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Malignant Hyperthermia and Muscular Dystrophies
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背景：據報導患有肌肉萎縮症（肌營養不良）的病人在全身麻醉時和麻醉後可能發生很多致命的併發症。作者對患有肌肉萎縮症的病人做了一項系統分析，旨在定義此類病人麻醉相關併發症的範疇，重點強調了惡性高熱的易感性。

方法：作者使用了多個搜尋引擎進行文獻檢索並對合適的文獻進行評價從而確定患肌肉萎縮症病人麻醉相關併發症。在所有肌肉萎縮症的類型中，Duchenne 型肌營養不良（DMD）和 Becker 型肌營養不良（BD）佔據了幾乎所有麻醉相關的報導。

結果：DMD 和 BD 病人麻醉相關併發症包括術中心力衰竭、吸入麻醉相關的橫紋肌溶解症（不用琥珀醯膽鹼）和琥珀醯膽鹼引起的橫紋肌溶解症及高鉀血症。

結論：與普通人群相比，並沒有發現 DMD 和 BD 病人增加了惡性高熱的易感性。但是，暴露於吸入麻醉藥的營養不良病人可能引起疾病相關的心臟併發症，或罕見的以橫紋肌溶解為特徵的惡性高熱相似症狀。後者也可能發生在術後。琥珀醯膽鹼可以引起致命性高鉀血症，應避免用於 DMD 和 BD 患者。

BACKGROUND: Patients with muscular dystrophy have been reported to experience a variety of life-threatening complications during and after general anesthesia. We performed a systematic analysis to define the spectrum of anesthetic-related complications in patients with muscular dystrophy, with an emphasis on malignant hyperthermia susceptibility.

METHODS: A literature search was undertaken using multiple search engines and the appropriate articles were reviewed by the authors to determine anesthetic-associated complications in patients with muscular dystrophy. Of all the types of muscular dystrophy,
Duchenne muscular dystrophy (DMD) and Becker dystrophy (BD) represent nearly all the anesthesia-related reports.

**RESULTS:** Anesthetic complications in patients with DMD and BD include intraoperative heart failure, inhaled anesthetic-related rhabdomyolysis (absence of succinylcholine), and succinylcholine-induced rhabdomyolysis and hyperkalemia.

**CONCLUSION:** We did not find an increased risk of malignant hyperthermia susceptibility in patients with DMD or BD compared with the general population. However, dystrophic patients who are exposed to inhaled anesthetics may develop disease-related cardiac complications, or rarely, a malignant hyperthermia-like syndrome characterized by rhabdomyolysis. This latter complication may also occur postoperatively. Succinylcholine administration is associated with life-threatening hyperkalemia and should be avoided in patients with DMD and BD.

**The Relationship Between Exertional Heat Illness, Exertional Rhabdomyolysis, and Malignant Hyperthermia**

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Exertional heat illness, exertional rhabdomyolysis, and malignant hyperthermia (MH) are complex syndromes with similar pathophysiology. All three are hypermetabolic states that include high demand for adenosine triphosphate, accelerated oxidative, chemical, and mechanical stress of muscle, and uncontrolled increase in intracellular calcium. Although there are no controlled clinical studies to support a relationship, there is evidence to suggest an association between unexpected heat/exercise intolerance and MH susceptibility. There are multiple case reports and a small number of clinical studies that have used *in vitro* muscle contracture testing and/or genetic testing to make the association. However, such methodology is problematic in that these tests are validated for clinical MH in association with anesthesia, and not for exertional heat illness or exertional rhabdomyolysis. Nevertheless, these relationships may have implications for some MH-susceptible patients and their capacity to exercise, as well as for clinicians treating and anesthetizing patients with histories of unexplained exertional heat and exercise illnesses.
Nitrous Oxide-Induced Analgesia Does Not Influence Nitrous Oxide's Immobilizing Requirements
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背景：氧化亞氮（N₂O）作用於脊髄上去甲腎上腺素神經元產生鎮痛，但尚不清楚這一作用是否與氧化亞氮的制動作用有關。本研究作者擬檢驗如下假設：在脊髄上去甲腎上腺素神經元選擇性清除或初次接受N₂O且鎮痛缺乏的動物（naïve animals）N₂O最低肺泡麻醉濃度（MAC）不變。

方法：研究者測定了70% N₂O、一個MACN₂O或一個MAC異氟醚下在腦室內注射抗多巴胺-β羥化酶共軛皂草素(SAP-DBH; n = 7)或對照抗體共軛皂草素(n = 5)前或後甩尾潛伏期(TFL)和後爪退縮潛伏期(HPL)。naïve animals組(n = 8) N₂O MAC在吸入N₂O25–45 min後測定（鎮痛作用高峰期），並在120–140 min（TFL和HPL恢復到基礎值後）後再測定。

結果：吸入N₂O30min後，TEL和HPL值顯著升高，但在120min內回到基礎值。接受SAP-DBH大鼠N₂O鎮痛未達到效果。然而，N₂O和異氟醚的MAC在SAP-DBH組和對照組間無顯著差異（N₂O平均值±標準差：1.7 ± 0.1 vs 1.7 ± 0.2；異氟醚：1.6 ± 0.2% vs 1.7 ± 0.2%）。naïve動物的N₂O吸入30min與120min時MAC沒有差別（1.8 ± 0.1 vs 1.8 ± 0.2%）。

結論：去除腦幹去甲腎上腺素能神經元或長期接觸N₂O將減弱其鎮痛效應，但不改變MAC。N₂O的制動作用的機制不依賴其鎮痛作用。

（陳毓雯譯 陳傑校）

BACKGROUND: Nitrous oxide (N₂O) acts on supraspinal noradrenergic neurons to produce analgesia, but it is unclear if analgesia contributes to N₂O's immobilizing effects. We tested the hypothesis that N₂O minimum alveolar anesthetic concentration (MAC) is unchanged after selective ablation of supraspinal noradrenergic neurons, or in naïve animals at N₂O exposure timepoints when analgesia is absent.

METHODS: We determined tailflick latency (TFL) and hindpaw withdrawal latency (HPL) under 70% N₂O, N₂O MAC, and isoflurane MAC before and after intracerebroventricular injections of anti-dopamine-β hydroxylase conjugated to saporin (SAP-DBH; n = 7), or a control antibody conjugated to saporin (n = 5). In a separate group of naive rats (n = 8), N₂O MAC was determined at 25–45 min after initiation of N₂O exposure (during peak analgesia) and again at 120–140 min (after TFL and HPL returned to baseline).

RESULTS: After 30 min of N₂O exposure, (TFL and HPL increased significantly but declined back to baseline within 120 min. N₂O did not produce analgesia in rats that received SAP-DBH. However, N₂O and isoflurane MAC were not significantly different between SAP-DBH and control-injected animals (Mean ± sd for N₂O: 1.7 ± 0.1 atm vs 1.7 ± 0.2 atm; isoflurane: 1.6 ± 0.2% vs 1.7 ± 0.2%). In naïve animals, N₂O MAC was not
different at the 30 min period compared with the 120 min period (1.8 ± 0.1 atm vs 1.8 ± 0.2 atm).

CONCLUSIONS: Destroying brainstem noradrenergic neurons or prolonged exposure to N₂O removes its analgesic effects, but does not change MAC. The immobilizing mechanism of N₂O is independent from its analgesic effects.

Monitoring with Head-Mounted Displays: Performance and Safety in a Full-Scale Simulator and Part-Task Trainer

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背景:頭戴式顯示器可以幫助麻醉醫師在任何時候都可以看到術中病人所監測的生命體征，即使麻醉醫師忙於操作或者無法看到監視器的時候。相關的麻醉文獻顯示使用 HMD（頭戴式顯示器）有其優點，但也有研究表明 HMD 會加重注意遲鈍（使用者很有可能因專注於顯示器而忽略眼前的其他事物），同時可能產生於焦距深度有關的知覺問題。本研究調查了兩種模擬器的差異。

方法:實驗一，研究戴上 HMD 是否會影響麻醉醫師發現病情的速度，以及 HMD 設置的不同焦距（近或遠）其結果是否會有差別。12 名麻醉醫師在三個自然場景中進行麻醉，這三個場景中均有模擬器模擬手術環境。在病人的監視器上或者手術室內出現 24 種不同的病情變化。實驗二，研究麻醉醫師由於進行操作而受到身體上的限制，使用 HMD 的麻醉醫師是否會比沒有使用 HMD 的麻醉醫師更快發現病情變化。12 名麻醉醫師在監測模擬病人生命體征的同時，要在部分任務訓練器上進行複雜的模擬臨床任務。所有的參與者在兩種場景中共會碰到 4 種不同的情況。

結果:實驗一表明戴上 HMD 或者調整設置的焦距都不會降低參與者發現病情變化的能力（包括發現病情情況的數量和時間）。總的來說，使用 HMD 後的參與者較只用標準監視器的時候會花更多的時間去看病人，更少的時間去看麻醉機、顯示器。參與者報告他們更喜歡近焦距的設置。實驗二顯示參與者使用 HMD 後發現其中 2 種病情變化的速度會更快，而另一種病情變化發現較慢。參與者使用 HMD 後去看麻醉機顯示器的頻率大大下降。使用 HMD 後，參與者表示他們沒這麼忙了，監測也更容易，而且他們相信發現異常情況變化的速度會更快。

結論: HMD 可以幫助麻醉醫師在身體受限的時候也能發現病情變化，而不是在身體不受限的時候。儘管沒有足夠的證據說明會加重不注意，但在航空方面發現，與 HMD 有關的知覺問題會影響到測試者是否能發現到情況的變化。麻醉醫師使用
BACKGROUND: Head-mounted displays (HMDs) can help anesthesiologists with intraoperative monitoring by keeping patients’ vital signs within view at all times, even while the anesthesiologist is busy performing procedures or unable to see the monitor. The anesthesia literature suggests that there are advantages of HMD use, but research into head-up displays in the cockpit suggests that HMDs may exacerbate inattentional blindness (a tendency for users to miss unexpected but salient events in the field of view) and may introduce perceptual issues relating to focal depth. We investigated these issues in two simulator-based experiments.

METHODS: Experiment 1 investigated whether wearing a HMD would affect how quickly anesthesiologists detect events, and whether the focus setting of the HMD (near or far) makes any difference. Twelve anesthesiologists provided anesthesia in three naturalistic scenarios within a simulated operating theater environment. There were 24 different events that occurred either on the patient monitor or in the operating room. Experiment 2 investigated whether anesthesiologists physically constrained by performing a procedure would detect patient-related events faster with a HMD than without. Twelve anesthesiologists performed a complex simulated clinical task on a part-task endoscopic dexterity trainer while monitoring the simulated patient’s vital signs. All participants experienced four different events within each of two scenarios.

RESULTS: Experiment 1 showed that neither wearing the HMD nor adjusting the focus setting reduced participants’ ability to detect events (the number of events detected and time to detect events). In general, participants spent more time looking toward the patient and less time toward the anesthesia machine when they wore the HMD than when they used standard monitoring alone. Participants reported that they preferred the near focus setting. Experiment 2 showed that participants detected two of four events faster with the HMD, but one event more slowly with the HMD. Participants turned to look toward the anesthesia machine significantly less often when using the HMD. When using the HMD, participants reported that they were less busy, monitoring was easier, and they believed they were faster at detecting abnormal changes.

CONCLUSIONS: The HMD helped anesthesiologists detect events when physically constrained, but not when physically unconstrained. Although there was no conclusive evidence of worsened inattentional blindness, found in aviation, the perceptual properties of the HMD display appear to influence whether events are detected. Anesthesiologists wearing HMDs should self-adjust the focus to minimize eyestrain and should be aware that some changes may not attract their attention. Future areas of research include developing principles for the design of HMDs, evaluating other types of HMDs, and evaluating the HMD in clinical contexts.

2001–2005 紐約州麻醉引起的惡性高熱的流行率

Prevalence of Malignant Hyperthermia Due to Anesthesia in New York State, 2001–2005

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BACKGROUND: Malignant hyperthermia (MH) is a pharmacogenetic syndrome that variably expresses itself on exposure to triggering agents. MH prevalence in the United States is not well documented. In this study, we assessed the prevalence of MH in New York State hospitals.

METHODS: Using New York hospital discharge data for the years 2001 through 2005, we identified all patients with a diagnosis of MH due to anesthesia using International Classification of Diseases, Ninth Revision, Clinical Modification code 995.86. MH prevalence was evaluated by demographic and clinical characteristics.

RESULTS: Of the 12,749,125 discharges from New York hospitals during the study period, 73 patients had a recorded diagnosis of MH due to anesthesia. Nearly three quarters of the MH patients were male and 71% were patients from emergency/urgent admissions. The estimated prevalence rate of MH was 0.96 (95% confidence interval [CI] 0.67–1.24) per 100,000 surgical discharges and 1.08 (95% CI 0.75–1.41) per 100,000 discharges in which there was any indication of exposure to anesthesia. The estimated prevalence of MH for males was 2.5 to 4.5 times the rate for females.

CONCLUSION: The prevalence of MH due to anesthesia in surgical patients treated in New York State hospitals is approximately 1 per 100,000. MH risk in males is significantly higher than in females.
背景：我們普遍認為病態肥胖症（MO）、阻塞性呼吸暫停（OSA）和頸圍是氣管插管的獨立危險因素。本研究中，作者試圖確定這些因素對於在經歷減肥手術的病人是否增加困難插管風險。通過測定呼吸暫停低通氣指數（AHI）、性別、頸圍和體重指數（BMI）的因素來確定阻塞性呼吸暫停（OSA）和它的嚴重程度。

方法：所有已登記的病態肥胖症病人術前描記多導睡眠圖。阻塞性呼吸暫停的嚴重程度是通過呼吸暫停低通氣指數和美國麻醉醫師協會的阻塞性呼吸暫停嚴重等級來確定。全部病人用統一標準的麻醉藥及方法，包括使用傾斜位直接喉鏡法。

結果：有180位連續病例入選，140位女性，40位男性。阻塞性呼吸暫停的發生率為68%，平均體重指數是49.4 kg/m²，平均呼吸暫停低通氣指數是31.3（範圍，0-135）。所有病人的氣管插管均未用急救氣道並由麻醉住院醫生完成。6例病人嘗試了3次及3次以上插管才成功。困難插管的發生率為3.3%，困難喉鏡暴露（Cormack and Lehane 3 級或 4 級）的發生率為8.3%。頸圍和困難氣管插管無關（優勢比 1.02, 95% 可信區間 0.93-1.11），阻塞性呼吸暫停和困難插管之間無顯著相關（P = 0.09），體重指數和困難插管之間也無顯著相關（優勢比 0.99, 95% 可信區間 0.92-1.06, P = 0.8）。插管的嘗試次數和體重指數 BMI (P = 0.8), 呼吸暫停低通氣指數 AHI (P = 0.82) 及頸圍 NC (P = 0.3)之間沒有關係。Mallampati 評級 III 或者更高預示著困難插管 (P = 0.02), 男性也是如此 (P = 0.02)。最後，Cormack and Lehane 分級與體重指數 BMI (P = 0.88)；呼吸暫停低通氣指數 AHI (P = 0.93)；阻塞性呼吸暫停 OSA (P = 0.6)無關。頸圍的增大與喉鏡暴露困難有關，但是和困難插管無關 (P = 0.02)。

結論：病態肥胖症病人斜坡位減肥手術時，困難插管或者喉鏡暴露困難和阻塞性呼吸暫停，體重指數，或者頸圍這些因素的有無及嚴重程度無關。只有 Mallampati 評分為 3 或者 4 和男性病人才預示著困難插管。

（陳靈科譯 陳傑校）

BACKGROUND: Morbid obesity (MO), obstructive sleep apnea (OSA), and neck circumference (NC) are widely believed to be independent risk factors for difficult tracheal intubation. In this study, we sought to determine whether these factors were associated with increased risk of difficult intubation in patients undergoing bariatric surgery. The predictive factors tested were OSA and its severity, as determined by apnea-hypopnea index (AHI), gender, NC, and body mass index (BMI).

METHODS: All sequentially enrolled MO patients underwent preoperative polysomnography. Severity of OSA was quantified using AHI and the American Society of Anesthesiologists’ OSA severity scale. All patients had a standardized anesthetic that included positioning in the "ramped position" for direct laryngoscopy.

RESULTS: One hundred eighty consecutive patients were recruited, 140 women and 40 men. The incidence of OSA was 68%. The mean BMI was 49.4 kg/m². The mean AHI was 31.3 (range, 0-135). All the patients’ tracheas were intubated successfully without the aid of rescue airways by anesthesiology residents. Six patients required three or more
intubation attempts, a difficult intubation rate of 3.3%. There was an 8.3% incidence of difficult laryngoscopy, defined as a Cormack and Lehane Grade 3 or 4 view. There was no relationship between NC and difficult intubation (odds ratio 1.02, 95% confidence interval 0.93-1.1), between the diagnosis of OSA and difficult intubation ($P = 0.09$), or between BMI and difficult intubation (odds ratio 0.99, 95% confidence interval 0.92-1.06, $P = 0.8$). There was no relationship between number of intubation attempts and BMI ($P = 0.8$), AHI ($P = 0.82$), or NC ($P = 0.3$). Mallampati Grade III or more predicted difficult intubation ($P = 0.02$), as did male gender ($P = 0.02$). Finally, there was no relationship between Cormack and Lehane grade and BMI ($P = 0.88$), AHI ($P = 0.93$), or OSA ($P = 0.6$). Increasing NC was associated with difficult laryngoscopy but not difficult intubation ($P = 0.02$).

CONCLUSIONS: In MO patients undergoing bariatric surgery in the "ramped position," there was no relationship between the presence and severity of OSA, BMI, or NC and difficulty of intubation or laryngoscopy grade. Only a Mallampati score of 3 or 4 or male gender predicted difficult intubation.

**PEEP 提高使用大劑量腎上腺素 CPR 大鼠模型的存活率**

Positive End-Expiratory Pressure Improves Survival in a Rodent Model of Cardiopulmonary Resuscitation Using High-Dose Epinephrine

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**背景**：多種干預措施用於心肺復蘇（CPR）的研究，以優化藥物的使用、胸外按壓和通氣功能。沒有研究顯示呼氣末正壓（PEEP）對於 CPR 結果的作用。作者推測，由於呼氣末正壓可扭轉肺不張，降低肺血管阻力，並有可能改善心輸出量，因此，CPR 中使用 PEEP 將提高存活率。

**方法**：麻醉的 Sprague-Dawley 大鼠暴露於 1 分鐘窒息心臟驟停。復蘇程式為標準化的胸部按壓、吸氧（$Fio_2 1.0$）和靜脈注射腎上腺素 30µg/kg（組 1）和 10µg/kg（組 2）。使用超聲心動圖評估左心功能（組 1），大鼠在 CPR 開始階段或者是整個復蘇過程隨機接受 5 cm H$_2$O PEEP 或 0 PEEP。存活定義為初步復蘇後，自主迴圈恢復並持續 60min 或者 120min（組 2）。

**結果**：組間基礎情況無差異。在組 1，與 0 PEEP 相比較，接受 5 cm H$_2$O PEEP ($Fio_2 1.0$ and 0.21) 可提升其存活率（7/9 and 6/6 vs 0/9, $P < 0.01$ and <0.001）。應用 5 cm H$_2$O PEEP ($Fio_2 1.0$) 能夠增加左室舒張末期容積，全身氧供和功能殘氣量。呼氣末正壓的使用並沒有影響左室收縮功能或動脈血壓。此結果差異不是因爲氧合的增加，因胞其存活率依示為 5 cm H$_2$O PEEP ($Fio_2 1.0$) vs 5 cm H$_2$O PEEP ($Fio_2 0.21$) >
BACKGROUND: Multiple interventions have been tested in models of cardiopulmonary resuscitation (CPR) to optimize drug use, chest compressions, and ventilation. None has studied the effects of positive end-expiratory pressure (PEEP) on outcome. We hypothesized that because PEEP can reverse pulmonary atelectasis, lower pulmonary vascular resistance, and potentially improve cardiac output, its use during CPR would increase survival.

METHODS: Anesthetized Sprague-Dawley rats were exposed to 1 min of asphyxial cardiac arrest. Resuscitation was standardized and consisted of chest compressions, oxygen (Fio2 1.0), and IV epinephrine 30 µg/kg (Series 1) and 10 µg/kg (Series 2). Left ventricular function was assessed by echocardiography (Series 1), and animals were randomized to receive either 5 cm H2O PEEP or zero PEEP at commencement of CPR and throughout resuscitation. Survival was defined as the presence of a spontaneous circulation 60 or 120 min (Series 2) after initial resuscitation.

RESULTS: There were no baseline differences between the groups. In Series 1, administration of 5 cm H2O PEEP (Fio2 1.0 and 0.21) was associated with improved survival compared with zero PEEP (7/9 and 6/6 vs 0/9, \(P < 0.01\) and <0.001, respectively). Application of 5 cm H2O PEEP (Fio2 1.0) increased left ventricular end-diastolic area, systemic oxygenation, and functional residual capacity. Use of PEEP during CPR did not adversely affect left ventricular systolic function or arterial blood pressure. The outcome differences were not due to increased oxygenation because the rank order of survival was 5 cm H2O PEEP (Fio2 1.0) > 5 cm H2O PEEP (Fio2 0.21) > zero PEEP (Fio2 1.0), whereas the rank order of Pao2 was 5 cm H2O PEEP (Fio2 1.0) > 5 cm H2O PEEP (Fio2 0.21) > zero PEEP (Fio2 1.0). In an additional series in which epinephrine 10 µg/kg was used (Series 2), the survival was 100% with no beneficial effects of PEEP.

CONCLUSION: In asphyxial cardiac arrest in a small rodent model, continuous application of PEEP (5 cm H2O) during and after CPR had beneficial effects on survival that were independent of oxygenation and without adverse cardiovascular effects.

BACKGROUND: 小鼠窒息心跳驟停模型，在 CPR 時間和之後持續呼氣末正壓通氣（5 cm H2O），對於存活率有提高的有益作用，且與吸入氧濃度無關，且無不良心血運效應。

(張育譯 陳傑校)
背景：從業者常常假定肥胖會增加妊娠患者神經阻滯技術的難度，但是很少有人系統地調查過與硬膜外或蛛網膜下腔阻滯相關的危險因素。作者設計這項前瞻性研究來預測妊娠患者神經阻滯技術困難的因素。

方法：使用一前瞻性、觀察表，觀察妊娠患者神經阻滯困難的多項潛在的危險因素，包括體重指數，能夠觸摸到棘突的程度，最大的背彎曲度，脊柱側凸和從業人員的經驗。用兩種方法來評估神經阻滯麻醉的難點：1）到達所需間隙的進針深度；2）從皮膚進針到蛛網膜下腔注射或硬膜外導管放置妥善所需的時間。將這些資料代入一個廣義的負誤差二項式線性模型從而決定總的進針過程的預測。神經阻滯麻醉時間的預測取決於其麻醉操作時間的線性模型。生存模型用來說明主治醫生干預住院醫生過程中的偏差。

結果：研究了427例妊娠患者的神經阻滯麻醉程式，對於進針深度和操作時間，重要的預測難點是醫生觸摸病人骨標誌的能力和病人的背彎曲程度。肥胖，即體重指數不是一個獨立的預測因數。儘管如此，肥胖的確能預測觸摸骨標誌的能力和背的彎曲度。

結論：儘管肥胖可能會導致神經阻滯困難，但一些肥胖病人令人驚訝的很容易進行神經阻滯。當進行任何一例妊娠患者尤其是肥胖產婦的神經阻滯麻醉時，背彎曲度和骨標誌的觸摸能預測神經阻滯技術的難度。

（唐穎譯 陳傑校）

BACKGROUND: Practitioners often presuppose that obesity will increase neuraxial technique difficulty in pregnant patients, but few investigators have systematically examined this population for risk factors associated with difficult epidural or spinal needle placement. We designed this study to prospectively identify factors that predict neuraxial technique difficulty in pregnant patients.

METHODS: Using a prospective, observational format, pregnant patients were examined for multiple potential risk factors for neuraxial technique difficulty, including current body mass index, ability to palpate spinous processes, maximum back flexion, scoliosis, and experience of the practitioner. Neuraxial technique difficulty was then assessed using two measures: 1) the number of needle passes needed to reach the desired space, and 2) the placement time from skin infiltration to either spinal injection or epidural catheter threading. Predictors of total needle passes were determined by fitting the data to a generalized linear model with negative binomial error. Predictors of neuraxial anesthetic time were determined by fitting a linear model to the log of neuraxial anesthetic placement time. A survival model was used to account for bias introduced when attending physicians intervened in resident physician procedures.

RESULTS: Neuraxial procedures in 427 pregnant patients were studied. For both the number of needle passes and the neuraxial anesthetic placement time, the significant predictors of difficulty were the practitioner’s ability to palpate the patient’s bony landmarks and the patient’s ability to flex her back. Obesity, as measured by body mass index, was not an independent predictor of either end point. Obesity did, however, strongly predict both the ability to palpate landmarks and flex the back.
CONCLUSIONS: Despite concerns that obesity may cause difficulty with neuraxial technique, some obese patients have surprisingly easy neuraxial block placements. When approaching any neuraxial anesthetic in a pregnant patient, and especially in the obese parturient, back flexion and landmark palpation predict neuraxial technique difficulty.

**CONCLUSIONS: 經絡與嗎啡在腹腔鏡子宮切除術後的病人靜脈自控鎮痛之比較**

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

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**背景**: 在這項研究中，作者研究了術後有內臟疼痛患者所需羥考酮和嗎啡的劑量，緩解疼痛的程度以及副作用。

**方法**: 91位行腹腔鏡子宮切除術的女患者在手術結束前接受羥考酮或嗎啡靜脈注射，並在術後 24 小時給予病人自控鎮痛術。

**結果**: 羥考酮的累積消耗量比嗎啡少（13.3 ± 10.4 mg 比 22.0 ± 13.1 mg, P = 0.001）。使用羥考酮，術後第一小時的視覺類比量表評分顯著低，但術後 24 小時的鎮靜效果差，P=0.006。

**結論**: 与嗎啡相比，羥考酮更適於緩解內臟疼痛，但不適用於鎮靜。

（鄭巧群 譯 陳傑 校）

**INTRODUCTION: 在這項研究中，我們研究了術後有內臟疼痛患者所需羥考酮和嗎啡的劑量，緩解疼痛的程度以及副作用。**

**METHODS**: Ninety-one women received IV oxycodone or morphine before the end of laparoscopic hysterectomy and then continued with patient-controlled analgesia for 24 h postoperatively.

**RESULTS**: The accumulated oxycodone consumption was less (13.3 ± 10.4 mg vs 22.0 ± 13.1 mg, P = 0.001) than morphine. With oxycodone, the visual analog scale scores were significantly lower in the first hour postoperatively and sedation was less during the 24-h postoperative period, P = 0.006.

**CONCLUSIONS**: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.

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**CONCLUSIONS**: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.
BACKGROUND: Several data suggest that both opioid and N-methyl-d-aspartate (NMDA) receptors are localized at the peripheral level, and drugs acting on these receptors may produce antinociception after topical administration; however, the antinociceptive effect of endogenous ligands at these receptors is poorly clarified. Our goal in this study was to determine the antinociceptive potency of the endogenous opioid peptide, endomorphin-1 (EM1), and the endogenous NMDA receptor antagonist, kynurenic acid (KYNA), and their interaction at the peripheral level in the rat inflamed joint model.

METHODS: Mechanical hypersensitivity was produced by injection of carrageenan (300 µg/20 µL) into the tibiotarsal joint of the right hind leg. The mechanical pain threshold was assessed by von Frey filaments (0.064-110 g). EM1 (30, 100, and 200 µg), KYNA (30, 100, 200, and 400 µg), and their combinations in a fixed-dose ratio (1:1) were injected into the inflamed joint, and the pain threshold was determined repeatedly for 75 min after the drug administrations.

RESULTS: Neither EM1 nor KYNA administered to the inflamed joint influenced the pain threshold at the noninflamed side. Both ligands produced dose-dependent antihyperalgesia, and the highest doses caused a prolonged effect. EM1 had higher potency (30% effective dose [ED30] and 50% effective dose [ED50] values were 112 µg [CI: 83-182] and 167 µg [CI: 135-220], respectively) compared
with KYNA (ED\textsubscript{30} and ED\textsubscript{50} values were 204 µg [CI: 160-251] and 330 µg [CI: 280-407], respectively). The antinociceptive effect of EM1 was prevented by subcutaneous naltrexone pretreatment. The coadministration of EM1 with KYNA caused an enhanced and/or prolonged antinociceptive effect. The ED\textsubscript{30} and ED\textsubscript{50} values of the combination were 141 µg [CI: 83-182] and 231 µg [CI: 190-293], respectively, which did not differ significantly from the theoretically additive values (ED\textsubscript{30} and ED\textsubscript{50} values were 145 µg [CI: 68-237] and 220 µg [CI: 144-230], respectively), thus the interaction between these ligands is additive. None of the treatments caused any sign of side effects.

**CONCLUSION:** Peripherally administered endogenous opioid agonist and NMDA receptor antagonist ligands might be beneficial in inflammatory pain. Because both drugs barely cross the blood-brain barrier, their local administration causes no central side effects.

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**Licking Decreases Phosphorylation of Extracellular Signal-Regulated Kinase in the Dorsal Horn of the Spinal Cord After a Formalin Test**

Taeko Fukuda, MD\*, Setsuji Hisano, PhD\†, and Makoto Tanaka, MD\*

From the *Department of Anesthesiology, Institute of Clinical Medicine, and †Laboratory of Neuroendocrinology, Institute of Basic Medical Sciences, Graduate School of Comprehensive Human Sciences, Tsukuba University, Tsukuba-city, Ibaraki, Japan. Anesth Analg 2009 109: 1318-1322.

**BACKGROUND:** Nociceptive behaviors might attenuate pain sensation. Phosphorylation of extracellular signal-regulated kinase (pERK) was recently reported to be induced by noxious stimuli in dorsal horn neurons. We investigated, in a formalin test, whether pERK of the dorsal horn is affected by licking.

**METHODS:** Twenty-four adult male rats were divided into four groups: control, formalin test, restricted control, and restricted formalin test. Ten percent formalin was

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**大鼠通過舔（Licking）後爪可減少福馬林致痛實驗後脊髓背角胞外信號調節激酶的磷酸化**

Licking Decreases Phosphorylation of Extracellular Signal-Regulated Kinase in the Dorsal Horn of the Spinal Cord After a Formalin Test

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**背景:** 傷害性行為可能減弱痛覺。最近研究表明胞外信號調節磷酸激酶（pERK）是由脊髓後角神經傷害性刺激引起的。作者研究福馬林實驗中脊髓後角的pERK是否受通過舔（licking）的影響。

**方法:** 將24只成年大鼠分為四組：對照組，福馬林致痛實驗組，活動受限對照組及活動受限福馬林致痛實驗組。福馬林致痛實驗組及活動受限福馬林致痛實驗組大鼠在其後爪皮下注射10%福馬林。對照組與福馬林致痛實驗組小鼠放置在一乾淨塑膠小室中，而活動受限對照組及活動受限福馬林致痛實驗組大鼠置於一改良制動管狀小室中。所有大鼠在25min後處死。使用免疫組化技術卵白素生物素過氧化物酶方法檢測腰椎十二節段的pERK值。

**結果:** 在活動受限福馬林致痛實驗中，患側淺層脊髓後角pERK陽性細胞數量顯著高於其它三組（P < 0.05）。福馬林致痛實驗組的pERK表達與其他兩組並無顯著性差異。

**結論:** 大鼠通過舔後爪減少福馬林致痛實驗中脊髓後角pERK的表達。這一發現表明通過舔後爪減弱了福馬林致痛實驗的疼痛。

（趙嫣紅譯 陳傑校）

**BACKGROUND:** Nociceptive behaviors might attenuate pain sensation. Phosphorylation of extracellular signal-regulated kinase (pERK) was recently reported to be induced by noxious stimuli in dorsal horn neurons. We investigated, in a formalin test, whether pERK of the dorsal horn is affected by licking.

**METHODS:** Twenty-four adult male rats were divided into four groups: control, formalin test, restricted control, and restricted formalin test. Ten percent formalin was
injected subcutaneously into the left rear paw of the formalin test and restricted formalin test groups. The control and formalin test group rats were kept in a clear plastic chamber, whereas the restricted control and restricted formalin test group rats were kept in a modified-restraint, pipe-shaped chamber. All rats were killed after 25 min. Twelve sections of the lumbar spinal cord were processed for p-ERK immunohistochemistry using the avidin-biotin peroxidase method.

**RESULTS:** The number of p-ERK positive cells in the restricted formalin test group was significantly higher than in the other three groups in the ipsilateral-side superficial dorsal horn \( (P < 0.05) \). However, there was no significant difference between the formalin test group and the two control groups in pERK expression.

**CONCLUSION:** Licking decreased pERK of the spinal cord of the formalin test group. The findings suggested that licking attenuated the pain of the formalin test.

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**The Median Effective Dose of Bupivacaine, Levobupivacaine, and Ropivacaine After Intrathecal Injection in Lower Limb Surgery**

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**Background:** Intrathecal injection is commonly used in lower limb surgery, and bupivacaine, levobupivacaine, and ropivacaine have been used as intrathecal drugs, but their relative potency is not fully established. In this study, we aimed to determine the median effective dose \( (ED_{50}) \) of these three local anaesthetics for intrathecal injection in lower limb surgery, and evaluate their relative potency.

**Methods:** Seventy-five patients undergoing lower limb surgery were randomly assigned to four groups, receiving intrathecal injection of bupivacaine or levobupivacaine or ropivacaine. The dosage of local anaesthetics was determined by the descending factorial design. Each patient received 1 mg of local anaesthetics as the initial dose, and the dosage was increased for each subsequent patient based on the successful or failed results. Intraoperative cold sensation was kept constant for 20 minutes, and the duration of surgery was up to 50 minutes, with no supplemental epidural anaesthesia. The ED_{50} was calculated using the Dixon and Massey method.

**Results:** The ED_{50} of bupivacaine was 5.5 mg (95% CI: 4.90-6.10 mg), levobupivacaine was 5.68 mg (95% CI: 4.92-6.44 mg), and ropivacaine was 8.41 mg (95% CI: 7.15-9.67 mg). The relative potency of levobupivacaine to bupivacaine was 0.97 (95% CI: 0.81-1.17), and that of ropivacaine to bupivacaine was 0.65 (95% CI: 0.54-0.80), while that of ropivacaine to levobupivacaine was 0.68 (95% CI: 0.55-0.84).
BACKGROUND: Intrathecal anesthesia is commonly used for lower limb surgery. Bupivacaine, levobupivacaine, and ropivacaine have all been used as intrathecal drugs, but their relative potency in this context has not been fully determined. In this study, we determined the median effective dose (ED$_{50}$) of these three local anesthetics for intrathecal anesthesia in lower limb surgery and hence their relative potencies.

METHODS: Seventy-five patients scheduled for lower limb surgery under combined spinal-epidural anesthesia were randomly allocated to one of three groups receiving intrathecal bupivacaine, levobupivacaine, or ropivacaine. The dose of local anesthetic was varied using up-down sequential allocation technique. The dose for the first patient in each group was 8 mg, and the dosing increment was set at 1 mg. Subsequent doses in each group were determined by the outcome in the previous patient using success or failure of the spinal anesthesia as the primary end point. A success was recorded if a bilateral T12 sensory block to cold was attained within 20 min after intrathecal injection, and the surgery proceeded successfully until at least 50 min after the intrathecal injection without supplementary epidural injection. The ED$_{50}$ was calculated using the method of Dixon and Massey.

RESULTS: The ED$_{50}$s were 5.50 mg for bupivacaine (95% confidence interval [CI]: 4.90–6.10 mg), 5.68 mg for levobupivacaine (95% CI: 4.92–6.44 mg), and 8.41 mg for ropivacaine (95% CI: 7.15–9.67 mg) in intrathecal anesthesia. The relative anesthetic potency ratios are 0.97 (95% CI: 0.81–1.17) for levobupivacaine/bupivacaine, 0.65 (95% CI: 0.54–0.80) for ropivacaine/bupivacaine, and 0.68 (95% CI: 0.55–0.84) for ropivacaine/levobupivacaine.

CONCLUSION: This study suggests that in intrathecal anesthesia for lower limb surgery, ropivacaine is less potent than levobupivacaine and bupivacaine, whereas the potency is similar between levobupivacaine and bupivacaine.

体外全血實驗發現抑制 XIII 因數會阻礙血凝形成，降低血凝塊穩定性並增加纖維蛋白溶解效應

In Vitro Inhibition of Factor XIII Retards Clot Formation, Reduces Clot Firmness, and Increases Fibrinolytic Effects in Whole Blood.
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背景：在圍手術期進行血栓彈力圖的檢查又重新引起了人們的興趣。血栓彈力圖檢查結果的主要決定因素包括凝血因數濃度（各種酶原和纖維原）和血小板計數，因此血小板抑制劑會使得主要受凝血因數影響的檢測指標變得無意義。從而使得合併應用血小板抑制劑與否的檢測結果逐漸被用於評估和檢測血液製品替代治療的效果。在本次研究中，我們評估了 XIII 因數抑制劑配伍應用糖蛋白 (GP) IIb/IIIa（血小板抑制）在全血血栓彈力圖中的效應，以及應用 XIII 因數抗體對常規檢測做一改進是否可用於檢測 XIII 因數缺乏症。

方法：正常全血會隨著非特異性抗體、抗 GPIIb/IIIa 抗體或者中性抗 XIII 因數抗體數量的增加而被孵化改變。樣本在經過組織因數啓動和血小板抑制的處理後進行分
BACKGROUND: Thrombelastography has received renewed interest in the perioperative setting. The main determinants of thrombelastographic results are coagulation factor concentrations (various zymogens and fibrinogen) and platelet count; thus, platelet inhibition renders these assays mainly coagulation factor dependent. Assays with and without platelet inhibition are thus increasingly used to trigger and monitor replacement therapy with blood products. In this study, we evaluated the effect of factor XIII inhibition and additional glycoprotein (GP) IIb/IIIa blockade on (platelet-inhibited) whole blood thrombelastography and whether a modified routine assay (using factor XIII antibody) can be used to detect factor XIII deficiency.

METHODS: Normal whole blood was incubated with increasing amounts of a nonspecific antibody, an anti-GP IIb/IIIa antibody, or a neutralizing anti-factor XIII antibody; samples were analyzed with a tissue factor-activated and platelet-inhibited whole blood thrombelastographic assay. Clotting time, clot formation time, maximum clot firmness, and clot lysis at 60 min were evaluated in triplicate. Also, 25 whole blood routine samples were evaluated for factor XIII deficiency using a new thrombelastographic assay incorporating a factor XIII antibody and using a standard factor XIII assay for comparison.

RESULTS: Although GP IIb/IIIa inhibition did not alter the results of the platelet-inhibited whole blood thrombelastography, factor XIII inhibition significantly reduced maximum clot firmness (P = 0.020) and increased clot formation time (P = 0.025) and clot lysis (P = 0.007), leaving clotting time unchanged; a ceiling effect seemed to be present with increasing antibody concentrations in whole blood (but not plasma). The thrombelastographic assay for factor XIII deficiency (<70% activity) had a 90% sensitivity and negative predictive value (area under receiver operating characteristic curve 0.803, P = 0.0015); for a deficiency <60%, sensitivity and negative predictive value were 100% (area under receiver operating characteristic curve 0.84, P = 0.0037).
CONCLUSION: Factor XIII has significant impact on platelet-inhibited activated whole blood thrombelastography. This phenomenon should be considered when interpreting thrombelastographic results in the bleeding patient, especially when the results trigger procoagulant therapy. Antibody-mediated factor XIII inhibition can be used to establish thrombelastography-based assays to detect factor XIII deficiency.

Malignant hyperthermia (MH) is a pharmacogenetic disorder of skeletal muscle in which volatile anesthetics trigger a sustained increase in intramyoplasmic $\text{Ca}^{2+}$ via release from sarcoplasmic reticulum and, possibly, entry from the extracellular milieu that leads to hypermetabolism, muscle rigidity, rhabdomyolysis, and death. Myotonias are a class of myopathies that result from gene mutations in various channels involved in skeletal muscle excitation-contraction coupling and sarcolemmal excitability, and unusual DNA sequence repeats that result in the inability of many proteins, including skeletal muscle channels that affect excitability, to undergo proper splicing. The suggestion has often been made that myotonic patients have an increased risk of developing MH. In this article, we review the physiology of muscle excitability and excitation-contraction coupling, the pathophysiology of MH and the myotonias, and review the clinical literature upon which the claims of MH susceptibility are based. We conclude that patients with these myopathies have a risk of developing MH that is equivalent to that of the general population with one potential exception, hypokalemic periodic paralysis. Despite the fact that there are no clinical reports of MH developing in patients with hypokalemic periodic paralysis, for theoretical reasons we cannot be as certain in estimating their risk of developing MH, even though we believe it is low.
Long-term propofol anesthesia is not associated with an increase in blood lactate.

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**BACKGROUND:** Lactic acidosis is considered an early sign of propofol infusion syndrome. In this study, we investigated the changes in lactate and pH with propofol versus volatile anesthesia (VA) of long duration.

**METHODS:** Demographic and intraoperative data were recorded retrospectively from the anesthesia records of patients who underwent elective spine surgery longer than 8 h. Propofol patients were matched 1:2 to VA patients, based on anesthesia time (AT) (±30 min) and blood loss (BL) (±500 mL).

**RESULTS:** Of 246 patients identified, 50 received propofol (AT = 10 ± 2 h, BL = 1955 ± 1409 mL) and were matched to 100 VA cases (AT = 10 ± 1 h, BL = 1801 ± 1543 mL), and of those, 40 and 72 patients, respectively, had complete lactate data at baseline and at 8 h after anesthesia and were included in the main analysis. The propofol group received 8.8 ± 2 mg · kg⁻¹ · h⁻¹ of propofol. The VA group age was older than the propofol group (58 ± 12 vs 51 ± 15 yr, respectively, P = 0.002), but there was no difference between the groups in gender, ASA grade, intraoperative hemodynamic variables, and use of vasopressors. After 8 h, the VA group had a larger increase in arterial lactate from baseline compared with the propofol group (change from baseline: propofol, 0.48 ± 0.72 mmol/L; VA, 1.2 ± 1.2 mmol/L, P = 0.001).
CONCLUSIONS: During prolonged spine surgery >8 h, VA was associated with higher serum lactate, when compared with propofol infusion. Prospective studies are needed to elucidate the exact mechanisms and clinical implications of this finding.

Isoflurane inhibits cyclic adenosine monophosphate response element-binding protein phosphorylation and calmodulin translocation to the nucleus of SH-SY5Y cells.

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BACKGROUND: Calmodulin (CaM) activation by Ca(2+), its translocation to the nucleus, and stimulation of phosphorylation of cyclic adenosine monophosphate response element-binding protein (CREB) (P-CREB) are necessary for new gene expression and have been linked to long-term potentiation, a process important in memory formation. Because isoflurane affects memory, we tested whether isoflurane interfered with the translocation of CaM to the neuronal cell nucleus and attenuated the formation P-CREB.

METHODS: SH-SY5Y cells, a human neuroblastoma cell line, were cultured. Cells were depolarized with KCl and the phosphorylation of CREB examined by Western blotting, enzyme-linked immunosorbant assay, and immunocytochemistry. The translocation of CaM from the cytosol to the nucleus was also examined after
depolarization. Cells were depolarized and lysed and fractionated by centrifugation to determine the amount of CaM translocated to the nucleus. CaM was localized by immunocytochemistry and quantitated by Western blotting and imaging. Before and during KCl depolarization, cells were exposed to isoflurane, isoflurane plus BΩay K 8644, nitrendipine, and Ω-conotoxin GVIa, respectively.

**RESULTS:** P-CREB increased after KCl depolarization. The increase of P-CREB peaked at depolarization duration of 30 s. The increase in P-CREB formation was inhibited by nitrendipine, but not omega-conotoxin, and by isoflurane in a concentration-dependent fashion. Pretreatment with the L-type Ca(2+) channel agonist, Bay K 8644, attenuated the inhibition of P-CREB formation by isoflurane. CaM presence in the nucleus occurred after KCl depolarization. CaM translocation was inhibited by nitrendipine and attenuated by isoflurane. Bay K 8644 pretreatment decreased the isoflurane inhibition of CaM translocation to the nucleus.

**CONCLUSIONS:** Our data demonstrate that isoflurane inhibits CaM translocation and P-CREB formation. This most likely occurs through isoflurane inhibition of Ca(2+)entry through L-type Ca(2+) channels.
BACKGROUND: Pediatric patients frequently receive continuous infusions of drugs via central venous catheters in the intensive care unit and the operating room. This study characterized drug delivery profiles in a quantitative laboratory model of a standard pediatric central venous infusion system.

METHODS: We evaluated drug delivery via a standard pediatric 8-cm, 4-F double-lumen catheter. One syringe pump infused normal saline as the carrier fluid through a limb of a Y-piece connected to the catheter's 22-gauge distal lumen. Through the other limb of the Y-piece, a second syringe pump infused methylene blue, the model drug, at a constant rate of 0.5 mL/h. The volume delivered was collected every minute for quantitative analysis. We compared 2 mL/h and 12 mL/h total flow rates to mimic volume delivery to a 3-kg infant, and priming of the Y-piece with the model drug, to mimic resumption of a stopped drug infusion, versus no priming, to mimic a new infusion. Drug pump system start-up performance was measured to estimate this factor's contribution to infusion onset profiles.

RESULTS: When initiating a new infusion of the model drug, the time to steady-state delivery at the catheter's end varied significantly among the studied scenarios as measured by the time to reach half of the targeted dose (t(50)). Onset of delivery with a low total flow was much slower (t(50) = 23.5 +/- 2.1 min) than with the high flow rate (t(50) = 15.7 +/- 2.9 min). Priming the drug limb of the connecting Y-piece with methylene blue substantially shortened the time to steady state (low flow t(50) = 12.7 +/- 0.6 min, high flow t(50) = 5.2 +/- 0.8 min). Time to cessation of drug delivery to the end of the catheter after stopping the drug pump was substantially shorter using the high carrier flow rate (t(50) = 3 +/- 0.5 min) compared with the low carrier flow rate (t(50) = 11.6 +/- 0.8 min). Drug pump system start-up performance contributed to onset delay.

CONCLUSIONS: Current infusion techniques in the pediatric care setting can result in significant, unrecognized, and potentially hazardous delays in achieving delivery of intended drug doses to the patient. Total flow rate, priming of the infusion system, the dead volume of the fluid path, and the start-up performance of the infusion pump system contribute to delays in achieving targeted rates of drug delivery.

鎮痛分娩過程中麻醉相關的併發症的流行病學研究
Epidemiology of Anesthesia-Related Complications in Labor and Delivery, New York State, 2002-2005
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背景：鎮痛分娩過程中麻醉相關的併發症的流行病學資料對於評估產科麻醉的安全性及有效性是非常有必要的，但是這方面的資料是缺乏的。在我們的這項研究中，我們對紐約醫院中產婦進行大規模的研究，旨在調查麻醉相關的併發症的流行病學情況。
BACKGROUND: Epidemiologic data on anesthesia-related complications occurring during labor and delivery are essential for measuring and evaluating the safety and quality of obstetric anesthesia care but are lacking. We aimed to fill this research gap by exploring the epidemiologic patterns and risk factors of anesthesia-related complications in a large sample of women giving birth in New York hospitals.

METHODS: Using the Healthcare Cost and Utilization Project State Inpatient Databases files, we identified all discharge records for labor and delivery from New York hospitals between 2002 and 2005. We then identified women who experienced any recorded anesthesia-related complication during labor and delivery as determined by International Classification of Diseases, Ninth Revision, Clinical Modification codes. The incidence of anesthesia-related complications was calculated by demographic and clinical characteristics. Multivariate logistic regression was performed to assess risk factors of anesthesia-related complications.

RESULTS: Of the 957,471 deliveries studied, 4438 (0.46%) had at least one anesthesia-related complication. The majority (55%) of anesthesia-related events occurring during labor and delivery were spinal complications, followed by systemic complications (43%) and overdose or adverse effects (2%). Multivariate logistic regression revealed five risk factors of anesthesia-related complications: cesarean delivery (odds ratio [OR] 2.51, 95% confidence interval [CI] 2.36-2.68), rural area (OR 1.33, 95% CI 1.21-1.46), Charlson-Deyo Comorbidity Index ≥1 (OR 1.47, 95% CI 1.28-1.69), Caucasian race (OR 1.37, 95% CI 1.24-1.52), and scheduled admission (OR 1.10, 95% CI 1.03-1.18). Anesthesia-related complications were associated with about a one-day increase in the average length of stay (3.89 ± 3.69 [mean ± sd] days vs 2.92 ± 2.38 days for deliveries without anesthesia-related complications, \( P < 0.0001 \)) and a 22-fold increased risk of maternal mortality (OR 22.26, 95% CI 11.20-44.24).

CONCLUSION: The incidence of anesthesia-related complications during labor and delivery seems to be low but remains a cause of concern, particularly in women.
undergoing cesarean delivery, living in rural areas, or having preexisting medical conditions.

**A Prediction Model for Out-of-Hospital Cardiopulmonary Resuscitation**

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**BACKGROUND:** We created a prediction model to be used in cardiopulmonary resuscitation (CPR) attempts as a decision tool to omit futile CPR attempts and to save resources.

**METHODS:** In this post hoc analysis, we assessed predictive parameters for neurological recovery after successful CPR. The original study was designed as a blinded, randomized, prospective, controlled, multicenter clinical trial.

**RESULTS:** We identified 1166 prehospital cardiac arrest patients being treated with advanced cardiac life support. Seven hundred eighty-six of 1166 patients (67.4%) died at the scene and 380 of 1166 (32.6%) were brought to the hospital. Two hundred sixty-five of 1166 patients (22.7%) died in the hospital. One hundred fifteen of 1166 (9.8%) were discharged from the hospital and 92 of the 115 patients (80%) could be followed-up. Good cerebral performance was regained by 54% of discharged patients (92/174; 72/955; 95% CI: 0.751-0.839).

**CONCLUSION:** For patients with good neurological recovery, this parameter cannot accurately predict in-hospital survival.
poor neurological recovery (9/42 = 21.4%). A score was developed to predict the probability of death using logistic regression analysis. Predicting death in the hospital revealed a sensitivity of 99.8% (953/955), but only a specificity of 2.9% (3/104; threshold 0.5). Predicting survival until discharge from the hospital revealed a sensitivity of 99% (103/104), but only a specificity of 8% (72/955; threshold 0.99). A receiver operating characteristic curve yielded an area under the curve of 0.795 (0.751-0.839) at a confidence interval of 95%.

CONCLUSION: For out-of-hospital patients with cardiac arrest, parameters documented in the field did not allow accurate prediction of hospital survival.

A Randomized Trial Comparing Colloid Preload to Coload During Spinal Anesthesia for Elective Cesarean Delivery
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BACKGROUND: Hypotension after spinal anesthesia for cesarean delivery is common. Previous studies have demonstrated that a crystalloid fluid "coload" (rapid administration of a fluid bolus starting at the time of intrathecal injection) is superior to the conventional crystalloid preload (fluid
administered before the intrathecal injection) for preventing hypotension. Colloid preload provides a sustained increase in central blood volume. We hypothesized that, in contrast to crystalloid, a colloid preload may be more effective than colloid coload for reducing the incidence of spinal anesthesia-induced hypotension.

METHODS: In this double-blind study, 178 patients were randomly assigned to receive a preload of 500 mL of hydroxyethyl starch over a period of 15–20 min before initiation of spinal anesthesia (n = 90) or an identical fluid bolus of hydroxyethyl starch starting at the time of identification of cerebrospinal fluid (n = 88). Vasopressors (ephedrine or phenylephrine) were administered if systolic arterial blood pressure decreased less than 80% of the baseline pressure and <100 mm Hg, or with smaller decreases in blood pressure if accompanied by nausea, vomiting, or dizziness. The primary outcome was the incidence of hypotension (defined as the administration of at least one dose of vasopressor).

RESULTS: There was no significant difference between the groups in the incidence of hypotension (68% in preload group and 75% in coload group, 95% confidence interval of difference –6%–20%; P = 0.28), doses of ephedrine and phenylephrine, and number of vasopressor unit doses. The incidence of severe hypotension (systolic blood pressure <80 mm Hg) was 16% in the preload group and 22% in the coload group (P = 0.30). There were no differences in the incidence of nausea and/or vomiting, or neonatal outcome between the groups.

CONCLUSION: There was no difference in the incidence of hypotension in women who received colloid administration before the initiation of spinal anesthesia compared with at the time of initiation of anesthesia. Both modalities are inefficient as single interventions to prevent hypotension.
BACKGROUND: The protective effect of sevoflurane preconditioning against spinal cord ischemia/reperfusion (I/R) is unclear. We designed this study to investigate whether sevoflurane preconditioning could induce rapid ischemic tolerance to the spinal cord in a rabbit model of transient spinal cord ischemia and how the role of extracellular signal-regulated kinase (ERK) is involved.

METHODS: To test whether preconditioning with sevoflurane induces rapid ischemic tolerance, New Zealand White male rabbits were randomly assigned to three groups. Animals in the Sev group received preconditioning with 3.7% sevoflurane (1.0 minimum alveolar anesthetic concentration) in 96% oxygen for 30 min, whereas animals in the O₂ group serving as controls inhaled only 96% oxygen for 30 min. The Sham group received the same anesthesia and surgical preparation but no preconditioning or spinal cord I/R. To evaluate the role of ERK activation in sevoflurane preconditioning, rabbits were randomly assigned to four groups. U0126, an ERK inhibitor, was administered IV 20 min before the beginning of preconditioning in the U0126 + O₂ and U0126 + Sev groups. Dimethylsulfoxide was administered IV at the same time in the vehicle + O₂ and vehicle + Sev groups. At 1 h after preconditioning, the animals were subjected to spinal cord I/R induced by infrarenal aorta occlusion. All animals were assessed at 48 h after reperfusion with modified Tarlov criteria, and the spinal cord segments (L5) were harvested for histopathological examination, TUNEL staining, and Western blot of phosphor-ERK1/2.

RESULTS: The animals in the Sev group had higher neurological scores and more normal motor neurons than those in the O₂ group (P < 0.01 for each comparison). Compared with vehicle + Sev group, the U0126 + Sev group had worse neurological outcomes, fewer viable neurons, more apoptotic neurons, and significantly decreased ERK1/2 phosphorylation (P ≤ 0.01 for each comparison). There were no significant differences in the outcomes among vehicle + O₂, U0126 + O₂, and U0126 + Sev groups.

CONCLUSIONS: This study demonstrates that sevoflurane preconditioning induces rapid tolerance to spinal cord I/R in rabbits, and the tolerance is possibly mediated through the activation of ERK. These data suggest that sevoflurane preconditioning might provide a new practical method for protecting perioperative spinal cord I/R.

Complete Freund's adjuvant-induced intervertebral discitis as an animal model for discogenic low back pain.
BACKGROUND: Although numerous animal models for low back pain associated with intervertebral disk (IVD) degeneration have been proposed, insufficient data have been provided to make any conclusions regarding pain. Our aim in this study was to determine the reliability of complete Freund's adjuvant (CFA) injection into the rat spine as an animal model representing human discogenic pain.

METHODS: We studied IVD degenerative changes with pain development after a 10-microL CFA injection into the L5-6 IVD of adult rats using behavioral, histologic, and biochemical studies. Serial histologic changes were analyzed to detect degenerative changes. Expression of calcitonin gene-related peptide (CGRP), prostaglandin E (PGE), and inducible nitric oxide synthase (iNOS) were determined using immunohistochemistry or real-time polymerase chain reaction as support data for pain development. In addition, CGRP immunoreactivity (ir) at the IVD was considered indirect evidence of neural ingrowth into the IVD.

RESULTS: There was a significant increase of the hindpaw withdrawal response in the CFA group until 7 wk postoperatively (P < 0.05). Histologic analyses revealed progressive degenerative changes of the disks without any damage in adjacent structures, including nerve roots. In the CGRP-ir staining study, the bilateral dorsal horns and IVD had positive ir after intradiscal CFA injection. CGRP mRNA expression was increased in the dorsal root ganglion (DRG) at 2 and 4 wk, whereas PGE and iNOS mRNAs were markedly increased at 2 wk. The increment of CGRP expression was higher in allodynic rats compared with nonallodynic rats.
CONCLUSION: Intradiscal CFA injection led to chronic disk degeneration with allodynia, which was suggested by pain behavior and expression of pain-related mediators. The increment of CGRP, PGE, and iNOS also suggest pain-related signal processing between the IVD and the neural pathway in this animal model. This animal model may be useful for future research related to the pathophysiology and development of novel treatment for spine-related pain.

大鼠鞘內注射嗎啡與馬普替林的協同效應
The Synergistic Interaction Between Morphine and Maprotiline After Intrathecal Injection in Rats
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背景:抗抑鬱藥物具有抑制去甲腎上腺素和/or 5-羥色胺重攝取的作用，常與阿片內聯合用於治療慢性疼痛。其增加鎮痛效果的機制尚未明確。我們使用大鼠熱撤離試驗比較鞘內注射嗎啡與非選擇性抗抑鬱藥阿米替林或選擇性抗抑鬱藥馬普替林、西他羅侖聯合使用時減弱傷害感受的效應。我們也觀察這些藥物間相互作用的可能機制。

方法:用七氟烷麻醉雄性 Wistar 大鼠，並分別向鞘內注射嗎啡、抗抑鬱藥或鹽水。給藥前後用熱撤離試驗評估減弱傷害感受效應。用最大可能效應百分比(MPE)表示撤離反應發生時間。爲了研究反應機制，所有動物均用非選擇性 α2 受體阻滯劑育亨賓和非選擇性阿片類阻滯劑納洛酮預處理。同時用等輻射分析法評估固定比例注射馬普替林和嗎啡的藥理學相互作用。

結果:單一鞘內注射嗎啡 2 µg、阿米替林 125 µg、西他羅侖 144 µg、馬普替林 1.25 µg 分別產生 51.6% ± 8.9%, 10.3% ± 3.2%, 33.8% ± 5.2% 和 48.5% ± 9.2% 的 MPE。嗎啡與阿米替林合用時減弱傷害感受效應增強至 91.3% ± 4.6% MPE，與馬普替林合用增強至 86.9% ± 9.2% MPE，而與西他羅侖合用無增強效果(40.6% ± 8.6% MPE)。馬普替林與嗎啡的減弱傷害感受時間增加4倍，由 120 分鐘增加至 480 分鐘，這一效應可被 α2 受體抑制劑育亨賓和阿片類 μ 受體拮抗劑納洛酮預處理逆轉。等輻射分析法證明了嗎啡和馬普替林的協調作用。

結論:選擇性去甲腎上腺素重攝取抑制劑通過 α2 受體抑制劑育亨賓和阿片類 μ 受體拮抗剂納洛酮能顯著增加嗎啡減弱傷害感受的強度和時間。選擇性 5-羥色胺抑制劑西他羅侖與嗎啡無此相互作用。

(朱蘭芳譯 薛張綱校)

BACKGROUND: Antidepressant drugs act as potent inhibitors of norepinephrine and/or serotonin reuptake and are widely used with opioids for the treatment of chronic pain. The mechanism of this increased analgesic action is unclear. We compared the anti-nociceptive effects of the intrathecal administration of morphine with that of a nonselective (amitriptyline) or selective (maprotiline or citalopram) antidepressant drug
using the thermal withdrawal test in rats. We also investigated the possible mechanisms involved in the interactions of these drugs.

**METHODS:** Male Wistar rats were anesthetized with sevoflurane and administered morphine and antidepressant drugs, or saline, through intrathecal injection. The antinociceptive effect was evaluated using the thermal withdrawal test before and after drug administration. The time for the withdrawal reaction was expressed as percentage of maximum possible effect (MPE). Animals were also pretreated with yohimbine (a nonselective alpha2-adrenergic antagonist) and naloxone (a nonselective opioid antagonist) for mechanism of action studies. Pharmacologic interaction was evaluated using isobolographic analysis of simultaneous administration of fixed proportions of maprotiline and morphine.

**RESULTS:** Single intrathecal administration of morphine (2 µg), amitriptyline (125 µg), citalopram (144 µg), and maprotiline (1.25 µg) produced 51.6% ± 8.9%, 10.3% ± 3.2%, 33.8% ± 5.2%, and 48.5% ± 9.2% MPE, respectively. The antinociceptive effect of morphine was increased when combined with amitriptyline (91.3% ± 4.6% MPE) and maprotiline (86.9% ± 9.2% MPE) but not with citalopram (40.6% ± 4.6% MPE). Coinadministration of maprotiline increased the antinociceptive duration of morphine by 4-fold (from 120 to 480 min), which was reversed by pretreatment with the α2-adrenoceptor inhibitor, yohimbine, and the mu-type opioid receptor antagonist, naloxone. Isobolographic analysis demonstrated a synergistic interaction between morphine and maprotiline.

**CONCLUSIONS:** Selective norepinephrine reuptake inhibitors can significantly increase the intensity and duration of morphine antinociceptive activity via both α2-adrenergic and opioid receptors. This interaction was not observed with the selective serotonin inhibitor, citalopram.
背景：在本研究中，我们评估了在静脉区域麻醉（IVRA）中加入对乙酰氨基酚对感觉和运动阻滞起效时间、止血带疼痛、和术后镇痛的影响。

方法：60名进行手部手术的患者随机且盲法地分为三组。所有组均接受静脉麻醉利多卡因（3 mg/kg）稀释至总容积40 mL。第一组接受静脉麻醉利多卡因加生理盐水，第二组接受静脉麻醉利多卡因和对乙酰氨基酚（300 mg）混合加生理盐水，第三组接受静脉麻醉利多卡因和对乙酰氨基酚（300 mg）。术中和术后阻滞生效时间和康复时间、止血带疼痛、和镇痛药使用情况被评估。手术期间，20、30和40分钟时的VAS评分显著较低（P < 0.05）。术中芬太尼使用总量分别为78 ± 12、58 ± 14、78 ± 11 µg；因止血带疼痛需要使用芬太尼的病人数量分别为13人、3人和9人。组2人数显著较少（P < 0.05）。组2术中使用芬太尼的时间间隔显著较长（分别为15 ± 6、25 ± 5、15 ± 4分钟）（P < 0.05）。组2术后VAS评分和镇痛药物使用的时间在各组中相似；组2术后使用双氯芬酸钠的总量较少（P < 0.05）。

结果：第二组运动阻滞起效时间较短，运动感觉恢复时间较长（P < 0.05）。第一组手术期间20、30和40分钟的VAS评分显著较低（P < 0.05）。组2使用双氯芬酸钠的总量较少（P < 0.05）。

结论：静脉区域麻醉时，利多卡因中加入对乙酰氨基酚可以降低止血带疼痛，提高麻醉的品质，减少术后镇痛药物使用的量。

背景：在外循环对体外循环对脑的微栓子数量和冠脉搭桥术后的认知障碍的影响

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背景：術後認知障礙（POCD）可能是冠脈搭橋術（CABG）後使患者虛弱的併發症。體外迴圈（CPB）中的腦微栓子被認為是POCD一個重要發病因素。在這個研究中，我們驗證在中國人群中不進行CPB的手術是否可以減少腦栓子的數量和CABG術後POCD的發生率。

方法：227例患者被選入這個前瞻性佇列研究。59例患者進行了CPB下的CABG手術，168例患者在不運用CPB下進行手術。腦微栓子通過雙側大腦中動脈經顱多普勒超聲檢查來持續檢測。一套神經心理學測試，包括七個試驗九個方面，在術前、術後1周和術後3月進行。POCD用國際POCD1研究的定義來進行定義。

結果：在CPB下手術患者的腦微栓子總數量的中位數為430（範圍：155－2088），不進行CPB的患者為2（0－66）(P < 0.001)。術後1周(55.2%或32/58[95%可信區間: 41.5%–68.3%]對47.0%或78/166[39.2%–54.9%], P = 0.283)和3月的POCD發生率(6.4%或3/47 [1.3%–17.5%]對13.1%或16/122 [7.7%–20.4%], P = 0.214)，進行CPB和不進行CPB手術的患者之間沒有差異。年齡的增加和較短的術後住院時間與術後1周的認知障礙獨立相關。年齡增加和有糖尿病史與術後3月認知障礙獨立相關。CPB或腦微栓子與POCD的發生沒有顯著的相關性。

結論：在中國人群中，CABG手術中不使用CPB能顯著減少腦微栓子的數量，但不能減少術後1周和3月POCD的發生。CPB和腦微栓子都不是與POCD獨立相關的風險因素。

（唐亮譯馬皓琳李士通校）

BACKGROUND: Postoperative cognitive dysfunction (POCD) can be a debilitating complication after coronary artery bypass graft (CABG) surgery. Cerebral microemboli during cardiopulmonary bypass (CPB) are believed to be an important etiologic factor of POCD. In this study, we examined whether avoidance of CPB with "off-pump" surgery reduces the number of cerebral microemboli and the incidence of POCD after CABG surgery in Chinese population.

METHODS: Two hundred twenty-seven patients were enrolled in this prospective cohort study. Fifty-nine patients underwent CABG surgery with CPB and 168 underwent off-pump surgery. Cerebral microemboli were measured continuously with bilateral transcranial Doppler ultrasonography of the middle cerebral arteries. A neuropsychological test battery that included seven tests with nine subscales was administered at baseline, as well as at 1 wk and 3 mo after surgery. POCD was defined using the international study of POCD1 definition.

RESULTS: The median total number of cerebral microemboli for the case was 430 (range: 155–2088) in patients undergoing surgery with CPB and 2 (0–66) in the off-pump patients (P < 0.001). There were no differences in the incidence of POCD between the patients having surgery with or without CPB either at 1 wk (55.2% or 32 of 58 patients [95% confidence interval: 41.5%–68.3%] vs 47.0% or 78 of 166 patients [39.2%–54.9%], P = 0.283) or 3 mo (6.4% or 3 of 47 patients [1.3%–17.5%] vs 13.1% or 16 of 122 of
patients [7.7%–20.4%, \( P = 0.214 \)] after surgery. Increasing age and shorter duration of postoperative hospital stay were independently associated with cognitive dysfunction at 1 wk after surgery. Increasing age and a history of diabetes mellitus were independently associated with cognitive dysfunction 3 mo after surgery. CPB or cerebral microemboli were not significantly related to the occurrence of POCD.

**CONCLUSIONS:** In Chinese population, avoidance of CPB during CABG surgery significantly decreased the number of cerebral microemboli, but it did not decrease the incidence of POCD at either 1 wk or 3 mo after CABG. Neither CPB nor cerebral microemboli was independently associated with the risk of POCD.

**Malignant Hyperthermia, Coexisting Disorders, and Enzymopathies: Risks and Management Options**

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Clinical episodes and abnormal laboratory tests compatible with a diagnosis of malignant hyperthermia have been observed in patients with a diversity of syndromes, enzymopathies, and coexisting disorders thereby raising the likelihood of causal associations and heightened perioperative risk in others carrying a shared diagnosis. In the present review, we survey available published series, case reports, and the results of contracture testing in patients identified by others to be potentially predisposed to malignant hyperthermia. For most conditions, evidence for a causal relationship with malignant hyperthermia susceptibility is weak. The review concludes with suggestions for clinical management when evidence for or against an association is uncertain.

**Neuromuscular Block Differentially Affects Immobility and Cortical Activation at Near–Minimum Alveolar Concentration Anesthesia**

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BACKGROUND: Anesthesia-induced immobility and cortical suppression are governed by anatomically separate, but interacting, areas of the central nervous system. Consequently, larger volatile anesthetic concentrations are required to suppress cortical activation than to abolish movement in response to noxious stimulation. We examined the effect of decreased afferent input, as produced by neuromuscular block (NMB), on immobility and cortical activation, as measured by Bispectral index (BIS) of the electrocardiogram, in the presence of noxious stimulation during approximately minimum alveolar concentrations (MACs) of desflurane anesthesia.

METHODS: The effect of NMB on the median effective end-tidal concentration of desflurane (EtDes<sub>50</sub>, or MAC<sub>tetanus</sub>) for immobility was estimated using the up-and-down method and isolated forearm technique in 24 healthy volunteers. Each volunteer sequentially received saline, mivacurium, and succinylcholine in a randomized order, while EtDes concentration during each of the treatments was determined based on the

結論：在接近於 MAC 的麻醉期間，司可林和美維庫銨增加了對體動反應的抑制。所有用藥均會引起傷害性刺激產生的小但顯著的 BIS 值增加。而司可林增加 BIS 值並不依賴於其對 EMG<sub>BIS</sub> 的影響。注射司可林增加了心血管系統的活性。有趣的是，儘管美維庫銨減弱了心血管對傷害刺激的反應，用 BIS 測定的皮層反應並沒有變化。

（黃麗娜 譯 馬皓琳 李士通 校）
movement response of the previous volunteer on the same treatment. Nonlinear mixed-effects modeling was used to evaluate the effect of NMB on BIS versus EtDes concentration relationship at baseline and after noxious stimulation, while the frontal electromyogram (EMG<sub>BIS</sub>) effect on BIS was also modeled as a covariate. Cardiovascular responses to noxious stimulation were compared across treatments.

**RESULTS:** Succinylcholine and mivacurium significantly reduced MAC<sub>tetanus</sub> (95% confidence interval) from 5.00% (4.85%–5.13%), during saline, to 4.05% (3.81%–4.29%) and 3.84% (3.60%–4.08%), respectively. Noxious stimulation significantly, although minimally, increased BIS response during all treatments. Succinylcholine increased BIS independently of an effect on EMG<sub>BIS</sub>. Succinylcholine administration increased cardiovascular activity. Interestingly, although cardiovascular reaction to the noxious event was ablated by mivacurium, cortical response, as determined by BIS, was retained.

**CONCLUSIONS:** Both succinylcholine and mivacurium enhanced immobility during near-MAC anesthesia. All treatments were associated with a small, although significant, BIS increase in response to noxious stimulation, whereas succinylcholine increased BIS independently of noxious stimulation or EMG<sub>BIS</sub>. Mivacurium suppressed autonomic response to a noxious event.

**短暫接觸七氟烷後，幹細胞樣人內皮祖細胞顯示集落形成能力增強：吸入麻醉藥對血管生成細胞的預處理**

**Stem Cell-Like Human Endothelial Progenitors Show Enhanced Colony-Forming Capacity After Brief Sevoflurane Exposure: Preconditioning of Angiogenic Cells by Volatile Anesthetics**

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**背景：**內皮祖細胞在組織修復中起關鍵作用，因此在“再生醫學”中被用於細胞的替代治療。我們檢驗麻醉藥七氟烷是否會調製這些血管生成細胞的生長或動員。

**方法：**在離體模型中，從健康捐獻者的外周血中分離出來的單核細胞用七氟烷預處理（2 vol%, 30 min 3次，間隔予30 min 空氣）。9天后在培養中測定集落形成單位，並與同期配對的未處理對照進行比較。使用磁性細胞分選法，從人臍帶血中富集 CD133+/CD34+ 的內皮祖細胞，並用即時逆轉錄多聚酶鏈式反應對七氟烷處理或未處理細胞內血管內皮生長因數（VEGF）、VEGFR2（KDR）、粒細胞集落刺激因數（G-CSF）、STAT3、c-kit 以及 CXCR4 的表達進行測定。在一個採用交叉試驗設計的志願者研究中，我們使用外周血樣流式細胞儀，檢驗吸入七氟烷（呼氣
末濃度<1 vol%）是否動員內皮祖細胞從骨髄生態位區進入迴圈。同時測定血漿中VEGF和G-CSF的水準。

結果：單核細胞體外接觸七氟烷增強CD133+/CD34+臍帶血細胞的集落形成能力並增加VEGF mRNA水準（P = 0.017）。健康志願者吸入七氟烷並不改變迴圈中CD133+/CD34+或KDR+/CD34+內皮祖細胞的數量，但增加了集落形成單位的數量（P = 0.034），而血漿中VEGF和G-CSF的水準保持不變。

結論：七氟烷預處理促使了幹細胞樣人類內皮祖細胞的生長和增殖，因此可能被用於促進圍手術期血管癒合並支持細胞替代治療。

BACKGROUND: Endothelial progenitor cells play a pivotal role in tissue repair, and thus are used for cell replacement therapies in "regenerative medicine." We tested whether the anesthetic sevoflurane would modulate growth or mobilization of these angiogenic cells.

METHODS: In an in vitro model, mononuclear cells isolated from peripheral blood of healthy donors were preconditioned with sevoflurane (3 times 30 min at 2 vol% interspersed by 30 min of air). Colony-forming units were determined after 9 days in culture and compared with time-matched untreated control. Using magnetic cell sorting, CD133+/CD34+ endothelial progenitors were enriched from human umbilical cord blood, and vascular endothelial growth factor (VEGF), VEGFR2 (KDR), granulocyte colony-stimulating factor (G-CSF), STAT3, c-kit, and CXCR4 expressions were determined in sevoflurane-treated and untreated cells by real-time reverse transcriptase polymerase chain reaction. In a volunteer study with crossover design, we tested whether sevoflurane inhalation (<1 vol% end-tidal concentration) would mobilize endothelial progenitor cells from the bone marrow niche into the circulation using flow cytometry of peripheral blood samples. VEGF and G-CSF plasma levels were also measured.

RESULTS: In vitro sevoflurane exposure of mononuclear cells enhanced colony-forming capacity and increased VEGF mRNA levels in CD133+/CD34+ cord blood cells (P = 0.017). Sevoflurane inhalation in healthy volunteers did not alter the number of CD133+/CD34+ or KDR+/CD34+ endothelial progenitors in the circulation, but increased the number of colony-forming units (P = 0.034), whereas VEGF and G-CSF plasma levels remained unchanged.

CONCLUSIONS: Sevoflurane preconditioning promotes growth and proliferation of stem cell-like human endothelial progenitors. Hence, it may be used to promote perioperative vascular healing and to support cell replacement therapies.

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背景：多路輸注裝置能夠同時輸注多種藥物，但也可能引起各投藥通路相互干擾，其原因是有效藥物的給藥速率的個體差異較大。我們在本研究中試圖闡明在多輸注治療期間多路輸注裝置屬性（死腔容量和抗反流閥[ARV]）對投藥的影響。

方法：對長度、死腔量以及有無 ARV 方面不同的輸注裝置進行評估。通過不同通路點同時輸注 3 種藥物，並通過紫外線分光亮度計分析流出液來得到其藥物濃度。評估以下參數來比較不同的輸注配置：(1) 每單位時間輸入病人體內的藥物量、(2) 輸注穩態（品質流速平臺）期間每單位時間輸入病人體內的平均藥量及(3) 流量變化效能——實驗暫態品質流率曲線下面積與對應的理論暫態品質流率曲線下面積的比值。

結果：無論流速如何變化，與高死腔量的輸注裝置（死腔量等於 6.16 mL 時流量變化效能 5.6% ± 8.2%）相比，低死腔量的輸注裝置明顯具有較高的流量變化效能（死腔量等於 0.046 mL 時開始輸注後 5 min 為 53.0% ± 15.4%）。即使存在較大死腔量，具有 ARV 的輸注裝置明顯抬高品質流率平臺（從沒有 ARV 時理論平臺的 92.4% 增加至有 ARV 時的 99.3%）。

結論：多輸注治療引起投藥干擾（輸注滯後時間，返流，單次注射量）。採用非常低死腔量和具有 ARV 的輸注裝置可以降低這種干擾。

(江繼宏 譯 馬皓琳 李士通 校)

BACKGROUND: Multiaccess infusion sets allow multiple simultaneous infusions but may induce interference in drug delivery resulting from large variations in the delivery rate of potent drugs. In this study, we sought to understand the influence of multiaccess infusion device properties (dead space volume and antireflux valve [ARV]) on drug delivery during multi-infusion therapy.

METHODS: Infusion sets differing in length, dead space volume, and presence of an ARV were assessed. Three drugs were infused simultaneously through different access points, and their concentrations were obtained using UV spectrophotometric analysis of the effluent. Different infusion configurations were compared by assessing (1) the amount of drug delivered to the patient per unit of time, (2) the mean amount of drug delivered to the patient per unit of time during the steady-state infusion (mass flow rate plateau), and (3) flow change efficiency calculated from the ratio of the area under the experimental instant mass flow rate curve to the area corresponding to theoretical instant mass flow rate curve.

RESULTS: Infusion sets with lower dead space volumes offered significantly higher flow change efficiency (53.0% ± 15.4% with a dead space volume equal to 0.046 mL 5 min after the start of infusion) than infusion sets with higher dead space volume (5.6% ± 8.2% with a dead space volume equal to 6.16 mL), whatever the flow rate changes. Even in case of large dead space volumes, the presence of an ARV significantly increased the mass flow rate plateau (from 92.4% to 99.3% of the theoretical plateau without and with the presence of an ARV, respectively).
CONCLUSIONS: Multi-infusion therapy induces perturbation in drug delivery. These perturbations (lag time, backflow, and bolus) could be reduced by using infusion sets including very low dead space volume and an ARV.

Core Myopathies and Risk of Malignant Hyperthermia

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In this article, we analyze myopathies with cores, for which an association to malignant hyperthermia (MH) has been suggested. We discuss the clinical features, the underlying genetic defects, subsequent effects on cellular calcium metabolism, and in vitro muscle responses to MH triggers. We describe in detail central core disease, multimicron core disease, and nemaline rod myopathy. We categorize the diseases according to the affected proteins and discuss the risk for MH, which is high or theoretically possible when the calcium-conducting proteins are affected.

The Relative Exposure of the Operating Room Staff to Sevoflurane During Intracerebral Surgery

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被放置在病人的嘴邊 (5cm以內)。被吸收劑吸附的七氟醚用色譜法由一名獨立的藥劑師進行定量測定。

結果：外科醫生呼吸區域吸收劑吸附的七氟醚量 (0.24 ± 0.04 ppm) 明顯低於麻醉醫生呼吸區域 (1.40 ± 0.37 ppm)，且與手術室最遠角落吸收劑吸附的七氟醚量 (0.25 ± 0.07 ppm) 相當。吸收劑吸附的七氟醚量與手術切口大小沒有相關性，即使調整了手術時間這一變數，兩者也沒有相關性。在第二個採樣系列中，病人嘴邊的吸收劑吸附了最高量的七氟醚 (1.54 ± 0.55 ppm)，其次是麻醉醫生呼吸區域 (1.14 ± 0.43 ppm) 和外科醫生呼吸區域 (0.15 ± 0.05 ppm)。

結論：外科醫生呼吸區域最接近的手術部位並不是增加七氟醚暴露的來源。我們觀察到麻醉醫生在手術室環境中暴露於七氟醚更多，這有必要深入研究。

（張瑩譯 馬皓琳 李士通校）

BACKGROUND: Our primary aim in this study was to investigate whether escape of the volatile anesthetic sevoflurane from the surgical site during craniotomy for tumor resection increases the exposure of the neurosurgeon to the anesthetic when compared with the anesthesiologist.

METHODS: Initially, the release of sevoflurane from the surgical site was measured during 35 tumorectomies starting from opening to closure of the dura. Volatile anesthetic absorbers were placed at three detection sites: 1) the surgeon’s breathing zone, 2) the anesthesiologist’s breathing zone, and 3) the farthest corner of the operation room. In the second sampling series that included 16 patients, the detector that had been in the corner of the operating room in the first series was now placed in the vicinity of the patient’s mouth (within 5 cm). Sevoflurane captured by the absorbers was quantified by an independent chemist using chromatography.

RESULTS: Absorbers in the surgeon’s breathing zone (0.24 ± 0.04 ppm) captured a significantly lower amount of sevoflurane compared with absorbers in the anesthesiologist’s breathing zone (1.40 ± 0.37 ppm) and comparable with that in the farthest corner of the operation room (0.25 ± 0.07 ppm). There was no correlation between the amount of absorbed sevoflurane and the size of craniotomy window, even when adjusting for the variation in duration of surgery. In the second series of sampling, absorbers in the proximity of the patient’s mouth captured the highest amount of sevoflurane (1.54 ± 0.55 ppm), followed by the anesthesiologist’s (1.14 ± 0.43 ppm) and the surgeon’s (0.15 ± 0.05 ppm) breathing zones.

CONCLUSIONS: The close proximity of the surgeon’s breathing zone to the craniotomy window does not appear to be a source of increased exposure to sevoflurane. The observed higher exposure of the anesthesiologist to sevoflurane in the operating room environment warrants further exploration.

The Effect of Gender on Compensatory Neuromuscular Response to Upper Airway Obstruction in Normal Subjects Under Midazolam General Anesthesia

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BACKGROUND: Upper airway patency may be compromised during sleep and anesthesia by either anatomical alterations (mechanical properties) or disturbances in the neural control (compensatory neuromuscular responses). The pathophysiology of upper airway obstruction during anesthesia may differ between men and women. Recently, we reported that the upper airway mechanical properties were comparable with those found during natural nonrapid eye movement sleep, as evaluated by measurements of passive critical closing pressure ($P_{CRIT}$) and upstream resistance ($R_{US}$) during midazolam sedation. In this study, we compared the effects of gender on compensatory neuromuscular responses to upper airway obstruction during midazolam general anesthesia.

METHOD: Thirty-two subjects (14 men and 18 women) were studied. We constructed pressure-flow relationships to evaluate $P_{CRIT}$ and $R_{US}$ during midazolam anesthesia. The midazolam anesthesia was induced with an initial dose of midazolam (0.07–0.08 mg/kg bolus) and maintained by midazolam infusion (0.3–0.4 µg · kg⁻¹ · min⁻¹), and the level of anesthesia was assessed by Ramsay score (Level 5) and Observer’s Assessment of Alertness/Sedation score (Level 2). Polysomnographic and hemodynamic variables were monitored while nasal pressure (via mask), inspiratory air flow (via pneumotachograph), and genioglossal electromyograph (EMG_GG) were recorded. $P_{CRIT}$ was obtained in both...
the passive condition, under conditions of decreased EMG (passive $P_{CRIT}$), and in an active condition, whereas EMG was increased (active $P_{CRIT}$). The difference between the active $P_{CRIT}$ and passive $P_{CRIT}$ ($\Delta P_{CRIT} = P_{A} - P_{P}$) was calculated in each subject to determine the compensatory neuromuscular response.

**RESULTS:** The difference between the active $P_{CRIT}$ and passive $P_{CRIT}$ ($\Delta P_{CRIT} = P_{A} - P_{P}$) was significantly greater in women than in men (4.6 ± 2.8 cm H2O and 2.2 ± 1.7 cm H2O, respectively; $P < 0.01$), suggesting greater compensatory neuromuscular response to upper airway obstruction independent of arousal.

**CONCLUSION:** We demonstrate that the arousal-independent compensatory neuromuscular responses to upper airway obstruction during midazolam anesthesia were partially maintained in women, and that gender may be a major determinant of the strength of compensatory responses during anesthesia.

從實驗室及理論角度分析安氟醚的皮質電效應

The Electrocortical Effects of Enflurane: Experiment and Theory

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背景：高濃度的安氟醚能引起典型的腦電圖：包括週期性抑制與大而短的突發性癲癇樣放電(PEDs)交替。在本研究中，我們比較了這種活性的理論性電腦模型與從麻醉大鼠中獲得的真實局部場電位(LFP)資料。

方法：將 8 x 8 的高密度電極植入視覺皮層後，記錄大鼠在 0.5、1.0、1.5 及 2.0 倍最小肺泡麻醉濃度(MAC)的安氟醚麻醉時 LFP 及多元峰活性。將來自於新皮層動力學平均場模型的電腦類比與這些記錄進行比較。通過延長抑制性突觸後電位(IPSP)衰減時間及數模擬增加安氟醚濃度所產生的神經元效應。與新皮層的激發率相反，我們調整了興奮性突觸後電位(EPSP)的幅。

結果：在麻醉大鼠中，安氟醚濃度的持續增加會始終引起 LFP 記錄中表現出抑制波型(>1.5 MAC)。多元電位的平均速率從 2.54/s (0.5 MAC) 下降到 0.19/s (2.0 MAC)。在高 MAC 時，大多數的多元動作電位事件變得與 PED 同步。在理論模型中，IPSP 衰減時間的延長及活性依賴 EPSP 的調整所導致的輸出結果與從實驗資料中所獲得的形態相似。通過分析方程的本征值來測定模型中節律性暴發樣活動的傾向。

結論：使用新皮層動力的平均場理論來複製安氟醚麻醉大鼠 LFP 中所觀察到的 PED 圖型是可能的。該圖型需要作一些綜合調整：適當增加 IPSP 下的總面積，延長 IPSP 衰減時間，及對 EPSP 的幅進行活性依賴的調整。

（裘毅敏譯，馬皓琳、李士通校）
BACKGROUND: High concentrations of enflurane will induce a characteristic electroencephalogram pattern consisting of periods of suppression alternating with large short paroxysmal epileptiform discharges (PEDs). In this study, we compared a theoretical computer model of this activity with real local field potential (LFP) data obtained from anesthetized rats.

METHODS: After implantation of a high-density 8 x 8 electrode array in the visual cortex, the patterns of LFP and multiunit spike activity were recorded in rats during 0.5, 1.0, 1.5, and 2.0 minimum alveolar anesthetic concentration (MAC) enflurane anesthesia. These recordings were compared with computer simulations from a mean field model of neocortical dynamics. The neuronal effect of increasing enflurane concentration was simulated by prolonging the decay time constant of the inhibitory postsynaptic potential (IPSP). The amplitude of the excitatory postsynaptic potential (EPSP) was modulated, inverse to the neocortical firing rate.

RESULTS: In the anesthetized rats, increasing enflurane concentrations consistently caused the appearance of suppression pattern (>1.5 MAC) in the LFP recordings. The mean rate of multiunit spike activity decreased from 2.54/s (0.5 MAC) to 0.19/s (2.0 MAC). At high MAC, the majority of the multiunit action potential events became synchronous with the PED. In the theoretical model, prolongation of the IPSP decay time and activity-dependent EPSP modulation resulted in output that was similar in morphology to that obtained from the experimental data. The propensity for rhythmic seizure-like activity in the model could be determined by analysis of the eigenvalues of the equations.

CONCLUSION: It is possible to use a mean field theory of neocortical dynamics to replicate the PED pattern observed in LFPs in rats under enflurane anesthesia. This pattern requires a combination of a moderately increased total area under the IPSP, prolonged IPSP decay time, and also activity-dependent modulation of EPSP amplitude.
pregabalin 300 mg 12 h apart for preventing and attenuating PLSP after laparoscopic cholecystectomy. The frequency and severity of PLSP, need for postoperative rescue analgesia, and side effect profiles were assessed for 48 h postoperatively. In both groups, the overall incidence of PLSP did not differ significantly, and the pain score for PLSP, time to first rescue analgesia, and cumulative ketorolac consumption were similar at each timepoint. However, the 2-h postoperative incidence of oversedation was higher with pregabalin.

Activation of Extracellular Signal-Regulated Kinase in Sciatic Nerve Contributes to Neuropathic Pain After Partial Sciatic Nerve Ligation in Mice
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BACKGROUND: The mitogen-activated protein kinase family plays an important role in several types of pain. However, the detailed role of phosphorylated extracellular signal-regulated kinase (pERK) in the region of injured peripheral nerve is poorly understood. In this study, we investigated whether pERK in injured sciatic nerve contributes to neuropathic pain induced by partial sciatic nerve ligation (PSL) in mice.

METHODS: Mice received PSL; pERK1/2 (p44/42) in sciatic nerve was measured by both Western blotting and immunohistochemistry. U0126 (an ERK kinase inhibitor) was
injected twice, an intraneural injection (20 nmol/2 µL) 30 min before PSL, and a perineural injection (20 nmol/10 µL) on Day 1 after PSL. Thermal hyperalgesia and tactile allodynia induced by PSL were evaluated by the thermal paw withdrawal test and the von Frey test, respectively.

RESULTS: As measured by Western blotting, in sham-operated mice, the levels of pERK1/2 in sciatic nerve were constant and the same as those in naive mice across Days 1-14. In PSL-operated mice, a significant increase in pERK1/2 was observed on Day 1 after PSL and persisted until Day 3. As measured by immunohistochemistry, immunoreactivity of pERK1/2 in PSL-operated sciatic nerve was markedly increased in comparison with that in sham-operated sciatic nerve on Day 1 after PSL. In the sciatic nerve on Day 1 after PSL, as indicated by double immunostaining, the increased immunoreactivity of pERK1/2 was colocalized with glial fibrillary acidic protein (GFAP), a marker of Schwann cells, but not F4/80, a marker of macrophages. PSL-induced thermal hyperalgesia was significantly attenuated by treatment with U0126 on Days 3, 7, and 14 after PSL. The PSL-induced tactile allodynia was also significantly attenuated by treatment with U0126 on Days 7 and 14 after PSL.

CONCLUSION: Activation of ERK in Schwann cells of the injured peripheral nervous system may play an important role in the development of neuropathic pain. Our results suggest that pERK itself and ERK-related mediators are potential therapeutic targets for the treatment of neuropathic pain.

脂肪乳剤可以改善從布比卡因引起的心搏驟停恢復，但對羅呱卡因或甲呱卡因引起的 心搏驟停無效

Lipid Emulsion Improves Recovery from Bupivacaine-Induced Cardiac Arrest, but Not from Ropivacaine- or Mepivacaine-Induced Cardiac Arrest
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BACKGROUND: Cardiac toxicity significantly correlates with the lipophilicity of local anesthetics (LAs). Recently, the infusion of lipid emulsions has been shown to be a promising approach to treat LA-induced cardiac arrest. As the postulated mechanism of action, the so-called "lipid sink" effect may depend on the lipophilicity of LAs. In this study, we investigated whether lipid effects differ with regard to the administered LAs.

METHODS: In the isolated rat heart, cardiac arrest was induced by administration of equipotent doses of bupivacaine, ropivacaine, and mepivacaine, respectively, followed by cardiac perfusion with or without lipid emulsion (0.25 mL · kg⁻¹ · min⁻¹). Subsequently, the times from the start of perfusion to return of first heart activity and to recovery of heart rate and rate-pressure product (to 90% of baseline values) were assessed.

RESULTS: In all groups, lipid infusion had no effects on the time to the return of any cardiac activity. However, recovery times of heart rate and rate-pressure product (to 90% of baseline values) were significantly shorter with the administration of lipids in bupivacaine-induced cardiac toxicity, but not in ropivacaine- or mepivacaine-induced cardiac toxicity.

CONCLUSIONS: These data show that the effects of lipid infusion on LA-induced cardiac arrest are strongly dependent on the administered LAs itself. We conclude that lipophilicity of LAs has a marked impact on the efficacy of lipid infusions to treat cardiac arrest induced by these drugs.

星狀神經節阻滯後分形心血管動力和壓力反射敏感性的狀態
Fractal Cardiovascular Dynamics and Baroreflex Sensitivity After Stellate Ganglion Block
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背景：研究現實星狀神經節阻滯可降低壓力反射的敏感性。本研究主要目的為確定心率和收縮壓變異性分形動力學（自體相似波動模式的動態改變）是否均參與了星狀神經節阻滯後壓力反射敏感性降低的機制。

方法：16名健康年輕志願者參與了本次研究。採用1%甲呱卡因6mL間隔1~1.25月對志願者行左或右星狀神經節阻滯。阻滯前，阻滯後30、60、90和120分鐘進行心率和收縮壓變異性頻譜分析。每次頻譜分析後即刻採用直立傾斜試驗評估壓力反射敏感性。

結果：經直立傾斜試驗評估，右側或左側星狀神經節阻滯後30分鐘壓力反射敏感性顯著降低（分別為1.26±0.18到0.46±0.08 bpm/mm Hg，P<0.05和1.17±0.35到0.51±0.13 bpm/min，P<0.01）。反映波動自體相似性程度的分形斜率在右側或左側星狀神經節阻滯後30分鐘顯著增加（右側星狀神經節阻滯－心率：−1.08±0.30
到 $-1.62 \pm 0.22, P < 0.01$；右星狀神經節阻滯－收縮壓：$-1.30 \pm 0.80$ 到 $-2.40 \pm 0.80, P < 0.05$；左星狀神經節阻滯－收縮壓：$-1.20 \pm 0.40$ 到 $-2.13 \pm 0.50, P < 0.05$。心率變異性分析顯示分形斜率在左星狀神經節阻滯後沒有改變。

結論：分形斜率的增加提示心率和收縮壓變異性的複雜性消失（保持複雜行爲的狀態），這是星狀神經節阻滯後壓力反射敏感性降低的機制之一。

（周雅春 譯 馬皓琳 李士通 校）

**BACKGROUND:** It has been shown that stellate ganglion block can attenuate baroreflex sensitivity. Our primary purpose in this study was to determine whether fractal dynamics (dynamic change of self-similar fluctuation patterns) of not only heart rate but also systolic blood pressure variability are involved in attenuation of baroreflex sensitivity after stellate ganglion block.

**METHODS:** Sixteen young, healthy volunteers entered the study. Spectral analysis of heart rate and systolic blood pressure variability was performed before and 30, 60, 90, and 120 min after either right or left stellate ganglion block, separated by a 1 to 1-mo interval, with 6 mL of 1% mepivacaine. Shortly after each spectral analysis, baroreflex sensitivity was assessed with the head-up tilt test.

**RESULTS:** Baroreflex sensitivity, assessed by the head-up tilt test, was significantly attenuated at 30 min after either right or left stellate ganglion block ($1.26 \pm 0.18$ to $0.46 \pm 0.08$ bpm/mm Hg, $P < 0.05$ and $1.17 \pm 0.35$ to $0.51 \pm 0.13$ bpm/min, $P < 0.01$, respectively). Fractal slopes reflecting the degree of self-similarity of fluctuations were significantly increased at 30 min after either right or left stellate ganglion block (right stellate ganglion block—heart rate; $-1.08 \pm 0.30$ to $-1.62 \pm 0.22, P < 0.01$; right stellate ganglion block—systolic blood pressure; $-1.30 \pm 0.80$ to $-2.40 \pm 0.80, P < 0.05$; left stellate ganglion block—systolic blood pressure; $-1.20 \pm 0.40$ to $-2.13 \pm 0.50, P < 0.05$). Fractal slope did not change after left stellate ganglion block with heart rate variability analysis.

**CONCLUSIONS:** Loss of complexity (status of being complex behavior) of both heart rate and systolic blood pressure variability, indicated by increased fractal slopes, is one mechanism in attenuating baroreflex sensitivity after stellate ganglion block.