

## 4th ERAS UK Conference

# *RECENT ADVANCES IN ANALGESIA*

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# Conflict of interests

- Paid honoraria lecturing and book chapters
- Editor of *Continuing Education in Anaesthesia, Critical Care & Pain*
- Assessor for MBBRACE-UK
- Committee member and website editor World ERAS® Society
- No shares in medical companies

# Analgesia

Good analgesia cornerstone of modern perioperative care. It may allow:

- Earlier mobilization
- Reduced organ dysfunction
- Reduced stress response
- Earlier nutrition
- Earlier discharge home

*Fawcett WJ. A Manual of Fast Track Recovery for Colorectal Surgery. 2012*

# Multimodal or balanced analgesia

Multimodal analgesia is achieved by combining different analgesics that act by different mechanisms, resulting in additive or synergistic analgesia with lowered adverse effects of sole administration of individual analgesics

Kehlet H, Dahl JB. *Anesth Analg* 1993 77: 1048-1056

# Multimodal or balanced analgesia

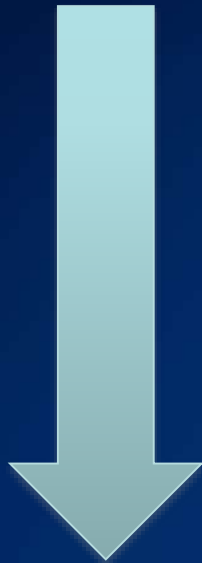
Reduce opioid consumption by using:

- Local anaesthetics
- Systemic analgesics

# Local anaesthetics

# Local anesthetics

*Central*

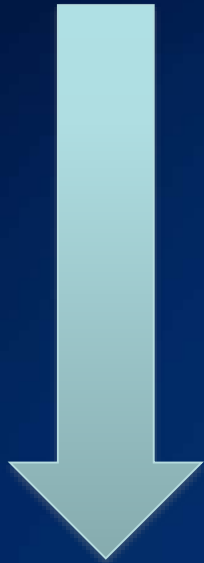


*Peripheral*

- Neuroaxial blockade (epidural and spinal)
- Paravertebral
- Nerve/plexus blocks
- TAP block
- Rectus sheath catheters
- Wound catheters/infiltration

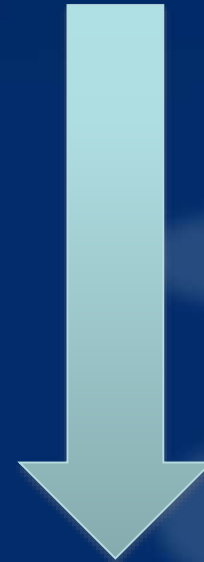
# Local anesthetics

*Central*



*Peripheral*

*Less popular*



*More popular*



# Why is central neuraxial block less popular?

## Epidurals

>

## Spinals

- Not necessary (for small incision surgery)
- Failure rate
- Fluid management and hypotension
- Mobility
- Risks
- Length of stay increased
- BUT good for open/prolonged surgery

- Work well
- Fluid management and hypotension
- Risks

# The non-working epidural

*British Journal of Anaesthesia* **109** (2): 144–54 (2012)

Advance Access publication 26 June 2012 · doi:10.1093/bja/aes214

## REVIEW ARTICLES



## Failed epidural: causes and management

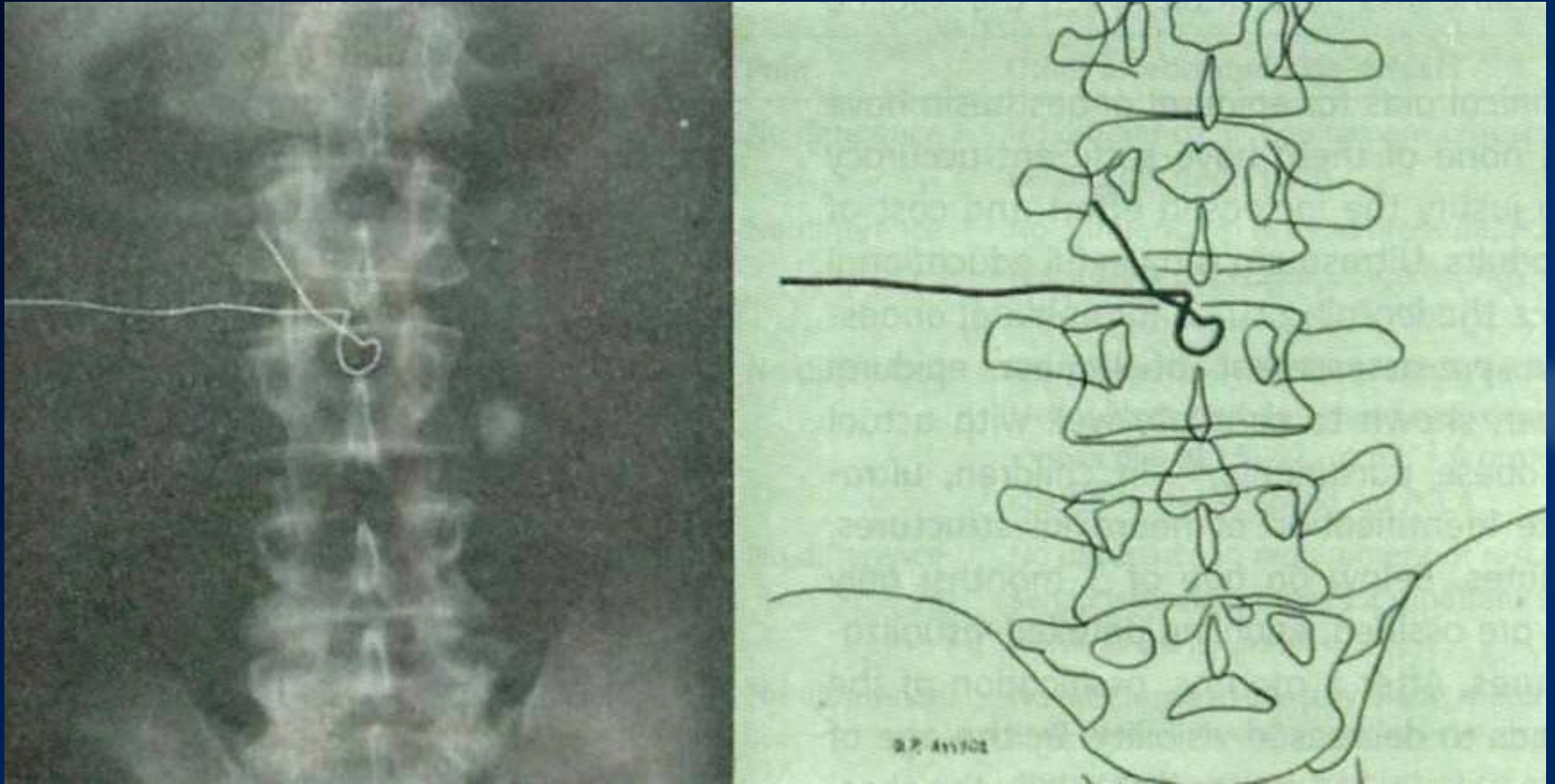
J. Hermanides, M. W. Hollmann\*, M. F. Stevens and P. Lirk

Department of Anaesthesiology, Academic Medical Center, University of Amsterdam, Meibergdreef 9,

# The non-working epidural

- Failure rate of epidurals up to 50% described
- Multifactorial
  - Technical
  - Pharmacological
- Active management
  - Adjuvants especially opioids
  - PCEA with background infusion

# Transforaminal epidural catheter



# Hypotension and fluids

- Hypotension and its effects on
  - Splanchnic and anastomotic perfusion
  - Other organs eg heart, brain, kidneys
- Treatment of hypotension
  - Fluids
  - Vasopressors
  - Pressure more important than flow

Gould TH. BJA 2002;89;446-51

# Laparoscopic colorectal surgery RCT

## epidural vs spinal vs PCA

Randomized clinical trial

*British Journal of Surgery* 2011; 98: 1068–1078

### Randomized clinical trial of epidural, spinal or patient-controlled analgesia for patients undergoing laparoscopic colorectal surgery

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# Fluids and weight gain

- More patients required further iv fluids after 24 hours in epidural group

	Spinal	Epidural	PCA	Kruskal-Wallis
% Patients	6.4%	22.6%	3.3%	p=0.028

- Weight gain (kg):

	Spinal	Epidural	PCA	Kruskal-Wallis
Median (IQR) maximum weight gain	1.8 (0.8-2.8)	2.73 (1.60-4.45)	1.6 (1.03-3.00)	p=0.029

# Mobilization – support for standing day one

	Spinal	Epidural	PCA
No help required	71%	20%	73%
One person required	29%	33%	27%
Two people required	0	44%	0
Not safe with two people	0	3%	0



# Risks of epidurals

## Neurological damage – NAP 3

- Permanent injury 1:24 000 to 1:54 000
- Death/paraplegia 1:50 000 to 1:140 000
- 2.5 x more likely epidurals cf spinals

<http://www.rcoa.ac.uk/nap3>

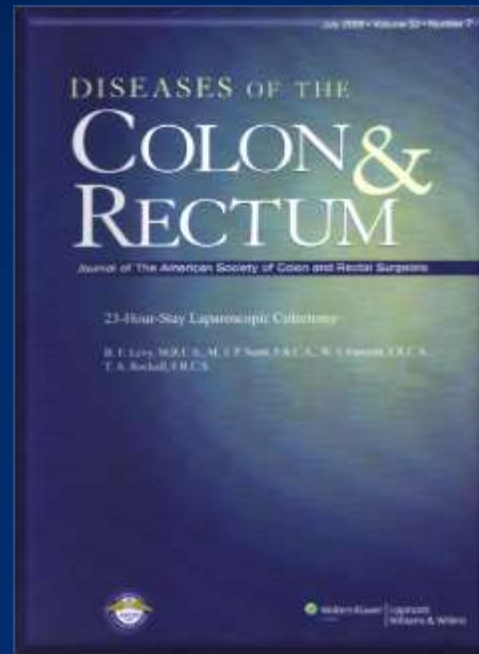
# Where to nurse epidural patients

Need location that has:

- Adequate patient throughput
- Main ward
- Regular observations
- Able to treat:
  - breakthrough pain
  - hypotension

# Spinals

- We used spinals successfully for first 23-hour stay laparoscopic colectomy paper.

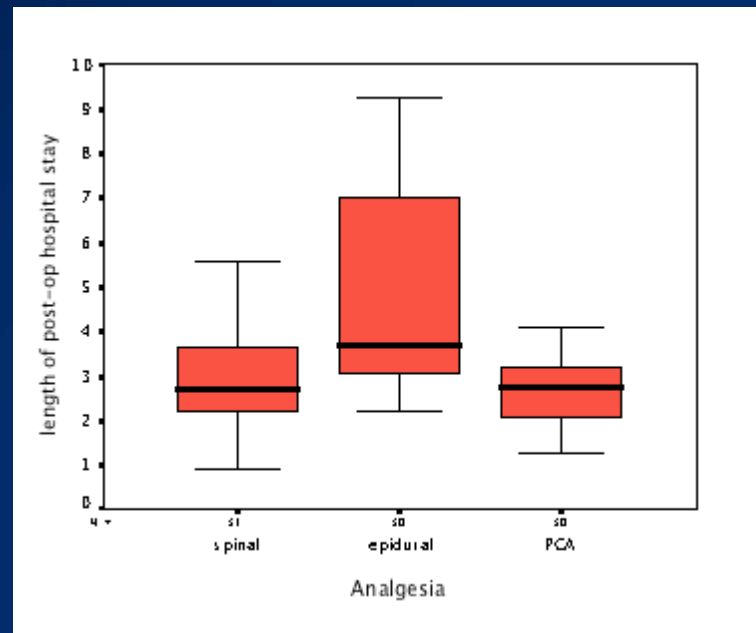


# Spinals

- Well tolerated
- Early pain scores similar to epidurals; both better than PCA
- Good opioid sparing effect
- Less postoperative fluids and weight gain than epidurals
- Quicker return of bowel function than both epidural and PCA
- Urinary catheter removed more quickly
- Improved mobilisation
- Reduced length of stay
- Not suitable for prolonged or open surgery

# Length of stay (days)

	Spinal	Epidural	PCA
Median	2.7	3.7*	2.75



# Rectus sheath blocks

- Limited good quality data
- Used especially for gynaecological and urological surgery
- Also herniae (children)
- Catheters can be inserted under direct vision, loss of resistance or by ultrasound
- LA via pump or bolus dosing

# Rectus sheath blocks

- Better than wound catheters (qv)
- Opioid sparing
- Avoids mobility/hypotension associated with epidural
- Training of staff
- RCT underway comparing Thoracic Epidural versus Rectus Sheath Catheters (TERSC)
- Early data suggests can be comparable to epidural

Crosbie EJ et al. *Eur J Obstet Gynecol Reprod Biol* 2012  
Wilkinson KA et al. *Trials* 2014;15:400

# TAP blocks

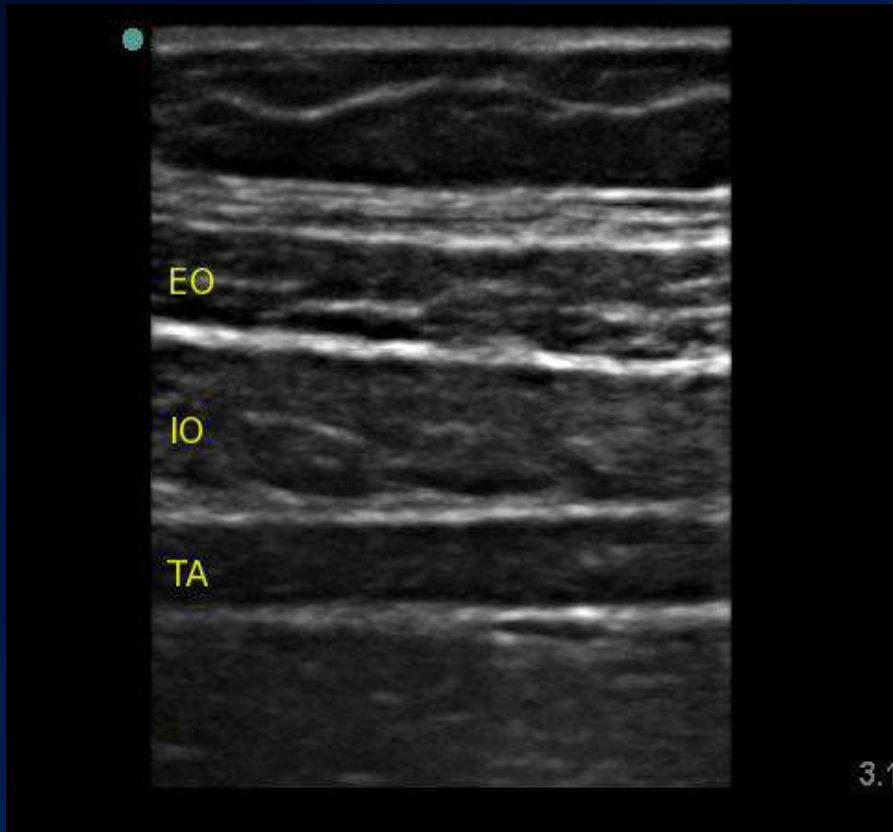
- Transversus abdominus plane block
- Many use ultrasound guidance
- Convincing opioid sparing effect for both open surgery (75%) and laparoscopic surgery (50%)
- Better evidence base than Rectus Sheath catheters
- Used in general surgical gynaecological, obstetrics and urology
- Subcostal TAP block now used for upper abdominal surgery

McDonnell JG et al. *Anesth Analg* 2007;104:193-197

El-Dawlatly AA et al. *BJA* 2009;102:763-7



# TAP blocks - ultrasound



Needle tip can be hard to visualise – infiltrate 2-4mls of saline to ensure correct placement

# TAP blocks

- TAP > iv paracetamol/oral analgesia > PCA
- Resumption of diet 12,12,36 hours respectively (P<0.001)
- Median LOS 2,3,5 days respectively (P<0.001)

Zafar N, *Colorectal Disease* 2010;12:119-124

- Meta analyses supports its use in both open surgery and laparoscopic colorectal surgery for systemic analgesia

Johns N et al. *Colorectal Disease* 2012;14: e635–e642

Zhao, X *Int J Clin Exp Med.* 2014; 7: 2966–2975

- However analgesic quality for TAP blocks generally inferior to central blocks for colorectal, LSCS and gastrectomy

# Surgical Site Catheter Analgesia

## Practical issues

- Catheter type
  - multiholed
- Catheter placement for abdominal surgery
  - preperitoneal > subcutaneous
- Bolus or Infusion. Flow rates
  - infusion > bolus.
  - high rates eg 10 mls/hr
- Duration
  - 48 hours
- For use at home ?

# Surgical Site Catheter Analgesia

- Varying results:
  - Opioid scores invariably reduced
  - Overall pain scores generally down
  - Some have shown reduced length of stay
  - Some have shown accelerated return of bowel function
  - Infection not increased

Karthikesalingham A et al. *World J Gastroenterol.* 2008 ;14: 5301-5305  
Beaussier M et al. *Anesthesiology* 2007; 07: 461-8

# Surgical Site Catheter Analgesia

- LSCS: better analgesia, less side effects, less need for nursing care, shorter duration of stay compared with epidural morphine

O'Neill P et al. *Anesth Analg* 2012;114:179-185

- Open colorectal surgery: Comparable pain scores (slightly worse on movement) but less for urinary retention.

Ventham NT *Br J Surg* 2013;100:1280-9.

- Orthopaedics: Also of benefit in following knee > hip surgery

Kuchalik J et al. *Br J Anaesth* 2013;111:793-9

Essving P et al. *Anesth Analg* 2011;113:926-33

# Peripheral 'novel' LA

- Local anaesthetic techniques demonstrated a significant reduction in opiate requirement at 48 hours. Local anaesthetic techniques were also associated with lower pain scores on movement at 24 and 48 hours, shorter length of stay, and earlier resumption of diet.

# Systemic analgesics

# Problems with systemic analgesics

- Opioids
- NSAIDs
- Paracetamol
- Local anaesthetics
- Steroids
- Clonidine
- Ketamine
- Magnesium



# Problems with systemic analgesics

- Opioids: *sedation, dysphoria, constipation, PONV*
- NSAIDs: *renal, bleeding, perforation, healing, CVS risk*
- Paracetamol: *hepatotoxicity*
- Local anaesthetics: *cardiac and CNS toxicity*
- Steroids: *hyperglycaemia, poor wound healing*
- Clonidine: *sedation, hypotension*
- Ketamine: *dysphoria*
- Magnesium: *hypotension, weakness*

## Healing and anti-inflammatory drugs

- Delayed bone union in some orthopedic models (< smoking!)
- Increased risk of anastomotic leakage with diclofenac treatment after laparoscopic colorectal surgery
- Cyclo-oxygenase 2 inhibitors and the risk of anastomotic leakage after fast track colonic surgery

Klein M et al. Digestive Surgery 2009;26:27-30  
Holte K et al. BJS 2009;96:650-4

- Unresolved after five years – hopefully answered soon?

Subendran J et al. J Gastrointest Surg 2014;18:1391-7  
Saleh F et al. J Gastrointest Surg 2014;18: 1398-404  
Nepogodiev D et al. BMJ Open 2014;4: e005164

# Lidocaine infusions

- Reduction in analgesic requirements, ileus and PONV
- Opioid consumption reduced by 2/3
- Reduced hospital stay

BUT

- May be less relevant in small incision vs classical open surgery

Marrett E et al BJS 2008;95:1331-1338

- Anti-cancer effect

Lirk P. Br. J. Anaesth 2012;109:200-207

# Lidocaine infusions

- Similar impact on bowel function to thoracic epidural

Wongyingsinn, M et al *Regional anesthesia and pain medicine* 2011;36:241-248

- Intraoperative infusion (only) also decreased opioid consumption and hospital LOS after gastrectomy

Kang KG et al. *Journal of Clinical Anesthesia* 2012;24:465-470

- Established and recommended as second line therapy

Joshi GP et al. *Colorectal Disease* 2013;15:146-155

# Ketamine

- Enjoying a resurgence 50 years after it was first synthesized
- *N*-methyl-D-aspartate (NMDA) glutamate receptor antagonist
- Synergistic/additive effect to morphine
- May prevent opioid-induced hyperalgesia (OIH) and chronic pain syndromes
- Dose and duration debated

# Ketamine

When used intraoperatively and via infusion for 48 hours post op (2 mcg/kg/min after a 0.5 mg/kg bolus):

- Morphine consumption halved
- Side effects: sedation, delusions, nightmares, psychiatric disorders not manifest at these doses

Zakine J et al. *Anesth Analg* 2008;106:1856–61

# Ketamine – 2 good reviews

Ketamine both reduces opioid consumption and improves analgesic quality:

- Less PONV, sedation but more nightmares/hallucinations
- Good for thoracic, upper GI and major orthopaedics
- Administered at different times
  - preemptively, intraoperatively, postoperatively
- and by different methods
  - bolus, infusion, PCA

Laskowski K et al. *Can J Anaesth* 2011;58:911-23

Adding ketamine to morphine PCA

- mixed drugs were superior to PCA opioid alone in thoracic surgery with significant reduction in
  - pain score
  - total morphine consumption
  - postoperative desaturation.
- ? benefit of adding ketamine for orthopaedic or abdominal surgery

Carstensen M et al *BJA* 2010;104:401-406

# Gabapentinoids

## Pregabalin and gabapentin:

- Reduce postoperative pain
- Good opioid sparing effect
- Reduced opioid side effects
- Dose, duration unknown
- BUT: Pregabalin produces visual disturbances

Tiippana EM et al. *A & A* 2007;6:1545-1556

Zhang J et al *BJA* 2011;106:454-462

- Not used for colorectal surgery but used successfully for laparoscopic cholecystectomy

Agarwal A et al *BJA* 2008;101: 700-704

- Recent review suggests they prevent chronic post surgical pain.

Clarke H et al. *Anesth Analg* 2012;115:428-42





## *Procedure Specific Postoperative Pain Management*

- Colonic Resection
- Radical Prostatectomy
- Breast (non cosmetic)
- Haemorrhoids
- Abdominal Hysterectomy
- Total Hip Arthroplasty
- Total Knee Arthroplasty
- Thoracotomy
- Hernia
- Laparoscopic Cholecystectomy

<http://www.postoppain.org/>

# The Future

# Analgesic effect on cancer outcome

- Regional anesthesia potentially improves outcome for some specialties (breast and prostate)
- ER patients may be fitter for adjuvant treatment more quickly (eg chemotherapy)
- Sympathetic block may improve cellular immunity
- Drug effects
  - Morphine and effects on NK cells
  - lignocaine demethylates DNA cancer cells

# Analgesic effect on cancer outcome

*British Journal of Anaesthesia* **105** (2): 106–115 (2010)  
doi:10.1093/bja/aeq164

BJA

## REVIEW ARTICLES



### Effect of anaesthetic technique and other perioperative factors on cancer recurrence

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<sup>1</sup> Department of Anesthesia and Perioperative Medicine and <sup>2</sup> Department of Oncology and Hematology, University of California San Francisco, 505 Parnassus Ave., San Francisco, CA 94143, USA

*British Journal of Anaesthesia* **109** (2): 140–3 (2012)  
doi:10.1093/bja/aes255

## EDITORIAL III

### Cancer biology, analgesics, and anaesthetics: is there a link?

L. A. Colvin<sup>1\*</sup>, M. T. Fallon<sup>2</sup> and D. J. Buggy<sup>3,4</sup>

<sup>1</sup> Department of Anaesthesia, Critical Care and Pain Medicine, Western General Hospital, Crewe Road, Edinburgh EH4 2XU, UK

<sup>2</sup> Edinburgh Cancer Research Centre, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh, UK

<sup>3</sup> Department of Anaesthesia, The Mater Misericordiae Hospital, Dublin 7, Ireland

<sup>4</sup> Outcomes Research Consortium, Cleveland Clinic, OH, USA

# Analgesic effect on cancer outcome

- Not so far in Colorectal in retrospective analysis

*British Journal of Anaesthesia* 109 (2): 185–90 (2012)  
Advance Access publication 23 April 2012 · doi:10.1093/bja/aes106

BJA

**CLINICAL PRACTICE**

**Retrospective analysis of the effect of postoperative analgesia on survival in patients after laparoscopic resection of colorectal cancer**

A. Day<sup>1\*</sup>, R. Smith<sup>1</sup>, I. Jourdan<sup>1</sup>, W. Fawcett<sup>2</sup>, M. Scott<sup>2</sup> and T. Rockall<sup>1</sup>

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<sup>2</sup> Department of Anaesthesia, The Royal Surrey County Hospital, Egerton Road, Guildford GU2 7XX, UK

- Nor gynaecological (ovarian or cervical)

# Analgesic effect on cancer outcome

- 503 patients longterm follow up from prospective RCT in which patients were randomly assigned to receive general anaesthesia with or without epidural block for at least 3 postoperative days.
- “Use of epidural block in abdominal surgery for cancer is not associated with improved cancer-free survival”

Myles PS et al. *BMJ* 2011;342:d1491

# Perhaps...

- Can anaesthetic technique improve long term survival?

*British Journal of Anaesthesia* **109** (5): 671–4 (2012)  
doi:10.1093/bja/oes358

## EDITORIAL I

### Enhanced recovery: more than just reducing length of stay?

W. J. Fawcett<sup>1\*</sup>, M. G. Mythen<sup>2</sup> and M. J. P. Scott<sup>1</sup>

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<sup>2</sup> Surgical Outcomes Research Centre (SOuRCe), UCL/UCLH, National Institute of Health Research Biomedical Research Centre, UCH, Euston Road, London NW1 2BU, UK

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# Summary

- Analgesia is key component of ERAS pathways
- Constantly challenge dogma
- Mainstay is multimodal analgesia
  - Regular oral analgesia (paracetamol/NSAIDs)
  - Opioid sparing
  - LA (peripheral) where feasible
- As surgery changes so does analgesia
  - Open ≠ Laparoscopic
  - Epidurals have a declining place
- Active management of problems
  - PONV
  - Weakness
  - Hypotension



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Mr Bruce Levy  
Mr Andrew Day

