



СЕВЕРО-ЗАПАДНЫЙ ГОСУДАРСТВЕННЫЙ МЕДИЦИНСКИЙ УНИВЕРСИТЕТ им. И.И.МЕЧНИКОВА  
САНКТ-ПЕТЕРБУРГ

*Не надо бояться стресса,  
его нет только у мертвых*

*Г.Селье*

# ХИРУРГИЧЕСКИЙ СТРЕСС

*А.Е. Карелов*

КАФЕДРА АНЕСТЕЗИОЛОГИИ И РЕАНИМАТОЛОГИИ им. В.Л.ВАНЕВСКОГО  
ЦЕНТР АНЕСТЕЗИОЛОГИИ И РЕАНИМАТОЛОГИИ  
Центр лечения боли

# ЗАЧЕМ НУЖНА КОНЦЕПЦИЯ ХИРУРГИЧЕСКОГО СТРЕССА?

- Риск анестезии
- Разработка/сравнение (новых) методик
- Прогноз послеоперационных осложнений
- Адекватность/качество анестезии в каждом конкретном клиническом случае

# ОПРЕДЕЛЕНИЕ

*Стресс-синдром* или *общий адаптационный синдром* определен как состояние, при котором появляются острые изменения функционирования нервной, эндокринной, сердечно-сосудистой, пищеварительной, дыхательной, репродуктивной систем, вызванные повреждающими (стрессовыми) агентами и направленные на интеграцию защитных механизмов

*Selye H. A syndrome produced by diverse noxious agents // Nature. – 1936. – V. 138. – P. 32*  
*Selye H. The alarm reaction // Canadian medical association journal. – 1936. – V. 34. – P. 706*

# ОПРЕДЕЛЕНИЕ

Стресс – это состояние, отличное от состояния покоя

*H.Selye, 1974*



# ОПРЕДЕЛЕНИЕ

Стресс (от англ. stress «нагрузка, напряжение; состояние повышенного напряжения») — совокупность неспецифических адаптационных (нормальных) реакций организма на воздействие различных неблагоприятных факторов–стрессоров (физических или психологических), нарушающее его гомеостаз, а также соответствующее **детерминирующее** состояние нервной системы организма (или организма в целом), **требующее в последующем период времени для восстановления**. В медицине, физиологии, психологии выделяют положительную (эустресс от др.-греч. εὖ- «хорошо») и отрицательную (дистресс от др.-греч. δυσ «потеря») формы стресса. По характеру воздействия выделяют нервно-психический, тепловой или холодовой (температурный), световой, голодовой и другие стрессы (облучения и т. д.).



# КОНЕЧНЫЙ РЕЗУЛЬТАТ

- Увеличение доступности энергосубстратов за счет имеющихся запасов
  - Гипергликемия
  - Гиперлипидемия
  - Аминоацидурия
- Усиление транспорта кислорода
  - Тахикардия
  - Артериальная гипертензия
  - Тахи- и гиперпноэ
- Системная воспалительная реакция – управление
- Гиперкоагуляция – сбережение
- Нарушение моторики кишечника – сбережение

# КОНЕЧНЫЙ РЕЗУЛЬТАТ

- Увеличение доступности энергосубстратов за счет имеющихся запасов **РЕЗУЛЬТАТ**
  - Гипергликемия
  - Гиперлипидемия
  - Аминоацидурия**начальное ухудшение состояния**
- Усиление транспорта **КРИТИЧНО**
  - Тахикардия
  - Артериальная гипертензия
  - Тахи- и гиперпноэ**объем резервов**
- Системное воспаление **ОПТИМАЛЬНЫЙ ПАРАМЕТР ПРОЦЕССА**
- Системное воспаление **обратно пропорционален тяжести**
- Гиперкоагуляция – сбережение
- Нарушение моторики кишечника – сбережение

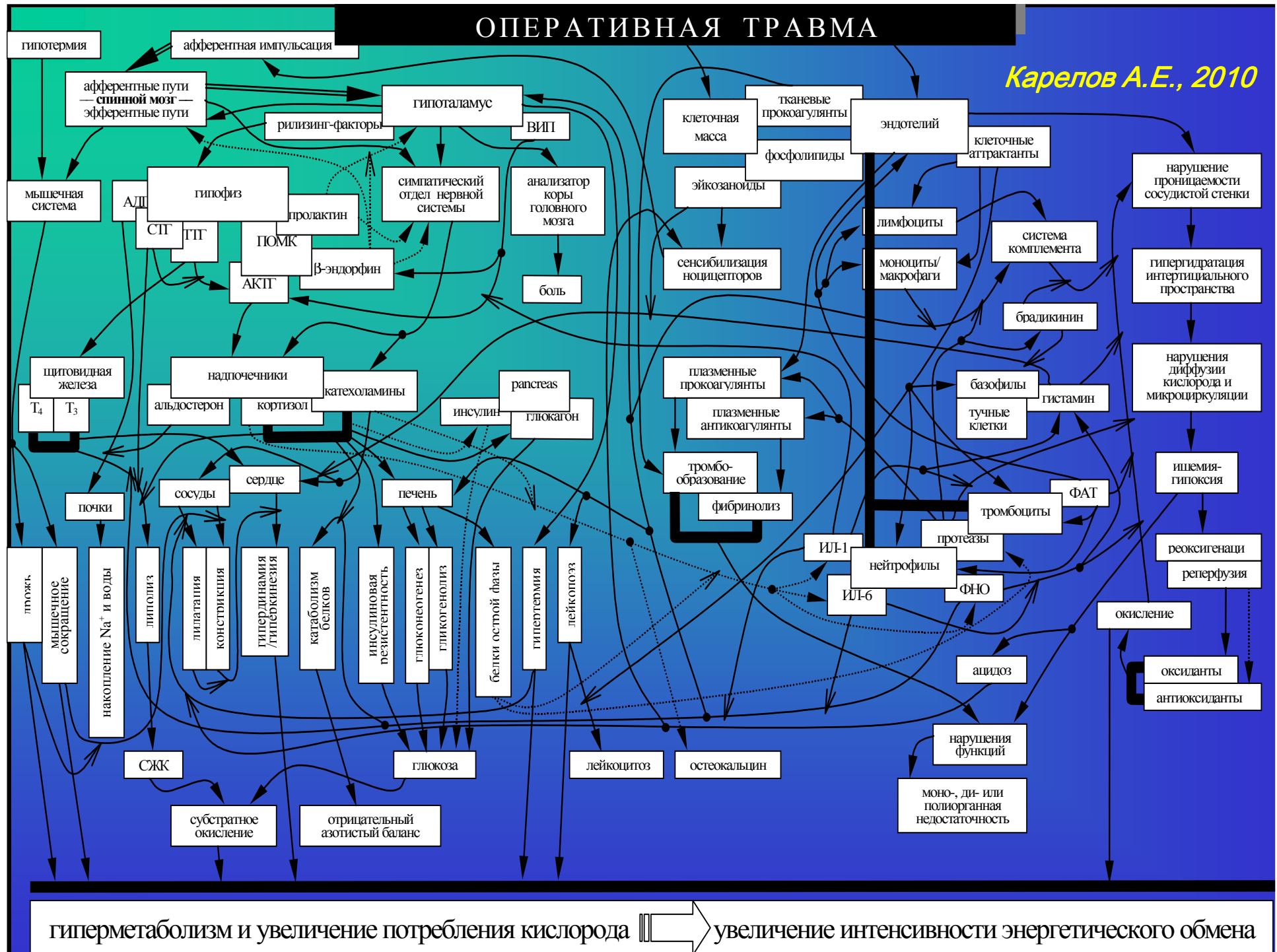


# ОСОБЕННОСТИ Х-СТРЕССА

- Присутствует мощнейший воспалительный компонент
- Возможны превентивные интервенции

# ОПЕРАТИВНАЯ ТРАВМА

Карелов А.Е., 2010

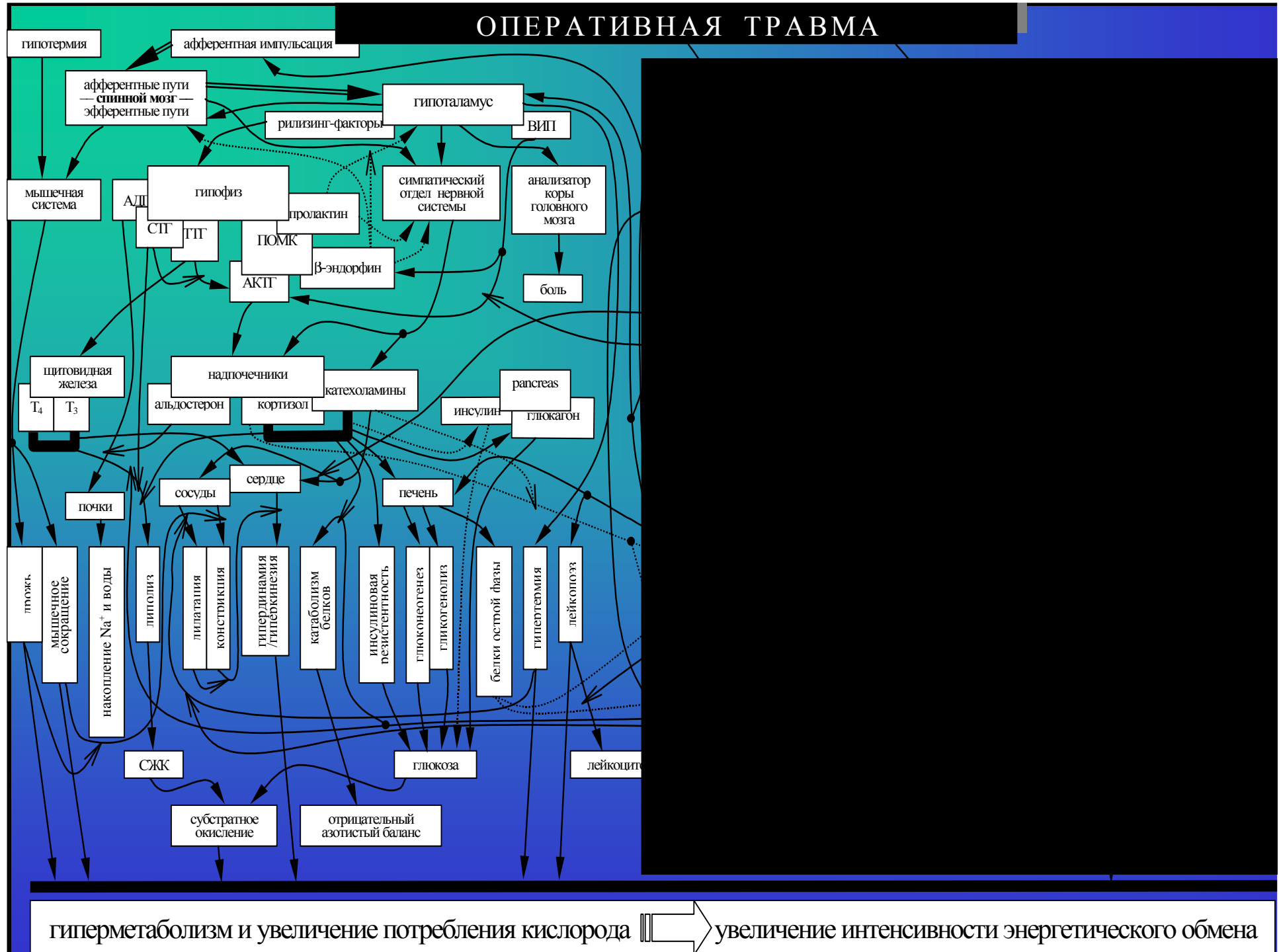


# КОМПОНЕНТЫ

- Нейроэндокринный ответ
  - Воспалительная реакция
- 
- Энергетический обмен
- 
- Иммунологические изменения



# ОПЕРАТИВНАЯ ТРАВМА



# СПИННОЙ МОЗГ

- Соматическая трехнейронная афферентная цепь (ноцицептивные пути)
- Вегетативные афферентные волокна

# ГИПОТАЛАМУС

- Рилизинг-факторы
- Активация симпатического отдела нервной системы

# ГИПОФИЗ

- Пролактин
- Проопиомеланокортин
  - Адrenокортикотропин
  - $\beta$ -эндорфин

# ГИПОФИЗ

- Антидиуретический гормон (вазопрессин)
- Соматотропный гормон
- Тиреотропный гормон



# ОРГАНЫ-МИШЕНИ

- Надпочечники
  - Глюкокортикоиды (кортизол)
  - Минералокортикоиды (альдостерон)
  - Катехоламины
    - адреналин
    - дофамин
    - норадреналин

# ОРГАНЫ-МИШЕНИ

- Поджелудочная железа
  - Глюкагон
  - Инсулин

# ОРГАНЫ-МИШЕНИ

- Щитовидная железа
  - Дийодтиронин
  - Трийодтиронин
  - Тетрайодтиронин (тироксин)

# УГЛЕВОДНЫЙ ОБМЕН

- Гипергликемия
  - нормо- или гипоинсулинемия
  - гликогенолиз (до 18 час)
  - глюконеогенез (2,0-2,5 → 4,4-5,1 мг/кг/мин)
  - инсулиновая резистентность (блокада GLUT-4)
- Инсулинзависимые и инсулинезависимые ткани

# ЛИПИДНЫЙ ОБМЕН

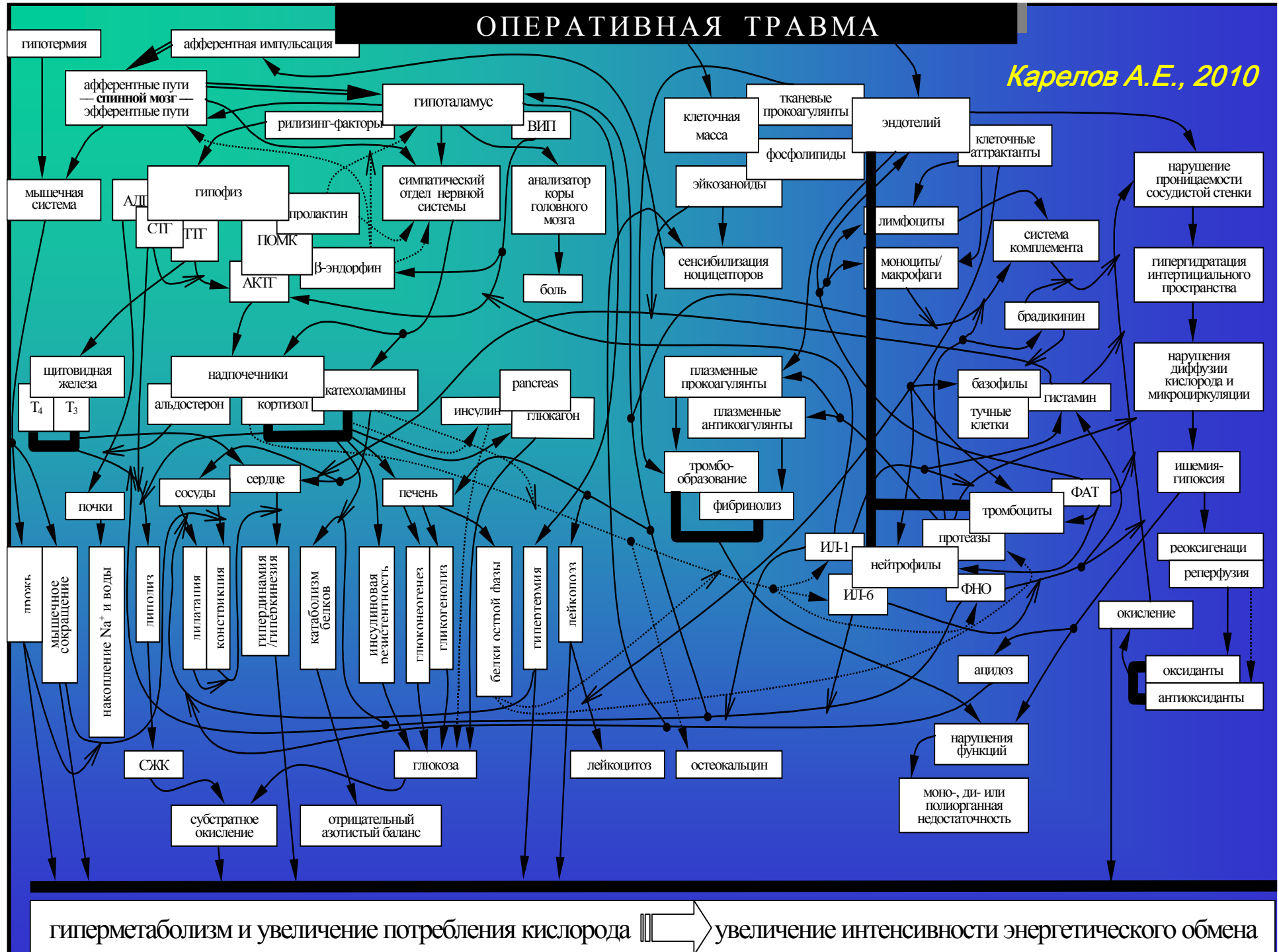
- Липолиз
  - свободные жирные кислоты
  - глицерол
- Дети и взрослые
- Последствия
  - жировая дистрофия печени
  - миокардиодистрофия
  - мышечная слабость

# БЕЛКОВЫЙ ОБМЕН

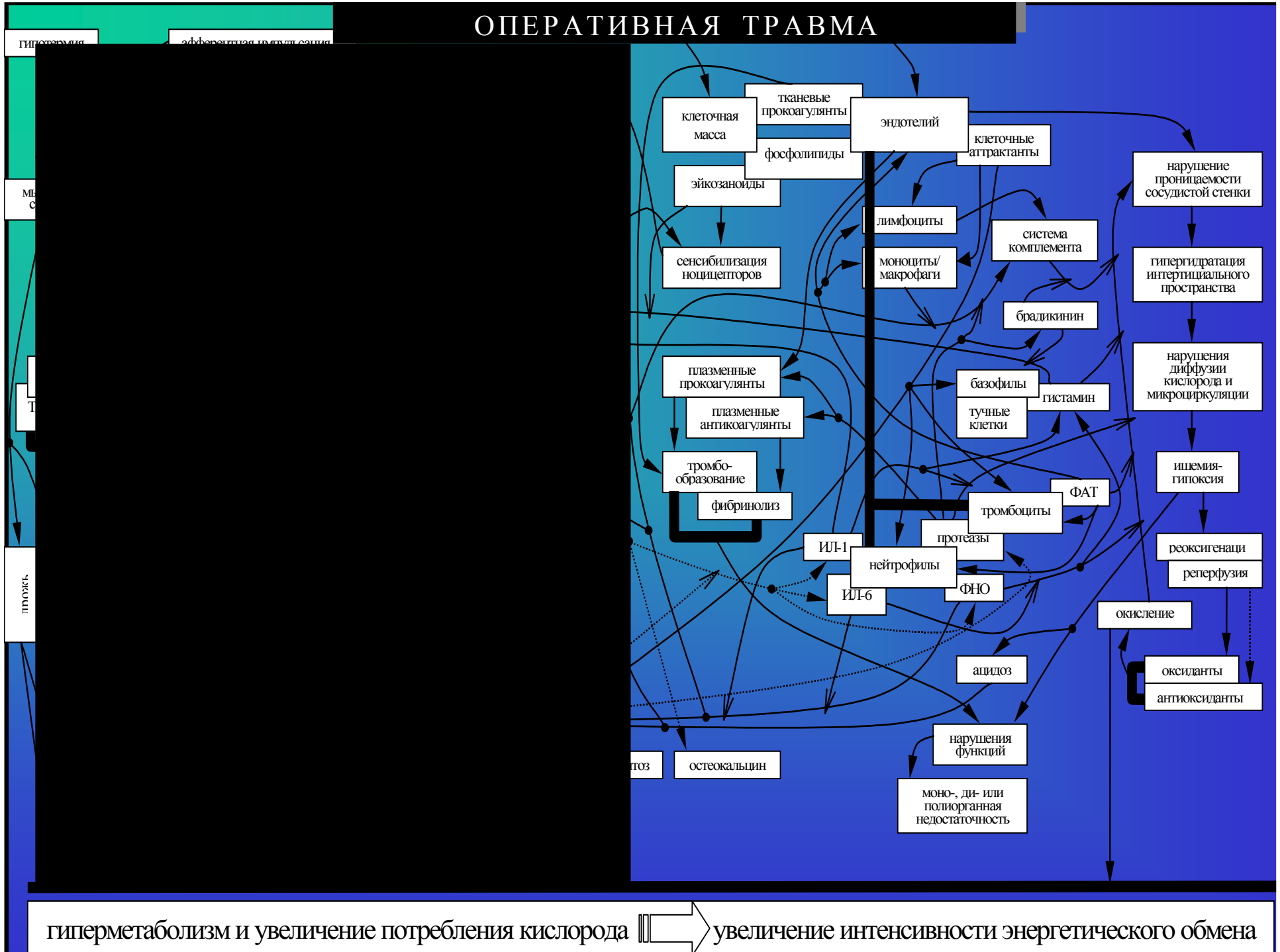
- Катаболизм белка (ФНО)
  - висцеральный
  - структурный
- Большие потери
  - глюконеогенез (аланин)
  - мочевая экскреция
- Анаболизм – заключительная часть восстановления

# ОПЕРАТИВНАЯ ТРАВМА

Карелов А.Е., 2010



# ОПЕРАТИВНАЯ ТРАВМА



гиперметаболизм и увеличение потребления кислорода → увеличение интенсивности энергетического обмена



# ГЕМОСТАЗ

- Повреждение эндотелия
  - Активация факторов свертывания
  - Образование тромбина
  - Выделение ТАФ
  - Активация тромбоцитов
- 
- Приобретение процессом системности
  - Нарушение микроциркуляции

# АНТИКОАГУЛЯЦИОННАЯ АКТИВНОСТЬ

- Активация коагуляционного каскада в системном кровотоке
- Активация антикоагуляционных факторов
- Истощение вовлеченных факторов
- ДВС-синдром:
  - лабораторный
  - клинический

# ВОСПАЛЕНИЕ

- Повреждение клеток с образованием свободных фосфолипидов
- Высвобождение
  - фосфолипазы  $A_2$
  - протеаз
  - гистамина
  - ЦИТОКИНОВ

# ФОСФОЛИПАЗА A<sub>2</sub>

- Образование из фосфолипидов арахидоновой кислоты, а затем медиаторов воспаления
  - простагландинов
  - лейкотриенов
- Сенситизация ноцицепторов

# ПРОТЕАЗЫ

- Неспецифический протеолиз
- Активация
  - Калликреин-кининовой системы (брадикинин)
  - Активация системы комплемента
    - Гемостаза и фибринолиза

# ГИСТАМИН

- Снижение сосудистого тонуса
- Усиление проницаемости сосудистой стенки

# ЦИТОКИНЫ

- Провоспалительные
  - ФНО, ИЛ-1, ТАФ, ..., ИЛ-6
- Противовоспалительные
  - ИЛ-10, ..., ИЛ-6

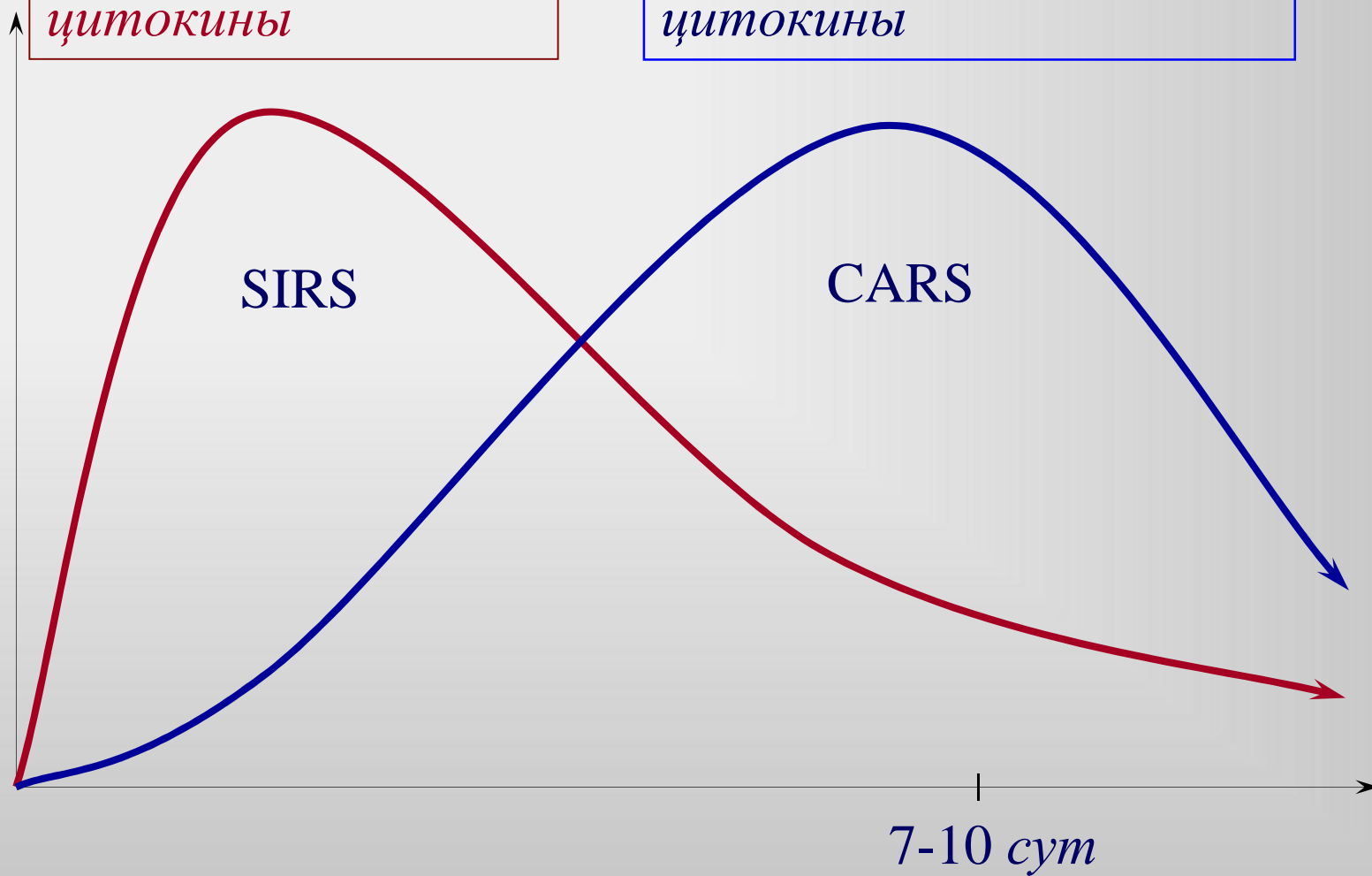
Белки острой фазы воспаления

позитивные: СРБ,  $\alpha_1$ -антихемотрипсин,  $\alpha_1$ -антитрипсин,  
ферритин, церуллоплазмин

негативные: альбумин, трансферрин

*Провоспалительные  
цитокины*

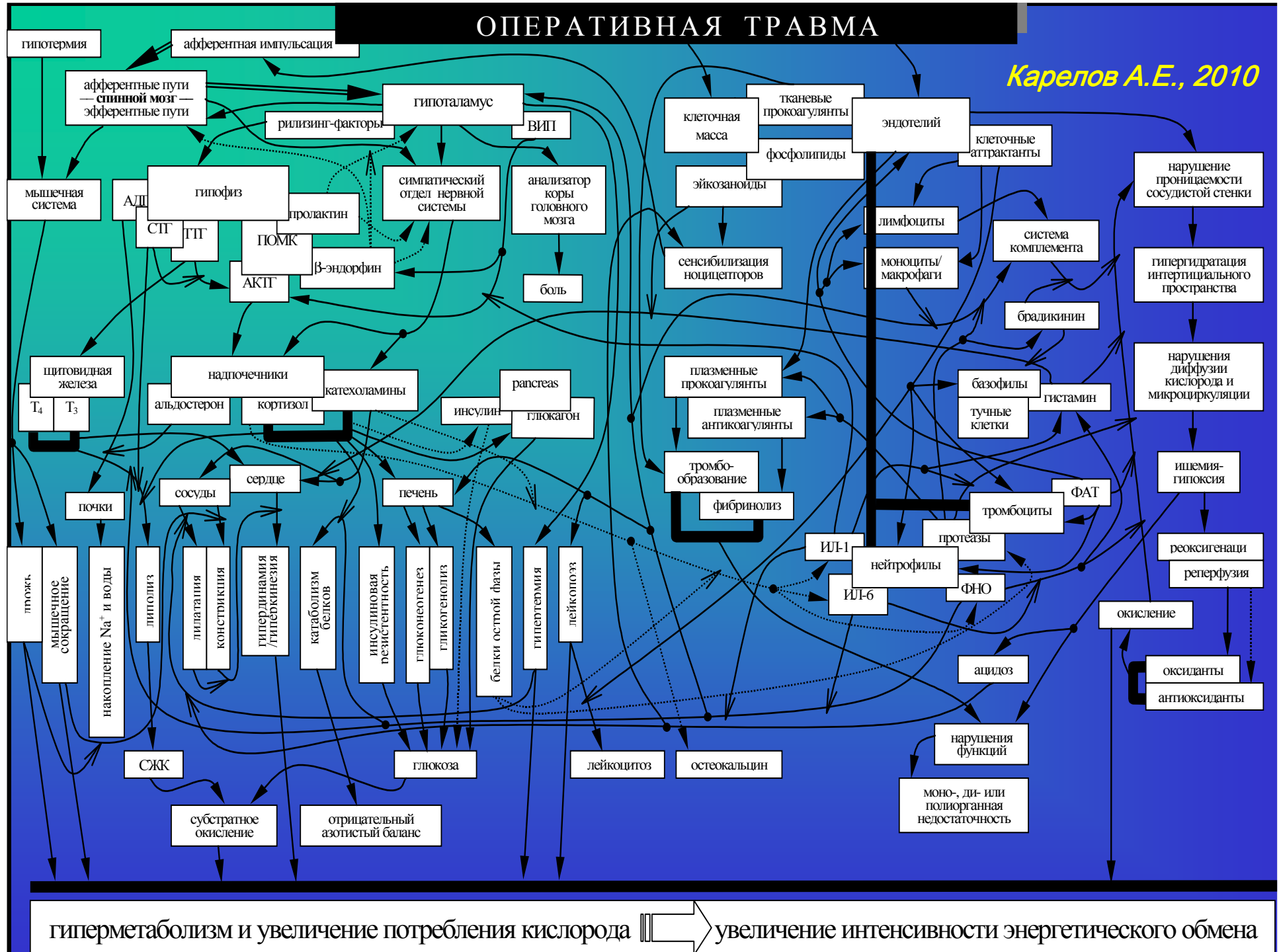
*Противовоспалительные  
цитокины*





# ОПЕРАТИВНАЯ ТРАВМА

Карелов А.Е., 2010

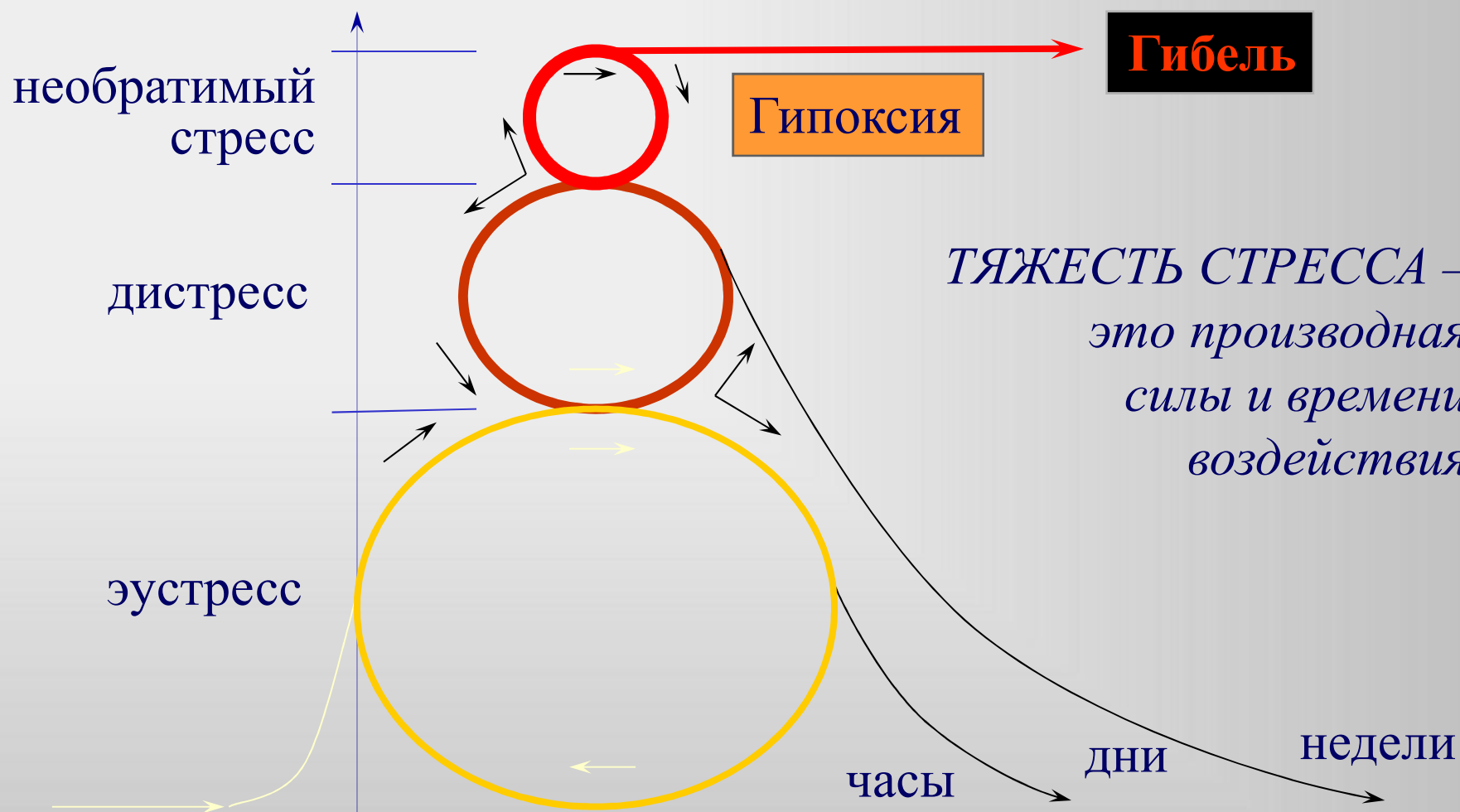


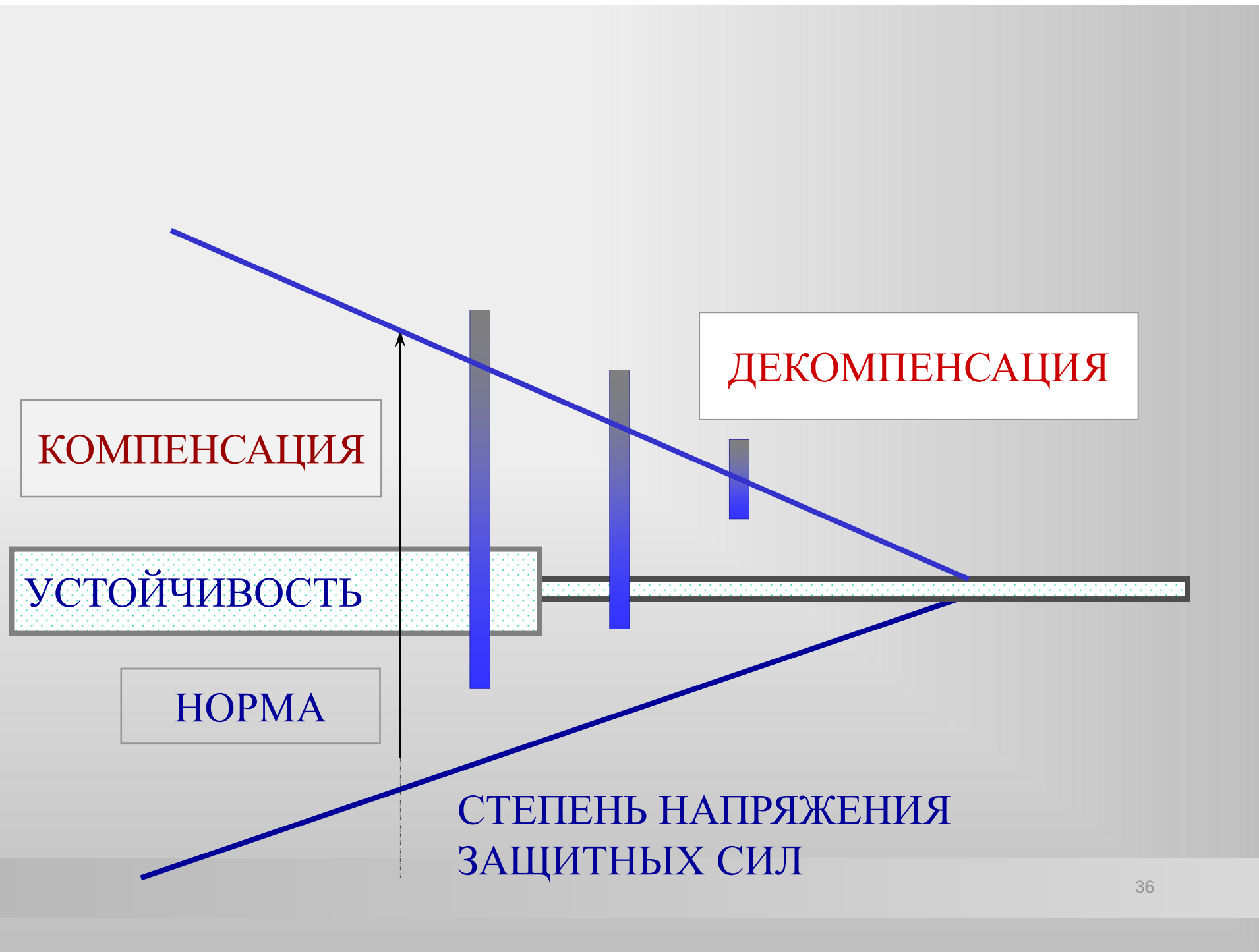
гиперметаболизм и увеличение потребления кислорода → увеличение интенсивности энергетического обмена

# ЭНЕРГОМЕТАБОЛИЗМ

- Увеличение затрат(/потребности) кислорода
- Гиперметаболизм

# КРИТИЧЕСКОЕ СОСТОЯНИЕ





# ОПЕРАЦИОННЫЙ СТРЕСС

THE LANCET Log in

SERIES | ANAESTHESIA | VOLUME 362, ISSUE 9399, P1921-1928, DECEMBER 06, 2003 PDF Purchase

## Anaesthesia, surgery, and challenges in postoperative recovery

Prof Henrik Kehlet, MD   • Jørgen B Dahl, MD

• Published: December 06, 2003 • DOI: [https://doi.org/10.1016/S0140-6736\(03\)14966-5](https://doi.org/10.1016/S0140-6736(03)14966-5)

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Summary

### Summary

Surgical injury can be followed by pain, nausea, vomiting and ileus, stress-induced catabolism, impaired pulmonary function, increased cardiac demands, and risk of thromboembolism. These problems can lead to complications, need for treatment in hospital, postoperative fatigue, and delayed convalescence. Development of safe and short-acting anaesthetics, improved pain relief by early intervention with multimodal analgesia, and stress reduction by regional anaesthetic techniques, β-blockade, analgesics, and

References

Uncited reference

Article Info

Related Series

- ~ катаболизм
- ~ боль
- ~ илеус
- ~ п/о тошнота и рвота
- ~ иммуносупрессия
- ~ повреждение миокарда
- ~ легочная дисфункция
- ~ нарушения системы гемостаза

*Kehlet H., 2003*

# ОПЕРАЦИОННЫЙ СТРЕСС

THE LANCET

Log in

SERIES | ANAESTHESIA

Anaesthesia

**КЛИНИЧЕСКИ** ~ катаболизм  
хирургический стресс рассматривается не  
как патогенетически единый – процесс, а как группа  
независимых процессов, объединенных в одно понятие  
**ПРОБЛЕМЫ**  
– как оценить хирургический стресс  
– как классифицировать  
послеоперационные осложнения

Summary

References

Uncited reference

Article Info

Related Series

Surgical injury can be followed by pain, nausea, vomiting and ileus, stress-induced catabolism, impaired pulmonary function, increased cardiac demands, and risk of thromboembolism. These problems can lead to complications, need for treatment in hospital, postoperative fatigue, and delayed convalescence. Development of safe and short-acting anaesthetics, improved pain relief by early intervention with multimodal analgesia, and stress reduction by regional anaesthetic techniques,  $\beta$ -blockade, analgesics, and

*Kehlet H., 2003*

# КОНЦЕПТЫ

- Глубина анестезии
- Маркеры стресса
- Стрессовый ответ и частота п/о осложнений
- Адекватность анестезии
- Ускоренное восстановление после хирургического вмешательства

# ГЛУБИНА АНЕСТЕЗИИ

## РАННИЙ ПЕРИОД

- Систематизация течения ингаляционной моноанестезии

*C. Snow, 1847  
A. Guedel, 1920, 1937  
G. Thomas et al., 1961*



# ГЛУБИНА АНЕСТЕЗИИ

## СОВРЕМЕННЫЙ ПЕРИОД

- Электронейрофизиология
  - Электроэнцефалограмма
  - Спектральный анализ
  - Вызванные потенциалы
- Сокращение лобной мышцы
- Сокращение нижней трети пищевода

# МАРКЕРЫ СТРЕССА

- Реакция вегетативного отдела нервной системы
- Показатели интенсивности воспалительной реакции
- Интенсивность аэробного метаболизма

# ВЕГЕТАТИВНЫЕ РЕАКЦИИ

- 
- Параметры системной гемодинамики (ЧСС, АД)
- Параметры внешнего дыхания (частота и глубина дыхания)
- Реакция зрачков и положение глаз
- Слезотечение и потоотделение

# ВЕГЕТАТИВНЫЕ РЕАКЦИИ

••

- Гормональный профиль (гормоны гипофиза, надпочечников, щитовидной и поджелудочной желез)  
и субстраты метаболизма (глюкоза, свободные жирные кислоты)

# ВОСПАЛИТЕЛЬНАЯ РЕАКЦИЯ

- Активность лейкоцитов
- Цитокины (ИЛ-6)
- С-реактивный белок
- Система комплемента

# АЭРОБНЫЙ МЕТАБОЛИЗМ

Интенсивность аэробного энергетического обмена

Метод – непрямой калориметрии

$$MR = VO_2 \times КЭК / ППТ,$$

где ППТ – площадь поверхности тела

КЭК – калорический эквивалент  $O_2$

$$VO_2 = V_I \cdot F_{IO_2} - V_E \cdot F_{EO_2}$$

# АДЕКВАТНОСТЬ АНЕСТЕЗИИ

Понятие *стресс-норма*

*В.А. Гологорский, 1988*

# СТРЕСС И ОСЛОЖНЕНИЯ

Постулировано, что чем больше выраженность  
операционного стресса, тем выше частота  
периоперационных осложнений

*Kehlet H. The stress response to anaesthesia and surgery:  
release mechanisms and the modifying factors //  
Clin. Anaesthesiol. – 1984. – V. 2. – P. 315-339*



# СТРЕСС И ОСЛОЖНЕНИЯ

OPEN ACCESS Freely available online

PLOS ONE

## High Postoperative Serum Cortisol Level Is Associated with Increased Risk of Cognitive Dysfunction Early after Coronary Artery Bypass Graft Surgery: A Prospective Cohort Study

Dong-Liang Mu<sup>1</sup>, Li-Huan Li<sup>2</sup>, Dong-Xin Wang<sup>1\*</sup>, Nan Li<sup>1</sup>, Guo-Jin Shan<sup>1</sup>, Jun Li<sup>1</sup>, Qin-Jun Yu<sup>2</sup>, Chun-Xia Shi<sup>2</sup>

**1** Department of Anesthesiology and Surgical Intensive Care Peking University First Hospital, Beijing, China, **2** Department of Anesthesiology, State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

### Abstract

**Context:** Stress response induced by surgery is proposed to play an important role in the pathogenesis of postoperative cognitive dysfunction.

**Objective:** To investigate the association between postoperative serum cortisol level and occurrence of cognitive dysfunction early after coronary artery bypass graft surgery.

**Design:** Prospective cohort study.

**Setting:** Two teaching hospitals.

**Patients:** One hundred and sixth-six adult patients who were referred to elective coronary artery bypass graft surgery from March 2008 to December 2009.

**Intervention:** None.

**Main Outcome Measures:** Neuropsychological tests were completed one day before and seven days after surgery. Cognitive dysfunction was defined using the same definition as used in the ISPOCD1-study. Blood samples were obtained in the first postoperative morning for measurement of serum cortisol concentration. Multivariate Logistic regression analyses were performed to assess the relationship between serum cortisol level and occurrence of postoperative cognitive dysfunction.

**Results:** Cognitive dysfunction occurred in 39.8% (66 of 166) of patients seven days after surgery. Multivariate Logistic regression analysis showed that high serum cortisol level was significantly associated with the occurrence of postoperative cognitive dysfunction (odds ratio [OR] 2.603, 95% confidence interval [CI] 1.371-4.944,  $P = 0.003$ ). Other independent predictors of early postoperative cognitive dysfunction included high preoperative New York Heart Association functional class (OR 0.402, 95% CI 0.207-0.782,  $P = 0.007$ ), poor preoperative Grooved Pegboard test score of nondominant hand (OR 1.022, 95% CI 1.003-1.040,  $P = 0.020$ ), use of penehyclidine as premedication (OR 2.565, 95% CI 1.109-5.933,  $P = 0.028$ ), and occurrence of complications within seven days after surgery (OR 2.677, 95% CI 1.201-5.963,  $P = 0.016$ ).

**Conclusions:** High serum cortisol level in the first postoperative morning was associated with increased risk of cognitive dysfunction seven days after coronary artery bypass graft surgery.

**Citation:** Mu D-L, Li L-H, Wang D-X, Li N, Shan G-J, et al. (2013) High Postoperative Serum Cortisol Level Is Associated with Increased Risk of Cognitive Dysfunction Early after Coronary Artery Bypass Graft Surgery: A Prospective Cohort Study. PLoS ONE 8(10): e77637. doi:10.1371/journal.pone.0077637

**Editor:** Jianzhong Sun, Thomas Jefferson University, United States of America

**Received:** May 31, 2013; **Accepted:** September 12, 2013; **Published:** October 15, 2013

Высокая концентрация кортизола в плазме утром после операции ассоциирована с более высокой частотой послеоперационной когнитивной дисфункции в первые 7 дней после кардиохирургической операции с искусственным кровообращением

Mu D.L., 2009

# СТРЕСС И ОСЛОЖНЕНИЯ



Journal of Anesthesia

December 2013, Volume 27, Issue 6, pp 942-944 | [Cite as](#)

Early postoperative cognitive dysfunction is associated with higher cortisol levels in aged patients following hip fracture surgery

Authors

[Authors and affiliations](#)

Mu-Huo Ji, Jin-Chun Shen, Rong Gao, Xiao-Yu Liu, Hong-Mei Yuan, Lin Dong, Jing Wu, Shan-Wu Feng, Wei-Yan Li, Jian-Jun Yang

Short Communication

First Online: 11 May 2013

617

Downloads

4

Citations

## Abstract

This study aimed to evaluate the relationship between plasma cortisol levels and the occurrence of postoperative cognitive dysfunction (POCD) in aged patients following hip fracture surgery. A total of 175 patients, aged 65 years or older, who were scheduled for hip fracture surgery with spinal anesthesia were enrolled. Perioperative plasma levels of cortisol and neurocognitive tests were determined at 1 day preoperatively and 7 days postoperatively. Seventy-seven patients completed both blood sample collections and neurocognitive tests. POCD occurred in 29.9 % of patients at 7 days postoperatively. POCD patients presented significantly higher cortisol levels compared with non-POCD patients ( $P < 0.05$ ). Furthermore, plasma cortisol levels were negatively correlated with mini-mental state examination (MMSE) scores at 7 days postoperatively ( $P < 0.0001$ ). A specificity of 93 % and a sensitivity of 35 % were identified for the plasma cortisol measurement to discriminate POCD patients from non-POCD patients. The results suggest higher plasma cortisol levels are associated with POCD in aged patients

Частота  
послеоперационной  
когнитивной  
дисфункции  
ассоциирована с  
высокой  
концентрацией  
кортизола в плазме

*Ji M.H., 2013*

# СТРЕСС И ОСЛОЖНЕНИЯ

International Journal of Colorectal Disease (2018) 33:1627–1634  
<https://doi.org/10.1007/s00384-018-3141-4>

ORIGINAL ARTICLE



## Perioperative risk prediction in the era of enhanced recovery: a comparison of POSSUM, ACPGBI, and E-PASS scoring systems in major surgical procedures of the colorectal surgeon

Nigel M. Bagnall<sup>1</sup> · Edward T. Pring<sup>1,2,3</sup> · George Malietzis<sup>1,2</sup> · Thanos Athanasiou<sup>1</sup> · Omar D. Faiz<sup>1,2</sup> · Robin H. Kennedy<sup>1,2</sup> · John T. Jenkins<sup>1,2</sup>

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### Abstract

**Purpose** This study aims to determine whether traditional risk models can accurately predict morbidity and mortality in patients undergoing major surgery by colorectal surgeons within an enhanced recovery program.

**Methods** One thousand three hundred eighty patients undergoing surgery performed by colorectal surgeons in a single UK hospital (2008–2013) were included. Six risk models were evaluated: (1) Physiology and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM), (2) Portsmouth POSSUM (P-POSSUM), (3) ColoRectal (CR-POSSUM), (4) Elderly POSSUM (E-POSSUM), (5) the Association of Great Britain and Ireland (ACPGBI) score, and (6) modified Estimation of Physiologic Ability and Surgical Stress Score (E-PASS). Model accuracy was assessed by observed to expected (O:E) ratios and area under Receiver Operating Characteristic curve (AUC).

**Results** Eleven patients (0.8%) died and 143 patients (10.4%) had a major complication within 30 days of surgery. All models overpredicted mortality and had poor discrimination: POSSUM 8.5% (O:E 0.09, AUC 0.56), P-POSSUM 2.2% (O:E 0.37, AUC 0.56), CR-POSSUM 7.1% (O:E 0.11, AUC 0.61), and E-PASS 3.0% (O:E 0.27, AUC 0.46). ACPGBI overestimated mortality in patients undergoing surgery for cancer 4.4% (O:E = 0.28, AUC = 0.41). Predicted morbidity was also overestimated by POSSUM 32.7% (O:E = 0.32, AUC = 0.51). E-POSSUM overestimated mortality (3.25%, O:E 0.57 AUC = 0.54) and morbidity (37.4%, O:E 0.30 AUC = 0.53) in patients aged  $\geq 70$  years and over.

**Conclusion** All models overestimated mortality and morbidity. New models are required to accurately predict the risk of adverse outcome in patients undergoing major abdominal surgery taking into account the reduced physiological and operative insult of laparoscopic surgery and enhanced recovery care.

**Keywords** Enhanced recovery · Colorectal surgery · Preoperative risk · ERAS · ERP

### Introduction

Colorectal surgery carries inherent perioperative risks, particularly for elderly patients with multi-morbidity [1]. Accurate risk stratification is essential to inform discussions with patients in order to facilitate informed consent, to enable surgical planning, and to anticipate the need for high

**Electronic supplementary material** The online version of this article (<https://doi.org/10.1007/s00384-018-3141-4>) contains supplementary material, which is available to authorized users.

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*Bagnall N.M., 2018*

# СТРЕСС И ОСЛОЖНЕНИЯ

## Neuroendocrine Stress Response and Heart Rate Variability: A Comparison of Total Intravenous Versus Balanced Anesthesia

Thomas Ledowski, MD, Berthold Bein, MD, Robert Hanss, MD, Andrea Paris, MD, Wolfgang Fudickar, MD, Jens Scholz, Prof. MD, and Peter H. Tonner, Prof. MD

Department of Anaesthesiology and Intensive Care Medicine, University Hospital Schleswig-Holstein Campus Kiel, Germany

Attenuating intraoperative stress is a key factor in improving outcome. We compared neuroendocrine changes and heart rate variability (HRV) during balanced anesthesia (BAL) versus total IV anesthesia (TIVA). Forty-three patients randomly received either BAL (sevoflurane/remifentanyl) or TIVA (propofol/remifentanyl). Depth of anesthesia was monitored by bispectral index. Stress hormones were measured at 7 time points (P1 = baseline; P2 = tracheal intubation; P3 = skin incision; P4 = maximum operative trauma; P5 = end of surgery; P6 = tracheal extubation; P7 = 15 min after tracheal extubation). HRV was analyzed by power spectrum analysis: very low frequency (VLF), low frequency (LF), high frequency (HF), LF/HF ratio, and to-

tal power (TP). LF/HF was higher in TIVA at P6 and TP was higher in TIVA at P3-7 (P3: 412.6 versus 94.2; P4: 266.7 versus 114.6; P5: 290.3 versus 111.9; P6: 1523.7 versus 658.1; P7: 1225.6 versus 342.6 ms<sup>2</sup>). BAL showed higher levels of epinephrine (P7: 100.5 versus 54 pg/mL), norepinephrine (P3: 221 versus 119.5; P4: 194 versus 130.5 pg/mL), adrenocorticotrophic hormone (P2: 10.5 versus 7.7; P5: 5.3 versus 3.6; P6: 10.9 versus 5.3; P7: 20.5 versus 7.1 pg/mL) and cortisol (P7: 6.9 versus 3.9 µg/dL). This indicates a higher sympathetic outflow using BAL versus TIVA during ear-nose-throat surgery.

(Anesth Analg 2005;101:1700-5)

The stress response to surgery is characterized by increased release of catabolic and immunosuppressive pituitary hormones and activation of the sympathetic nervous system (1). Excessive intraoperative stress may influence outcome, length of hospital stay, and overall costs of hospital care (2,3). Because there is evidence that the choice of anesthetic may influence the intraoperative stress response (4), we compared sevoflurane-based balanced anesthesia (BAL) with total IV anesthesia (TIVA). Although both regimens are commonly used, there are no data comparing the stress response during administration of TIVA versus BAL technique in a consistent surgical

Measurement of circulating stress hormones requires blood samples and laboratory analyses and is therefore not suitable for bedside monitoring of intraoperative stress. Thus, noninvasive measurement of stress-related physiological changes is highly desirable. Heart rate variability (HRV) may reflect autonomic nervous system (ANS) activity. Different frequency bands of the HRV power spectrum are related to the sympathetic and parasympathetic activity of the ANS (5). Thus, stress-related sympathetic activation may induce a similar change in the HRV pattern observed.

Because HRV is influenced both by volatile and IV

Сбалансированная анестезия в большей степени активирует симпатический отдел нервной системы, чем тотальная внутривенная анестезия

Ledowski T, 2005

# СТРЕСС И ОСЛОЖНЕНИЯ

Clinical Research Article

Korean J Anesthesiol 2010 October 59(4): 265-269  
DOI: 10.4097/kjae.2010.59.4.265

## Comparison of the neuroendocrine and inflammatory responses after laparoscopic and abdominal hysterectomy

Tae Kwane Kim, and Jun Rho Yoon

Department of Anesthesiology and Pain Medicine, College of Medicine, The Catholic University of Korea, Bucheon, Korea

**Background:** Laparoscopic surgery is associated with a more favorable clinical outcome than that of conventional open surgery. This might be related to the magnitude of the tissue trauma. The aim of the present study was to examine the differences of the neuroendocrine and inflammatory responses between the two surgical techniques.

**Methods:** Twenty-four patients with no major medical disease were randomly assigned to undergo laparoscopic (n = 13) or abdominal hysterectomy (n = 11). Venous blood samples were collected and we measured the levels of interleukin-6 (IL-6), CRP and cortisol at the time before and after skin incision, at the end of peritoneum closure and at 1 h and 24 h after operation.

**Results:** The laparoscopic hysterectomy group demonstrated less of an inflammatory response in terms of the serum IL-6 and CRP responses than did the abdominal hysterectomy group, and the laparoscopic hysterectomy group had a shorter hospital stay (P < 0.05). The peak serum IL-6 (P < 0.05) and CRP concentrations were significantly less increased in the laparoscopic group as compared with that of the abdominal hysterectomy group (P < 0.05), while the serum cortisol concentration showed a similar time course and changes and there were no significant difference between the groups. The response of interleukin-6 showed a significant correlation with the response of CRP (r = 0.796; P < 0.05).

**Conclusions:** The laparoscopic surgical procedure leaves the endocrine metabolic response largely unaltered as compared with that of open abdominal hysterectomy, but it reduces the inflammatory response as measured by the IL-6 and CRP levels. (Korean J Anesthesiol 2010; 59: 265-269)

**Key Words:** Cytokines, Hysterectomy, Interleukine-6, Laparoscopy, Surgical procedures.

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Corresponding author: Jun Rho Yoon, M.D., Department of Anesthesiology and Pain Medicine, College of Medicine, The Catholic University of Korea, 2, Sosa-dong, Wonmi-gu, Bucheon 420-717, Korea. Tel: 82-32-340-7075, Fax: 82-32-340-2255, E-mail: pauly@catholic.ac.kr  
This work was supported by the Institute of Clinical Medicine Research of Bucheon St.Mary's Hospital, Research Fund.

Лапароскопическая  
гистерэктомия не оказала  
положительного влияния на  
нейроэндокринный ответ  
(концентрацию кортизола),  
но значительно снизила  
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операцией, выполненной  
открытым доступом

*Kim T.K., 2010*

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# *Отказ от курения*

за 4 недели до операции

Krogh F., et al., 1998

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## Preoperative Smoking Habits and Postoperative Pulmonary Complications

Leslie G. Bluman, MPH, [Lori Mosca](#), MD, MPH, PhD , [Nancy Newman](#), MS, [David G. Simon](#), MD, MSc

 PlumX Metrics

DOI: <https://doi.org/10.1378/chest.113.4.883>

Abstract **Full Text** References

**Objective**  
To examine the effect of preoperative smoking behavior on postoperative pulmonary complications.

**Design**  
Prospective cohort study.

**Setting**  
The Veterans Administration Medical Center, Syracuse, NY.

**Participants**  
Patients scheduled for noncardiac elective surgery (n=410).

**Measurements and results**

за 4 недели до операции – не  
выявлено преимуществ

*Bluman L.G., 1998*

# Отказ от курения

CLINICAL ORTHOPAEDICS AND RELATED RESEARCH  
Number 367, pp. 172–180  
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## Smoking and Joint Replacement: Resource Consumption and Short Term Outcome

*Carlos J. Lavernia, MD\*;* *Rafael J. Sierra, MD\*;*  
*and Orlando Gomez-Marin, MSc, PhD\*\**

Smoking has been shown to increase morbidity and mortality in surgical procedures. Microvascular and trauma surgeons have documented the adverse effect of smoking in the healing of skin flaps and increased complication rates in the treatment of nonunions. In addition, spine surgeons have shown the adverse effects of smoking in fusion rates. The objective of this study was to assess the effects of smoking on the incidence of short term complications, resource consumption, and length of hospital stay of patients undergoing arthroplasty of the hip and knee. Two hundred two patients who underwent joint replacement surgery were evaluated. A smoking history was assessed for all patients. The number of packs multiplied by the number of years as a smoker were calculated. Operative and anesthesia time and medical severity of illness were documented on all patients. Short term outcome was assessed using hospital charges, length of stay, inpatient consults, and the presence and number of complications during the acute hospitalization. One hundred forty-one primary and 61 revision procedures were done. The mean age of the patients was 66.07 years. Sixty-one percent of the patients

had osteoarthritis, 3.9% had rheumatoid arthritis, 4.9% had osteonecrosis, 28% had a failed total knee or hip arthroplasty and 2% had a periprosthetic fracture. There were 25 patients who smoked and 177 patients who did not smoke. For patients who currently smoke, the mean number of packs of cigarettes smoked per day multiplied by the number of years as a smoker was 28.3. The average length of stay in the hospital was 5.1 days and the average hospital charges were \$31,315. Patients who smoked were younger and had fewer comorbidities than patients who did not smoke. However, patients who smoked were found to have statistically longer surgical time and higher charges adjusted for age, procedure, and surgeon than patients who did not smoke. Patients who smoked also had longer anesthesia times. A history of smoking is obtained easily on all patients. Preoperative screening for nicotine use can predict operative time and health resource consumption. The exact reasons why patients who smoked had higher hospital charges remain elusive. Probable reasons include higher degree of operative complexity (orthopaedic severity of illness). In addition patients who smoked previously also had better short term outcome than patients who currently smoke. This

за 4 недели до операции –  
улучшает краткосрочные  
показатели исхода  
хирургического лечения

*Lavernia C.J., 1999*

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## Relationship Between the Duration of the Preoperative Smoke-Free Period and the Incidence of Postoperative Pulmonary Complications After Pulmonary Surgery

Masashi Nakagawa, MD , Hideo Tanaka, MD, Hideaki Tsukuma, MD, Yoshihiko Kishi, MD

PlumX Metrics  
DOI: <https://doi.org/10.1378/chest.120.3.705>

Abstract Full Text Images References

### Abstract

**Study objective**  
To examine the relationship between the duration of the preoperative smoke-free period and the development of postoperative pulmonary complications (PPCs) in patients who underwent pulmonary surgery, and the optimal timing of quitting smoking.

**Design**  
Retrospective cohort study.

**Setting**  
Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan.

за 4 недели до операции –  
снижает частоту  
осложнений при  
операциях на легких

*Nakagawa M., 2001*

# Отказ от курения

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February 1, 2005

## Smoking Is a Risk Factor for Incisional Hernia

Lars Tue Sørensen, MD; Ulla B. Hemmingsen, RN; Lene T. Kirkeby, MD; [et al](#)  
» Author Affiliations | Article Information  
Arch Surg. 2005;140(2):119-123. doi:10.1001/archsurg.140.2.119

### Abstract

**Hypothesis** A number of risk factors for incisional hernia have been identified, but the pathogenesis remains unclear. Based on previous findings of smoking as a risk factor for wound complications and recurrence of groin hernia, we studied whether smoking is associated with incisional hernia.

**Design** Cohort study. Clinical follow-up study for incisional hernia 33 to 57 months following laparotomy for gastrointestinal disease. Variables predictive for incisional hernia were assessed by multiple regression analysis.

**Setting** Department of Surgery, Bispebjerg Hospital, Copenhagen, Denmark.

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послеоперационных  
осложнений при устранении  
послеоперационной грыжи

*Sorensen L. T., 2005*

# Отказ от употребления алкоголя

Papers

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## Effect of preoperative abstinence on poor postoperative outcome in alcohol misusers: randomised controlled trial

Hanne Tønnesen, Jacob Rosenberg, Hans J Nielsen, Verner Rasmussen, Christina Hauge, Ib K Pedersen, Henrik Kehlet

### Abstract

**Objective** To evaluate the influence of preoperative abstinence on postoperative outcome in alcohol misusers with no symptoms who were drinking the equivalent of at least 60 g ethanol/day.

**Design** Randomised controlled trial.

**Setting** Copenhagen, Denmark.

**Subjects** 42 alcoholic patients without liver disease admitted for elective colorectal surgery.

**Interventions** Withdrawal from alcohol consumption for 1 month before operation (disulfiram controlled) compared with continuous drinking.

**Main outcome measures** Postoperative complications requiring treatment within the first month after surgery. Perioperative immunosuppression measured by delayed type hypersensitivity; myocardial ischaemia and arrhythmias measured by Holter tape recording; episodes of hypoxaemia measured by pulse oximetry. Response to stress during the operation were assessed by heart rate, blood pressure, serum concentration of cortisol, and plasma concentrations of glucose, interleukin 6, and catecholamines.

**Results** The intervention group developed significantly fewer postoperative complications than the continuous drinkers (31% v 74%,  $P=0.02$ ).

Delayed type hypersensitivity responses were better in the intervention group before ( $37 \text{ mm}^2$  v  $12 \text{ mm}^2$ ,  $P=0.04$ ), but not after surgery ( $3 \text{ mm}^2$  v  $3 \text{ mm}^2$ ).

Development of postoperative myocardial ischaemia (23% v 85%) and arrhythmias (33% v 86%) on the second postoperative day as well as nightly hypoxaemic episodes (4 v 18 on the second postoperative night) occurred significantly less often in the intervention group. Surgical stress responses were lower in the intervention group ( $P<0.05$ ).

stay and need more secondary surgery. The most common complications are infections, cardiopulmonary insufficiency, and episodes of bleeding. The pathogenic mechanisms are probably preoperative immunosuppression, preclinical cardiac insufficiency, haemostatic imbalance, and an exaggerated response to surgical stress.<sup>7</sup> In non-surgical patients such dysfunctions are often reversible after withdrawal from alcohol.<sup>5</sup>

We investigated the influence of 1 month of preoperative abstinence from alcohol on postoperative morbidity in a controlled randomised design.

### Methods

#### Protocol

We planned to evaluate a minimal relevant difference above 50% between the groups. The complication rate in the alcohol misusers was estimated as 67-75%.<sup>2-4</sup> We were willing to accept a high type I failure because of the relatively few side effects of intervention compared with the poor outcome otherwise, whereas we would not overlook a possible benefit in this high risk group ( $2\alpha=0.10$ ,  $\beta=0.05$ ). The number of included patients was then calculated to  $2 \times 18$ . The inclusion criteria were alcohol misuse of five or more drinks (60 g of ethanol) a day without clinical or historical evidence of alcohol related illness (cirrhosis, hepatitis, pancreatitis, polyneuropathy, Wernicke-Korsakoff syndrome) in patients suffering from colorectal disease who probably required elective surgical intervention. Only patients without disseminated malignant disease or signs of bowel obstruction scheduled for intended radical surgery were included.

To avoid surgical delay the patients were included in the trial before the final decision for operation was

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Verner Rasmussen, consultant

Department of Surgical Gastroenterology, Bispebjerg Hospital, University of Copenhagen, DK-2400 Copenhagen NV, Denmark  
Christina Hauge, senior surgeon

Department of Surgery, Herlev Hospital, University of Copenhagen, DK-2730 Herlev, Denmark  
Ib K Pedersen, chief surgeon

за 4 недели до операции для тех, кто бессимптомно употреблял более 60 г/сут этанола

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– аритмии

– эпизоды апноэ во сне

Tønnesen H., 1999

# Психологическая подготовка

## – Боль

*Egbert LD, Bant GE, Welch CE, et al. Reduction of postoperative pain by encouragement and instruction of patients. N Engl J Med 1964;207:824-7*

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*Daltroy LH, Morlino CI, Eaton HM, et al. Preoperative education for total hip and knee replacement patients. Arthritis Care Res 1998;11:469-78*

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*Klafta JM, Roizen MF. Current understanding of patients' attitudes toward and preparation for anesthetic: a review. Anesth Analg 1996; 83:1314-21*

# Адекватная премедикация

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March 3, 2015

## Effect of Sedative Premedication on Patient Experience After General Anesthesia

### A Randomized Clinical Trial

Axel Maurice-Szamburski, MD<sup>1</sup>; Pascal Auquier, MD, PhD<sup>2</sup>; Véronique Viarre-Oreal, PhD<sup>1</sup>; et al

> [Author Affiliations](#) | [Article Information](#)

JAMA. 2015;313(9):916-925. doi:10.1001/jama.2015.1108

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### Abstract

**Importance** Sedative premedication is widely administered before surgery, but little clinical evidence supports its use.

**Objective** To assess the efficacy of sedative premedication on perioperative patient experience.

**Design, Setting, and Participants** A randomized clinical trial, the PremedX study, enrolled 1062 adult patients who had been scheduled for various elective surgical procedures in 10 French teaching hospitals (in Marseille).

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Премедикация

бензодиазепином не

улучшает самочувствие

пациентов, но отсрочивает

пробуждение и экстубацию

*Maurice-Szamburski A., 2015*



# Адекватная премедикация



[Intervention Review]

## Clonidine premedication for postoperative analgesia in children

Paul Lambert<sup>1</sup>, Allan M Cyna<sup>1</sup>, Nicholas Knight<sup>2</sup>, Philippa Middleton<sup>3</sup>

<sup>1</sup>Department of Women's Anaesthesia, Women's and Children's Hospital, Adelaide, Australia. <sup>2</sup>Department of Anaesthesia, Royal Adelaide Hospital, Adelaide, Australia. <sup>3</sup>ARCH: Australian Research Centre for Health of Women and Babies, The Robinson Institute, Discipline of Obstetrics and Gynaecology, The University of Adelaide, Adelaide, Australia

Contact address: Allan M Cyna, Department of Women's Anaesthesia, Women's and Children's Hospital, 72 King William Road, Adelaide, South Australia, 5006, Australia. [allan.cyna@health.sa.gov.au](mailto:allan.cyna@health.sa.gov.au).

**Editorial group:** Cochrane Anaesthesia, Critical and Emergency Care Group.

**Publication status and date:** New, published in Issue 1, 2014.

**Citation:** Lambert P, Cyna AM, Knight N, Middleton P. Clonidine premedication for postoperative analgesia in children. *Cochrane Database of Systematic Reviews* 2014, Issue 1. Art. No.: CD009633. DOI: 10.1002/14651858.CD009633.pub2.

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### ABSTRACT

#### Background

Postoperative pain remains a significant problem following paediatric surgery. Premedication with a suitable agent may improve its management. Clonidine is an alpha-2 adrenergic agonist which has sedative, anxiolytic and analgesic properties. It may therefore be a useful premedication for reducing postoperative pain in children.

#### Objectives

To evaluate the evidence for the effectiveness of clonidine, when given as a premedication, in reducing postoperative pain in children less than 18 years of age. We also sought evidence of any clinically significant side effects.

Премедикация клонидином  
снижает тяжесть  
послеоперационного  
болевого синдрома у  
детей

*Lambert P., 2014*

# Проведение предоперационной антибиотикопрофилактики

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## Current Guidelines for Antibiotic Prophylaxis of Surgical Wounds

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RONALD K. WOODS, M.D., PH.D., and E. PATCHEN DELLINGER, M.D., University of Washington Medical Center, Seattle, Washington  
*Am Fam Physician.* 1998 Jun 1;57(11):2731-2740.

**Appropriately administered antibiotic prophylaxis reduces the incidence of surgical wound infection. Prophylaxis is uniformly recommended for all clean-contaminated, contaminated and dirty procedures. It is considered optional for most clean procedures, although it may be indicated for certain patients and clean procedures that fulfill specific risk criteria. Timing of antibiotic administration is critical to efficacy. The first dose should always be given before the procedure, preferably within 30 minutes before incision. Readministration at one to two half-lives of the antibiotic is recommended for the duration of the procedure. In general, postoperative administration is not recommended. Antibiotic selection is influenced by the organism most commonly causing wound infection in the specific procedure and by the relative costs of available agents. In certain gastrointestinal procedures, oral and intravenous administration of agents with activity against gram-negative and anaerobic bacteria is warranted, as well as mechanical preparation of the bowel. Cefazolin provides adequate coverage for most other types of procedures.**

Postoperative wound infections have an enormous impact on patients' quality of life and contribute substantially to the financial cost of patient care. The potential consequences for patients range from increased pain and care of an open wound to sepsis and even death. Approximately 1 million patients have such wound infections each year in the United States, extending the average hospital stay by one week and increasing the cost of hospitalization by 20 percent.<sup>1</sup> This translates to an additional \$1.5 billion in health care costs annually.<sup>2</sup>

– снижает частоту нагноения  
послеоперационной раны

*Woods R.K., 1998*

# Регионарная анальгезия/анестезии местными анестетиками при операциях на органах малого таза и нижних конечностях

## Papers

### Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials

Anthony Rodgers, Natalie Walker, S Schug, A McKee, H Kehlet, A van Zundert, D Sage, M Futter, G Saville, T Clark, S MacMahon

#### Abstract

**Objectives** To obtain reliable estimates of the effects of neuraxial blockade with epidural or spinal anaesthesia on postoperative morbidity and mortality.  
**Design** Systematic review of all trials with randomisation to intraoperative neuraxial blockade or not.

**Studies** 141 trials including 9559 patients for which data were available before 1 January 1997. Trials were eligible irrespective of their primary aims, concomitant use of general anaesthesia, publication status, or language. Trials were identified by extensive search methods, and substantial amounts of data were obtained or confirmed by correspondence with trialists.

**Main outcome measures** All cause mortality, deep vein thrombosis, pulmonary embolism, myocardial infarction, transfusion requirements, pneumonia, other infections, respiratory depression, and renal failure.

**Results** Overall mortality was reduced by about a third in patients allocated to neuraxial blockade (103 deaths/4871 patients versus 144/4688 patients, odds ratio = 0.70, 95% confidence interval 0.54 to 0.90, P = 0.006). Neuraxial blockade reduced the odds of deep vein thrombosis by 44%, pulmonary embolism by 55%, transfusion requirements by 50%, pneumonia by 39%, and respiratory depression by 59% (all P < 0.001). There were also reductions in myocardial infarction and renal failure. Although there was limited power to assess subgroup effects, the proportional reductions in mortality did not clearly differ by surgical group, type of blockade (epidural or

#### Introduction

Anaesthesia is commonly classified into two main techniques: general anaesthesia, in which gaseous or intravenous drugs achieve central neurological depression, and regional anaesthesia, in which drugs are administered directly to the spinal cord or nerves to locally block afferent and efferent nerve input.<sup>1</sup> Regional anaesthesia for major thoracic, abdominal, or leg surgery relies on neuraxial blockade by injection of local anaesthetic drugs into either the subarachnoid space (spinal anaesthesia) or into the epidural space surrounding the spinal fluid sac (epidural anaesthesia).

The risks of fatal or life threatening events are increased several fold after major surgery, but there is debate about whether the type of anaesthesia has any substantive effect on these risks. Neuraxial blockade has several physiological effects that provide a rationale for expecting to improve outcome with this technique.<sup>2</sup> However, the few clinical trials of epidural or spinal anaesthesia that have focused specifically on fatal or life threatening events have generally been too small to detect effects of plausible size reliably. To provide more reliable estimates of the effects of neuraxial blockade on postoperative morbidity and mortality, we conducted a systematic review of all relevant randomised trials.

#### Methods

##### Identification of trials and data collection

We sought to identify all trials in which patients were randomised to receive intraoperative neuraxial blockade (with epidural or spinal anaesthesia) or not. We did

Clinical Trials Research Unit, Department of Medicine, University of Auckland, Private Bag 92019, Auckland, New Zealand

Anthony Rodgers *co-director*  
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Department of Anesthesiology, Intensive Care and Pain Therapy, Catharina Hospital

## МЕТА-АНАЛИЗ

141 рандомизированное исследование (1971-1999);

9559 пациентов

Сравнение групп пациентов с нейро-аксиальным блоком и общей анестезией

Rogers et al., 2000

# Регионарная анальгезия/анестезии местными анестетиками при операциях на органах малого таза и нижних конечностях

## Papers

### Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials

Anthony Rodgers, Natalie Walker, S Schug, A McKee, H Kehlet, A van Zundert, D Sage, M Futter, G Saville, T Clark, S MacMahon

#### Abstract

**Objectives** To obtain reliable estimates of the effects of neuraxial blockade with epidural or spinal anaesthesia on postoperative morbidity and mortality.  
**Design** Systematic review of all trials with randomisation to intraoperative neuraxial blockade or not.

**Studies** 141 trials including 9559 patients for which data were available before 1 January 1997. Trials were eligible irrespective of their primary aims, concomitant use of general anaesthesia, publication status, or language. Trials were identified by extensive search methods, and substantial amounts of data were obtained or confirmed by correspondence with trialists.

**Main outcome measures** All cause mortality, deep vein thrombosis, pulmonary embolism, myocardial infarction, transfusion requirements, pneumonia, other infections, respiratory depression, and renal failure.

**Results** Overall mortality was reduced by about a third in patients allocated to neuraxial blockade (103 deaths/4871 patients versus 144/4688 patients, odds ratio = 0.70, 95% confidence interval 0.54 to 0.90, P = 0.006). Neuraxial blockade reduced the odds of deep vein thrombosis by 44%, pulmonary embolism by 55%, transfusion requirements by 50%, pneumonia by 39%, and respiratory depression by 59% (all P < 0.001). There were also reductions in myocardial infarction and renal failure. Although there was limited power to assess subgroup effects, the proportional reductions in mortality did not clearly differ by surgical group, type of blockade (epidural or

#### Introduction

Anaesthesia is commonly classified into two main techniques: general anaesthesia, in which gaseous or intravenous drugs achieve central neurological depression, and regional anaesthesia, in which drugs are administered directly to the spinal cord or nerves to locally block afferent and efferent nerve input.<sup>1</sup> Regional anaesthesia for major thoracic, abdominal, or leg surgery relies on neuraxial blockade by injection of local anaesthetic drugs into either the subarachnoid space (spinal anaesthesia) or into the epidural space surrounding the spinal fluid sac (epidural anaesthesia).

The risks of fatal or life threatening events are increased several fold after major surgery, but there is debate about whether the type of anaesthesia has any substantive effect on these risks. Neuraxial blockade has several physiological effects that provide a rationale for expecting to improve outcome with this technique.<sup>2</sup> However, the few clinical trials of epidural or spinal anaesthesia that have focused specifically on fatal or life threatening events have generally been too small to detect effects of plausible size reliably. To provide more reliable estimates of the effects of neuraxial blockade on postoperative morbidity and mortality, we conducted a systematic review of all relevant randomised trials.

#### Methods

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We sought to identify all trials in which patients were randomised to receive intraoperative neuraxial blockade (with epidural or spinal anaesthesia) or not. We did

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Результаты для регионарных методик:  
Снижение общей летальности на 30 %  
Снижение частоты:

- легочных инфекционных осложнений на 39%
- депрессии дыхания на 55%
- случаев тромбэмболии легочной артерии на 55%
- острого инфаркта миокарда на 33 %
- объема перелитой крови на 50%
- острой почечной недостаточности на 43%

Rogers et al., 2000

# Борьба с непреднамеренной гипотермией

Anesthesiology  
82:85-95, 1995  
© 1995 American Society of Anesthesiologists, Inc.  
J. B. Lippincott Company, Philadelphia

## The Catecholamine, Cortisol, and Hemodynamic Responses to Mild Perioperative Hypothermia

### A Randomized Clinical Trial

Steven M. Frank, M.D.,\* Michael S. Higgins, M.D.,† Michael J. Breslow, M.D.,‡ Lee A. Fleisher, M.D.,\* Randolph B. Gorman, M.D.,† James V. Sitzmann, M.D.,§ Hershel Raff, Ph.D.,|| Charles Beattie, M.D.#

**Background:** Unintended hypothermia occurs frequently during surgery and may have adverse effects on the cardiovascular system. Although the mechanisms responsible for the cardiovascular manifestations of hypothermia are unclear, it is possible that they are sympathetically mediated. In this prospective study, relationships between body temperature, the neuroendocrine response, and hemodynamic changes in the perioperative period were examined.

**Methods:** Seventy-four elderly patients, undergoing abdominal, thoracic, or lower extremity vascular surgical procedures, were randomly assigned to either "routine care" (n = 37) or "forced-air warming" (n = 37) groups. Throughout the intraoperative and early postoperative periods, the routine care group received standard thermal care, and the forced-air warming group received forced-air skin-surface warming. Core temperature, forearm minus fingertip skin-surface temperature gradient, and plasma concentrations of epinephrine, norepinephrine, and cortisol were measured throughout the perioperative period, and the two groups were compared. In

addition, heart rate and arterial blood pressure were compared between groups.

**Results:** The routine care and forced-air warming groups did not differ with regard to age, sex, type of surgical procedures, anesthetic techniques, or postoperative analgesia. Mean core temperature was lower in the routine care group on admission to the postanesthetic care unit (routine care,  $35.3 \pm 0.1^\circ\text{C}$ ; forced-air warming,  $36.7 \pm 0.1^\circ\text{C}$ ;  $P = 0.0001$ ) and remained lower during the early postoperative period. Forearm minus fingertip skin-surface temperature gradient (an index of peripheral vasoconstriction) was greater in the routine care group in the early postoperative period. The mean norepinephrine concentration (pg/ml) was greater in the routine care group immediately after surgery ( $480 \pm 70$  vs.  $330 \pm 30$ ,  $P = 0.02$ ) and at 60 min ( $530 \pm 50$  vs.  $340 \pm 30$ ,  $P = 0.002$ ) and 180 min ( $500 \pm 80$  vs.  $320 \pm 30$ ,  $P = 0.004$ ) postoperatively. Mean epinephrine concentrations were not significantly different between groups. Mean cortisol concentrations were increased in both groups during the early postoperative period ( $P < 0.01$ ), but the differences between groups were not significant. Systolic, mean, and diastolic arterial blood pressures were significantly higher in the routine care group.

**Conclusions:** Compared with patients in the forced-air warming group, patients receiving routine thermal care had lower core temperatures, a greater degree of peripheral vasoconstriction, higher norepinephrine concentrations, and higher arterial blood pressures in the early postoperative period. These findings suggest a possible mechanism for hypothermia-related cardiovascular morbidity in the perioperative period. (Key words: Hormones: cortisol. Hypothermia: perioperative. Sympathetic nervous system, catecholamines: epinephrine; norepinephrine. Thermoregulation: vasoconstriction.)

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§ Associate Professor, Department of Surgery, The Johns Hopkins Medical Institutions, Baltimore, Maryland.

|| Professor, Department of Medicine, St. Luke's Medical Center, The Medical College of Wisconsin, Milwaukee, Wisconsin.

UNINTENDED perioperative hypothermia occurs in

Гипотермия – фактор  
риска осложнений и  
летальности

Frank S.M., 1995  
Sessler D.I., 1997

# Борьба с непреднамеренной гипотермией

SAGE journals

Perfusion

## Lowest core body temperature and adverse outcomes associated with coronary artery bypass surgery

Gordon R DeFoe, Charles F Krumholz, Christian P DiDato, more...

Show all authors

First Published March 1, 2003 | Research Article

<https://doi.org/10.1191/0267659103pf660oa>

Article information



### Abstract

To examine the effect of lowest core body temperature on adverse outcomes associated with coronary artery bypass graft (CABG) surgery, data were collected on 7134 isolated CABG procedures carried out in New England from 1997 to 2000. Excluded from the analysis were patients with pump times <60 and >120 min and those operated upon using continuous warm cardioplegia. Data for lowest core temperature were divided into quartiles for analysis ( $\leq 31.4^\circ\text{C}$ ,  $31.5\text{--}33.1^\circ\text{C}$ ,  $33.2\text{--}34.3^\circ\text{C}$ , and  $\geq 34.4^\circ\text{C}$ ).

Patients with lower core body temperature on cardio-pulmonary bypass (CPB) had higher in-hospital mortality rates. Crude mortality rates were 2.9% in the  $\leq 31.4^\circ\text{C}$  group, 2.1% in the  $31.5\text{--}33.1^\circ\text{C}$  group, 1.3% in the  $33.2\text{--}34.3^\circ\text{C}$  group and 1.2% in the  $\geq 34.4^\circ\text{C}$  group. The trend toward higher mortality as core temperature decreased was statistically significant ( $p_{\text{trend}} < 0.001$ ). Adjustment for differences in patient and disease characteristics did not significantly change the results and the test of trend remained significant ( $p < 0.001$ ).

**Rates of perioperative stroke were somewhat lower in the colder groups. Rates in the two colder groups were 0.9% compared with 1.6% and 1.4% in the warmer groups ( $p_{\text{trend}} = 0.082$ ). This remained a marginal but significant trend after adjustment for possible confounding factors ( $p = 0.044$ ).**

Low core body temperatures on CPB are associated with higher rates of in-hospital mortality among isolated CABG patients. Rates of intra- or postoperative use of an intra-aortic balloon pump are also higher with lower core temperatures. We concluded that temperature management strategy during CABG surgery has an important effect on patient outcomes.

Гипотермия повышает частоту осложнений и уровень летальности в кардиохирургии

DeFoe G.R., 2003

# Борьба с непреднамеренной гипотермией

AJG

KNEE | SHOULDER & E

## Inadvertent Perioperative Hypothermia During Orthopedic Surgery

Publish date: July 12, 2018

AUTHORS: Chandrakanth Boddu, MD, Joseph Cushner, Giles R. Scuderi, MD

AUTHOR AFFILIATION | DISCLOSURES ▼

### ABSTRACT

Inadvertent perioperative hypothermia is a significant problem in patients undergoing either emergency or elective orthopedic surgery, and is associated with increased morbidity and mortality. Though in general the incidence of inadvertent perioperative hypothermia in postoperative recovery rooms has been decreasing over the last 2 decades, it still remains a significant risk in certain specialty practices, such as orthopedic surgery. This review article summarizes the currently available evidence on the incidence, risk factors, and complications of inadvertent perioperative hypothermia. Also, the effective preventive strategies in dealing with inadvertent perioperative hypothermia are reviewed and essential clinical guidelines to be followed are summarized.

Inadvertent perioperative hypothermia, defined as an involuntary drop in core body temperature to  $<35^{\circ}\text{C}$  ( $95^{\circ}\text{F}$ ), is a condition associated with significant morbidity and mortality.<sup>1</sup> This phenomenon has been reported in both emergency orthopedic admissions, such as fracture management, as well as in the elective setting such as arthroscopy, arthroplasty, and spine surgery.

In a study conducted in the United Kingdom including 781 elderly patients with a mean age of 80 years who presented with hip fractures, the 30-day mortality rate was 15.3% in patients who were admitted with a tympanic temperature of  $<36.5^{\circ}\text{C}$  and only 1% in patients who maintained a tympanic temperature of  $36.5^{\circ}\text{C}$  to

Гипотермия повышает частоту послеоперационных осложнений в виде инсульта и сепсиса, а также и уровень летальности в травматологии и ортопедии

*Boddu C., 2018*

# Медикаментозное ингибирование чрезмерной активации гипофизарно- надпочечниковой секреции



Volume 67, Issue 6  
1 December 1988

< Previous Next >

## Fast Cortisol-Induced Inhibition of the Adrenocorticotropin Response to Surgery in Humans

HERSHEL RAFF, ROBERT J. FLEMMA, JAMES W. FINDLING, DEBRA K. NELSON

*The Journal of Clinical Endocrinology & Metabolism*, Volume 67, Issue 6, 1  
December 1988, Pages 1146–1148, <https://doi.org/10.1210/jcem-67-6-1146>

Published: 01 December 1988 Article history ▾

Glucocorticoid negative feedback is exerted in at least two time domains: fast feedback (within minutes of the feedback signal) and delayed feedback (within hours of the feedback signal). Although delayed feedback is known to inhibit ACTH responses to a variety of stimuli in humans, whether there is fast feedback inhibition of the ACTH responses to such stimuli is not known. The purpose of this study was to evaluate the efficacy of a pharmacological injection of cortisol sodium succinate (CORT) as a rapid inhibitor of the ACTH response to surgery in patients undergoing thoracotomy for myocardial revascularization.

Thirty patients were premedicated with diazepam and induced with thiopental sodium. They were assigned to one of four groups: group I, general anesthesia was maintained with enflurane (n = 8); group II, patients were anesthetized as in group I, but received a bolus injection of 500 mg CORT within 5 s of the start of surgery (n = 7); group III, anesthesia was maintained with 50–100 mg fentanyl (FENT; n = 8); and group IV, patients were anesthetized as in group III and given CORT as in group II (n = 7). Surgery induced a large increase in plasma ACTH in group I (no CORT, no FENT); the mean plasma ACTH level was  $57 \pm 14$  ( $\pm$ SE) pmol/L 10 min after the start of surgery, and it peaked at  $92 \pm 18$  pmol/L 50 min after the start of

Гидрокортизон в дозе  
500 мг, введенный в  
момент начала операции  
снижает уровень  
адренокортикотропина и  
кортизола

Raff H., 1988



# Снижение объема гемотрансфузий

## RESEARCH

OPEN ACCESS



### Effect of restrictive versus liberal transfusion strategies on outcomes in patients with cardiovascular disease in a non-cardiac surgery setting: systematic review and meta-analysis

Annemarie B Docherty,<sup>1,2</sup> Rob O'Donnell,<sup>2</sup> Susan Brunskill,<sup>3</sup> Marialena Trivella,<sup>3</sup> Carolyn Doree,<sup>4</sup> Lars Holst,<sup>5</sup> Martyn Parker,<sup>6</sup> Merete Gregersen,<sup>7</sup> Juliano Pinheiro de Almeida,<sup>8</sup> Timothy S Walsh,<sup>1,2</sup> Simon J Stanworth<sup>3,9</sup>

For numbered affiliations see end of article.

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2016;352:i1351  
<http://dx.doi.org/10.1136/bmj.i1351>

#### ABSTRACT

##### OBJECTIVE

To compare patient outcomes of restrictive versus liberal blood transfusion strategies in patients with cardiovascular disease not undergoing cardiac surgery.

##### DESIGN

Systematic review and meta-analysis.

##### DATA SOURCES

Randomised controlled trials involving a threshold for red blood cell transfusion in hospital. We searched (to 2 November 2015) CENTRAL, Medline, Embase, CINAHL, PubMed, LILACS, NHSBT Transfusion Evidence Library, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform, ISRCTN Register, and EU Clinical Trials Register. Authors were contacted for data whenever possible.

##### TRIAL SELECTION

Published and unpublished randomised controlled trials comparing a restrictive with liberal transfusion threshold and that included patients with cardiovascular disease.

##### DATA EXTRACTION AND SYNTHESIS

Data extraction was completed in duplicate. Risk of bias was assessed using Cochrane methods. Relative risk ratios with 95% confidence intervals were presented in all meta-analyses. Mantel-Haenszel random effects models were used to pool risk ratios.

##### MAIN OUTCOME MEASURES

30 day mortality, and cardiovascular events.

##### RESULTS

41 trials were identified; of these, seven included data on patients with cardiovascular disease. Data from a further four trials enrolling patients with cardiovascular disease were obtained from the authors. In total, 11 trials enrolling patients with cardiovascular disease (n=3033) were included for meta-analysis (restrictive transfusion, n=1514 patients; liberal transfusion, n=1519). The pooled risk ratio for the association between transfusion thresholds and 30 day mortality was 1.15 (95% confidence interval 0.88 to 1.50, P=0.50), with little heterogeneity (I<sup>2</sup>=14%). The risk of acute coronary syndrome in patients managed with restrictive compared with liberal transfusion was increased (nine trials; risk ratio 1.78, 95% confidence interval 1.18 to 2.70, P=0.01, I<sup>2</sup>=0%).

##### CONCLUSIONS

The results show that it may not be safe to use a restrictive transfusion threshold of less than 80 g/L in patients with ongoing acute coronary syndrome or chronic cardiovascular disease. Effects on mortality and other outcomes are uncertain. These data support the use of a more liberal transfusion threshold (>80 g/L) for patients with both acute and chronic cardiovascular disease until adequately powered high quality randomised trials have been undertaken in patients with cardiovascular disease.

##### REGISTRATION

PROSPERO CRD42014014251.

#### WHAT IS ALREADY KNOWN ON THIS TOPIC

Restrictive red cell transfusion policies are recommended as safe for most hospital patients with anaemia

Uncertainty exists for patients with cardiovascular disease, whose hearts may be more susceptible to limited coronary oxygen supply

#### Introduction

Approximately seven million people in the United Kingdom have cardiovascular disease,<sup>1</sup> and it is a prevalent

Гемоглобин ниже 80 г/л ухудшает исходы хирургического лечения пациентов с ишемической болезнью сердца

*Docherty A.B., 2016*

## *Снижение объема интраоперационной инфузии (поддержание нормоволемии)*

- Избыточная инфузия – фактор риска повреждения легких  
*Licker M. et al., 2007*
- Последний прием «немутной» жидкости, в т.ч. содержащей глюкозу, разрешается за 2 часа до операции  
*Smith et al., 2011 (Guidelines from the European Society of Anaesthesiology)*
- Механическая подготовка кишечника перед операцией способствует относительной гиповолемии  
*Holte K., 2010*
- Вода выводится легче и быстрее, чем соли  
*Lobo D.N., 2002*

# Медикаментозное блокирование факторов вызывающих или поддерживающих воспаление и гиперальгезию (упреждающая анальгезия)

Anesthesiology  
77:439-446, 1992

## Preemptive Analgesia

### Clinical Evidence of Neuroplasticity Contributing to Postoperative Pain

Joel Katz, Ph.D.,\* Brian P. Kavanagh, M.B., B.Sc., M.R.C.P.I.,† Alan N. Sandler, M.Sc., M.B., Ch.B., F.R.C.P.C.,‡  
Hilary Nierenberg, B.Sc.N.,§ John F. Boylan, M.B., F.F.A.R.C.S.I.,¶ Mark Friedlander, M.B., Ch.B., F.R.C.P.C.,‡  
Brian F. Shaw, Ph.D., C.Psych.\*\*

Recent evidence suggests that surgical incision and other noxious perioperative events may induce prolonged changes in central neural function that later contribute to postoperative pain. The present study tested the hypothesis that patients receiving epidural fentanyl before incision would have less pain and need fewer analgesics postoperatively than patients receiving the same dose of epidural fentanyl after incision. Thirty patients (ASA physical status 2) scheduled for elective thoracic surgery through a posterolateral thoracotomy incision were randomized to one of two groups of equal size and prospectively studied in a double-blind manner. Epidural catheters were placed via the L2-L3 or L3-L4 interspaces preoperatively, and the position was confirmed with lidocaine. Group 1 received epidural fentanyl (4 µg/kg, in 20 ml normal saline) before surgical incision, followed by epidural normal saline (20 ml) infused 15 min after incision. Group 2 received epidural normal saline (20 ml) before surgical incision, followed by epidural fentanyl (4 µg/kg, in 20 ml normal saline) infused 15 min after incision. No additional analgesics were used before or during the operation. Anesthesia was induced with thiopental (3-5 mg/kg) and maintained with N<sub>2</sub>O/O<sub>2</sub> and isoflurane. Paralysis was achieved with pancuronium (0.1 mg/kg). Postoperative analgesia consisted of patient-controlled intra-

venous morphine. Visual analogue scale pain scores were significantly less in group 1 (2.6 ± 0.44) than in group 2 (4.7 ± 0.58) 6 h after surgery ( $P < 0.05$ ), by which time plasma fentanyl concentrations had decreased to subtherapeutic levels (<0.15 ng/ml) in both groups. Patient-controlled morphine usage in group 2 (26.1 ± 5.2 mg) was significantly ( $P < 0.008$ ) greater than in group 1 (11.7 ± 2.2 mg) between 12 and 24 h after surgery, even though visual analogue scale pain scores at these times were not significantly different ( $P > 0.05$ ). The results suggest that preemptive analgesia may reduce the central consequences of surgical incision and rib retraction by preventing noxious neural impulses from gaining entry into the central nervous system. (Key words: Analgesia; postoperative. Analgesics, epidural; fentanyl. Anesthetic techniques: Epidural. Pain; neuroplasticity.)

RECENT LABORATORY and clinical studies show that injury produces a prolonged change in central nervous system function that influences responses to subsequent afferent inputs. In rodents, high-intensity electrical stimulation of afferent nerve fibers or injury to nociceptors in skin induces neural and behavioral changes that persist even when inputs from the injured region are later blocked by local anesthesia<sup>1-3</sup> or interrupted by nerve section<sup>4-7</sup> or dorsal rhizotomy.<sup>8</sup> Simply cutting afferent nerve fibers in the absence of a prior noxious conditioning stimulus produces a long-term facilitation in spinal cord cells that persists in the absence of sustaining inputs from the transected nerve.<sup>9</sup> Clinical evidence that central neural plasticity contributes to persistent pain comes from studies of amputees who complain of phantom limb pain that resembles a painful preamputation lesion in the quality of sensation and the location in the limb.<sup>10,11</sup> Taken together, the evidence suggests that noxious stimulus-induced changes in central neural function may contribute to pain long after the offending stimulus has been removed or the peripheral injury has healed.

Physiologic and behavioral studies of animals also show that noxious stimulus-induced neuroplasticity can be prevented or "preempted" by administration of analgesic agents prior to injury. Bathing peripheral nerves in a local anesthetic solution prior to nerve transection reduces the

Снижает интенсивность боли и потребность в опиоидных агонистах после операции

Katz J., 1992

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† Research Resident in Anesthesia, Department of Anaesthesia, The Toronto Hospital, Toronto General Division.

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Received from the Departments of Psychology and Anesthesia, The Toronto Hospital, Toronto General Division, and the Department of Anaesthesia, University of Toronto. Accepted for publication May 20, 1992. Supported in part by fellowships from the Ontario Ministry of Health and the Medical Research Council of Canada (J.K.). Presented in part at the Canadian Pain Society Annual Meeting, Vancouver, British Columbia, October 1991 and at the Annual Meeting of the American Society of Anesthesiologists, San Francisco, California, October 1992.

# Применение бета-адреноблокаторов в интра- и послеоперационном периоде

The New England  
Journal of Medicine

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VOLUME 335

DECEMBER 5, 1996

NUMBER 23



## EFFECT OF ATENOLOL ON MORTALITY AND CARDIOVASCULAR MORBIDITY AFTER NONCARDIAC SURGERY

DENNIS T. MANGANO, PH.D., M.D., ELIZABETH L. LAYUG, M.D., ARTHUR WALLACE, PH.D., M.D., AND IDA TATEO, M.S., FOR THE MULTICENTER STUDY OF PERIOPERATIVE ISCHEMIA RESEARCH GROUP\*

### ABSTRACT

**Background** Perioperative myocardial ischemia is the single most important potentially reversible risk factor for mortality and cardiovascular complications after noncardiac surgery. Although more than 1 million patients have such complications annually, there is no effective preventive therapy.

**Methods** We performed a randomized, double-blind, placebo-controlled trial to compare the effect of atenolol with that of a placebo on overall survival and cardiovascular morbidity in patients with or at risk for coronary artery disease who were undergoing noncardiac surgery. Atenolol was given intravenously before and immediately after surgery and orally thereafter for the duration of hospitalization. Patients were followed over the subsequent two years.

**Results** A total of 200 patients were enrolled. Ninety-nine were assigned to the atenolol group, and 101 to the placebo group. One hundred ninety-four patients survived to be discharged from the hospital, and 192 of these were followed for two years. Overall mortality after discharge from the hospital was significantly lower among the atenolol-treated patients than among those who were given placebo over the six months following hospital discharge (0 vs. 8 percent,  $P < 0.001$ ), over the first year (3 percent vs. 14 percent,  $P = 0.005$ ), and over two years (10 percent vs. 21 percent,  $P = 0.019$ ). The principal effect was a reduction in deaths from cardiac causes during the first six to eight months. Combined cardiovascular outcomes were similarly reduced among the atenolol-treated patients; event-free survival throughout the two-year study period was 68

**M**ORTALITY and morbidity due to cardiovascular disease are prevalent and costly for the 30 million patients who undergo noncardiac surgery annually in the United States, affecting more than 1 million of them.<sup>1,2</sup> In the subgroup of 3 million patients who require noncardiac surgery who have or are at risk for coronary artery disease, the most significant risk factors for mortality and cardiovascular morbidity are myocardial ischemia and nonfatal myocardial infarction during the first week after surgery; these factors increase the risk of serious cardiovascular outcomes by a factor of 2 to 20 over the two years after surgery.<sup>3-5</sup> Postoperative ischemic events appear to be related to the persistently exaggerated sympathetic response that is associated with substantial increases in the heart rate throughout the hospitalization.<sup>6-10</sup> Several small clinical trials have investigated the effect of the preoperative or intraoperative use of nitrates,<sup>11,12</sup> beta-blockers,<sup>13-15</sup> calcium-channel blockers,<sup>16,17</sup> or  $\alpha_2$ -agonists<sup>18,19</sup> on hemodynamics and measures of myocardial ischemia. Although several of the preliminary findings were encouraging, previous trials have not investigated the effects of such therapies when administered over the entire postoperative hospital stay. Even more important, the effects of such intensive therapy on long-term mortality (i.e., mortality after discharge from the hospital) and the incidence of cardiovascular events remained to be determined.

We hypothesized that in patients who had or were

Проспективное  
рандомизированное  
исследование на 200 пациентах  
высокого риска  
некардиохирургического  
профиля

Препарат – атенолол

Летальность по сравнению с  
контролем:

- через 6 месяцев – 0 против 8%
- через 2 года – 10% против 21%

Mangano D.T., 1996

# Применение бета-адреноблокаторов в интра- и послеоперационном периоде

EFFECT OF BISOPROLOL ON MORBIDITY AND MORTALITY IN PATIENTS UNDERGOING VASCULAR SURGERY

## THE EFFECT OF BISOPROLOL ON PERIOPERATIVE MORTALITY AND MYOCARDIAL INFARCTION IN HIGH-RISK PATIENTS UNDERGOING VASCULAR SURGERY

DON POLDERMANS, PH.D., ERIC BOERSMA, PH.D., JEROEN J. BAX, PH.D., IAN R. THOMSON, PH.D., LOUIS L.M. VAN DE VEN, PH.D., JAN D. BLANKENSTEIJN, PH.D., HUBERT F. BAARS, M.D., TIK-LEN YO, PH.D., GIUSEPPE TROCINO, M.D., CARLO VIGNA, M.D., JOS R.T.C. ROELANDT, PH.D., AND HERO VAN URK, PH.D., FOR THE DUTCH ECHOCARDIOGRAPHIC CARDIAC RISK EVALUATION APPLYING STRESS ECHOCARDIOGRAPHY STUDY GROUP\*

### ABSTRACT

**Background** Cardiovascular complications are the most important causes of perioperative morbidity and mortality among patients undergoing major vascular surgery.

**Methods** We performed a randomized, multicenter trial to assess the effect of perioperative blockade of beta-adrenergic receptors on the incidence of death from cardiac causes and nonfatal myocardial infarction within 30 days after major vascular surgery in patients at high risk for these events. High-risk patients were identified by the presence of both clinical risk factors and positive results on dobutamine echocardiography. Eligible patients were randomly assigned to receive standard perioperative care or standard care plus perioperative beta-blockade with bisoprolol.

**Results** A total of 1351 patients were screened, and 846 were found to have one or more cardiac risk factors. Of these 846 patients, 173 had positive results on dobutamine echocardiography. Fifty-nine patients were randomly assigned to receive bisoprolol, and 53 to receive standard care. Fifty-three patients were excluded from randomization because they were already taking a beta-blocker, and eight were excluded because they had extensive wall-motion abnormalities either at rest or during stress testing. Two patients in the bisoprolol group died of cardiac causes (3.4 percent), as compared with nine patients in the standard-care group (17 percent,  $P=0.02$ ). Nonfatal myocardial infarction occurred in nine patients given standard care only (17 percent) and in none of those given standard care plus bisoprolol ( $P<0.001$ ). Thus, the primary study end point of death from cardiac causes or nonfatal myocardial infarction occurred in 2 patients in the bisoprolol group (3.4 percent) and 18 patients in the standard-care group (34 percent,  $P<0.001$ ).

**Conclusions** Bisoprolol reduces the perioperative incidence of death from cardiac causes and nonfatal myocardial infarction in high-risk patients who are undergoing major vascular surgery. (N. Engl. J. Med.

**P**ATIENTS undergoing major vascular surgery are at risk for serious perioperative cardiac complications, such as nonfatal myocardial infarction and death.<sup>1</sup> A combination of clinical assessment and noninvasive cardiac testing can be used to identify patients at high risk.<sup>2</sup> Various interventions have been proposed to reduce the risk of cardiac complications in such patients after noncardiac surgery, but none have been found to be efficacious.

Drugs that block beta-adrenergic receptors prevent cardiac complications in patients with acute myocardial infarction, silent ischemia, and heart failure.<sup>3-6</sup> Perioperative blockade of beta-adrenergic receptors has been proposed to reduce the risk of perioperative cardiac complications.<sup>7-9</sup> However, previous trials lacked the statistical power to evaluate the cardioprotective effect of beta-blockade on the incidence of serious cardiac events, such as death or nonfatal myocardial infarction.

We hypothesized that perioperative beta-blockade with bisoprolol would reduce the perioperative incidence of death from cardiac causes and nonfatal myocardial infarction in high-risk patients undergoing major vascular surgery. We therefore performed a multicenter study of a subgroup of high-risk patients who had clinical predictors of cardiac risk together with positive results on dobutamine echocardiography.

### METHODS

#### Study Protocol

Between 1996 and 1999, we prospectively screened all patients undergoing elective abdominal aortic or infrainguinal arterial reconstruction at seven participating centers. The ethics committee at each center approved the study protocol. The patients were

Проспективное  
рандомизированное  
исследование на 114 пациентах  
высокого риска  
некардиохирургического  
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Кардиологическая летальность по  
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3,4% против 17%

Poldermans D., 1999

# Применение продленной центральной анальгезии в течении 24 часов у новорожденных

## The New England Journal of Medicine

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Volume 326

JANUARY 2, 1992

Number 1

### HALOTHANE-MORPHINE COMPARED WITH HIGH-DOSE SUFENTANIL FOR ANESTHESIA AND POSTOPERATIVE ANALGESIA IN NEONATAL CARDIAC SURGERY

K.J.S. ANAND, M.B., B.S., D.PHIL., AND P.R. HICKEY, M.D.

**Abstract Background.** Extreme hormonal and metabolic responses to stress are associated with increased morbidity and mortality in sick adults. We hypothesized that administering deep opioid anesthesia to critically ill neonates undergoing cardiac surgery would blunt their responses to stress and might improve clinical outcomes.

**Methods.** In a randomized trial, 30 neonates were assigned to receive deep intraoperative anesthesia with high doses of sufentanil and postoperative infusions of opiates for 24 hours; 15 neonates were assigned to receive lighter anesthesia with halothane and morphine followed postoperatively by intermittent morphine and diazepam. Hormonal and metabolic responses to surgery were evaluated by assay of arterial blood samples obtained before, during, and after the operations.

**Results.** The neonates who received deep anesthesia (with sufentanil) had significantly reduced responses of beta-endorphin, norepinephrine, epinephrine, glucagon,

aldosterone, cortisol, and other steroid hormones; their insulin responses and ratios of insulin to glucagon were greater during the operation. The neonates who received lighter anesthesia (with halothane plus morphine) had more severe hyperglycemia and lactic acidemia during surgery and higher lactate and acetoacetate concentrations postoperatively ( $P < 0.025$ ). The group that received deep anesthesia had a decreased incidence of sepsis ( $P = 0.03$ ), metabolic acidosis ( $P < 0.01$ ), and disseminated intravascular coagulation ( $P = 0.03$ ) and fewer postoperative deaths (none of 30 given sufentanil vs. 4 of 15 given halothane plus morphine,  $P < 0.01$ ).

**Conclusions.** In neonates undergoing cardiac surgery, the physiologic responses to stress are attenuated by deep anesthesia and postoperative analgesia with high doses of opioids. Deep anesthesia continued postoperatively may reduce the vulnerability of these neonates to complications and may reduce mortality. (N Engl J Med 1992;326:1-9.)

OPIOID anesthetic agents in high doses can blunt endocrine and metabolic responses to cardiac or noncardiac operations in adults, as demonstrated by perioperative changes in the levels of cortisol,<sup>1,2</sup> catecholamines,<sup>3</sup> vasopressin,<sup>4</sup> and growth hormone.<sup>1</sup> These drugs may also reduce the mobilization of metabolic substrates that follows stimulation of glycogenolysis, gluconeogenesis, lipolysis, and protein breakdown.<sup>2,3</sup> Deeper levels of opioid anesthesia produce a dose-dependent inhibition of responses to the stress of surgery; such effects may be due to central or peripheral neuroendocrine regulatory mechanisms or may be the direct effects of opioids on endocrine glands.<sup>5</sup>

The metabolic balance of neonates is precarious.

noncardiac<sup>7,8</sup> operations is substantially greater than that of adults. A physiologic basis has been proposed<sup>9</sup> for the use of deep levels of anesthesia and postoperative analgesia to attenuate the extreme responses of newborns to perioperative pain and stress. We report the results of a test of this hypothesis in critically ill neonates undergoing severe surgical stress. We measured perioperative changes in the circulating levels of stress hormones and metabolic substrates and monitored postoperative morbidity and mortality in 45 neonates undergoing cardiac surgery, in a randomized trial of two regimens of intraoperative anesthesia and postoperative analgesia. The hypothesis to be tested proposed that the stress responses of newborns to cardiac operations are not altered by the use of opiates in

Снижение концентрации  
кортизола, катехоламинов и  
глюкагона в  
экспериментальной группе  
Частота сепсиса,  
метаболического ацидоза,  
ДВС-синдрома и смерти по  
сравнению с контролем:

0 из 30 против 4 из 15

Anand K.J.S., 1992

## *Дыхание газовой смесью с высоким FiO<sub>2</sub> более двух часов после операции*

- Тошнота и рвота
- Нагноение раны
- Тахикардия и энцефалопатия

*Knighon DR, Halliday B, Hunt TK. Oxygen as an antibiotic, the effect of inspired oxygen on infection. Arch Surg 1984;119:199–204.*

*Greif P., et al. 1999, 2000;*

*Rosenberg-Adamsen S. et al., 1999*

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)

## GUIDELINES

### Perioperative fasting in adults and children: guidelines from the European Society of Anaesthesiology

Ian Smith, Peter Kranke, Isabelle Murat, Andrew Smith, Geraldine O'Sullivan, Eldar Søreide, Claudia Spies and Bas in't Veld

This guideline aims to provide an overview of the present knowledge on aspects of perioperative fasting with assessment of the quality of the evidence. A systematic search was conducted in electronic databases to identify trials published between 1950 and late 2009 concerned with preoperative fasting, early resumption of oral intake and the effects of oral carbohydrate mixtures on gastric emptying and postoperative recovery. One study on preoperative fasting which had not been included in previous reviews and a further 13 studies published since the most recent review were identified. The searches also identified 20 potentially relevant studies of oral carbohydrates and 53 on early resumption of oral intake. Publications were classified in terms of their evidence level, scientific validity and clinical relevance. The Scottish Intercollegiate Guidelines Network scoring system for assessing level of evidence and grade of recommendations was used. The key recommendations are that adults and children should be encouraged to drink clear fluids up to 2 h before elective surgery (including caesarean section) and all but one member of the guidelines group consider that tea or coffee with milk added (up to about one fifth of the total volume) are still clear fluids. Solid food should be prohibited for 6 h before elective

surgery in adults and children, although patients should not have their operation cancelled or delayed just because they are chewing gum, sucking a boiled sweet or smoking immediately prior to induction of anaesthesia. These recommendations also apply to patients with obesity, gastro-oesophageal reflux and diabetes and pregnant women not in labour. There is insufficient evidence to recommend the routine use of antacids, metoclopramide or H<sub>2</sub>-receptor antagonists before elective surgery in non-obstetric patients, but an H<sub>2</sub>-receptor antagonist should be given before elective caesarean section, with an intravenous H<sub>2</sub>-receptor antagonist given prior to emergency caesarean section, supplemented with 30 ml of 0.3 mol l<sup>-1</sup> sodium citrate if general anaesthesia is planned. Infants should be fed before elective surgery. Breast milk is safe up to 4 h and other milks up to 6 h. Thereafter, clear fluids should be given as in adults. The guidelines also consider the safety and possible benefits of preoperative carbohydrates and offer advice on the postoperative resumption of oral intake.

*Eur J Anaesthesiol* 2011;28:556–569

Published online 28 June 2011

#### Why were these guidelines produced?

Widespread consultation suggested that guidelines on perioperative fasting would be useful to European Society of Anaesthesiology (ESA) members.

Our guideline aims to provide an overview of the present knowledge on perioperative fasting with assessment of the quality of the evidence in order to allow anaesthesiologists all over Europe to integrate this knowledge in their daily care of patients.

#### What is similar to previous guidelines?

The ESA guidelines endorse a 2-h fasting interval for clear fluids and a 6-h interval for solids.

#### What is different from previous guidelines?

The ESA guidelines:

- are recent and include several studies published since previous guidelines;
- increase the emphasis on encouraging patients not to avoid fluids for any longer than is necessary;
- offer practical, pragmatic advice on chewing gum, smoking and drinks containing milk;
- consider the safety and possible benefits of preoperative carbohydrates;
- offer advice on the postoperative resumption of oral intake.

Последний прием «немутной»  
жидкости, в т.ч. содержащей  
глюкозу, разрешается за 2 часа  
до операции

*Smith et al., 2011*

*(Guidelines from the European Society of Anaesthesiology)*



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Effects of preoperative oral carbohydrates and peptides on  
postoperative endocrine response, mobilization, nutrition and  
muscle function in abdominal surgery

M. G. Henriksen, I. Hessov, F. Dela, H. Vind Hansen, V. Haraldsted, S. Å. Rodt

First published: 07 March 2003 | <https://doi.org/10.1034/j.1399-6576.2003.00047.x> | Cited by: 105

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## Abstract

**Background:** Surgery is succeeded by long-lasting state of relative peripheral insulin resistance, which is reduced by giving glucose infusion or oral carbohydrate-rich drinks immediate before operating instead of fasting. The aim of the present study was to investigate whether oral carbohydrate or carbohydrate with peptide drinks preoperatively instead of fasting would improve postoperative voluntary muscle strength, nutritional intake and ambulation, decrease postoperative fatigue, anxiety and discomfort, and reduce the endocrine response to surgery.

**Methods:** Forty-eight patients were included and randomized into three groups to receive 2 × 400 ml of carbohydrate-rich drinks or to fast overnight and allowed only water. Voluntary grip and quadriceps strength, body composition, pulmonary function, VAS-score of eight parameters of wellbeing, muscle biopsies and insulin, glucagon, IGF-1 and free fatty acids were measured before and after the operation. The basic postoperative regimen for all groups were immediate oral nutrition and early enforced mobilization.

Пероральный прием или  
внутривенная инфузия  
раствора глюкозы перед  
операцией снижает  
выраженность инсулиновой  
резистентности

*Henriksen M.G., 2003*

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)

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## Tight glucose control and hypoglycemia

Preiser, Jean-Charles MD, PhD; Brunkhorst, Frank

Critical Care Medicine: April 2008 - Volume 36 - Issue 4 - p 1391  
doi: 10.1097/CCM.0b013e31816a16d0  
Letters to the Editors

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CONTENT NOT FOR REUSE

### Letters to the Editors

From "inconvenient truth" to "assault on reason"

**To the Editor:**

Strict glycemic control (SGC) carries the risk of severe hypoglycemia (SH). Indeed, with SGC the incidence of SH (defined as a blood glucose concentration <40 mg/dL) is five- to ten-fold higher as compared with a conventional blood glucose strategy (1, 2).

neuronal NADPH oxidase during glucose reperfusion. Of note, the degree of oxidative stress and neuronal death increased with increasing glucose concentrations during the reperfusion period. These results suggest that not SH by itself, but high blood glucose concentration following hypoglycemic coma, can initiate neuronal death. The study by Drs. Krinsley and Crover (3) is retrospective in its design, and it may not be possible to retrieve data on how severe hypoglycemia

and Spronk that "we consider the risk of SH [severe hypoglycemia] to not be a reason for failing to implement" tight glycemic control. In fact, the sensitivity analysis included in our manuscript makes the point that the beneficial effect of tight glycemic control would not have been eliminated unless the rate of SH quadrupled and the mortality attributable to an episode doubled. Recognition of the potential for harm should foster efforts for safer implementation of insulin treat-

Интенсивная  
инсулиноterapia приводит к  
гипогликемии с  
неврологическими  
последствиями

Preiser J.C., 2008

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)

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## Effect of an Intensive Glucose Management Protocol on the Mortality of Critically Ill Adult Patients

James Stephen Krinsley, MD  

 PlumX Metrics

DOI: <https://doi.org/10.4065/79.8.992> 

**Abstract** Full Text Images References

### OBJECTIVE

To assess the effect of an intensive glucose management protocol in a heterogeneous population of critically ill adult patients.

### PATIENTS AND METHODS

This study consisted of 800 consecutive patients admitted after institution of the protocol (treatment group, between February 1, 2003, and January 10, 2004) and 800 patients admitted immediately preceding institution of the protocol (baseline group, between February 23, 2002, and January 31, 2003). The setting was a 14-bed medical-surgical intensive care unit (ICU) in a university-affiliated community teaching hospital. The protocol involved intensive monitoring and treatment to maintain plasma glucose values lower than 140 mg/dL. Continuous intravenous insulin was used if glucose values exceeded 200 mg/dL on 2 successive occasions.

### RESULTS

The 2 groups of patients were well matched, with similar age, sex, race, prevalence of diabetes mellitus, Acute Physiology and Chronic Health Evaluation II scores, and distribution of diagnoses. After institution of the protocol, the mean glucose value decreased from 152.3 to 130.7 mg/dL ( $P < .001$ ), marked by a 56.3% reduction in the percentage of glucose values of 200 mg/dL or higher, without a significant change in hypoglycemia. The development of new renal insufficiency decreased 75% ( $P = .03$ ), and the number of patients undergoing transfusion of packed red blood cells decreased 18.7% ( $P = .04$ ). Hospital mortality decreased 29.3% ( $P = .002$ ), and length of stay in the ICU decreased 10.8% ( $P = .01$ ).

Гипергликемия ухудшает  
прогноз пациентов в  
критическом состоянии

*Krinsley J.S. et al., 2005*

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)

## The New England Journal of Medicine

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VOLUME 345

NOVEMBER 8, 2001

NUMBER 19



### INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.Sc., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.

#### ABSTRACT

**Background** Hyperglycemia and insulin resistance are common in critically ill patients, even if they have not previously had diabetes. Whether the normalization of blood glucose levels with insulin therapy improves the prognosis for such patients is not known.

**Methods** We performed a prospective, randomized, controlled study involving adults admitted to our surgical intensive care unit who were receiving mechanical ventilation. On admission, patients were randomly assigned to receive intensive insulin therapy (maintenance of blood glucose at a level between 80 and 110 mg per deciliter) or conventional treatment (infusion of insulin only if the blood glucose level exceeded 215 mg per deciliter and maintenance of glucose at a level between 180 and 200 mg per deciliter).

**Results** At 12 months, with a total of 1548 patients enrolled, intensive insulin therapy reduced mortality during intensive care from 8.0 percent with conventional treatment to 4.6 percent ( $P < 0.04$ , with adjustment for sequential analyses). The benefit of intensive insulin therapy was attributable to its effect on mortality among patients who remained in the intensive care unit for more than five days (20.2 percent with conventional treatment, as compared with 10.6 percent with intensive insulin therapy;  $P = 0.005$ ). The greatest reduction in mortality involved deaths due to multiple-organ failure with a proven septic focus. Intensive insulin therapy also reduced overall in-hospital mortality by 34 percent, bloodstream infections by 46 percent, acute renal failure requiring dialysis or hemofiltration by 41 percent, the median number of red-cell transfusions by 50 percent, and critical-illness polyneuropathy by 44 percent, and patients receiving in-

**C**RITICALLY ill patients who require intensive care for more than five days have a 20 percent risk of death and substantial morbidity.<sup>1</sup> Critical-illness polyneuropathy and skeletal-muscle wasting prolong the need for mechanical ventilation.<sup>2,5</sup> Moreover, increased susceptibility to severe infections and failure of vital organs amplify the risk of an adverse outcome.

Hyperglycemia associated with insulin resistance<sup>6-8</sup> is common in critically ill patients, even those who have not previously had diabetes. It has been reported that pronounced hyperglycemia may lead to complications in such patients,<sup>9,13</sup> although data from controlled trials are lacking. In diabetic patients with acute myocardial infarction, therapy to maintain blood glucose at a level below 215 mg per deciliter (11.9 mmol per liter) improves the long-term outcome.<sup>14-16</sup> In nondiabetic patients with protracted critical illnesses, high serum levels of insulin-like growth factor-binding protein 1, which reflect an impaired response of hepatocytes to insulin, increase the risk of death.<sup>17,18</sup>

We hypothesized that hyperglycemia or relative insulin deficiency (or both) during critical illness may directly or indirectly confer a predisposition to complications,<sup>11,19,20</sup> such as severe infections, polyneuropathy, multiple-organ failure, and death. We performed a prospective, randomized, controlled trial at one center to determine whether normalization of blood glucose levels with intensive insulin therapy reduces mortality and morbidity among critically ill

Гипергликемия после  
операции – фактор риска  
осложнений и  
летальности,  
инсулинотерапия

Van den Berghe G., 2001

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)

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September 20, 2010September 2010

## Postoperative Hyperglycemia and Surgical Site Infection in General Surgery Patients

Ashar Ata, MBBS, MPH; Julia Lee, BS; Sharon L. Bestle, RN; et al

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Arch Surg. 2010;145(9):858-864. doi:10.1001/archsurg.2010.179

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### Abstract

**Hypothesis** Postoperative hyperglycemia is an independent risk factor for postoperative surgical site infection (SSI).

**Design** Retrospective medical record review.

**Setting** Academic tertiary referral center.

**Patients** A total of 2090 general and vascular surgery patients in an institutional quality improvement database between November 1, 2006, and April 30, 2009.

**Main Outcome Measure** Postoperative SSI.

**Results** Postoperative glucose levels v

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послеоперационной  
гипергликемии – нагноение  
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Ata A., 2010

# Коррекция стрессовой гипергликемии (поддержание нормогликемии или пермиссивной гипергликемии)



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## Insulin Therapy for the Management of Hyperglycemia in Hospitalized Patients

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<sup>a</sup>Department of Medicine, Boston University School of Medicine, 88 East Newton Street, Boston, MA 02118, USA

<sup>b</sup>Department of Medicine, Emory University School of Medicine, 49 Jesse Hill Jr. Drive, Atlanta, GA 30303, USA

### Abstract

It has long been established that hyperglycemia with or without a prior diagnosis of diabetes increases both mortality and disease-specific morbidity in hospitalized patients<sup>1–4</sup> and that goal-directed insulin therapy can improve outcomes.<sup>5–9</sup> During the past decade, since the widespread institutional adoption of intensified insulin protocols after the publication of a landmark trial,<sup>5,10</sup> the pendulum in the inpatient diabetes literature has swung away from achieving intensive glucose control and toward more moderate and individualized glycemic targets.<sup>11,12</sup> This change in clinical practice is the result of several factors, including challenges faced by hospitals to coordinate glycemic control across all levels of care,<sup>13,14</sup> publication of negative prospective trials,<sup>15,16</sup> revised recommendations from professional organizations,<sup>17,18</sup> and increasing evidence

- Пермиссивная гипергликемия – 6,1-10,0 ммоль/л;
- Оптимально – 6,1-7,8 ммоль/л

*McDonnell M.E., 2012*

# Анальгезия высокими дозами опиоидов

European Review for Medical and Pharmacological Sciences

2017; 21: 4419-4422

## Relationship between blood remifentanyl concentration and stress hormone levels during pneumoperitoneum in patients undergoing laparoscopic cholecystectomy

P. ACETO<sup>1</sup>, C. DELLO RUSSO<sup>2</sup>, C. LAI<sup>3</sup>, V. PERILLI<sup>1</sup>, N. FUCCI<sup>4</sup>,  
N. DE GIOVANNI<sup>4</sup>, A. PIRAS<sup>5</sup>, P. NAVARRA<sup>2</sup>, L. SOLLAZZI<sup>1</sup>

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<sup>4</sup>Institute of Public Health, Section of Legal Medicine, Catholic University Medical School, Rome, Italy

<sup>5</sup>Institute of Clinical Pediatrics, Catholic University Medical School, Rome, Italy

**Abstract.** – **OBJECTIVE:** The effect of remifentanyl on stress response to surgery is unclear. However, there are not clinical studies investigating the relationship between blood remifentanyl concentrations and stress hormones. Therefore, the aim of the present study was to assess the association between blood remifentanyl concentrations measured after pneumoperitoneum and cortisol (CORT) or prolactin (PRL) ratio (intraoperative/preoperative value), in patients undergoing laparoscopic cholecystectomy.

**PATIENTS AND METHODS:** Patients did not receive any pre-anesthetic medication. Anesthesia induction was standardized. Anesthesia maintenance was performed with inhaled sevoflurane at age-adjusted 1.0 minimum alveolar concentration and intravenous remifentanyl at infusion rate ranging from 0.1 to 0.4 mcg/kg/min. Blood samples were withdrawn before anesthesia induction and 5 min after achieving a pneumoperitoneum pressure of 12 mmHg. Correlation analyses were performed to evaluate the relationship between measured blood remifentanyl concentrations, CORT or PRL ratio (intraoperative/preoperative value) and remifentanyl dose delivered by the pump.

**RESULTS:** A significant inverse correlation was found between CORT ratio and measured

### Introduction

It has been demonstrated that laparoscopic surgery may produce a moderate stress response although this approach is considered as minimally invasive<sup>1</sup>. Intravenously administered remifentanyl, combined with general anesthetics, provides stable hemodynamic during laparoscopic surgery<sup>2,3</sup>. Previous studies regarding remifentanyl effect on stress response in laparoscopic surgery are conflicting. Some authors reported remifentanyl dose-independent stress hormone variations in response to pneumoperitoneum, whereas other studies demonstrated reduced hormone release only at high doses<sup>4</sup>. In this regard, it may be suggested that remifentanyl, as other opioids, could mitigate stress response activation in a dose-dependent manner<sup>5,6</sup>. Currently, there are not clinical studies investigating the relationship between blood concentrations of remifentanyl and stress hormones during surgery. In this scenario, the aim of the present study was to assess the association between blood remifentanyl concentration measured after pneumoperitoneum and stress hormones (cortisol and prolactin) ratio (intraoperative/preoperative)

Концентрация кортизола в  
плазме крови обратно  
пропорциональна  
концентрации  
ремифентанила

Aceto P., 2017

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## Anaesthesia, surgery, and challenges in postoperative recovery

Prof Henrik Kehlet, MD   • Jørgen B Dahl, MD

• Published: December 06, 2003 • DOI: [https://doi.org/10.1016/S0140-6736\(03\)14966-5](https://doi.org/10.1016/S0140-6736(03)14966-5)

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Summary

### Summary

Surgical injury can be followed by pain, nausea, vomiting and ileus, stress-induced catabolism, impaired pulmonary function, increased cardiac demands, and risk of thromboembolism. These problems can lead to complications, need for treatment in hospital, postoperative fatigue, and delayed convalescence. Development of safe and short-acting anaesthetics, improved pain relief by early intervention with multimodal analgesia, and stress reduction by regional anaesthetic techniques,  $\beta$ -blockade, analgesics, and

References

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Summary

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Surgical injury can be followed by pain, nausea, vomiting and ileus, stress-induced catabolism, impaired pulmonary function, increased cardiac demands, and risk of thromboembolism. These problems can lead to complications, need for treatment in hospital, postoperative fatigue, and delayed convalescence. Development of safe and short-acting anaesthetics, improved pain relief by early intervention with multimodal analgesia, and stress reduction by regional anaesthetic techniques,  $\beta$ -blockade, analgesics, and

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## Effect of local wound infiltration with ropivacaine on postoperative pain relief and stress response reduction after open hepatectomy

Jing-Xian Sun, Ke-Yun Bai, Yan-Feng Liu, Gang Du, Zhi-Hao Fu, Hao Zhang, Jin-Huan Yang, Ben Wang, Xiu-Yu Wang, Bin Jin

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**Author contributions:** Sun JX collected the data and drafted the manuscript; Liu YF, Fu ZH, Zhang H, Yang JH and Wang XY contributed to data collection and statistical analysis; Du G and Wang B helped revise the manuscript; Jin B and Bai KY contributed to the study design and revised the manuscript; all authors read and approved the final manuscript.

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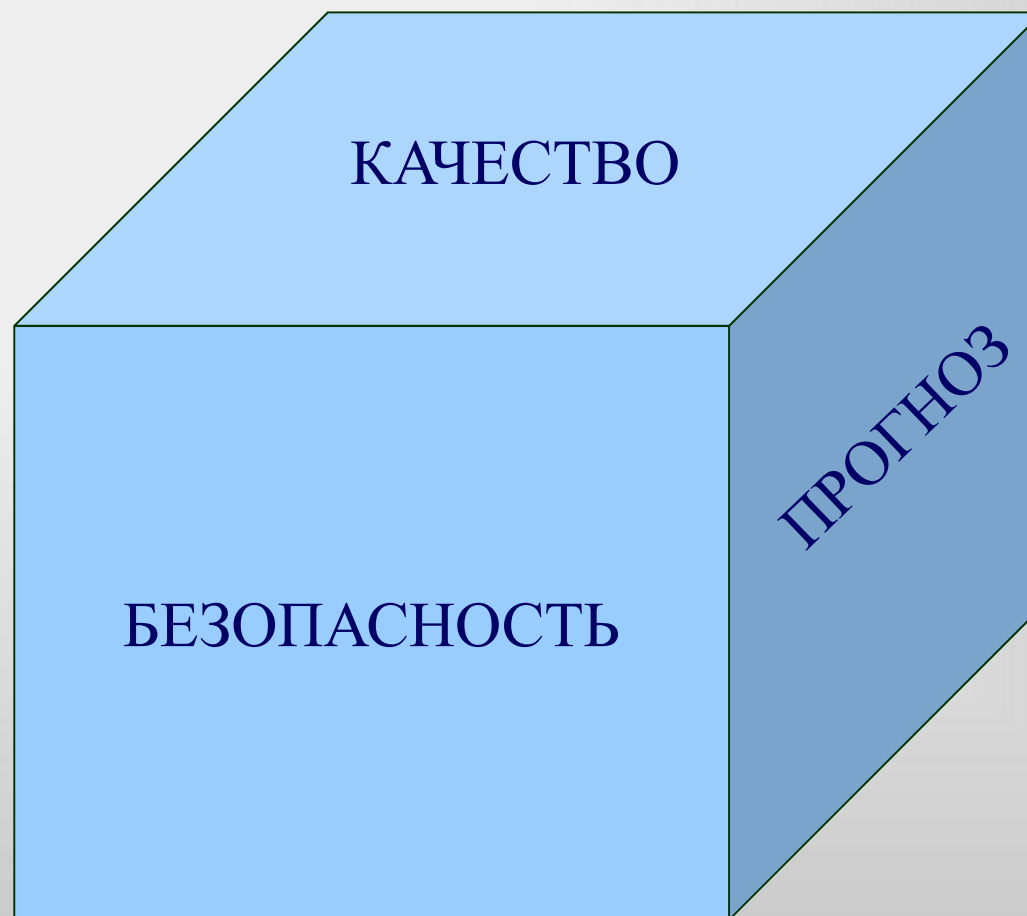
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