FACULTY OF PAIN MEDICINE
AUSTRALIAN AND NEW ZEALAND COLLEGE OF ANAESTHETISTS
ABN 82 055 042 852

EXAMINATION HELD ON 4th then 26th NOVEMBER 2016

at regional centres (4 Nov 2014) then at AMC National Test Centre, Melbourne, Victoria.

THIS REPORT IS PREPARED TO PROVIDE CANDIDATES AND SUPERVISORS OF TRAINING WITH INFORMATION ABOUT THIS EXAMINATION AND TO ASSIST WITH PREPARATION FOR FUTURE EXAMINATIONS. THE EDUCATIONAL RESOURCE CONCERNING EACH WRITTEN QUESTION IN APPENDIX A IS NOT A MODEL ANSWER FOR THE QUESTION. THE INFORMATION CONTAINED IN EACH WILL BE MORE INFORMATION THAN COULD BE COVERED IN THE FIFTEEN MINUTES. THE INFORMATION PROVIDED IS CONSIDERED CURRENT AND EVIDENCE-BASED, BUT MAY BE SUBJECT TO CHANGE IN THE FUTURE.

CANDIDATES SHOULD DISCUSS THE REPORT WITH THEIR MENTORS SO THAT THEY MAY PREPARE OPTIMALLY FOR FUTURE EXAMINATIONS.

The Examination is an integral part of the pain medicine training program, leading to the award of Fellowship of the Faculty of Pain Medicine.

The 2015 Curriculum guides the range of content which may be assessed.

The Examination consists of written and oral sections and covers the theory and practice of pain medicine.

It is acknowledged that standardisation of the assessment process across the candidature is imperfect, vulnerable to an array of potential confounders. The Faculty of Pain Medicine attempts to optimise the accuracy and fairness of the examination process by including multiple assessment points, ensuring that all stages are assessed by a pair of examiners. Where possible, members of the Court of Examiners are paired such that an examining duo will come from different primary specialties and different geographical locations.

The 2016 FPM Examinations were observed by Dr Michael Jones, Chairman of Examinations, ANZCA.

1. EXAMINATION — OVERALL PASS RATE 67%

This year, 24 candidates presented for the examination and 16 were successful.

2. WRITTEN SECTION

See Appendix A for the educational resources regarding each question.

General information:
Always, candidates need to:

1. *Answer the question.*
2. Plan the answer in a logical fashion and demonstrate an organised approach.
3. Give succinct answers and avoid repetition.
4. Use headings and dot points if asked to list or discuss briefly.
5. Give definitions of specialist terms (e.g. neuropathic pain, placebo response or breakthrough analgesia). Examiners are unable to assume understanding or meaning of a particular term without clear definition. Similarly for abbreviations.
6. Start answer with "I would do…" if asked to "outline your approach to…"

Candidates were required to answer ten compulsory questions of equal mark value. Where there were more than one section to the question, all sections were to be answered.

General comments: Candidates should endeavour to introduce their responses with accurate definitions of the pivotal terminology in the question. Consideration of the broad sociopsychobiomedical aspects of the question must be provided. As always legibility of responses continues to challenge the markers. Needless to say, there is no substitute for a sound knowledge of the subject matter.

As has occurred with all recent sittings, many answers lacked the sophistication expected of specialist pain medicine physicians. Once again, there was concern about the lack of knowledge in some key and basic areas given the candidates are supposed to be specialists in the area and know more than the referrer. **It remains apparent that the trainees are not digesting the content of recent journals, nor is adequate priority being accorded to on-line resources provided by the Faculty, including the curriculum and training handbook.**

Candidates are reminded to read the questions carefully, and to attempt to write legibly.

Many candidates continue to use generic templates to answer questions, and whilst these are not specific to task, they are then poorly adapted to it.

Abbreviations always, and specific medical terms generally, require definition when used for the first time.

* * *

Question 1 (92%) successful

1. Define 'Opiate Tolerance'.
2. How does it develop?
3. When admitted for total knee replacement patient, what preoperative strategy do you give a 57 year old opiate tolerant man with failed back surgery syndrome?

Question 2 (79%) successful

Describe how you distinguish clinically between active visceral nociception, visceral hyperalgesia, and referred pain.

Question 3 (79%) successful

What information would you include in a submission aiming to inform about over-the-counter (OTC) availability of codeine-containing analgesics79

Question 4 (46%) successful

Discuss the diagnosis and management of a patient with Post Traumatic Stress Disorder (PTSD) and persistent pain

Question 5 (58%) successful

Write brief notes on the main concepts involved in culturally responsive care in pain management for patients from diverse backgrounds.

Question 6 (67%) successful

In a patient with renal or hepatic impairment, the changes may affect the pharmacokinetics of analgesics prescribed.
Summarise the key changes and indicate how they might influence your choice and/or the dose of medications used for pain management in these patients.
Include both opioid and non-opioid drugs in your answer

Question 7 (63%) successful

Your tertiary pain management centre needs to improve community access and reduce waiting times to your pain services.

a) What are the issues to consider?
b) What strategies can be used to address these problems?

Question 8 (79%) successful

Write short notes on the use of Lidocaine in the management of pain

Question 9 (58%) successful

A 22 year old sales clerk is referred to you by a neurologist with "medically unexplained" pain, weakness and numbness of the entire left "hemi-body" after a minor motor vehicle accident two years ago. She is wheelchair bound and holds her left hand in a claw-like posture.
Describe your approach to assessment and management of this patient.

Question 10 (4 %) successful

The number needed to treat (NNT) has become widely utilised to compare the efficacy of chronic pain treatments.

1. Define NNT
2. Outline the potential problems associated with its calculation and interpretation
3. A systematic review of clinical trials of morphine establishes the NNT is 2.5 (95% confidence interval 1.82 - 4.0). Explains what this confidence interval means and why is it important.

3. VIVA VOCE SECTION (88 %)

In accordance with the Faculty of Pain Medicine Training Handbook, in the course of the examination day each candidate was required to undertake 8 *viva voce* stations of 15 minutes each, undertaken in two rounds of four vivas each. Each viva attracted equal marks.
The following qualities were assessed:

- clinical judgement
- the application of principles of acceptable and safe pain medicine practice
- prioritisation
- interpretation of complex clinical situations
- an ability to make decisions based on changing clinical situations
- anticipation of clinical actions and their sequelae
- effective communication.

Actors were utilised in some stations. Examiners in-training observed in some stations.

3.1 OBSERVED STRUCTURED CLINICAL EXAMINATION (OSCE) PASS RATE (88 %)

This section consisted of four highly structured viva voces which were carefully scripted to assess specific educational objectives.

OSCE1:
You are called to see a 44 year old patient in the surgical ward who had a L4-5/S1 spinal fusion the day before. The patient started to complain of increasing pain around 0300 hrs that did not seem to be covered well enough with the Patient Controlled Analgesia (PCA).

The overnight anaesthetic registrar was called and increased the PCA bolus dose at 0600 hrs. Since then, the patient's pain has seemed to increase even more rapidly and is now reported as 8/10 at rest.

The patient had a previous surgery: an L4/5 laminectomy 2 years ago and says he/ she was taking only paracetamol, amitriptyline and gabapentin prior to admission.

Please outline the brief pain history you would obtain from the patient?

OSCE 2:
You have been referred a 56-year-old woman who has had widespread pain for 20 years. She saw a rheumatologist 1 year ago who diagnosed Rheumatoid Arthritis. She was rheumatoid factor positive with a titre of more than 100 in addition to being anti-CCP positive. She is now on Abatacept injections after not responding to three months of methotrexate. Her inflammatory markers are all now completely normal

Past history of Hypertension and Obesity with borderline Blood Sugar Levels. She admits with time weight gain.

On examination she has widespread tenderness in all four quadrants. Her MCP joints are tender but not swollen and no more tender than other joints of her hands.

This case study will focus on her management.

How do you interpret her presentation?

OSCE 3:
As a Specialist Pain Medicine Physician, you are asked by a local GP to consult on a 38-year-old woman

called Jodie, who has presented with a history of increasingly severe and disabling bifrontal headache for the past three weeks.

She is a smoker but otherwise in good general health. She has had intermittent lumbar pain in the last six months, which has been put down to her work as a clothes retailer.

Please consider your clinical approach to the assessment of this patient.

OSCE 4:
Mr Smith is a 45 year old man from interstate seeking the continuation of medication for the management of his chronic abdominal pain. He has moved to your city to live with his girlfriend.

He claims to be on OxyContin 80mg TDS prescribed by his previous GP. He brought a letter from the GP to you stating his GP could not be contacted as he was on holiday.

Mr Smith was 20 minutes late to his initial appointment scheduled for 0900. He apologised to you for being late stating the bus was delayed. Your impression was that this man's breath smelt of alcohol.

What is your differential diagnosis for this man's abdominal pain?

3.2 STRUCTURED ORAL VIVAS PASS RATE (92 %)

VIVA 1
A 43 year old woman presents to you as an outpatient for pain management. 12 months ago she presented for a micro-discectomy at C5/6 because of a herniated intervertebral disc causing a left C6 radiculopathy. Following this operation the patient awoke quadriplegic and has remained so. She complains of ongoing chronic pain and spasticity in the neck, trunk and all 4 limbs.

What is the prevalence of chronic pain following spinal cord injury?

VIVA 2
Your patient reports to you that your trainee is being bullied by your co-worker.

How is workplace bullying defined?

VIVA 3
A patient who warrants but refuses palliative care for pancreatic carcinoma and assertively requests that they want pain control via coeliac plexus block.

Re Ashley Brown DOB 24/4/1969 Leawarra Way Clifton Beach VIC 3245
Dear Dr,
Many thanks for seeing Ashley who has had a recent diagnosis of carcinoma of the pancreas. He was not a suitable candidates for a Whipple's procedure and we are currently undertaking some palliative chemotherapy (Gemcitabine, 5-fluorouracil (5-FU) Oxaliplatin). His pain is being managed by his GP with OxyContin, pregabalin and some endone. He is unwilling to consider palliative care at the moment however would like to discuss the possibility of a coeliac plexus block with you. He has developed some uncomfortable peripheral neuropathy also.
Ashley is a teacher married with two children aged nine and 13. Obviously this recent devastating diagnosis has been a shock to him and his family.

VIVA 4

35-year-old man admitted to hospital 1 week ago following an aircraft crash. He sustained 3rd degree fuel burns to 40 % of his body (torso and legs). Four days ago, he had surgical debridement of this injury. He requires daily dressings on the burns ward for the next 2 weeks.

What are your first priorities in this situation?

4. OVERALL EXAMINATION COMMENTS:

The Faculty has continued working towards optimised assessment processes, which enquire into the competence with which the candidates have mastered the 2015 Curriculum.

Written short answer questions were chosen from across the curriculum, and the viva voces were carefully designed to ensure, as much as was possible, the full breadth of the subject material was examined.

The FPM Examinations Committee remains concerned that some areas of the curriculum are not well understood. Practice of an organised approach to tasks is essential both for success in the examination but more importantly for clinical practice. So as to improve overall performance in the vivas, candidates are encouraged to practice synthesising impromptu responses and presenting these in an organised fashion, such as to display one's ability to discuss intelligently and maturely a wide range of relevant topics.

The Court of Examiners acknowledges the External Observer for 2016, Dr Michael Jones, ANZCA Councillor and Chair Examinations (ANZCA) who provided valuable reflections on the examination processes.

I am most grateful for the support and assistance provided by the Faculty staff, both in Melbourne and the regions, as well as the team at the AMC Assessment Centre. In particular I gratefully acknowledge the tremendous generosity of self which has been provided by the members of the Examination Committee and the Court of Examiners.

5. THE BARBARA WALKER PRIZE / CERTIFICATES OF MERIT

The Barbara Walker prize was not awarded for the 2016 examination.
Certificates of Merit were awarded to Dr Anthony Carrie (NZ), Dr Megan Eddy (VIC), Dr Irina Hollington (SA) and Dr Alan Nazha (NSW).

NEWMAN L. HARRIS
Chairman

GRETA M. PALMER
Deputy Chair

February 2017

2016 FPM WRITTEN EXAMINATION
APPENDIX A

An educational resource regarding the written short answer questions is appended to the report as follows.

Question 1

4. **Define 'Opiate Tolerance'.**
5. **How does it develop?**
6. **When admitted for total knee replacement patient, what preoperative strategy do you give a 57 year old opiate tolerant man with failed back surgery syndrome?**

Definition:

A common clinical observation in patients receiving opioid medication is the need to escalate opioid dose over time to maintain adequate analgesia. This is commonly attributed to the development of tolerance to the analgesic effects of opioids.

Development

There are many proposed mechanisms.

Examples:

1. A single opioid receptor can activate simultaneously different signalling pathways such ACase, MAP kinases or ion channels and it is possible to observe different levels of desensitization when considering those cellular responses. For instance, we recently showed that Remifentanil, a MOR selective agonist, produces a significant desensitization by 60% on the cAMP pathway after 10 min while at the same time desensitization of the MAP kinases ERK1/2 signalling pathway was not significantly affected.
   Two types of desensitization, homologous and heterologous, were described. In homologous desensitization, only agonist-activated receptors are desensitized while in heterologous desensitization, both agonist-activated and non-activated receptors sharing the same signalling pathways are inactivated. Those types of desensitization are related to different mechanisms especially in terms of receptor phosphorylation and kinases.
2. Glial cell activation: reciprocal signaling between immunocompetent cells in the central nervous system (CNS) has emerged as a key phenomenon underpinning pathological and chronic pain mechanisms. Neuronal excitability can be powerfully enhanced both by classical neurotransmitters derived from neurons, and by immune mediators released from CNS-resident microglia and astrocytes, and from infiltrating cells such as T cells.

Preoperative strategy do you give a 57 year old opiate tolerant man with failed back surgery syndrome and sleep apnoea who is to have total knee joint surgery in 6 weeks?

1) Establish a rapport through an empathetic approach.
2) Take a history and examination including a developmental history, social history and current psychological status.
3) Exclude red flags as appropriate eg Bone scan of the lumbar spine, blood tests including FBC, Iron studies Thyroid function tests.
4) Obtain consent from the patient to educate them about the health and pain issues that are important. Offer the patient your insight into the specific strengths that they have that will allow them to manage the total knee joint replacement.

5) The main issues are:

Opioid tolerance

Debilitation- likely to have reduced exercise tolerance

Sleep apnoea- risk of hypoventilation peri-operatively

Limited employment opportunities

Potential for low mood

6) Alternatives for analgesia and their limitations:
    - Partial agonist- Norspan. The withdrawal from the full agonist opiate needs to be managed.
    - A slow reduction of oxycodone HCL SR is required.
    - Changing to another full agonist opiate- this is unlikely to be effective
    - Assisted reduction using alternative drugs eg ketamine , lidocaine
    - ? Referral to Drug Health for Suboxone/ methadone if aberrant behavior is noted
    - Is there a role for simple analgesia peri-operatively?
    - What are the instructions for the anaesthetist? For example, Continuing Norspan with sublingual buprenorphine, regional techniques eg Adductor Canal block recommended, alternatives to full agonist opiates eg Tapentadol
7) Support for these changes: This may require psychological assistance through the withdrawal process. Management of global anxiety that can develop after withdrawal. Hopefully he is open to engaging in program to increase his physical strength and stamina. He will require a one on one program aimed at improving his transversus abdominis and multifidus tone. As he develops truncal strength, balance and whole body stamina will be required. There should be a specific focus on his knee strength especially the Vastus Medialis Muscle.
8) Consider a healthy diet regimen in conjunction with what he has found to be helpful in the past. Offer support with a nutritionist to assist with calorie management and encouragement.
9) Contact his local GP for assistance with medication management.
10) Review 1 month preoperatively, peri-operatively and postoperatively. Offer support to his anaesthetist and surgeon.

References:

(1) Chu, Larry F. et al Analgesic tolerance without demonstrable opioid-induced hyperalgesia: A double-blinded, randomized, placebo-controlled trial of sustained-release morphine for treatment of chronic nonradicular low-back pain. Pain. 153(8): 1583-1592, August 2012.

(2) Allouche S, Noble F, Marie N. Opioid receptor desensitization: mechanisms and its link to tolerance. Frontiers in Pharmacology. 2014;5:280. doi:10.3389/fphar.2014.00280.

(3) Peter M. Grace1,2, Mark R. Hutchinson1,2, Steven F. Maier1 and Linda R. Watkins. NATURE REVIEWS | IMMUNOLOGY VOLUME 14 | APRIL 2014 | 217 Mark Hutchinson et al

(4) Clifford Woolff J Clin Invest. 2010 Nov 1; 120(11): 3742–3744.

Question 2

Describe how you distinguish clinically between active visceral nociception, visceral hyperalgesia, and referred pain.

DEFINITIONS:

1. **Visceral nociception** – nociception arising from neural sources in deep organs of the body due to tissue insult
2. **Visceral hyperalgesia (really visceral allodynia)** – non-noxious stimuli interpreted as pain i.e. "sensitised" organ
3. **Referred pain** – pain experienced in a location remote from the inciting structure two types depending on location of inciting structure.

Possible explanations for hyperalgesia and referred pain

Relatively sparse distribution of somatic nerves in visceral structures compared with somatic structures. Autonomic nervous system has much greater influence with extensive innervation throughout visceral structures. Parasympathetic fibres are the important descending pathways and sympathetic fibres provide the ascending, excitatory fibres.

Acute tissue injury, irritation, and inflammation typically provoke sensitisation and neuroplastic modulation of the peripheral afferents, spinal circuits and spinobulbospinal circuits which may results in a transient, and sometimes prolonged, upregulation of afferent sensitivity. Varying types of stressors of varying severity have been shown to up- or down-regulate visceral pain responses in animal models. Allodynia of somatic structures, especially muscles, is attributed to the process of central sensitisation – convergence-facilitation. Visceral nociception is often associated with referral of pain to somatic structures (skin, subcutis, muscle), thought to be due to viscero-somatic convergence of afferent fibres in the dorsal horn through nociceptive input from viscera sensitising dorsal horn neurons that also process somatic input so that sensitised dorsal horn second-order neurons are now responsible for non-noxious somatic input being perceived as painful e.g. flank muscle tenderness persisting after removal of kidney or ureteric calculi. Clinically, tenderness is elicited on muscle palpation which will reproduce the characteristic "visceral pain" felt by patient.

Proposed mechanisms for persistent visceral hyperalgesia include

- increased responsiveness of visceral afferents outlasting the acute inflammatory event e.g. prolonged sensitisation of afferent pathways underlying post-infectious IBS
- intermittent peripheral sensitisation of primary afferents possibly triggered by subclinical infections or dysbiosis of microflora e.g. acute, transient bouts of abdominal or pelvic pain
- neuroplastic changes affecting response patterns of primary afferents (including peripheral endings of the spinal and vagal afferents) e.g. alteration in sensitivity of bladder mechanosensitive nerve endings reducing the threshold for voiding, increasing urgency and frequency, and changing the normally non-noxious sensation of bladder filling to painful
- changes in sensitivity of reflex pathways at spinal cord e.g. micturition reflex pathway between lower thoracic/pelvic spinal cord and bladder appears to be sensitised after initial tissue damage such as bladder infection
- ineffective engagement of descending pain inhibition systems
- enhanced responses seen on fMRI shown to expectation of visceral pain
- neuroimmune activation in spinal cord – activation of glia can produce proinflammatory cytokines such as TNFα, and down regulate glutamate transporter on astrocytes which may increase synaptic glutamate concentrations. Both result in upregulation of glutamate/NMDA receptor signalling which contributes to central sensitisation

Clinical approach to assessment

A traditional biomedical approach (history, examination and appropriate investigations) can be used

initially seeking to rule out disease or organ pathology driving a nociceptive response, aiming to identify any potential life-threatening or organ-threating problem that requires urgent management.

Relevant history of the pain (location, quality, severity, time of and from onset etc..)
Acute visceral nociception -Provoked by acute stretch, ischaemia or distension in the viscera. Often rapid onset, high pain severity, may be well localised but more often poorly localised, often felt in the midline, associated with autonomic features such as nausea and sweating, has a strong emotional quality associated e.g. severe angina.
Physical examination - may be clearly defined physical signs and changes identifiable on investigations Examples could include ECG changes in acute myocardial infarction, causative bacterium on stool culture in acute gastroenteritis, or urine culture for urinary tract infection, renal calculus on radiology, bloody stool, altered bowel habit in inflammatory bowel disease or carcinoma with characteristic radiological changes and proven with colonoscopy with biopsy, dysmenorrhoea and menorrhagia in endometriosis and adenomyosis.

Visceral hyperalgesia - Characteristic is pain or discomfort associated with non-noxious stimuli (really visceral allodynia), may occur acutely or persist in chronic states; thought to underlie a large number of chronic visceral pain disorders
Enhanced perception of afferent stimuli –common examples from GIT or GUT
Manifest as lower threshold for discomfort and pain, increased intensity and affective stimulus rating and atypical viscero-somatic referral areas e.g. IBS patients report discomfort at much lower levels of experimental bowel distension, larger areas of referral of pain than controls
Physical examination more often shows diffuse, widespread tenderness on light palpation; investigations may be negative in chronic phase.

Risk factors for development of persistent symptoms include:

- Female sex
- Duration of inciting event (e.g. from gastroenteritis or UTI)
- Psychosocial stressors at the time of the inciting event
- Psychological factors such as anxiety and depression

Symptoms are more likely to arise in individuals with a history of other somatic symptoms probably reflecting a generalised sensory augmentation state which produces an enhanced perception of noxious and non-noxious impulses coming from slowly healing tissue e.g. epithelium in post-infectious IBS. However, the cause for many chronic visceral pain states remains unknown e.g. in 90% of men with urological chronic pelvic pain syndrome.

In addition need to assess other indicators of organic disease i.e. “red flags” including:

- Weight loss
- Anaemia
- Fever
- Bloody stool or melaena
- Stearorrhoea
- Haematuria
- Non-menstrual PV bleeding
- Elevated inflammatory markers
- Extra-visceral manifestations suggestive of systemic disease process – skin changes, joint changes in inflammatory arthritides
- Personal or strong family history of carcinoma

Referred pain – 3 possible sub-types
-viscero-somatic hyperalgesia – visceral pain felt in skin, subcutis, muscle
-somato-visceral hyperalgesia- sensitised soma triggers visceral pain

-**viscero-visceral hyperalgesia** – one sensitised organ causes sensitisation of another organ e.g. persistent pelvic pain from endometriosis is often associated with bladder pain and IBS; urological chronic pelvic pain syndrome is often associated with IBS

Patterns of viscero-somatic referred pain

Typical referral patterns include:
Cardiac- left chest radiating down left arm, through to small area T2,3 posterior chest
Lung and diaphragm- supra clavicular radiating to neck anteriorly and posteriorly
Thymus- right supraclavicular radiating to right suprascapular area
Liver and gall bladder- anterior subcostal on right side of epigastrium radiating posteriorly through to right subscapular area T5-T9
Pancreas- anteriorly right of epigastrium radiating through to the back centrally towards left side
Stomach- central epigastrium radiating posteriorly to right of midline approx. T3-6
Small intestine- central supra-umbilical
Ovary- bilateral radiation to supra-umbilical area mid-clavicular line
Colon- periumbilical
Kidney- from renal angle possible radiation to wide area of referral involving whole of abdomen, lateral and medial thigh sparing anterior thigh area
Urinary bladder- suprapubic radiating through to coccygeal area
Ureter- broader suprapubic area radiating to medial thigh

References:

FPM Essential Topical Area 5 eLearning module, accessed on *Networks*, ANZCA 2/10/16
Pain 2016: Refresher Courses Part VI Visceral and abdominopelvic pain, Chapters 15-17, pp. 117-147, 16 World Congress on Pain, IASP Press, Washington DC

Question 3

What information would you include in a submission aiming to inform about over-the-counter (OTC) availability of codeine-containing analgesics?

1. Introduction

Codeine phosphate is a weak opioid analgesic, which is widely available in Australia and New Zealand at low dose in combination with non-opioid analgesics such as ibuprofen and paracetamol as over the counter dispensing (S3, pharmacist only) for the treatment of mild to moderate pain. High dose codeine preparations (>30 mg) are available on prescription (S4, S8 in Australia). The predominant opioid effect of codeine is believed to be via its active metabolites, morphine (via de-methylation) and codeine-6-glucuronide.

2. Dosage efficacy

OTC combination analgesic preparations contain codeine in unit doses ranging from 8 mg to 15 mg. Doses below 30 mg of codeine are unlikely to produce any additional pain-relieving benefit than the non-opioid analgesic alone, although few studies have been performed. Codeine alone does not compare favourably to commonly used alternatives such as non-steroidal anti-inflammatory drugs (NSAIDs) or paracetamol, however appears more clinically useful when combined with these agents.

The numbers needed to treat (NNT) of various combinations has been reported based on mild-moderate acute pain and demonstrate lack of efficacy of low dose codeine in combination products compared with paracetamol or NSAID alone.

The NNTs (vs. placebo unless otherwise specified) include:

Codeine 60 mg	7
Paracetamol 1gm /ibuprofen 400 mg	1.5
Paracetamol 1gm/codeine 60	2.2
Paracetamol 1gm/codeine 60 vs. paracetamol alone	6.1

The low doses of codeine available in OTC products are unlikely to produce clinical benefit greater than paracetamol or NSAID alone, but increases adverse effects and potential for risk. The Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists suggested that codeine in OTC combination analgesics had “no analgesic purpose but increased the risk of physiological and psychological dependence and, consequently, morbidity”.

3. Risk of harm:

A consequence of the inability to separately titrate the doses of drugs combined in OTC codeine analgesics is that an individual escalating codeine dose in OTC products to gain efficacy risks secondary harm from the non-opioid analgesic it is combined with. Cases of misuse and dependence on OTC codeine-ibuprofen resulting in life-threatening morbidity including gastric ulceration and haemorrhage, protein losing enteropathy, renal tubular acidosis with hypokalaemia have been reported.

Similarly, excessive use of paracetamol/codeine OTC products risks hepatic impairment secondary to accumulation of a toxic paracetamol metabolite.

Further risk of harm is implied in those with renal impairment (morphine and codeine glucuronide metabolite accumulation) and the older person (increased risk of constipation and falls). The incidence of constipation and medication overuse headache appears to be higher with codeine containing combination preparations.

4. CYP2D6 metabolism:

Genetic variability (including with different ethnic background) in CYP2D6 metabolism (ranging from

ultra-rapid and rapid metabolisers to poor metabolisers) creates inter-individual differences in metabolite (morphine) production, such that clinical effect may be high (with risk of morphine toxicity, breast milk transference) or low (lack of effect) respectively. In addition, rapid metaboliser patients may be at higher risk of euphoria (? higher addiction risk) whilst poor metaboliser may escalate dosing to achieve therapeutic effect (with associated adjuvant toxicity).

The metabolism of codeine to morphine via CYP2D6 activity is subject to inhibition with certain SSRI antidepressants or induction with enzyme inducers (e.g. phenytoin). Poor metabolisers, despite poor analgesic effect, will still experience many of the side effects of codeine.

Specific risks relate to infants and children, where genetic variability in codeine metabolism has been implicated in adverse effects (including death) in breastfeeding mothers or young children who are rapid or ultra-rapid metabolisers, with subsequent excessive morphine activity.

5. Risk of neuroinflammation/tolerance/addiction – mechanisms of action:
Codeine, even at low doses, appears to active glia cells within the CNS, which may contribute to the development of opioid tolerance and hyperalgesia, possibly via toll-like receptor activation. This is believed to be the basis of observation of increased use of opioid post-operatively via PCA opioid delivery systems in those administered codeine pre-operatively.

The risk of addiction secondary to codeine exposure via OTC products is not quantified, although is believed to be significant based on case series of overt addition following exposure. Risk factors for opioid addiction include past history of alcohol or opioid addiction, psychiatric illness, childhood sexual abuse and family history of addiction: the easy availability of an opioid product via OTC access puts those with risk factors for addiction at risk.

6. Practical/public health considerations:
Due to varied legislative requirements, current information provision regarding the potential for dependence formation and adverse effects appears inadequate. Access is not overseen by a regulated medical practitioner, nor is supply from pharmacies overseen/monitored. Regulatory bodies enforce no limits on the provision of pack numbers, advertising of products or guidelines regarding appropriate advice regarding OTC use.

References:

1. Derry S, Karlin SM, Moore RA. Single dose oral ibuprofen plus codeine for acute postoperative pain in adults. *Cochrane Database of Systematic Reviews* 2015, Issue 2; CD010107.
2. Frei MY, Nielsen S, Dobbin MD et al. Serious morbidity associated with misuse of over-the-counter codeine-ibuprofen analgesics: a series of 27 cases. *Medical Journal of Australia* 2010; 193(5): 294-6.
3. Iedema J. Cautions with Codeine. *Australian Prescriber* 2011; 34(5): 133-5.
4. Murnion BP. Combination analgesics in adults, *Australian Prescriber* 2010; 33(4): 113-5.
5. Schug SA, Palmer GM, Scott DA, Halliwell R, Trinca J. *Acute Pain Management: Scientific Evidence.* Melbourne: ANZCA & FPM, 2015.
6. Tobin CL, Dobbin M & McAvoy B. Regulatory responses to over-the-counter codeine analgesic misuse in Australia, New Zealand and the United Kingdom. *Aust N Z J Public Health* 2013; 37(5): 483-8.

Question 4

Discuss the diagnosis and management of a patient with Post Traumatic Stress Disorder (PTSD) and persistent pain

Trauma is the major leading cause of death and morbidity in the under 45 year age group with most trauma secondary to falls, motor vehicle accidents, homicide and injury caused by either self or another person. Furthermore, mortality secondary to motor vehicle accidents is within the top ten causes worldwide. Of those who survive approximately 16% develop long-term disabilities including psychological morbidity. Motor vehicle accidents (MVAs) account for the most common causes of post-traumatic pain with significant comorbidities involving psychological disorders including post-traumatic stress disorder (PTSD). It is not surprising that chronic pain occurs following trauma in the setting of MVAs. With MVAs there are often multiple sites of injury requiring extensive and frequent surgical procedures with significant disruption and distortion of normal tissue. Coexistent with chronic pain and PTSD are also high prevalence levels of depression, anxiety, substance abuse and acquired brain injury.

Comorbid persistent pain and post-traumatic stress disorder are common. However the literature remains fairly sparse about their shared aetiology and 'mutual maintenance'.

One of the difficulties in examining their comorbid association is the evolving definition that occurs in the literature for PTSD, making an examination of what literature does exist, challenging. These definitions resulted from earlier studies involving the association of PTSD based on DSM-IV criteria and chronic post-traumatic pain. This has been likened in its definition to persistent post-surgical pain, making aspects more difficult to interpret. One of these aspects is the prevalence for each, individually and, in association. Studies have demonstrated that the rates of chronic post-traumatic pain across the adult populations are in the order of 20-80%, whilst that of PTSD varies between 10-50% of those with chronic post-traumatic pain. US figures quote an 8% life-time prevalence of PTSD with women affected more frequently than men.

It should also be noted that PTSD may occur in patients who have not personally experienced a traumatic event e.g. first responders. The prevalence of chronic pain in this group is also noted to be high with non-traumatic chronic pain including chronic headache and chronic widespread pain ("fibromyalgia") being commonly associated.

PTSD has taken on different terms, definitions and qualifications over the years. Initially described as "war neurosis" or "shell shock", PTSD has morphed from combat situations to involve the psycho-behavioural and physiological responses. These follow situations where, according to the DSM-5 it is frequently found (at least 30 days after a traumatic event) in patients following *specified traumatic exposure*. These traumatic events compose the first of 8 criteria used to define the diagnosis of PTSD and include:

(i) personal experience of death, near-death or sexual assault, witnessing trauma of these types in another person, experiences that involve the death or near-death experiences of relatives or close friends and recurrent exposure to aversive events (except via the media, other than when this is for work) e.g. in first responders. This constitutes criterion A of the diagnosis.

(ii) Criterion B consists of symptoms of intrusion including recurrent nightmares, recurrent memories of the trauma and dissociative flashbacks.

(iii) Criterion C focuses on avoidance of thoughts or feelings related to the traumatic event or avoidance of people, places, activities or objects that serve as external reminders of the event.

(iv) Criterion D involves negative cognitions and mood.

(v) Criterion E centres on arousal symptoms such as hypervigilance, poor sleep, problems of concentration, or reckless behavior.

(vi) For PTSD to be diagnosed, the symptoms must persist for at least a month (criterion F) and
(vii) cause significant impairment or distress (criterion G) and
(viii) must not be due to medication, substance abuse or other illness (criterion H).

Present in the DSM -5 and not in earlier editions is an acknowledgement of PTSD occurring in children younger than 6 years. For a diagnosis of PTSD, criteria A and F-H must be met along with at least one symptom in each of criteria B-E. In DSM-5 it should also be noted that PTSD is no longer categorized as an anxiety disorder but now sits separately from these in spite of much overlap existing. ICD-11 (due for release in 2017) has a different proposed set of criteria for a diagnosis of PTSD. There are fewer criteria (similar to DSM-IV) proposed to make a diagnosis.

It is significant that there is commonality between many of the symptoms and signs of patients who describe both chronic pain and PTSD. These include such symptoms as hyperarousal, anxiety, avoidance, emotional lability and an increased somatic focus. In both, anxiety sensitivity (i.e. a tendency for an individual to become fearful, specifically, the fear of anxiety symptoms attributing their presence to harm) has often been demonstrated to be elevated. Two dominant psychological theories have been used to explain chronic pain. The first proposes that pain behaviours will persist indefinitely if they occur in the context of reward or gain e.g. Pavlov's dog, (operant theory). The second proposes that the meanings ascribed to the pain influence the patient's interpretation and responses. These include their behavior, use of coping strategies and affect (cognitive behavioural theory). These theories have both contributed to the idea of "mutual maintenance" through:

(i) attentional biases where pain recurrently reminds the patient of the trauma
(ii) anxiety sensitivity is where PTSD-related anxiety contributes to maintaining the patient's belief that the pain is 'harmful' thereby further contributing to the patient's distress
(iii) persistent reminders of the trauma contribute by reliving the experience e.g. flashbacks which sustain the association between chronic pain and PTSD
(iv) avoidant coping style which is characteristic of PTSD and results in deconditioning with constant reminders of the pain
(v) depression and reduced levels of behavioural activity resulting in both incapacity and trauma avoidance
(vi) pain perception that is exacerbated by anxiety and highlights the patient's experience of pain, emotional distress and disability
(vii) exhaustion of cognitive resources by the patient's need to manage both the chronic pain and PTSD such that, they are unable to develop more adaptive strategies in response to either.

Certain drugs may contribute to mutual maintenance of chronic pain and PTSD include the use of opioids which have both analgesic and anxiolytic effects. The analgesia while helpful in the management of acute pain has not been demonstrated to be helpful in chronic pain but often provides the default when patients report pain and increasing levels of distress. These drugs operate by both a reinforcing effect in that they contribute to reducing the PTSD-related anxiety as well as to the deconditioning and mood disturbance, sleep disruption and distress that occurs in the patient with chronic pain. Similarly, other drugs with anxiolytic effects that are used in the management of pain (gabapentinoids for neuropathic pain; the benzodiazepines for pain associated with acute muscular spasm) may produce similar anxiolytic effects with 'emotional numbing' and avoidance as part of their side-effect profiles.

Treatments

Cognitive Behavioural Therapy (CBT) - Cognitive Behavioural Theorists believe that behaviour is an expression of the patient's negative cognitions such that by changing the way in which the patient evaluates and responds to situations, thoughts and feelings and addresses unhealthy behaviours (e.g. resting on the couch) is the optimum treatment for both PTSD and chronic pain. Programs may be individual or group with the cohesion of the group providing the support and safety required.

Exposure therapy aims to reduce a person's fear, anxiety and avoidance behaviour by exposing the person to feared thoughts, feelings and situations in a graduated and controlled fashion. This is achieved through both imagined and in vivo exposure to traumatic events in a safe environment. This allows the patient to re-contextualise the trauma memory and its associated beliefs.

Acceptance and commitment therapy is based on the idea that suffering arises not from the experience of pain but from the attempted avoidance of that experience. This results in an inflexibility that prevents the sufferer from adopting the behavioural steps in accord with their values.

Psychodynamic psychotherapy emphasises the role of the unconscious brain in behavior. It is based on the premise that all behavior is 'learned' through previous experiences. Therapy involves a "shorter" and less intense form of psychoanalysis with a trusted therapist.

Selective Serotonin Reuptake inhibotors (SSRI's) are the drug of choice in the management of PTSD (if required) provided only that the patient is not suicidal. Other drug therapies that may be considered include the use of beta-blockers (to mitigate symptoms of hyperarousal); prazosin, clonidine, donepezil and dexamphetamine. Sleep disturbance may be treated using mirtazapine. For short term use only, a nocturnally administered short acting benzodiazepine (alprazolam or lorazepam) can be employed. Buprenorphine, ketamine and hallucinogens may also be occasionally used as well. Patients will often resort to self-prescription of cannabis. Co-existent depression must be aggressively treated.

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Question 5

Write brief notes on the main concepts involved in culturally responsive care in pain management for patients from diverse backgrounds.

Culture is defined as the customary beliefs, social norms, and material traits of a racial, religious, or social group. Culturally-specific attitudes and beliefs about the origin, role, and meaning of pain influence the manner in which individuals view and respond to their pain, and the pain of those around them. Culture has a significant impact on shaping the beliefs, behaviour, and responses of an individual to pain. Both Australia and NZ are culturally diverse countries with indigenous populations (Aboriginal and Torres Strait Islanders in Australia, Maori in NZ) and migrant populations from the Pacific Islands, Asia, Africa, the Middle East, Europe, and South America.
The Aboriginal and Torres Island population comprises 2.5% of the total Australian population. In NZ, Maori comprise just under 15% of the population (Statistics NZ 2013) while Pacific Islanders account for 7% of the population. Culture, language, and religious beliefs have a significant impact on both the assessment and management of pain.

The culture and attitudes of both the clinician and patient are important. Health professionals need to consider their own cultural assumptions and address cross-cultural differences in pain expression and beliefs during the consultation. An inability to do so may have a significant negative impact on the therapeutic relationship.
Some of the factors that need to be considered include:

1. Spoken language – potential difficulty with pain assessment, consent for interventions, understanding of analgesic modalities/medication use. Professional interpreter needed – family, friends, staff members are inappropriate as their skills are not validated and they may omit/edit information.
2. Methods of communication – pain may not be verbally communicated.
3. Linguistic expression.
4. Metaphorical language.
5. Health beliefs and attitudes.
6. Attitude toward and expectations of Westernised healthcare.
7. Framework of meaning.
8. Health literacy and education level.
9. Socioeconomic status – contributes to inequalities in access to and quality of healthcare.
10. Norms of behaviour and pain-related behaviour – overt pain behaviour perceived as weakness in some cultures so patients may be more stoic during their assessment. Other cultures display more overt pain behaviours. Both should be treated in an equally respectful manner.
11. Analgesic preferences and cultural beliefs regarding non-pharmacological management. Some cultures embrace the multidimensional approach to pain management whereas other cultures may be less amenable to exploring pain self- management strategies.
12. Migration history – forced immigration for personal/family safety – (victims of torture, war, genocide), political refugees, older age at migration may be associated with more difficulty with integration into a new community.
13. Medical comorbidities more prevalent in certain cultures (eg. renal impairment in Torres Strait Islanders and Pacific Islanders) and may impact on the choice of analgesic agent.
14. Pharmacogenetic factors affecting drug metabolism also need to be considered in deciding analgesic choices.
15. Higher rates of substance abuse and some psychiatric disorders in the indigenous populations of NZ and Australia may make patient engagement in pain management services problematic.

Patients may have difficulty understanding pain assessment tools and many tools have not undergone cross-cultural validation. Use of multi-lingual assessment tools and educational documents (eg. Pain

Toolkit online resource available in many languages) is recommended. A verbal descriptor pain assessment scale may be more appropriate than a numerical rating scale.
Disparity in effective pain treatment may occur. Research suggests pain may be under-treated. Cultural differences in opioid consumption and opioid prescribing have also been reported.
To ensure culturally responsive care, health professionals need to improve cultural competency by increasing cross-cultural knowledge, skills, and self-awareness through attending cultural competency courses or utilising the ANZCA online learning resources.

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Question 6

In a patient with renal or hepatic impairment, the changes may affect the pharmacokinetics of analgesics prescribed.

Summarise the key changes and indicate how they might influence your choice and/or the dose of medications used for pain management in these patients. Include both opioid and non-opioid drugs in your answer.

In a patient with renal or hepatic impairment, the changes may affect the pharmacokinetics of analgesics prescribed. Summarise the key changes and indicate how they might influence your choice and/or the dose of medications used for pain management in these patients. Include both opioid and non-opioid drugs in your answer.

Key changes:

1) Renal impairment can result in:
    a) Decreased excretion of parent drugs that are cleared by the kidney
    b) Decreased excretion of active metabolites

2) Hepatic impairment causes fewer problems but:
    a) Some drugs may have increased oral bio-availability due less first pass metabolism
    b) Some metabolised for clearance less rapidly → prolonged effects

Influence on choice of drug/dose	**Renal impairment**	**Hepatic impairment**
Opioids, tramadol and tapentadol	*No dose adjustment required as none, minimal amount, or only weakly active metabolites* • alfentanil (unless impairment is severe; no active metabolites) • fentanyl (good choice if severe renal impairment; no active metabolites) • buprenorphine (unchanged PK as mainly biliary excretion of metabolites) • methadone (unless impairment is severe) • oxycodone (OK if mild-moderate renal impairment)[a] • tapentadol (do not use in severe renal impairment) *Active metabolites so dose adjustment suggested or, sometimes in preference, use alternative agent:* • codeine (morphine) • hydromorphone (H3G) • morphine (M6G & M3G) • tramadol (M1) *Avoid:* • pethidine (norpethidine)	*No dose adjustment generally required*: [b] • alfentanil • fentanyl • morphine (decrease if oral administration as ↑ bioavailability) • buprenorphine • oxycodone • methadone (no dose adjustment needed in stable chronic liver disease) *Dose adjustment may be needed if impairment severe:* • hydromorphone • tramadol • tapentadol (avoid in severe hepatic impairment; adjust dose in moderate *Avoid:* • pethidine

	dextropropoxyphene (nordextropropoxyphene)	
Paracetamol	Safe to use in most patients – may need to increase dose interval if severe renal impairment	Short-term use at therapeutic dose is reasonable in patients with chronic liver disease; reduce dose for long-term use; preferred to NSAIDs
NSAIDs including non-selective and coxibs	Use with caution if mild renal impairment and avoid if severe. Limited renal reserve. Same for coxibs	May be used in mild chronic liver disease; avoid in cirrhosis; coxibs might be safer
Gabapentin, pregabalin	Dose adjustments suggested based on creatinine clearance	Suitable for use – non-hepatic metabolism
Tricyclic antidepressants (TCAs)	Metabolite accumulation may occur but limited evidence about need for dose reductions	Reduced doses suggested if severe hepatic impairment
SNRIs	Duloxetine and venlafaxine – dose reduction if creatinine clearance < 30 mL/min	Duloxetine should not be used in hepatic impairment and the dose of venlafaxine should be reduced
Clonidine	Limited data; dose adjustment has been recommended	
Older anticonvulsants		Avoid carbamazepine and valproate if severe impairment; otherwise dose adjustments may be required
Ketamine[c]	Limited data but probably no dose adjustment needed	Limited information
Local anaesthetic drugs	No significant difference in plasma concentrations unless renal impairment is severe	Dose adjustment may be required with repeated or prolonged use as clearance may be significantly impaired [b]

Question 7

Your tertiary pain management centre needs to improve community access and reduce waiting times to your pain services.

c) What are the issues to consider?
d) What strategies can be used to address these problems?

Rationale (issues to consider):

- High prevalence of persistent pain in community – significant interference with quality of life
- Not all who are referred can have access – there are more demands than there are services
- There is lack of access to evidenced based pain treatment which improves **self management** and reduces pain
- Patients are kept on a sequential biomedical model without getting better

Strategies to reduce waiting times and improve access:

- Triaging: develop a scoring system that attempts to prioritise referrals such that:
    - those with most urgent problems get earlier access e.g. cancer pain
    - early intervention (i.e. recent onset cases) – higher priority score e.g. patient with persistent severe acute pain / subacute pain which may transition to chronic pain
    - those who have had multiple previous contacts with pain services (implying failure to get better) are scored lower priority
    - use local knowledge of available resources and allocate higher priority to patients with problems for which the available resources are highly likely to help improve their QOL
- Recognise those who are in litigation looking for support for claims vs. those who are seeking treatment
- Implement a Pre-screening education program. The best known of these was developed in Western Australia, and is called STEPS, or "Self-Training Educative Pain Sessions", consisting of multidisciplinary sessions in an intensive group manner providing information and skills in a broad pain management plan designed to optimise treatment outcomes for patients with pain
    - Elaborate on the components of the programme – orientation, pacing, patient stories, moving with pain, response to pain, medical options (or the principles of the programme). This delivers enough information to attendees such that it has been shown that many choose not to go ahead with further individual assessments in the unit, saving valuable appointment spaces.
    - Patients requiring / requesting further individual assessment are expected to have attended a STEPS program before acceptance.
- Increase the knowledge and skill levels of Primary Care physicians because most patients with pain make their earliest contacts with Primary Care. Pain unit should work cooperatively with Primary Care, upskilling of Primary Care physicians including
    - Accurate recognition of patients with neuropathic pain in particular helps to choose better pathways for care.
    - Alternatives to inappropriate opioid prescribing in primary care, especially for neuropathic pain for which opioids are often ineffective.
    - Offering 'telephone clinics' where GPs can discuss a case and receive advice without actually referring- can save time, get more timely and appropriate care – especially where pharmacological Rxs are indicated.
- Adequate resourcing of the Pain centre. This will require advocacy to hospital administrations.
    - Need adequate level of skilled multidisciplinary staffs to perform work especially in clinical psychology and physiotherapy to complement pain medicine specialists.

- An effective acute pain management service to treat acute pain effectively to reduce the transition to chronicity
- Develop effective interdisciplinary collaboration with other departments to treat pain early and comprehensively
- Need adequate educational resources to equip staffs etc
- Measurement of outcomes to better tailor services

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Question 8

Write short notes on the use of Lidocaine in the management of pain.

Pharmacology

- Amide local anaesthetic, sodium channel blocker
- 60 – 90 mins duration
- Metabolised by liver MEGX

Adverse issues/contraindications

- Allergy to amide anaesthetics, Localised sepsis, myasthenia gravis, coagulation issues
- Toxicity doses 4 mg/kg or 7 mg / kg with adrenaline in any one hour as SC infiltration
- Blood/serum levels toxic >5mcg/ml
- Clinical spectrum of toxicity
    - Primarily CNS (circumoral tingling, convulsions), less evident CVS (Hypotension palpitations)

Uses

- Topical mucosal as gel, inhaled, drops,
- Transdermal as 5% patch
- Central
    - Intrathecal / epidural and specific indications
- Peripheral
    - Local infiltration
    - Peri-neurally as a local anaesthetic for nerve block
    - Prolong use by catheter techniques
- Intravenous use
- Levels of evidence for use
    - Acute peri operative pain Level 1
    - Analgesic, anti-hyperalgesic, anti-inflammatory, gastrointestinal pro-peristaltic effects
    - Chronic neuropathic pain Level 1
    - Level 1 evidence of variable efficacy for chronic migraine

Reference:

Eipe N, Gupta, S et al. BJA Education 2016, 1 – 7

Question 9

A 22 year old sales clerk is referred to you by a neurologist with "medically unexplained' pain, weakness and numbness of the entire left "hemi-body" after a minor motor vehicle accident two years ago. She is wheelchair bound and holds her left hand in a claw-like posture.
Describe your approach to assessment and management of this patient.

This patient has multiple symptoms in addition to pain, namely weakness and numbness affecting the left side of the body, is wheelchair-bound, and holds her left hand in a claw-like posture. In this particular patient, in the absence of an objectively demonstrable organic cause for the various symptoms, as well as the presence of "medically unexplained pain", the diagnosis is Conversion Disorder. If the patient presented only with medically unexplained pain, the diagnosis would have been Pain Disorder Associated With Psychological Factors (DSM-IV-TR). "Medically unexplained pain" (MUP) is not an uncommon scenario, with up to 30% of chronic pain patients exhibiting medically unexplained symptoms.

The presence of additional physical symptoms and loss of function, without an organic cause, indicates that the diagnosis of Conversion Disorder is appropriate. Both Conversion Disorder and Pain Disorder are included among the Somatoform Disorders according to both DSM-IV-TR and ICD-10. This diagnosis assumes that the symptoms and signs are not intentionally produced or feigned (as in Factitious Disorder or Malingering respectively).

Somatoform Disorders are those where symptoms suggest a medical condition but no underlying physical disorder can be found. Specific disorders in this group include Hypochondriasis, Body Dysmorphic Disorder and Somatization Disorder, in addition to Conversion Disorder and Pain Disorder. In Conversion Disorders symptoms could include deficits in motor or sensory function. Conversion Disorder with sensory deficit has also been referred to as Non-Dermatomal Somatosensory Deficits (NDSDs) (with reduced sensory response) described as "unexplainable hypoaesthesia not conforming to the distribution of peripheral nerves". NDSDs are reportedly common and present in up to 40% of chronic pain patients.

Assessment and Differential Diagnosis:
Review and confirm physical status to ensure that an organic cause for symptoms has not been overlooked and no physical diagnosis is missed:

- It is important to review history and investigations: take a comprehensive history, confirm nature of accident, treatment, psychological history, school/ work history, social history, do a full physical examination and review radiology.
- Consider whether there has been acute onset of "CRPS" in one limb that has extended (although CRPS typically has sensory "gain"/ allodynia rather than sensory deficit). Claw hand can follow severe CRPS.

Assess psychosocial factors:

- Assess mood, support persons, consider secondary gain, tertiary gain.

Management:
Management is likely to be challenging, and given the presence of symptoms for two years, change might not be achievable. Enlist the help of a skilled rehabilitation team that includes a psychologist, physiotherapist, occupational therapist.
A period of inpatient rehab might be required initially.
Psychological techniques are central to successful management of conversion disorders and include:

- avoid confronting the patient or trivialising symptoms
- avoid reinforcement
- provide benign explanatory model of symptoms, review tests results, create an expectation of recovery

- evaluate patient's emotional adjustment, consider psychotherapy.

The use of behaviour therapy might be helpful, and "behavioural modification and shaping techniques" are useful in the physical therapy management. Abnormal movement patterns are ignored, and correct movement patterns reinforced using feedback and praise. The patient should be advanced through a progressively more difficult therapy programme based on treatment approaches used with analogous neurological conditions.

Create a structured graduated programme of activity with achievable goals.

- Is independent ambulation achievable?
- Is the hand able to be treated or should patient be looking to adaptive one handed independence?

Some might suggest the use of interventional management to activate the claw like hand such as analgesic blocks, with stretching and strengthening – consider management as per dystonia, and with adjuvant medications for pain including baclofen, anticonvulsant drugs, and antidepressants (either TCA or SNRI).
Graded motor imagery might be useful, again with skilled therapy and structured approach (might include mirror box therapy)
Be wary of using opioids, particularly avoid high doses.
Use reward and subtle reinforcement of gains made.
Work closely with the family to achieve independence, reduce reinforcement of illness.

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Question 10

The number needed to treat (NNT) has become widely utilised to compare the efficacy of chronic pain treatments.

6. **Define NNT**
7. **Outline the potential problems associated with its calculation and interpretation**
8. **A systematic review of clinical trials of morphine establishes the NNT is 2.5 (95% confidence interval 1.82 - 4.0). Explains what this confidence interval means and why is it important.**

1. Definition:

- NNT = "the number of patients one would need to treat in order to get one more responder on the active treatment than one would have gotten had they been treated with control"(1).
- NNT = "single unitary measure of a drug's efficacy that was meant to provide an intuitive means for evaluating the relative efficacy of different drugs in order to rank them as to their efficacy"(1).
- NNT = "inverse of the absolute risk difference" (1/ARD)(1).
- ARD = "difference in proportion of patients who manifest a response to a treatment and the proportion of patients who manifest a response to control"(1).
- NNT is usually used to compare the efficacy* of different drugs for the same indication (1). *Efficacy can be defined as "the performance of an intervention under ideal and controlled circumstances, whereas effectiveness refers to its performance under 'real-world' conditions" (cited in (2)).
- Example: "If half (50%) the patients on active treatment respond (response rate = 0.5), and one quarter (25%) of the placebo-treated patients respond (response rate = 0.25), then the ARD is 0.5-0.25 = 0.25. The NNT is 1/0.25 = 4. This can be interpreted as 4 patients would have to be treated with the treatment to get 1 more responder than with placebo. In other words, treating 4 patients with treatment would yield 2 responders, whereas treating 4 patients with placebo would yield only 1 responder" (1).

2. Potential problems associated with its calculation and interpretation:

Most of the problems associated with NNT are shared by other summary measures of efficacy and relate to the quality and comparability of the research being pooled (3). The golden rule to reduce such problems is use only data from trials or systematic reviews that are methodologically sound and free from bias. This is often difficult to achieve however (3). The practice of dichotomised data is of concern to some given most of the source data are quantitative (continuous or integer scales) or at least ordinal qualitative data. The choice of response threshold can appear arbitrary at times.

2.1. Problems associated with calculation (1)

- Calculation from multiple trials can be subject to bias
- NNT can have an infinite value
- At times the confidence interval (CI, i.e. precision) of the NNT can be hard to define, particularly when NNT is high
- The CI is skewed (due to it being the inverse of the ARD confidence interval)
- NNT is dependent on using similar outcomes and similar comparisons (controls)
  Outcomes: If NNT is calculated using data that does not compare "like with like" i.e. different outcomes, duration of treatment, different conditions the results hold little meaning.
  The NNT dichotomises outcome into responders or non-responders. Response most commonly = reduction in pain (from baseline). A predefined definition is used to determine response e.g. ≥30% reduction in pain OR not. Different response definitions result in profoundly different NNTs e.g. ≥30% vs ≥50% reduction (1).
  Comparisons: If the control for comparison is not the same (e.g. placebo vs non-treatment vs alternative active treatment) the NNT will not be valid (3).

These general problems are summarised by Katz (1) as

- The NNT is sensitive to the level of efficacy in the placebo group

- The NNT depends on the endpoint
- The NNT is dependent on the selection of outcome measured
- The NNT is dependent on the cut-off chosen for the dichotomous outcome
- The NNT is dependent on the time point of outcome
- The NNT depends on factors internal and external to the study aside from study drug
- NNT does not reflect effectiveness of treatment in clinical practice

Katz (1) describes a number of specific problems with NNT

- The NNT can have an infinite value, creating problems for meta-analyses and causing a disproportionate impact of failed versus successful studies
- The precision of the NNT is difficult to estimate
- The NNT has a skewed CI

2.2. Problems associated with interpretation (1)

- A clear understanding of the definition varies and wrong definitions can be found on the internet including: "NNT = the number of people needed to treat to get one responder" (1).

3. A systematic review of clinical trials of morphine establishes the NNT is 2.5 (95% confidence interval 1.82 - 4.0). Explains what this confidence interval means and why is it important.

"Statisticians use a confidence interval to express the degree of uncertainty associated with a sample statistic. A confidence interval is an interval estimate combined with a probability statement" (4).

Considering the above example, an average of 2.5 patients (point estimate) would needed to be treated with morphine (dose and response would need to be predefined) to get one more responder than if treated with control (also needs to be defined). We are 95% confident the ***true population NNT*** for morphine[1] (at x dose to achieve y response) would lie between 1.82 and 4 patients needing to be treated.

A *confidence intervals is important* as it provides (a) the precision of the estimate and (b) the uncertainty of the estimate (4).

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[1] To be more precise we would expect 95% of the hypothetical samples of the same size from the population would contain the true value of the NNT within these two boundaries.