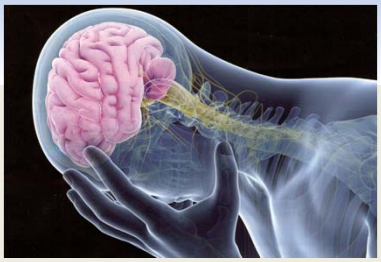
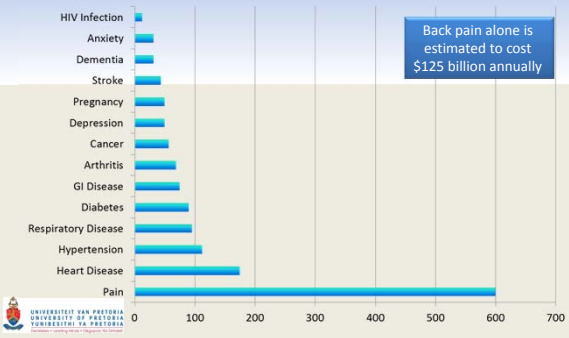
Pain Management
Current perspectives



Helgard Meyer, FCFP(SA)
Department of Family Medicine
University of Pretoria
Wilgers MR Medical Centre

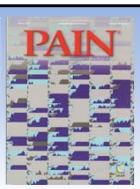
Cost of pain
Painter in J Clin Rheum, 2013



Topical Review

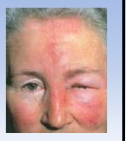
PAIN

Updating the definition of pain
Williams et al in Pain, 2016



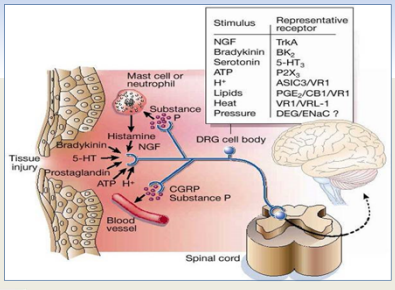
"Pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components."

Acute pain
Holdcroft in Core topics in Pain, 2005

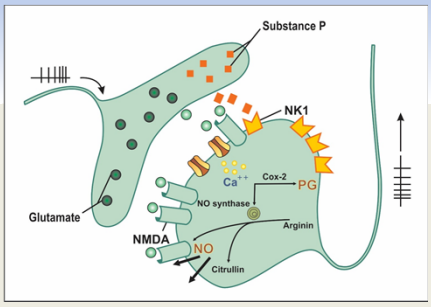


- Normal biological response
- Protects / promotes healing
- Unrelieved acute pain:
  - ↑ catecholamines
  - ↑ heart rate
  - Shallow breathing
  - Shock
  - Delayed healing
  - Nervous system effects
  - May evolve into chronic pain
- Must be treated and its cause be removed

Peripheral sensitization
Woolf in Pain, 1986



Central sensitization
Woolf in Rheum Dis Clin, 2002



Chronic pain

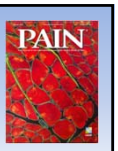
Holdcroft in Core topics in Pain, 2005

- Persists longer than the expected time for healing (>3 months)
- No "warning" function
- Underlying disease may be absent
- Pain becomes the "disease"
- Emotional / psychosocial factors important
- Complex to treat
  - Interdisciplinary approach
- Management *vs* eradication

Warning

Focussing only on pain intensity in the assessment of chronic pain patients

Sullivan in Pain, 2016



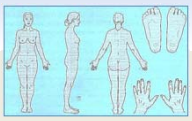
➢ Results in the strongest analgesics for the wrong patients.

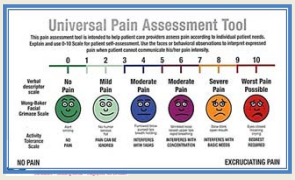
'Higher pain intensity in chronic musculo-skeletal pain mostly indicates more emotional and psychosocial factors."

Assessment of patients in chronic pain

Mackichan in Rheum Dis Clin North Am, 2008
Meyer in SA Fam Pract, 2011

- Unique and personal experience
- Personal report
- Subjective (*PQRST*)
  - DN4
- Measure





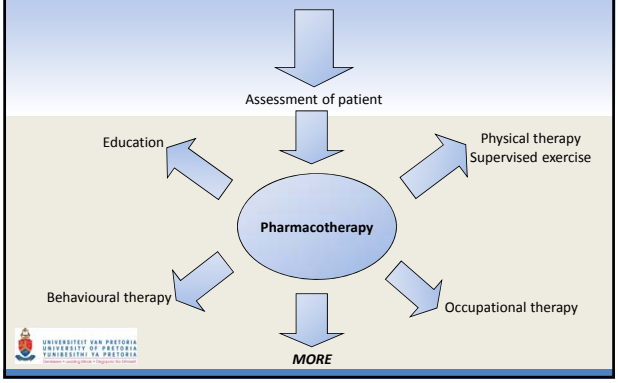
Treatment goals for chronic pain patients

Ashburn in Lancet, 1999
Meyer in SA Fam Pract, 2007

- Reduction of pain (30% is clinically significant)
- Improvement in co-morbidities (e.g. mood and sleep)
- Improve patient's functioning

Return to work

Chronic pain – multimodal approach



Pharmacotherapy

Gronow in Anaes and Int Care, 2010

Primary analgesics

- Paracetamol
- NSAID's / COX-2 inhibitors
  - *Ibuprofen*
  - *Diclofenac*
  - *Naproxen*
  - *Celecoxib*
  - *Etoricoxib, etc*
- Opioids
  - Mild
    - *Codeine*
    - *Tramadol*
  - Strong:
    - *Morphine*
    - *Hydromorphone*
    - *Buprenorphine*
    - *Oxycodone*
    - *Fentanyl*
    - *Tapentadol*

Adjuvant analgesics

- Tricyclics
  - *Amitriptyline, Cyclobenzaprine*
- SNRI's
  - *Duloxetine, etc.*
- Anticonvulsants:
  - *Carbamazepine*
  - *Gabapentin*
  - *Pregabalin*

Local anaesthetics

Diverse analgesics

- *Ketamine*
- *Cannabinoids*
- *Muscle relaxants*

Topical analgesics

- *Lidocaine patch*
- *Capsaicin patch*

New adaptation of the analgesic ladder

Vargas-Schaffer in Can Fam Phys, 2010

Chronic cancer and non-cancer pain

Acute pain
Chronic pain without control
Acute flare-up of chronic pain

STEP 1
Non-opioid analgesics
Paracetamol
NSAIDs
COX-2 inhib

STEP 2
Weak opioids
Codeine
Tramadol

STEP 3
Strong opioids

STEP 4
Nerve block
Epidurals
PCA pump

NSAIDs (with or without adjuvants at each step)

Mechanism-based pain classification

Woolf in Ann Int Med, 2009

NOCICEPTIVE PAIN
Tissue damage activates nociceptors
e.g. osteo-arthritis
surgery

Mixed pain
Both types of pain co-exist

NEUROPATHIC PAIN
Lesion or disease of nervous system

Symptoms:
Numbness
Paraesthesia
Hyperalgesia
Electric-shocks
Burning, etc

Low back pain
Cancer pain
etc

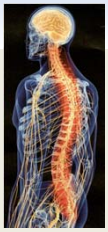
IDIOPATHIC

Neuropathic pain

Price in Clin J of Pain, 2004
Management of Pain. Philadelphia, 2006

Disease / lesion of the somato-sensory nervous system

- Diabetic polyneuropathy
- Post herpetic neuralgia
- HIV neuropathy
- Trigeminal neuralgia
- *Low back pain*
- *Chronic post-surgery pain (CPSP)*
- Mechanical compression
- Post-injury (CRPS)
- Cancer
- Chemotherapy
- Amputation ("Phantom pain")



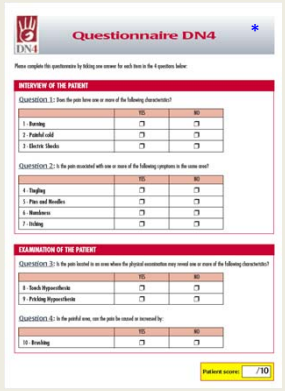
DN4

Douleur Neuropathique 4

Bouhassira et al Pain, 2005.

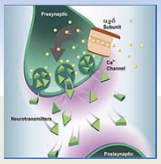
Score ≥ 4/10

Specificity: 90%
Sensitivity: 83%



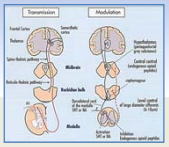
Pharmacotherapy in chronic neuropathic pain

Dworkin et al in Pain, 2007



First line

- **Antidepressants**
  - Tricyclics *(amitriptyline)*
  - SNRI's *(duloxetine)*
- **α2-δ ligands**
  - Pregabalin
  - Gabapentin



Second line

- **Tramadol**
  - Severe pain
  - Acute flare-up

Third line

- **Strong opioids**
  - Very careful patient selection
- **Cannabinoids**

Algorithm for osteoarthritis of knee

Briyere et al in Sem Arthr Rheum, 2014

Step 1: Core set

- Information / education
- Weightloss
- Exercise (aerobic, strengthening)
- Combinations of treatment

Algorithm for osteoarthritis of knee

Briyere et al in Sem Arthr Rheum, 2014

Step 2: Background treatment

Paracetamol
or
Chronic SYSADOA
(*Symptomatic Slow-acting Drugs for Osteo-arthritis*)

- *Glucosamine-sulphate*
- *Chondroitin-sulphate*

Still symptomatic: Add

Topical NSAIDS
Topical capsaicin

Refer to physio for assessment
(e.g. mal-alignment)

Algorithm for osteoarthritis of knee

Briyere et al in Sem Arthr Rheum, 2014

Step 3: Advanced pharmacological management

Oral NSAIDS / COXIBS *(Intermittently)*

Increased GI risk:
Avoid non-selective NSAIDS
COX-2 selective NSAIDS (±PPI)

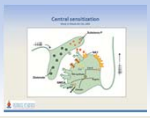
Increased CV risk:
Prefer naproxen

Increased renal risk:
Avoid NSAIDS

Intra-articular hyaluronate
Intra-articular corticosteroid

Algorithm for osteoarthritis of the knee

Briyere et al in Sem Arthr Rheum, 2014



Short-term tramadol
Duloxetine

End-stage disease

Joint replacement surgery

If contra-indicated

Strong opioid analgesics (NB: guidelines)
"Last resort"

Paracetamol

Nikles in Am J Ther, 2005
Schug in Clin Rheum, 2006
Nikles in Am J Ther, 2005
Schug in Clin Rheum, 2006

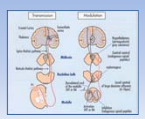
Central effect?

- *COX-2* inhibition (central prostaglandins)
- Serotonergic anti-nociceptive
- *NMDA* receptor (via NO)
- **Cannabinoid receptors**

Proven synergy
- **NSAIDs**
- **Tramadol**
- **Opioids**

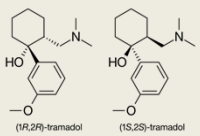
Tramadol

Cicero et al in Drug Alcohol Dep, 1999
Schug in Anaesth Int Care, 2000
Epstein et al in Biol Psych, 2006
Rafa in J Clin Pharm, 2008
Barkin in Am J Therap, 2008
Park et al in Clin Rheum, 2012
Smith et al in Drug Eval, 2013



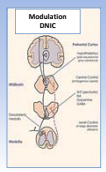
- Central acting atypical opioid
- Both mono-aminergic and opioid effects
- Also NMDA antagonist activity
- **Much less opioid receptor affinity than morphine**

Very low abuse potential (< 1/100 000)



Tramadol

Schug in Anaesth Int Care, 2000
Epstein et al in Biol Psych, 2006
Rafa in J Clin Pharm, 2008
Barkin in Am J Therap, 2008
Park et al in Clin Rheum, 2012
Smith et al in Drug Eval, 2013



- ***Pro-drug (CYP2-D-6)***
- ***Adverse effects (serotonergic)***
  - Nausea, vomiting
  - Dizziness, headache, sweating
  - Lowers convulsion threshold
  - *Serotonin syndrome (very rare)*

Analgesic combinations

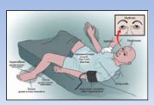
Schug in Clin Rheum, 2006

Rational combinations:

- Different receptors / mechanisms
- Improved efficacy (NNT)
- Reduced individual dosages
- Less side effects
- NB in mixed pain states

Serotonin syndrome

Boyer et al in New Eng J Med, 2005
Backley et al in BMJ, 2014
www.drugs.com (±1000 drugs)



Clinical diagnosis

- Neuromuscular:
  - *Tremor, shivering*
  - *Hyper-reflexia, ankle clonus, ocular clonus*
- Autonomic:
  - *Tachycardia, mydriasis*
  - *Sweating, hyperthermia*
- Mental:
  - *Anxious, agitation*
  - *Confusion, delirium*

High potency opioids in chronic pain

Evans in Best Practice, 2000
Russell in Pain Medicine, 2002
Niesch et al in Cochrane Rev, 2009
Noble et al in Cochrane Rev, 2010

Short term use for acute pain

End-of-life pain

Chronic non-cancer pain – controversial

- ***Morphine sulphate***
- ***Fentanyl***
- ***Oxycodone, etc***

SA Guidelines for long term high potency opioid therapy in *chronic non-cancer pain*

Raff et al in SAMJ, 2014 (Suppl)

"… appropriate and very careful patient selection and follow-up is paramount …"

- Opioid risk assessment
- Psycho-social assessment

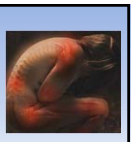
Adverse effects of opioid therapy

Raff et al in SAMJ, 2014

- Respiratory depression
- Nausea, vomiting
- Constipation
- Bladder dysfunction
- Pruritus
- Tolerance / dependence / addiction
- Endocrinological e.g. ↓ testosterone and libido
- Opioid induced hyperalgesia

Chronic widespread pain

Gran in Res Clin Rheum, 2003
Yunus in Best Pract Rheum, 2007



- ±10-12% of general population
- Mostly musculo-skeletal
- Mostly a spectrum of disorders
  - *Psychiatric disorders*
  - *Rheumatic disorders*
  - *Pain disorders*
  - *Sleep disorders*
- Fibromyalgia in 30-40% of patients with CWP

Other causes of chronic widespread pain

Daoud et al in Curr Pain and Headache Rep, 2002
Gerwin in J of Musc Skel Pain, 2004

Psychiatric disorders
- Mood disorders
- Somatoform pain disorders
- Unresolved emotional issues (*chronic anger*)

Spondyloarthritis
- Ankylosing spondylitis
- Reactive arthritis
- Psoriatic arthritis, etc.

Sleep disorders
- Primary insomnia
- Obstructive sleep apnoea
- Restless legs syndrome

Chronic fatigue syndrome

Drugs
- Opioid induced hyperalgesia (including OTC's)
- Statins
- ARV's
- Antipsychotics

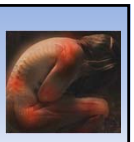
Neoplastics conditions
- Myeloma
- Metastatic breast cancer etc.

Hormonal / Metabolic
- Hypothyroidism
- Hyperparathyroidism
- Type 2 diabetis mellitus
- Iron deficiency
- Vit D deficiency

Infections
- HIV
- Tuberculosis
- "Brucellosis"

Statin-induced myalgia

Thompson et al in JAMA, 2003
Joy et al in Ann Int Med, 2009



- Up to 10% of patients on statins (rhabdomyolysis rare)
- Often long lag period
- Often generalized myalgia
  (More severe in hip- and shoulder girdles)
- Intensity varies
- Risk factors
  - ➡ *Family history*
  - ➡ *Females*
  - ➡ *Low BMI*
  - ➡ *Physically very active*
  - ➡ *Alcohol*
  - ➡ *Grapefruit*

1990 ACR classification criteria for FMS

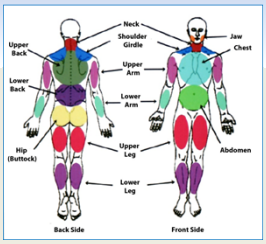
Woolfe et al in Arthr Rheum, 1990

- Widespread musculoskeletal pain > 3 months in all 4 quadrants
- ≥ 11/18 painful tender points with digital pressure of 4kg/cm²

2010 ACR diagnostic criteria for FMS

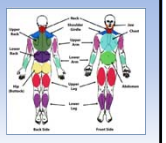
Wolfe et al in Arth Care Res, 2010

- Widespread Pain Index (WPI)
  - *19 body areas*
- Symptom Severity Scale (SS)
  - *Fatigue: 0-3*
  - *Sleep: 0-3*
  - *Cognitive: 0-3*
  - *Somatic symptoms: 0-3*
- Diagnostic
  - *WPI ≥ 7 SS ≥ 5*
  - *WPI 3-6 SS ≥ 9*
  - *At least 3 months*



Canadian guidelines for diagnosis and management of FMS

Canadian Guidelines for FMS in Rheum Arthr, 2013
Fitzcharles et al in Pain Res Manag, 2013



Recognized as a valid pain syndrome based on recent neurophysiological evidence

- ➡ Paradigm shift in diagnosis:
  - ➡ *Diagnose and manage most "concentrated" in primary care*
  - ➡ *Do not "over-investigate"*
- ➡ Not "all-or-nothing" phenomenon ***("fibromyalgia-ness")***

Emphasis on non-pharmacological strategies

Diagnosis of FMS

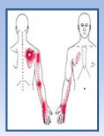
Clauw in Am J of Med, 2009
Canadian Guidelines for FMS in Rheum Arthr, 2013
Clauw in JAMA, 2014

- ➡ Physical examination *("mandatory")*
  - *Exclude other causes of widespread MSK pain*
  - *Detect peripheral pain generators*
  - ***NB:*** *Soft tissue pressure tenderness*
- ➡ Blood tests:

  "Excessive testing contributes to uncertainty and fear and worsens prognoses"
  - *FBC/ESR*
  - *CRP*
  - *TSH/T4*
  - *Creatinekinase (CK)*
  - *25-OH-D*
  - *Calcium*

Peripheral pain generators in FMS

Borg-Stein J in Rheum Dis Clin N Am, 2002
Meyer in Curr Pain Headache Rep, 2002
Bennett in Rheum Dis Clin North Am, 2002
Ablin et al in Joint Bone Spine, 2008
Clauw in J Clin Psych, 2008
Giamberardino in IASP Clin Updates, 2008
Gerwin in Phys Med Rehab Clin N Am, 2014



- *Myofascial trigger points*
- Osteo-arthritis
- Endometriosis
- Disc herniation
- Headaches
- Tendonitis
- Surgery

Treatment of FMS
Non-Medication

Goldenberg in JAMA, 2004
Pooks in Curr Opin Rheum, 2007
Clauw in J of Clin Rheum, 2007

Non-pharmacological

Strong evidence

- **Cardiovascular exercise**
- Patient education
- Cognitive behavioral therapy
- Multimodal approach

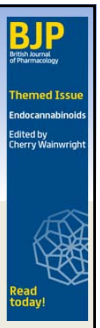
Pharmacological

Modest evidence

- Pregabalin } **FDA approved**
- Duloxetine }
- Amitriptyline
- Cyclobenzaprine
- Tramadol ± paracetamol

Cannabinoids for treatment of chronic non-cancer pain; a systematic review of randomized trials

Lynch et al in British J of Clin Pharm, 2012



20 recent good quality randomized trials:

- Cannabinoids are *modestly effective and a safe treatment option* for chronic non-cancer (*predominantly neuropathic*) pain.
- Smoked cannabis *effective* in HIV-neuropathy
- Some evidence in FM and RA
- Evidence base is growing
- Need more long-term studies