



Cancer Pain

- 50% will develop cancer over lifetime – ICS
- 30-45% pain at diagnosis, intermediate stages
- 80-90% pain with advanced cancer

- 40-50% moderate to severe pain
- 25-30% very severe pain

Cancer Pain

- Tumour progression / tissue destruction
- Metastases, bone
- Neuropathic
- Chemo / radiotox toxicity
- Operations
- MSK, reduced physical activity
- Non cancer related

Cancer Pain, Plexopathy

- Cervical
- Brachial
- Lumbosacral

- Infiltration
- Fibrosis

Plexopathy

- Cervical Cervical nodes
 Head and neck tumours
- Brachial Breast, lung, lymphoma
 Metastases
 Upper and lower
- Lumbar Infiltration of psoas
 Abdominal and pelvic cancers
 colorectal, endometrial, renal, sarcoma,
 lymphoma
 Metastases

Peripheral Neuropathy

- Tumour invasion

- Fibrosis

- Chemo

- Surgery

BONE METASTASES

- Solid tumours regularly metastasise to bone.
 - breast, prostate, lung, thyroid, kidney, colorectal.
- Multiple Myeloma commonly associated with skeletal disease.
- 70% of patients with bone mets develop pain.
- Usually discovered after diagnosis but in 20% skeletal pain may be the presenting complaint.
- Regular indicator of recurrence, e.g. 40% of women with breast cancer.
- 4% of all back pains...

BONE METASTASES – COMMON SITES

- Thoracic and lumbar spine
- Pelvis
- Cervical spine
- Long bones
- Some sites are pathognomonic e.g. renal/scapula and breast/skull.
- Axial pain is the most common presenting symptom.

VERTEBRAL METASTASES

- Pain
- Reduced ambulation
- Vertebral fractures
- Hypercalcaemia
- Spinal cord compression
- Neurological deficit.

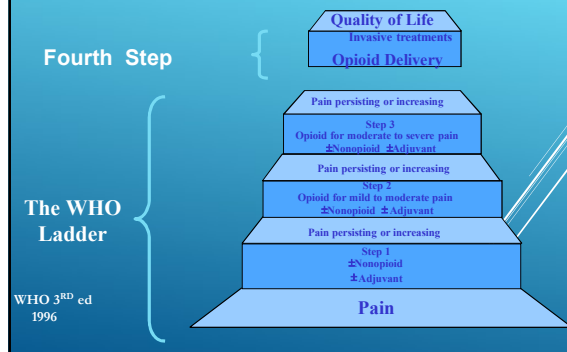
VERTEBRAL PAIN

- Altered physiological equilibrium between osteoclasts and osteoblasts with structural degradation of bone.
- Mass effect, stretching of the periosteum.
- Increased expression of chemical/inflammatory mediators of pain e.g. prostaglandins, bradykinin, histamine, substance P.
- Invasion of nerve cells
- Muscle spasm.

TREATMENT OPTIONS – ESMO / NICE GUIDELINES

- Analgesics. WHO ladder.
- Corticosteroids
- Bisphosphonates
- Denosumab
- Hormone therapy
- Radiotherapy
- Radiolotopes
- Vertebroplasty / Kyphoplasty
- Surgery
- RF
- Interventional techniques e.g. continuous epidural/IT pump

MODIFIED WHO ANALGESIC LADDER



CANCER PAIN – THE ROLE OF INTERVENTIONAL PROCEDURES

- Step 4 in World Health Organization (WHO) ladder approach
- Earlier use if risk/benefit is favourable
- Understand limitations and contraindications
- Interventional procedures sometimes needed for chronic ongoing pain
- Can be beneficial in very end-stage situations
- Adjuvant to the existing multimodal analgesia

INTERVENTIONAL THERAPY INDICATIONS

- Intractable pain*
- Intractable side effects*
- Pain likely to be relieved with a nerve block and/or intervention
- Failure to achieve adequate analgesia without intolerable side effects of oral medications

NCCN 2006 Pain Guidelines

INTERVENTIONS

- ▶ Somatic nerve / plexus blocks
- ▶ Sympathetic nerve blocks
- ▶ Continuous epidural / intra-thecal infusions
- ▶ Local anaesthetics with steroids
- ▶ Destructive

SOMATIC

- ▶ Brachial plexus
- ▶ Lumbar plexus
- ▶ Epidural – translaminal
_ transforaminal, nerve root block
- ▶ Intercostal / Paravertebral
- ▶ Individual Nerve blocks

BRACHIAL PLEXUS

- ▶ Plexus invasion
- ▶ Pain in distribution of plexus
- ▶ Various approaches, interscalene, supraclavicular
- ▶ Ultrasound control, stimulating needle

LUMBAR PLEXUS

- ▶ Invasion / distribution
- ▶ Hip, femur, knee
- ▶ X ray control
- ▶ Transverse process L3 / L4. 3cm deeper in psoas

INTERCOSTAL

- ▶ Rib infiltration etc
- ▶ X ray control, walk off rib, transverse process
- ▶ Pneumothorax

EPIDURAL

- ▶ "One shot"
- ▶ Translaminar / transforaminal / caudal
- ▶ Cervical, thoracic, lumbar, sacral (caudal)
- ▶ Vertebral metastases, nerve root compression
- ▶ X-ray control

SYMPATHETIC BLOCKS

- ▶ Coeliac Plexus Block
- ▶ Superior Hypogastric Plexus Block
- ▶ Stellate Ganglion Block

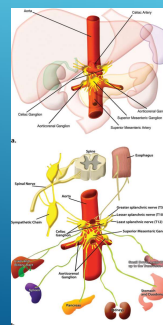
COELIAC PLEXUS

- ▶ Ganglia and interconnecting nerves
- ▶ Coeliac, aortorenal, superior mesenteric ganglia (variable number and location)
- ▶ Preganglionic sympathetic efferents
 - Greater Splanchnic (T5-T9)
 - Lesser Splanchnic (T10-T11)
 - Least Splanchnic (T12)
- ▶ Preganglionic Psymp (vagus)
- ▶ Visceral afferent fibres

ANATOMY

- ▶ T12 or L1 level
- ▶ Left more caudal (0.9cm v's 0.6cm to coeliac)
- ▶ 2.7cm long (0.5 - 4.5)
- ▶ Relationship to coeliac artery most consistent

ANATOMY




- ▶ Distal oesophagus to proximal transverse colon
- ▶ Pancreas
- ▶ Liver
- ▶ Biliary tract
- ▶ Gall bladder
- ▶ Spleen
- ▶ Kidneys
- ▶ Adrenals
- ▶ Mesentery
- ▶ Small & large bowel, stomach

BLOCKADE

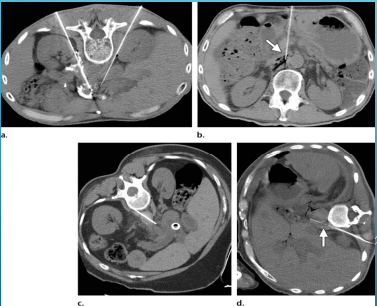
- ▶ Fluoroscopy
- ▶ Ultrasound
- ▶ CT
- ▶ MRI
- ▶ Laparoscopic
- ▶ Endoscopic
- ▶ Anterior vs Posterior approaches
- ▶ Retrocrural vs Antecrural approaches

FLUOROSCOPY

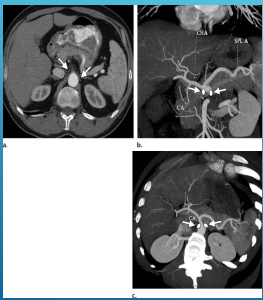
- ▶ Simple
- ▶ Retrocrural
- ▶ Splanchnic nerve blocks
- ▶ L1, anterolateral surface
- ▶ LA, steroid, neurolysis, radiofrequency lesioning
- ▶ Can't see structures:
 - ▶ Blood vessels
 - ▶ Abdominal organs
 - ▶ Lung
 - ▶ Diffusion of neurolytic solution
- ▶ Transaortic approach (antecrural)



CT



CT



- ▶ Retroperitoneal structure/tumour visualisation
- ▶ Coeliac plexus itself
- ▶ Planning
 - ▶ needle puncture angle
 - ▶ course
 - ▶ depth
 - ▶ location of tip
- ▶ Diffusion/exact spread of neurolytic solution
- ▶ Safer

ENDOSCOPIC

- ▶ Oesophagus/Upper stomach
- ▶ Endoscope with Ultrasound
- ▶ Can pass needle
- ▶ Real time monitoring
- ▶ Snowstorm
- ▶ Infection (abscess, pancreatitis)



INDICATIONS

- ▶ Upper GI tumour
- ▶ Liver metastases
- ▶ Nausea & vomiting
- ▶ Chronic pancreatitis

SUPERIOR HYPOGASTRIC PLEXUS

- ▶ Pelvic Pain
- ▶ Antero lateral border L5
- ▶ Fluoroscopic

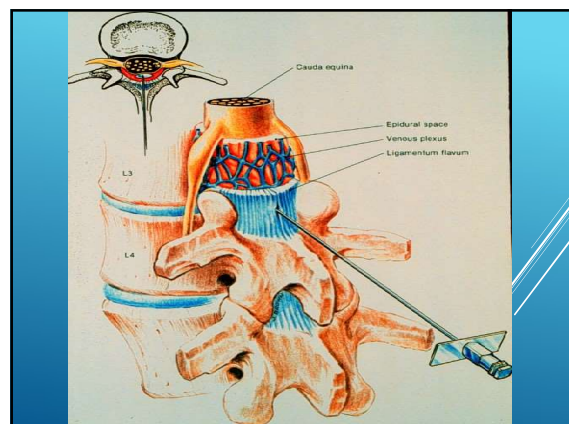
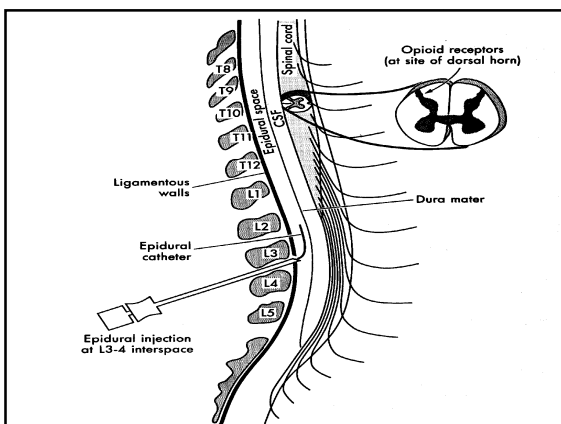
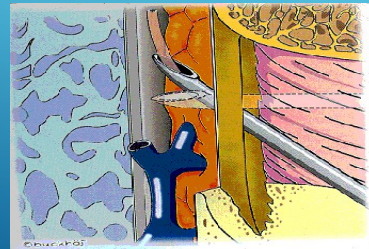
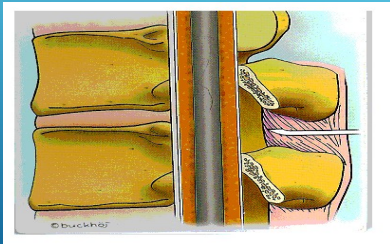
THE EPIDURAL / INTRATHECAL SPACES

"The epidural space is a **potential space** that contains fatty tissue and blood vessels; and is located between the bony vertebral canal and the outer surface of the dura mater"

"The epidural space contains fat which surrounds and pads the spinal cord. This fat acts as a **depot** for opioid and LA."

Intrathecal space contains CSF

EPIDURAL ANALGESIA





DRUG OPTIONS

- ▶ Various drugs
- ▶ Opioids
- ▶ Local Anaesthetics
- ▶ Clonidine
- ▶ Baclofen
- ▶ Ziconotide
- ▶ Ketamine, midazolam

LOCAL ANAESTHETICS

- ▶ Bupivacaine / ropivacaine
- ▶ Block nerves
- ▶ Na channel blockade, DH and nerve roots
- ▶ Sensory, motor, autonomic

EXTENT OF BLOCK

- ▶ Level of epidural
- ▶ Volume
- ▶ Concentration
- ▶ Surgical anaesthesia
- ▶ Preferential sensory block
- ▶ Hypotension, bradycardia, resp muscles
- ▶ Epidural:intrathecal 5/10:1
- ▶ Neurotoxicity

OPIOIDS

- ▶ X 10 epidural
- ▶ X 100 intrathecal

SCIENTIFIC RATIONALE

- ▶ Discovery of opioid receptors in the dorsal horn of the spinal cord, Pert 1973
- ▶ Powerful Analgesic, Yaksh 1976
- ▶ Selective Spinal Analgesia, Cousins 1979
- ▶ Epidural Morphine, Behar 1979
- ▶ Intrathecal Morphine, Wang 1979

- ▶ Dorsal horn, pre and post synaptic, hyperpolarisation of membranes

EPIDURAL OPIOIDS

Three main pathways:

- ▶ Diffusion through the dura -CSF, spinal cord, nerve roots
- ▶ Vascular uptake by the vessels in the epidural space into the systemic circulation
- ▶ Uptake by the fat in epidural space; creating a depot from which drug can eventually enter CSF or systemic circulation

SPINAL ANALGESIC AGENTS

Opioids:

Morphine - low lipid solubility/slow onset of action, produces prolonged analgesia.

Fentanyl - High lipid solubility/ faster onset, shorter duration of action.

INTRATHECAL OPIOIDS

- ▶ Better analgesia, much lower doses, fewer SE's
- ▶ Respiratory depression
- ▶ Tolerance
- ▶ Neuropathic pain, visceral, incident
- ▶ Endocrine problems
- ▶ Weight gain, water retention, perspiration, mood

CLONIDINE

- ▶ Epidural Clonidine 1984
- ▶ Alpha 2 agonist
- ▶ Inhibits release of Sub P, CGRP
- ▶ Inhibits pre gang sympathetic outflow
- ▶ Synergistic with opioids and LA's

BACLOFEN

- ▶ Spasm
- ▶ GABA agonist
- ▶ Much lower doses intra thecally

ZICONOTIDE

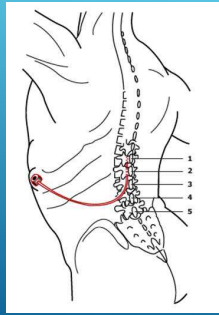
- ▶ N type Ca channel antagonist
- ▶ Specific to Presyn Terminals in DH
- ▶ High SE's profile
- ▶ Slow titration

INFUSION SYSTEMS

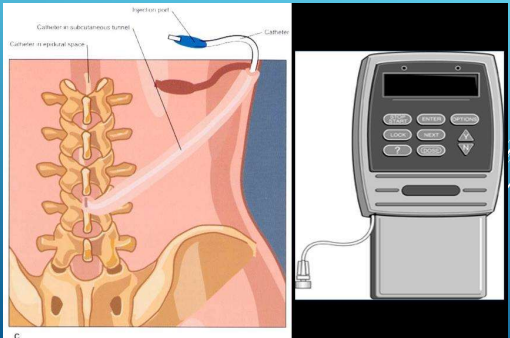
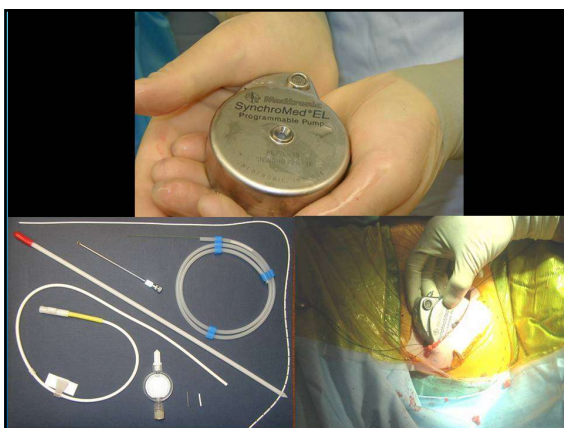
- External pump, percutaneous catheter tunneled
- External pump, implanted catheter, Subcut port
- Implanted pump
 - Programmable
 - Non Programmable

Permanent Epidural Catheter With A Subcutaneous Port

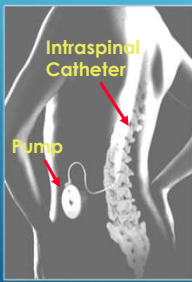
▶ Tunneled catheters are appropriate for patients with a life expectancy less than three months.



TUNNELED/TEMPORARY EPIDURAL OR PLEXUS INFUSIONS

POSITION OF IMPLANTED PUMP AND CATHETER



- ▶ Pump placement
 - ▶ Left or right abdomen
 - ▶ Enough skin / subcutaneous tissue for support
- ▶ Catheter placement
 - ▶ Tunneled subcutaneously from spinal column to pump

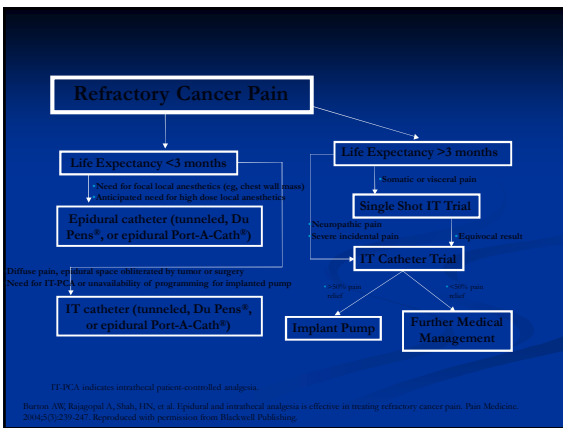
CATHETER PLACEMENT

Drug movement in CSF

- ▶ CSF motion
- ▶ Injection rate
- ▶ Brownian motion

CSF MOTION

- ▶ Cardiac cycle / Intrathecal vasculature
- ▶ Max in cervical area, min caudally
- ▶ Rostocaudally, not circumferentially
- ▶ 3 channels
- ▶ Hydrophilic



PATIENT SELECTION

- ▶ Failed medical therapy
- ▶ Side effects
- ▶ Unresponsive to nerve blocks
- ▶ Radiotherapy

CONTRAINDICATIONS

- ▶ Infection
- ▶ Coagulopathy
- ▶ Debility

CHOICE OF SYSTEM

- ▶ Prognosis
- ▶ 3 months
- ▶ Cost
- ▶ Ease of insertion
- ▶ Infection
- ▶ Maintenance

TRIALS FOR INTRATHECAL

- ▶ Bolus
- ▶ Temporary intrathecal catheter
- ▶ Epidural catheter

COMPLICATIONS

- Infections: Staph aureus, epidermidis, strep vir
- Pump Displacement
- Catheter problems
- Filling errors / Programming errors
- Pump failures
- Catheter tip inflammatory masses
- Headache, CSF leak, Hygroma, Seroma
- Usual Drug Complications

MANAGEMENT

- ▶ Refills 1 to 2 months
- ▶ Dose alteration by telemetry
- ▶ PCA
- ▶ Epidural infusion change 2 to 4 days

SUCCESS

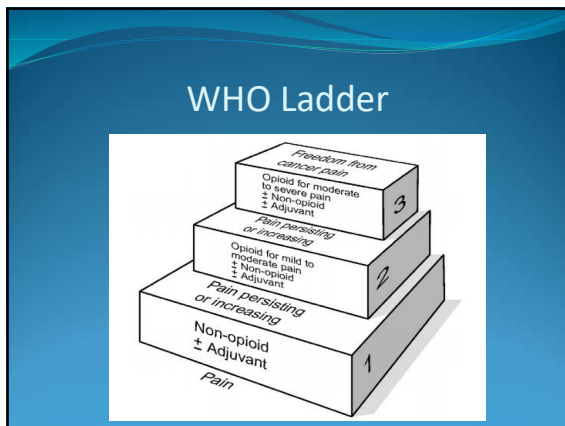
- ▶ Better control
- ▶ Fewer SE's
- ▶ Longer survival
- ▶ Cost effective

EVIDENCE

- ▶ Cochrane 2006
- ▶ Smith et al 2002, 2004, 2005

CORK EXPERIENCE

- ▶ Failed medical control
- ▶ Trial with epidural catheter
- ▶ Immediate oral dose reduction
- ▶ Neurosurgical assistance
- ▶ Morphine 40mg/ml / Bupivacaine 40mg/ml mixture 1:5
- ▶ Start low and titrate
- ▶ Generally good success






Cancer pain

- WHO ladder may not be successful in up to 30% of cancer pain sufferers
- Breivik 2009, a pan-European survey
- Valberg 2008
- Discussion document British Pain Society 2011
- Smith and Saiki 2015
- O'Brien and Kane 2014* 48000 patients suffer uncontrolled cancer pain per year

Step 4

- Revised WHO ladder, Miguel 2000, Cancer Control
- Step 4, major interventions e.g. destructive blocks, intrathecal pumps, continuous infusions
- Case should be made for earlier, simpler interventions

- The effective management of cancer-related pain is a top priority for patients, families and health care professionals.
- Between 85-90% of patients with advanced cancer can have their pain well controlled with analgesic drugs and adjuvants.
- However, in 10-30% of cancer patients, systemic analgesics fail to provide adequate control of cancer pain.
- Up to 80% of these patients may benefit from interventional techniques.

ESMO Clinical Practice Guidelines 2012.





However...

- Linklater 2002 Palliative Medicine

Evidence suggests the gross under-utilization of interventional pain management techniques in the treatment of cancer pain. This may be multifactorial in origin but typically results from poor interdisciplinary communication (i.e. palliative care, oncology and pain medicine), ad hoc referral arrangements and a lack of integrated services

- Findings borne out by Kay et al 2007
- Low referral rates from Palliative Medicine
- 31% received more than 12 per year
- 50% less than 5
- 25% had dedicated time (short)
- Less than 1000 interventions per year

Lack of Integration

- Lack of communication
- Lack of knowledge
- Inadequate resources, funding, planning
- Territorial?
- Difficulty accessing Pain Medicine, lack of cancer training

The History....

Traditionally in Cork very strong links between Palliative Medicine/Medical & Radiation Oncology and Pain Medicine.

Significant numbers of patients until recently treated in acute hospital setting.

However this required:

- Transfer out of hospice environment.
- Outpatient oncology patients sharing facilities with non-oncology outpatients.

This was not always appropriate for the patient population, nor was it efficient.



Development...

- New hospice officially opened in 2011
- Strong relationship, Michael 2010
- After multidisciplinary collaboration between Palliative Care/Medical & Radiation Oncology/Pain Medicine it was decided that a dedicated Interventional Pain Management Unit would be established in the new Marymount Hospice.

Comprising:

- Reception / secretarial / admin area
- Outpatient suite
- Procedure room, C-arm and ultra sound facilities
- Recovery, 3 bedded, full monitoring

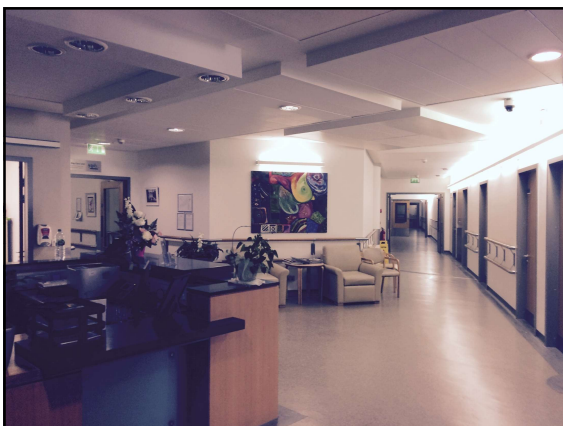
Development continued...

Staffing required:

- Pain Specialist Consultant & NCHD
- CNS Pain Relief
- 3 Staff nurses
- Secretarial support
- Radiography

Funding:

- Proposal to HSE highlighting clinical need, benefits, costing.
- Marymount a registered charity, private funding also sought.



Procedure Room

A photograph of a procedure room. It contains a large medical table, a computer monitor, and various medical devices. The room is equipped for medical procedures.

Procedure Room



Problems

- Introducing the concepts of monitoring, recovery, possible resuscitation into a hospice setting
- Multidisciplinary co-operation – Medicine (Anaesthetic and Palliative Medicine), Nursing, Pharmacy, Radiography, Administration
- Multiple meetings – protocols, staffing, equipment



Team Talk



Presently...


- 2 outpatient sessions – Consultant
SpR
CNS
- 1 Interventional session – Consultant
3 staff nurses
Radiographer
- Admin support
- Ward consultations

Procedures

- Relatively simple procedures
- Nerve and plexus blocks +/- continuous infusion
- Epidural injections +/- continuous infusion
- Miscellaneous procedures, minor injections
- Procedures for non cancer pain
- Complex procedures (coeliac plexus block, intrathecal pumps) done in main hospital

Audit of first years' Activity...

- The retrospective review examined the first year's activity of the interventional pain service (June 2015-June 2016).
- 150 new referrals, 620 consultations
- 175 blocks, some repeat (age range 28 - 89), 102 female : 73 male
- Palliative Care accounted for the majority of referrals (44%) Medical and Radiation Oncology 36% and Breast surgery 10%
- Breast disease comprised the largest percentage of cancers referred to the service @ 58%
- Lumbar and thoracic metastatic disease (53% & 26% respectively) were the main indications.
- Epidural blocks (caudal, thoracic and lumbar) accounted for



- Collaborative approach between Pain Medicine and Palliative Care, Medical Oncology, Radiation Oncology, other cancer specialists.
- Rapid Access. New patients invariably seen at next clinic
- 82% of patients had an intervention within two weeks of first review. Delays typically occurred only if patients had commenced antibiotics, issues with anticoagulants, staff leave
- Patients treated in an appropriate environment
- Destigmatizes hospice treatment
- Good results from simple, safe procedures



Epidural steroids

- First used in 1885, Corning "seminal incontinence" & "addiction to masturbation"
- 1901 treatment of radicular pain (Sicard & Cathelin)
- 1955 - first use of epidural steroids (Lievre)
- Mode of action.
 - anti inflammatory, phospholipase A2
 - effect on C fibres

Epidural steroids

- Various uses.
 - Back pain with leg pain.
 - prolapsed disc
 - spinal ,foraminal, lateral recess stenosis.
- Various controversies
 - Which steroid to use?
 - route??
 - dose??
 - volume
 - Xray guidance?
- (Cohen et al 2013)



Epidural steroids

- Minimal reference in the literature to the use of epidural steroids for pain associated with vertebral metastases.
- In our institution we have been using epidural steroids for this indication for some time.
- Hence we carried our a prospective audit to evaluate efficacy.

audit

- Patients with severe pain from vertebral metastases (back or leg pain)
- Referred from Palliative care/Medical Oncology
- Reviewed in Cancer Pain OPD
- All patients had been treated using the WHO ladder and Radiotherapy

audit

- Patients reviewed at 1,2 and 4 months post procedure
- Pain VAS (visual analogue score)
- % Improvement – Patient Self-assessment
- Patient satisfaction
- Medications
- Side effects

Procedure

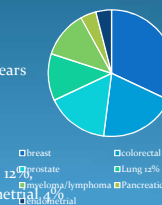
- Epidurals done by one of two operators (Consultant or Pain Fellow)
- X ray guided, prone
- Level depended on metastatic location and pain distribution
- Saline & Depomedrone (80 – 120 mg) injected into epidural space
- Low volume used, 5mls
- Lie on affected side post procedure

results

- A total of 68 epidurals in 37 patients
- Results for 63 epidurals in 32 patients
- 3 patients had 4 epidurals
- 5 patients had 3 epidurals
- 12 patients had 2 epidurals
- 12 patients had 1 epidural

results

- Male V Female 28% V 72%
- Age 45 – 87 years, mean 68 years
- Breast 32%
- Colorectal 20%,
- Prostate 16 %,
- Lung 12%,
- Myeloma/Lymphoma 12%
- Pancreatic 4%, Endometrial 4%





Results – 1 month

- 72% had $\geq 50\%$ reduction in VAS
- 82% had $\geq 50\%$ improvement (self assessment)

Results – 2 months

- 65% had $\geq 50\%$ reduction in VAS
- 78% had $\geq 50\%$ improvement (self assessment)

Results - 4 months

- 53% had $\geq 50\%$ reduction in VAS
- 67% had $\geq 50\%$ improvement (self assessment)
- 64% Very/Completely Satisfied.

Results - 4 months

- 66% had $\geq 30\%$ reduction in VAS
- 78% had $\geq 30\%$ improvement (self assessment)

Results – 4 months

- Between 1/2 and 2/3 of patients had 50% relief
- Between 2/3 and 3/4 had 30% relief
- 2/3 were very satisfied with the procedure.

Side effects

- None apart from temporary tenderness at the site

discussion

- Simple, safe & cheap intervention
- Effective, results comparable to radiotherapy
- Can be repeated - effect likely to be repeated
- Good duration of relief in patients with poor prognosis
- Logistical difficulties, communication, Linklater & Kay
- Epidural steroids should routinely be part of the treatment of pain associated with vertebral metastases
- No reason why procedure cannot be done early in the diagnosis, to compliment pharmacology & radiotherapy





175 interventions performed per year in the Cork / Kerry area vs about 1000 done in Britain

Good success

Step 4?

- In non malignant pain we don't wait until all pharmacological combinations have been exploited before we carry out simple interventions
 - So why should we do so in cancer pain
 - Adjuvants on the WHO ladder should include blocks
 - Pain Specialists should be involved at an early stage
 - O'Brien and Kane
- The era of ad hoc arrangements is over
Pain Specialists should be fully integrated into the Palliative Care team
There is always more to analgesia than analgesics

Future

- Increase our activity
- Earlier intervention
- New consultant in Pain Medicine position with specific sessions in Hospice, and part funded by Hospice / Palliative Care





This purpose-built self-contained hospice-based Interventional Pain Management Unit is unique, providing rapid access to patients suffering from cancer pain.

 **Summary** 

- Evidence suggests the gross under-utilization of interventional pain management techniques in the treatment of cancer pain.
- Previous system not effective or efficient.
- This intergrated service resulted from a collaborative approach between Palliative Care, Oncology and Pain Medicine in response to patient need.
- Present system is cost effective & efficient from both humanitarian and economic perspectives, a unique facility providing rapid access to interventional pain management techniques.
- Model of integrated care undoubtedly to be replicated elsewhere.

Críoch
Go raibh maith agaibh

