells expressing hTRPV1 or hTRPA1 compared with capsaicin (a TRPV1 agonist) or the allyl isothiocyanate (AITC, a TRPA1 agonist), respectively. Furthermore, in HEK293 cells expressing hTRPV1, pretreatment with tramadol or M1 for 5 minutes did not change the increase in [Ca\(^{2+}\)]\(_i\) induced by capsaicin. Conversely, pretreatment with tramadol (0.1–10 μM) and M1 (1–10 μM) significantly suppressed the AITC-induced [Ca\(^{2+}\)]\(_i\) increases in HEK293 cells expressing hTRPA1. In addition, the patch-clamp study showed that pretreatment with tramadol and M1 (10 μM) decreased the inward currents induced by AITC.

CONCLUSIONS: These data indicate that tramadol and M1 selectively inhibit the function of hTRPA1, but not that of hTRPV1, and that hTRPA1 may play a role in the analgesic effects of these compounds.
Transmission Dynamics of Gram-Negative Bacterial Pathogens in the Anesthesia Work Area

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BACKGROUND: Gram-negative organisms are a major health care concern with increasing prevalence of infection and community spread. Our primary aim was to characterize the transmission dynamics of frequently encountered gram-negative bacteria in the anesthesia work area environment (AWE). Our secondary aim was to examine links between these transmission events and 30-day postoperative health care-associated infections (HCAIs).

METHODS: Gram-negative isolates obtained from the AWE (patient nasopharynx and axilla, anesthesia provider hands, and the adjustable pressure-limiting valve and agent dial of the anesthesia machine) at 3 major academic medical centers were identified as possible intraoperative bacterial transmission events by class of pathogen, temporal association, and phenotypic analysis (analytical profile indexing). The top 5 frequently encountered genera were subjected to antibiotic disk diffusion sensitivity to identify epidemiologically related transmission events. Complete multivariable logistic regression analysis and binomial tests of proportion were then used to examine the relative contributions of reservoirs of origin and within- and between-case modes of transmission, respectively, to epidemiologically related transmission events. Analyses were conducted with and without the inclusion of duplicate transmission events of the same genera occurring in a given study unit.
RESULTS: The top 5 frequently encountered gram-negative genera included Acinetobacter, Pseudomonas, Brevundimonas, Enterobacter, and Moraxella that together accounted for 81% (767/945) of possible transmission events. For all isolates, 22% (167/767) of possible transmission events were identified by antibiotic susceptibility patterns as epidemiologically related and underwent further study of transmission dynamics. There were 20 duplicates involving within- and between-case transmission events. Thus, approximately 19% (147/767) of isolates excluding duplicates were considered epidemiologically related. Contaminated provider hand reservoirs were less likely (all isolates, odds ratio 0.12, 95% confidence interval 0.03-0.50, P = 0.004; without duplicate events, odds ratio 0.05, 95% confidence interval 0.01-0.49, P = 0.010) than contaminated patient or environmental sites to serve as the reservoir of origin for epidemiologically related transmission events. Within- and between-case modes of gram-negative bacilli transmission occurred at similar rates (all isolates, 7% between-case, 5.2% within-case, binomial P value 0.176; without duplicates, 6.3% between-case, 3.7% within-case, binomial P value 0.036). Overall, 4.0% (23/548) of patients suffered from HCAIs and had an intraoperative exposure to gram-negative isolates. In 8.0% (2/23) of those patients, gram-negative bacteria were linked by pulsed-field gel electrophoresis to the causative organism of infection. Patient and provider hands were identified as the reservoirs of origin and the environment confirmed as a vehicle for between-case transmission events linked to HCAIs.

CONCLUSIONS: Between- and within-case AWE gram-negative bacterial transmission occurs frequently and is linked by pulsed-field gel electrophoresis to 30-day postoperative infections. Provider hands are less likely than contaminated environmental or patient skin surfaces to serve as the reservoir of origin for transmission events.

双层手套，一个减少手术室污染的简单策略评估的随机对照试验

Double Gloves: A Randomized Trial to Evaluate a Simple Strategy to Reduce Contamination in the Operating Room

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背景：对于病人和医护人员，口腔菌群失调，血源性病原体和细菌污染造成感染的直接风险。我们采用新验证的技术在模拟手术室环境中，研究是否使用双层手套，并在气管插管后立即脱去外层手套可减少这种风险。

方法：41位麻醉住院医师（培训2-4年）被纳入研究（包括个人及团体模拟）。进入模拟手术室后，住院医师行麻醉诱导及气管插管（定时约6分钟），他们并不知研究设计。22个模拟试验中，11位住院医师在气管插管时佩戴单层手套，11位佩戴双层手套并在插管完成后立即脱去外层。在模拟实验开始前，我们在模型的嘴巴及口腔涂沫荧光标记的胶体替代病原体。实验后，观察者手持紫外线灯检查手术环境的40处，来确认替代病原体是否转移到病人或病人所处环境中。佩戴双层手套的住院医师在护士的引导下于完成气管插管后立即脱去外层手套，40个潜在病原体传播地点确定并分级。

结果：两组的污染率存在临床及统计学显著差异。单层手套组污染处数量为20.3±1.4（mean±SE）;双层手套组污染处数量为5.0±0.7（P <0.001）。
BACKGROUND: Oral flora, blood-borne pathogens, and bacterial contamination pose a direct risk of infection to patients and health care workers. We conducted a study in a simulated operating room using a newly validated technology to determine whether the use of 2 sets of gloves, with the outer set removed immediately after endotracheal intubation, may reduce this risk.

METHODS: Forty-one anesthesiology residents (PGY 2-4) were enrolled in a study consisting of individual or group simulation sessions. On entry to the simulated operating room, the residents were asked to perform an anesthetic induction and tracheal intubation timed to approximately 6 minutes; they were unaware of the study design. Of the 22 simulation sessions, 11 were conducted with the intubating resident wearing single gloves, and 11 with the intubating resident using double gloves with the outer pair removed after verified intubation. Before the start of the scenario, we coated the lips and inside of the mouth of the mannequin with a fluorescent marking gel as a surrogate pathogen. After the simulation, an observer examined 40 different sites using a handheld ultraviolet light in the operating room to determine the transfer of surrogate pathogens to the patient and the patient's environment. Residents who wore double gloves were instructed by a confederate nurse to remove the outer set immediately after completion of the intubation. Forty sites of potential intraoperative pathogen spread were identified and assigned a score.

RESULTS: The difference in the rate of contamination between anesthesiology residents who wore single gloves versus those with double gloves was clinically and statistically significant. The number of sites that were contaminated in the operating room when the intubating resident wore single gloves was 20.3 ± 1.4 (mean ± SE); the number of contaminated sites when residents wore double gloves was 5.0 ± 0.7 (P < 0.001).

CONCLUSIONS: The results of this study suggest that when an anesthesiologist wears 2 sets of gloves during laryngoscopy and intubation and then removes the outer set immediately after intubation, the contamination of the intraoperative environment is dramatically reduced.

Web-Based Tailored Intervention for Preparation of Parents and Children for Outpatient Surgery (WebTIPS): Development

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背景：由于费用控制的强制，目前的门诊手术前准备程序无法应用于大多数孩子与父母。最近网上流行了一种教孩子和父母术前准备的好方法。在这篇文章中，我们主要讲述网络版门诊手术前准备的运行操作（网络小贴士）。

程序运行：一个多学科工作组认为基于网络的干预首先是由输入，矩阵，输出三大模块组成。接下来，输入的各种变量的内容，矩阵的逻辑及输出的内容是发展的。输出产品有一个大人模块和一个小孩模块，详见 http://surgerywebtips.com/about.php。小孩模块使用的准备策略是信息提供，建模，玩耍和应对技能训练。贴士的大人模块提供的策略是信息提供，应对技能训练，放松及分散注意力技能。著名的动画和网页设计公司开发出一种安全的连网产品基于上述描述。
BACKGROUND: As a result of cost-containment efforts, preparation programs for outpatient surgery are currently not available to the majority of children and parents. The recent dramatic growth in the Internet presents a unique opportunity to transform how children and their parents are prepared for surgery. In this article, we describe the development of Web-based Tailored Intervention for Preparation of parents and children undergoing Surgery (WebTIPS).

DEVELOPMENT OF PROGRAM: A multidisciplinary task force agreed that a Web-based tailored intervention consisting of intake, matrix, and output modules was the preferred approach. Next, the content of the various intake variables, the matrix logic, and the output content was developed. The output product has a parent component and a child component and is described in http://surgerywebtips.com/about.php. The child component makes use of preparation strategies such as information provision, modeling, play, and coping skills training. The parent component of WebTIPS includes strategies such as information provision, coping skills training, and relaxation and distraction techniques. A reputable animation and Web design company developed a secured Web-based product based on the above description.

CONCLUSIONS: In this article, we describe the development of a Web-based tailored preoperative preparation program that can be accessed by children and parents multiple times before and after surgery. A follow-up article in this issue of Anesthesia & Analgesia describes formative evaluation and preliminary efficacy testing of this Web-based tailored preoperative preparation program.

EN3427: A Novel Cationic Aminoindane with Long-Acting Local Anesthetic Properties

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Background: Currently approved local anesthetic drugs provide relatively simple local anesthesia, which is appropriate in some cases, even advantageous, but the duration of action is insufficient to affect clinical situations. We aimed to identify the molecules of a new local anesthetic, specifically demonstrating the potential of a long-acting drug discovery program, which targets the allosteric modulation of transient receptor potential (TRP) channels. We tested the hypothesis that cationic molecules, if they can permeate the membrane of the nerve cells, can provide a persistent anesthetic effect, as long as the neuronal access is via TRP channels. The current work describes the step from discovery of the en3427 molecule via in vivo studies in rodents to the establishment of some pain models in rats.

Method: Male SD rats were used, and acute mechanical paw and hindlimb models were characterized. Animals were tested for baseline sensitivity. Pain was induced using transcutaneous electrical nerve stimulation and von Frey filaments. Sensory thresholds were determined, and the pain model was established. Tail flick was used to measure pain. Mechanical paw paw thresholds were measured using a C-shaped paw deflection device. Pain was induced by subcutaneous injection of drugs, and mechanical paw and paw withdrawal thresholds were measured at different time points.

Results: Intravenous injection of lidocaine (2%) produced paw withdrawal pain relief, with thresholds similar to baseline values at 1 hour. Intravenous injection of en3427 (0.2%) produced analgesia that was significantly higher than baseline at 1 hour. Intravenous injection of lidocaine (2%) produced pain relief that was not significantly different from baseline at 1 hour. Intravenous injection of en3427 (0.2%) produced analgesia that was not significantly different from baseline at 1 hour.
BACKGROUND: Currently approved local anesthetic drugs provide relatively brief local anesthesia that is appropriate and even desirable in some settings, but an extended duration of action beyond their capabilities would be a distinct benefit in other clinical situations. We implemented a drug discovery program that sought to identify novel local anesthetic molecules that specifically demonstrated a long-acting, preferential action on nociceptor sensory afferents that expressed transient receptor potential (TRP) channels. The hypothesis we tested was whether relatively membrane-impermeant local anesthetic molecules could confer long-lasting anesthesia if neuronal access was facilitated by TRP channel activation. The current work describes in vivo studies on a lead molecule that emerged from the discovery program, EN3427, in several rodent pain models.

METHODS: Studies were performed on male Sprague-Dawley rats using 2 models of acute mechanical paw-pinched and pinprick-evoked nociceptive pain. Behavioral responses to noxious stimuli were assessed at baseline, that is, before any pharmacologic intervention, and at various timepoints after a single perisciatic or subcutaneous administration of either EN3427 alone or in combination with lidocaine. Paw withdrawal thresholds or cutaneous trunci reflexes were quantified, and pre-post drug values were compared statistically with analysis of variance followed by post hoc Dunnett multiple range test.

RESULTS: A single perisciatic injection of lidocaine (2%) produced relief of paw-pinched-evoked pain that was significantly different from baseline through to the 1-hour timepoint (Dunnett multiplicity-adjusted P = 0.0081), as assessed using paw withdrawal or vocalization end points. EN3427 (0.2%), in the same model, produced a long-lasting block, with pain thresholds being significantly above baseline through to the 18-hour timepoint (Dunnett multiplicity-adjusted P = 0.0002); the combination of EN3427 (0.2%) plus lidocaine (2%) produced even longer lasting analgesia, with pain thresholds being significantly above baseline through to the 24-hour timepoint (Dunnett multiplicity-adjusted P = 0.0073). Similar results were obtained with use of the pinprick approach. A single subcutaneous injection of lidocaine (2%) produced complete loss of sensation to cutaneous pinprick through 0.5 hours, but sensitivity thresholds were no different to baseline by the 1-hour timepoint, a similar injection of EN3427 alone (0.2%) produced a loss of sensation that was significantly different from baseline through the 8-hour timepoint (Dunnett multiplicity-adjusted P = 0.0045), and the combination of lidocaine (2%) plus EN3427 (0.2%) appeared to further enhance duration of analgesia, although this was significantly different from baseline only through the 10-hour timepoint (Dunnett multiplicity-adjusted P = 0.0048). Analgesic efficacy was dose related; using the combined injection approach, we found that increases in the dose of EN3427 with a fixed 2% lidocaine led to substantially extended analgesia and increasing doses of lidocaine combined with a fixed dose of EN3427 (0.2%) led to only modestly increased duration of action.

CONCLUSIONS: The present studies demonstrate that a new molecular entity, EN3427, produces effective and long-lasting analgesia in 2 rodent pain models. The analgesic effects of EN3427 are significantly longer-lasting than lidocaine and are further extended when EN3427 is combined with lidocaine. The results are discussed with respect to a possible lidocaine-mediated
TRP channel activation and facilitated neuronal access of EN3427, with subsequent entrapment conferring extended-duration efficacy.