Buprenorphine use in the perioperative period-From “here to there”-Where to now?-Back “here”?....stay “there”? or go “somewhere else”?

Coran Lang
Pain Specialist and Anaesthetist
Western Health

“In the face of Fentanyl shortage: the use of Buprenorphine”

Coran Lang
Pain Specialist and Anaesthetist
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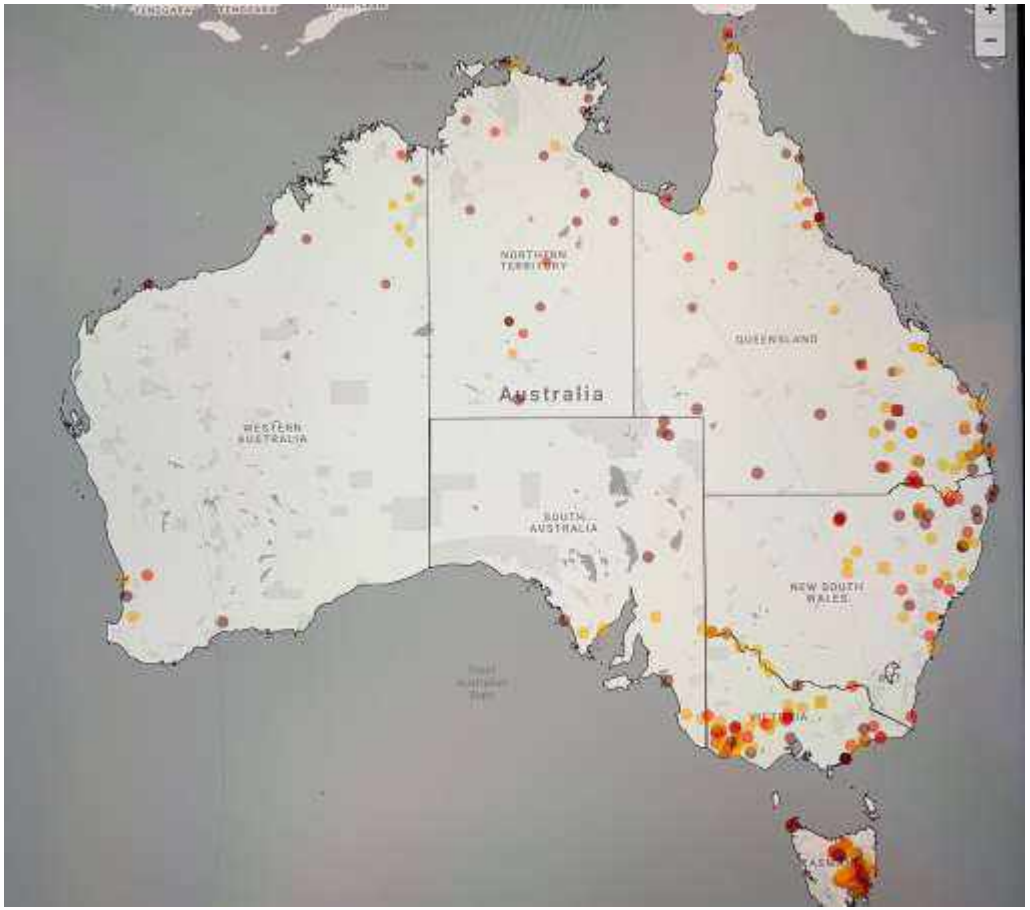
“Traditional Owners” rather than actual Owners



Conflicts of Interest

Nil

BEYOND ATTENDING OVER GENEROUSLY SPONSORED SCIENTIFIC MEETINGS.

Dunning-Kruger effect

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Key points

- **Intravenous buprenorphine is a useful "3rd" opioid for use in acute pain especially if Fentanyl shortages become commonplace**
- **Buprenorphine may have a significant role in the OIH associated with Remifentanil infusions.**
- **Opioid tolerance in patients and management of acute pain is still a major pain management problem.**
- **?A more nuanced approach to providing perioperative analgesia-especially the hyperalgesic patient.**

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Buprenorphine-An Introduction

- Potent Mu opioid receptor (MOR) agonist-in clinically relevant doses behaves as full agonist
- Anti-hyperalgesic
- Kappa opioid receptor antagonist
- Less DOR agonist effect/? DOR antagonist
- Reduced tendency towards tolerance.
- Reduced OIBD
- Patients often already on it with ORT
- Ceiling dose for Sedation/OIVI
- PROBABLY NOT ceiling dose analgesia.
- Safe in Renal/Liver failure
- Cheaper than morphine

Buprenorphine…a bit more

- **Semi synthetic THEBAINE derived Mu OPIOID AGONIST**
- **Developed in the 1970-80's.**
- **Initially used in Australia as ORT ("Suboxone" or "Subutex")- T1/2, S/L bioavailability, and Safety profile.**
- **More recently available for "Chronic Pain" as a Transdermal prep. ("Norspan")**
- **Good sublingual bioavailability (0.3-0.5)**
- **Poor oral bioavailability due to first pass enterohepatic metabolism**

OIVI ceiling/cap

(Dahan et al BJA 2005)

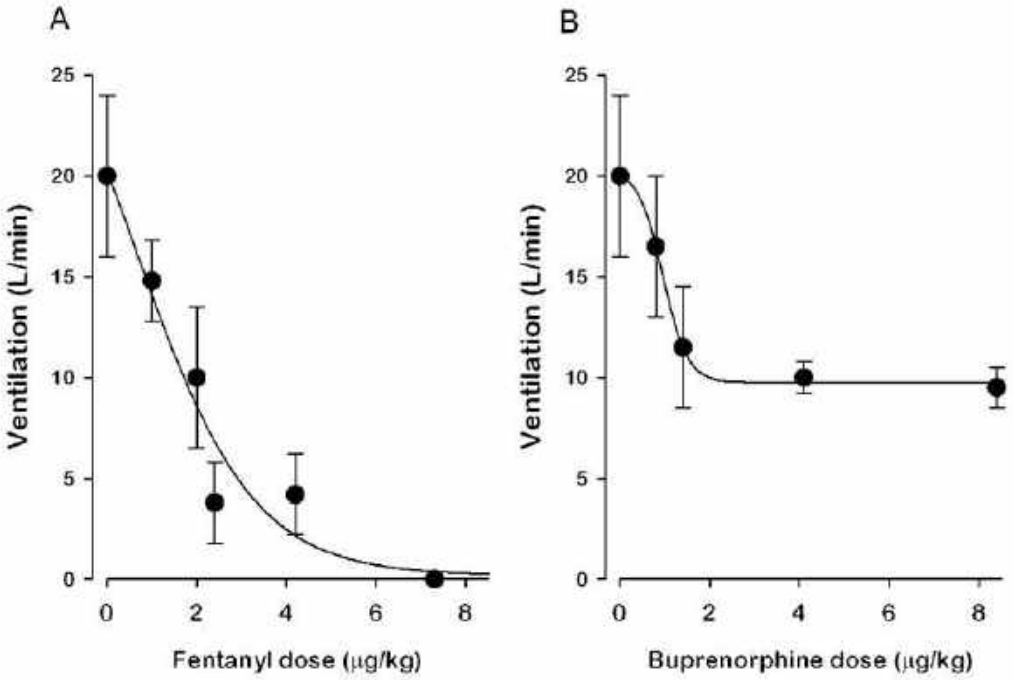
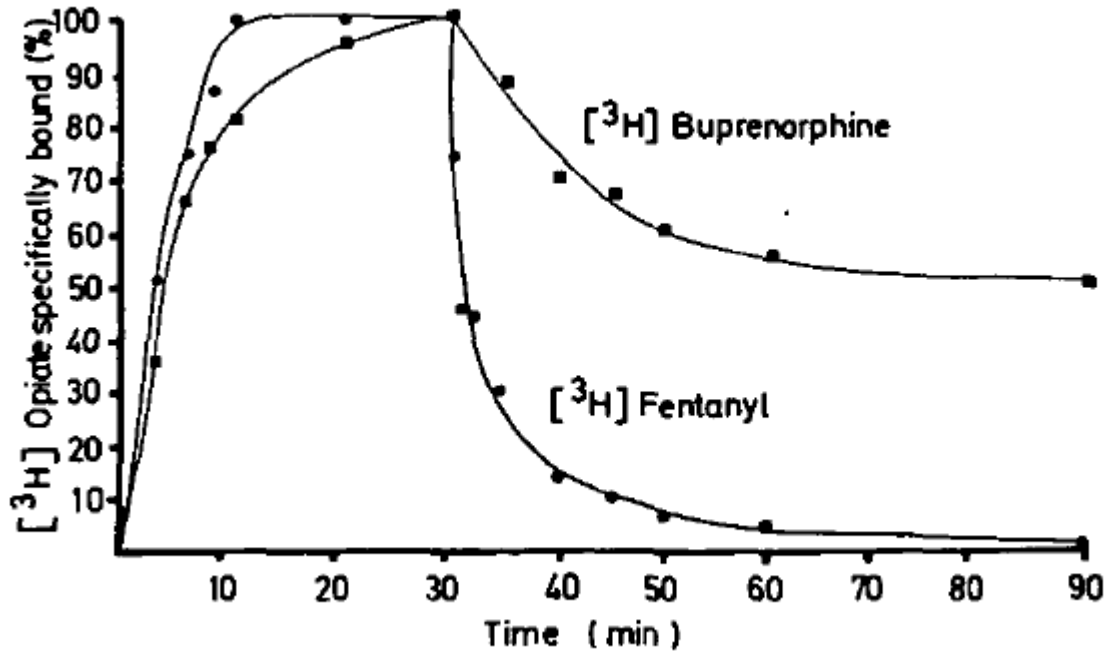


Figure 4. Dose–response relationships for (A) fentanyl and (B) buprenorphine (Dahan).[34]

(BBB) “Crosses like oil, binds (slowly to Mu receptors) like syrup, but sticks like concrete"



“HERE”
(At Western Health)

Sublingual buprenorphine available only as “Individual patient usage” (IPU) til 2014 for long term nociception/opioid tolerance in NBM patients

“THERE” (At Western Health)

- **Eric Visers’s statement at 2008 FPM Spring meeting!**
- **2014 DTC application to use S/L (and IV) in patients on pre-existing Buprenorphine with proviso of auditing first 12 months**
- **From 2015 onwards expanded to use in selective opioid naïve patients as well.**
- **Then increasing use in perioperative rotations from select patients on >100 MEQ of either oxycodone variants or fentanyl patches**.

Where to now?
Buprenorphine-No?

Case Report

Buprenorphine-related complications in elderly hospitalised patients: a case series

S. Richards*, L. Torre†, B. Lawther‡

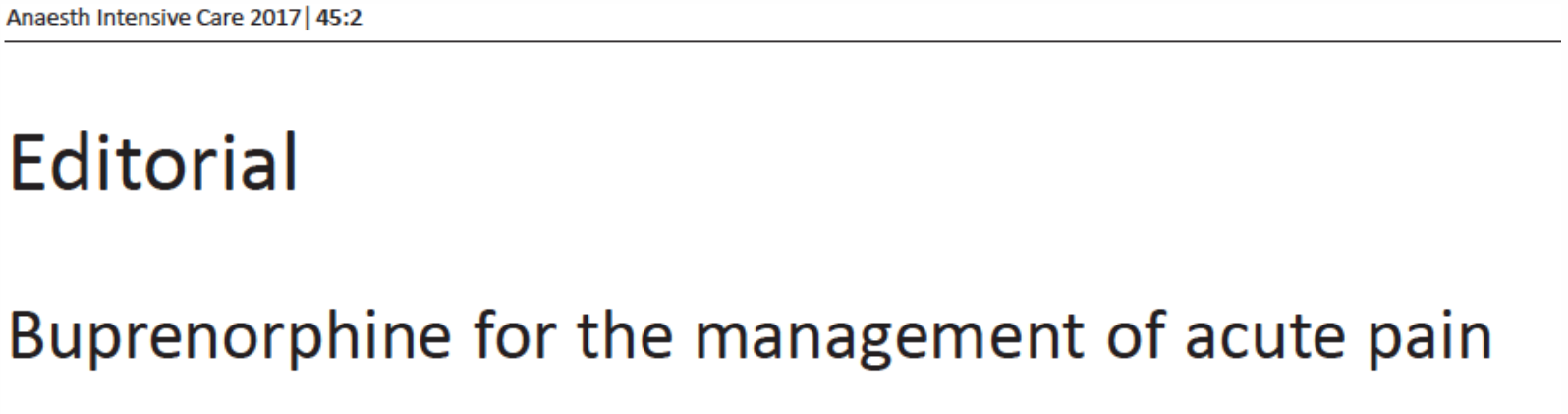
Richards et al AIC 2017

Western Health

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	85 yrs	92 yrs	78 yrs	82 yrs	91 yrs	68 yrs
Sex	Female	Female	Female	Male	Male	Female
Primary condition §	EVAR	Fall, clinical rib fractures	TKR	Arthroplasty of MCP and IP	CCF	Elbow arthroplasty + ORIF
Presentation ¶	Elective	Emergency	Elective	Elective	Emergency	Elective
Buprenorphine #	200 µg sl	400 µg sl	1 mg sl, 300 µg sc, 5 µg/hr td	1.4 mg sl	400 µg sl	3 mg sl
Renal function ³	65	66	52	82	31	80
Time interval *	6 hrs	2 hrs	6 hrs	2.5 hrs	4.5 hrs	4 hrs
Concomitant medication ø	-	Codeine	Oxycodone Clonidine	Midazolam	Gabapentin Oxycodone	Oxycodone Pregabalin
Neurological depression ¥	Yes	Yes	Yes	Yes	Yes	Yes
Respiratory depression $	Yes	Yes	Yes	Yes	Yes	Yes
Naloxone administration Æ	1.2 mg IV bolus	1 mg IV bolus 600 µg/hr infusion x 20 hrs	-	400 µg IV bolus	400 µg IV bolus 200 µg/hr infusion x 9 hrs	2.2 mg IV bolus Infusion 40 µg/hr X 7 hrs
Time to resolution of symptoms ¤	16 hrs	§	14 hrs	2 hrs	12 hrs	11 hours

Where to now? Buprenorphine-No?

Anaesth Intensive Care 2017 **45:2**



Anaesth Intensive Care 2017 | 45:2

Editorial

Buprenorphine for the management of acute pain

Opioids and Local anaesthesia

- **The back bone of acute pain management in the perioperative period……**
- **A more nuanced approach?**

Where to Now?

- **Coincidentally a Fentanyl “shortage”….**
- **Three cases observed whereby high dose remifentanil infusions used intraoperatively from 4-8 hours duration**
- **Rescue IV buprenorphine at end of case at 2-3 micrograms kg-1**
- **Little ongoing need for breakthrough analgesia**

Hyperalgesia

- **Nociceptive stimulus “more painful”**
- **Thermal/pinprick/mechanical/pressure**
- **Peripheral mechanisms (at the nociceptor)**
- **Central mechanisms (at DRG/Spinal cord) “Central Sensitisation**
- **?”Tertiary” mechanisms……**
- **Opioid induced Hyperalgesia**

Buprenorphine as an anti hyperalgesic…2005

Pain 118 (2005) 15–22

PAIN

www.elsevier.com/locate/pain

Research papers

Different profiles of buprenorphine-induced analgesia and antihyperalgesia in a human pain model

Wolfgang Koppert[a,*], Harald Ihmsen[a], Nicole Körber[a], Andreas Wehrfritz[a], Reinhard Sittl[a], Martin Schmelz[b], Jürgen Schüttler[a]

[a]*Department of Anaesthesiology, University Hospital Erlangen, Krankenhausstrasse 12, D-91054 Erlangen, Germany*
[b]*Department of Anaesthesiology Mannheim, University of Heidelberg, Theodor-Kutzer Ufer 1-3, D-61087 Mannheim, Germany*

Received 7 February 2005; received in revised form 17 May 2005; accepted 20 June 2005

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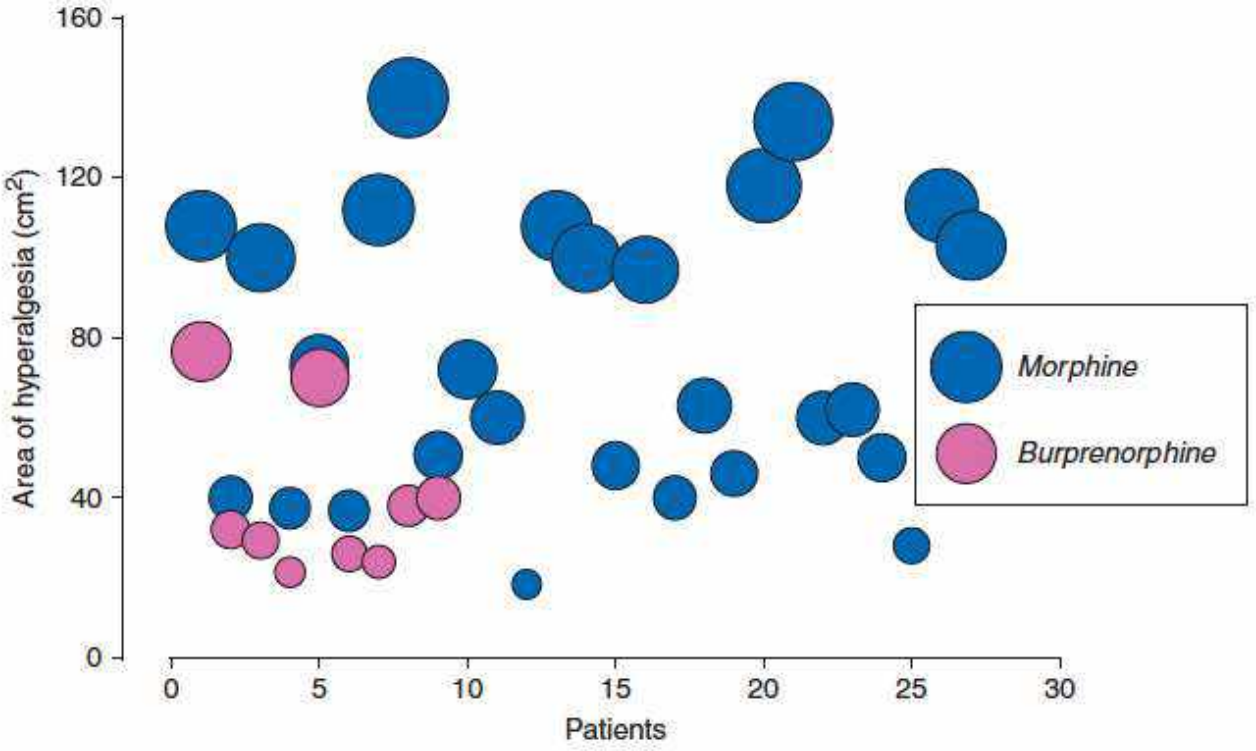
Buprenorphine-as an anti hyperalgisic? BJA 2017

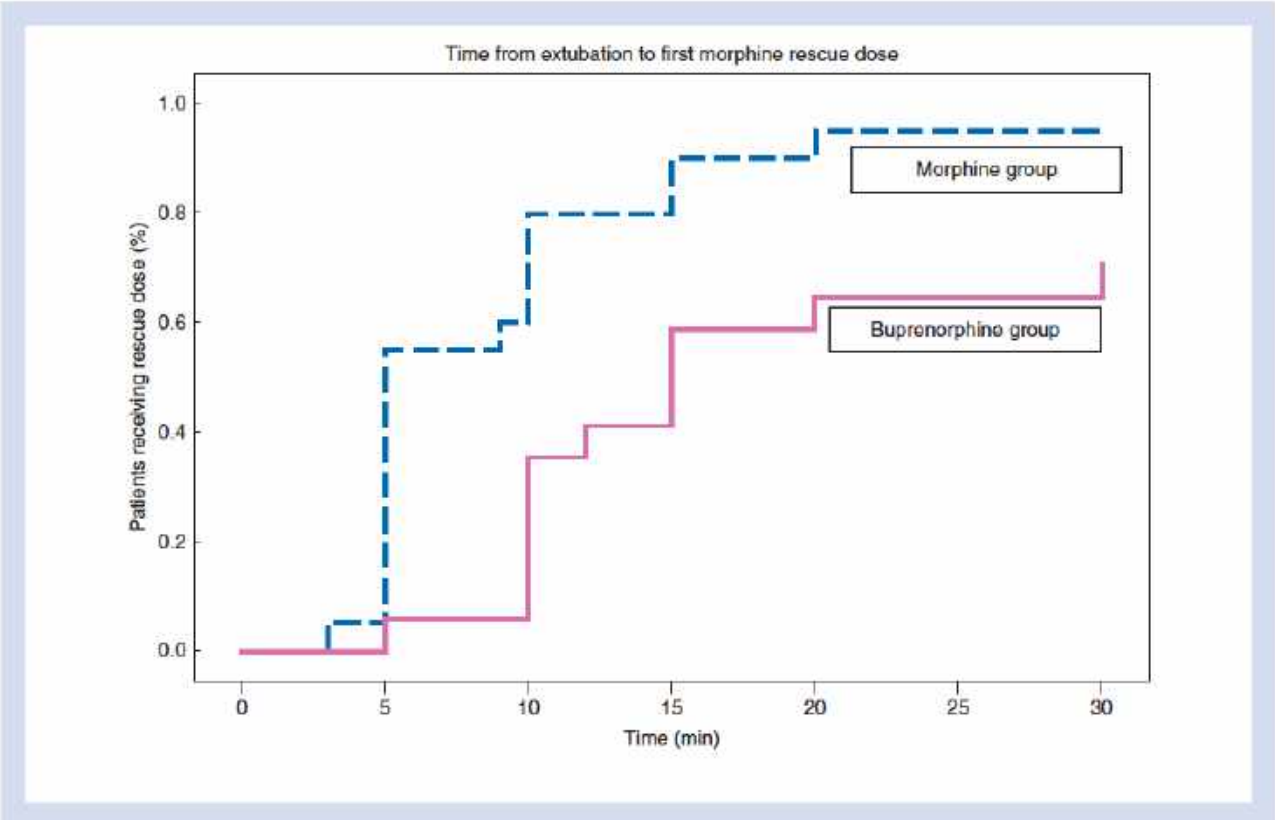
Low-dose buprenorphine infusion to prevent postoperative hyperalgesia in patients undergoing major lung surgery and remifentanil infusion: a double-blind, randomized, active-controlled trial

Marco Mercieri[1,*,†], Stefano Palmisani[1,2,†], Roberto A. De Blasi[1], Antonio D'Andrilli[1], Alessia Naccarato[1], Barbara Silvestri[1], Sara Tigano[1], Domenico Massullo[1], Monica Rocco[1] and Roberto Arcioni[1]

Mercieri BJA 2017



Mercieri BJA 2017



Why the “Epidemic” of CPSP?

- More opioid tolerance?
- More awareness of CPSP?
- Higher patient expectations?
- More nerve “damaging” procedures.
- What role “Hyperalgesia” (concept of hyperacute central sensitisation in postop period).

“Somewhere Else”-Rational use of IV Perioperative Buprenorphine

- **Buprenorphine ORT (“Suboxone”) tolerant patients with acute pain.**
- **Topical buprenorphine Chronic pain patients with acute pain**
- **Systemically Hyperalgesic patients (such as Fibromyalgia)?**
- **Post Remifentanil infusion rescue analgesia**
- **Chemical copers/?others.**
- **Perioperative rotation to Transdermal Buprenorphine for the patient on “high risk opioids/opioid doses”**

But is it.....?
Anthanasos et al

Pain Medicine 2019; 20: 119–128
doi: 10.1093/pm/pny025

Original Research Article

Buprenorphine Maintenance Subjects Are Hyperalgesic and Have No Antinociceptive Response to a Very High Morphine Dose

Western Health

Thank you.
Questions?