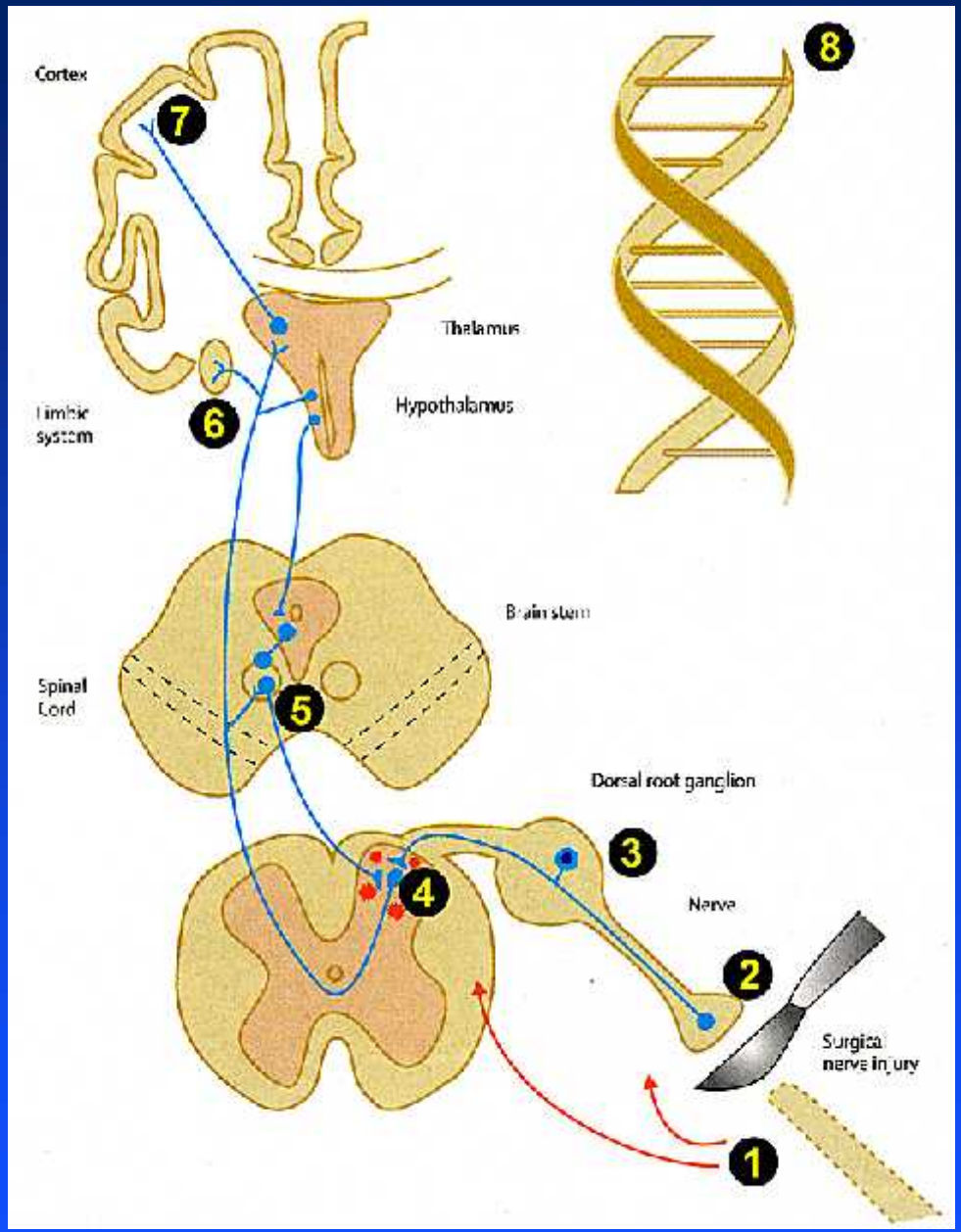
Professor Narinder Rawal, MD, PhD, FRCA (Hon)
Department of Clinical Medicine
Division of Anaesthesiology and Intensive Care
University Hospital
Örebro, Sweden

Persistent postsurgical pain

- **Mechanism – pathophysiology**
- **Prevalence**
- **Risk factors**
- **Role of surgical technique**
- **Issue of unnecessary surgery**
- **Can persistent postsurgical pain be prevented? The role of analgesic techniques**



1. Local and systemic chemicals drive pain signalling
2. Neuroma at injury site - excitability in sensory fibres
3. Changes in gene expression in dorsal front ganglion
4. Dorsal horn - central sensitization
5. Descending controls modulate transmission in spinal cord
6. Limbic system and hypothalamus - altered mood, behaviour
7. Sensation of pain generated in cortex (past experiences, cultural inputs, expectations)
8. Genomic DNA predispose (or not) patient for chronic pain

Persistent postsurgical pain – the incidence

• Craniotomy	6-12 %	Kaur 2000 Harner 1993
• Leg amputation	50-80 %	Finch 1980 Fisher 1998 Sherman 1984
• Thoracotomy	50 %	Bertrand 1996 Katz 1996
• Breast surgery	11-57 %	Jung 2003 Tasmuth 1996
• Lap cholecystectomy	3-56 %	Stiff 1994 Ure 1995 de Povourville 1997
• Inguinal hernia	12 %	Aasvang 2005

Chronic postsurgical pain

Genetic predisposition

Surgical

- Severity of postopertaive pain
- Surgical factors
  - site and extent of surgery
  - damage to nerves
  - reoperations
  - bleeding, infection

Psychological

- Patient attiudes
- Preop anxiety
- Expectation of chronicity

Environmental

- Poor education
- Low income
- Poor self-rated health

Preoperative

- Female gender
- Younger age
- Pain before surgery
- Analgesic use

*Different pain syndromes after same surgery**

- **Lower limb amputation**
  - **phantom pain**
  - **stump pain**
  - **back pain**
- **Breast surgery**
  - **phantom pain**
  - **neuropathic pain (damage to intercostobrachial nerve)**
  - **scar pain**

* ***Patients may complain of a range of unpleasant symptoms after surgery such as numbness, tingling, swelling pain***

It´s not only nerve damage

"Damage to nerves during surgery is obviously an important cause of chronic pain after surgery ----- but this is a complex issue.

Merely avoiding the sectioning of major nerve trunks is not sufficient to prevent CPSP and sectioning nerves clearly does not always result in chronic pain.

It is not possible to perform operations without injuring elements of the nervous system at some level"

Macrae W A
Br J Anaesth 2008;1001:77-86

Chloroform has done a great deal of harm.
It allows any fool to be a surgeon.

George Bernard Shaw
In: A doctor's dilemma 1906

Persistent postsurgical pain – role of surgical technique

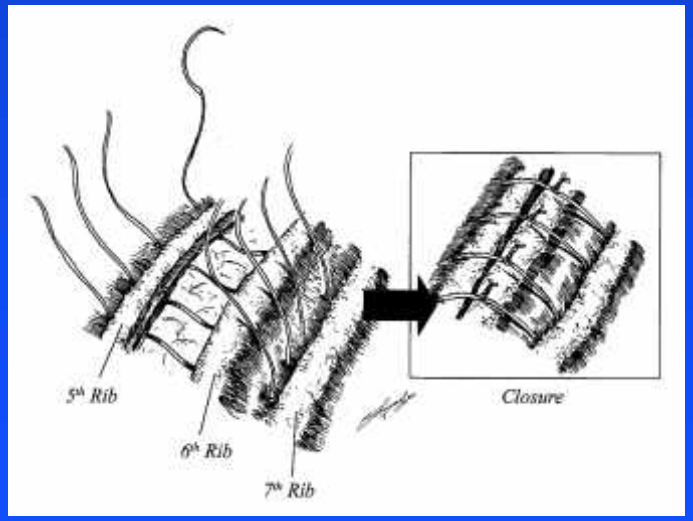
- **Laparascopic surgery (*vs.* open)**
- **Mastectomy - preservation of intercostal-brachial nerve**
  - sentinel lymph node biopsy (avoids axillary dissection and intercostal nerve damage)
- **Thoracoscopic techniques (spare intercostal nerves) avoid use of rib retractors**
  - intercostal suture technique to avoid nerve compression
- **Muscle sparing thoracotomy**
- **Minimally invasive surgery (nephrectomy, sternotomy etc.)**

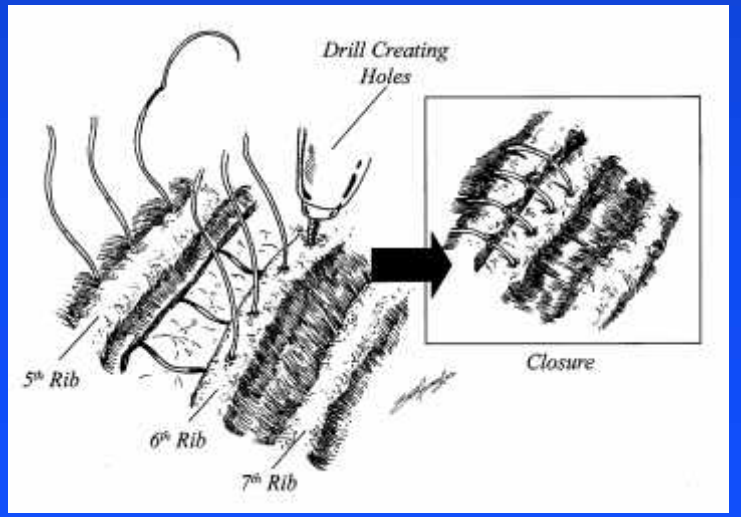
Intracostal Sutures Decrease the Pain of Thoracotomy

Robert J. Cerfolio, MD, FACS, Theolynn N. Price, MD, Ayesha S. Bryant, MSPH, Cynthia Sale Bass, RN, MSN, and Alfred A. Bartolucci, PhD

Ann Thorac Surg 2003;76:407-12

- **Elective thoracotomy, n = 280, single surgeon**
- **Preoperative EDA**
- **Pericostal sutures (stitches on top of 5th and 7th rib (n = 140) *vs.* intracostal sutures (stitches on top onf 5th rib and through 6th rib (n = 140)**
- **Pain scores lower in intracostal group at 2 weeks, 1 month, 2 months, 3 months**





Non-opioid analgesic techniques

- **Analgesic drugs**
  - **Paracetamol**
  - **NSAID's (including COX-2-inhibitors)**
  - **NMDA antagonists (ketamine, dextromethorphan)**
  - **α_2 receptor agonists (clonidine, dexmedetomidine)**
  - **others (gabapentin, corticosteroids, capsaicin, nicotine, neostigmine etc.)**
- **Regional techniques (including catheter techniques)**
  - **Central blocks (EDA, spinal, CSE)**
  - **Peripheral blocks**
  - **Incisional**
  - **Intraarticular**
- **Non-pharmacological techniques**

Anesthesiology 2005; 103:1079–88

Efficacy of Postoperative Patient-controlled and Continuous Infusion Epidural Analgesia versus *Intravenous Patient-controlled Analgesia with Opioids*

A Meta-analysis

Christopher L. Wu, M.D., Seth R. Cohen, B.S.,† Jeffrey M. Richman, M.D.,‡ Andrew J. Rowlingson, B.A.,§ Genevieve E. Courpas, B.A.,§ Kristin Cheung, M.D.,|| Elaina E. Lin, B.A.,# Spencer S. Liu, M.D.***

- **299 RCT's**
- **Epidural analgesia in every combination superior to i.v. PCA upto 3-days (exception epidural morphine alone)**
- **Continuous infusion superior to PCEA for pain at rest and activity (but more PONV and motor block, less pruritus)**
- **Epidural l.a. □ opioid better than epidural opioid alone**

"In summary, almost without exception, epidural analgesia, regardless of analgesic agent, epidural regimen, and type and time of pain assessment, provided superior postoperative analgesia compared with intravenous patient-controlled analgesia"

Preincisional Paravertebral Block Reduces the Prevalence of Chronic Pain After Breast Surgery

Pekka M. Kairaluoma, MD

Martina S. Bachmann, MD, PhD

Per H. Rosenberg, MD, PhD

Pertti J. Pere, MD, PhD

Anesth Analg 2006;103:703-8

- **n = 60, 1 year follow-up, control sham block**
- **14-day symptom diary, tel. interviews, 1, 6, 12 months after surgery**
- **At 12 months**
  - **reduction of pain symptoms (43 % *vs.* 77 %)**
  - **decreased intensity of motion-related pain**
  - **lower intensity of pain at rest**
- **Low incidence of neuropathic pain (2/30 *vs.* 3/30)**

"In addition to providing acute postoperative pain relief, preoperative PVB seems to reduce the prevalence of chronic pain 1 yr after breast cancer surgery"

Does Continuous Peripheral Nerve Block Provide Superior Pain Control to Opioids? A Meta-Analysis

Jeffrey M. Richman, MD*, Spencer S. Liu, MD‡, Genevieve Courpas, BA*, Robert Wong, MD*, Andrew J. Rowlingson, BA*, John McGready, MS†, Seth R. Cohen, BS§, and Christopher L. Wu, MD*

Anesth Analg 2006;102:248-57

- **19 RCT's (only 11 double-blind)**
- **Better analgesia for all time periods (mean and max VAS) at 24, 48 and 72 h**
- **Superior analgesia for all catheter locations and time periods**
- **Reduction in opioid use with perineural analgesia**
- **PONV (49 % *vs.* 21 %), sedation (52 % *vs.* 27 %), pruritus (27 *vs.* 10 %) more common with opioid analgesia**
- **Improved patient satisfaction (4 RCT's only)**

"CPNB analgesia, regardless of catheter location, provided superior postoperative analgesia and fewer opioid-related side effects when compared with opioid analgesia"

COLLECTIVE REVIEWS

Efficacy of Continuous Wound Catheters Delivering Local Anesthetic for Postoperative Analgesia: A Quantitative and Qualitative Systematic Review of Randomized Controlled Trials

Spencer S Liu, MD, Jeffrey M Richman, MD, Richard C Thirlby, MD, FACS, Christopher L Wu, MD

J Am Coll Surg
2006;203:914-932

- 39 RCT's (n = 1761) qualitative analysis, 45 RCT's (n = 2031), qualitative analysis
- Surgical subgroups (abdominal, cardiothoracic, gynecologic, orthopedic, minor)
- Benefits of wound catheters:
  - decreased pain scores at rest and activity (32 % reduction)
  - decreased need for opioids (25 % reduction)
  - decreased risk of PONV (16 % reduction)
  - increased patient satisfaction (30 % increase)
  - decreased LOS in hospitalized patients (limited data, 1 day, p = 0.01)
- No increase in adverse effects
- Qualititative systematic review supported same benefits

"Continuous wound catheters appear to be an effective modality for management of postoperative pain"

Regional anaesthesia and chronic postsurgical pain*

RA is beneficial

• Hysterectomy	Brandsborg	2007
• Thoracotomy	Richardson	1994
	Obata	1999
	Senturk	2002
	Tiippana	2003
• C. Section	Nikolajsen	2004
• Iliac crest bone harvesting	Reuben	2001
• Breast surgery	Kairaluoma	2006

No benefit of RA

• Inguinal hernia	Kalliomäki	2008
• Gyn. Surgery	Katz	2004
• Hand surgery	McCartney	2004
• Thoracotomy	Ochroch	2002

** Preemtive RA is also controversial for phantom pain*

Analgesic methods for prevention of chronic postsurgical pain

• **Gabapentin**	**Fassoulaki**	**2005**
	Fassoulaki	**2007**
• **Ketamine**	**Katz**	**2004**
	Wilson	**2008**

British Journal of Anaesthesia **96 (2)**: 152–5 (2006)
doi:10.1093/bja/aei318

Editorial II

Gabapentin: a new drug for postoperative pain?

Rowbotham D J

- **Improves quality of opioid analgesia**
- **Reduces opioid requirements**
- **Prevents or reduces opioid tolerance**
- **Relieves anxiety**

Acta Anaesthesiol Scand 2011; 55: 927–943
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ACTA ANAESTHESIOLOGICA SCANDINAVICA
doi: 10.1111/j.1399-6576.2011.02471.x

Review Article

Efficacy and safety of perioperative pregabalin for post-operative pain: a meta-analysis of randomized-controlled trials

E. Engelman and F. Cateloy
Department of Anaesthesia, CUB Hopital Erasme, Brussels, Belgium

British Journal of Anaesthesia 106 (4): 454–62 (2011)
Advance Access publication 25 February 2011 doi:10.1093/bja/aer027

BJA

REVIEW ARTICLES

Efficacy of pregabalin in acute postoperative pain: a meta-analysis

J. Zhang[1], K.-Y. Ho[2]* and Y. Wang[1]

- **11 and 12 RCTs, n=521, mostly minimal invasive surgery**
- **Pain intensity not reduced**
- **Opioid consumption reduced by 8-13 mg, vomiting by 30%**
- **300mg/day or 600 mg/day have identical effects**
- **Risks: dizziness, visual disturbances**

Ketamine as Adjuvant Analgesic to Opioids: A Quantitative and Qualitative Systematic Review

Kathirvel Subramaniam, MD, Balachundhar Subramaniam, MD, and Richard A. Steinbrook, MD

From the Department of Anesthesiology, Critical Care & Pain Management, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts

Anesth Analg 2004;99:482-95

- **37 RCT's, n= 2385, 5 subgroups: i.v. ketamine single dose, cont. Infusion, PCA, epidural, pediatric**
- **I.v. morphine + ketamine not better than i.v. Morphine**
- **I.v. ketamine infusion decreased i.v. and epidural opioid requirements in 6/11 studies***
- **Single bolus ketamine decreased opioid requirements in 7/11 studies***
- **Epidural ketamine beneficial in 5/8 trials**
- **Adverse effects not increased with small dose (0.15-1 mg/kg bolus, 0.12-0.6 mg/kg/h infusion**

"…small dose ketamine is a safe and useful adjuvant to standard practice opioid analgesia"**

May prevent central sensitization and chronic neuropathic pain

** No reduction of opioid adverse effects, ** in 54 % studies*

Low sub-analgesic doses of ketamine to prevent opioid-induced tolerance and hyperalgesia

Yes

Cholecystectomy (open)	Royblat L, et al, Anesth Analg 1993
Human volunteers	Ilkjaer S, et al, Br J Anaesth 1996
C. section	Ngan Kee WB, et al, Anesth Analg 1997
Colorectal	De Kock M, et al. Pain 2001
Colorectal	Guignard B, et al. Anesth Analg 2002
Hysterectomy	Gilabert MA, et al. Rev Esp Anaesthesiol Reanim 2002
Gyn. lap.	Kwok RF, et al, Anesth Analg 2004

No

Abd. hysterectomy	Dahl V, et al, Anesth Analg 2000
ACL repair	Jaksch W, et al, Anesth analg 2002
ENT	Ganne O, et al, Eur J Anaesthesiol 2005

British Journal of Anaesthesia **101 (1):** 77–86 (2008)
doi:10.1093/bja/aen099 Advance Access publication April 22, 2008

BJA

Chronic post-surgical pain: 10 years on

W. A. Macrae

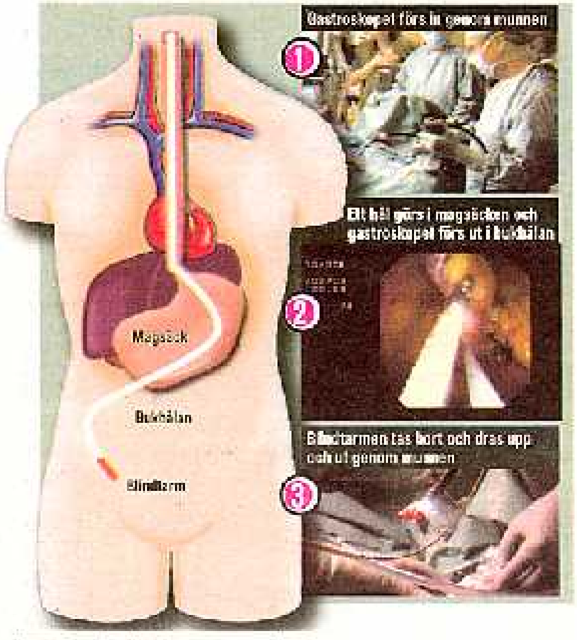
Ninewells Hospital and Medical School, Dundee DD1 9SY and The Bute Medical School, University of St Andrews, St Andrews, KY16 9TS, Scotland

E-mail: w.a.macrae@dundee.ac.uk

In the past ten years there has been recognition that chronic post-surgical pain is a significant problem. This is a complex area of research and although the quality of studies has improved many difficulties remain. Several recent publications have examined risk factors. Severe acute postoperative pain emerges as a factor that we may be able to influence. There is a need for education of the medical profession and the general public, so that effective measures are introduced and unnecessary and inappropriate operations minimized.

Br J Anaesth 2008; 101: 77–86

Aftonbladet
Torsdag 21 februari 2008



Blindtarm togs bort – genom munnen

Här opererar de bort blindtarmen – genom munnen.
Nu hoppas läkarna att den revolutionerande metoden ska kunna användas vid andra typer av ingrepp.

Ny metod ska minska besvär efter operation

SCIENCE

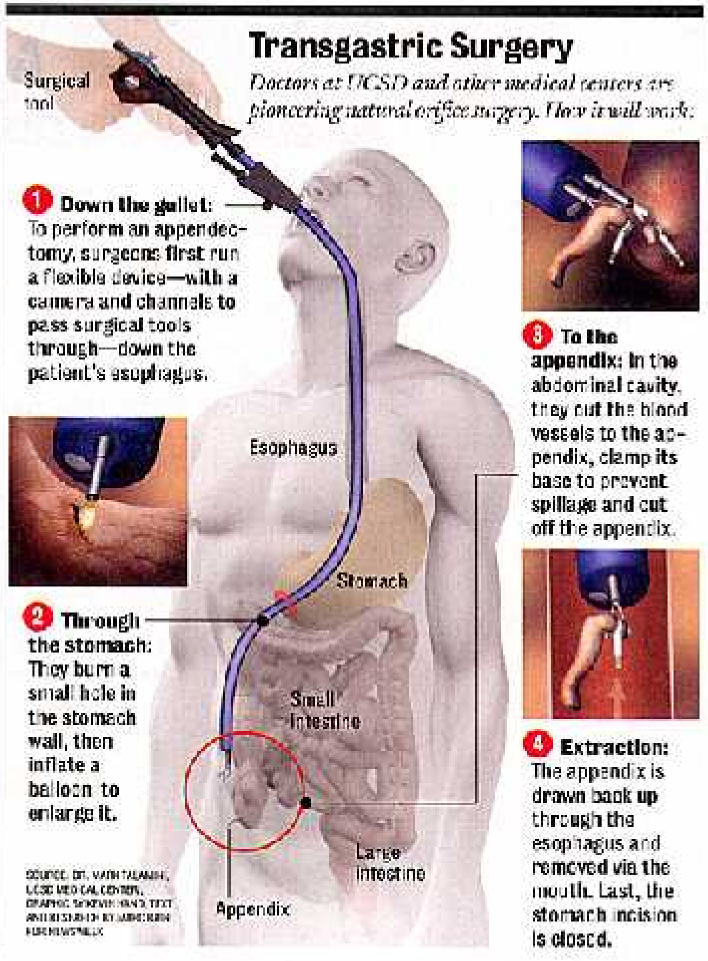
Open Wide. No, Wider.

Are we ready for an era of 'natural-orifice surgery'?

By TINA PENG

TWENTY-FIVE YEARS AGO, TYPIcal appendectomy patients could expect to spend as many as seven

says natural orifice surgery is being oversold. Most of the procedures worldwide have been gallbladder removals, which are usually performed laparoscopically and are already almost painless and scarless with



Newsweek
April 14, 2008

Tuesday, September 19, 2000

USA TODAY

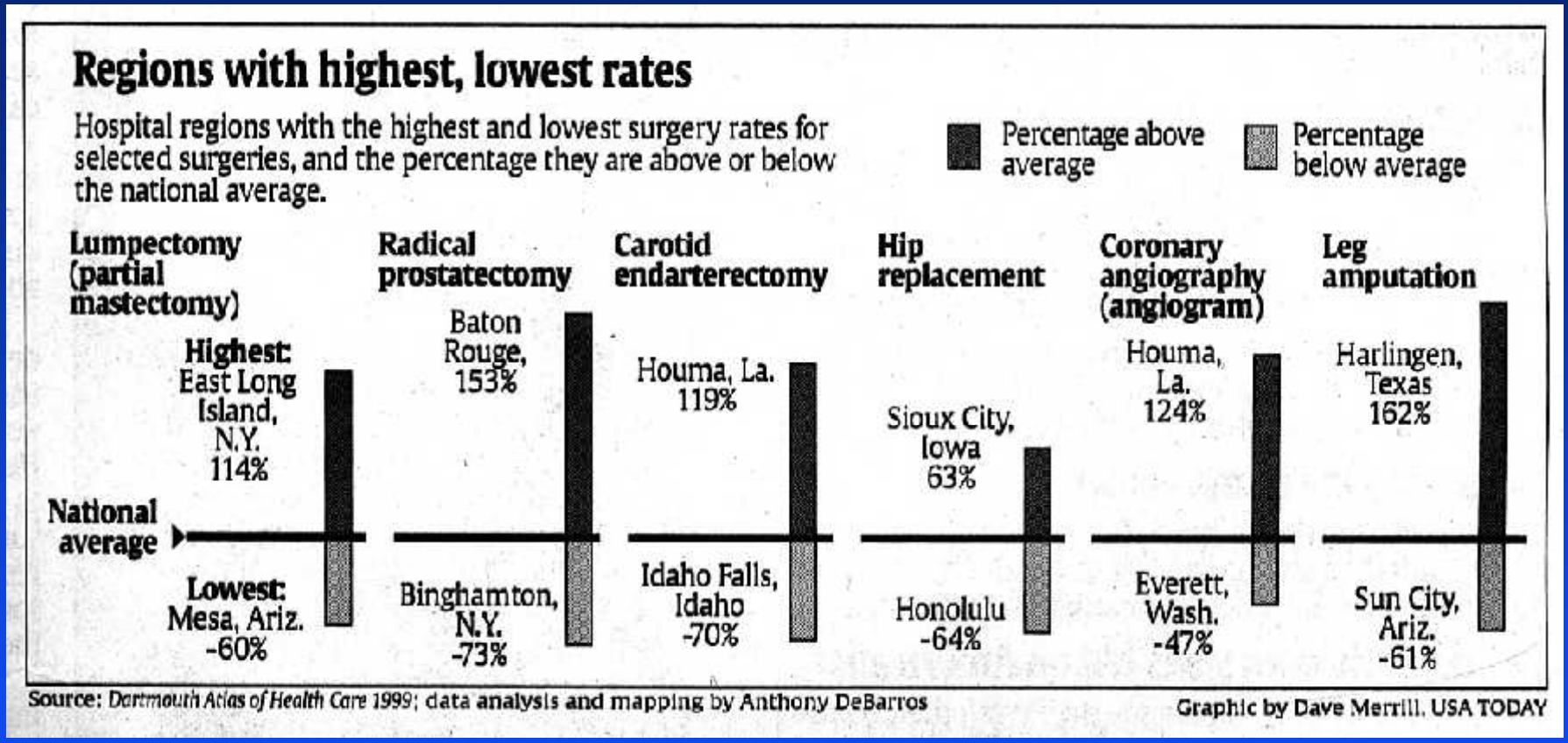
AVAILABLE AROUND THE WORLD

The operation you get often depends on where you live

Medical researchers question whether patients everywhere are fully informed before surgery

The geography of Surgery

For surgery data on all regions of the USA: http://health.usatoday.com


Regions with highest, lowest rates
Hospital regions with the highest and lowest surgery rates for selected surgeries, and the percentage they are above or below the national average.
Percentage above average
Percentage below average
Lumpectomy (partial mastectomy)
Highest: East Long Island, N.Y. 114%
National average
Lowest: Mesa, Ariz. -60%
Radical prostatectomy
Baton Rouge, 153%
Binghamton, N.Y. -73%
Carotid endarterectomy
Houma, La. 119%
Idaho Falls, Idaho -70%
Hip replacement
Sioux City, Iowa 63%
Honolulu -64%
Coronary angiography (angiogram)
Houma, La. 124%
Everett, Wash. -47%
Leg amputation
Harlingen, Texas 162%
Sun City, Ariz. -61%
Source: Dartmouth Atlas of Health Care 1999; data analysis and mapping by Anthony DeBarros
Graphic by Dave Merrill, USA TODAY

US Presidential Commission on Health Care

1. ***Extensive overuse of some services and underuse of others***

   - **20% of surgeries and medical tests are unnecessary or inappropriate (e.g. about 80.000 unnecessary hysterectomies/year)**

   - **About 33% heart attack victims do not get necessary betablockers leading to 18.000 deaths/year**

2. ***Unacceptably high rate of medical errors***

   - **Every year about 180.000 people die and about 1 000.000 are injured from medical mishaps**

3. ***Wide variations in patterns of care across US***

USA Today
March 13, 1998

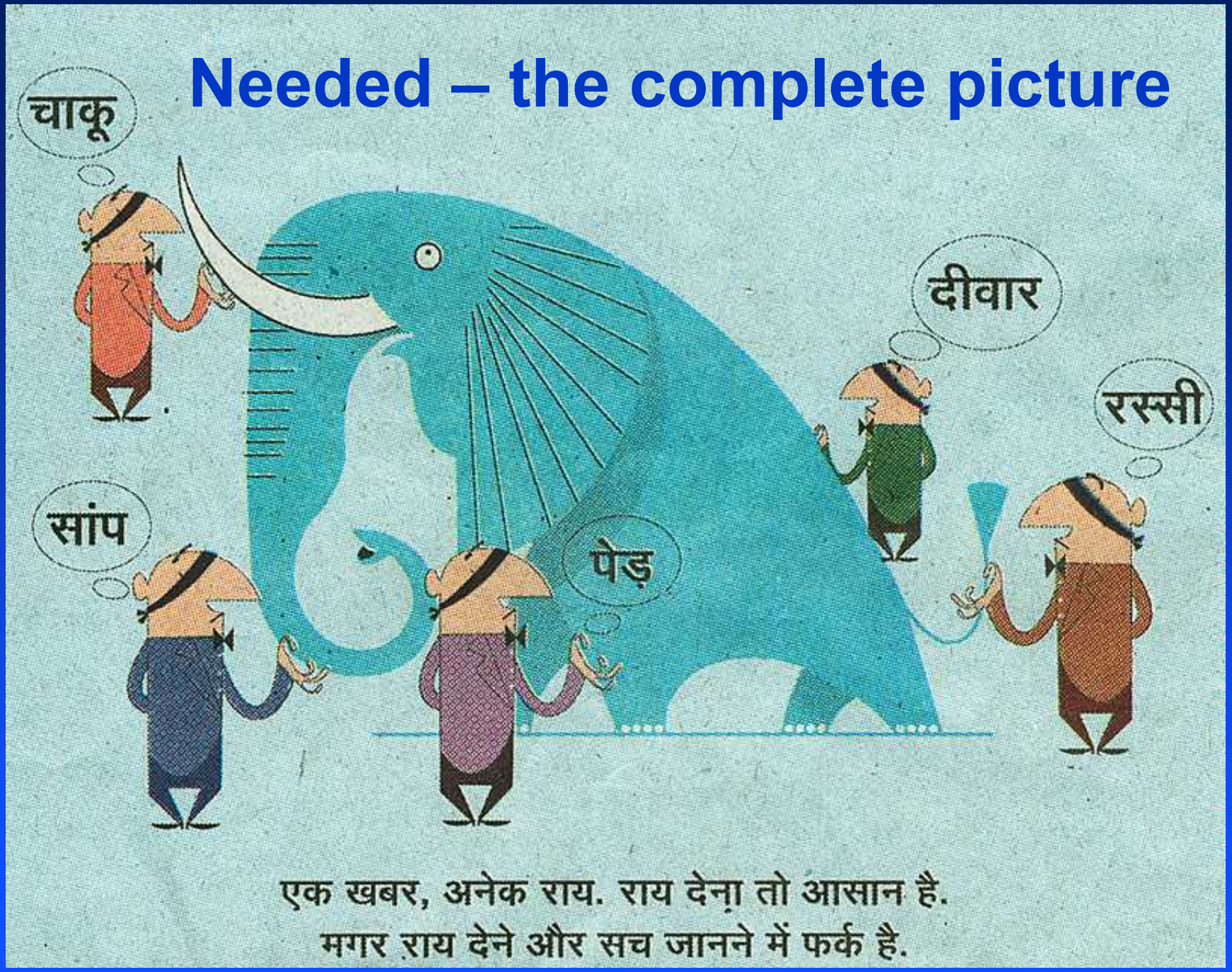
APRIL 2 2006 SUNDAY TELEGRAPH

news.telegraph.co.uk

'Too posh to push' mothers cost NHS £80m

- **About 55 000 unnecessary C. Sections annually**
- **Survey of 100 obstetricians - half of all C. Sections not for medical reasons**
- **C. Section rate in many hospitals above 30 % (WHO recommendations not higher than 15 %)**

Needed – the complete picture



APS - Örebro model

Pre-set goals

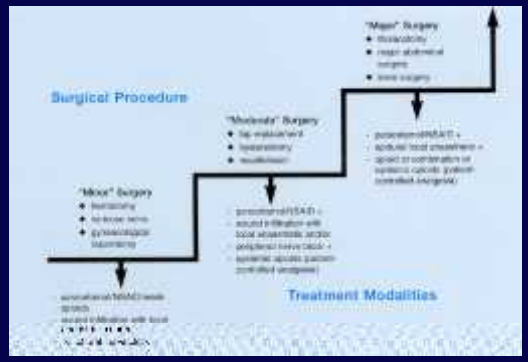
- Patient satisfaction (VAS ≤ 3)
- Postop rehabilitation

Ward nurse training

- Upgrading nursing role
- ”Smärtombud” (nurse, surgeon)
- APN/Anaesthesiologist-based

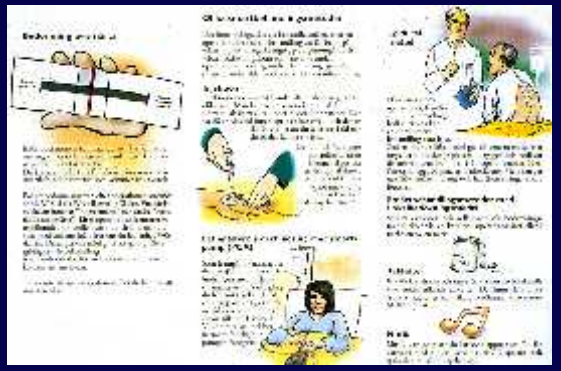
Standardized protocols

- In collaboration with surgeons



Pain management routines integrated into surgical clinical pathways

Patient information



Annual audits

- Assess successes and failures
- Are goals achieved?

Editorial

Red-Hot Chili Peppers: A Spicy New Approach to Preventing Postoperative Pain

Paul F. White, PhD, MD, FANZCA

Anesth Analg 2008;107:6-8

To summarize...

Pain 137 (2008) 233–234

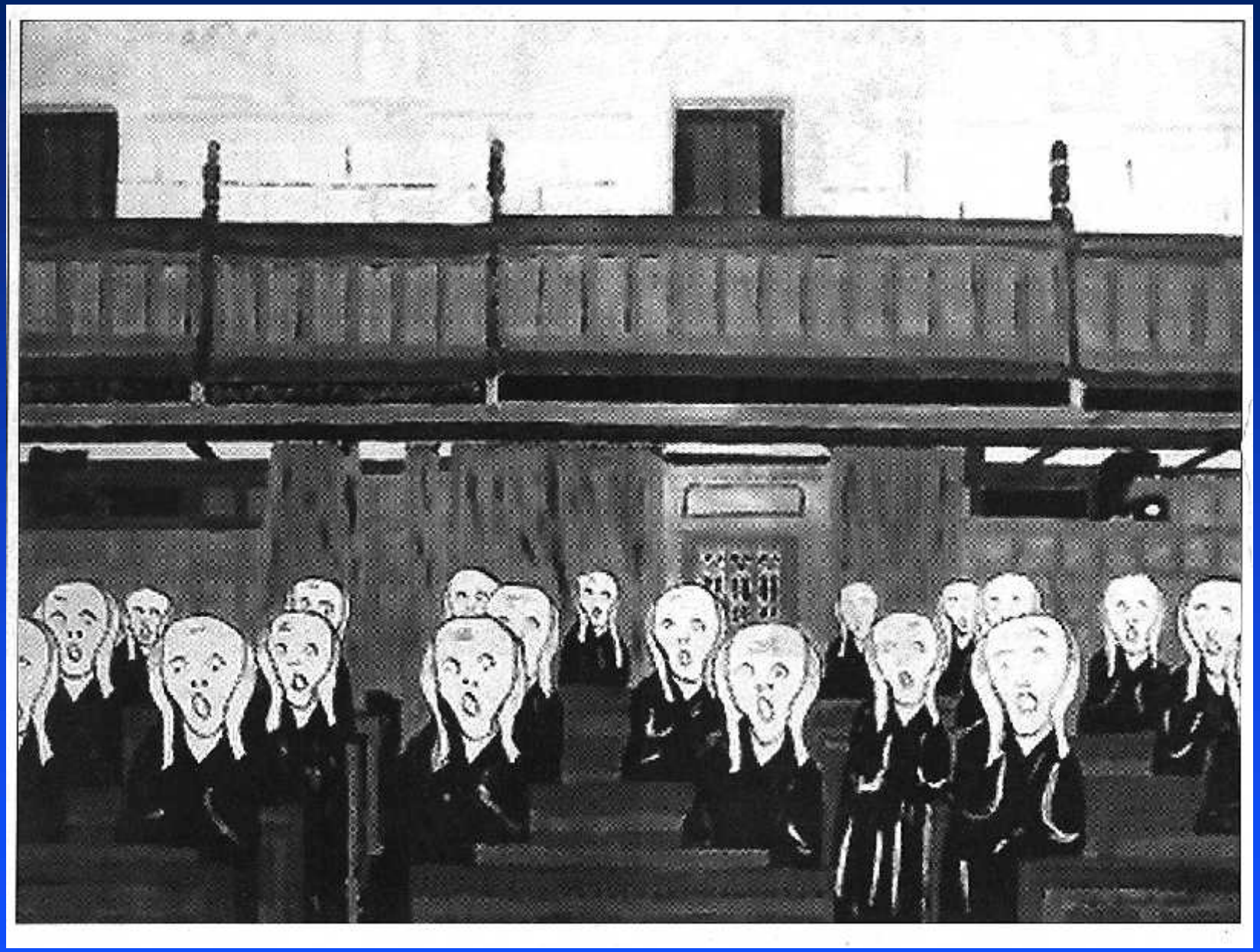
PAIN

www.elsevier.com/locate/pain

Editorial

Management of acute postoperative pain: Still a long way to go!

Breivik H, Stubhaug A
Pain 2008;137:233-234



Chronic postsurgical pain

Genetic predisposition

Surgical

- Severity of postopertaive pain
- Surgical factors
  - site and extent of surgery
  - damage to nerves
  - reoperations
  - bleeding, infection

Psychological

- Patient attiudes
- Preop anxiety
- Expectation of chronicity

Environmental

- Poor education
- Low income
- Poor self-rated health

Preoperative

- Female gender
- Younger age
- Pain before surgery
- Analgesic use

EDITORIAL VIEWS

Anesthesiology 2010; 112:509–10

ACTION on the Prevention of Chronic Pain after Surgery

Public–Private Partnerships, the Future of Analgesic Drug Development

Rappaport Bob A. et al
Anesthesiology 2010 112;509-10

Anesthesiology 2010; 112:511–3

Preclinical Research on Persistent Postsurgical Pain

What We Don't Know, but Should Start Studying

Scholz J. et al
Anesthesiology 2010 112;511-13

Anesthesiology 2010; 112:514–5

Persistent Postsurgical Pain

The Path Forward through Better Design of Clinical Studies

Kehlet H. et al
Anesthesiology 2010 112;514-15

Anesthesiology 2010; 112:516–8

Preventing Chronic Postsurgical Pain

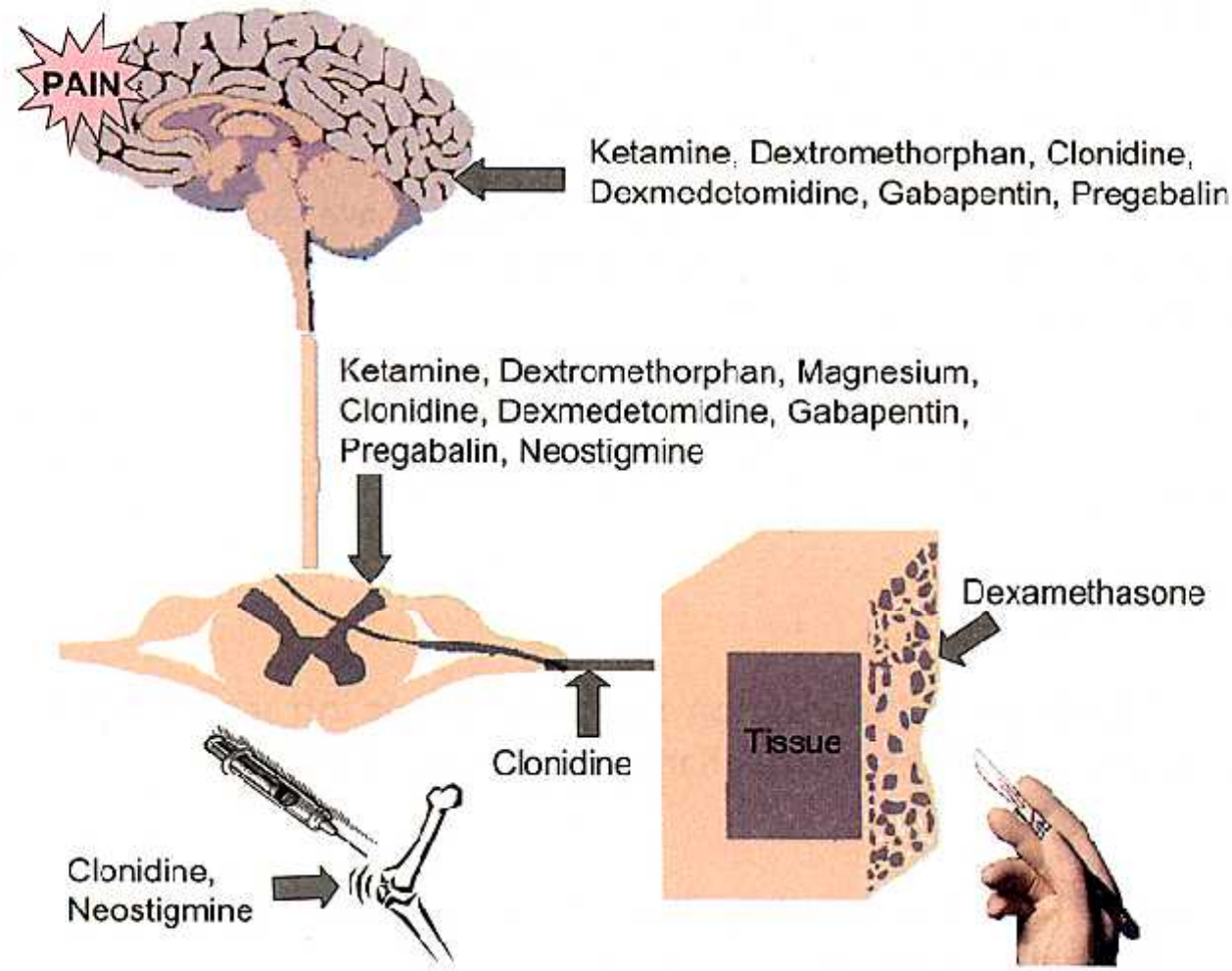
How Much of a Difference Makes a Difference?

Dworkin Robert H. et al
Anesthesiology 2010 112;516-18

Persistent postsurgical pain

Summary

- **Acute postoperative pain is followed by chronic pain in 10-50 % of patients**
- **Several risk factors have been identified**
- **Regional techniques may be beneficial in some procedures (thoracotomy, mastectomy, spine surgery)**
- **Preventive multimodal techniques using ketamine, gabapentin, coxibs seem to have potential**
- **Opioid sparing strategies are beneficial (opioids should be avoided)**
- **Need for further studies**



Anatomical sites where adjuvants can act to enhance opioid or local anesthetic activity to reduce postoperative pain.

Buvanendran A, Kroin J S
Best Practice and Reasearch Clin Anaesthesiology 2007;21:31-49

Anesthesiology 2005; 103:813-20

Intraoperative Epidural Analgesia Combined with Ketamine Provides Effective Preventive Analgesia in Patients Undergoing Major Digestive Surgery

Patricia Lavand'homme, M.D., Ph.D., Marc De Kock, M.D., Ph.D.,† Hilde Waterloos, R.N.‡*

- **RCT, colon surgery, n = 85, 72 hour study**
- **TEA + GA + ketamine i.v.**
- ***Before incision*: i.v. or epidural ketamine 0,25 mg/kg/h**
- ***Intraoperative*: i.v. lido + sufenta + clonidine *or* epidural bupi + sufenta + clonidine**
- ***Postoperative*: i.v. lido + morphine + clondine *or* epidural bupi + sufenta + clondine**
- **Pain scores, analgesia consumption, wound hyperalgesia, residual pain 2 w-12 months**
- **Higher hyperalgesia and residual pain upto 1 year (28 %) in i.v./i.v. group**
- **Postoperative epidural less effective in preventing residual pain at 1 year (11 %) than intraoperative epidural (0 %)**

"Combined with an antihyperalgesic dose of ketamine, intraoperative epidural analgesia provides effective preventive analgesia after major digestive surgery"

Anesthesiology 2007; 107:371–3

Glucocorticoids for Acute and Persistent Postoperative Neuropathic Pain

What Is the Evidence?

Romundstad L, Stubbhaug A

In summary, there is evidence that glucocorticoids alleviate acute and continued postoperative pain by suppressing inflammatory mediators, glial activation, reducing neural activity, sympathetic sprouting, and central neuroplastic changes such as central sensitization.

…there is evidence supporting the perioperative use of glucocorticoids for the relief of acute and sustained postoperative pain. What we now need is properly sized studies investigating long-term effects of perioperative glucocorticoids on human postoperative pain

Anesthesiology 2005; 103:681–5

Preventive Analgesia to Reduce Wound Hyperalgesia and Persistent Postsurgical Pain

Not an Easy Path

Brennan T J, Kehlet H

In summary… relation between the area of wound hyperalgesia, analgesic intervention and the intensity of acute and persistent postsurgical pain may not appear as an easy path for the anesthesiologist and surgeon.