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CHRONIC PAIN

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ABSTRACT:

Chronic pain, defined as pain persisting beyond three months, affects approximately 20% of adults globally. Unlike acute pain, which serves as a warning signal, chronic pain is a maladaptive condition involving complex neuroplastic changes in the central and peripheral nervous systems. This article explores the pathophysiology of chronic pain, its distinction from acute pain, the biopsychosocial model of management, pharmacological interventions (NSAIDs, opioids, adjuvants), and non-pharmacological strategies (CBT, physical therapy, mindfulness). The article concludes with an original crossword puzzle to reinforce key terminology.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. While acute pain resolves with healing, chronic pain persists long after the initial injury has healed—or without any identifiable injury at all. Conditions such as fibromyalgia, diabetic neuropathy, rheumatoid arthritis, and chronic back pain fall under this umbrella. The societal cost of chronic pain includes billions in lost productivity and healthcare expenses, as well as immense personal suffering. Understanding chronic pain requires shifting from a purely biomedical lens to a biopsychosocial framework.

Pathophysiology – How Pain Becomes Chronic

Mechanisms of Chronic Pain

The transition from acute to chronic pain involves three primary processes:

Peripheral Sensitization

Following tissue injury, inflammatory mediators (prostaglandins, bradykinin, nerve growth factor) lower the threshold of nociceptors (pain receptors). Normally, a high-intensity stimulus is required to fire a pain signal. In peripheral sensitization, even a light touch can trigger pain (allodynia). This is protective in the short term but maladaptive in chronic states.

Central Sensitization

Repeated high-intensity pain signals from the periphery cause functional and structural changes in the dorsal horn of the spinal cord and the brain. NMDA receptors become hyperactive, and inhibitory pathways (GABAergic) weaken. The "pain volume knob" is turned up permanently. Wind-up phenomenon—progressively stronger pain responses to the same stimulus—is a hallmark of central sensitization.

Neuroplastic Changes in the Brain

fMRI studies show that chronic pain shrinks grey matter in the prefrontal cortex and anterior cingulate cortex (areas involved in emotion and decision-making). Simultaneously, the default mode network (active during rest) becomes overconnected, meaning the brain cannot "turn off" pain even during sleep or relaxation.

Types of Chronic Pain

Classification

Chronic pain is broadly divided into three categories based on etiology:

Type Definition Examples

Nociceptive Pain from actual or threatened damage to non-neural tissue; activates nociceptors. Osteoarthritis, rheumatoid arthritis, mechanical low back pain, cancer bone metastasis.

Neuropathic Pain caused by a lesion or disease of the somatosensory nervous system. Diabetic peripheral neuropathy, postherpetic neuralgia (shingles), spinal cord injury, phantom limb pain.

Nociplastic Pain arising from altered nociception despite no clear evidence of tissue or nerve damage. Fibromyalgia, irritable bowel syndrome (IBS), non-specific chronic low back pain, tension headaches.

The distinction is crucial because treatment differs: NSAIDs work for nociceptive pain, while gabapentinoids (gabapentin, pregabalin) are first-line for neuropathic pain.

The Biopsychosocial Model

Beyond Biology – Psychological & Social Factors

The biopsychosocial model, proposed by Engel in 1977, is the gold standard for understanding chronic pain.

Psychological Factors

· Fear-avoidance model: Patients who catastrophize ("this pain means I am dying") avoid movement → deconditioning → more pain → more fear (vicious cycle).

· Depression & Anxiety: 50% of chronic pain patients meet criteria for major depression. Serotonin and norepinephrine dysregulation is common to both conditions.

Self-efficacy: Belief in one's ability to function despite pain predicts better outcomes than pain intensity itself.

Social Factors

· Catastrophizing partners: Spouses who respond with excessive concern reinforce pain behavior.

· Workplace ergonomics and job satisfaction: Low job control + high physical demands = higher disability rates.

· Healthcare system: Fragmented care, long wait times, and opioid stigma can worsen outcomes.

. Pharmacological Management

Medications for Chronic Pain

The WHO Analgesic Ladder, originally designed for cancer pain, is adapted for chronic non-cancer pain.

· NSAIDs (ibuprofen, naproxen, celecoxib): Effective for inflammatory pain. Risk: GI bleeding, nephrotoxicity.

· Acetaminophen (paracetamol): Weaker anti-inflammatory but safer for long-term use (monitor liver).

Step 2: Weak Opioids (only for breakthrough pain in select cases)

· Tramadol, codeine. Risk: tolerance, hyperalgesia (opioid-induced increased pain sensitivity).

Step 3: Strong Opioids (controversial for chronic non-cancer pain)

· Morphine, oxycodone, fentanyl. Evidence shows minimal long-term benefit for function and high risk of addiction, respiratory depression, and opioid-induced hyperalgesia. Current guidelines recommend against chronic opioids except for palliative care.

Adjuvant Analgesics (First-line for most chronic pain)

· Gabapentinoids: Gabapentin, pregabalin (neuropathic pain, fibromyalgia).

· Antidepressants: Amitriptyline (tricyclic), duloxetine (SNRI) – modulate descending inhibitory pathways.

· Topical agents: Lidocaine patches, capsaicin cream.

Non-Pharmacological & Interventional Approaches

Non-Drug Treatments (Evidence-Based)

Physical Therapy & Exercise

Graded exposure to movement reverses fear-avoidance. Aerobic exercise (walking, swimming) increases endogenous opioids (endorphins) and reduces pro-inflammatory cytokines.

Cognitive Behavioral Therapy (CBT)

CBT targets catastrophic thinking, pacing of activities, and relaxation techniques. Meta-analyses show moderate effect sizes on pain interference and distress, though not on pain intensity itself.

Mindfulness-Based Stress Reduction (MBSR)

8-week programs teaching non-judgmental awareness of pain sensations reduce activation in the default mode network and improve pain acceptance.

Interventional Procedures

· Nerve blocks: Temporary diagnostic or therapeutic relief (e.g., medial branch block for facet joint pain).

· Radiofrequency ablation: Destroys nerve fibers transmitting pain (lasts 6–12 months).

· Spinal cord stimulation (SCS): Electrodes placed in epidural space produce paresthesia that replaces pain. Effective for failed back surgery syndrome and complex regional pain syndrome.

Page 8: The Opioid Crisis and Chronic Pain

A Cautionary Tale – The Opioid Epidemic

In the 1990s, pharmaceutical companies aggressively marketed opioids as "low-risk" for chronic pain, leading to a fivefold increase in prescriptions by 2010. The result:

· 500,000+ opioid-related deaths in the US (1999–2019).

· Widespread addiction and diversion to illicit fentanyl and heroin.

· Stigma now prevents legitimate chronic pain patients from accessing needed medication.

Current CDC Guidelines (2022):

· Opioids are not first-line for chronic pain.

· If used, start with immediate-release formulations at the lowest effective dose.

· Combine with non-pharmacological therapy.

· Monitor for risk of addiction using urine drug screens and prescription drug monitoring programs (PDMPs).

The Pendulum Swing Problem: Overly restrictive prescribing has led to "opioid abandonment" – some patients with legitimate severe pain (e.g., sickle cell disease, post-surgical pain) are now under-treated. The future lies in precision medicine and non-addictive alternatives.

Emerging Therapies

The Future of Chronic Pain Management

8.1 Sodium Channel Blockers (NaV1.7, NaV1.8)

Genetic studies show that people lacking NaV1.7 channels feel no pain.

[05.04.2026 23:10] Ismoilxon: Selective blockers are in clinical trials for congenital insensitivity to pain and erythromelalgia.

8.2 Monoclonal Antibodies

· Tanezumab (anti-NGF): Blocks nerve growth factor. Effective for osteoarthritis but caused rapid joint destruction in some patients (now restricted).

· CGRP antagonists: Already approved for migraine (a neurovascular pain disorder).

8.3 Psychedelic-Assisted Therapy

Psilocybin (magic mushrooms) and MDMA are in Phase 2 trials for fibromyalgia and phantom limb pain. Mechanism: disrupting the default mode network and increasing neuroplasticity.

8.4 Virtual Reality (VR)

VR distracts the brain and modulates pain perception through immersive environments. EaseVRx (prescription VR) is FDA-approved for chronic low back pain.

8.5 CRISPR Gene Editing

Preclinical models show that knocking out the NaV1.7 gene reverses inflammatory pain. Human trials are likely a decade away.

Conclusion & Practical Takeaways

Conclusion

Chronic pain is not merely a prolonged version of acute pain; it is a distinct disease of the nervous system. Successful management requires abandoning the simplistic "pain equals tissue damage" model. Instead, clinicians must address biological contributors (inflammation, nerve damage), psychological factors (catastrophizing, depression), and social determinants (work environment, family dynamics). The future is multimodal: a combination of central nervous system-targeted medications (gabapentinoids, SNRIs), physical rehabilitation, cognitive restructuring, and, when appropriate, interventional procedures. For patients, the goal is not zero pain but improved function and quality of life.

1. Move despite pain – graded exercise reduces disability.
2. Challenge catastrophic thoughts – "This pain is not causing damage."
3. Use adjuvants before opioids – gabapentin and duloxetine are safer.
4. Address sleep and mood – insomnia and depression amplify pain.
5. Set functional goals (e.g., "walk 15 minutes daily") rather than pain intensity goals.

Crossword Puzzle (Reinforcement of Key Terms)

Cronic Pain Crossword Puzzle

Instructions: Solve the crossword using the clues below. All answers are key terms from this article

2. Type of pain caused by a lesion or disease of the somatosensory nervous system (e.g., diabetic neuropathy) (11 letters)

5. Drug class including gabapentin and pregabalin, first-line for neuropathic pain

7. Psychological process of magnifying the threat of pain (e.g., "This pain will ruin my life") .

9. The brain's inability to stop processing pain signals even at rest; involves the default mode network (16 letters – two words)

11. A non-pharmacological therapy that teaches non-judgmental awareness of sensations (10 letters – abbreviation)

13. This antidepressant (SNRI) is FDA-approved for fibromyalgia and musculoskeletal pain (9 letters)

14. The "pain volume knob" turned up permanently in the spinal cord (12 letters – two words)

1. Pain from actual tissue damage, e.g., osteoarthritis (10 letters)

2. Model of pain that includes biological, psychological, and social domains (17 letters – one word)

3. A procedure using electrodes in the epidural space to replace pain with tingling (7 letters – abbreviation)

4. The phenomenon where opioids actually increase pain sensitivity over time (10 letters – two words)

5. A topical agent derived from chili peppers that depletes substance P (7 letters)

6. A non-opioid analgesic with weak anti-inflammatory effects but safer for long-term use (12 letters)

7. Loss of grey matter in this brain region is seen in chronic pain patients (13 letters – two words)

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