

1997; 78:606-617

BJA
British Journal of Anaesthesia

Multimodal approach to control postoperative pathophysiology and rehabilitation

H. Kehlet

- **every operation can be ambulatory ?**
- **why is the patient in hospital today ?**
- **what is it that we cannot control ?**

1

Lancet 2003; 362: 1921

Anaesthesia, surgery, and challenges in postoperative recovery

Henrik Kehlet, Jørgen Dahl

- **organ dysfunction ("surgical stress")**
- **hypothermia-induced morbidity**
- **pain**
- **PONV / ileus**
- **fluid excess/ hypovolaemia**
- **cognitive dysfunction/sleep disturbances**
- **immobilisation/semi-starvation**
- **blood management**
- **fatigue (early/late)**
- **traditions (tubes, drains, restrictions, etc.)**

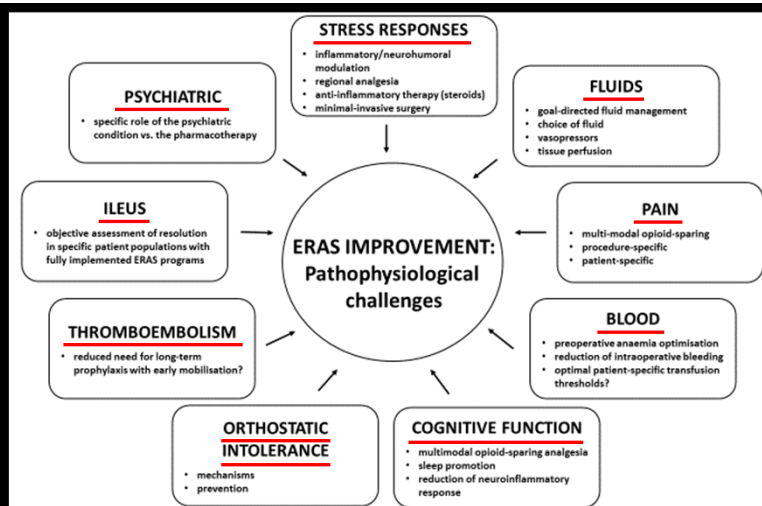
2

Anaesthesia 2020;75 Suppl 1:e54-e61.

Anaesthesia
Journal of the Association of Anaesthetists of
Great Britain and Ireland

Enhanced postoperative recovery: Good from afar, but far from good?

Henrik Kehlet, Prof., PhD, FACS(Hon), ASA(Hon)



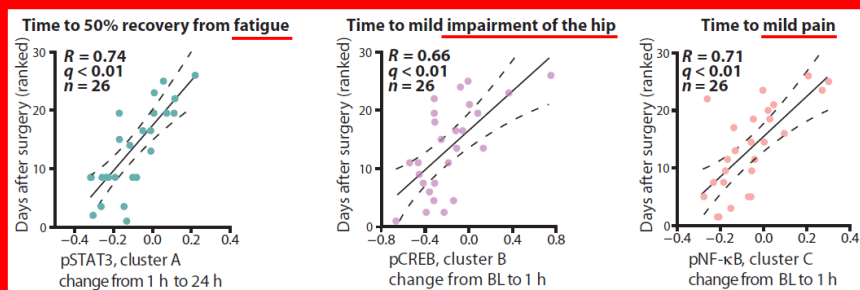
3

Sci Transl Med 2014;6:255ra131.

Science Translational Medicine

Clinical recovery from surgery correlates with single-cell immune signatures

Brice Gaudillière,^{1,2*} Gabriela K. Fragiadakis,^{2,3*} Robert V. Bruggner,^{2,4} Monica Nicolau,^{2,5,6} Rachel Finck,^{2,3} Martha Tingle,¹ Julian Silva,¹ Edward A. Ganio,¹ Christine G. Yeh,¹ William J. Maloney,⁷ James I. Huddleston,⁷ Stuart B. Goodman,⁷ Mark M. Davis,³ Sean C. Bendall,^{2,3} Wendy J. Fantl,^{2,3,8} Martin S. Angst,^{1†‡} Garry P. Nolan^{2,3†‡}



see also Fragiadakis Anesthesiology 2015;123:1241

4

Nat Neurosci 2017;20:156-66.

nature
neuroscience

Neural regulation of immunity: molecular mechanisms and clinical translation

Valentin A Pavlov^{1,2} & Kevin J Tracey^{1,2}

Anesthesiology 2016; 124:1174-89.

Anesthesiology
The Journal of the American Society of Anesthesiologists, Inc.

Neural Control of Inflammation

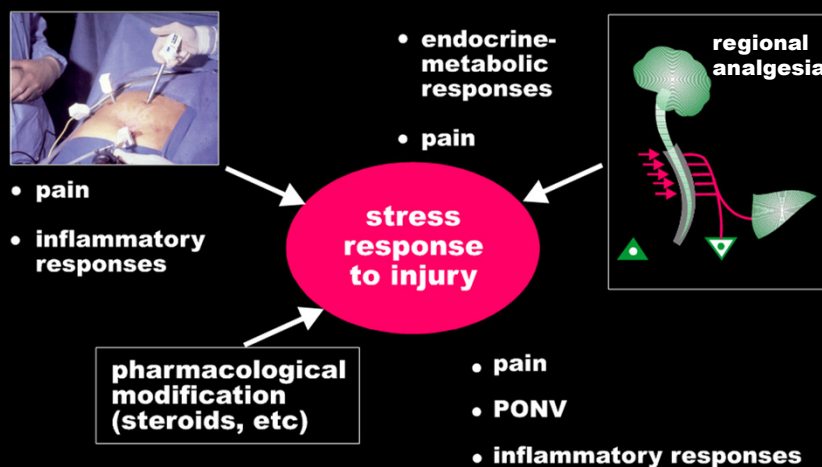
Implications for Perioperative and Critical Care

Benjamin E. Steinberg, M.D., Ph.D., Eva Sundman, M.D., Ph.D., Niccolo Terrando, Ph.D.,
Lars I. Eriksson, M.D., Ph.D., F.R.C.A., Peder S. Olofsson, M.D., Ph.D.

**basis for novel therapeutic strategies in
the context of perioperative medicine**

5

modification of the surgical stress responses



Kehlet

Anaesthesia 2020;75 Suppl 1:e54.

6

Ann Surg 2014;260:540-9.

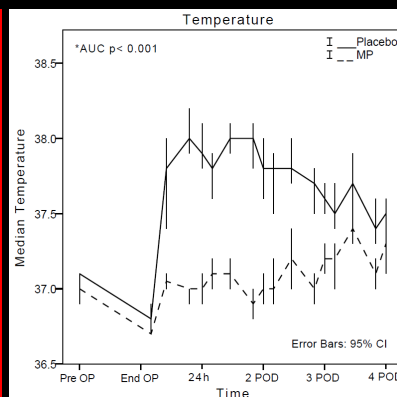
ANNALS OF SURGERY
A Monthly Review of Surgical Science Since 1885

Preoperative Methylprednisolone Enhances Recovery After Endovascular Aortic Repair

A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

Louise de la Motte, MD, PhD,* Henrik Kehlet, Prof. MD, PhD, FACS (Hon),† Katja Vogt, MD, DMSc,*
Claus H. Nielsen, MD, PhD,‡ John B. Groenvall, MD,§ Henning B. Nielsen, MD, DMSc,¶ Andreas Andersen,*
Torben V. Schroeder, Prof. MD, DMSc,|| and Lars Lönn, Prof. MD, PhD*§

- **n = 150**
- **pro-inflammatory mediators ↓**
- **SIRS ↓ 27 vs 92 % (p< 0.001)**
- **discharge criteria 2 vs 3 days (p< 0.001)**



7

Acta Orthop 2018;89:477-9.

Acta Orthopaedica

High-dose glucocorticoid before hip and knee arthroplasty: To use or not to use—that's the question

Kehlet H. & Lindberg-Larsen V.

pain ↓ fatigue ↓ safety ↑
CRP ↓ endothelial function ↑
glucose homeostasis (↓)

need for dose-finding and repeat-dosing studies in "high" and "low" pain responders

see also Kehlet & Joshi Anaesthesia 2020;75:856.

8

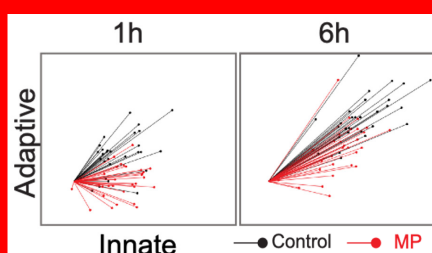
Nat Commun 2020;11:3737.



Preferential inhibition of adaptive immune system dynamics by glucocorticoids in patients after acute surgical trauma

Edward A. Gano^{1,6}, Natalie Stanley^{1,6}, Viktoria Lindberg-Larsen^{2,6}, Jakob Einhaus¹, Amy S. Tsai¹, Franck Verdonk¹, Anthony Culos¹, Sajjad Gahemi^{1,3}, Kristen K. Rumer¹, Ina A. Stelzer¹, Dyani Gaudilliere⁴, Eileen Tsai¹, Ramin Fallahzadeh¹, Benjamin Choisy¹, Henrik Kehlet⁵, Nima Aghaeepour^{1,6}, Martin S. Angst^{1,6} & Brice Gaudilliere^{1,6,8}

- **RCT n=58 +/- 125 mg MP**
- **high-dimensional cytometry (Gaudilliere 2014)**



MP: inhibition of adaptive components (0-48 h), but not innate

9

Br J Anaesth 2017; 119:720-2.



Guidelines For Perioperative Pain Management: Need For Re-evaluation

Joshi G, Kehlet H

- **dynamic, balanced analgesia is a prerequisite for optimal recovery**
- **procedure-specific (www.postoppain.org)**
- **must be assessed in an ERAS setting**

Joshi & Kehlet Best Pract Res Clin Anaesthesiol 2019;33:259.

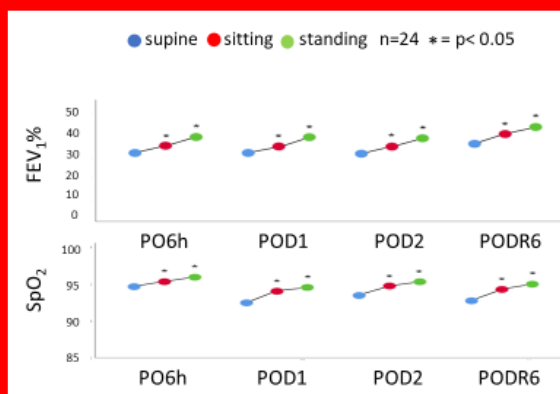
10

Periop Med 2021;10:26.

Perioperative
Medicine

Effect of posture on pulmonary function
and oxygenation after fast-tracking video-
assisted thoracoscopic surgery (VATS)
lobectomy: a prospective pilot study

Lin Huang¹, Henrik Kehlet^{2*} and René Horsleben Petersen²



11

patient blood management

1st pillar

**optimize
hemato-
poiesis**

2nd pillar

**minimize
blood loss
and
bleeding**

3rd pillar

**optimize
tolerance
of anemia**

multidisciplinary team approach

Munting & Klein
Elhenawy et al.

Anaesthesia 2019;74:suppl 1:49
Systematic reviews 2021;10:36

12

Anesthesiology 2019;130:825-32.

Anesthesiology
The Journal of the American Society of Anesthesiologists, Inc.

Perioperative Fluid Therapy for Major Surgery

Timothy E. Miller, M.B., Ch.B., F.R.C.A., Paul S. Myles, M.B., B.S., M.P.H., D.Sc., F.A.N.Z.C.A.

- **positive balance approach (1 – 1.5 L)**
- **balanced solutions**
- **colloids controversial**
- **goal-directed therapy promising, but...**
- **need for "fast-track" studies !**

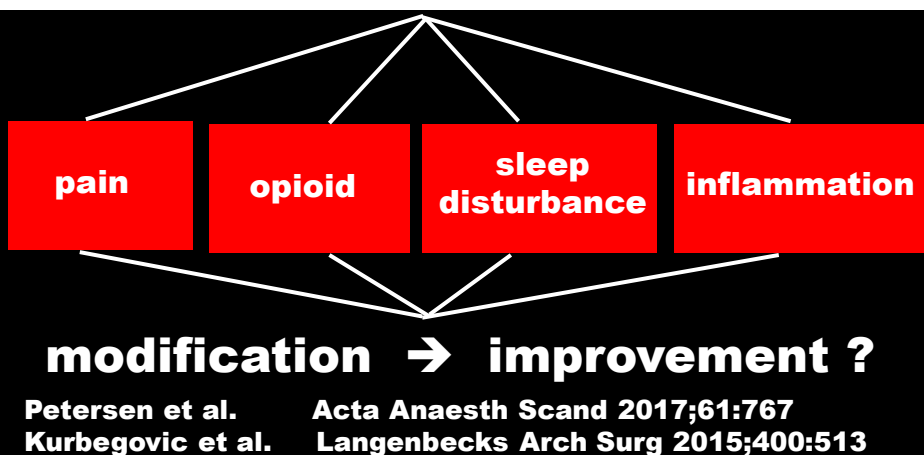
13

Acta Anaesthesiol Scand 2010;54:951-6

Acta Anaesthesiologica
Scandinavica
AN INTERNATIONAL JOURNAL OF ANAESTHESIOLOGY AND INTENSIVE CARE, PAIN AND EMERGENCY MEDICINE

New insights into the pathophysiology of postoperative cognitive dysfunction

L. KRENK^{1,2,3}, L. S. RASMUSSEN¹ and H. KEHLET^{2,3}



14

Br J Anaesth 2021;126:348-9.



Fast-track hip and knee arthroplasty...how fast?

Thomas W. Wainwright¹, Stavros G. Memtsoudis^{2,3,4} and Henrik Kehlet^{5,6,*}

- **outpatient set-up natural evolution**
- **patient selection and monitoring !**
- **no extra post-discharge facilities**
- **first LOS 1-2 days, then try outpatient**
- **“first better – then faster” !**

15

Br J Anaesth 2019;123:671-8.



Days alive and out of hospital after fast-track total hip and knee arthroplasty: an observational cohort study in 16 137 patients

Christoffer C. Jørgensen^{1,2,*}, Pelle B. Petersen^{1,2}, Henrik Kehlet^{1,2} on behalf of the Lundbeck Foundation Center for Fast-track Hip and Knee Replacement Collaborative Group[†]

Eur Urol Open Sci 2021;28:1-8.



Morbidity and Days Alive and Out of Hospital Within 90 Days Following Radical Cystectomy for Bladder Cancer

Sophia L. Maibom^{a,b,*}, Martin A. Røder^{a,b}, Alicia M. Poulsen^a, Peter O. Thind^a, Marie L. Salling^a, Lisbeth N. Salling^a, Henrik Kehlet^{b,c}, Klaus Brasso^{a,b}, Ulla N. Joensen^{a,b}

new interesting method to assess overall surgical outcome - LOS, readmissions and mortality

16

Anaesthesia 2018;73:799-803.



Large pragmatic randomised controlled trials in peri-operative decision making: are they really the gold standard?

Joshi G, Alexander JC, Kehlet H.

- **why not ERAS discussion ?**
- **no "large" trials with low ERAS adherence**
- **more focus on organ- and procedure – specific functional recovery parameters**
- **first detailed pathophysiological studies – then RCT/multicenter cohort studies**

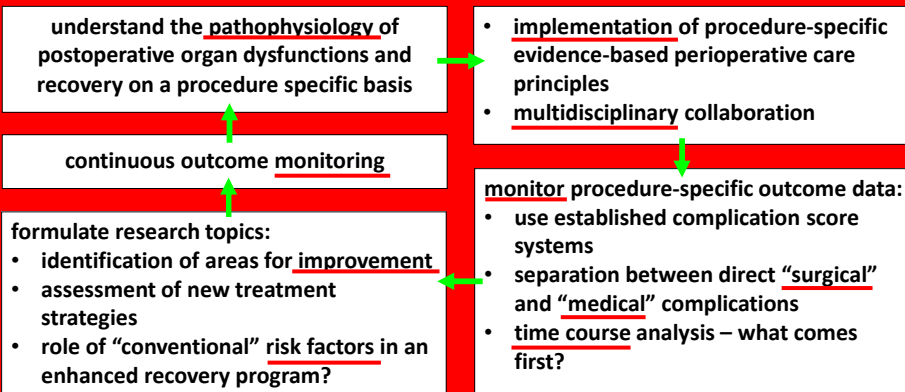
17

Ann Surg 2016;264:237-8.



Advancing Surgical Outcomes Research and Quality Improvement Within an Enhanced Recovery Program Framework

Henrik Kehlet, MD, PhD and Christoffer C. Jørgensen, MD



18

Anaesthesia 2020;75 Suppl 1:e54-e61.

Anaesthesia
Journal of the Association of Anaesthetists of
Great Britain and Ireland

Enhanced postoperative recovery: Good from afar, but far from good?

Henrik Kehlet, Prof., PhD, FACS(Hon), ASA(Hon)

- **focus on pathophysiology of recovery**
- **need for better procedure-specific evidence of ERAS components**
- **improved study design of ERAS**
- **better implementation of evidence**
- **“first better – then faster”**