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STATE OF THE ART REVIEW

Advances in the diagnosis and management of neck pain

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ABSTRACT

Neck pain imposes a considerable personal and socioeconomic burden—it is one of the top five chronic pain conditions in terms of prevalence and years lost to disability—yet it receives a fraction of the research funding given to low back pain. Although most acute episodes resolve spontaneously, more than a third of affected people still have low grade symptoms or recurrences more than one year later, with genetics and psychosocial factors being risk factors for persistence. Nearly half of people with chronic neck pain have mixed neuropathic-nociceptive symptoms or predominantly neuropathic symptoms. Few clinical trials are dedicated solely to neck pain. Muscle relaxants and non-steroidal anti-inflammatory drugs are effective for acute neck pain, and clinical practice is mostly guided by the results of studies performed for other chronic pain conditions. Among complementary and alternative treatments, the strongest evidence is for exercise, with weaker evidence supporting massage, acupuncture, yoga, and spinal manipulation in different contexts. For cervical radiculopathy and facet arthropathy, weak evidence supports epidural steroid injections and radiofrequency denervation, respectively. Surgery is more effective than conservative treatment in the short term but not in the long term for most of these patients, and clinical observation is a reasonable strategy before surgery.

Introduction

Neck pain is a common condition and a leading cause of disability worldwide.[1 2] Despite the enormous burden that neck pain exacts on society, it attracts only a fraction of the research money and publicity given to back pain.[3] In this article, we explore the epidemiology, diagnosis, and treatment of neck pain. Emphasis is given to controversial topics and treatments that are most commonly used and investigated (such as integrative and interventional treatments), with particular attention paid to areas that are most relevant to academics and specialists.

Sources and selection criteria

In February 2017, we searched the Medline database, Embase, Google Scholar, and the Cochrane Database of Systematic Reviews using the search terms “cervical pain”, “neck pain”, “cervical radiculopathy”, “cervical radicular pain”, and “cervical myelopathy”, with no restrictions. For individual sections, key words relating to the relevant topics (for example, facet joint, epidural steroid injections, physical examinations, antidepressants, acupuncture, and surgery) were identified and cross referenced with the initial search terms using the above databases. We considered animal and experimental studies, systematic and other reviews, meta-analyses, clinical trials, and for certain sections in which higher grade evidence was lacking (such as treatment and complications) case reports and case series. Systematic reviews and clinical trials, particularly larger randomized studies, were prioritized over lower grade evidence. We also obtained additional articles by examining reference lists.

Epidemiology

Neck pain has a high prevalence in developed countries. One systematic review estimated mean point, annual, and lifetime prevalence rates of 7.6% (range 5.9-22.2%), 37.2% (range 16.7-75.1%), and 48.5% (range 14.2-71%), respectively.[1] According to the Global Burden of Disease 2010 study, neck pain is the fourth most common cause of disability in the United States, after back pain, depression, and other musculoskeletal disorders.[2] Women are more likely to experience neck pain, with peak prevalence occurring in middle age.[1 4] A recent review estimated that the annual cost of low back and neck pain was $87.6bn (£67.8bn; €77.2bn) in the US, ranking third behind diabetes and heart disease.[5]

Risk factors

Several risk factors predispose to the development of neck pain, including psychopathology, genetics, sleep problems, smoking, obesity, sedentary lifestyle, previous neck pain, trauma, back pain, and poor general health.[6-9]

Sports and work injuries have also been associated with neck pain, with the highest incidence noted for race car driving, wrestling, and ice hockey.[4] Although office and computer workers, manual laborers, healthcare workers, and occupational drivers are more likely than others to experience neck and shoulder pain, low job satisfaction and poorly perceived work support are the major work related factors associated with neck pain.[10]

Classification

Neck pain can be classified in several ways—for example, acute versus chronic or associated versus not associated with occipital headaches. However, the most relevant classification separates neck pain into neuropathic, which requires discrete identifiable nerve(s) injury as the cause of symptoms, and non-neuropathic, because this distinction affects diagnostic assessments and treatment at all levels of care. In the lumbar region, studies have reported prevalence rates of 16-55% for neuropathic pain,[11 12] with one review reporting an aggregate rate of 36.6%.[13] The only study performed in the cervical region found that 43% of 100 patients had non-neuropathic pain, 7% had predominantly neuropathic pain, and 50% had mixed pain.[14] The low proportion of patients with solely neuropathic pain probably resulted from the methodology used because selection criteria required patients to have neck pain (those with arm pain without neck pain were excluded). The high proportion of patients with mixed neuropathic-nociceptive pain was attributed to the fact that radicular pain is usually caused by degenerative conditions that predispose a person to nociceptive pain (for example, herniation occurring in a degenerative disc or facet hypertrophy resulting in foraminal stenosis).[3] People with neuropathic pain had higher levels of functional impairment and psychopathology, similar to what has been reported for low back pain.[11] Not surprisingly, those with neuropathic or mixed pain states were more likely to receive procedural interventions such as surgery and epidural steroid injections (ESIs).[14]

Natural course

Acute neck pain

Most episodes of acute neck pain resolve within two months, although about half of patients continue to have low grade symptoms or recurrences and to seek healthcare for their symptoms for more than one year.[15-18] Ironically, neither early treatment nor radiographic degeneration seems to have a meaningful impact on prognosis.[16 19] Variables that predict persistence include female sex, older age, presence of radiculopathy, higher baseline pain intensity, multiple pain sites, smoking, obesity, poor general health, and a variety of psychosocial factors.[15-21]

Cervical radiculopathy

Although cervical radicular pain is associated with a worse prognosis than axial pain, most patients improve.[21] A retrospective study of 561 patients with cervical radicular pain reported that although recurrences were common (31.7%), 90.5% of people had minimal or no pain at a mean follow-up of 5.9 years.[18] A systematic review evaluating the natural course of cervical radicular pain from a herniated disc found that although most patients improved within six months, complete improvement, which was seen in 83% of people, took two to three years. The main factor associated with poor outcome was an ongoing worker's compensation claim.[22] These findings are consistent with radiological studies showing that about half of cervical disc herniations will decrease within the first six months and about 75% will decrease by more than 50% within two years.[23] Data on the natural progression of cervical stenosis are scant, but unlike disc herniations, the anatomical derangements of spinal stenosis do not regress with time.

Cervical myelopathy

Cervical myelopathy results from disease (for example, myelitis) or injury (for example, trauma or syrinx) affecting the spinal cord, which causes upper motor neuron signs. In young people, trauma is the most common cause of myelopathy, whereas spondylosis is the most common cause later in life.[24] The incidence and point prevalence rates of cervical myelopathy are conservatively estimated to be 41 per million and 605 per million, respectively.[25] The natural course of cervical myelopathy is highly variable and is characterized by periods of quiescence and stepwise progression.

Whereas myelopathy is sometimes considered an indication for surgery, studies comparing surgical and non-surgical outcomes have been mixed. A randomized trial comparing surgical to non-surgical treatment for mild to moderate spondylotic myelopathy reported that more than 80% of both groups exhibited no progression or improvement at three year follow-up.[26] Another prospective study also described a 20% deterioration rate at a mean follow-up of three years.[27] A prospective study in 62 patients found that about three quarters of surgically and non-surgically treated patients were satisfied with treatment at a mean follow-up of 11 months, although those managed medically experienced more neurological deterioration.[28]

Other retrospective studies have reported worse outcomes for spondylotic myelopathy. One found that 10 of 27 patients treated conservatively over six months experienced deterioration that necessitated surgery,[29] whereas another found that all 22 patients with cervical myelopathy reported progression, with 21 proceeding to surgery.[30] The authors of a literature review combined with a systematic review[31] as well as a consensus statement on conservative management[32] concluded that 20-60% of patients will deteriorate at three to six year follow-up, with only the area of compression weakly predicting disease progression. About 23% of patients with spondylotic cord decompression without myelopathic symptoms will progress to myelopathy within four years.[32] Other factors associated with poorer prognosis with conservative management include small spinal canal area, greater cord compression, younger age, and more severe symptoms.[27 33]

Prevention

Many biological and psychosocial factors can predispose to chronic neck pain, but it is less well known that

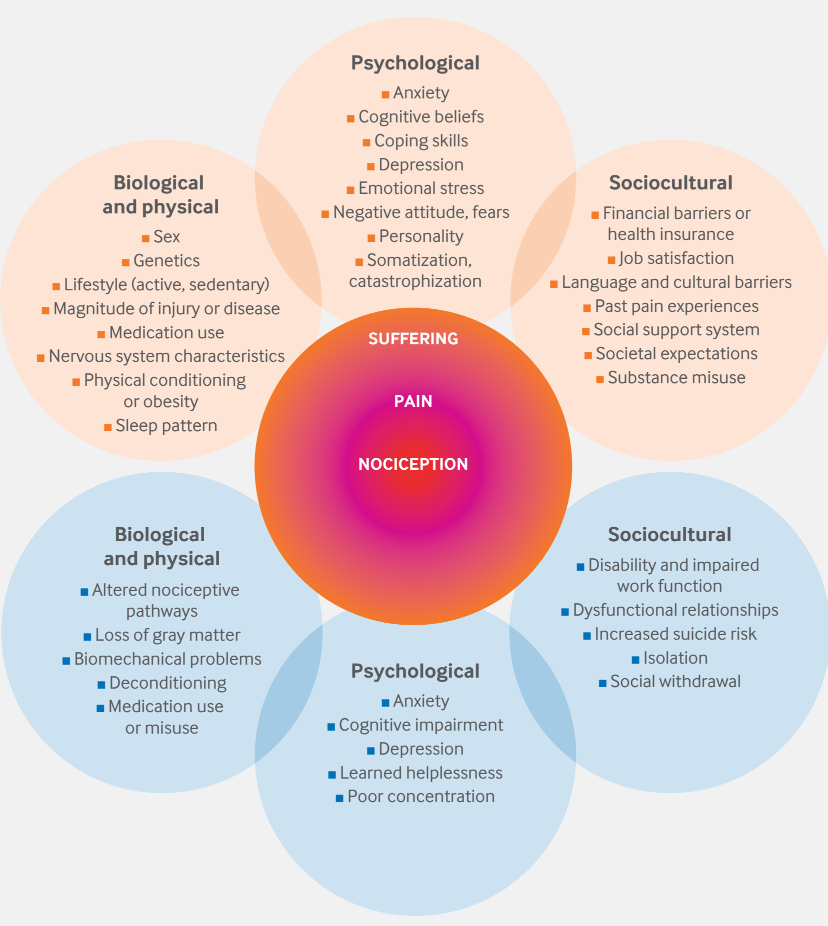

Fig 1 | The biopsychosocial model of pain posits that biological, psychological, and social factors influence who develops chronic pain (pink circles) and that chronic pain has biological, psychological, and social consequences (blue circles). Courtesy of Frank Corl (Mayo Clinic), Steven Cohen, and W Michael Hooten

chronic pain is often associated with anatomical, psychological, social, and professional factors. This is consistent with the biopsychosocial model, which considers pain to be a dynamic interaction between biological, psychological, and social factors unique to each individual (fig 1). Consequently, researchers have examined whether a variety of interventions can prevent the development of neck pain and its transition to chronic pain and disability.

The risks and costs of using drugs and other interventions to prevent neck pain in asymptomatic high risk populations outweigh the benefits so this approach is not indicated. One meta-analysis found that education did not prevent neck and back pain.[34] Another review of multiple controlled trials found that exercise was effective in preventing neck and low back pain but there was no evidence to support or refute the effectiveness of ergonomic or risk factor modification.[35] In people with acute whiplash injury, one large randomized controlled study performed in 405 patients who presented to the emergency department found that an educational video added to usual care resulted in a 7.9% (95% confidence interval −2.0 to 17.8) decrease in the proportion of people who still had pain at 24 weeks compared with usual care alone.[36]

Box 1 | Uncommon medical and systemic causes of neck pain

Neoplastic
- Metastatic tumor
- Multiple myeloma
- Spinal cord tumors
- Chordoma

Inflammatory
- Rheumatoid arthritis
- Seronegative spondyloarthropathies

Infectious
- Osteomyelitis
- Epidural abscess
- Discitis
- Herpes zoster
- Meningitis

Vascular
- Arteriovenous fistula or malformation

Endocrinological
- Paget's disease
- Osteoporotic fractures

Neurologic
- Peripheral neuropathy
- Amyotrophic lateral sclerosis
- Transverse myelitis
- Guillain-Barré syndrome
- Brachial plexus lesion

Evaluation

A thorough history and physical examination is needed to distinguish neuropathic pain from mechanical neck pain because treatment decisions are based on this distinction. Medical and systemic disorders can cause neck pain (box 1; fig 2), and most are regional musculoskeletal or neuropathic in nature.

Suspected neuropathic pain

Nerve root compression caused by an acute intervertebral disc herniation may initially produce neck pain, followed by arm pain. A history of physical exertion or trauma is often assumed to be a causative factor but is present in less than 15% of patients.[18] Radicular pain typically occurs in a dermatomal pattern, although more than half of people have multiple nerve root involvement and there is considerable dermatomal overlap.[37] Clinical symptoms of nerve root compression may also be secondary to foraminal stenosis, which is typically associated with an insidious onset.[38] Exacerbating factors can include coughing, sneezing, or other activities that increase subarachnoid pressure. Another common source of neuropathic pain is cervical spinal stenosis. Presenting symptoms can include neck pain, stiffness, and upper extremity radicular pain. One potential consequence of cervical spine stenosis is the development of cervical myelopathy, which is characterized by symptoms of upper motor neuron impairment.[39] In patients with presumed cervical myelopathy, amyotrophic lateral sclerosis should be suspected when fasciculations and bulbar signs are evident.

Signs of nerve root compression can be identified on physical examination but may be obscured by the

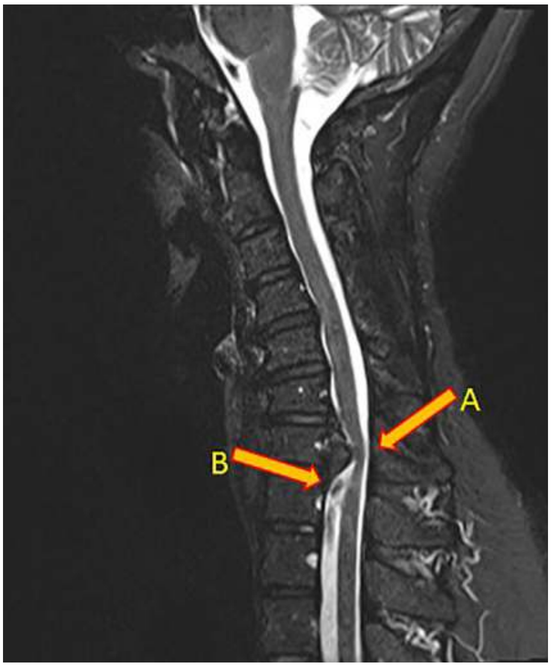

Fig 2 | Short T1 inversion recovery (STIR) magnetic resonance image showing an osteochondroma causing spinal cord compression (A) in a patient with multiple hereditary exostoses. The patient presented with myelopathy and mild spinal cord signal changes. Arrow B indicates decreased signal within the cerebrospinal fluid representing a flow related artefact. Courtesy of Brandon Childers, Department of Radiology, Johns Hopkins

presence of active myofascial trigger points, which were found in one study to occur in 51.2% of people with cervical radiculopathy.[40] On inspection, the head and neck may be slightly tilted towards the affected side. Muscles of the neck, shoulder, arm, and hand should be observed for atrophy, which may indicate the presence of long standing nerve root dysfunction. However, numbness in the hands and fingers is often indicative of carpal or cubital tunnel syndrome and not spinal nerve root compression. Physical examination maneuvers may help establish a diagnosis of nerve root compression. For example, Spurling's test and upper limb tension tests have sensitivities exceeding 50%, and the specificities of Spurling's test, shoulder abduction and neck distraction tests range between 80% and 90% (table 1).[41-44] When performing physical examination maneuvers, shoulder pain elicited during rotation and abduction of the arm suggests a primary shoulder problem rather than nerve root compression. Physical examination findings are often non-specific for cervical stenosis but include reduced cervical range of motion and paraspinal tenderness. In general, tests may be more accurate in acute than in chronic radiculopathy and for herniated discs compared with stenosis, but the use of multiple tests increases precision.[44]

Diagnostic tests

Diagnostic imaging is recommended for the evaluation of neuropathic neck pain. Although magnetic resonance imaging (MRI) is superior to computed tomography for evaluating soft tissue abnormalities, computed tomography or computed tomography-myelography may help distinguish osteophytes from soft tissue abnormalities and can be used when MRI is contraindicated. For the evaluation of nerve root compression, MRI findings should be interpreted in the context of the clinical presenation.[45] In an MRI study of 78 patients with cervical radiculopathy for less than one month, the clinically affected root was identified in 73% of patients.[46] However, the false positive rate was 45% and the false negative rate was about 26%, indicating the absence of compression at the affected level. Regardless of the performance characteristics of imaging modalities, brachial plexus pathology should be considered in patients with upper extremity pain, weakness, sensory loss, and a non-diagnostic imaging study.

Electromyography and nerve conduction studies are the key electrodiagnostic tests used to identify physiological nerve root abnormalities. The two main objectives of electrodiagnostics are:

- To confirm the existence of nerve root dysfunction and exclude other peripheral nerve disorders, such as plexopathy
- To identify which nerve root(s) is involved and determine the type of nerve root dysfunction, such as demyelination, axonal loss, and conduction block.

The sensitivity of electrodiagnostic testing for cervical radiculopathy ranges from 50% to 71%,[47 48] so a non-diagnostic test result does not exclude nerve root dysfunction.[49] In clinical practice, the utility of electromyography could be affected by confounding musculoskeletal disorders such as myofascial pain and lateral epicondylitis, which are often present in patients referred for electrodiagnostic testing.[50]

Evaluation of mechanical non-radicular neck pain

The onset of non-radicular neck pain is usually insidious, but pain referral patterns may help distinguish between common sources of pain. For example, axial neck pain referred to the occipital, suboccipital, shoulder, or mid-back regions is suggestive of cervical facet joint pain.[51] Specifically, the atlanto-occipital, and atlanto-axial joints can be associated with occipital and posterior auricular pain, pain emanating from the C2-3 or C3-4 facet joints can extend into the occipital and suboccipital regions, C4-5 or C5-6 facet joint disease can cause pain radiating into the shoulder, and the C6-7 and C7-T1 joints typically refer pain to the mid-back and scapular regions.[51] Cervical facet pain does not usually extend distal to the shoulder and is not associated with neurological deficits, which can help distinguish it from radicular pain. Axial neck pain associated with headaches, unilateral or bilateral shoulder pain, non-radicular arm pain, ocular and vestibular dysfunction, and anterior chest wall pain is suggestive of cervical discogenic pain.[52] Activities that may provoke or aggravate discogenic pain include coughing, lifting, or applying pressure on the cervical spinous processes, whereas lying supine may relieve pain.[52] Regardless of the underlying source, studies have shown increased myoelectric activity in patients with chronic neck pain,[53] and the prevalence of trigger points in the neck musculature of people with chronic neck pain can exceed 50%.[54] This suggests that myofascial pain is often associated with primary pain generators.

Table 1 | Clinical and diagnostic evaluation of neck pain*[3-44]

Source of pain	Risk factors	History	Clinical signs	Physical examination	Diagnostic imaging	Electrodiagnostics
Axial (non-radicular)						
Facet joint	Motor vehicle collision Trauma Whiplash injury	Insidious onset	Axial neck pain Referred pain to occiput, shoulder, mid-back	Reduced neck ROM Paraspinal tenderness No neurological deficits	Weak association with facet arthrosis on plain films	Not indicated
Intervertebral disc	Smoking Advancing age Repetitive neck motions Trauma	Insidious onset	Axial neck pain Shoulder pain Non-radicular arm pain Vestibular findings	Reduced range of motion (extension > flexion; lateral bending > rotation) Midline tenderness	Plain films show reduced disc height Annular tears or fissures on MRI	Not indicated
Muscles and ligaments	Strenuous occupation Repetitive movements High impact sports	Acute or insidious onset History of whiplash injury	Axial neck pain Possible referral to shoulders and mid-back	Paraspinal tenderness Muscle guardingReduced neck ROM No neurological deficits	Plain films for fracture CT for fracture MRI for soft tissues	Not indicated
Radicular						
Nerve root compression	Middle age when caused by disc herniation Advanced age when caused by foraminal stenosis Smoking Lumbar radiculopathy Strenuous occupation	May have acute onset with disc herniationInsidious onset with spondylosis	Neck pain UE weakness in myotomal pattern Sensory changes in dermatomal pattern Upper extremity neurological weakness or numbness	Spurling's test 40-60% sen, 85-95% spec Shoulder abduction 40-50% sen; 80-90% spec Neck distraction 40-50% sen; 90% spec Upper limb tension 70-90% sen; 15-30% spec Valsalva 22% sen; 94% spec	MRI for nerve root compression False positive 45%False negative 26% CT or CT myelography to distinguish osteophytes from soft tissue changes	Electromyography 50-71% sen; 56-85% spec
Spinal stenosis	Advanced age Congenitally small spinal canal	Insidious onset	Neck pain Neck stiffness UE radicular pain	Reduced neck ROM Paraspinal tenderness	MRI for soft tissuesCT for osseous diameter of spine canal	Used for radiculopathy
Cervical myelopathy	Age >50 years Male Spinal cord trauma Syrinx	Insidious onset	Neck pain UE weakness and numbness Gait deficits Loss of dexterity	Lhermitte's sign <20% sen; >90% spec Hoffman's sign 50-80% sen; 78% spec Babinski's reflex 10-75% sen; >90% spec Hyper-reflexia >65% sen Clonus <50% sen	MRI for intramedullary hyperintensity	Used for spinal cord conduction deficits and anterior horn cell dysfunction

*Abbreviations: CT=computed tomography; MRI=magnetic resonance imaging; ROM=range of motion; sen=sensitivity; spec=specificity; UE=upper extremity.

The abrupt onset of axial neck pain is often the result of trauma; exposure of the cervical spine, including its muscles and ligaments, to excessive forces; or an underlying medical condition. When trauma is suspected, the clinical history should focus on identifying the potential mechanism of injury. On physical examination, guarding may result in a reduced range of motion and the neck musculature may be tender to palpation. The absence of midline cervical spine tenderness, focal neurological deficits, intoxication, and painful distracting injury (clinically apparent pain that might distract the patient from the pain of a cervical spine injury), together with a normal level of consciousness indicates a low probability of serious cervical spine injury after blunt trauma.[55]

Whiplash refers to an "acceleration-deceleration mechanism of energy transfer to the neck" often stemming from rear or side impact motor vehicle collisions.[56] Although neck pain after whiplash injury can be attributed to the facet joints in about 50% of people,[57] other structures are important contributors to pain including the discs,[56 58] muscles,[56 59] and ligaments.[56 60] Consequently, pain associated with whiplash injury is often referred to the trapezius muscle, shoulder, mid-back, and, to a lesser extent, the face.[61] Up to 80% of people will experience neck pain within one day of sustaining a whiplash injury and about 50% will continue to report neck pain one year after the initial injury.[62] Although acute pain after whiplash may be secondary to subclinical disease (soft tissue injury or trauma involving the spine),[56] no reliable link has been established to account for persistent chronic pain. Diagnostic imaging should include flexion-extension radiographs of the cervical spine to look for fractures or vertebral body malalignment; however, radiographs may yield limited diagnostic information.[63] Depending on the extent of injury, computed tomography and MRI may be warranted to look for fractures and ligamentous injury,[64] although studies have generally found no association between MRI findings and persistent pain after whiplash.[65]

Red flags

A key component of the clinical evaluation of neck pain is to identify serious pathology and non-musculoskeletal diseases that may be the source of pain and related symptoms. The differential diagnosis of neck pain is broad but includes trauma and non-musculoskeletal disease processes that can be classified as neoplastic, inflammatory, infectious, vascular, endocrinological, and neurologic in origin (box 1). Red flags refer to signs and symptoms that raise suspicion of something more serious than conventional musculoskeletal disorders, such as spinal cord injury, infection, tumors, or cardiovascular disease. In contrast to low back pain,[66] the diagnostic accuracy of red flag findings for identifying life threatening or critical disease involving the neck has not been reported. In addition to trauma and other factors that predispose a person to dangerous neurological sequelae, such as atlanto-axial subluxation in Down's syndrome and inflammatory arthritis,[3 67] important risk factors and clinical features suggestive of a non-musculoskeletal disease process can be generally categorized as: age related, physical signs and symptoms, neurological findings, and serum markers of inflammation (figs 3-5).[52]

Causes and treatments

There are as many potential pain generators in the neck as there are anatomical structures, and in the absence of a pathognomonic means for diagnosis, it can be difficult

RED FLAGS

AGE RELATED FACTORS

Age < 20 years
- Congenital abnormalities
- Birthmarks
- Altered hair distribution
- Skin tags
- Family history
- Infections related to substance misuse

Age > 50 years
- History of cancer
- Vascular disease

PHYSICAL SIGNS AND SYMPTOMS
- Fever
- Neck stiffness
- Nausea or vomiting
- Unexplained weight loss
- Torticollis
- Limited neck mobility
- Erythema or exudate
- Severe neck tenderness

MISCELLANEOUS
- Raised erythrocyte sedimentation rate
- Raised C reactive protein
- Raised white blood cell count
- New symptoms in the context of inflammatory arthritis
- Trauma

NEUROLOGICAL FINDINGS
- Hoffmann's and Babinski's sign
- Hyper-reflexia
- Altered muscle tone
- Incontinence
- Altered cognitive status
- Ataxia
- Visual loss
- New or severe headache
- Photophobia or phonophobia

Fig 3 | Red flags for neck pain necessitating further investigation. Courtesy of Frank Corl (Mayo Clinic), Steven P Cohen, and W Michael Hooten

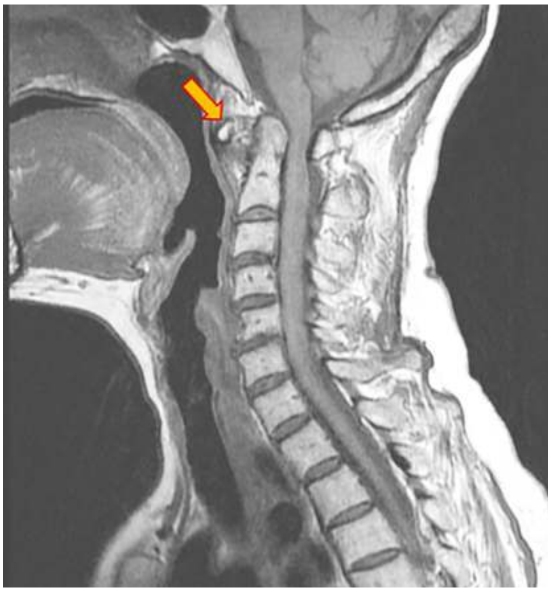

Fig 4 | T1 weighted sagittal magnetic resonance image showing increased distance between the posterior aspect of the anterior arch of C1 and the anterior margin of the dens of C2 (arrow), indicating atlanto-axial subluxation in a patient with rheumatoid arthritis. There is also anterior positioning of the posterior arch of C1 resulting in mild to moderate spinal cord compression without edema. Courtesy of John Carrino (Weil Cornell Medical College)

to identify the source of pain. Many treatments are predicated on precise diagnoses, often in the form of "diagnostic blocks," but in the absence of any confirmatory reference standard the validity of diagnostic injections can never truly be known. Given the interdependent association between adjacent structures, most people probably have multiple concurrent pain generators (fig 6).

Mechanical non-neuropathic causes

Non-specific neck pain

Few clinical trials have evaluated drugs for neck pain, so treatment is often based on generalization from studies performed for back pain. Because no study evaluating pharmacotherapy for non-neuropathic spinal pain has ever "diagnosed" a specific cause on the basis of injections (such as facet blocks), the study population

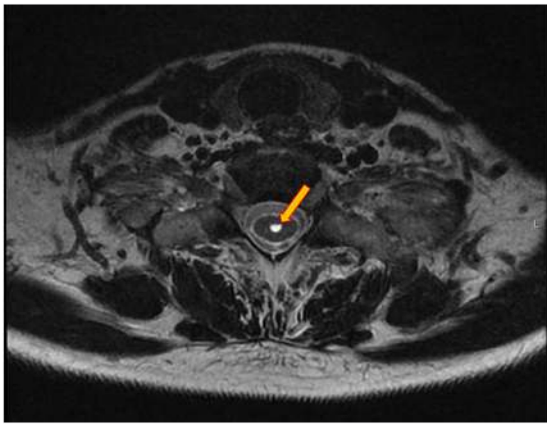

Fig 5 | T2 weighted axial magnetic resonance image through C7-T1 showing a syrinx (arrow). Courtesy of John Carrino (Weill Cornell Medical College)

is often referred to as having "non-specific" neck pain. This denotes pain that cannot be attributed to a specific cause often because a proper investigation has not been conducted. It is unclear whether drugs that are effective for non-specific spinal pain would yield similar benefit in a more homogeneous population, such as those with discogenic pain. Given that these drugs have small effect sizes even in ideal circumstances, it is reasonable to try non-pharmacological treatment options first.

Reviews have concluded that systemic non-steroidal anti-inflammatory drugs (NSAIDs) are effective in back pain, but they carry a risk of adverse effects in people over 60 years and have not been evaluated in neck pain. Two moderately sized placebo controlled trials established short term (2-8 days) benefit for topical diclofenac in people with neck and upper back pain secondary to suspected muscle and joint disease (mean difference 63% in pain scores in the treatment group versus 24% in the control group),[68 69] which is consistent with reviews showing efficacy for topical NSAIDs in acute and chronic musculoskeletal pain.[70]

Muscle relaxants can alleviate pain and improve function in patients with spinal pain and are more effective for acute pain than for chronic pain. Two randomized controlled trials (RCTs) evaluating cyclobenzaprine in 1405 patients with acute neck (more than a third of patients)

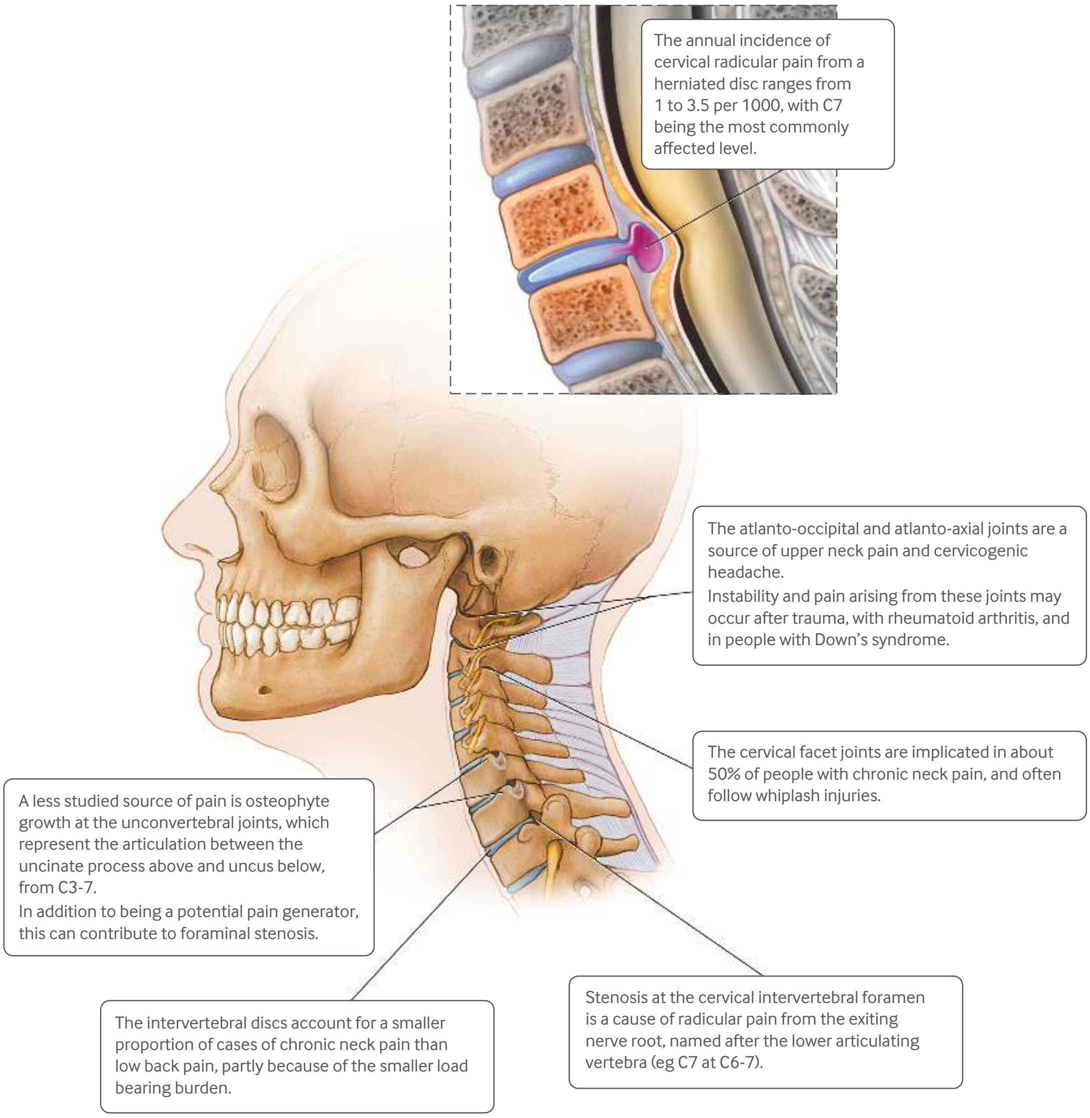

Fig 6 | Sagittal view of cervical spine showing potential pain generators. Courtesy of Frank Corl (Mayo Clinic)

or back pain secondary to muscle spasm found that intermediate doses (15 mg/d) and high doses (30 mg/d) were more effective than placebo (P<0.03), but that low doses (7.5 mg/d) were ineffective (responder rate for intermediate dose 11-20% higher than placebo group).[71] A double blind crossover study in 90 people with joint or back pain, compared the anti-inflammatory drug benorylate alone to benorylate and chlormezanone. It found no benefit for add-on muscle relaxant therapy, although subgroup analysis found significant improvement in patients with neck pain for pain reduction and sleep.[72] Comparative effectiveness research is one of the top chronic pain research priorities of the National Institutes of Health (NIH), yet few pain studies have compared treatments. A three arm randomized trial compared spinal manipulation; home exercise and advice; and pharmacotherapy with NSAIDs, acetaminophen, or muscle relaxants (or a combination of these drugs) in 272 people with acute and subacute neck pain. Patients in the manipulation and exercise groups fared statistically significantly better than those who received pharmacological treatment up to 12 month follow-up (50% responder rates 82%, 77%, and 69%, respectively, at week 12).[73]

Collectively, these studies provide moderate evidence that topical NSAIDs such as diclofenac are effective for acute and chronic neck pain and weak evidence supporting muscle relaxants for subacute neck pain associated with muscle spasm. However, neither drug is better than non-pharmacological alternative treatments.

Myofascial pain

Myofascial pain is a common cause of neck pain that involves discrete or diffuse areas of sensitivity within one or more muscle. The causes of myofascial pain are poorly understood, but muscle pain can develop secondary to biomechanical imbalances, trauma, emotional stress, and even endocrine and hormonal abnormalities. Tender muscles release excess acetylcholine, which can result in dysfunctional motor endplates, sustained muscle contractions, local ischemia, sarcomere shortening, and the release of inflammatory mediators, in what can devolve into a vicious circle.[74]

A hallmark of myofascial pain is the presence of palpable trigger points, which are taut muscle bands that refer pain in a defined pattern spontaneously or after stimulation, although their clinical relevance is controversial. In the neck, primary (key) trigger points often elicit satellite (remote) trigger points.[75] Studies that have evaluated trigger points with electromyography have found both increased (amplitude and duration)[76] and decreased[77] myoelectric activity, with the decreased activity being attributed to muscle weakness. Irritable muscles can lead to stiffness, spasms, and muscle fiber shortening, which impedes relaxation and reduces strength.[78]

Although ultrasound and other tests have been advocated to identify trigger points and myofascial neck pain, physical examination remains the reference standard.[79] One meta-analysis performed in people with chronic neck pain found that the point prevalence of active trigger points ranged from 14.8% in the right levator scapula to 38.5% in the right upper trapezius.[80]

The treatment of myofascial pain should be multimodal and should include correcting underlying structural and postural imbalances, physical therapy (for example, massage and range of motion exercises), drugs, and psychotherapy (including cognitive behavioral therapy and biofeedback).[81] When conservative options fail, trigger point injections should be considered as adjunctive therapy. This procedure involves inserting a small needle into the taut muscle band(s) in the area of maximal tenderness, which should elicit a local twitch response. A small amount of drug is injected, after which the needle is withdrawn and redirected into the hyperirritable region from different directions. The precise mechanism by which injections inactivate trigger points is unknown, but hypotheses include mechanically disrupting the abnormal taut bands, inhibiting nociceptive feedback loops, increasing local endorphin levels, and releasing cellular potassium, which interferes with nerve conduction.[81]

Many randomized trials have evaluated trigger point injections, but they generally have methodological flaws such as use as a standalone treatment and the lack of a true placebo group (dry needling could be beneficial).[82] Some evidence suggests that trigger point injections alone are not more effective than less invasive treatments such as laser and ultrasound, and that injections with anything, including saline, are better tolerated and more effective than dry needling.[83-85] One randomized trial in 80 people with chronic whiplash disorders found no significant benefit for dry needling with exercise compared with exercise and sham needling.[86] There is little evidence to support one injectate over any other including botulinum toxin,[84,85] which purportedly works by inhibiting excessive release of acetylcholine, thereby diminishing aberrant muscular contractions.[87] An RCT in people with neck and shoulder pain after a whiplash injury found that up to three injections with sterile water significantly reduced pain scores compared with saline three months after treatment (mean decrease in pain score 1.7 *v* –0.4; P<0.02).[88]

Cervical facet joint pain

On the basis of medial branch (facet joint nerve) blocks, the prevalence of cervical facet joint pain is estimated at 40-55% in patients with neck pain with or without whiplash.[89] In the absence of a history of cervical facetogenic pain or physical examination signs correlating with such pain,[90] injections of the medial branches innervating the joints, or the joints themselves, are considered the reference standard for diagnosis.[91] However, without a standard for comparison, the accuracy of cervical facet blocks cannot be known, and their utility is controversial. Consequently, the best way to view these blocks may be as "prognostic" blocks before radiofrequency ablation (RFA). Many experts advocate performing placebo controlled or comparative local anesthetic blocks to improve accuracy, because single blocks carry a false positive rate of 27-60%.[89,92] However, having a prevalence (true positive) rate of 50% coupled with a false positive rate approaching 50% is irreconcilable, leaving little room for true and false negative blocks. Moreover, the prevalence rate in studies does not significantly change with the diagnostic criteria—it is similar regardless of the threshold for a positive block or whether double blocks are used.[89] No studies have examined the utility of multiple blocks in the neck, but a comparative effectiveness study done for suspected lumbar facet joint pain found that double blocks resulted in a lower overall success rate and higher cost than proceeding straight to RFA without a screening block.[93] The only study that evaluated outcomes of cervical facet RFA in people selected without diagnostic blocks reported 55% and 30% success rates at two months and three years, respectively.[94] In one three phase crossover study that compared local anesthetic blocks with lidocaine and bupivacaine versus placebo controlled blocks, comparative blocks were shown to have a specificity of 88% but a sensitivity of only 54%.[95] As a screening tool for a relatively safe and effective treatment in which alternative treatments include opioids or surgery, a high sensitivity and negative predictive value are desirable.

The higher prevalence of facet joint pain in the neck than in the low back is attributable to the relatively larger size of the joints compared with the discs and differences in function (less motion in the lower back).[91] Given the lower prevalence of facet joint pain in the lumbar spine, a higher false positive rate might be expected in the lumbar spine, but this is not the case.[96] This underscores the inherent limitations of using diagnostic blocks to identify a painful structure in the absence of a reference standard. A crossover study evaluating the accuracy of diagnostic intra-articular facet blocks found no significant difference in positive rates between anesthetic, placebo, and sham injections.[97]

Intra-articular steroid injections are sometimes used to treat cervical facet joint pain, but the technical failure rate is high, the only controlled trial evaluating steroid injections found no benefit,[98] and most systematic reviews have concluded that these injections are ineffective.[91] Clinical studies have found C2-3 and C5-6 to be the most commonly symptomatic levels,[99,100] whereas radiological studies have found C3-4, C4-5, and C2-3 to be more commonly affected.[101 102] Radiological evidence of degeneration is also common in asymptomatic people.[103] Along with the facet joints, the atlanto-axial and atlanto-occipital joints can be a source of pain. These joints are not amenable to ablation, and the evidence supporting intra-articular steroids is anecdotal.[104]

RFA of the medial branches is considered by many to be the standard for treating cervical facet joint pain. However, the evidence supporting RFA is mixed. In the cervical spine, a placebo controlled randomized trial performed in 24 patients with whiplash injury who experienced concordant relief with three controlled diagnostic injections reported significant improvement in the treatment group compared with sham lesioning for a median duration of 263 days (58% of patients were pain free at six months in the treatment group *v* 8% in the control group; P=0.04).[99] The only other controlled trial randomized 12 people with cervicogenic headache to RFA or sham treatment of the C2-6 medial branches.[105] Although patients received comparative local anesthetic blocks before treatment, the results were not part of the inclusion criteria. Three months after treatment, four people in the RFA group versus two people in the sham group reported 30% or more improvement in pain, although no differences were noted afterwards. Thus, the evidence supporting RFA for facetogenic pain is weak.

Cervical discogenic pain

Degenerated discs contain high levels of pro-inflammatory mediators.[106] More than 70% of people without neck pain have clinically significant disc degeneration by their mid-40s,[107] with the prevalence rising above 85% by age 60.[108] Disc degeneration also increases the likelihood of herniation.[109] No markers can distinguish a painful from a non-painful degenerative disc,[106] although there is evidence to support the role of low grade infection in some people.[110] The high prevalence of neck pain and disc abnormalities in asymptomatic people provides the conceptual appeal for discography, which is advocated as the only test that connects disease to symptoms.

Provocation discography operates on the premise that increasing intradiscal pressure by contrast injection will provoke concordant symptoms at painful levels, but prevalence studies performed in the neck have yielded disparate findings. Retrospective studies (n=173 and n=31) [111 112] reported at least one positive level that provoked concordant symptomatology in 86% and 84% of patients, respectively. In contrast to the lumbar spine, a negative control disc was not required for a positive discogram. Another retrospective study evaluating a battery of diagnostic injections in 143 people with chronic neck pain reported a 16% prevalence rate of discogenic pain.[113] A similar prevalence study found that 41% of patients with chronic neck pain had both positive discography and positive facet blocks, whereas 20% had only positive discography.[114] Along with differences in technique, another reason for the discrepancies relates to the clinical acumen of the referral source. For example, an experienced surgeon who selects discography candidates carefully will have a higher positive rate than a less experienced practitioner. A systematic review evaluating the accuracy of cervical discography found prevalence rates of 16-53%.[115]

Discography is an invasive procedure that carries a small risk of catastrophic consequences and a high false positive rate in certain populations.[116] Consequently, the evidence for using discography as a screening tool to improve surgical selection is limited. Whereas two studies reported improved fusion outcomes and a lower incidence of postsurgical adjacent segment disease when discography was used to select patients for surgery, these studies were retrospective and conducted before radiological imaging was routine.[117 118]

High quality studies of treatments for cervical discogenic pain without radicular symptoms are lacking, and surgery is a mainstay of treatment in some circles. In general, surgical treatment for common degenerative conditions is widely acknowledged to be inferior to the treatment for mechanical pain accompanied by neurological symptoms, including in the neck. As noted in the surgical section, cervical disc arthroplasty and fusion are the two main surgical treatments for degenerative spondylosis, although in clinical trials and practice these are generally used in people with radicular or myelopathic symptoms (see surgical section for evidence). One review found no evidence to support the use of cervical disc arthroplasty and fusion in the absence of radiculopathy, although cervical spine fusion is often used to treat instability or spinal deformities such as cervical kyphosis in people with neck pain who present without neuropathic symptoms.[119] The evidence supporting other treatments for discogenic pain, including epidural and intradiscal injections, and thermal ablation, is weak and inconsistent.[120-124]

Neuropathic pain

Cervical disc herniation

The annual incidence of cervical radiculopathy resulting from disc protrusion or degenerative spondylosis (or both) is estimated at 1-3.5 per 1000 person years, peaking in the sixth decade of life.[18-126] A population based study reported a 0.055% incidence of radicular pain secondary to a cervical herniated disc, although estimates based on patients seeking medical attention underestimate incidence.[127] Studies in asymptomatic volunteers report the prevalence of disc herniation as 2-23%, with a median of 11%. Most studies reported no significant differences between the sexes.[108-130]

Unlike the lumbar spine, where the traversing nerve root is most commonly irritated, in the cervical spine disc herniations and spondylosis most often affect the exiting nerve root, so a C6-7 disc herniation will usually cause C7 symptoms. The most commonly affected levels are C7 (45-60%), C6 (20-25%), and C5 and C8 (10%).[3 18] Not all radicular symptoms result from mechanical nerve root compression. Similar to the lumbar spine, cytokines and other inflammatory mediators play a pivotal role in cervical radicular pain.[131 132]

Few non-surgical treatments have been studied for cervical radiculopathy. Two RCTs evaluating ESIs yielded mixed results,[133 134] with the study that used a

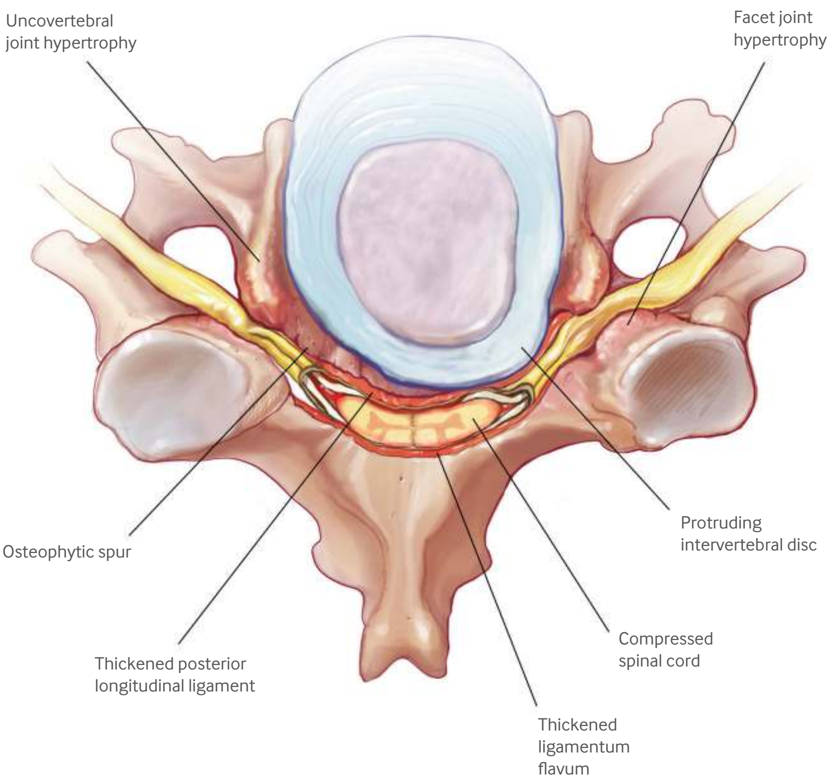

Fig 7 | Axial view of the cervical spine showing potential causes of spinal stenosis. Courtesy of Frank Corl (Mayo Clinic)

transforaminal approach reporting a negative outcome.[134] Most systematic and evidence based reviews have concluded that transforaminal ESI provides more benefit than interlaminar injections, but its use in the neck is limited because of the risk of catastrophic complications such as spinal cord infarction, particularly with depo-steroids.[124 135] Comparative effectiveness studies by one group showed similar benefit in pain relief, function, and other outcome measures such as opioid consumption and employment for both steroids and local anesthetic in a variety of cervical diseases including disc hernation.[120-138] Another randomized study in 169 patients with radicular pain found the combination of ESI and conservative treatment consisting of physical therapy and the adjuvants nortriptyline or gabapentin (or both) provided superior relief compared with either treatment alone (mean reduction in pain score of 3.1 in the combination group versus 1.9 in the others at one month; P=0.035).[139] Together, these studies provide limited evidence that ESI is more effective than epidural non-steroid injections but moderate evidence that a series of epidural injections can provide sustained relief. One criticism about ESI studies that use epidural injections as a control group is that epidural non-steroids are not a true placebo.[140] The only placebo controlled study to evaluate pulsed radiofrequency of the dorsal root ganglia reported benefit at three months in 23 patients with chronic cervical radicular pain (82% *v* 33% experienced positive outcome at three months; P=0.02).[141]

The results of controlled trials evaluating first line neuropathic drugs for radicular pain have been disappointing. Apart from the aforementioned study that found only small differences between adjuvants and ESI,[139] no randomized studies have evaluated drugs solely for cervical radicular pain. Studies evaluating antidepressants and gabapentinoids for lumbosacral radiculopathy have yielded mixed results,[142-147] with the best studies being negative.[143-147] A placebo controlled trial evaluating pregabalin in 19 people with cervical and lumbar radicular pain found no benefit for pregabalin.[146]

Cervical spinal stenosis

Spinal stenosis can be classified as central, involving the lateral recesses, or foraminal, with the last two types generally affecting the exiting nerve root(s). The incidence of symptomatic central cervical spinal stenosis, in which the spinal canal diameter measures less than 10 mm, is estimated to be one in 100 000 but significantly increases over the age of 50 years.[148] Spinal stenosis has many causes, which can broadly be categorized as congenital (for example, short pedicles), spondylotic (for example, degenerative discs, hypertrophied facet joints and ligaments, and osteophytes), iatrogenic (for example, surgery), traumatic, metabolic (for example, Paget's disease), and rheumatologic (for example, spondyloarthropathy). In adults, degenerative spondylosis is by far the most common. Risk factors for stenosis include genetics, older age, and possibly occupation—for example, porters, high performance aviators, and athletes such as rugby players are thought to be at increased risk.[25] Unlike radicular pain from a herniated disc, spinal stenosis often results in multi-level neuropathic symptoms. When spinal cord compression occurs (for example, myelopathy), symptoms may also include gait and balance disturbances, deterioration in fine motor skills, and incontinence. Hypotheses for the pathogenesis of symptoms include chronic neurogenic compression and ischemia of the spinal cord and nerve roots from venous congestion (fig 7).[148 149]

Few studies have evaluated epidural steroids for cervical stenosis. Among the randomized trials that assessed cervical ESI, two included patients with stenosis; the first found that one to three cervical ESIs performed with steroid and local anesthetic resulted in superior pain relief and range of motion compared with the same solution injected intramuscularly for up to one year (68% *v* 11.8% experienced >50% pain relief; P<0.001), a positive study.[133] The second found that conservative therapy and a series of ESIs provided significantly greater improvement than either treatment as stand-alone therapy in 169 patients, as noted above.[139] Another study comparing a series of ESIs to epidural local anesthetic found that both groups experienced significant, comparable, long term improvement.[136] In both the lumbar and cervical regions, it is widely acknowledged that the benefits afforded by ESI for herniated discs are superior to those for spinal stenosis (table 2).[124]

Exercise and integrative medicine

Exercise is often touted as an effective treatment for chronic pain, although a recent Cochrane review found that the quality of evidence is low.[158] Exercise may be beneficial for neck pain by stimulating endorphin secretion,

Table 2 | Randomized controlled trials evaluating procedural interventions for neck pain*

Reference	Patients	Treatments	Selection criteria	Results	Comments
Cervical facet joint studies					
Barnsley 1994[98]	41 patients with chronic neck pain >3 months after motor vehicle collision	Intra-articular LA or steroid	Complete concordant relief with lidocaine and bupivacaine; MBB from C2-3 to C6-7	No difference between groups; <50% had pain relief for >1 week	Saline control; intra-articular block not used
Lord 1996[99]	24 patients with neck pain >3 months after motor vehicle collision	RFA or sham denervation	Complete concordant relief with 3 placebo controlled MBBs from C3-4 to C6-7 using lidocaine and bupivacaine but not saline	RFA better than sham at 27 weeks; mean time to return of 50% of baseline pain 263 days	Excluded patients with putative C2-3 pain
Stovner 2004[105]	12 patients with chronic unilateral cervicogenic headache	RFA or sham denervation	Neck pain radiating to arm or shoulder and unilateral headache	4 patients in RFA group *v* 2 in sham group had ≥30% pain relief at 3 months but no differences afterwards	Greater occipital nerve and C2-6 MBBs were performed but not used for selection; study terminated early
Cervical epidural steroid injection studies					
Stav1993[133]	42 patients with cervicobrachialgia	1-3 cervical interlaminar ESI with LA and steroid or intramuscular injection with LA and steroid	Clinical signs and symptoms and radiological imaging	≥50% relief obtained in 76% of ESI *v* 35% of control patients after 1 week, and 68% *v* 12% after 1 year	Not all patients had radiculopathy
Anderberg 2007[134]	40 patients with cervical radiculopathy	Transforaminal LA and steroid or LA and saline from C5-8	Clinical symptoms and MRI pathology along with (+) diagnostic selective nerve root block	No difference between groups up to 3 weeks	11 patients had 2 levels treated
Manchikanti 2012[136]	120 patients with cervical central spinal stenosis	Multiple interlaminar ESI with LA or LA and steroid as needed	Neck and arm pain with MRI showing spinal stenosis	More than 70% of patients in both groups had ≥50% improvement at 2 years, with no differences between groups	High number of patients on opioids; all patients received exercise program; more injections done in patients with positive outcome
Manchikanti 2012[137]	56 patients with cervical postsurgical pain	Multiple interlaminar ESI with LA or LA and steroid as needed	Persistent neck and arm pain after surgery	More than 70% of patients in both groups had ≥50% improvement at 2 years, with no differences between groups	High number of patients on opioids; all patients received exercise program; more injections done in patients with positive outcome
Manchikanti 2013[138]	120 patients with cervical disc herniation	Multiple interlaminar ESI with LA or LA and steroid as needed	MRI showing disc herniation; patients did not have to have arm pain	More than 70% of patients in both groups had ≥50% improvement at 2 years, with no differences between groups	High number of patients on opioids; all patients received exercise program; more injections done in patients with positive outcome
Manchikanti 2014[120]	120 patients with axial neck pain	Multiple interlaminar ESI with LA or LA and steroid as needed	Negative facet blocks; imaging not noted; included patients with arm pain	More than 70% of patients in both groups had ≥50% improvement at 2 years, with no differences between groups	Same group has multiple studies with same findings; high number of patients on opioids; all patients received exercise program; more injections done in patients with positive outcome
Cohen 2014[139]	169 patients with cervical radicular symptoms from herniated disc or spinal stenosis	3 groups:1. Up to 3 interlaminar ESI with LA and steroid2. Gabapentin or nortriptyline + physical therapy (or both)3. ESI + drugs + physical therapy	Clinical symptoms and MRI pathology	Group 3 > groups 1 and 2; persisted on some measures up to 6 months	Treatments designed to replicate those faced by primary care physicians; evaluator blinded; placebo effect from multiple treatments probably higher in combination group
Pulsed radiofrequency studies					
Van Zundert 2007[141]	23 patients with cervical radicular pain	1 cycle of pulsed RFA of affected DRG or sham radiofrequency	Clinical signs and symptoms and positive diagnostic selective nerve root block	Pulsed RFA > sham up to 3 months	Study terminated early; MRI not used as selection criterion; effectiveness of blinding questionable
Trigger point injections					
Wheeler 1998[150]	33 patients with unilateral cervicothoracic, paraspinal pain	3 groups: injection of the most sensitive trigger point with 50 units of botulinum toxin A, 100 units, or saline	Clinical symptoms and presence of trigger points	No differences between groups up to 4 months	More patients asymptomatic in botulinum toxin groups; sponsorship not noted
Ferrante 2005[151]	132 patients with cervicothoracic myofascial pain	Injection of botulinum toxin type A or saline into 1-5 trigger points	Clinical symptoms of myofascial pain with up to 5 trigger points	No differences between groups up to 12 weeks	Patients started on physical therapy and a pharmacological regimen of amitriptyline, ibuprofen, and rescue opioids at time of treatment; sponsorship not noted
Kamanli 2005[152]	29 patients with myofascial pain of the neck, upper back, or shoulder region	3 groups: dry needling, injection of lidocaine, and injection of botulinum toxin type A	Clinical signs and symptoms of myofascial pain	Lidocaine > botulinum toxin > dry needling at 1 month	87 total trigger points injected; only injected one side; sponsorship not noted
Gobel 2006[153]	145 patients with myofascial pain affecting the neck or shoulders (or both)	Injection of botulinum toxin type A or saline into 10 most painful trigger points	Clinical symptoms of myofascial pain with at least 10 trigger points	Botulinum toxin > saline at 12 weeks	Industry sponsored
Ojala 2006[154]	31 patients with myofascial pain in the neck-shoulder region	Crossover study evaluating injections of botulinum toxin type A and saline 4 weeks apart into 3-7 trigger points	Clinical symptoms of myofascial pain with presence of trigger points	No differences between groups at 4 weeks	Non-industry sponsored; effect of botulinum toxin lasts longer than 4 week crossover period

Table 2 | Continued

Reference	Patients	Treatments	Selection criteria	Results	Comments
Pecos-Martin 2014[155]	72 patients with mechanical neck pain and active trigger points	Dry-needling into an active trigger point in the trapezius muscle or 1.5 cm medial to trigger point	Clinical signs and symptoms of myofascial pain	Dry needling into trigger point > control up to 1 month	Effectiveness of blinding questionable
Nicol 2014[156]	54 patients with myofascial neck and shoulder pain who responded to botulinum toxin type A	Botulinum toxin type A or saline injections into painful neck and shoulder muscles	Myofascial pain responsive to botulinum toxin	Botulinum toxin > saline at 12 weeks	Enriched study design; industry sponsored
Kwanchuay 2015[157]	33 patients with myofascial pain in the neck-shoulder region and 48 trigger points	Botulinum toxin type A or saline injected into 24 trigger points each	Myofascial pain for > 3 months and active trigger points	No differences between groups at 3 or 6 weeks	Patients acted as their own controls; botulinum toxin associated with greater reduction in pressure pain threshold
Sterling 2015[86]	80 patients with axial pain from whiplash disorder	Dry needling and exercise or sham dry needling and exercise for 6 weeks	Neck pain after whiplash injury for >3 months but <2 years, with no radicular symptoms	No differences between groups at 6 and 12 weeks; small differences at 6 and 12 months favoring treatment	Sham dry needling performed in the same muscles with sham acupuncture needles; differences at 6 and 12 months deemed clinically insignificant

*Abbreviations: DRG=dorsal root ganglia; ESI=epidural steroid injection; LA=local anesthetic; MBB=medial branch block; MRI=magnetic resonance imaging; RFA=radiofrequency ablation of the cervical medial branches.

improving sleep and mood, and reversing or preventing deconditioning. Exercise programs have been shown to prevent spinal pain in general,[35] but few studies have been performed in neck pain alone, and these have yielded mixed results.[159 160]

The effects of exercise on whiplash injuries have also been mixed, with one randomized trial comparing six weeks of exercise in addition to advice with advice alone (n=134),[161] and another comparing a 10 week multimodal physical therapy program with self management (n=71).[162] The first found small to moderate effect sizes in the short term (immediately after treatment) but no long term benefit.[161] The second study found that people allocated to receive the multimodal program reported significantly better pain relief and functional capacity, again assessed immediately after the treatment period (effect size 0.48; P=0.04).[160] A larger more recent randomized study in patients with chronic whiplash found no difference between advice and a physical therapy exercise program up to 12 months of follow-up (table 3).[176]

Integrative medicine, also known as complementary and alternative medicine, encompasses a broad range of treatments including acupuncture, spinal manipulation, massage, meditation, and yoga. Integrative treatments can be delivered by licensed practitioners (such as acupuncturists), physicians, or by self care (for example, meditation). In addition to treatments that require specialized training (such as Tai Chi and yoga), herbal therapies such as soy, turmeric (curcumin), polyphenols, and omega 3 fatty acids have been shown in clinical studies to exert analgesic effects, although none has been specifically studied for cervical pain.[177] Despite the fact that integrative therapies are often not reimbursed by insurance companies, population based surveys suggest that the use of such therapies exceeds 50% in some countries, being slightly higher in Asia and Australia. Moreover, people often use several different integrative treatments concurrently.[178 179] Consequently, clinicians should be aware of the effectiveness of the integrative medicine treatments that are commonly used for neck pain and need to understand which patients might benefit. Table 3 summarizes studies of integrative medicine for neck pain.

Surgery

A broad range of surgical techniques are used to treat neck pain, with the indications for surgery being dependent on the underlying source of pain. For cervical radiculopathy, a randomized trial that compared anterior cervical decompression and fusion plus physiotherapy with physiotherapy alone (n=59) showed that patients allocated to surgery experienced significantly greater reductions in neck pain (39 mm *v* 19 mm; P=0.01) and neck disability (21% *v* 11%; P=0.03) compared with the non-operative group at five to eight year follow-up.[180] However, no significant differences were seen for arm pain or self assessed health status. A three arm randomized study compared anterior decompression and fusion surgery, physical therapy, and cervical collar immobilization in 81 patients with cervical radiculopathy. It found significantly greater short term reductions in pain and neurological dysfunction in the surgical group compared with the collar group and non-significantly greater decreases in pain compared with the physical therapy group (present mean pain reduction in surgical group −10 *v* −9 in the therapy group and −1 in the immobilization group; P<0.01 *v* the immobilization group), although no significant differences were seen at 15 months.[181]

Various surgical options are available for the treatment of cervical spondylotic myelopathy including corpectomy and fusion, anterior cervical discectomy and fusion, laminoplasty, and laminectomy and fusion.[182] However, randomized trials provide limited clinical outcomes to guide treatment. In a small (n=64) randomized study comparing surgery with conservative care for cervical myelopathy, measures of physical and neurological functioning were similar between the two groups at two and 10 year follow-up.[183 184] In addition, surgical treatment of spondylotic myelopathy is associated with a complication rate of 11-38%.[185] Predictors of complications include older age, longer duration of surgery, and two stage surgery.[185] Given the natural course of cervical radiculopathy and myelopathy, and the modest predominantly short term benefits of surgery, conservative treatment with surveillance for neurological progression is a reasonable course for both conditions.

Table 3 | Summary of systematic reviews and meta-analyses of exercise and integrative medicine treatments for neck pain*

Reference	Definition of treatment	Study selection	Subjects	Meta-analysis results	Comments
Exercise					
Gross 2016[163]	Planned repetitive activities to improve aerobic fitness or strength (or both)	27 moderate quality RCTs of exercise for chronic neck pain	2485 patients with chronic neck pain	Immediate (<1 day)/short-term (>1 day to 3 months) effects of neck/UE strengthening on pain (pSMD −0.71) Intermediate (3-12 months) effects of neck strengthening on pain and function (pSMD −14.9)	Low quality evidence suggests general fitness training and stretching may not change pain and function at immediate or short term follow-up
Southerst 2016[164]	Series of movements to train the body by routine practice	9 RCTs of exercise for neck pain1 RCT of exercise for WAD	1415 patients with neck pain134 patients with WAD	Meta-analysis not performed	For persistent neck pain and WAD, combined strengthening, ROM, and flexibility exercises more effective than waitlist
Bertozzi 2013[165]	Therapeutic exercise not defined	9 medium quality RCTs of exercise for neck pain7 RCTs included in the meta-analysis	889 patients with chronic neck pain included in the meta-analysis; mean age 39 years	Short term (<1 month) and intermediate (1-6 months) effects of exercise on neck pain (Hedges g −0.53 and −0.45, respectively)	No significant long term (>6 months) effects on painNo significant short, intermediate, or long term effects on disability
Massage					
Wei 2017[166]	Chinese massage (Tui Na) uses the fingers or hands to act on the muscle or soft tissue of the painful body part to increase blood flow, relieve muscle spasm, and suppress pain	5 low-very low quality RCTs for cervical radiculopathy3 studies compared Tui Na *v* cervical traction2 studies compared Tui Na and cervical traction *v* cervical traction	448 patients with cervical radiculopathy; mean age 48 years	Immediate (<1 day) effects on radicular pain *v* cervical traction (SMD −0.58)Immediate effects on radicular pain with Tui Na and cervical traction *v* cervical traction alone (SMD −2.01)	No significant longer term (>1 day) effects on painDuration of Tui Na treatment 14-20 days
Kong 2013[167]	Therapeutic soft tissue manipulation with hand or mechanical device	8 high quality RCTs of massage for neck pain6 studies included in meta-analysis	479 patients with neck pain; mean age 38 years	Immediate (<1 day) effects on neck pain *v* inactive therapies (SMD 1.79)No significant effects for pain *v* active therapies	No significant longer term (>1 day) effects on painNo significant effects on functional status
Spinal manipulation					
Zhu 2016[168]	Rapid high velocity, low amplitude thrust directed at the cervical joints	3 RCTs of spinal manipulation for cervical radiculopathy	502 patients with cervical radiculopathyMean age range 45-53.6 years	Moderate quality evidence of immediate (time period not specified) effects on pain *v* cervical traction (SMD 1.28)	2 of 3 RCTs had no follow-upFunctional status not assessed
Gross 2010[169]	Localized force of varying velocity and varying amplitude directed at specific spinal segments	27 RCTs of spinal manipulation for neck pain9 RCTs had low risk of bias	1522 patients with neck pain	Low quality evidence of short term (>1 day to <4 weeks) effects on neck pain *v* control (pSMD −0.90)Low quality evidence for pain reduction (NNT 5) and increased function (NNT 5) in acute neck painLow quality evidence for immediate (<1 day) pain reduction (NNT 5) in chronic neck pain	No significant long term (6-12 months) effects on pain or function
Acupuncture					
Yuan 2015[170]	No definition provided	17 RCTs of acupuncture for neck pain	1434 patients with neck pain	Short term (<3 months) effects on pain *v* sham acupuncture (SMD −0.72)Immediate (≤1 week) effects on pain *v* drugs (SMD −0.57)Immediate (≤1 week) effects on pain *v* massage (SMD −1.63)	No significant effects on pain *v* inactive therapiesNo significant effects on pain *v* spinal manipulationNo significant effects on pain *v* cervical traction
Fu 2009[171]	A technique of inserting needles into certain body points to restore health and prevent disease	14 RCTs of acupuncture for neck pain	4249 patients with neck pain	Limited evidence for short term (<3 months) effects on pain *v* control (SMD −0.45)Limited evidence for short term effects on pain *v* sham acupuncture (SMD −0.53)	No significant long term (>3 months) effects on painNo significant short term (<3 months) effects on disability
Yoga and qigong					
Cramer 2017[172]	Yoga defined as "physical activity, breath control, meditation, and/or lifestyle advice"	3 RCTs of yoga for neck pain2 of 3 RCTs with low risk of bias	188 patients with neck pain; mean age 46 years	Short term (time period not specified) effects on pain *v* usual care (SMD −1.28)Short term effects on disability *v* usual (SMD −0.97)Short term effects on quality of life *v* usual care (SMD 0.57)Short term effects on mood *v* usual care (SMD −1.02)	Long term outcomes not assessed
Kim 2016[173]	Yoga—physical postures, breathing exercises, meditation, and relaxation	3 RCTs of yoga for neck painAll RCTs assessed as high risk of bias	184 patients with neck pain; mean age 51 years	Meta-analysis not performed	Low quality evidence suggests yoga is associated with lower pain and functional disability scores *v* control
Yuan 2015[170]	Qigong defined as mind-body training focusing on breathing adjustment, physical activity modulation and willing adjustment	3 RCTs of qigong for neck painStudy quality assessed as fair	280 patients with neck pain	Short term (<3 months) effects on pain *v* waitlist (WMD −15.27)Intermediate (3-6 months) effects on pain *v* waitlist (WMD −10.18)Short term effects on disability *v* waitlist (WMD −7.67)	No significant intermediate effects on disability *v* waitlistNo significant short-intermediate effects on pain or disability *v* exercise
Electrotherapy					
Kroeling 2013[174]	Therapies using electric current to reduce pain and improve muscle tension and function	20 RCTs of electrotherapy for neck pain	1239 patients with neck pain	Meta-analysis not performed	Very low quality evidence that PEMF, rMS, and TENS are more effective for pain *v* placeboLow quality evidence that permanent magnets were more effective for pain *v* placeboNo significant effects of electrotherapies on function

Table 3 | Continued

Reference	Definition of treatment	Study selection	Subjects	Meta-analysis results	Comments
Other treatments					
Yuan 2015[170]	Cupping induces local blood stasis to promote healing by creating a vacuum over the selected body area	5 RCTs of cupping for neck painStudy quality assessed as fair	241 patients with neck pain	Immediate effects (≤1 week) on neck pain *v* waitlist (MD −6.65)Immediate effects (≤1 week) on disability *v* waitlist	No long term effects reported
Graham 2011[175]	Traction involves a pulling force applied to the neck through a mechanical system	7 RCTs of traction for neck disorders with radicular symptoms1 RCT with low risk of bias	958 patients with radicular symptoms	No significant effects (follow-up period not specified) of continuous traction on pain or function *v* placebo (SMD −0.16)	No evidence supporting traction for neck disorders with radicular symptoms

*Abbreviations: MD= mean difference; NNT=number needed to treat; PEMF=pulsed electromagnetic field therapy; pSMD=pooled standardized mean difference; RCTs=randomized controlled trials; rMS=repetitive magnetic stimulation; ROM=range of motion; SMD=standardized mean difference; TENS=transcutaneous electrical nerve stimulation; UE=upper extremity; WAD=whiplash associated disorder; WMD=weighted mean difference.

Two widely used surgical options for cervical degenerative disc disease are anterior cervical discectomy with fusion (ACDF) and cervical disc arthroplasty (CDA). Few randomized trials have compared either procedure with non-surgical treatment. However, randomized studies performed for back pain suggest that less than 40% of people who undergo spinal fusion or disc arthroplasty for mechanical pain associated with common degenerative conditions can expect meaningful pain relief or a highly functional outcome that lasts for two years, and that benefits diminish over time.[186 187] Given the anatomical, functional, and technical differences between surgery for low back and neck pain, it is unclear how generalizable these findings are. In a small (n=47) randomized trial that compared CDA and ACDF, improvements in neck and arm pain were similar for both groups at seven and 10 year follow-up, but patients in the CDA group experienced statistically significantly greater reductions in neck disability scores (8% *v* 16%) and reoperation rates were lower (9% *v* 32%).[188]

Although outcome data from randomized trials are available, the potential benefits of CDA compared with ACDF are still unclear. However, recent systematic reviews suggest that CDA is associated with greater reductions in neck disability, greater satisfaction, fewer complications, lower reoperation rates, and lower rates of adjacent segment degeneration than ACDF.[189 190] Systematic reviews also suggest that multilevel CDA is as effective as single level CDA and may be associated with greater preservation of cervical motion than ACDF.[191 192]

Emerging treatments

Biological therapies including stem cell therapy, nerve growth factor inhibitors, and platelet rich plasma have been evaluated in other chronic pain conditions and have yielded mixed results. These treatments have yet to be critically studied for neck pain. Future studies should assess their utility for both degenerative and neuropathic conditions.

The use of ketamine to treat refractory chronic pain has generated enormous interest. Ketamine acts as an antagonist at the *N*-methyl-*D*-aspartate receptor and is purported to act through the reversal of central sensitization. Controlled trials evaluating ketamine have generally shown short term benefit for neuropathic pain conditions and disorders characterized by central sensitization (such as fibromyalgia) but this drug has not been studied for neck pain.[193]

Guidelines

In 2013, the Spine Intervention Society updated its guidelines on cervical facet RFA.[194] Similar to previous guidelines,[195] they advocate performing double blocks before ablation to reduce the false positive rate, either with two different local anesthetics or an anesthetic agent and saline. The guidelines also recommended placing large bore electrodes parallel to the target nerves and performing multiple lesions to increase the success rate but do not mandate sensory or motor testing, the last of which is usually used to minimize the chance of accidental spinal nerve ablation.[91] One case report described a case of head drop after multilevel cervical radiofrequency ablation in which motor testing was not used that required eventual spinal fusion.[196] A previous article by the guidelines' author acknowledges that performing two diagnostic blocks before treatment may not be cost effective in some countries, such as the US.[197]

In the past few years, several guidelines have been published on ESI. A multidisciplinary group representing the neuropathic pain special interest group of the International Association for the Study of Pain provided a weak recommendation for ESI to treat cervical and lumbar radiculopathy, with most of the evidence derived from lumbar studies.[198] In a multispecialty working group panel convened under the US Food and Drug Administration's (FDA) Safe Use Initiative, experts from different organizations provided recommendation on the performance of cervical ESI, which included always reviewing radiological studies, using image guidance with contrast for needle placement, not injecting particulate steroids for transforaminal injections, and not injecting above C6-7. These recommendations were developed because more than 50 cases of paraplegia or death have been reported after cervical transforaminal ESI was performed with depo-steroids. This resulted in the FDA convening a panel in 2014 to evaluate the effectiveness and safety of ESI; the panel concluded that for some ESI (such as cervical transforaminal ESI performed with depo-steroids) the risks may outweigh the benefits.[199]

Comprehensive guidelines published in 2013 by the American Society of Interventional Pain Physicians on the management of spinal pain found limited evidence for cervical discography and good evidence for the diagnostic validity of cervical medial branch blocks, which they recommended performing before discography.[200] However, the accuracy of cervical medial branch blocks

QUESTIONS FOR FUTURE RESEARCH

- How can we better identify people at high risk of developing acute neck pain and those with acute pain who will to transition to chronic neck pain?
- Can pre-emptive measures (such as ergonomic modification and exercise) and preventive measures (such as advice and mass media campaigns, physical therapies, and drugs) prevent acute pain and prevent pain from becoming chronic, respectively?
- How effective will registries be in determining effectiveness in large scale populations, identifying phenotypes likely to respond to treatment (precision medicine), and establishing differences in treatment responses between healthcare providers (identifying individuals who select inappropriate candidates for treatment)?
- Will the growing emphasis on comparative effectiveness and cost effectiveness studies enable providers and third party payers to make long term economically sustainable treatment decisions that improve patient care?
- What is the role of biological therapies such as cytokine inhibitors, nerve growth factor inhibitors, and stem cell injections in the treatment of neuropathic and degenerative spinal pain?

to identify a painful joint was not based on an independent test but on double blocks performed with different anesthetics. They reported good evidence for cervical ESI for disc herniation and fair evidence for axial neck pain, spinal stenosis, and post-laminectomy syndrome. For the treatment of facet joint pain, they found fair evidence for therapeutic medial branch blocks and RFA and limited evidence for intra-articular injections. However, this contradicts the rationale for performing diagnostic cervical medial branch blocks with two different local anesthetics, based on concordant relief for the duration of the action of the drugs, which is measured in hours not months.

Guidelines by the Motor Accident Commission of Australia in 2008 provide guidance on the assessment, diagnosis, and prognosis of whiplash associated disorders, as well as recommendations for treatment stratified by chronicity.[201] For chronic whiplash, recommended treatments included exercise and advice (grade B), cognitive behavioral therapy (grade C), RFA (grade B), and subcutaneous "trigger point" injections with water (grade C). For acute whiplash, exercise (grade A), advice (grade B), and non-opioid drugs (grade B) were among the treatments advocated. Despite the date, these recommendations are still appropriate.

Conclusions

Neck pain imposes an enormous personal and socioeconomic burden on society, with a prevalence approaching that of low back pain and disability rates ranking within the top five in the US. Yet only a fraction of the resources and attention devoted to low back pain have been dedicated to neck pain. Most cases of acute neck pain, regardless of whether or not they are radicular in nature, will resolve within three months, although a substantial proportion of people will continue to experience low grade symptoms or frequent recurrences. It is crucially important to categorize neck pain as either neuropathic or non-neuropathic because this information is needed to guide investigations (necessity for imaging) and treatment decisions. The facet joints have been implicated as the primary pain generator in nearly half of people with whiplash injuries, but there is a poor correlation between imaging and symptom severity. Topical NSAIDs can be beneficial in people with non-specific neck pain and muscle relaxants are a reasonable treatment choice for acute non-radicular pain. In patients with cervical radiculopathy there is weak evidence to support the use of ESI, and in patients with mechanical pain who respond to diagnostic blocks there is weak evidence to support the use of RFA. Similar to back pain, surgical decompression for patients with radiculopathy can provide short term benefit compared with non-surgical treatment, but the benefits diminish with time. In addition to controlled and comparative effectiveness studies evaluating various treatment options for neck pain, future research should endeavor to determine whether chronic pain can be prevented after an acute pain episode and establish registries to determine large scale treatment outcomes.

HOW PATIENTS WERE INVOLVED IN THIS ARTICLE

The article was sent for review to Geoffrey Chesbrough, who has a long history of neck pain and occipital headaches that developed over the course of his military career. Although no changes were suggested, he emphasized the importance of an accurate diagnosis and the need for doctors to try to tailor treatments to individual patients. He previously underwent a "shotgun" approach, which included epidural steroid injections, cervical facet blocks and radiofrequency ablation, occipital nerve blocks, and trigger point injections, before finally obtaining good, albeit short lasting (less than three months) relief from atlanto-axial joint blocks, which he continues to receive as needed.

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