CANCER PAIN: EXPECTATIONS vs REALITY

Dr Andrew Davies FRCP
Consultant in Palliative Medicine
Royal Surrey County Hospital, Guildford

Supportive & Palliative Care Team

ESMO Designated Centers of Integrated Oncology and Palliative Care

Introduction

Pain

Pain is “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage”.

IASP, 1994

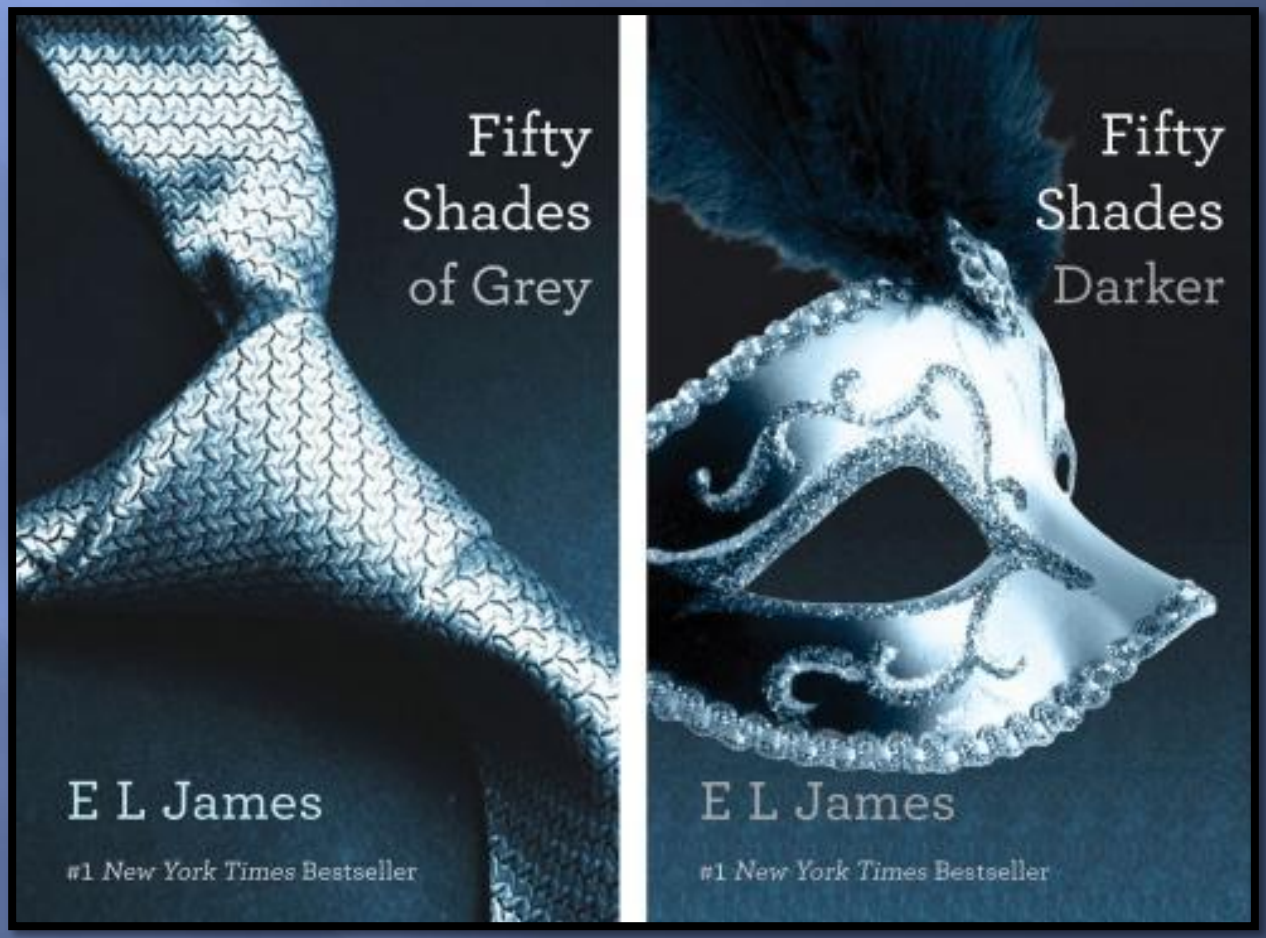
Pain

Pain

"Pain is always subjective".

IASP, 1994

Pain


Fifty
Shades
of Grey
E L James
#1 New York Times Bestseller
Fifty
Shades
Darker
E L James
#1 New York Times Bestseller

Pain

"It is unquestionably a sensation in a part or parts of the body, but it is also always unpleasant and therefore also an emotional experience".

IASP, 1994

Pain

Pain

"Many people report pain in the absence of tissue damage or any likely pathophysiological cause; usually this happens for psychological reasons. There is usually no way to distinguish their experience from that due to tissue damage if we take the subjective report. If they regard their experience as pain, and if they report it in the same ways as pain caused by tissue damage, it should be accepted as pain".

IASP, 1994

Epidemiology

Epidemiology

review

Annals of Oncology 18: 1437–1449, 2007
doi:10.1093/annonc/mdm056
Published online 12 March 2007

Prevalence of pain in patients with cancer: a systematic review of the past 40 years

M. H. J. van den Beuken-van Everdingen[1]*, J. M. de Rijke[1], A. G. Kessels[2], H. C. Schouten[3], M. van Kleef[4] & J. Patijn[1]

[1]Pain Management and Research Centre, University Hospital Maastricht; [2]Department of Clinical Epidemiology and Medical Technology Assessment, University Hospital Maastricht; [3]Department of Internal Medicine, University Hospital Maastricht; [4]Department of Anaesthesiology, University Hospital Maastricht, PO Box 5800, 6202 AZ Maastricht, The Netherlands

Received 18 December 2006; revised 11 January 2007; accepted 12 January 2007

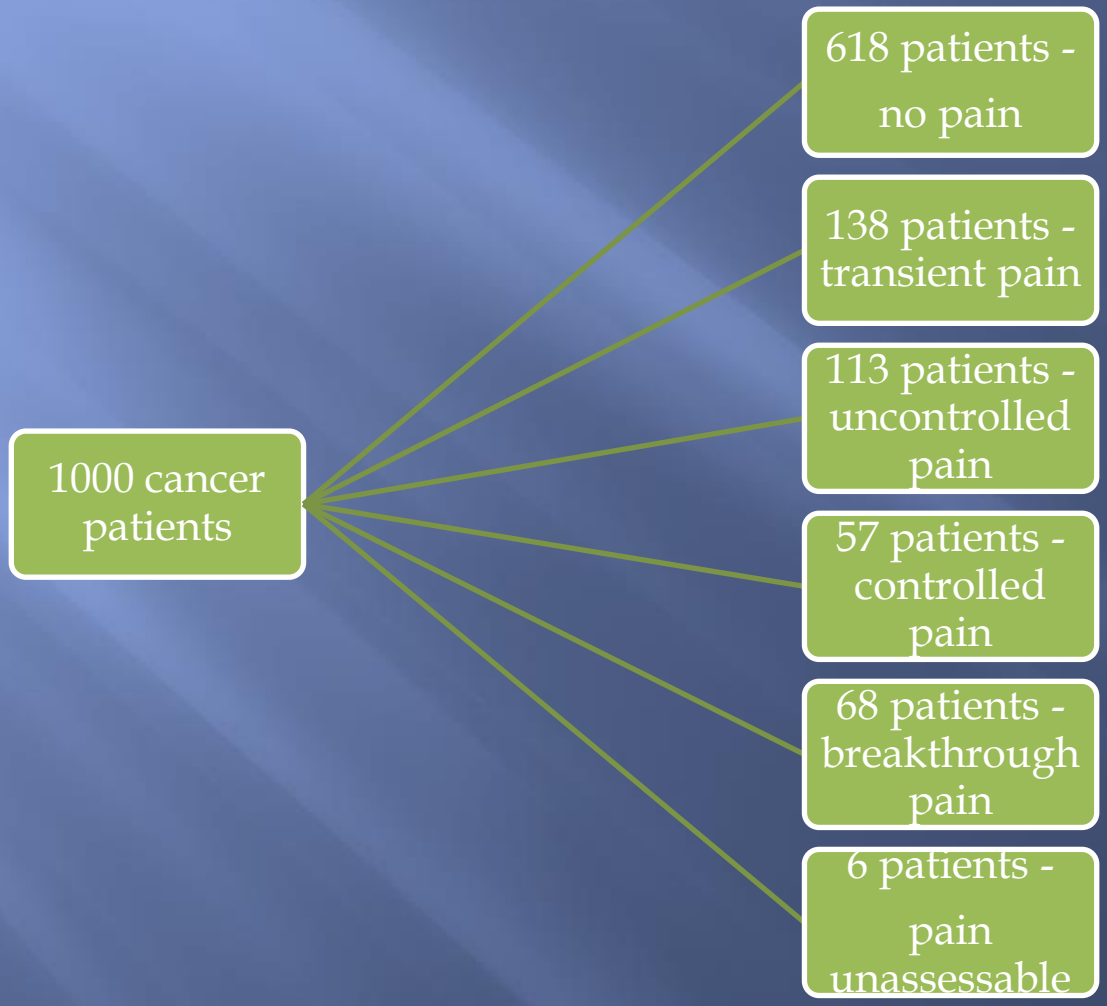
Epidemiology

PATIENT GROUP	PREVALENCE PAIN
Patients with cancer (mixed group)	53% [95% CI: 43-63%]
Patients with advanced cancer	64% [95% CI: 58-69%]
Patients receiving anticancer Rx	59% [95% CI: 44-73%]
Patients following anticancer Rx ("curative" Rx)	33% [95% CI: 21-46%]

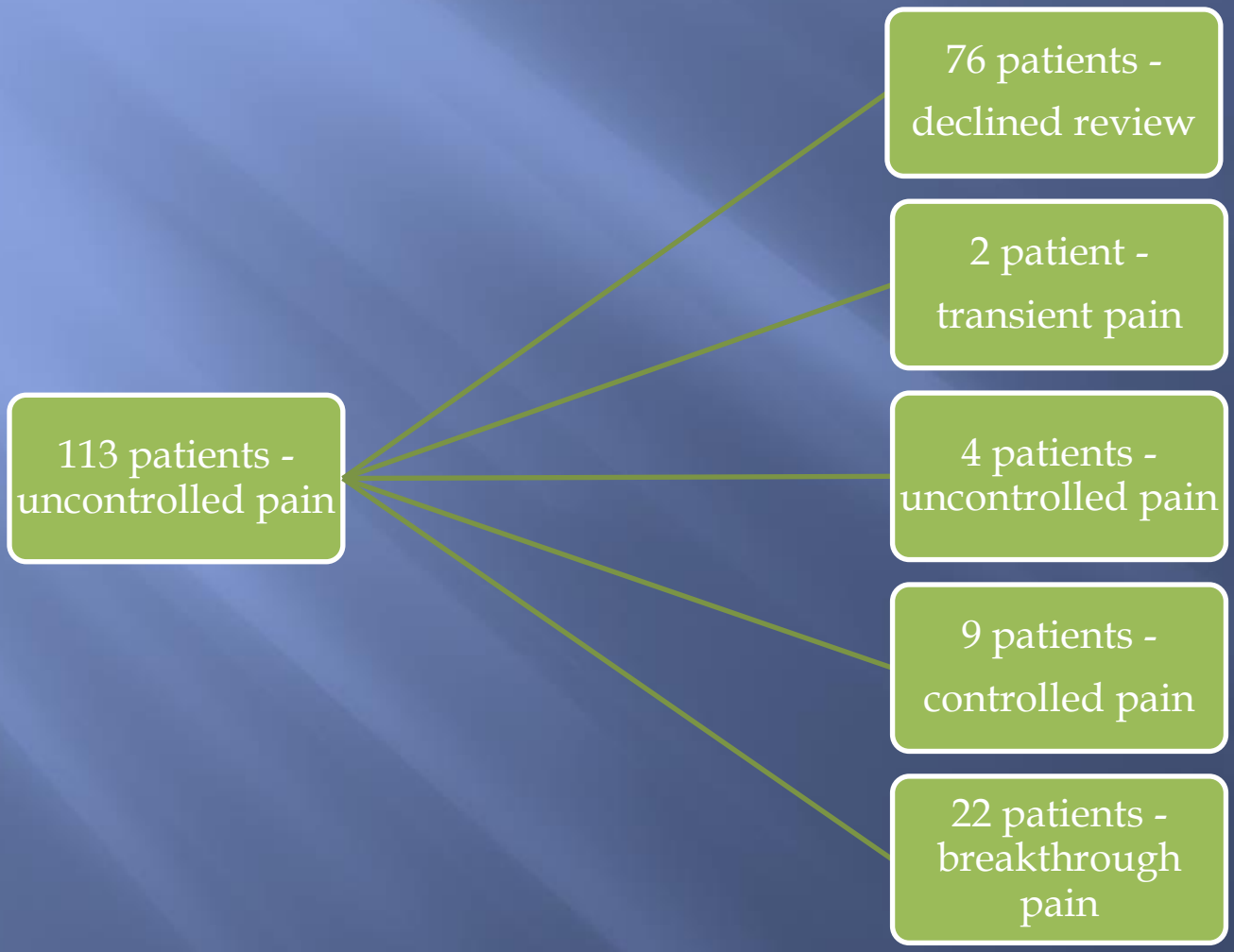
Epidemiology

"More than one-third of the patients with pain in the reviewed articles graded their pain as moderate or severe."

Epidemiology



Epidemiology



Aetiology

Pain

Cause of pain	Frequency
Cancer	92.5%
Cancer treatment	20.8%
Unrelated cancer	2.3%

Caraceni, 1999

Pain

Type of pain	Frequency
Nociceptive	58.3%
Neuropathic	7.7%
Mixed	32.1%
Psychogenic	1.8%
Unknown	1.7%

Caraceni, 1999

Pain

"Activity induced in the nociceptor and nociceptive pathways by a noxious stimulus is not pain, which is always a psychological state, even though we may well appreciate that pain most often has a proximate physical cause".

IASP, 1994

Pain

PAIN IN MEN WOUNDED IN BATTLE

LT. COL. HENRY K. BEECHER, M.C., A.U.S.

CONSULTANT IN ANESTHESIA AND RESUSCITATION, MEDITERRANEAN THEATER OF OPERATIONS

THERE IS A COMMON BELIEF that wounds are inevitably associated with pain, and, further, that the more extensive the wound the worse the pain. Observation of freshly wounded men in the Combat Zone showed this generalization to be misleading. If one may speak of such a subjective experience as pain in exact terms, the generalization can be said to hold in only about one-quarter of severely wounded men; it fails in the remaining three-quarters. There are practical reasons for examining this problem, for a clear appreciation of its nature will lead to improved treatment of the distress of the wounded.

The widespread tendency to serious error in the employment of one of the most useful drugs in medicine, morphine, also suggested that the treatment of pain in wounded men needed to be reviewed. An opportunity to do this was made possible during the prolonged action on the Venafro and Cassino Fronts and later at the Anzio Beachhead and in France.

Pain

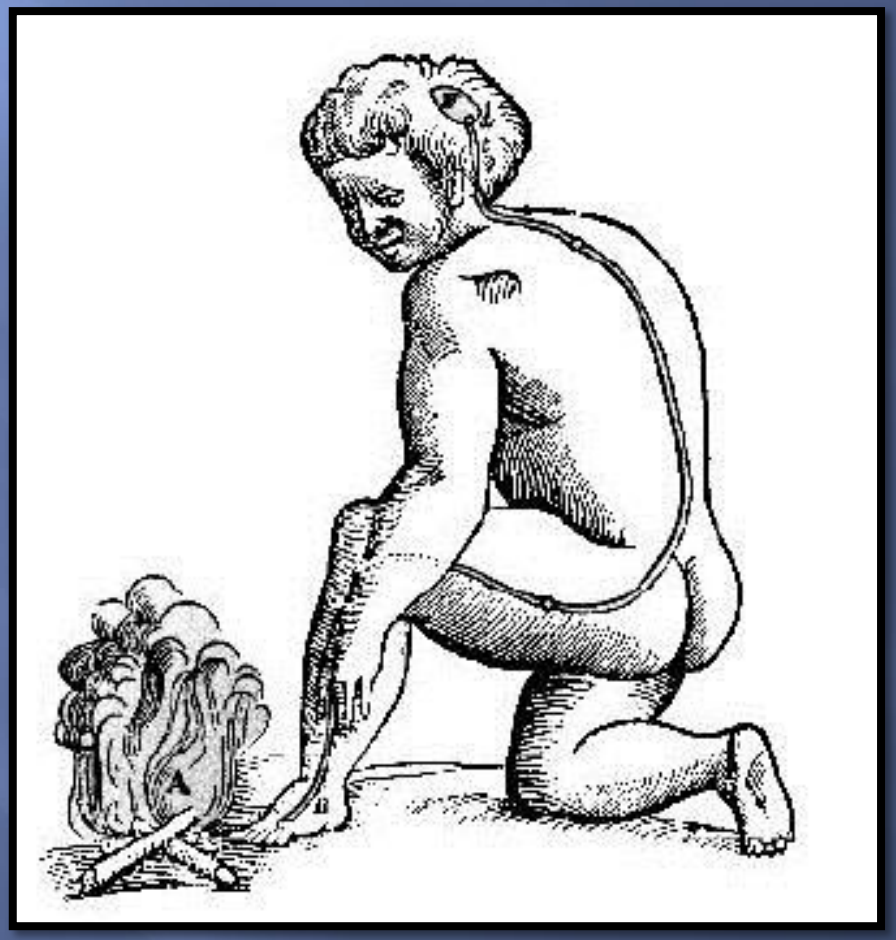
TABLE I

215 PATIENTS WITH MAJOR WOUNDS

(Standard Errors of the Mean are Shown)

Type of Wound	Compound Fractures of Long Bones	Extensive Soft-tissue Wounds	Penetrating Wounds of Thorax	Penetrating Wounds of Abdomen	Penetrating Wounds of Cerebrum
Number of pts.	50	50	50	50	15
Pt's age (yrs.)	24.8 ± 0.9	24.5 ± 1.1	24.5 ± 0.8	22.7 ± 0.6	25.1 ± 1.4
Time since wounding (hrs.)	12.5 ± 1.3	11.3 ± 1.4	9.8 ± 1.0	7.2 ± 0.7	7.9 ± 1.4
Avg. total dose of morphine (mg.)	1 pt.: none* 49 pts. avgd. 27.0 ± 1.5	11 pts.: none* 39 pts. avgd. 27.0 ± 2.7	11 pts.: none* 39 pts. avgd. 25.0 ± 1.8	5 pts.: none* 45 pts. avgd. 29.0 ± 2.2	8 pts.: none* 7 pts. avgd. 19.8 ± 4.2
Avg. latest dose of morphine (mg.) (spread as above)	22.6	19.5	21.2	25.0	19.8
Time since latest morphine (hrs.)	7.0 ± 0.8	7.2 ± 0.6	6.5 ± 0.6	4.8 ± 0.7	6.2 ± 1.5
Pain (degree). (Number of pts. in each group)	19 none 12 slight 7 moderate 12 bad	19 none 15 slight 8 moderate 8 bad	15 none 18 slight 11 moderate 6 bad	7 none 5 slight 14 moderate 24 bad	9 none 5 slight 0 moderate 1 bad
Further pain relief therapy wanted (pts.)	11 yes 39 no	9 yes 41 no	10 yes 40 no	27 yes 23 no	1 yes 14 no

Pain

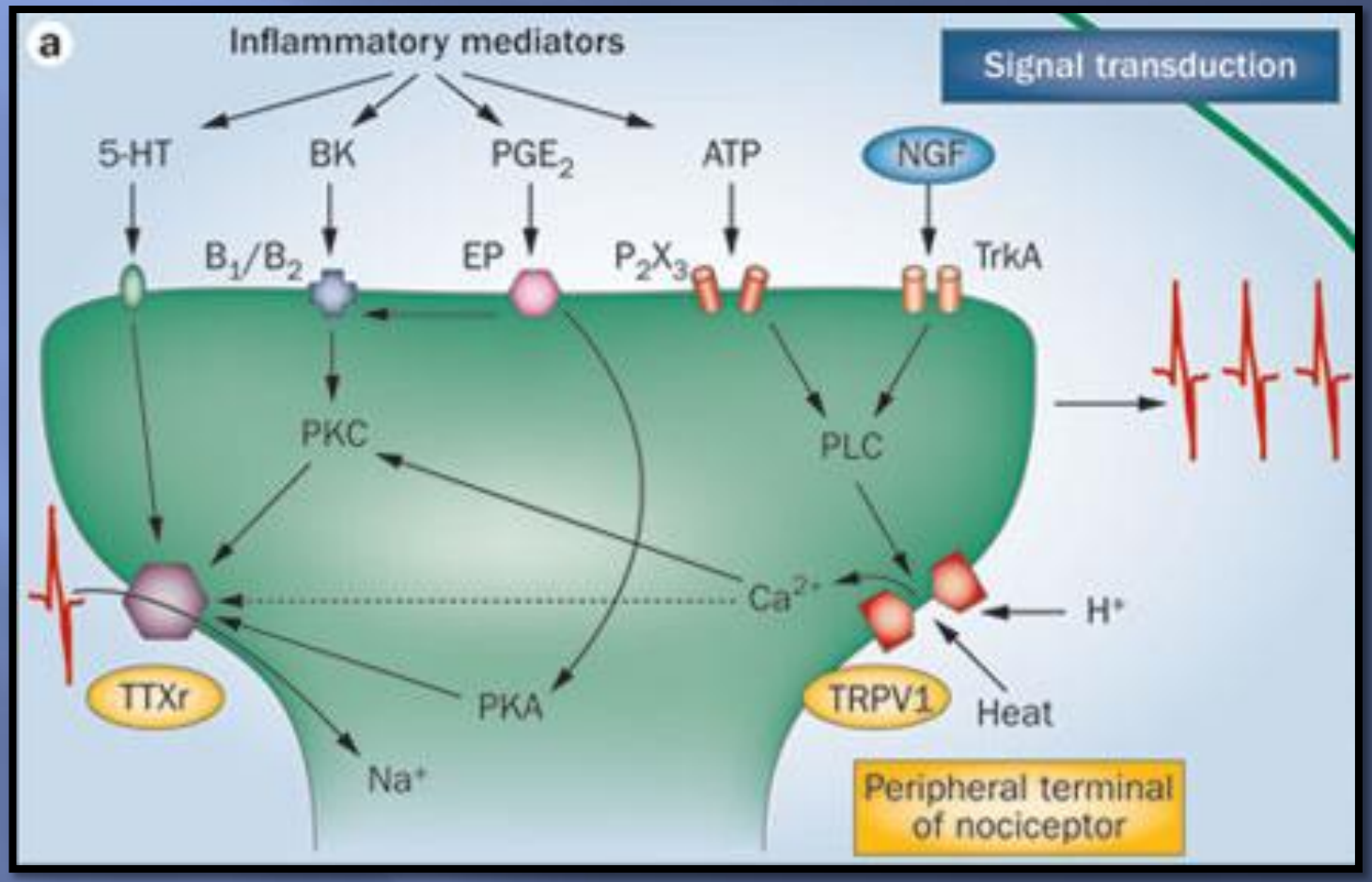


Pain

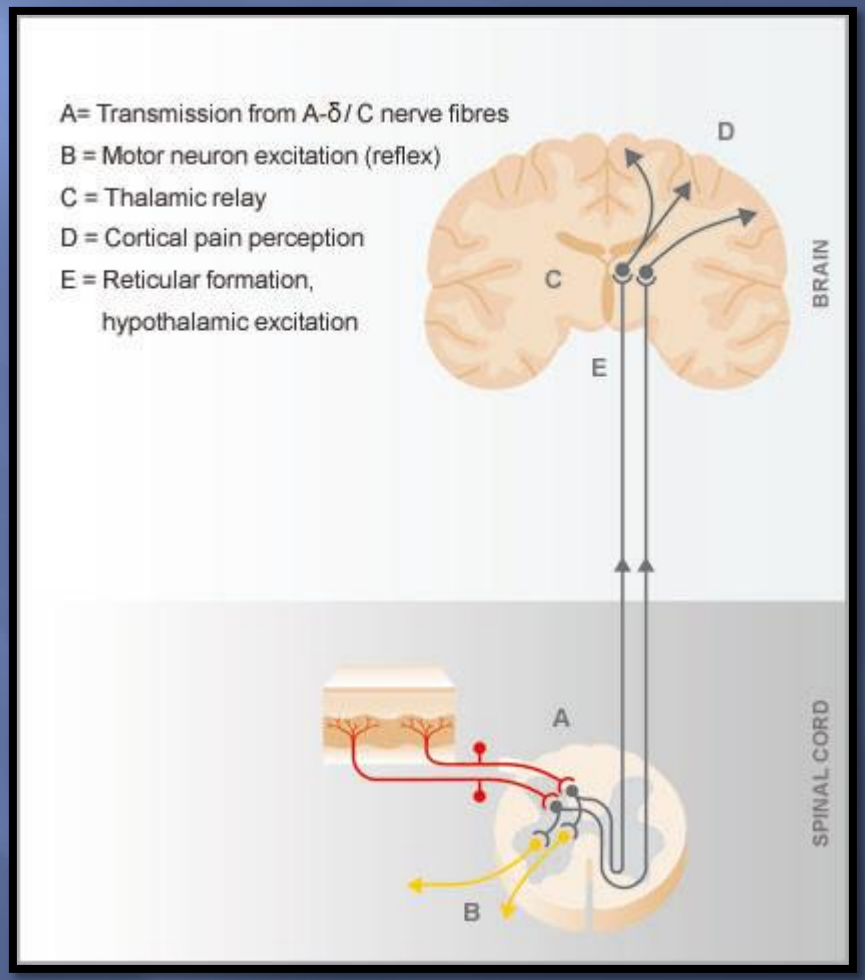
Nociception:

- Transduction
- Transmission
- Modulation (up / down)
- Perception

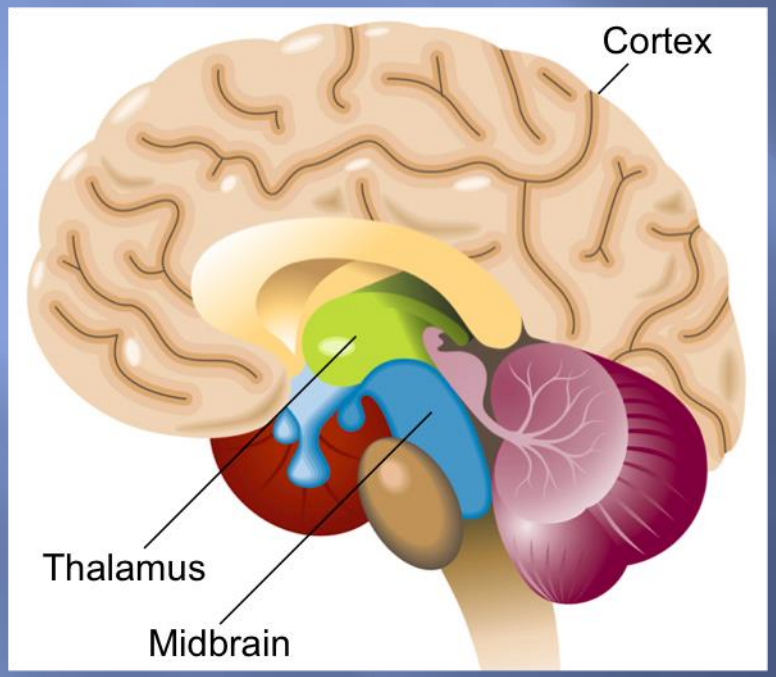
Pain


a
Inflammatory mediators
Signal transduction
5-HT
BK
PGE2
ATP
NGF
B1/B2
EP
P2X3
TrkA
PKC
PLC
Ca2+
H+
TTXr
PKA
TRPV1
Heat
Na+
Peripheral terminal of nociceptor

Pain


A= Transmission from A-δ / C nerve fibres
B = Motor neuron excitation (reflex)
C = Thalamic relay
D = Cortical pain perception
E = Reticular formation,
hypothalamic excitation
D
C
E
BRAIN
A
B
SPINAL CORD

Pain



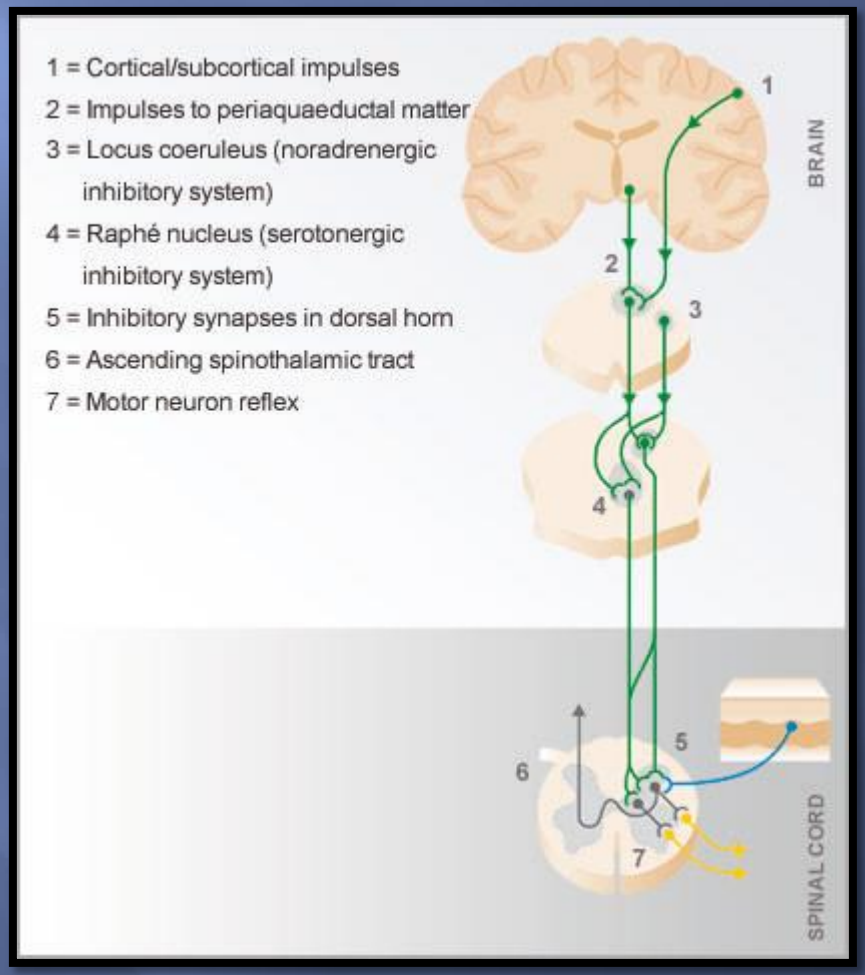
Thalamus - "relay station"

Limbic system – involved in regulation of pain threshold; governs emotional response to pain

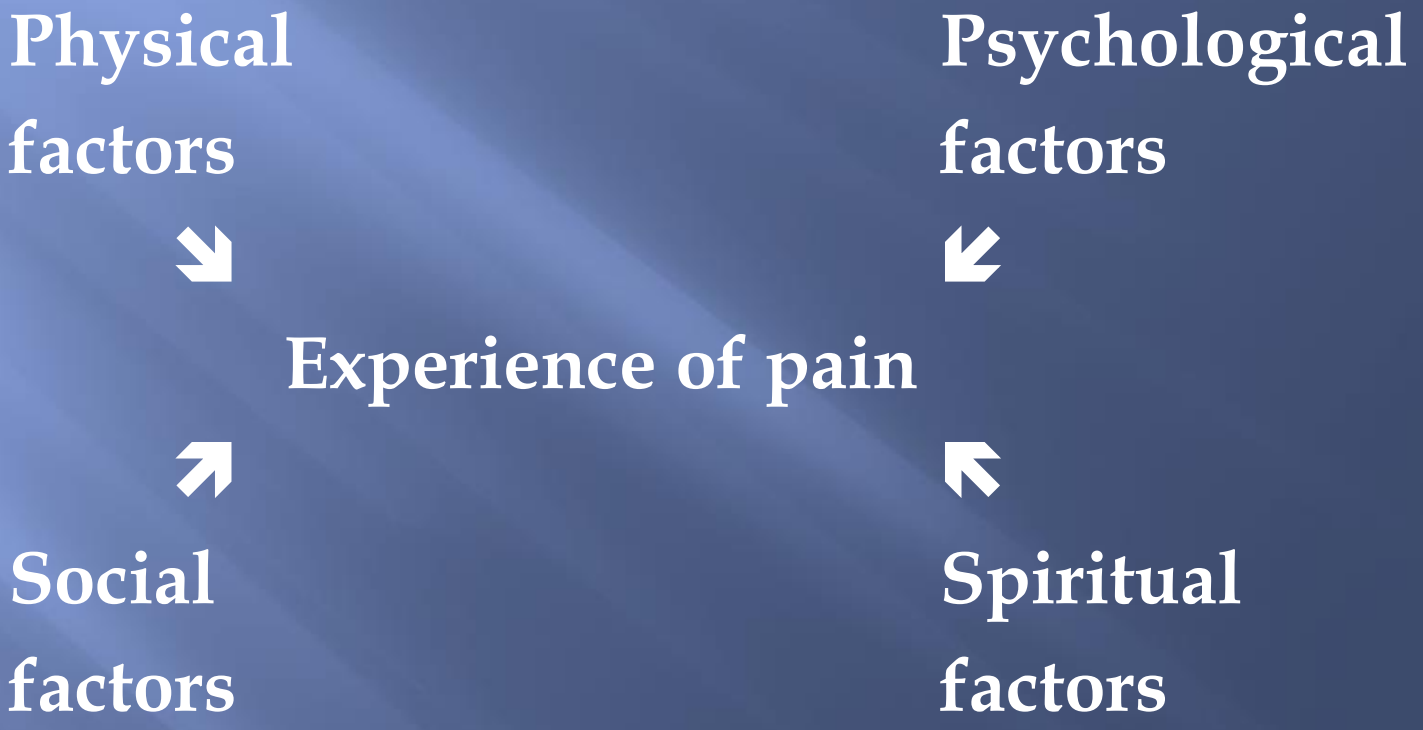
Periaquaeductal grey – involved in modulation of pain

Cerebral cortex – involved in perception of pain

Pain


1 = Cortical/subcortical impulses
2 = Impulses to periaquaeductal matter
3 = Locus coeruleus (noradrenergic inhibitory system)
4 = Raphé nucleus (serotonergic inhibitory system)
5 = Inhibitory synapses in dorsal horn
6 = Ascending spinothalamic tract
7 = Motor neuron reflex
BRAIN
SPINAL CORD

Pain


Physical factors
Psychological factors
Experience of pain
Social factors
Spiritual factors

Pain

"The second principle developed in the early work at St. Joseph's was that 'We have to consider the whole person'. This emphasis led by 1964 to the concept of 'total pain', the complex of physical, psychological, social and spiritual elements that make up the patient's whole experience and that has proved important in the development of this specialty".

Saunders, 1978

Clinical features

Clinical features

"You can't find it [inner peace] in that darkness of pain...I can't emphasize that the pain blinds you to all of that, blinds you to all that's positive. I mean the real bad pain…it just closes you down. You just can't get through it…it's an iron door and it's one thing you don't wanna go through…you just wanna, wanna stop"

Coyle, 2004

Clinical features

Complications:

- Physical
  - direct
  - indirect
- Psychological
- Social
- Health economic

- [↑ Mortality]

Clinical features

Sensitization:

Increased responsiveness of nociceptive neurons to their normal input, and / or recruitment of a response to normally subthreshold inputs.

Sensitization can include a drop in threshold and an increase in suprathreshold response. Spontaneous discharges and increases in receptive field size may also occur. Clinically, sensitization may only be inferred indirectly from phenomena such as hyperalgesia or allodynia.

Management

Management

"Cancer pain can be controlled with simple treatments in more than 80% of cases. In the remaining 20%, it is important to use a multidimensional approach that includes a careful reassessment of the pain syndrome and the use of second line agents and / or nonpharmacological interventions".

Bruera, 2003

Barriers

Barriers to pain control:

- Government / society
- Healthcare system
- Healthcare professionals
- Patients
- Carers
- Pain-related factors

Barriers (patient)

Reluctance to report pain:

- Desire to be a "good patient"
- Concerns about distraction
- Concerns about meaning

Reluctance to take medication:

- Concerns about side effects
- Concerns about addiction

Barriers (patient)

Misconceptions:

- Fatalism
- Concerns about tolerance

Other issues:

- Miscommunication
- Polypharmacy
- Practical issues
- Carer concerns

Barriers (pain)

Edmonton Classification System for Cancer Pain

- Pain mechanism (neuropathic pain)
- Incident pain
- Psychological distress
- Addictive behaviour
- Cognitive function
- [Pain intensity]

Barriers

Heath care professionals

- Education*
  - Increase in knowledge
  - Change in opinion
  - ? Decrease in pain intensity

- Co-ordination of management

- Support from pain specialists

Barriers

Patients

- Education*
  - Increase in knowledge
  - Change in opinion
  - Increase in adherence
  - Decrease in pain intensity
- Support from health care professionals
- Engagement of carers

Barriers

Pain

- Assessment*
  - adequate assessment
  - assessment tools*

- Treatment*
  - appropriate treatment
  - protocols / algorithms*
  - pain-specific treatments*

Barriers

Barriers

Pain

- Re-assessment

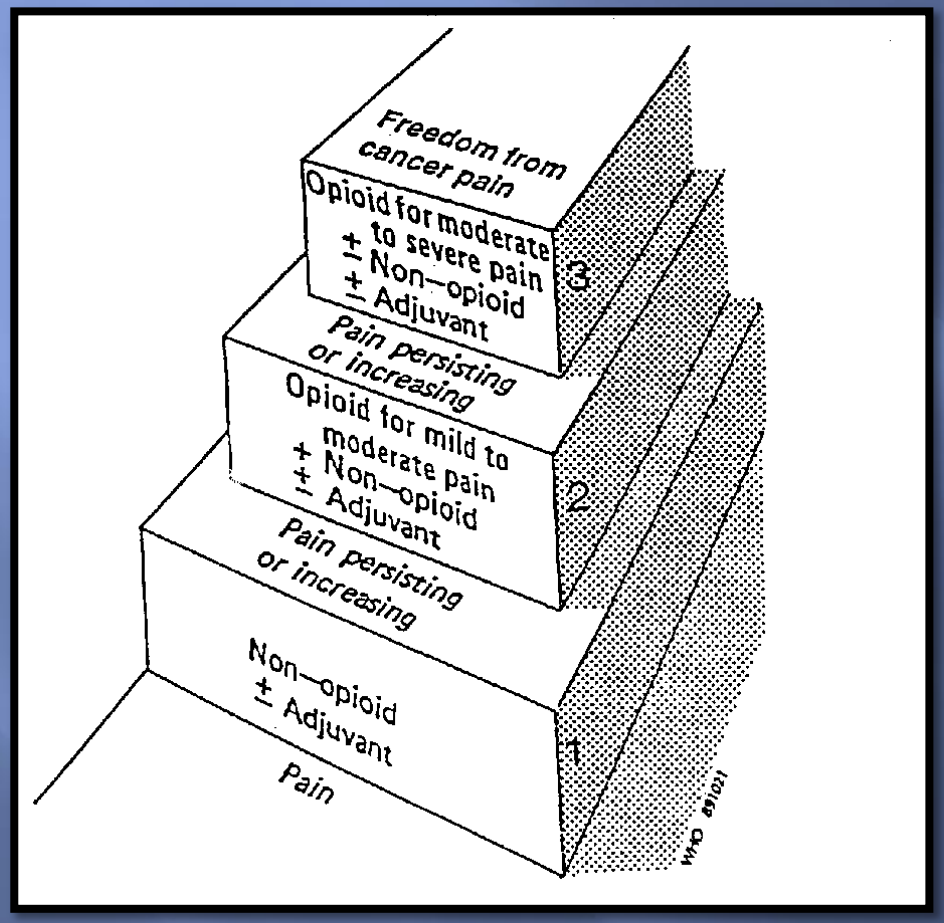
  - adequate re-assessment

- Referral*

  - assessment*

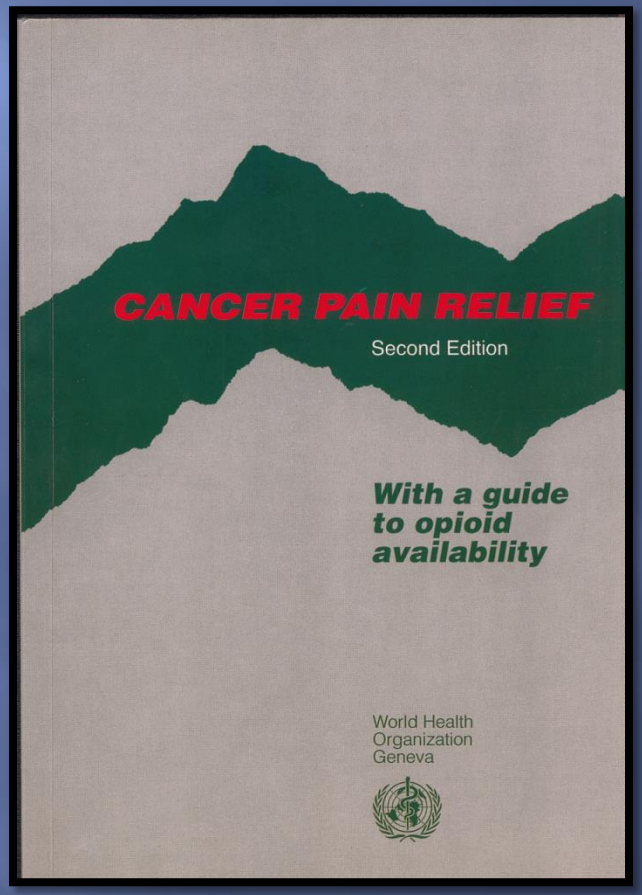
  - treatment*

Management



- "By mouth"
- "By the clock"
- "By the ladder"
- "For the individual"
- "Attention to detail"

Management


CANCER PAIN RELIEF
Second Edition
With a guide to opioid availability
World Health Organization
Geneva

Management

review

Annals of Oncology 19: 1985–1991, 2008
doi:10.1093/annonc/mdn419
Published online 15 July 2008

Prevalence of undertreatment in cancer pain. A review of published literature

S. Deandrea[1,2*], M. Montanari[3,4], L. Moja[5] & G. Apolone[3,4]

[1]Laboratory of Epidemiological Methods, Department of Epidemiology, Mario Negri Institute for Pharmacological Research, Milano; [2]Department of Epidemiology, Institute of Medical Statistics and Biometry, University of Milano, Milano; [3]Center for the Evaluation and Research on Pain, Department of Oncology, Mario Negri Institute for Pharmacological Research, Milano; [4]Laboratory of Translational and Outcome Research, Department of Oncology, Mario Negri Institute for Pharmacological Research, Milano; [5]Department of Oncology, Italian Cochrane Centre, Mario Negri Institute for Pharmacological Research, Milano

Received 5 March 2008; revised 2 June 2008; accepted 9 June 2008

Management

"Our analysis of 26 relevant studies showed that 43% of cancer patients have a negative PMI [Pain Management Index] score: nearly one of two patients is undertreated".

Management

Articles

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup, Nadine Attal*, Sindhu Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace*

Lancet Neurol 2015; 162–73

Published Online January 7, 2015

http://dx.doi.org/10.1016/S1474-4422(14)70251-0

See Comment page 129

Summary

Background New drug treatments, clinical trials, and standards of quality for assessment of evidence justify an update of evidence-based recommendations for the pharmacological treatment of neuropathic pain. Using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE), we revised the Special Interest Group on Neuropathic Pain (NeuPSIG) recommendations for the pharmacotherapy of neuropathic pain based on the results of a systematic review and meta-analysis.

Management

DRUG / GROUP OF DRUGS	NNT
TCAs	3.6
Strong opioids	4.3
Tramadol	4.7
SNRI (duloxetine)	6.4
Gabapentin	7.2
Pregabalin	7.7

Conclusion

Conclusion

"Once the pain was relieved it was the most beautiful experience of my life, to be able to participate and control the pain".

Coyle, 2004