KONTINUIRANA LOKALNA ANALGEZIJA U PREVENCIJI PERZISTENTNOG I HRONICNOG POSTOPERATIVNOG BOLA

Prof dr Ljubica Pejakov
Specijalista anesteziolog
Subspecijalista klinicki farmakolog
Medicinski fakultet u Podgorici

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OD POSTOPERATIVNOG DO HRONICNOG BOLA

- Perzistentni bol: ne prestaje, ili traje duze od postoperativnog oporavka (3-6 mes)*
- Incidenca: 10-50% pacijenata
- Hronicni postoperativni bol, CNS plasticitet kao odgovor na ostecenje tkiva
- Eticki, socioekonomski problemi, perioperativni morbiditet…

- **Kehlet H et al. Lancet 2006*

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Chronic Pain after surgery – How serious is the problem ?

Patrick Narchi, MD

Centre Clinical
Anesthesia Department
16800 Soyaux
France

Introduction

Persistent pain after surgical healing is a major and often overlooked problem. Pain that is unlikely to resolve or pain that lasts longer than the usual healing time after surgery have been suggested, as well as various time scales, usually 6 or 3 months. Changes in the nervous system may well lie behind many of these syndromes. Neural plasticity can result in amplification of sensory input, which may result in somatic or visceral hyperalgesia. This could well have a bearing on chronic postsurgical pain. Peripheral neural mechanisms such as nociceptor sensitization and neuroma formation have previously been regarded as the most likely explanations for such chronic pain phenomena. In recent years, evidence has been accumulating, indicating that changes in central neural functions may also play a significant role in persisting pain (1). There is also evidence from animal work that some strains of rat and mice are more likely to develop neurogenic pain after nerve injury than others. It may be that certain people are at particularly high risk of developing pain after surgery. There is evidence that postoperative pain is influenced by psychological and familial factors.

UTICAJ NA POSTOPERATIVNI BOL

- **Preoperativno:**

  - srednji do jak intenzitet bola duze od 1 mesec preoperativno na istoj lokalizaciji, anksioznost, hiperalgezicni odgovor na bol, ocekivanja pacijenta…

- **Intraoperativno:**

  - ostecenje nerva, amputacija ekstremiteta, torakotomija, mastektomija, sternotomija, ortopedske operacije

- **Postoperativno**:

  -intenzivan postoperativni bol, kvalitet i trajanje analgezije, anksioznost

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HRONICNI POSTHIRURSKI BOL-UZROCI

- Promene u **centralnom nervnom sistemu**: plasticitet-amplifikovanje senzornog inputa= somatska/visceralna hiperalgezija*
- **Periferni neuralni mehanizmi:** senzitizacija nociceptora, formiranje neuroma
- Psihosocijalne okolnosti, komorbiditeti (druga hronicna bolna stanja), genetski faktori

* *Reuben SS. Curr Pain Headache Rep 2007; 11:5-13*

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HRONICNI POSTOPERATIVNI BOL-GENETSKI FAKTORI

- **Genetske razlike**: inter-individualna varijabilnost (polna, odgovor na analgetike)
- **Genetski polimorfizmi**: identifikacijom SNP ili haplotipova i uticaja na medikamente u akutnom i hronicnom bolu -strategije za personalizciju i popravljanje perioperativnih ishoda prema genetskom profilu ("One size does not fit all")
  Cilj: naci rizicne pacijente za razvoj hronicnog postoperativnog bola kao preventivni i terapijski model

Landau R. Int Anesthesiol Clin 2007

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EPIDEMIOLOGIJA PERZISTENTNOG/HRONICNOG BOLA

- Operacija ingvinalne hernije: otvorena 14%, laparoskopska 2-10%
- Torakotomija 22-14% (nakon 2 i 12 meseci)
- Hirurgija dojke: mastektomija sa rekonstrukcijom 49%, operacija redukcije 22%
- Ortopedija: hronicni regionalni bolni sindrom (CRPS) 2-40%, postamputacioni fantomski bol 3-80%, bol u patrljku 63%
- Holecistektomija: 35-40%

Neumayer L et al. N. Engl J Med 2004

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PERIOPERATIVNI TOK-ISHOD

- Savremeni model perioperativnog toka : brzi oporavak /ishod
- **Intenzivan put oporavka**
  - ERP (enhanced recovery pathways) *
- **Intenziviran oporavak nakon hirurgije**
  - ERAS (enhanced recovery after surgery)

**Ljungqvist O et al, JAMA 2017*

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BOL KAO "PETI VITALNI ZNAK"

- Nepovoljan uticaj bola na perioperativni tok- program za monitoring i kontrolu bola: **BOL KAO "PETI VITALNI ZNAK"**
- Dramaticno **povecanje** primene opioida i s njima povezanih nezeljenih dejstava*

Levy N et al. BJA, 2018

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NEZELJENA DEJSTVA OPIOIDA

- Mucnina I povracanje
- Ileus
- Retencija urina
- Respiratorna depresija
- Ograniceno kretanje
- Sedacija
- Konfuzija
- Opstipacija
- Tolerancija
- Adikcija

PRODUZENA HOSPITALIZACIJA

⇨

POVECANJE TROSKOVA

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"EPIDEMIJA OPIOIDA"

- Prekomeno propisivanje opioida u postoperativnom periodu vezano za skoro sve hirurske grane- "Kriza opioidne epidemije"*
- Nedovoljno poznavanje ne-opioidnih alternativa za postoperativnu analgeziju**
- Multimodalna, minimalno opioidna analgezija kljucni element u modelu ERAS poboljsanja fiziologije oporavka nakon bolnih operacija

**Chen EY et al, JAMA 2018*
***Tan W.et al Jam Coll Surg, 2018*

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NE-OPIOIDNI REZIM MULTIMODALNE ANALGEZIJE

- Perioperativne epiduralne tehnike
- Perineuralne kateter tehnike
- **INCIZIONE KATETER TEHNIKE LOKALNIM ANESTETICIMA**
- Regionalne blokade
- Paracetamol
- NSAIL

.

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OPTIMALNA EFIKASNOST TEHNIKE ANALGEZIJE:

- - Bez nezeljenih dejstava
  - Jeftina
  - Visoka komplijansa pacijenta
  - Dobar ishod

- Rezim multimodalne analgezije kljucan za smanjenje potrosnje opioida u postoperativnom periodu

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KONTROLA POSTOPERATIVNOG BOLA

- Razlicite hirurske procedure = razlicite vrste, intenziteti i lokacija bola*
- Koncept "postoperativna terapija bola specificna za proceduru" PROSPECT**

  (www.postoppain.org)

**Apfelbaum et al. Anesth Analg 2003*

***Neugebauer EAW et al. Surg Endosc 2007*

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INCIZIONE KATETER TEHNIKE LOKALNIM ANESTETICIMA

- Incizione tehnike lokalnim anesteticima vazan deo multimodalne analgezije u programu ERAS (enhanced recovery after surgery)

- Nova tehnika?
  - Capelle 1936. god
  - Blades and Ford 50`
  - Thomas 80`

  Novi lokalni analgetici, oprema- nacin isporucivanja

Capelli W. Dtsch Z Chirurgie, 1936
Blades B, Ford WB. Surg Gynecol Obstet ,1950
Thomas DFM et al. Ann R Coll Surg Engl, 1983

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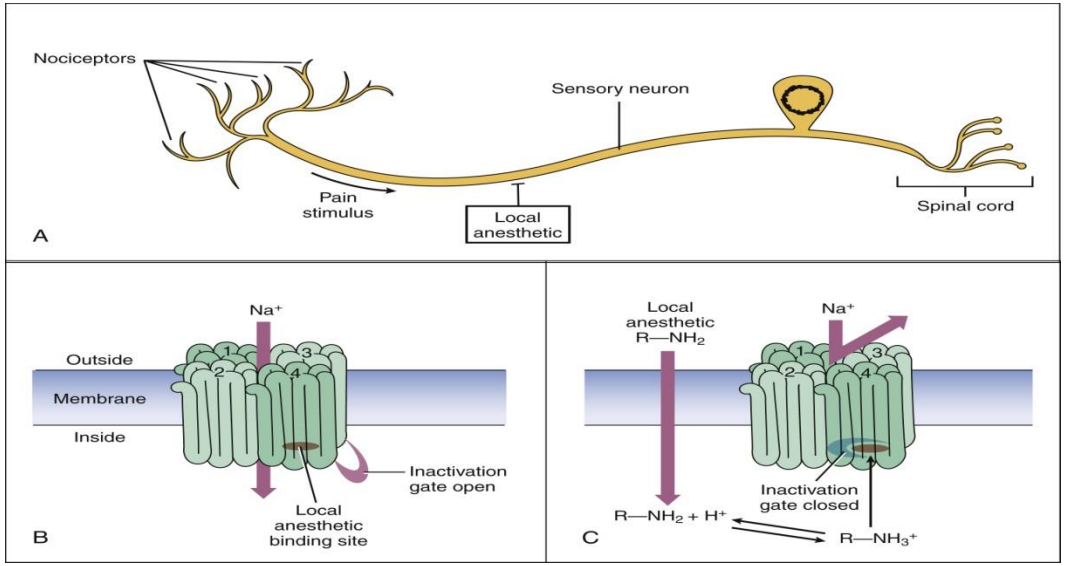
INCIZIONE KATETER TEHNIKE LOKALNIM ANESTETICIMA

- Mehanizam dejstva:

  - Direktna blokada transmisije bolnih impulsa iz nociceptivnih aferentnih vlakana na povrsini rane

  - Vezivanjem za brze Na^+ kanale u membrani aksona sprecava se propagacija akcionog potencijala



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INCIZIONE KATETER TEHNIKE LOKALNIM ANESTETICIMA

- Prednost:
- Redukcija postoperativnog bola uz ogranicenje sistemskih nezeljenih dejstava analgezije
- Lokalni anestetici inhibisu lokalni inflamatorni odgovor na povredu tkiva (sto senzitizuje nociceptivne receptore i doprinosi bolu i razvoju hiperalgezije)
- Infiltracija lokalnih anestetika smanjuje adheziju neutrofila za endotel, otpustanje inflamatornih medijatora iz njih kao i stvaranje slobodnih kiseonickih radikala i edema

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INCIZIONE KATETER TEHNIKE - PREDNOSTI

- Bezbednost, jednostavnost, niska cena
- Kateter se pravilno postavlja direktnom vizualizacijom ili artroskopski
- Nizi rizik probijanja u vaskularne / neuralne / pleuralne/ interskalenus strukture od perineuralnih kateter tehnika
- Analgezija na ogranicenom polju operativnog zahvata- normalna upotreba ekstremiteta, rana rehabilitacija (trnjenje – senzorna blokada...)

Liu SS et al. J Am Coll Surg 2006

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INCIZIONE KATETER TEHNIKE - PREDNOSTI

- Korist kod kontraindikacija za centralne blokove (krvarenje, infekcije)
- Minimalni sistemski efekti
- Ambulantni i bolnicki pacijenti (odeljenje)
- Dobra prihvacenost od strane pacijenta (komplijansa)

Liu SS et al. J Am Coll Surg 2006

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INCIZIONE KATETER TEHNIKE LOKALNIM ANESTETICIMA

- **Nacini isporucivanja lokalnih anestetika**

- Bolus : infiltracija lokalnim anestetikom efikasna -kratko dejstvo

- Kontinuirana infuzija: eliminacija “pikova” i padova analgetickog efekta kod intermitentnog davanja i sistemskih analgetika

- **BAZALNA INFUZIJA + “ON DEMAND” BOLUS DOZE (PCRA- pacijent kontrolisana regionalna anestezija)***

** Rawal N. Best Pract Res Clin Anaesthesiol 2007*

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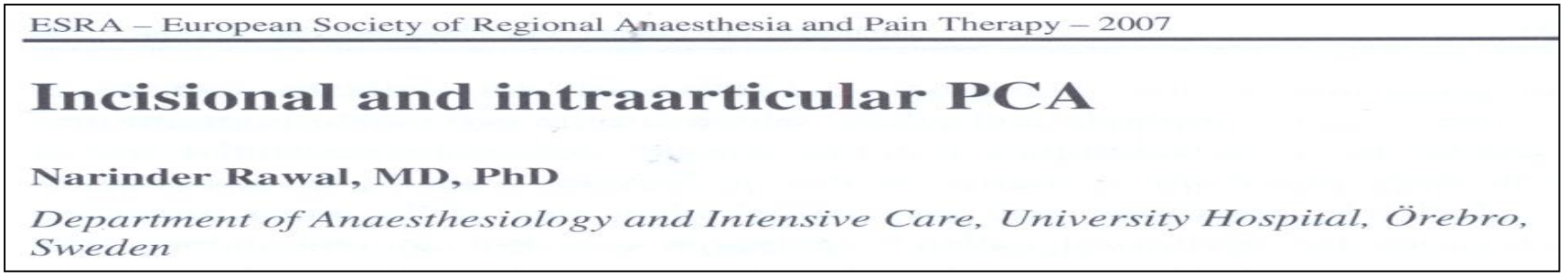
PERIFERNE KATETER TEHNIKE


ESRA – European Society of Regional Anaesthesia and Pain Therapy – 2007

Incisional and intraarticular PCA

Narinder Rawal, MD, PhD

Department of Anaesthesiology and Intensive Care, University Hospital, Örebro, Sweden

- **"PCRA" - pacijent kontrolisana regionalna anestezija***
  interindividualne razlike za analgeticima postoperativno
  (bolus doza: na 3-12h)
- **PACIJENTI KORIGUJU RAZLIKE U INTENZITETU I TRAJANJU POSTOPERATIVNOG BOLA**

  - Odgovara dinamicnoj prirodi postoperativnog bola.

  - Niza ukupna doza, manje nezeljenih efekata, vece zadovoljstvo pacijenta.*

* *Ryck Y et al. Reg Anesth Pain Med 2001*

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INCIZIONE KATETER TEHNIKE

- Kateter se plasira u ranu na kraju operacije, tehnicki jednostavno
- Konektovanje katetera i pumpe sa prethodno proracunatom kolicinom lokalnog anestetika na sat

"Pain buster" I kateter

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INCIZIONE KATETER TEHNIKE

- Parametri za ishod?

  Efikasnost analgezije: opsta hirurgija, abdominalna, kardiotorakalna, ortopedija, spinalna, ginekologija, mali ambulantni zahvati

  - 32% niza ocena bola (u mirovanju i pokretima)
  - 25%-70% manja potreba za opioidima
  - 16% manje PONV
  - 30% vece zadovoljstvo pacijenta
  - kraca hospitalizacija (1-3 dan)
  - 22% manje hronicnog bola nakon 6 meseci

* ***Liu SS et al. J Am Coll Surg 2006***

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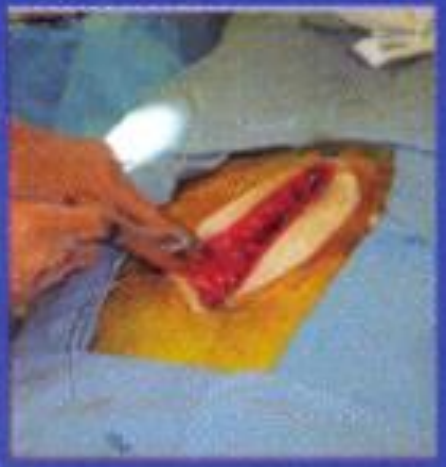
Continuous local anaesthetic infusion is associated with decreased postoperative analgesic requirement

SC catheter – 300 mL of bupivacaine over 72 h (4 mL/h)

50% less opioid consumption



	Control $n = 35$	Bupivacaine $n = 35$
Morphine consumption (mg)	60.1 ± 62	33.7 ± 32
Mobilisation (D)	2.3 ± 0.6	2.0 ± 0.6
GI function resumption (D)	4.2 ± 1.6	3.6 ± 1.3
Duration of hospitalisation (D)	10.1 ± 6	9.8 ± 5

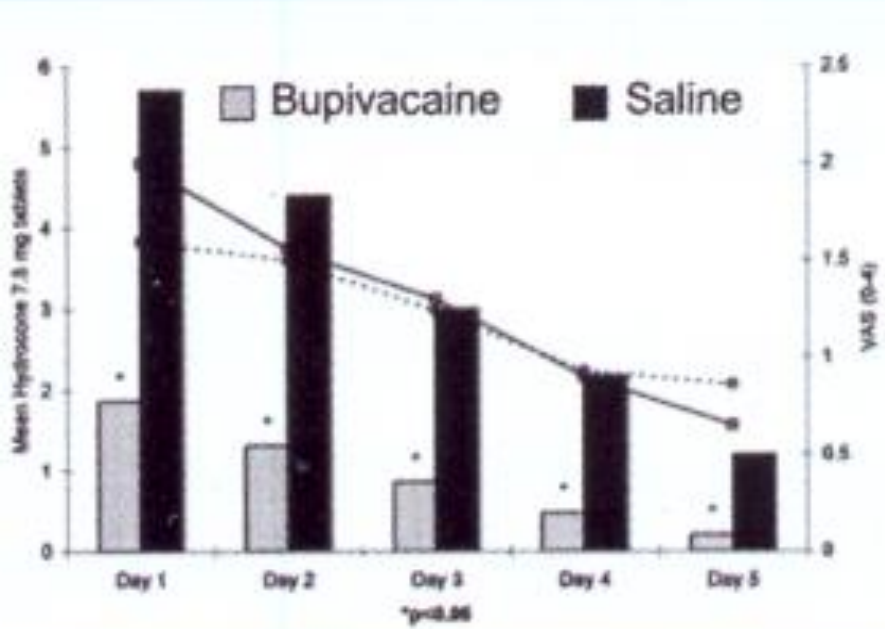
No difference in pain relief

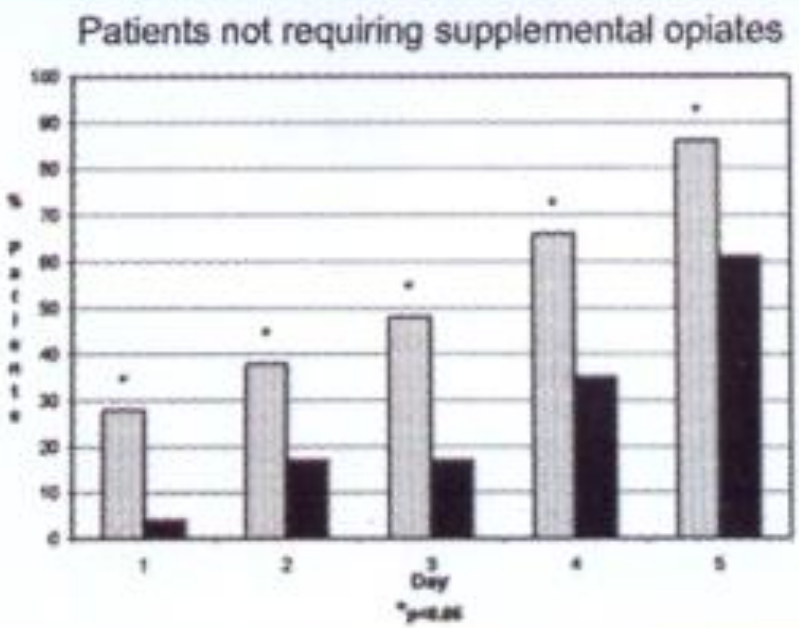
Baig *et al. J Am Coll Surg* 2006;202:297-305

KONTINUIRANA INFUZIJA NAKON INGVINALNE HERNIJE

- Kateter sa multiperforacijama- subfascijalno
- Bupivakain 0,5% 2 ml/h u toku 48h
- Bez nezeljenih dejstava

ISPLATIVOST? HRONICNI BOL?





LebBlanc et al. *J Am Coll Surg* 2005;200:198-202

NEZELJENA DEJSTVA?

- Rizik incizione hernije: 1% (starost, dijabetes, gojaznost, vaskularna oboljenja)*
- Dehiscencija rane: 0,5-3%
- Vaskularna punkcija (oko 5% slucajeva)
- Sistemska toksicnost lokalnih anestetika – preciznost doziranja (400 mg bupivakaina u toku 24 h)
- Direktna tkivna toksicnost (miotoksicnost, mionekroza) izuzetno retko**

** Brower MC. Reg Anesth Pain Med 2003*
***Zinck W, Graf BM. Reg Anesth Pain Med 2004*

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NEZELJENA DEJSTVA?

- Infekcija rane – nije zapazena veza sa tehnikom (inhibicija>70% *Staph aureus* infiltracijom 2% lidocaina)
- Antibakterijski filtri

- Lokalni anestetici- bakteriostatski/cidno i fungistatsko/cidno dejstvo (eksperimentalno)*

**Stratford AF. Plast Reconstr Surg 2002*

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ZARASTANJE RANE

- *In vivo* animalni modeli, *in vitro* celijski sistemi: usporeno *
- **Uticaj lokalnih anestetika na oksigenaciju tkiva subkutano :** bupivakain-oksigenacija na rani
  - razlika intaktna koza i rana ~ 25,9 mm Hg (pritisak kiseonika u subkutanom tkivu sa polarografskim elektrodama)
  - redukcija bola povisava nivo O2 u tkivu i imuni odgovor
  -"Iznad 15 mm Hg- dobra analgezija, prevencija infekcije" **
- **Dalja istrazivanja?**

** Brower MC, Johnson ME. Reg Anesth Pain Med, 2003*

***M. Ahmad, ASA Annual Meeting, Las Vegas, 2009*

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OPREMA

- ASEPTICNA TEHNIKA
- BEZBEDNOST (pumpe, kateteri)
- PUMPE: ELASTOMERNE ILI BATERIJSKE
  - Prevencija akcidentalnog praznjenja pumpe
  - Ujednaceno sirenje lokalnog anastetika
- KATETERI:

  epiduralni, jedan ili vise otvora, dugacki, bez lateksa, “radio-opaque”

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OPREMA- PUMPE

- Elastomerne pumpe- prednosti

  - lake, portabilne, jednokratne

  - balon sa lokalnim anestetikom, splasnjava srazmerno odavanju izabrane kolicine anestetika na sat

  - jednostavne, laka obuka

  Nedostaci- mala kolicina anesetika moze biti apsorbovana u balon

- Electricne pumpe

  -precizne ali

  - skupe, ograniceno trajanje baterije, alarmi, obuka

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Ambulatory Perineural Local Anesthetic Infusion

Brian M. Ilfeld, MD, and F. Kayser Enneking, MD

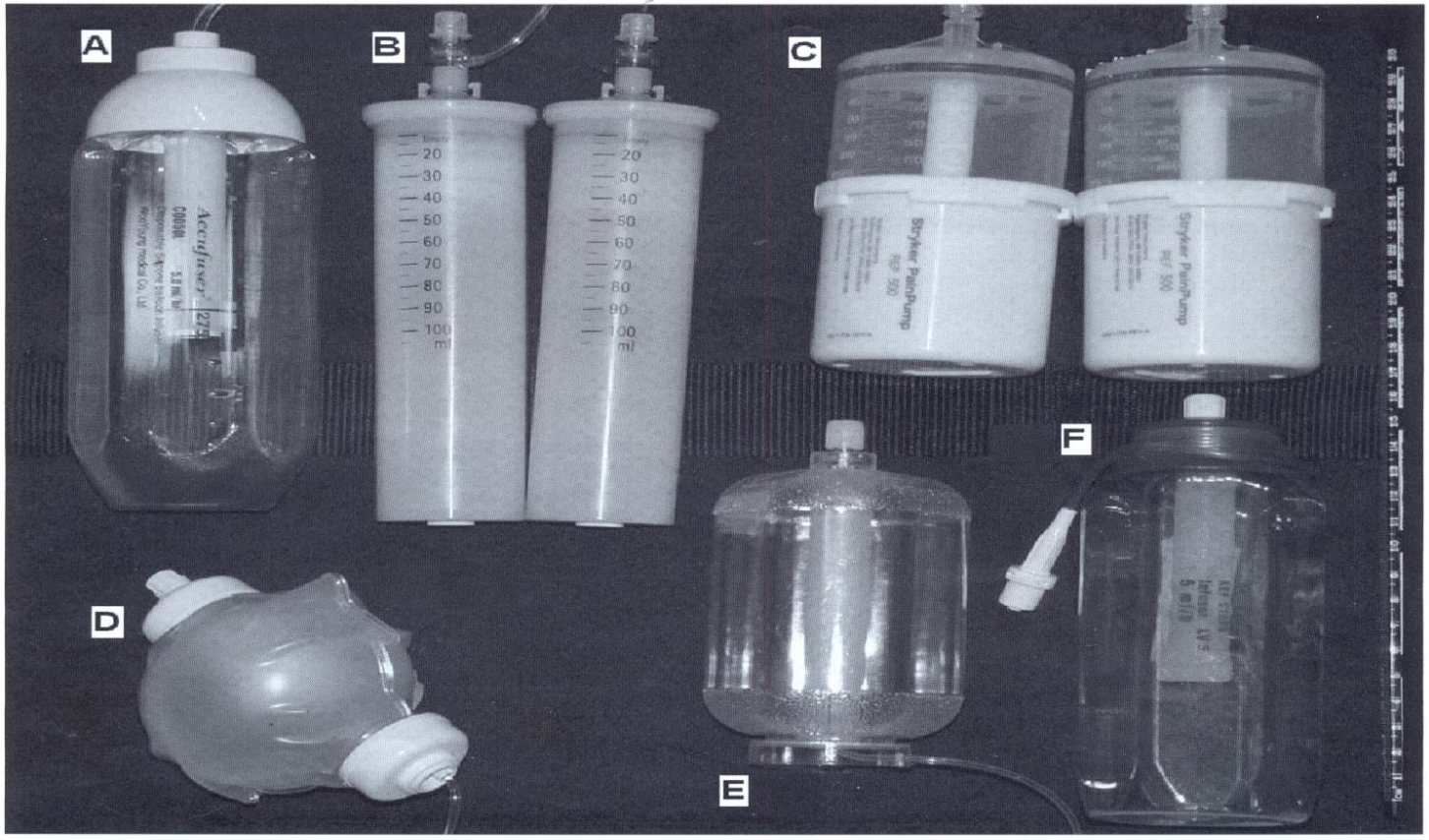

Fig 2. Portable basal-only or bolus-only infusion pumps. (A) Accufuser, (B) Sgarlato, (C) Pain Pump, (D) C-Bloc, (E) MedFlo II, and (F) Infusor LV5. Manufacturer information is included in Table 1.

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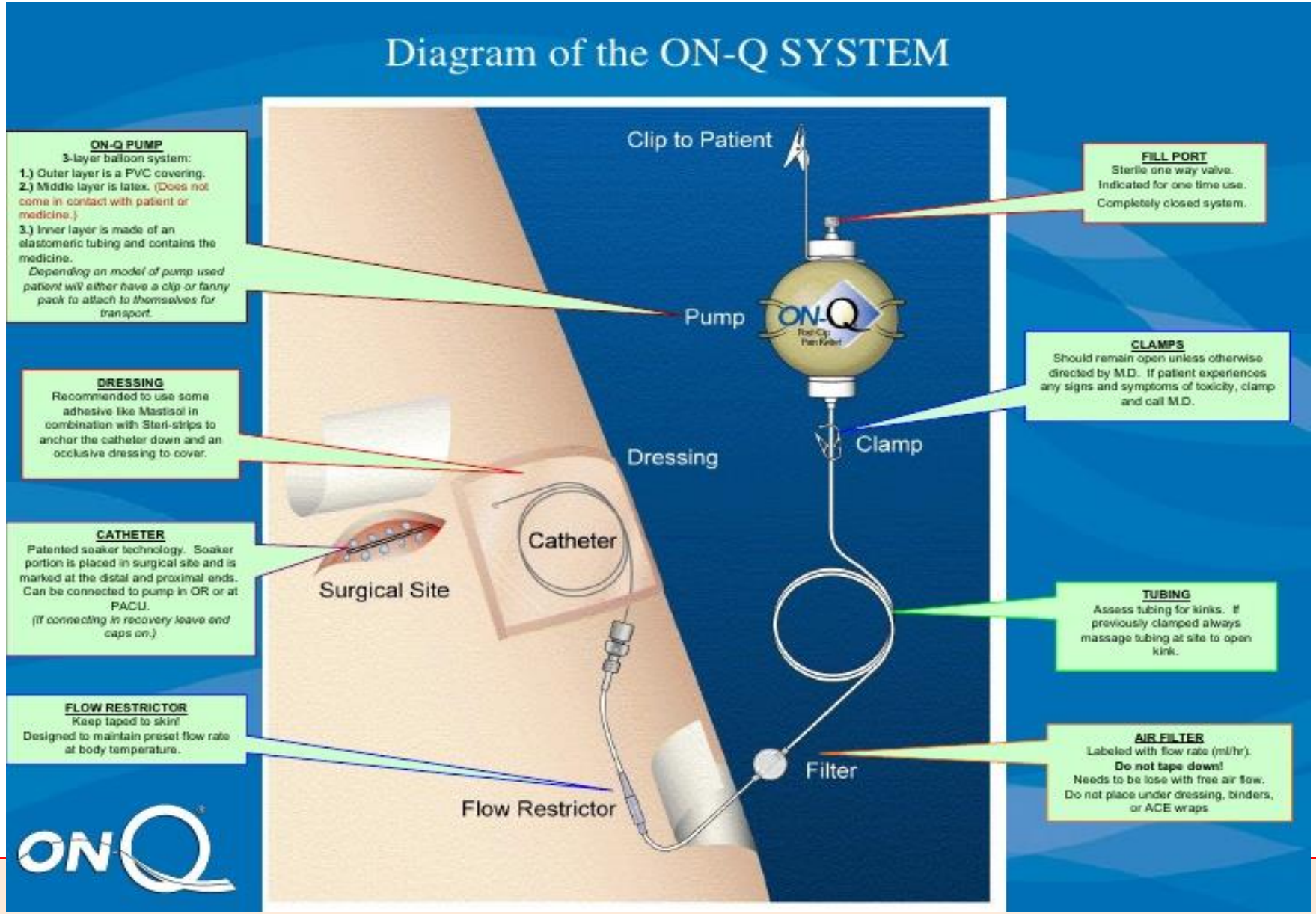

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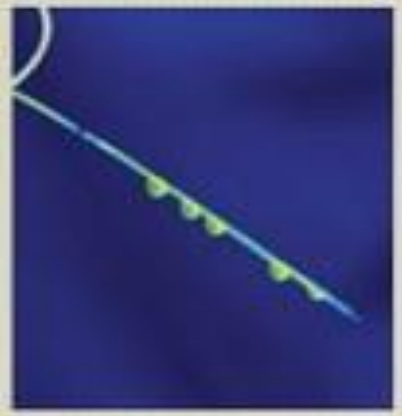
On Q Pain Buster catheter



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