

# Table of Contents

## July 2011

### Cardiovascular Anesthesiology

[圍術期收縮壓變異性是否能預測心臟手術後的死亡率？一項關於 ECLIPSE 試驗的探索性分析](#)

(陳毓雯譯 陳傑校)

#### **Does Perioperative Systolic Blood Pressure Variability Predict Mortality After Cardiac Surgery? An Exploratory Analysis of the ECLIPSE trials**

- Solomon Aronson,
- Cornelius M. Dyke,
- Jerrold H. Levy,
- Albert T. Cheung,
- Philip D. Lumb,
- Edwin G. Avery,
- Ming-yi Hu,
- and Mark F. Newman

*Anesth Analg July 2011 113:19-30; published ahead of print February 23, 2011*

[多重電極全血血小板聚集試驗、血小板功能分析儀-100 及體內出血時間在阿司匹林介導的血小板功能障礙患者術前重點照護評估中的作用](#)

(范羽譯 薛張綱校)

#### **Multiple Electrode Whole Blood Aggregometry, PFA-100, and In Vivo Bleeding Time for the Point-of-Care Assessment of Aspirin-Induced Platelet Dysfunction in the Preoperative Setting**

- Csilla Jámbor,
- Klaus-Werner von Pape,
- Michael Spannagl,
- Wulf Dietrich,
- Andreas Giebl,
- and Heike Weisser

*Anesth Analg July 2011 113:31-39; published ahead of print April 25, 2011*

[術中經食道心臟超聲介導放置主動脈內球囊反搏泵](#)

(唐亮 譯 馬皓琳 李士通 校)

### **Echo Didactics: Positioning an Intraaortic Balloon Pump Using Intraoperative Transesophageal Echocardiogram Guidance**

- Matthew A. Klopman,
- Edward P. Chen,
- and Roman M. Sniecinski

*Anesth Analg July 2011 113:40–43; published ahead of print April 5, 2011*

## **Ambulatory Anesthesiology**

[麻醉恢復室中 CYP2D6-和 CYP3A-依賴的昂丹司瓊血漿濃度具有對映體選擇性](#)

(張婷譯 陳傑校)

### **CYP2D6- and CYP3A-Dependent Enantioselective Plasma Concentrations of Ondansetron in Postanesthesia Care**

- Ulrike M. Stamer,
- Eun-Hae Lee,
- Neele I. Rauers,
- Lan Zhang,
- Maren Kleine-Brueggeney,
- Rolf Fimmers,
- Frank Stuber,
- and Frank Musshoff

*Anesth Analg July 2011 113:48–54; published ahead of print May 19, 2011*

## **Anesthetic Pharmacology**

[關於標準體重對於肥胖患者丙泊酚麻醉誘導劑量關係的研究](#)

(侯文婷譯 薛張綱校)

### **Lean Body Weight Scalar for the Anesthetic Induction Dose of Propofol in Morbidly Obese Subjects**

- Jerry Ingrande,
- Jay B. Brodsky,
- and Hendrikus J. M. Lemmens

*Anesth Analg July 2011 113:57–62; published ahead of print September 22, 2010*

[一項地氟烷與丙泊酚的對比：對超重病人術後早期肺功能的影響](#)

(張怡譯 馬皓琳 李士通校)

### **A Comparison of Desflurane Versus Propofol: The Effects on Early Postoperative Lung Function in Overweight Patients**

- M. Zoremba,
- F. Dette,
- T. Hunecke,
- L. Eberhart,
- S. Braunecker,
- and H. Wulf

*Anesth Analg July 2011 113:63–69; published ahead of print October 21, 2010*

[通過七氟醚濃度和腦電雙頻指數間滯後效應的測量證實肥胖不影響七氟起效和失效時間](#)

(孫曉瓊譯 陳傑校)

### **Obesity Does Not Influence the Onset and Offset of Sevoflurane Effect as Measured by the Hysteresis Between Sevoflurane Concentration and Bispectral Index**

- Luis I. Cortínez,
- Pedro Gambús,
- Iñaki F. Trocóniz,
- Ghislaine Echevarría,
- and Hernán R. Muñoz

*Anesth Analg July 2011 113:70–76; published ahead of print May 19, 2011*

## **Technology, Computing, and Simulation**

[健康個體中交感神經阻斷對手指光學體積描記圖和手指溫度的影響](#)

(黃劍譯 薛張綱校)

### **The Effects of Sympathectomy on Finger Photoplethysmography and Temperature Measurements in Healthy Subjects**

- Pekka Talke,
- Amir Snapir,
- and Matti Huiku

*Anesth Analg July 2011 113:78–83; published ahead of print April 25, 2011*

[麻醉前準備程式的疏漏步驟](#)

(劉朝輝譯，馬皓琳，李士通校)

### **Missed Steps in the Preanesthetic Set-Up**

- Samuel Demaria, Jr.,
- Kimberly Blasius,
- and Steven M. Neustein

*Anesth Analg July 2011 113:84–88; published ahead of print April 5, 2011*

## **Patient Safety**

[胃部超聲檢查在禁食外科患者中的應用：一項前瞻性描述性研究](#)

(陸秉璋譯 陳傑校)

### **Gastric Sonography in the Fasted Surgical Patient: A Prospective Descriptive Study**

- Anahi Perlas,
- Liisa Davis,
- Masood Khan,
- Nicholas Mitsakakis,
- and Vincent W. S. Chan

*Anesth Analg July 2011 113:93–97; published ahead of print May 19, 2011*

[克-特二氏綜合征患者行手術的麻醉管理：一項 136 例的綜述](#)

(劉珏瑩譯 薛張綱校)

### **Anesthesia for Surgery Related to Klippel–Trenaunay Syndrome: A Review of 136 Anesthetics**

- David W. Barbara and
- Jack L. Wilson

*Anesth Analg July 2011 113:98–102; published ahead of print April 5, 2011*

[用於直接喉鏡檢查的頭頸部位置](#)

(安光惠譯 馬皓琳 李士通校)

### **Review Article: Head and Neck Position for Direct Laryngoscopy**

- Mohammad El–Orbany,
- Harvey Woehlck,
- and M. Ramez Salem

*Anesth Analg July 2011 113:103–109; published ahead of print May 19, 2011*

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

[羥乙基澱粉（130kD）抑制脂多糖激發的小鼠肺臟 Toll 樣受體 4 信號轉導通路](#)

(趙嫣紅譯 陳傑校)

### **Hydroxyethyl Starch (130 kD) Inhibits Toll-Like Receptor 4 Signaling Pathways in Rat Lungs Challenged with Lipopolysaccharide**

- Jie Tian,
- Yunxia Wang,
- Zhengyu He,
- Yuan Gao,
- Joyce E. Rundhaug,
- and Xiangrui Wang

*Anesth Analg July 2011 113:112–119; published ahead of print March 17, 2011*

[毛細血管再充盈時間：這還是一個有用的臨床標誌？](#)

(陸麗虹譯 薛張綱校)

### **Medical Intelligence Article: Capillary Refill Time: Is It Still a Useful Clinical Sign?**

- Amelia Pickard,
- Walter Karlen,
- and J. Mark Ansermino

*Anesth Analg July 2011 113:120–123; published ahead of print April 25, 2011*

## **Obstetric Anesthesiology**

[在產科中用於硬膜外血斑的血量：一項隨機、盲法臨床試驗](#)

(陳彬彬 譯 馬皓琳 李士通 校)

### **The Volume of Blood for Epidural Blood Patch in Obstetrics: A Randomized, Blinded Clinical Trial**

- Michael J. Paech,
- Dorota A. Doherty,
- Tracey Christmas,
- Cynthia A. Wong,

- and Epidural Blood Patch Trial Group

*Anesth Analg July 2011 113:126–133; published ahead of print May 19, 2011*

## **Pediatric Anesthesiology**

[雞蛋過敏的兒童對丙泊酚的過敏反應](#)

(周姝婧譯 陳傑校)

### **Allergic Reactions to Propofol in Egg-Allergic Children**

- Andrew Murphy,
- Dianne E. Campbell,
- David Baines,
- and Sam Mehr

*Anesth Analg July 2011 113:140–144; published ahead of print April 5, 2011*

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

[麻醉藥異氟醚對缺氧誘導的含半胱氨酸的天冬氨酸蛋白水解酶 3 啟動和  \$\beta\$  位澱粉樣前體蛋白裂解酶增加潛在的雙重作用](#)

(任雲譯 薛張綱校)

### **The Potential Dual Effects of Anesthetic Isoflurane on Hypoxia-Induced Caspase-3 Activation and Increases in $\beta$ -Site Amyloid Precursor Protein-Cleaving Enzyme Levels**

- Chuxiong Pan,
- Zhipeng Xu,
- Yuanlin Dong,
- Yiyang Zhang,
- Jun Zhang,
- Sayre McAuliffe,
- Yun Yue,
- Tianzuo Li,
- and Zhongcong Xie

*Anesth Analg July 2011 113:145–152; published ahead of print April 25, 2011*

[活性氧清除劑抑制大鼠短暫局灶性腦缺血-再灌注損傷後 SATA3 活化](#)

(江繼宏 譯 馬皓琳 李士通 校)

**Reactive Oxygen Species Scavenger Inhibits STAT3 Activation After Transient Focal Cerebral Ischemia–Reperfusion Injury in Rats**

- Chong Lei,
- Jiao Deng,
- Bairen Wang,
- Dandan Cheng,
- Qianzi Yang,
- Hailong Dong,
- and Lize Xiong

*Anesth Analg July 2011 113:153–159; published ahead of print April 27, 2011*

## **Analgesia**

### **Pain Mechanisms**

[神經肽通過調節角質細胞白介素-1 \$\beta\$ 的產生導致周圍神經痛覺過敏](#)

(黃丹譯 陳傑校)

**Neuropeptides Contribute to Peripheral Nociceptive Sensitization by Regulating Interleukin-1 $\beta$  Production in Keratinocytes**

- Xiaoyou Shi,
- Liping Wang,
- Xiangqi Li,
- Peyman Sahbaie,
- Wade S. Kingery,
- and J. David Clark

*Anesth Analg July 2011 113:175–183; published ahead of print May 19, 2011*

[對嗎啡耐藥的小鼠鞘內注射依那西普能減低谷氨酸能傳遞途徑，從而部分恢復嗎啡的抗傷害性刺激的作用。](#)

(翁梅琳譯 薛張綱校)

**Intrathecal Etanercept Partially Restores Morphine's Antinociception in Morphine-Tolerant Rats via Attenuation of the Glutamatergic Transmission**

- Ching–Hui Shen,
- Ru–Yin Tsai,
- Yueh–Hwa Tai,

- Shinn-Long Lin,
- Chih-Cheng Chien,
- and Chih-Shung Wong

*Anesth Analg July 2011 113:184-190; published ahead of print April 13, 2011*

[美金剛對大鼠浸潤性皮膚鎮痛的局部麻醉作用](#)

(瞿亦楓 譯 馬皓琳 李士通 校)

**The Local Anesthetic Effect of Memantine on Infiltrative Cutaneous Analgesia in the Rat**

- Yu-Wen Chen,
- Chin-Chen Chu,
- Yu-Chung Chen,
- Jhi-Joung Wang,
- and Ching-Hsia Hung

*Anesth Analg July 2011 113:191-195; published ahead of print April 27, 2011*

## **Regional Anesthesia**

[簡報:蛛網膜下腔阻滯的評價：一項包括 175 篇文獻以及改進意見的調查](#)

(懷曉蓉譯 陳傑校)

**Brief Reports: An Assessment of Subarachnoid Block: A Survey of 175 Articles and Recommendations for Improvement**

- Argyro Fassoulaki,
- Konstantinos Chondrogiannis,
- and Anteia Paraskeva

*Anesth Analg July 2011 113:196-198; published ahead of print April 25, 2011*

[臂叢阻滯在術中對氧平衡的影響](#)

(張玥琪譯，薛張綱校)

**Brief Reports: Influence of Brachial Plexus Blockade on Oxygen Balance During Surgery**

- David B. Lumenta,
- Werner Haslik,
- Harald Beck,
- Andreas Pollreisz,



- Harald Andel,
- and Manfred Frey

*Anesth Analg July 2011 113:199-201; published ahead of print April 27, 2011*

### 術中經食道心臟超聲介導放置主動脈內球囊反搏泵

#### **Positioning an Intraaortic Balloon Pump Using Intraoperative Transesophageal Echocardiogram Guidance**

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*Anesth Analg July 2011 113:40-43*

一名射血分數 25% 的 72 歲老年男性計畫在體外迴圈下擇期行擇期性冠狀動脈搭橋術。由於手術的高風險性，外科醫生想在體外迴圈開始前置入主動脈內球囊反搏泵 (IABP)。需要術中食道心臟超聲 (TEE) 以確保放置在正確的位置。

(唐亮 譯 馬皓琳 李士通 校)

A 72-year-old man with an ejection fraction of 25% is scheduled to undergo elective coronary artery bypass graft using cardiopulmonary bypass. Because of the high-risk nature of the operation, the surgeon wants to insert an intraaortic balloon pump (IABP) before initiating cardiopulmonary bypass. An intraoperative transesophageal echocardiogram (TEE) is requested to ensure correct placement.

### 一項地氟烷與丙泊酚的對比：對超重病人術後早期肺功能的影響

#### **A Comparison of Desflurane Versus Propofol: The Effects on Early Postoperative Lung Function in Overweight Patients**

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**背景：**在這項研究中，我們評估並比較了丙泊酚與地氟烷麻醉對超重病人術後肺功能和脈搏血氧飽和度值的影響。

**方法：**我們前瞻性地研究了 134 名體重指數在 25 到 35 kg/m<sup>2</sup> 之間並正在進行持續 40 到 120 分鐘的小型外周手術病人。病人被隨機分配接受丙泊酚 (全靜脈麻醉) 或經氣管導管的地氟烷麻醉，控制腦電雙頻指數在 40 到 60 之間。術前用藥、輔助藥物使用和通氣經過標準化。我們測定了術前 (基線) 和氣管導管拔出後 10 分鐘、0.5 小時、2 小時和 24 小時的血氧飽和度和肺功能。所有數值測定時病人均處於仰臥且頭抬高 30° 體位。與術前基線數值比較的變化首先使用單變數方法分析體重指數和麻醉方式不同的影響，然後用線性回歸和多元方差分析。

**結果：**在術後 2 小時內，丙泊酚組相對地氟烷組表現出較低的血氧飽和度（2 小時，平均值±標準差，93.8% ± 2.0%比 94.6% ± 2.1%； $P < 0.007$ ）和肺功能（用力肺活量、第一秒用力呼氣量[FEV<sub>1</sub>]、呼氣峰流量、呼氣中流量[MEF]、用力吸氣肺活量和吸氣峰流量；在丙泊酚組相對基線有 11%至 20%的較大減少，所有  $P < 0.001$ ）。甚至術後 24 小時，FEV<sub>1</sub>、呼氣峰流量、MEF、用力吸氣肺活量和吸氣峰流量在丙泊酚組也降低更多（所有指標  $P < 0.01$ ）。在拔管後 2 小時，肥胖程度加重使丙泊酚而非地氟烷麻醉的病人 FEV<sub>1</sub>和 MEF 降低（ $P < 0.01$ ）。

**結論：**我們推斷，對於最長達 120 分鐘的表淺手術過程，使用丙泊酚維持麻醉對術後早期肺功能和血氧飽和度的損害較使用地氟烷大。而且，體重增加會降低丙泊酚麻醉術後 2 小時的肺功能，但地氟烷麻醉不會。

（張怡譯 馬皓琳 李士通校）

**BACKGROUND:** In this study, we evaluated the influence of propofol versus desflurane anesthesia in overweight patients on postoperative lung function and pulse oximetry values.

**METHODS:** We prospectively studied 134 patients with body mass indices of 25 to 35 kg/m<sup>2</sup> undergoing minor peripheral surgery lasting 40 to 120 minutes. Patients were randomly assigned to receive propofol (total IV anesthesia) or desflurane anesthesia via a tracheal tube targeting bispectral index values of 40 to 60. Premedication, adjuvant drug usage, and ventilation were standardized. We measured oxyhemoglobin saturation and lung function preoperatively (baseline), and at 10 minutes, 0.5 hour, 2 hours, and 24 hours after tracheal extubation. All values were measured with the patient supine, in a 30° head-up position. Changes from preoperative baseline values were first analyzed for the impact of body mass index and type of anesthesia using univariate methods, followed by linear regression and multivariate analysis of variance.

**RESULTS:** Within the first 2 hours after surgery, the propofol group displayed lower oxyhemoglobin saturation (at 2 hours, mean ± SD, 93.8% ± 2.0% vs 94.6% ± 2.1%;  $P < 0.007$ ) and lung function (forced vital capacity, forced expiratory volume exhaled in 1 second [FEV<sub>1</sub>], peak expiratory flow, midexpiratory flow [MEF], forced inspiratory vital capacity, and peak inspiratory flow; between 11% and 20% larger reduction from baseline in the propofol group, all  $P < 0.001$ ) compared with the desflurane group. Even 24 hours after surgery, FEV<sub>1</sub>, peak expiratory flow, MEF, forced inspiratory vital capacity, and peak inspiratory flow were reduced more in the propofol group (all  $P < 0.01$ ). At 2 hours after extubation, increasing obesity was associated with decreasing FEV<sub>1</sub> and MEF in patients anesthetized with propofol but not desflurane ( $P < 0.01$ ).

**CONCLUSION:** We conclude that, for superficial surgical procedures of up to 120 minutes, maintenance of anesthesia with propofol impairs early postoperative lung function and pulse oximetry values more than with desflurane. Furthermore, increasing obesity decreases pulmonary function at 2 hours after propofol anesthesia but not after desflurane anesthesia.

### 麻醉前準備程式的疏漏步驟

#### Missed Steps in the Preanesthetic Set-Up

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**背景：**麻醉醫師在誘導麻醉時快速完成許多工作。誘導準備的關鍵需要最大化患者的安全。考慮到手術室緊張的環境，準備步驟因為無意識或甚至可能有意為了節約時間而疏漏。我們做這研究來探究在手術室中誘導前即刻遺失步驟的發生率。

**方法：**在本研究中，我們用一個修正的麻醉程式來隨機核實 200 個外科手術在麻醉誘導前可能的疏漏步驟。另外記錄多種其他手術房間/病例變數來探測疏漏步驟與某些變數（例如手術房間病例負荷和區域與全身麻醉比較）是否存在相關性。

**結果：**我們發現 23 個疏漏步驟。手動復蘇裝置可用性和一個處於工作狀態的吸引器配備是最常見的疏漏步驟。計畫的麻醉方法為區域麻醉的病例、在具有較多手術負荷（ $\geq 5$  個計畫手術）的手術房間中以及在主治麻醉醫師完成配備的手術房間中疏漏步驟的發生率較高。

**結論：**疏漏步驟確實有顯著且可測量的發生率。我們需要採取降低疏漏步驟數量的措施來改善患者的安全。

（劉朝輝譯，馬皓琳，李士通校）

**BACKGROUND:** Anesthesiologists accomplish many tasks rapidly during induction of an anesthetic. Key preparation for induction is needed to maximize patient safety. Given the intense environment of the operating room, preparatory steps may be missed either unintentionally or possibly even intentionally to save time. We conducted this study to determine the incidence of missed steps in the operating room immediately before induction.

**METHODS:** In this study, 200 surgical procedures were randomly checked for missed steps before induction of anesthesia using a “Revised Preanesthetic Set-Up.” Additionally, multiple other operating room/case variables were recorded to determine whether there was correlation between the missed steps and certain variables such as room case load and regional versus general anesthesia.

**RESULTS:** Twenty-three missed steps were discovered. Manual resuscitation device availability and a working suction set-up were the most frequently missed steps. A higher percentage of missed steps was found in cases in which regional was the planned anesthesia technique, in rooms with higher case loads ( $\geq 5$  cases scheduled), and in rooms that attending anesthesiologists completed the set-up.

**CONCLUSIONS:** Missed steps do occur at a significant and measurable rate. Measures need to be taken to decrease the number of missed steps to improve patient safety.

### 用於直接喉鏡檢查的頭頸部位置

#### Head and Neck Position for Direct Laryngoscopy

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嗅花位（SP）歷來被認為是直接喉鏡檢查（DL）的最佳頭位。但是它相對於其他頭位的優勢近十年來一直受到質疑。我們回顧了有關這一主題的稀有文獻，來檢查支持或者反對嗅花位常規使用的證據。為了避免對於什麼是合適的嗅花位產生混淆以及便於比較從不同研究得到的結果，必須使用一個嗅花位的標準定義（如頸屈 35°和頭伸 15°）。雖然有人提出一些理論來解釋嗅花位優越性，但是三軸成一線理論仍然被認為是有充分根據的解剖學解釋。為了達到想得到的頸部前屈位元，需要將頭抬高，但是由於頭頸部的解剖和胸廓的大小不同，每個人頭部抬高的程度都不一樣。比如，對於嬰幼兒就不需要抬高頭位元，因為頭的大小和形狀的關係，在水平頭位時三軸就很接近。胸骨與外耳道水準對齊可以作為肥胖以及非肥胖患者嗅花位元的定位標記。對於所能獲得的文獻的分析是支持直接喉鏡時採用嗅花位。在肥胖病人，為了達到合適的嗅花位，應該採用“斜坡”（或背部抬高）體位。嗅花位不能保證對於所有的患者都暴露充分，因為有很多其他解剖因素會影響暴露的最終分級。但是，嗅花位應該作為直接喉鏡檢查的初始頭位，因為這個體位提供了暴露充分的最佳機會。為了達到合適的體位，必須要注重調整體位時的細節，避免小的技術失誤。操作直接喉鏡檢查應該是不斷修正的過程，在嗅花位元遇到暴露困難的情況下應該調整體位元。

(安光惠譯 馬皓琳 李士通校)

The sniffing position (SP) has traditionally been considered the optimal head position for direct laryngoscopy (DL). Its superiority over other head positions, however, has been questioned during the last decade. We reviewed the scarce literature on the subject to examine the evidence either in favor or against the routine use of the SP. A standard definition for the position should be used (e.g., 35° neck flexion and 15° head extension) to avoid confusion about what constitutes a proper SP and to compare the results from different studies. Although several theories were proposed to explain the superiority of the SP, the three axes alignment theory is still considered a valid anatomical explanation. Although head elevation is needed to achieve the desired neck flexion, the elevation height may vary from one patient to another depending on head and neck anatomy and size of the chest. In infants and small children, for example, no head elevation is needed because the size and shape of the head allow axes approximation in the head-flat position. Horizontal alignment of the external auditory meatus with the sternum, in both obese and non-obese patients, indicates, and can be used as a marker for, proper positioning. Analysis of the available literature supports the use of the SP for DL. To achieve a proper SP in obese patients, the “ramped” (or the back-up) position should be used. The SP does not guarantee adequate exposure in all patients, because many other anatomical factors control the final degree of visualization. However, it should be the starting head position for DL because it provides the best chance at adequate exposure. Attention to details during positioning and avoidance of minor technical errors are essential to achieve the proper position. DL should be a dynamic procedure and position adjustment should be instituted in case poor visualization is encountered in the SP.

**在產科中用於硬膜外血斑的血量：一項隨機、盲法臨床試驗**

**The Volume of Blood for Epidural Blood Patch in Obstetrics: A Randomized, Blinded Clinical Trial**

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**背景：**此項多國、多中心、隨機、盲法試驗的目的在於確定用於硬膜外血斑的自體血 3 種容量中的最適容量。

**方法：**在硬膜外置管過程中非故意硬膜穿破後需行硬膜外血斑的產科患者，分別注入 15、20 或 30mL 血液，根據硬膜外血斑的時間和中心分組。隨訪受試者 5 天。主要研究指標為頭痛持續或部分緩解的合成，次要指標包括頭痛持續緩解、部分緩解、持續頭痛的嚴重性以及操作過程中和操作後的腰痛。

**結果：**121 例女性患者完成了本試驗。容量的中位數（四分位數間距）為 15（15-15）、20（20-20）和 30（22-30）mL，15、20 和 30mL 組分別有 98%、81% 和 54% 的患者接受了安排的容量。三組頭痛持久或部分緩解率分別為 61%、73% 和 67%，頭痛完全緩解率為 10%、32% 和 26%。15mL 組的 0-48 小時內頭痛評分—時間曲線下面積最大。硬膜外血斑操作過程中和操作後的腰痛發生率各組相似，且程度較輕，但是 15mL 組操作後腰痛評分最高。未出現嚴重併發症。

**結論：**儘管硬膜外血斑的最適容量仍需要進一步確定，我們相信以上發現提示，在治療產科患者硬膜穿破後頭痛時，可嘗試給予 20mL 自體血。

（陳彬彬 譯 馬皓琳 李士通 校）

**BACKGROUND:** Our aim in this multinational, multicenter, randomized, blinded trial was to determine the optimum of 3 volumes of autologous blood for an epidural blood patch.

**METHODS:** Obstetric patients requiring epidural blood patch after unintentional dural puncture during epidural catheter insertion were allocated to receive 15, 20, or 30 mL of blood, stratified for the timing of epidural blood patch and center. Participants were followed for 5 days. The primary study end point was a composite of permanent or partial relief of headache, and secondary end points included permanent relief, partial relief, persisting headache severity, and low back pain during or after the procedure.

**RESULTS:** One hundred twenty-one women completed the study. The median (interquartile range) volume administered was 15 (15–15), 20 (20–20), and 30 (22–30) mL, with 98%, 81%, and 54% of groups 15, 20, and 30 receiving the allocated volume. Among groups 15, 20, and 30, respectively, the incidence of permanent or partial relief of headache was 61%, 73%, and 67% and that of complete relief of headache was 10%, 32%, and 26%. The 0- to 48-hour area under the curve of headache score versus time was highest in group 15. The incidence of low back pain during or after the epidural blood patch was similar among groups and was of low intensity, although group 15 had the highest postprocedural back pain scores. Serious morbidity was not reported.

**CONCLUSIONS:** Although the optimum volume of blood remains to be determined, we believe these findings support an attempt to administer 20 mL of autologous blood when

treating postdural puncture headache in obstetric patients after unintentional dural puncture.

### 活性氧清除劑抑制大鼠短暫局灶性腦缺血-再灌注損傷後 STAT3 活化

#### Reactive Oxygen Species Scavenger Inhibits STAT3 Activation After Transient Focal Cerebral Ischemia–Reperfusion Injury in Rats

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**背景：**已證實信號傳導子及轉錄啟動子 3 (STAT3) 在缺血性腦組織中被活化。然而，腦缺血-再灌注後 STAT3 活化的機制及其作用還不甚明瞭。本研究中，我們試圖驗證這一假設：腦缺血-再灌注後 STAT3 的活化與活性氧 (ROS) 的產生相關。

**方法：**採用阻斷成年雄性 SD 大鼠大腦中動脈法建立局灶性腦缺血模型。用免疫組織化學和蛋白質免疫印跡法評估 STAT3 活化程度。通過大鼠持續性缺血或缺血-再灌注來明確 STAT3 活化的時間分佈特性。給予 ROS 清除劑二甲叉三脲 (DMTU) 來評估 ROS 在誘導 STAT3 活化中起的作用。採用神經行為學評分和計算腦梗死體積法評估 DMTU 及 STAT3 活化抑制劑 AG490 對腦缺血損傷的影響。

**結果：**大腦中動脈阻斷後缺血組織周圍範圍內神經元和星形膠質細胞 STAT3 的活化明顯增加。STAT3 活化主要發生在再灌注時相而不是缺血相。此外，DMTU 以劑量依賴性方式抑制 STAT3 活化，提示 STAT3 活化或許是 ROS 產生後的繼發性事件。DMTU 和 AG490 明顯減少梗死面積且改善神經系統結果。

**結論：**相比缺血，再灌注能更強地刺激 STAT3 活化。ROS 清除與 STAT3 活化的抑制緊密相關。通過 ROS 的清除和 STAT3 活化的下調可達到神經保護作用。

(江繼宏 譯 馬皓琳 李士通 校)

**BACKGROUND:** Signal transducer and activator of transcription 3 (STAT3) activation in ischemic brain has been verified. However, the mechanism and the role of STAT3 activation after cerebral ischemia–reperfusion are poorly elucidated. In the present study, we sought to test the hypothesis that STAT3 activation after cerebral ischemia–reperfusion was related to reactive oxygen species (ROS) production.

**METHODS:** Adult male Sprague–Dawley rats were subjected to focal cerebral ischemia induced by middle cerebral artery occlusion. STAT3 activation was evaluated by immunohistochemistry and Western blotting. Rats were subjected to permanent ischemia or ischemia–reperfusion to clarify the temporal profile of STAT3 activation. The role of ROS in inducing STAT3 activation was assessed by administration of the ROS scavenger dimethylthiourea (DMTU). The effects of DMTU and the STAT3 activation inhibitor AG490 administration on brain ischemic injuries were evaluated by neurologic behavior scores and brain infarct volumes.

**RESULTS:** The activation of STAT3 after middle cerebral artery occlusion was significantly increased within peri-ischemia neurons and astrocytes. STAT3 activation mainly occurred in the reperfusion phase rather than in the ischemia phase. In addition,

DMTU suppressed STAT3 activation in a dose-dependent manner, indicating that STAT3 activation may be a subsequent event after ROS production. DMTU and AG490 significantly reduced infarct sizes and improved neurologic outcomes.

**CONCLUSION:** In comparison with ischemia, reperfusion is a more powerful stimulus for STAT3 activation. ROS scavenging is closely correlated with an inhibition of STAT3 activation. Neuroprotective effects are achieved through ROS scavenging and down-regulation of STAT3 activation.

### 美金剛對大鼠浸潤性皮膚鎮痛的局部麻醉作用

#### The Local Anesthetic Effect of Memantine on Infiltrative Cutaneous Analgesia in the Rat

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背景：美金剛可阻滯 N-甲基-D-天冬氨酸受體以及 Na<sup>+</sup>離子流，這是局部麻醉的主要機制之一。迄今尚無研究提及美金剛有局部麻醉作用，因此我們研究了美金剛的局麻作用。

方法：在皮下注藥阻滯表皮軀幹肌肉反射後，我們評估了美金剛、利多卡因和地佐環平（MK-801）。將美金剛對大鼠的皮膚鎮痛作用的劑量依賴性效應與利多卡因和 MK-801 進行比較。每種藥物的作用時間通過等效基線（20%有效劑量 [ED<sub>20</sub>], ED<sub>50</sub> 和 ED<sub>80</sub>）來評估和比較。局麻藥中頻繁使用的利多卡因被視為對照組。

結果：我們證明了美金剛、利多卡因和 MK-801 在浸潤性皮膚鎮痛中產生劑量依賴性局麻作用。相對藥效為 MK-801(10.4 [9.7–11.1]) > 美金剛(17.6 [15.2–20.4]) > 利多卡因(25.9 [23.8–28.1]) ( $P < 0.01$ )。在等效基線中，美金剛的作用時間較利多卡因( $P = 0.012$ )和 MK-801 ( $P = 0.008$ )長。聯合給予美金剛(13.3 μmol/kg)和 MK-801(1.3 μmol/kg)的作用較單獨給予美金剛(13.3 μmol/kg)或 MK-801 (1.3 μmol/kg)強，時間也較長。而局部注射生理鹽水或腹膜內給予大劑量美金剛、利多卡因或 MK-801 均不產生皮膚鎮痛作用（資料未顯示）。

結論：本研究表明美金剛的效能弱於 MK-801，美金剛比利多卡因和 MK-801 可產生更長的鎮痛時間。當與 MK-801 合用時，美金剛顯示出皮膚鎮痛的協同作用。我們的結論是美金剛比利多卡因提供更好的局部鎮痛，而且 N-甲基-D-天冬氨酸受體同樣促進了美金剛的鎮痛作用。

（瞿亦楓 譯 馬皓琳 李士通 校）

**BACKGROUND:** Memantine blocks N-methyl-D-aspartate receptors and the Na<sup>+</sup> current, one principal mechanism of local anesthesia. Until now, no study mentioned that memantine had a local anesthetic effect, and therefore we investigated the local anesthetic effect of memantine.

**METHODS:** After blockade of cutaneous trunci muscle reflex with subcutaneous injections, we evaluated the cutaneous analgesic effect of memantine, lidocaine, and dizocilpine (MK-801) in rats. The dose-dependent response of memantine on cutaneous analgesia was compared with lidocaine and MK-801 in rats. The duration of action for each drug was evaluated and compared on an equipotent basis (20% effective dose [ED<sub>20</sub>], ED<sub>50</sub>, and ED<sub>80</sub>). Lidocaine, a frequently used local anesthetic, was used as control.

**RESULTS:** We demonstrated that memantine, lidocaine, and MK-801 produced dose-dependent local anesthetic effects as infiltrative cutaneous analgesia. The relative potency was MK-801 (10.4 [9.7–11.1]) > memantine (17.6 [15.2–20.4]) > lidocaine (25.9 [23.8–28.1]) ( $P < 0.01$ ). On an equipotent basis, memantine showed longer duration than lidocaine ( $P = 0.012$ ) and MK-801 ( $P = 0.008$ ). Coadministration of memantine (13.3  $\mu\text{mol/kg}$ ) and MK-801 (1.3  $\mu\text{mol/kg}$ ) produced greater blockade and duration than memantine (13.3  $\mu\text{mol/kg}$ ) or MK-801 (1.3  $\mu\text{mol/kg}$ ) alone. Neither local injection of saline nor intraperitoneal administration of a large dose of memantine, lidocaine, or MK-801 produced cutaneous analgesia (data not shown).

**CONCLUSIONS:** This study indicated that memantine is less potent than MK-801, and that memantine elicits longer analgesic duration than both lidocaine and MK-801. When combined with MK-801, memantine demonstrates a synergistic effect of cutaneous analgesia. We conclude that memantine produces better local analgesia than lidocaine and that *N*-methyl-D-aspartate receptors also contribute to the analgesic effect of memantine.

### 圍術期收縮壓變異性是否能預測心臟手術後的死亡率？一項關於 ECLIPSE 試驗的探索性分析

#### Does Perioperative Systolic Blood Pressure Variability Predict Mortality After Cardiac Surgery? An Exploratory Analysis of the ECLIPSE trials

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**背景：**對圍術期血壓穩定性與手術預後關係進行探討的相關報導較罕見。本研究驗證接受心臟手術患者收縮壓（SBP）變異性與術後 30 天死亡率相關的假設。

**方法：**評估 ECLIPSE 試驗中隨機選取的 1512 名圍術期高血壓患者的圍術期血壓變異性。使用偏離設定收縮壓範圍所產生的壓力幅度×持續時間（曲線下面積）來評



估血壓變異度。以 10mmHg 為最小單位,將 SBP 下限逐步提高,在使術中設定 SBP 範圍從 65-135 mmHg 升至 105-135 mmHg; 術前術後設定 SBP 範圍從 75-145 mmHg 升至 105-135 mmHg 的過程中,進行各個設定下的變異度分析。採用多因素 Logistic 回歸評估得出血壓變異度與 ECLIPSE 試驗得出的術後 30 天死亡率間關係。

**結果：**當設定 SBP 範圍為術中 75 - 135 mm Hg，術前術後 85 - 145 mm Hg 時, 血壓變異度與術後 30 天內死亡率顯著相關。每增加收縮壓 60 mm Hg × min/h，30 天內死亡率比值比增加 1.16 (95% 可信區, 1.04-1.30)。如果曲線下面積從 0 提高至 300 mm Hg × min/h，預計低風險患者的 30 天死亡率將從 0.2% 增至 0.5%，而高風險患者將從 42.4% 增至 60.7%。

**討論：**圍術期血壓變異度與心臟手術患者 30 天死亡率相關，術中偏離 75 to 135 mm Hg，以及術前或術後偏離 85 to 145 mm Hg 範圍的收縮壓變異度與術後 30 天內死亡率顯著相關。高風險患者預計死亡率大於低風險患者。

(陳毓雯 譯 陳傑 校)

**BACKGROUND:** Few studies describe an association of perioperative blood pressure stability with postoperative outcome. We tested the hypothesis that systolic blood pressure (SBP) variability in patients undergoing cardiac surgery is associated with 30-day mortality.

**METHODS:** Perioperative blood pressure variability was evaluated in the 1512 patients who were randomized and had perioperative hypertension in the ECLIPSE trials. Blood pressure variability was assessed as the product of magnitude × duration of SBP excursions outside defined SBP ranges (area under the curve). SBP ranges were analyzed from 65 to 135 mm Hg intraoperatively and 75 to 145 mm Hg pre- or postoperatively, up to 105 to 135 mm Hg intraoperatively and 115 to 145 mm Hg pre- or postoperatively, with the narrower ranges defined by progressively increasing the lower SBP limit by 10 mm Hg increments. Multiple logistic regression was used to assess the association of blood pressure variability with 30-day mortality obtained from the primary ECLIPSE trial results.

**RESULTS:** Increased SBP variability outside a range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively is significantly associated with 30-day mortality. The odds ratio was 1.16 (95% confidence interval, 1.04–1.30) for 30-day mortality risk per incremental SBP excursion of 60 mm Hg × min/h. The predicted probability of 30-day mortality increased for low-risk patients from 0.2% to 0.5%, and for high-risk patients from 42.4% to 60.7% if the area under the curve increased from 0 to 300 mm Hg × min/h.

**CONCLUSIONS:** Perioperative blood pressure variability is associated with 30-day mortality in cardiac surgical patients, proportionate to the extent of SBP excursions outside the range of 75 to 135 mm Hg intraoperatively and 85 to 145 mm Hg pre- and postoperatively. Predicted mortality was greater for high-risk patients than for low-risk patients.

麻醉恢復室中 CYP2D6-和 CYP3A-依賴的昂丹司瓊血漿濃度具有對映體選擇性  
**CYP2D6- and CYP3A-Dependent Enantioselective Plasma Concentrations of Ondansetron in Postanesthesia Care**

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**背景:**細胞色素 P450 (CYP2D6)基因多態性會影響昂丹司瓊的止吐作用,這一點已經被證實。然而, CYP3A 對於昂丹司瓊代謝和藥效影響的機制還不清楚。本研究的目的是評估基因型依賴的 CYP2D6 和 CYP3A 活性對昂丹司瓊對映體血漿濃度的影響。另外,還評估了昂丹司瓊加倍劑量對其基因型依賴的血漿濃度影響。

**方法:**病人麻醉前,靜脈給予 4mg 或者 8mg 的昂丹司瓊防止嘔吐。CYP2D6 依賴活性評分包括 CYP2D6 酶活性無影響、降低、正常或增加,而 CYP3A 主要分為低表達(CYP3A5\*3/\*3)和高表達狀態(CYP3A5 wt/wt or wt/\*3)。使用液相質譜分析檢測 R-昂丹司瓊和 S-昂丹司瓊對映體的血漿藥物濃度。R-昂丹司瓊和 S-昂丹司瓊血漿濃度-時間曲線下面積(AUC)與 CYP2D6 和 CYP3A 基因型依賴的酶活性有關。

**結果:**共分析了 141 個完整資料。S-昂丹司瓊的濃度隨 CYP2D6 活性的不同而改變(P=0.01),沒有 CYP2D6 活性組中濃度最高(95%CI: 362.5 [238.3/486.7] h · ng/mL),而 CYP2D6 活性增加組中,S-昂丹司瓊的濃度則最低(95%CI: 149.6 [114.5/184.8] h · ng/mL),CYP2D6 活性減少和正常的基因型組中的 S-昂丹司瓊的濃度分別為(263.6 [228.8/298.8], 255.4 [228.2/282.7] h · ng/mL),與 CYP3A5 高表達的基因型相比,低表達的 CYP3A5 基因型依賴的 R-昂丹司瓊的 AUC 是其兩倍多(281.5 [248.6/314.3] vs 142.5 [92.4/192.7] h · ng/mL; P = 0.003)。對於低活性 CYP3A 的個體,昂丹司瓊劑量加倍會增加血漿藥物濃度,而在高活性 CYP3A 的個體則無此現象(P<0.001)。

**結論:**昂丹司瓊代謝是對映體選擇性的。在麻醉恢復室中,CYP2D6 活性評分與 S-昂丹司瓊的濃度相關聯,而 CYP3A5 表達情況則主要影響 R-昂丹司瓊的濃度。基因和環境決定了 CYP2D6 和 CYP3A 的酶活性,從而影響著昂丹司瓊的止吐作用。

(張婷 譯 陳傑 校)

**BACKGROUND:** An influence of polymorphic cytochromes P450 (CYP) 2D6 genetic variants on antiemetic efficacy of ondansetron has been suggested. However, the role of CYP3A in ondansetron metabolism and efficacy has been unclear. In this study, we evaluated the hypothesis that genotype-dependent CYP2D6 and CYP3A activity selectively influences plasma concentrations of ondansetron enantiomers. Additionally, the effects of doubling the ondansetron dose on genotype-dependent plasma concentrations were investigated.

**METHODS:** Patients received IV ondansetron 4 or 8 mg for emesis prophylaxis before emergence from anesthesia. The CYP2D6-dependent activity score representing no, decreased, normal, or increased CYP2D6 enzyme activity as well as CYP3A low (CYP3A5\*3/\*3) and high expressor status (CYP3A5 wt/wt or wt/\*3) were determined. Plasma concentrations of R- and S-ondansetron enantiomers were measured by liquid

chromatography–tandem mass spectrometry. Area under the plasma concentration–time curves (AUCs) of *R*- and *S*-ondansetron were associated with CYP2D6 and CYP3A5 genotype-dependent enzyme activity.

**RESULTS:** Complete data of 141 subjects were analyzed. Concentrations of *S*-ondansetron differed between CYP2D6 activity groups ( $P = 0.01$ ) with highest values in patients with no CYP2D6 activity (mean [95% confidence interval]: 362.5 [238.3/486.7] h · ng/mL) and lowest values in those with increased activity (149.6 [114.5/184.8] h · ng/mL) compared with subjects displaying genotypes resulting in reduced or normal CYP2D6 activity (263.6 [228.8/298.8], 255.4 [228.2/282.7] h · ng/mL). AUC of *R*-ondansetron was 2 times higher in CYP3A5 low expressors compared with high expressors (281.5 [248.6/314.3] vs 142.5 [92.4/192.7] h · ng/mL;  $P = 0.003$ ). Doubling the ondansetron dose increased plasma concentrations only in individuals with low CYP3A activity, but not in individuals with high enzyme activity ( $P < 0.001$ ).

**CONCLUSIONS:** The metabolism of ondansetron seems to be enantioselective. In this postoperative setting, CYP2D6 activity scores correlated with concentrations of *S*-ondansetron, whereas CYP3A5 expressor status mainly influenced concentrations of *R*-ondansetron. Genetically and environmentally determined CYP2D6 and CYP3A enzyme activity might have implications for antiemetic efficacy.

通過七氟醚濃度和腦電雙頻指數間滯後效應的測量證實肥胖不影響七氟起效和失效時間

### Obesity Does Not Influence the Onset and Offset of Sevoflurane Effect as Measured by the Hysteresis Between Sevoflurane Concentration and Bispectral Index

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**背景：**在肥胖患者中，可能因患者的呼吸變化和氣體交換改變而推遲麻醉氣體的起效和失效的時間。這項研究評估了肥胖對於七氟醚顯效滯後現象的影響。七氟醚的顯效是通過腦電雙頻指數（BIS）測量來證實。由於呼氣末正壓（PEEP）可改善肥胖病人氣體交換能力，作者還評估了 PEEP 對於滯後現象的影響。

**方法：**本研究對 15 名肥胖和 15 名體重正常，ASA 分級 I 級和 II 級，20 至 50 歲，接受全身麻醉的擇期腹腔鏡手術的患者進行前瞻性研究。使用異丙酚進行麻醉誘導，七氟醚和芬太尼進行麻醉維持。在手術結束後並使 BIS 值穩定在 60 至 65，增加七氟醚吸入濃度至 5% 維持 5 分鐘後或直到 BIS 值 < 40 時降低吸入濃度。此項七氟醚的轉換過程在體重正常的受試者（無 PEEP）進行一次，在肥胖患者中進行兩次（PEEP 為 0 和 8cmH<sub>2</sub>O）。使用 NONMEM 6 法建立人群藥代學/藥效動力學（PK / PD）相關的抑制 E<sub>max</sub> 模型，應用此模型描述在轉換過程中七氟醚呼氣末濃

度和 BIS 值之間的遲滯效應。關於七氟醚吸入和呼出濃度、BIS 值以及達到不同 BIS 值終點的時間的描述性分析也用來比較 PK 和 PD 的特性。

**結果：**所有患者完成了研究。這些資料符合 PK / PD 模型。而體重指數或 PEEP ( $P > 0.05$ ) 不會影響代表滯後效應的效應室消除速率常數。肥胖和 PEEP 不會對任何的 PK / PD 的描述性指標產生影響。

**結論：**此項研究結果並不支持以下假設：肥胖延長七氟醚-這一難溶麻醉劑的麻醉誘導時間或麻醉維持 90-120 分鐘患者的麻醉恢復時間。

(孫曉瓊 譯 陳傑 校)

**BACKGROUND:** The onset and offset of action of anesthetic gases might be delayed by respiratory changes and gas exchange alterations present in obese patients. In this study, we assessed the influence of obesity on the hysteresis between sevoflurane and its effect as measured by the bispectral index (BIS). Because the use of positive end-expiratory pressure (PEEP) in obese patients has improved gas exchange, we also assessed the influence of PEEP on hysteresis.

**METHODS:** Fifteen obese and 15 normal-weight patients, ASA physical status I and II, 20 to 50 years old, scheduled to undergo general anesthesia for elective laparoscopic surgery, were prospectively studied. Anesthesia was induced with propofol and maintained with sevoflurane and fentanyl. At the end of surgery and after stable BIS values of 60 to 65, the inspired concentration of sevoflurane was increased to 5 vol% for 5 minutes or until BIS was  $<40$  and then decreased. Sevoflurane transitions were performed once in normal-weight subjects (without PEEP) and twice in obese patients (one without PEEP and one with a PEEP of 8 cm H<sub>2</sub>O). The hysteresis between sevoflurane end-tidal concentrations and BIS during these transition periods was modeled with an inhibitory Emax model using a population pharmacokinetic/ pharmacodynamic (PK/PD) approach with NONMEM VI. A descriptive analysis of sevoflurane inspired and expired concentrations, BIS values, and time to reach different BIS end points was also used to compare the PK and PD characteristics.

**RESULTS:** All patients completed the study. The data were adequately fit with the PK/PD model. The hysteresis expressed as the effect-site elimination rate constant was not influenced by body mass index or PEEP ( $P > 0.05$ ). Neither obesity nor PEEP showed any influence on the PK/PD descriptors.

**CONCLUSIONS:** Our results do not support the hypothesis that obesity prolongs induction or recovery times when sevoflurane, a poorly soluble anesthetic, is used to maintain anesthesia from 90 to 120 minutes.

### 胃部超聲檢查在禁食外科患者中的應用：一項前瞻性描述性研究

#### Gastric Sonography in the Fasted Surgical Patient: A Prospective Descriptive Study

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**背景：**吸入性肺炎目前仍然是一項嚴重的麻醉相關併發症。目前缺少一種可靠的診斷工具來評估胃容量。不久前一項研究已經證實了在健康志願者身上採用胃部超聲檢查可以提供可靠的關於胃容量和內容物的定性和定量資訊。此項前瞻性研究將對 200 例接受擇期手術的空腹患者的胃竇進行定性及定量分析。

**方法：**在全麻誘導前完成標準化胃部掃描程式。分別對仰臥位和右側臥位患者進行胃竇超聲的定性掃描後，採用三分制分級系統進行患者分類。

**結果：**86 例患者為 0 級（空胃竇），107 例為 1 級（僅在右側臥位發現極少的液體體積），7 例為 2 級（在平臥位和右側臥位均可清晰發現胃竇內液體伴有明顯擴張）。3 分制分級系統與預先通過數學建模估計的全胃液體容量有相關性。0 級對應完全排空的胃，1 級對應可忽略不計的液體容量（ $16\pm 36\text{ml}$ ），在達到空腹要求的可接受範圍內，2 級對應明顯比預期大的胃液體容量（ $180\pm 83\text{ml}$ ），已經超過之前報導的“安全”限制。胃竇達到 2 級的一名患者在麻醉開始時發生了明顯胃內容物返流。

**結論：**我們單獨根據胃竇部超聲結果定性分析，提出的 3 分制分級系統與預計的胃容量結果良好相關。此分級系統有希望成為術前評估吸入風險的“生物標記”。在廣泛運用於臨床實踐之前，這項診斷技術還需要進一步進行認證和設計。

（陸秉璋 譯 陳傑 校）

**BACKGROUND:** Aspiration pneumonia remains a serious anesthetic-related complication. A reliable diagnostic tool to assess gastric volume is currently lacking. We recently demonstrated that gastric sonography can provide reliable qualitative and quantitative information about gastric content and volume in healthy volunteers. In the current study, we performed a prospective qualitative and quantitative analysis of the gastric antrum in 200 fasted patients undergoing elective surgery.

**METHODS:** A standardized gastric scanning protocol was applied before anesthetic induction. Patients were classified following a 3-point grading system based solely on qualitative sonographic assessment of the antrum in the supine and right lateral decubitus positions.

**RESULTS:** Eighty-six patients were classified as grade 0 (empty antrum); 107 patients as grade 1 (minimal fluid volume detected only in the right lateral decubitus position); and 7 patients were classified as grade 2 (antrum clearly distended with fluid visible in both supine and lateral positions). The 3-point grading system correlated with total gastric fluid volume as predicted by a previously reported mathematical model. Essentially grade 0 corresponds to a completely empty stomach, grade 1 corresponds to negligible fluid volumes ( $16 \pm 36 \text{ mL}$ ) within normal ranges expected for fasted patients, and grade 2 correlates with significantly higher predicted gastric fluid volumes ( $180 \pm 83 \text{ mL}$ ) beyond previously reported “safe” limits. One patient with a grade 2 antrum had an episode of significant regurgitation of gastric contents on emergence from anesthesia.

**CONCLUSION:** We propose a 3-point grading system based exclusively on qualitative sonographic assessment of the gastric antrum that correlates well with predicted gastric volume. This grading system could be a promising “biomarker” to assess perioperative aspiration risk. Before it can be applied widely to clinical practice, this diagnostic tool needs to be further validated and characterized.

羥乙基澱粉（130kD）抑制脂多糖激發的小鼠肺臟 Toll 樣受體 4 信號轉導通路

## Hydroxyethyl Starch (130 kD) Inhibits Toll-Like Receptor 4 Signaling Pathways in Rat Lungs Challenged with Lipopolysaccharide

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**背景：**大量研究表明，羥乙基澱粉（HES）液體用於膿毒血症患者及其他嚴重炎症反應患者，能下調炎症介質的表達並抑制中性粒細胞介導的組織損傷。然而，我們對於潛在機制仍不甚瞭解。Toll 樣受體 4（TLR4）信號在炎症反應中有著重要的作用。在此次實驗中，筆者研究了 TLR4 信號在 HES 抗炎效應中的作用。

**方法：**選取雄性 Sprague-Dawley 大鼠，靜脈注射脂多糖（LPS）10mg/kg。三組大鼠分別注射生理鹽水(30 mL/kg)、HES 130/0.4 (15 及 30 mL/kg)。當使用脂多糖激發後六小時，處死大鼠並提取其肺組織。通過蘇木精-伊紅染色測定大鼠肺損傷。通過定量聚合酶鏈式反應（PCR）技術和免疫印跡技術以及蛋白電泳遷移率變動分析法分別測定：大鼠肺組織中的 TLR4 mRNA 表達、p38 絲裂原活化蛋白激酶（MAPK）、細胞外信號調節激酶 1/2MAPK 活性以及啟動蛋白（AP-1）活性。

**結果：**與生理鹽水組相比，兩組不同給藥量的 HES 均大大減少大鼠肺組織中由 LPS 引起的組織學改變。分子生物學分析表明，15 及 30 mL/kg 的 HES 均顯著減少脂多糖激發小鼠的 TLR4 mRNA 水準並抑制大鼠肺組織中 p38 MAPK 及 AP-1，而兩種劑量的 HES 均未對細胞外信號調節激酶 1/2MAPK 有所影響。

**結論：**這些研究結果表明 HES 130/0.4 至少部分通過 TLR4/p38 MAPK/AP-1 轉導通路對脂多糖激發大鼠肺組織產生抗炎反應。

（趙嫣紅 譯 陳傑 校）

**BACKGROUND:** A number of studies have shown that hydroxyethyl starch (HES) solutions are able to down-regulate the expression of inflammatory mediators and inhibit neutrophil-mediated tissue injuries when they are used in patients with sepsis or other diseases with severe inflammatory responses. However, our knowledge about the underlying mechanisms is limited. Toll-like receptor 4 (TLR4) signaling has a pivotal 關鍵的 role in inflammatory processes. In this study, we examined the possible involvement of TLR4 signaling in the antiinflammatory effects of HES.

**METHODS:** Male Sprague-Dawley rats were exposed to lipopolysaccharide (LPS) (10 mg/kg, IV) and received IV saline (30 mL/kg) or HES 130/0.4 (15 or 30 mL/kg). Six hours after LPS challenge, rats were killed and their lungs harvested. Lung injury was examined by hematoxylin 蘇木精 and eosin staining 伊紅染色. TLR4 mRNA expression, p38 mitogen-activated protein kinase (MAPK) and extracellular signal-regulated kinases 1/2 MAPK activation, and activator protein 1 (AP-1) activity in the lungs were detected

with quantitative polymerase chain reaction, Western blotting, and electrophoretic mobility shift assay, respectively.

**RESULTS:** Compared with saline, HES profoundly attenuated the histological changes induced by LPS in the lungs at both dose levels. Molecular analysis showed that both 15 and 30 mL/kg HES significantly decreased TLR4 mRNA levels and inhibited activation of p38 MAPK and AP-1 in rats challenged with LPS, whereas activation of extracellular signal-regulated kinases 1/2 MAPK was not affected by either dose of HES.

**CONCLUSIONS:** These findings indicate that the beneficial effects of HES 130/0.4 on inflammation are mediated at least in part by inhibiting the TLR4/p38 MAPK/AP-1 pathway in lungs from rats challenged with LPS.

### 雞蛋過敏的兒童對丙泊酚的過敏反應

#### Allergic Reactions to Propofol in Egg-Allergic Children

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**背景：**雞蛋和/或豆類過敏通常是丙泊酚應用的禁忌症。本次研究的目的是在於評估患有免疫球蛋白 E 介導的雞蛋和/或豆類過敏症的兒童是否也在應用丙泊酚治療後發生過敏反應。

**方法：**作者對悉尼 Westmead 兒童醫院 1999 年至 2010 年間患有 IgE 介導的雞蛋和/或豆類過敏症的兒童同時接受丙泊酚治療的病例採取回顧性病例分析。

**結果：**研究共納入 28 位雞蛋過敏的患兒，他們共接受了 43 次丙泊酚治療。沒有患兒因為對豆類過敏並應用了丙泊酚而納入研究。在被納入的患兒中，21 位（75%）為男孩，患兒在接受麻醉時的平均年齡為 2.4 歲（範圍為 1 至 15 歲），並且這些患兒通常合併有其他的過敏性疾病（61% 患有濕疹，32% 患有哮喘，43% 對花生過敏）。大多數患兒（n=19，68%）對雞蛋發生過由 IgE 介導的臨床反應，並且經蛋清皮膚點刺激試驗（skin prick test, SPT）強陽性（≥7 mm）證實。其中，有兩位患兒發生過對雞蛋的過敏反應，其餘的 9 位患兒由於 SPT 強陽性（≥7 mm）而從未進食過雞蛋。所有對雞蛋的 SPT 實驗均在應用丙泊酚後 12 個月內進行。研究中有一位患兒在應用丙泊酚 15 分鐘後發生了非過敏性休克性過敏反應（n=1，2%），該患兒為一位 7 歲的男孩，既往有雞蛋過敏史，並對其他多種物質均有 IgE 介導的過敏症（如牛奶、堅果，和芝麻），患兒對丙泊酚的 SPT 為 3mm。其他對雞蛋過敏的患兒應用丙泊酚後均無反應。

**結論：**儘管目前澳大利亞的標籤上仍注明相關警告，丙泊酚還是被頻繁應用於對雞蛋過敏的患兒。對於大多數有雞蛋過敏史但既往未發生過雞蛋源性的過敏性休克的患兒來說，丙泊酚是可以安全使用的。

（周姝婧 譯 陳傑 校）

**BACKGROUND:** Egg and/or soy allergy are often cited as contraindications to propofol administration. Our aim was to determine whether children with an immunoglobulin (Ig)E-mediated egg and/or soy allergy had an allergic reaction after propofol use.

**METHODS:** We performed a retrospective case review over an 11-year period (1999–2010) of children with IgE-mediated egg and/or soy allergy who had propofol administered to them at the Children's Hospital Westmead, Sydney.

**RESULTS:** Twenty-eight egg-allergic patients with 43 propofol administrations were identified. No child with a soy allergy who had propofol was identified. Twenty-one children (75%) were male, the median age at anesthesia was 2.4 years (range, 1–15 years), and the presence of other atopic disease was common (eczema 61%, asthma 32%, peanut allergy 43%). Most children ( $n = 19$ , 68%) had a history of an IgE-mediated clinical reaction to egg with evidence of a significantly positive egg white skin prick test (SPT) reaction ( $\geq 7$  mm). Two of these had a history of egg anaphylaxis. The remaining children ( $n = 9$ , 32%) had never ingested egg because of significantly positive SPT ( $\geq 7$  mm). All SPTs to egg were performed within 12 months of propofol administration. There was one nonanaphylactic immediate allergic reaction ( $n = 1$  of 43, 2%) that occurred 15 minutes after propofol administration in a 7-year-old boy with a history of egg anaphylaxis and multiple other IgE-mediated food allergies (cow's milk, nut, and sesame). SPT to propofol was positive at 3 mm. No other egg-allergic child reacted to propofol.

**CONCLUSIONS:** Despite current Australian labeling warnings, propofol was frequently administered to egg-allergic children. Propofol is likely to be safe in the majority of egg-allergic children who do not have a history of egg anaphylaxis.

### 神經肽通過調節角質細胞白介素-1 $\beta$ 的產生導致周圍神經痛覺過敏

#### Neuropeptides Contribute to Peripheral Nociceptive Sensitization by Regulating Interleukin-1 $\beta$ Production in Keratinocytes

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**背景：**越來越多的證據表明：對於複雜性區域疼痛綜合症（CRPS）的患者，皮膚炎症細胞因數的產生與增高的神經肽信號表達有密切的關係。在此之前一項研究觀察到在脛骨骨折的CRPS大鼠模型上，角質細胞產生白介素(IL)-1 $\beta$ 需要包含NALP1炎性因數在內的蛋白酶-1的活化，且白介素-1受體拮抗劑（anakinra）的應用降低了骨折導致的後爪機械性痛覺過敏。因此，本研究假設神經肽通過提高炎症因數表達和蛋白酶-1的活性來啟動皮膚的天然免疫系統從而導致痛覺過敏。

**方法：**考察向大鼠後爪皮膚注射神經肽P物質（SP）和降鈣素基因相關肽（CGRP）後，出現的痛覺致敏是否有白介素-1 $\beta$ 的參與。接著研究是否這些神經肽能夠刺激角質細胞產生白介素-1 $\beta$ ，並且可以增加包括NALP-1和蛋白酶-1在內的炎症因數蛋白質成分的表達。最後，確定神經肽刺激產生白介素-1 $\beta$ 是否需要蛋白酶-1和組織蛋白酶B的啟動。

**結果：**在大鼠足底注射P物質和降鈣素基因相關肽導致痛覺過敏，降鈣素基因相關肽的效應大約較前者小10倍。此外，靜脈注射白介素-1受體拮抗劑阿那白滯素（anakinra），可預防神經肽產生的痛覺過敏。同樣，局部應用神經肽後大鼠皮膚角質細胞白介素-1受體表達上調。體外實驗資料證明，P物質和降鈣素基因相關



肽都會劑量依賴性提高角質細胞內白介素-1 $\beta$ 和蛋白的表達。此外，P物質能時間和劑量依賴性地上調角質細胞內NALP-1和蛋白酶1的mRNA和蛋白水準。相比之下，降鈣素基因相關肽時間和劑量依賴性地增加角質細胞內NALP-1和蛋白酶1的mRNA水準，但NALP-1和蛋白酶1的蛋白水準並沒有顯著改變。應用蛋白酶1選擇性抑制劑Ac-YVAD-CHO可減少P物質和降鈣素基因相關肽（效應較弱）引起的角質細胞內IL-1 $\beta$ 產生增加。選擇性組織蛋白酶B抑制劑CA-74Me也抑制角質細胞內神經肽刺激白介素-1 $\beta$ 的產生。

**結論：**結果表明，神經肽通過增加角質細胞白介素-1 $\beta$ 的產生誘發痛覺過敏。神經肽的增加角質細胞白介素-1 $\beta$ 的產生是依賴蛋白酶-1和組織蛋白酶B。神經皮膚信號包括天然免疫神經肽的啟動可能導致了複雜性區域疼痛綜合症患者的疼痛。

（黃丹 譯 陳傑 校）

**BACKGROUND:** It is increasingly evident that there is a close connection between the generation 產生 of cutaneous inflammatory cytokines and elevated neuropeptide signaling in complex regional pain syndrome (CRPS) patients. Previously, we observed in the rat tibia fracture model of CRPS that activation of caspase-1 containing NALP1 inflammasomes was required for interleukin (IL)-1 $\beta$  production in keratinocytes, and that administration of an IL-1 receptor antagonist (anakinra) reduced the fracture-induced hindpaw mechanical allodynia. We therefore hypothesized that neuropeptides lead to nociceptive sensitization through activation of the skin's innate immune system by enhancing inflammasome expression and caspase-1 activity.

**METHODS:** We determined whether the neuropeptides substance P (SP) and calcitonin gene-related peptide (CGRP) require IL-1 $\beta$  to support nociceptive sensitization when injected into mouse hindpaw skin by testing mechanical allodynia. We then investigated whether these neuropeptides could stimulate production of IL-1 $\beta$  in a keratinocyte cell line (REKs), and could increase the expression of inflammasome component proteins including NALP1 and caspase-1. Finally, we determined whether neuropeptide-stimulated IL-1 $\beta$  production required activation of caspase-1 and cathepsin.

**RESULTS:** Intraplantar injections of SP and CGRP lead to allodynia in mouse hindpaws but CGRP was approximately 10-fold less potent in causing this response. Moreover, systemic administration of the IL-1 receptor (IL-1R) antagonist anakinra prevented sensitization after neuropeptide injection. Also, mouse skin keratinocytes express IL-1R, which is up-regulated after local neuropeptide application. In vitro data demonstrated that both SP and CGRP increased IL-1 $\beta$  gene and protein expression in REKs in a dose-dependent manner. Furthermore, SP time- and dose-dependently up-regulated NALP1 and caspase-1 mRNA and protein levels in REKs. In contrast, CGRP time- and dose-dependently enhanced NALP1 and caspase-1 mRNA levels without causing a significant change in NALP1 or caspase-1 protein expression in REKs. Inhibition of caspase-1 activity using the selective inhibitor Ac-YVAD-CHO reduced SP and, less effectively, CGRP induced increases in IL-1 $\beta$  production in REK cells. The selective cathepsin B inhibitor CA-74Me inhibited neuropeptide induced IL-1 $\beta$  production in REKs as well.

**CONCLUSIONS:** Collectively, these results demonstrate that neuropeptides induce nociceptive sensitization by enhancing IL-1 $\beta$  production in keratinocytes. Neuropeptides rely on both caspase-1 and cathepsin B for this enhanced production. Neurocutaneous signaling involving neuropeptide activation of the innate immunity may contribute to pain in CRPS patients.

簡報:蛛網膜下腔阻滯的評價：一項包括 175 篇文獻以及改進意見的調查

**Brief Reports: An Assessment of Subarachnoid Block: A Survey of 175 Articles and Recommendations for Improvement**

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**背景：**蛛網膜下腔阻滯的評估，尤其是感覺部分，可能不完整並且會影響蛛網膜下腔阻滯麻醉研究的結論，以及在日常臨床實踐中的應用。

**方法：**作者手動搜索了出版時間在 2006 年至 2009 年之間的 8 本麻醉期刊，發現 175 篇關於蛛網膜下腔阻滯的文章，用來確定蛛網膜下腔麻醉過程記錄的組成部分以及交感神經和運動阻滯的程度。

**結果：**86% 文章記錄了蛛網膜下腔注射的部位，84% 記錄局麻藥配比，77% 記錄局麻藥濃度，75% 記錄患者的體位元，77% 記錄穿刺針大小，以及 71% 記錄穿刺針類型。69% 文章記錄了用於評估感覺阻滯的刺激，17% 記錄了阻滯是單側或雙側，以及 11% 記錄刺激應用的界限。運動和交感神經阻滯分別在 40% 和 18% 研究中進行了評估。

**結論：**這些結果表明涉及蛛網膜下腔麻醉的研究，存在不完整的方法描述和感覺阻滯的評估。建議建立一份清單，以促進一個更加規範的有關蛛網膜下腔麻醉的評估。

(懷曉蓉 譯 陳傑 校)

**BACKGROUND:** Assessment of subarachnoid block, particularly the sensory component, may be incomplete and influence the conclusions of studies involving subarachnoid anesthesia, as well as their application in routine clinical practice.

**METHODS:** We manually searched 175 articles concerning subarachnoid block published from 2006 to 2009 in 8 anesthesia journals to determine the components of the subarachnoid anesthetic procedure recorded as well as the extent of sympathetic and motor block.

**RESULTS:** The level of subarachnoid injection was reported in 86% of the articles, baricity in 84%, concentration of local anesthetic in 77%, patient's position in 75%, needle size in 77%, and needle type in 71%. The stimulus used for assessing sensory block was reported in 69% of the articles; 17% described the block as unilateral or bilateral, and 11% described the lines along which the stimulus was applied. Motor and sympathetic block were assessed in 40% and 18% of studies, respectively.

**CONCLUSIONS:** These results suggest incomplete description of tools and assessment of sensory block in studies involving subarachnoid anesthesia. We propose a checklist to facilitate a more standardized evaluation of the extent of subarachnoid anesthesia.

多重電極全血血小板聚集試驗、血小板功能分析儀-100 及體內出血時間在阿司匹林介導的血小板功能障礙患者術前重點照護評估中的作用

## **Multiple Electrode Whole Blood Aggregometry, PFA-100, and In Vivo Bleeding Time for the Point-of-Care Assessment of Aspirin-Induced Platelet Dysfunction in the Preoperative Setting.**

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**背景：**因服用阿司匹林引起的獲得性血小板功能障礙可能導致圍手術期出血傾向增加。因此，本研究旨在測定體內出血時間（BT）及另兩項血小板功能試驗在阿司匹林治療患者術前殘餘抗血小板功能評估中的診斷精確度。

**方法：**陸續選取擇期手術患者進入該前瞻性研究。“阿司匹林效應完全組”患者于血樣採集前 48 小時最後服用阿司匹林；而“阿司匹林效應變動組”與“阿司匹林效應修復組”患者最後服用阿司匹林的時間分別為采血前 48-96 小時和 96 小時以上。對照組患者不服用阿司匹林。通過多重電極全血血小板聚集試驗、血小板功能分析儀（PFA）-100 及體內出血時間對阿司匹林的效應進行評估。運用位元列於因果多重比較程式（Dunn）中的單向方差分析對各組間的差異進行檢測。使用 z 檢驗比較各分類資料。創建受試者工作特徵（ROC）曲線對所研究的血小板功能試驗的診斷精確度進行判定。分別計算 ROC 曲線下面積（AUC）及血小板功能試驗的靈敏度和特異性。統計學顯著性水準設定為  $P < 0.05$ 。

**結果：**共有 394 名患者納入研究（其中包括 133 名對照組患者與 261 名阿司匹林治療組患者）。所有 3 種方法均能檢測出阿司匹林效應完全組患者阿司匹林的抗血小板作用。但在阿司匹林效應修復組與對照組，不論進行何種檢測，兩組的檢測值均無統計學差異。在使用多重電極全血血小板聚集試驗及 PFA-100 進行阿司匹林敏感患者鑒定試驗與血小板閉鎖功能試驗時發現，阿司匹林效應變動組患者的測試值不同于對照組患者；但在 BT 測定中，兩組並未顯現差異。ROC 分析表明，在排除阿司匹林殘餘功能的試驗中，阿司匹林敏感患者鑒定試驗具有最高的診斷精確度（AUC 0.81， $P < 0.001$ ），其次分別為血小板閉鎖功能試驗（AUC 0.78， $P < 0.001$ ）與 BT（AUC 0.56， $P = 0.05$ ）。阿司匹林敏感患者鑒定試驗排除阿司匹林殘餘功能的臨界值為 53U，靈敏度和特異性分別為 88% 和 71%。

**結論：**在患者服用阿司匹林後 48 小時內，阿司匹林能充分發揮其抗血小板治療效應。本研究發現，阿司匹林撤藥 96 小時以上（大於 4 天），血小板功能即可修復；因此，對於這些患者，術前進行血小板功能試驗是毫無幫助的。若要測定術前 48-96 小時內停用阿司匹林患者阿司匹林的殘餘效應，阿司匹林敏感患者鑒定試驗可能具有最高的診斷精確度。

（范羽譯 薛張綱校）

**Background:** Acquired platelet dysfunction due to aspirin ingestion may increase bleeding tendency during surgery. Thus, we examined the diagnostic accuracy of in vivo bleeding time (BT) and 2 platelet function assays for the preoperative assessment of a residual antiplatelet effect in patients treated with aspirin.

**Methods:** Consecutive patients scheduled for surgery were prospectively enrolled in this study. The patients' last aspirin ingestion had occurred within the previous 48 hours

before blood sampling in the "full aspirin effect" group, between 48 and 96 hours before in the "variable aspirin effect" group, and >96 hours before in the "recovered aspirin effect" group. The control group had not taken any aspirin. Multiple electrode aggregometry, platelet function analyzer (PFA)-100, and in vivo BT were performed to assess the effects of aspirin. One-way analysis of variance on ranks with a post hoc multiple-comparison procedure (Dunn) was used to detect differences among the groups. Categorical data were compared using the z test. Receiver operating characteristic (ROC) curves were created to determine the diagnostic accuracy of the platelet function assays investigated. The area under the ROC curve (AUC), sensitivity, and specificity of the assays were calculated. The level of statistical significance was set at  $P < 0.05$ .

**Results:** Three hundred ninety-four patients were included in the analysis (133 control and 261 aspirin-treated patients). All 3 methods were able to detect the antiplatelet effect of aspirin in the full aspirin effect group. Furthermore, no difference in the measurement values between the recovered aspirin effect and control group was found, irrespective of the assay performed. Measurement values in the variable aspirin effect group were different from those of the control group in the ASPItest using multiple electrode aggregometry and COL-EPI using PFA-100 but not in BT. ROC analysis showed the highest diagnostic accuracy in excluding the residual aspirin effect in the ASPItest (AUC 0.81,  $P < 0.001$ ), followed by COL-EPI (AUC 0.78,  $P < 0.001$ ) and BT (AUC 0.56,  $P = 0.05$ ). The cutoff value of 53 U in the ASPItest excluded the effect of aspirin with a sensitivity of 88% and specificity of 71%.

**Conclusions:** The full therapeutic antiplatelet effects of aspirin can be expected within 48 hours of the patient's last aspirin ingestion. Platelet function recovered in our study if aspirin cessation occurred >96 hours (4 days) before; thus, in these patients, preoperative platelet function testing is not useful. To quantify any residual aspirin effect in patients who ceased their intake of aspirin between 48 and 96 hours before surgery, the ASPItest might have the highest diagnostic accuracy.

### 關於標準體重對於肥胖患者丙泊酚麻醉誘導劑量關係的研究

#### **Lean Body Weight Scalar for the Anesthetic Induction Dose of Propofol in Morbidly Obese Subjects.**

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**背景：**病態肥胖相關的特殊的麻醉風險已經有所記錄，由於和肥胖有關的生理和人體的變化藥物管理會有所改變。不幸的是，對於極度肥胖的麻醉藥效學的研究還很薄弱。儘管丙泊酚作為誘導藥物頻繁使用在肥胖病人身上，但是適合這些患者的丙泊酚誘導劑量尚存爭議。因此，我們對肥胖病人丙泊酚麻醉誘導劑量的不同體重標量進行了對比。

**方法：**選60名肥胖患者（體重指數 $\geq 40\text{kg/m}^2$ ）進行丙泊酚麻醉誘導，他們隨機接受以總體重或標準體重為標量的藥物劑量。選30名正常體重的患者（體重指數 $\leq 25\text{kg/m}^2$ ）接受以總體重為基礎的丙泊酚注射（ $100\text{mg/kg/h}$ ），注射器讀數用於標

記意識喪失，在這一點上丙泊酚注射停止。丙泊酚的劑量需要記錄意識喪失的注射讀數和時間。

**結果：**按標準體重給予丙泊酚，達到意識喪失的丙泊酚注射器讀數和時間所需的丙泊酚總量在正常體重和病態肥胖者中相似。按照標準體重注射丙泊酚，病態肥胖者達到意識喪失所需丙泊酚的劑量相當大且時間相當短。三組中，標準體重與丙泊酚總劑量之間有很大相關性。

**結論：**在病態肥胖患者全麻誘導中，標準體重是丙泊酚誘導的體重基本標量。  
(侯文婷譯 薛張綱校)

**Background:** The unique anesthetic risks associated with the morbidly obese (MO) population have been documented. Pharmacologic management of these patients may be altered because of the physiologic and anthropometric changes associated with obesity. Unfortunately, studies examining the effects of extreme obesity on the pharmacology of anesthetics have been sparse. Although propofol is the induction drug most frequently used in these patients, the appropriate induction dosing scalar for propofol remains controversial in MO subjects. Therefore, we compared different weight-based scalars for dosing propofol for anesthetic induction in MO subjects.

**Methods:** Sixty MO subjects (body mass index  $\geq 40$  kg/m<sup>2</sup>) were randomized to receive a propofol infusion (100 mg kg<sup>-1</sup> h<sup>-1</sup>) for induction of anesthesia based on total body weight (TBW) or lean body weight (LBW). Thirty control subjects (body mass index  $\leq 25$  kg/m<sup>2</sup>) received a propofol infusion (100 mg kg<sup>-1</sup> h<sup>-1</sup>) based on TBW. Syringe drop was used as the marker for loss of consciousness (LOC), at which point the propofol infusion was stopped. The propofol dose required for syringe drop and time to LOC were recorded.

**Results:** Total propofol dose (mg/kg) required for syringe drop and time to LOC were similar between control subjects and MO subjects given propofol based on LBW. MO subjects receiving a propofol infusion based on TBW had a significantly larger propofol dose and significantly shorter time to LOC. There was a strong relationship between LBW and total propofol dose received in all 3 groups.

**Conclusion:** LBW is a more appropriate weight-based scalar for propofol infusion for induction of general anesthesia in MO subjects.

### 健康個體中交感神經阻斷對手指光學體積描記圖和手指溫度的影響

#### The effects of sympathectomy on finger photoplethysmography and temperature measurements in healthy subjects

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**背景：**光學體積描記術是一種通過光線的傳播情況來測量組織容量變化的技術。光學體積描記結果圖像是由AC和DC兩部分組成。關於血管舒張時對AC與DC的光學體積描記信號的影響，目前所掌握的資料還很有限。我們的研究目的有兩個，一

是交感神經阻斷對於光學體積描記圖不同元件的影響；二是比較交感神經阻斷所引起的變化與外周溫度所引起的變化有何不同。

**方法：**在10名健康志願者中，進行單側腋路臂叢神經阻滯，從而使得交感神經阻斷，血管擴張。未進行臂叢神經阻滯的一側做為對照。使用光學體積描記法連續測量雙側的手指血容量和手指的溫度。將手指的光學體積描記圖像分離出AC和DC組分。並且計算AC與DC的比值(AC/DC)。所有資料從臂叢神經阻滯完成開始連續記錄30分鐘。使用鄧尼特檢驗法重複測量分析各個變數以確定臂叢神經阻滯對手指光學體積描記圖和手指溫度的影響。

**結果：**臂叢神經阻滯後2.7分鐘開始，被阻滯的手臂血管擴張，手指光學體積描記圖的DC部分明顯減少( $P < 0.0001$ )。阻滯後30分鐘，DC減少的平均值為 $-51\% \pm 19\%$  (95%可信區間為 $-61\% - -42\%$ )。光學體積描記圖的其他組分與基線值相比，無明顯變化。臂叢神經阻滯後5.7分鐘開始手指溫度明顯上升( $P < 0.0001$ )。阻滯後30分鐘，溫度上升的平均值為 $7.1^{\circ}\text{C} \pm 3.8^{\circ}\text{C}$  (95%可信區間為 $5.1^{\circ}\text{C} - 9.0^{\circ}\text{C}$ )。光學體積描記圖中的DC組分對於預測神經阻滯的效果敏感性和特異性均為最優。

**結論：**本研究闡明了交感神經阻斷所引起的手指光學體積描記圖中AC和DC組分的變化情況。本次試驗模型中，我們發現DC組分對於監測外周血管擴張情況最為敏感。

(黃劍譯 薛張綱校)

**BACKGROUND:** Photoplethysmography uses light transmission to measure changes in tissue volume. The resulting photoplethysmogram is composed of AC and DC components. Limited data are available on the effects of vasodilation on the AC and the DC components of the photoplethysmograph signal. The aims of our study were (1) to investigate the effects of sympathectomy on different components of the photoplethysmogram, and (2) to compare sympathectomy-induced changes in the photoplethysmogram with changes in peripheral temperature.

**METHODS:** In 10 healthy subjects, sympathectomy-induced peripheral vasodilation was achieved using an axillary brachial plexus block. The nonblocked arm served as control. We obtained measurements of bilateral continuous measurements of finger blood volume (by photoplethysmography) and finger temperature. We separated the finger photoplethysmogram into its AC and DC components. In addition, we calculated the ratio of AC to DC (AC/DC). All data were recorded until 30 minutes after the end of brachial plexus block. Repeated-measures analysis of variance followed by the Dunnett post hoc test determined the effect of brachial plexus block on the finger photoplethysmogram and finger temperature.

**RESULTS:** The DC component of the finger photoplethysmogram decreased (vasodilation) significantly ( $P < 0.0001$ ) after brachial plexus block in the blocked arm starting 2.7 minutes after the block. Average decrease in DC values was  $-51\% \pm 19\%$  (95% confidence interval:  $-61\%$  to  $-42\%$ ) at 30 minutes after the block. None of the other photoplethysmogram components changed significantly from preblock baseline values. On average, the finger temperature increased significantly ( $P < 0.0001$ ) starting 5.7 minutes after brachial plexus block in the blocked arm. Average increase in temperature was  $7.1^{\circ}\text{C} \pm 3.8^{\circ}\text{C}$  (95% confidence interval:  $5.1^{\circ}\text{C} - 9.0^{\circ}\text{C}$ ) 30 minutes after the block. The DC component of the photoplethysmogram had the highest sensitivity and specificity to predict a successful block.

**CONCLUSIONS:** This study characterizes sympathectomy-induced changes in the AC and DC components of the finger photoplethysmogram. In this experimental model, we found the DC component to be most sensitive in detecting peripheral vasodilation.

### 克-特二氏綜合征患者行手術的麻醉管理：一項 136 例的綜述

#### **Anesthesia for Surgery Related to Klippel–Trenaunay Syndrome: A Review of 136 Anesthetics**

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**背景：**克-特二氏綜合征是一種很少見的先天的畸形以靜脈曲張或靜脈畸形，毛細血管畸形，其中包括神經血管的結構，在受影響的四肢有骨或軟骨組織的肥大三聯症。在軀幹，結腸，膀胱，或脊髓也可能有。克-特二氏綜合征不應當與克-費二氏綜合征相混淆，克-費二氏綜合征有椎骨或頸部的異常。對於有克-特二氏綜合征的病人的麻醉方案中只有少數的案例報導需小心可能的困難氣道但沒有報導外科手術的大出血而需要輸血的。

**方法：**我們在梅奧診所的醫學資料庫內做了一個電子搜索，想找到進行 KTS 手術的麻醉的病人的資料。回顧了這類手術的醫學記錄，麻醉的設備，氣道管理，藥物的使用，手術中液體的管理，輸液的設備，血管通路，術後的併發症。

**結果：**82 個少見病人進行了與 KTS 相關的手術，共進行了 134 個一般的麻醉，2 個腰麻。外科手術前，27% 的病人有週期性的出血，24% 有週期性的蜂窩織炎，9% 有深靜脈血栓，2% 有肺栓塞。主要進行手術的年齡是  $21 \pm 15$  歲。主要的手術的步驟有鐳射抗凝，曲張靜脈硬化療法或剝脫，

**結論：**有 KTS 的患者都有複雜的相關的並存的疾病。相反於以前的報導，氣道管理的困難並不是偶然遇到的。在嚴重的 KTS 的患者手術中，儘管用了止血帶，仍有大量的出血，麻醉醫生應該配合需要進行適當的液體復蘇。脊髓的麻醉只在神經血管的畸形的外傷被排除後才可以考慮使用。

(劉珏瑩譯 薛張綱校)

**BACKGROUND:** Klippel-Trenaunay syndrome (KTS) is a rare congenital malformation characterized by the triad of varicose veins or venous malformations, capillary malformations that may involve neurovascular structures, and bony or soft tissue hypertrophy in affected limbs. Areas such as the trunk, bowel, bladder, and spinal cord may be involved as well. KTS should not be confused with Klippel-Feil syndrome, which involves abnormalities of the cervical vertebrae. Anesthetic management for patients with KTS has only been described in limited case reports that caution about potential airway difficulty but do not report surgical hemorrhage requiring transfusion.

**METHODS:** We performed an electronic search of the Mayo Clinic medical record database to identify patients who had undergone an anesthetic for surgery related to KTS. Review of medical records was performed for type of surgery, anesthetic technique, airway management and difficulty, medications used, intraoperative fluid administration, transfusion requirements, vascular access used, and postoperative complications.

**RESULTS:** Eighty-two unique patients were identified who underwent 134 general anesthetics and 2 lumbar neuraxial anesthetics for surgeries related to KTS. Preoperatively, 27% of patients had a history of recurrent bleeding, 24% recurrent cellulitis, 9% deep vein thrombosis, and 2% pulmonary embolism. The mean age at time of surgery was  $21 \pm 15$  years. The majority of surgical procedures involved laser coagulation or varicose vein sclerotherapy or stripping. All of the 74 direct laryngoscopies and tracheal intubations were performed on the first attempt without difficulty. Mask ventilation was possible in all 131 patients for whom this was attempted, with only 1 requiring an oral airway. Documented estimated blood loss ranged from 20 to 18,000 mL, with a mean of  $740 \pm 2739$  mL. Use of a tourniquet did not obviate the possibility of substantial blood loss. The only significant postoperative complication involved a calf hematoma after vein stripping and avulsion that required return to the operating room for evacuation.

**CONCLUSIONS:** Patients with KTS have multiple associated comorbidities relevant to perioperative management. In contrast to previous reports, difficulty with airway management was not encountered. Surgery related to severe KTS may be associated with massive hemorrhage despite tourniquet use, and the anesthesiologist should anticipate the need for appropriate fluid resuscitation. Neuraxial techniques may be considered only if the possibility of trauma to neurovascular malformations has been excluded with recent spine imaging.

**毛細血管再充盈時間：這還是一個有用的臨床標誌？**

**Medical Intelligence Article: Capillary Refill Time: Is It Still a Useful Clinical Sign?**

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毛細血管再充盈時間（CRT）作為對危重病人快速心肺評估的一部分被衛生保健工作者廣泛運用。其測量包括血液回流到遠端毛細血管的目視檢查。據推測，CRT 是對周圍灌注改變的一個簡單的測量方法。目前，麻醉狀態下 CRT 的測量尚缺乏證據，尚需進一步研究。但可從其他領域的研究證據中得到借鑒。在這篇論文中，我們研究這方面的證據和影響 CRT 測量的影響因素。新的方法來評估的 CRT 正在研究中。在未來，CRT 測量可能使用新技術，如數位錄影或進化後的血氧飽和度探頭，這些新的方法將消除與臨床 CRT 顯示器測量的限制，甚至可以提供一個自動化的 CRT 測量方法。

（陸麗虹譯 薛張綱校）

Capillary refill time (CRT) is widely used by health care workers as part of the rapid, structured cardiopulmonary assessment of critically ill patients. Measurement involves the visual inspection of blood returning to distal capillaries after they have been emptied by pressure. It is hypothesized that CRT is a simple measure of alterations in peripheral perfusion. Evidence for the use of CRT in anesthesia is lacking and further research is required, but understanding may be gained from evidence in other fields. In this report,



we examine this evidence and factors affecting CRT measurement. Novel approaches to the assessment of CRT are under investigation. In the future, CRT measurement may be achieved using new technologies such as digital videography or modified oxygen saturation probes; these new methods would remove the limitations associated with clinical CRT measurement and may even be able to provide an automated CRT measurement.

### 麻醉藥異氟醚對缺氧誘導的含半胱氨酸的天冬氨酸蛋白水解酶 3 啟動和 $\beta$ 位澱粉樣前體蛋白裂解酶增加潛在的雙重作用

#### The Potential Dual Effects of Anesthetic Isoflurane on Hypoxia-Induced Caspase-3 Activation and Increases in $\beta$ -Site Amyloid Precursor Protein-Cleaving Enzyme Levels.

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**背景：**  $\beta$  澱粉樣蛋白(A $\beta$ )積聚、含半胱氨酸的天冬氨酸蛋白水解酶啟動、細胞凋亡和缺氧導致的神經毒性都被提出與阿爾茨海默病神經病理髮生機制有關。  $\beta$  澱粉樣蛋白是澱粉樣前體蛋白由天冬氨酸蛋白水解酶  $\beta$  位澱粉樣前體蛋白裂解酶(BACE)和  $\gamma$  分泌酶蛋白酶加工產生。吸入麻醉藥長久以來被認為有針對神經毒性的保護作用。但是，近期的研究提出吸入麻醉藥異氟醚可能通過誘導含半胱氨酸的天冬氨酸蛋白水解酶啟動和凋亡，以及增加  $\beta$  位澱粉樣前體蛋白裂解酶和  $\beta$  澱粉樣蛋白的水準來促進神經毒性。因此我們尋求明確異氟醚是否可誘導劑量相關性的雙重作用：含半胱氨酸的天冬氨酸蛋白水解酶啟動和  $\beta$  位澱粉樣前體蛋白裂解酶水準增加，是神經保護作用還是促進神經毒性作用。

**方法：** 人類 H4 神經膠質瘤細胞由單純缺氧(3% O<sub>2</sub>)、不同濃度異氟醚 (0.5%和 2%)和缺氧聯合 0.5%或 2%異氟醚處理。我們通過蛋白印跡分析測量含半胱氨酸的天冬氨酸蛋白水解酶 3 裂解(啟動)、 $\beta$  位澱粉樣前體蛋白裂解酶和 B 細胞淋巴瘤-2 基因水準。

**結果：** 結果顯示初次經過 0.5%異氟醚處理 8 小時減弱了缺氧誘導的含半胱氨酸的天冬氨酸蛋白水解酶 3 啟動和  $\beta$  位澱粉樣前體蛋白裂解酶水準增加作用，而 2%異氟醚處理 8 小時可增強這種作用。2%異氟醚處理也促進了缺氧誘導的 B 細胞淋巴瘤-2 基因水準降低。

**結論：**結果提示一種潛在性概念異氟醚有對缺氧誘導的毒性有雙重作用（保護和助長作用），這可能通過 B 細胞淋巴瘤-2 基因家族蛋白作用產生。這些發現可引發更多系統性研究來確定麻醉藥對阿爾茨海默病相關神經毒性的潛在雙重作用。

（任雲譯 薛張綱校）

**BACKGROUND:**  $\beta$ -Amyloid protein ( $A\beta$ ) accumulation, caspase activation, apoptosis, and hypoxia-induced neurotoxicity have been suggested to be involved in Alzheimer disease neuropathogenesis.  $A\beta$  is produced from amyloid precursor protein through proteolytic processing by the aspartyl protease  $\beta$ -site amyloid precursor protein-cleaving enzyme (BACE) and  $\gamma$ -secretase. Inhaled anesthetics have long been considered to protect against neurotoxicity. However, recent studies have suggested that the inhaled anesthetic isoflurane may promote neurotoxicity by inducing caspase activation and apoptosis, and by increasing levels of BACE and  $A\beta$ . We therefore sought to determine whether isoflurane can induce concentration-dependent dual effects on hypoxia-induced caspase-3 activation and increases in BACE levels: protection versus promotion.

**METHODS:** H4 human neuroglioma cells were treated with hypoxia (3%  $O_2$ ) alone, different concentrations of isoflurane (0.5% and 2%), and the combination of hypoxia and 0.5% or 2% isoflurane. The levels of caspase-3 cleavage (activation), BACE, and Bcl-2 were determined by Western blot analysis.

**RESULTS:** We show for the first time that treatment with 0.5% isoflurane for 8 hours attenuated, whereas treatment with 2% isoflurane for 8 hours enhanced, hypoxia-induced caspase-3 activation and increases in BACE levels. The 2% isoflurane treatment also enhanced a hypoxia-induced decrease in Bcl-2 levels.

**CONCLUSIONS:** These results suggest a potential concept that isoflurane has dual effects (protection versus promotion) on hypoxia-induced toxicity, which may act through Bcl-2 family proteins. These findings could lead to more systematic studies to determine the potential dual effects of anesthetics on Alzheimer disease-associated neurotoxicity.

對嗎啡耐藥的小鼠鞘內注射依那西普能減低谷氨酸能傳遞途徑，從而部分恢復嗎啡的抗傷害性刺激的作用。

### **Intrathecal Etanercept Partially Restores Morphine's Antinociception in Morphine-Tolerant Rats via Attenuation of the Glutamatergic Transmission**

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**背景：**長期暴露於嗎啡可以導致鎮痛耐受。嗎啡耐受除了阿片類受體的構型會受到改變，谷氨酸能傳遞途徑增強也與之有關。腫瘤壞死因數 $\alpha$ 通過啟動谷氨酸能傳遞途徑，與神經元的可塑性有關。我們檢驗了依那西普的作用，它是一種腫瘤壞死因數 $\alpha$ 能抑制小鼠身上的嗎啡耐受。

**方法：**在雄性為 Wister 小鼠體內植入兩根鞘內導管，一根導管連接一個微泵，用來注射嗎啡(15 µg/h)或者生理鹽水(1 µL/h)各 5 天。在第 5 天，嗎啡停用後，給予注射依那西普(50 µg)或者生理鹽水(10 µL)。3 個小時以後，給予急性的嗎啡治療(15 µg/10 µL, 靜脈注射)，所有的小鼠之後都接受了傷害性的尾巴輕拍試驗。

**結果：**結果顯示對於嗎啡耐受的小鼠，急性的依那西普(50 µg)治療可以提高嗎啡抗傷害性刺激的作用。對嗎啡耐受的小鼠，蛋白電泳提示依那西普能降低細胞膜谷氨酸運載蛋白 GLT-1 和 GLAST 的下調。依那西普能抑制 AMP 受體和 N-methyl-d-aspartate 受體亞單位（包括 GluR1/GluR2 和 NR1/NR2A.）的上調。

**結論：**這些結果顯示在嗎啡耐受後，依那西普能部分恢復嗎啡的抗傷害性刺激的作用。依那西普對減輕臨床疼痛治療有潛在價值，特別是對於長期接受阿片類藥物治療的患者，它能阻止耐受，更好地發揮阿片類藥物的作用。

（翁梅琳譯 薛張綱校）

**BACKGROUND:** Long-term exposure to morphine leads to analgesic tolerance. In addition to an opioid receptor conformational change, enhancing the glutamatergic signal transmission is also involved in morphine tolerance. Tumor necrosis factor- $\alpha$  has been demonstrated to correlate with neuronal plasticity via activation of glutamatergic transmission. We examined the effect of etanercept, a tumor necrosis factor- $\alpha$  inhibitor on morphine tolerance in rats.

**METHODS:** Male Wistar rats were implanted with 2 intrathecal (IT) catheters, and 1 IT catheter was connected to a mini-osmotic pump, used for either morphine infusion (15 µg/h) or saline (1 µL/h) infusion for 5 days. On day 5, either etanercept (50 µg) or saline (10 µL) was injected after discontinued morphine infusion. Three hours later, acute morphine (15 µg/10 µL, IT) treatment was given and all rats received a nociceptive tail-flick test.

**RESULTS:** The results showed that acute etanercept (50 µg) treatment caused a significant antinociceptive effect of morphine in morphine-tolerant rats. Western blotting indicated that etanercept attenuated the downregulation of membrane glutamate transporters GLT-1 and GLAST in morphine-tolerant rats. Etanercept also inhibited the upregulation of surface AMPA-receptor and N-methyl-d-aspartate-receptor subunits, including GluR1/GluR2 and NR1/NR2A.

**CONCLUSIONS:** These results demonstrate that etanercept partially restores the antinociceptive effect of morphine in morphine tolerance after a morphine challenge. Etanercept has potential for use in the clinical management of pain, particularly in patients who require long-term opioid treatment, and the effectiveness of which can be hampered by tolerance.

### 臂叢阻滯在術中對氧平衡的影響

#### **Influence of Brachial Plexus Blockade on Oxygen Balance During Surgery**

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有選擇性地在四肢局部疾病手術中實施臂叢神經阻滯會產生一個集合麻醉、運動阻滯和藥物性交感阻滯的有利的效果。爲了在未來的治療中更好地利用臂叢神經阻滯的持久效應，我們進行了一個健康病人行擇期手部手術的可控的前瞻性研究，研究中利用可靠的靜脈血氣監測技術，肯定了四肢阻滯區氧平衡的情況較爲阻滯區地有改善。

（張玥琪譯，薛張綱校）

The combined effects of anesthesia, motor blockade, and chemically induced sympathectomy after brachial plexus blockade can have a beneficial impact, when applied in selected, isolated diseased states of the upper limb. With the aim of using the prolonged effects of brachial plexus blockade for a future therapeutic application, we demonstrated a dependable methodology of venous blood gas monitoring and confirmed an improved oxygen balance of the blocked versus nonblocked upper extremity in a controlled, prospective study in healthy patients undergoing elective hand surgery.