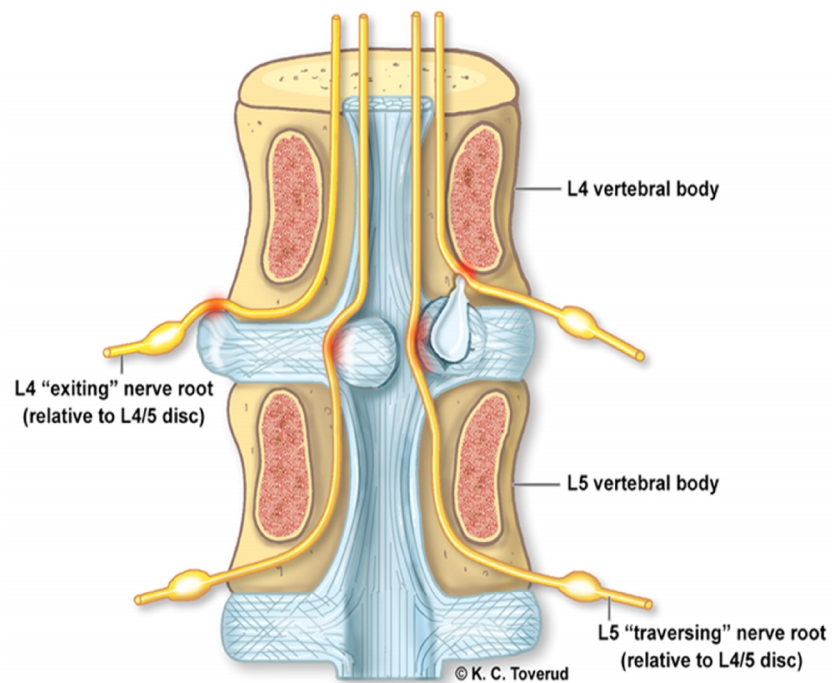


## Lumbosacral radiculopathy managed in multidisciplinary back clinics

*Diagnostic accuracy, prognostic factors and efficacy of epidural injection therapy.*

*A thesis for the degree of Philosophiae Doctor – 12 July 2015*

**Trond Iversen**





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## 2. NORWEGIAN ABSTRACT – NORSK SAMMENDRAG

I perioden 2005–2010 ble det ved fem norske sykehus utført en randomisert kontrollert studie over effekten av epidurale steroidinjeksjoner i behandlingen av kronisk (> 12-ukers varighet) isjias. Det ble til sammen undersøkt 461 pasienter i aldersgruppen 18–60 år for deltagelse i studien; 116 av disse ble etter grundig forundersøkelse inkludert og randomisert til tre ulike behandlingsgrupper.

Alle pasientene fikk utført magnetic resonance imaging (MRI) eller computer tomography (CT) av korsryggen for å kartlegge tilstedeværelsen av skiveprolaps med eventuell avklemming av spinal nerverot, og det ble det tatt opp en grundig sykehistorie og utført en standardisert nevrologisk undersøkelse for å kartlegge hvilken nerverot i korsryggen som mest sannsynlig forårsaket pasientens isjias. Alle pasientene fylte ut validerte spørreskjema for å kartlegge grad av smerter i rygg og ben (visual analogue scale), livskvalitet (the European quality of life (EuroQol) measure, EQ-5D) og ryggfunksjon (Oswestry Disability Index (ODI)). I tillegg ble en rekke psykososiale faktorer og pasientenes jobbstatus kartlagt.

Etter forundersøkelsen fikk en pasientgruppe to epidurale injeksjoner av en kombinasjon av steroider og saltvann (behandlingsgruppe); en gruppe fikk to epidurale injeksjoner med saltvann (placebogruppe) og en gruppe fikk to subkutane injeksjoner med saltvann (shamgruppe). Injeksjonene ble gitt med 2 ukers intervall av erfarne anestesileger.

Alle pasientene ble fulgt opp etter 6, 12 og 52 uker. Ved oppfølgingsundersøkelsene gjennomgikk alle nevrologisk undersøkelse og pasientene fylte ut spørreskjema for å kartlegge smerter, livskvalitet og ryggfunksjon.

Resultatene etter 52 uker viste at det ikke var noen forskjell mellom gruppene på bedring i smerter, livskvalitet og ryggfunksjon. Til sammen 15 pasienter ble ryggoperert i oppfølgingstiden, men det var ingen forskjell i antall opererte pasienter mellom gruppene. På basis av disse funnene ble det konkludert med at epidural steroidinjeksjon for å behandle isjias er uvirksom.

I studien ble det også undersøkt hvor presis den nevrologiske undersøkelsen er for å avklare hvilken nerverot som avklemmes av et skiveprolaps påvist på MRI eller CT. Vi fant at nytten av de ulike nevrologiske testene som brukes for å stille diagnosen isjias var lav.

I studien ønsket vi også å kartlegge hvilke faktorer som er viktig for å kunne si noe om forløpet (prognosen) til isjias. Vi fant at lav alder, høy utdanning, det å være i full jobb og det å ha lav frykt for at det å være i jobb skulle skade ryggen var gode indikatorer (prediktorer) for at isjiasplagene var bedre etter 52-ukers oppfølging.

### 3. LIST OF PAPERS

The following papers were produced during the course of this study. They are provided in Appendices 1 to 3.

#### 3.1 Paper I

Iversen T, Solberg TK, Romner B, Wilsgaard T, Nygaard Ø, Waterloo K, Brox JI, Ingebrigtsen T (2013) Accuracy of physical examination for chronic lumbar radiculopathy. *BMC Musculoskelet Disord.* 2013 Jul 9;14:206. doi: 10.1186/1471-2474-14-206.

#### 3.2 Paper II

Iversen T, Solberg TK, Wilsgaard T, Waterloo K, Brox JI, Ingebrigtsen T (2015) Outcome prediction in chronic unilateral lumbar radiculopathy: prospective cohort study. *BMC Musculoskeletal Disord.* 2015 Feb 7;16:17. doi: 10.1186/s12891-015-0474-9.

#### 3.3 Paper III

Iversen T, Solberg TK, Romner B, Wilsgaard T, Twisk J, Anke A, Nygaard O, Hasvold T, Ingebrigtsen T (2011) Effect of caudal epidural steroid or saline injection in chronic lumbar radiculopathy: multicentre, blinded, randomised controlled trial. *BMJ* 2011 Sep 13;343:d5278. doi: 10.1136/bmj.d5278.

The papers will be referred to by their Roman numerals.



## 4. ABBREVIATIONS

ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
APS	American Pain Society
ASIPP	American Society of Interventional Pain Physicians
AUC	Area under the curve
CI	Confidence interval
CMS	Centers for Medicare & Medicaid Services
CONSORT	Consolidated Standards of Reporting Trials
CT	Computer tomography
EuroQol	European quality of life
FABQ	Fear Avoidance Beliefs Questionnaire
FABQ-PA	Fear Avoidance Beliefs Questionnaire for physical activity
FABQ-W	Fear Avoidance Beliefs Questionnaire for work
FDA	Food and Drug Administration
IASP	International Association for the Study of Pain
LR	Likelihood ratio
MRI	Magnetic resonance imaging

NASS	North American Spine Society
NSAID	Non-steroidal anti-inflammatory drug
ODI	Oswestry Disability Index
OR	Odds ratio
PET	Positron emission tomography
PROM	Patient reported outcome measure
RCT	Randomized controlled trial
ROC	Receiver operating characteristic
SD	Standard deviation
SLR	Straight leg raise
STARD	STAndards for the Reporting of Diagnostic accuracy
TNFA	Tumour necrosis factor alfa
UNN	University Hospital of North Norway Tromsø
VAS	Visual analogue scale
WMD	Weighted mean difference

## 5. WHAT IS THE THESIS ABOUT?

This thesis deals with some of the key issues in evidence-based medicine, i.e. to provide knowledge about diagnostic accuracy, prognostic factors and treatment efficacy, which can be used in the clinical decision-making process for patients with lumbosacral radiculopathy. Scientific evidence for diagnostic workup and treatment recommendations are still lacking (1). Few areas of clinical medicine are therefore as controversial as the non-surgical management of patients with lumbosacral radiculopathy, and treatment recommendations are often made with much ambiguity.

It is hoped that the results presented in this thesis can be used in clinical guideline development, to improve health care for patients.





## 6. INTRODUCTION

Patients with degenerative disorders in the lumbosacral spine often have chronic low back pain and/or radiating leg pain, with or without neurological deficits. The consequences are disability, reduced quality of health and reduced working capability. In western societies, lumbar spine disorders account for higher costs resulting from disability and absenteeism from work than any other somatic disease category (2).

### 6.1 Prevalence, incidence and risk factors

The lifetime prevalence of low back pain in Norway is around 60–80%. Half of the population have suffered from low back pain during the past year, and approximately 40% in the past month. The yearly incidence of low back pain varies between 20 and 28% (3) and 70% can have relapses during the course of a year (2), but for the individual episode, the prognosis is good. The majority get better during the course of a few weeks. Variations in occurrence are associated with risk factors such as age, education, occupation, culture/ethnicity, lifestyle and psychosocial issues (4).

A specific cause can be found in only 10–15% of patients with low back pain and radiation pain to the leg; the causes include prolapse, spinal stenosis, and other underlying pathology such as rheumatic disease, infection, fractures or tumours. For the majority of the cases, our understanding of the pathophysiology, i.e. the cause of low back pain and lumbosacral radiculopathy is uncertain. Knowledge about risk factors is limited and conflicting (5-8).

Lifetime prevalence of lumbosacral radiculopathy due to a prolapsed disc is estimated to be 5.3% in men and 3.7% in women (9, 10). The annual prevalence of lumbosacral radiculopathy due to disc-related problems reported in the literature varies considerably ranging from 1.6% in the general population to 43% in selected working populations (10-12). A number of studies have estimated the annual incidence of lumbosacral radiculopathy to be 1–2% in the general population (13, 14). The variation in estimates is probably due to differences in the definition of symptoms and the interpretation of clinical and radiological findings (10, 15, 16).

There is a general belief that the course and prognosis of acute lumbosacral radiculopathy is favourable (17-21), but at 1 year up to 30% will still have significant symptoms, 20% will be out of work, and 5–15% will undergo surgery (21-26).

Two important risk factors associated with the occurrence of lumbosacral radiculopathy, and important predictors of pain and disability, are higher age and male gender (27, 28).

Lumbosacral radiculopathy is more common among persons over 40, and men show high prevalence rates of radicular syndromes. However, past the age of 40, the risk for women increases much faster than for men (28). In a study of lumbar intervertebral discs using magnetic resonance imaging (MRI), the prevalence of degenerative intervertebral discs was shown to increase linearly with age. The exact pathophysiological mechanism for the observed phenomenon is unclear. The underlying cause may be tissue weakening occurring primarily from genetic inheritance, ageing, nutritional compromise, and loading history (29).

Other known risk factors are: worrying and health anxiety, sick leave and fear avoidance about physical activity. Smoking also seems to increase the risk of disc disease, low back pain and lumbosacral radiculopathy. The hypothesis is that smoking may impair the blood supply to the vertebral endplate, thereby decreasing the nutrition of the intervertebral disc.

Many work-related factors are also relevant for the prognosis of lumbar radiculopathy, such as heavy physical work, static work posture, lifting and forceful movements, repetitive bending and whole-body vibration (30).

Identification of prognostic factors for persistent pain and disability is important for better understanding of the clinical course of lumbar radiculopathy and to assist clinical decision-making. There is, however, a lack of scientific evidence concerning which prognostic factors are most relevant to predict the course of the disease.

## 6.2 Costs

Every year there are around 2 million back-related consultations in Norway, constituting a major challenge in the daily workflow for doctors and physiotherapists (4). In primary care, musculoskeletal diseases represent the largest diagnostic group. Among the somatic conditions, back pain was the most important cause of sick leave and social benefit payments in Norway in 2010 (31).

The relative proportion of back pain as the cause of sick leave (>16 days) decreased from 17 to 11% in Norway in the period 1994 to 2008 (31). One possible explanation for the decline is that clinicians to a much greater extent emphasized that patients should maintain normal activity, and they recommended early return to work according to new

clinical guidelines. The decline is not unique to Norway, but is also registered in several other European countries, particularly in the UK (31). There is, however, in the same period observed a corresponding increase in sick leave for depression and mild psychological disorders (31).

### 6.3 Definition of spinal pain

Despite the efforts of the International Association for the Study of Pain (IASP) (32) to reach consensus about terminology and definitions, confusion still persists among clinicians about how to distinguish between back pain, referred pain, radicular pain, and radiculopathy.

Nociceptive back pain is evoked by noxious stimulation of structures in the lumbar spine but can also produce referred pain. Referred pain is provoked by noxious stimulation of nerve endings in the spine and is perceived in other regions that share the same segmental innervation. Referred pain is not caused by impingement of nerve roots and there are no neurological signs. Radicular pain is pain evoked by ectopic discharges emanating from a dorsal root or its ganglion. Neurological signs arise due to a conduction block corresponding to that spinal nerve or its root(s).

Radiculopathy is defined by objective neurological signs. Although radiculopathy and radicular pain commonly occur together, radiculopathy can occur in the absence of pain, and radicular pain can occur in the absence of radiculopathy (33).

In this thesis the focus is on chronic lumbosacral radiculopathy.

## 6.4 Clinical presentation

The most common clinical presentation of a lumbosacral radiculopathy is radicular leg pain below knee level with neurological deficits in the distribution of the lumbosacral nerves (10, 17). Radicular pain has a typical lancinating, shocking or electric quality travelling into the lower limb along a narrow band. In approximately 90% of cases, radiculopathy is caused by a prolapsed disc involving nerve root impingement (34, 35). Leg pain is often accompanied by both motor and sensory deficits, and back pain. The leg pain is typically more intense than the back pain. Numbness in the dermatome, a positive straight leg raise (SLR) test, and muscle weakness and reflex changes can be found (17, 36). Diminished reflexes occur as a result of either sensory or motor block. If this clinical syndrome is present for more than 12 weeks, it is defined as chronic lumbosacral radiculopathy (17, 37-39).

Systematic reviews of the diagnostic properties of clinical diagnostic tests for lumbosacral radiculopathy report variable accuracy, with low to moderate sensitivities for sensory deficits and impaired tendon reflexes (0.14 to 0.61) (40, 41) and motor weakness (0.27 to 0.62) (42, 43), and low to high sensitivities for the SLR test (0.35 to 0.81) (44). The ability of neurological testing procedures to detect a disc herniation is poor. Standardization of protocols for the neurological testing procedures would allow better evaluation of their sensitivity, specificity and reliability.

A recent Cochrane review confirmed poor performance of diagnostic tests to detect the presence of lumbosacral radiculopathy in 18 studies from specialized care (45). None of these studies discriminated between nerve root impingement and just the presence of a

disc herniation on the images they used as reference standard. This could be a major bias, since the prevalence of disc herniation in unselected populations without radiculopathy symptoms is high, and the presence of radicular pain is likely to be linked to radiological evidence of root impingement (46).

Vroomen (47) reported a strong inter-rater reliability for reduced muscle strength and sensory deficits ( $\kappa$  0.57 to 0.82) in patients with lumbosacral radiculopathy and moderate agreement for reflex impairments ( $\kappa$  0.42 to 0.53), whereas McCarthy (48) reported moderate inter-rater agreement for both reflexes and motor deficits ( $\kappa$  0.41 to 0.56). Another study found strong to high agreement among doctors assessing sensibility to pain ( $\kappa$  0.50 to 0.71) (49).

The clinical course of back pain and lumbosacral radiculopathy has been assessed in many cohort studies (50, 51). For low back pain and lumbosacral radiculopathy the course of the disease often follows a pattern of general improvement that starts rapidly and plateaus over time, independent of choice of treatment. It has been suggested that the mere participation in a study influences the course of symptoms (52, 53). This might be explained by benefits perceived by participants and assumed to be related to intensive assessment and monitoring. The so-called 'Hawthorne effect' is quoted as an example of how individuals change behaviour due to the attention they receive from researchers (54-56). This pattern of the clinical course of pain and disability entails a huge challenge to the researcher concerning interpretation of the outcome of treating lumbosacral radiculopathy.

## 6.5 Pathophysiology of pain

For centuries, the origin of pain in lumbosacral radiculopathy was believed to be an inflammation of the sciatic nerve (57). In 1934, Mixter and Barr recognized the mechanical origin of radiculopathy (58, 59), namely nerve root impingement by a herniated lumbar disc. Mixter and Ayers demonstrated in 1935 that radiculopathy can also occur without mechanical nerve root impingement (60). Later, several studies have shown a prevalence of disc herniation ranging from 20 to 76% among asymptomatic individuals (61, 62), and many patients with symptoms of radiculopathy have no radiological findings on MRI (17, 63, 64). Inflammation of the nerve root may therefore be an important factor for developing radiculopathy (65-67). A recent study using gadolinium-enhanced MRI (68) showed that annular disc tears may cause radiculopathy without any signs of nerve root impingement. Lauder (69) reported that in patients with radiculopathy confirmed by neurophysiological investigations, nearly 31% had no signs of weakness and up to 45% had no sensory deficits detected on clinical examination. Studies also demonstrate that in patients with severe lumbosacral radiculopathy, weakness may not be observed on examination, unless a large conduction block of the nerve root is present (70, 71). More than finding effective treatments for radiculopathy, research has revealed an increasingly complex pathophysiology of pain and new knowledge gaps over the years (33, 72).

## 6.6 Imaging

There is a weak correlation between the anatomical level of the disc herniation found on MRI and the clinical level that is suspected based on an examination of the patients.

Laupacis (73) argues that the increasing power of new technologies, such as computer tomography (CT) and MRI, has led to an inappropriate de-emphasis on clinical skills and a greater dependence on imaging.

Since the detection of abnormalities on physical examination may affect the decision to pursue epidural steroid injections, back surgery, or further diagnostic testing, bias in the physical examination may have substantial implications for the practice of spine care. High numbers of incidental findings on MRI (74, 75) may result in expectance bias among investigators and systematic errors in the results for the physical examination. Evidence suggests that sensory testing is most prone to bias due to prior knowledge of MRI results (76). The finding is consistent with observations that the potential for bias increases with increasing subjectivity in the interpretation of the clinical tests (77).

In a recent longitudinal cohort study of the associations between incident lumbar spine MRI findings and radiculopathy, only three MRI findings had large magnitude associations with symptoms and clinical findings. Annular fissures were associated with chronic low back pain, and patients with disc extrusions and nerve root impingement had a high incidence of radiculopathy (78, 79).

## 6.7 Treatment

Conservative treatment for radiculopathy is primarily aimed at pain reduction, using pure analgesics or non-steroidal anti-inflammatory drugs (NSAIDs), or more specific drugs against neuropathic pain (80-84). Other treatment options are steroid injections (20, 37), traction (85) and physiotherapy (86). Systematic reviews of conservative



interventions for lumbosacral radiculopathy have failed to identify an intervention that is superior to the others. However, large unbiased studies are scarce (87, 88).

Epidural steroid injections are increasingly applied (89), and this is the most widely used intervention for back pain and radiculopathy, with frequency doubling over the past 8 years (90). Unfortunately the clinical evidence supporting such treatment is insufficient (1) and use of steroids may have significant side effects. Surgery rates have also more than doubled over the past decade (91). There seems to be a consensus that surgery is indicated in carefully selected patients for lumbosacral radiculopathy in the presence of a herniated lumbar disc (34) with serious or progressive neurologic deficits and imaging demonstrating lumbar disc herniation at the nerve root level correlating with the patient's examination findings (19, 92).

There is, to date, no consensus about the right indication for epidural steroid injections.

## **6.8 Recurrent pain, disability and cost-effectiveness**

Recurrent radicular pain after non-surgical treatment of acute lumbar disc herniation occurs in 25% of cases over 1 year. Recurrent back pain is more common, 43% (93).

Despite the increase in back pain interventions, disability rates continue to rise (94-96).

Epidural steroid injections have increased by more than 25% from 2000 to 2011 in the USA (97), representing a significant increase in costs for society and patients (98). In the UK, the use of therapeutic epidural injections increased by 49% from 2000 to 2010 (99).

## 6.9 The physiology of pain and the pharmacology of steroids

Exposed nuclear material is known to irritate the spinal nerve roots and probably also the sinuvertebral nerve endings (100). Inflammation makes nociceptors hyperexcitable by the release of pro-inflammatory mediators, resulting in a lowered firing threshold leading to a state called peripheral sensitization (101). Central sensitization results from longstanding changes in the properties of neurons; the pain is no longer coupled, as acute nociceptive pain is, to the presence, intensity or duration of particular peripheral stimuli. Central sensitization represents a major functional shift in the somatosensory system from high-threshold nociception to low-threshold pain hypersensitivity (102, 103).

Steroid injections gained wide popularity after Lievre in 1953 (104) reported improvement in 5 out of 20 patients with lumbosacral radiculopathy. The mechanisms of action and the local anti-inflammatory effect at the injection site have still not been fully elucidated and clinical effects are uncertain (105). The anti-inflammatory and pain reducing effect of steroids seems to be mediated via a steroid receptor complex in the cell nucleus inhibiting the formation of cyclo-oxygenase 2 (cox-2) enzymes, and thereby the prostaglandin synthesis resulting in reduced inflammation. Steroids also suppress the immunological response of lymphocytes, stimulate production of the anti-inflammatory mediator lipocortin and reduce inflammatory oedema around an affected nerve root (106).

## 6.10 Anatomy of the lumbosacral spine

The lumbar vertebrae consist of a body anteriorly, two pedicles that project posteriorly from the body, and two laminae that connect the pedicles, which together form the vertebral canal, which contains the spinal cord, spinal nerves, and epidural space. The spinal nerves exit the vertebral canal under the pedicles.

The five sacral vertebrae are fused forming the wedge-shaped sacrum. The fifth sacral vertebra is not fused posteriorly, giving rise to an opening known as the sacral hiatus. The hiatus can be identified by bony prominences on either side of it, the sacral cornua.

The epidural space is the space that lies between the spinal meninges and the bony structures and communicates with the paravertebral space through the intervertebral foramen (107). The epidural space is composed of a series of discontinuous compartments that can be opened by the volume of an injection (108). The compartments consist of a rich network of valveless veins, lymphatics and segmental arteries. The proximal parts of the nerve roots pass through the epidural space. The epidural fat appears to have clinically important effects on the pharmacology of epidural drug deposits (109, 110).

The dura mater is the outermost and thickest meningeal tissue and is composed of collagen and elastin fibres. It extends laterally along the spinal nerve roots and ends at approximately S2, where it fuses with the filum terminale. The inner edge of the dura mater is highly vascular and can be important for clearance from the epidural space (111).

The spinal cord gives rise to 31 pairs of spinal nerves, each composed of an anterior motor root and a posterior sensory root. The nerve roots are in turn composed of multiple rootlets. The portion of the spinal cord that gives rise to all of the rootlets of a single spinal nerve is called a cord segment. The skin area innervated by a given spinal nerve and its corresponding cord segment is called a dermatome. The intermediolateral grey matter of the T1 through L2 spinal cord segments contains the cell bodies of the preganglionic sympathetic neurons. These sympathetic neurons run with the corresponding spinal nerve to a point just beyond the intervertebral foramen where they exit to join the sympathetic chain ganglia. In the lumbar region the nerve roots are named for the vertebrae forming the cephalad half of the intervertebral foramen; for example, L4 emerges through an intervertebral foramen formed by L4 and L5. Those nerves that extend beyond the end of the spinal cord at L2 to their exit site are collectively known as the cauda equina (112).

The meningeal branches of the spinal nerves (also known as recurrent meningeal nerves, sinuvertebral nerves, or recurrent nerves of Luschka) are a number of small branches of the spinal nerve (Figure 1). They re-enter the intervertebral foramen, and innervate the annulus fibrosus of the intervertebral disc, the dura mater, facet joints and the ligaments of the spinal canal, carrying pain sensation. The ventral dura mater seems to contain a rich polysegmental innervation of both autonomic and nociceptor fibres (113), but the evidence for this is conflicting (114). The ventral dural nerves may extend up to eight segments, with a great amount of overlap between adjacent nerves. This may be the anatomical substrate for understanding extrasegmental, referred dural pain (115).

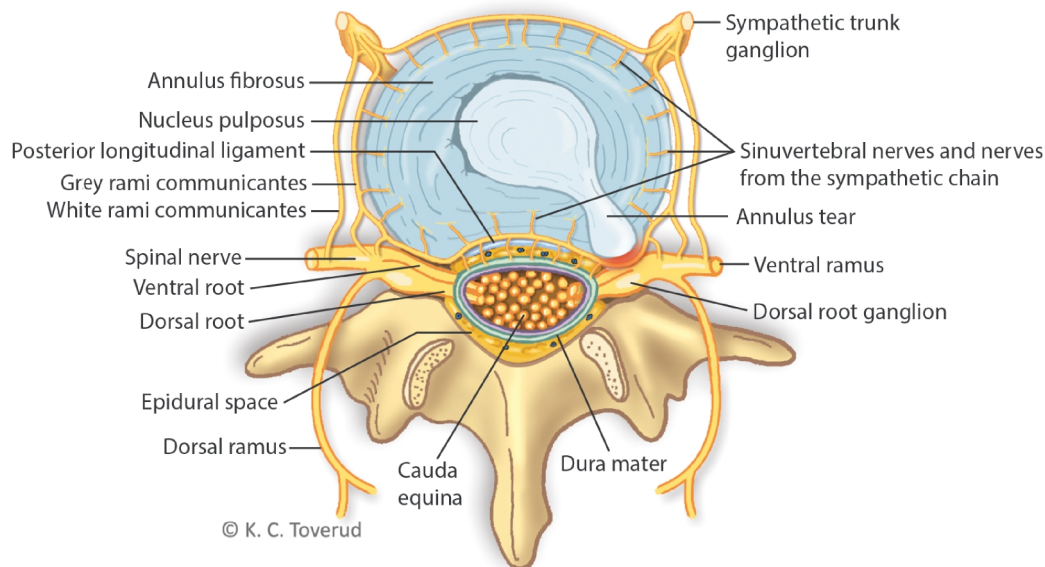


Figure 1. Anatomy of the lumbosacral spine.

## 6.11 Technical aspects of giving epidural injections

Epidural injections can be administered by three common methods – the transforaminal (perineural) (Figure 2), the interlaminar (Figure 2) and the caudal (Figure 3).

Caudal epidural injections are considered the safest and easiest method, with minimal risk of accidental dural puncture, even though relatively high volumes (10–30 ml) are required to reach the level where the pathology is situated. A caudal injection is placed through the sacral hiatus (located at S5 and occasionally S4). Ultrasound or fluoroscopic guidance is often used.

Interlaminar entry delivers the medication closer to the site of pathology and requires less volume (5–10 ml). It is performed by placing the needle between the spinous processes in the midline (or paramedian) traversing it through the ligamentum flavum using the resistance technique.

The transforaminal approach is considered even more targeted both with respect to pathology and pain generator (nerve ganglion), and an even smaller volume of injection is needed (2–5 ml). The transforaminal approach is a selective injection aimed at a specific level and is always done under fluoroscopic guidance. The foraminae are the small lateral openings between the vertebrae through which the nerve roots exit the spinal canal (116).

Caudal and interlaminar injection of steroids have been the main methods used, but more recently transforaminal epidural injections have gained increased popularity (117).

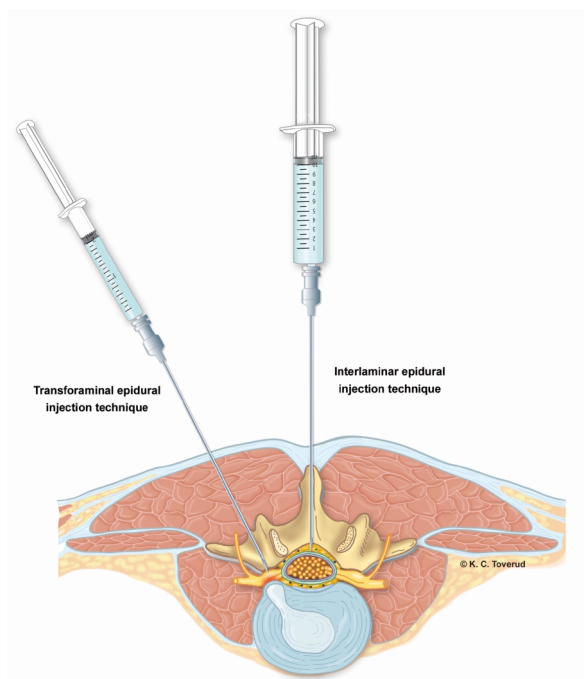


Figure 2. Interlaminar and transforaminal epidural injection techniques against a lateral herniated disc with nerve root displacement at level L4/5.

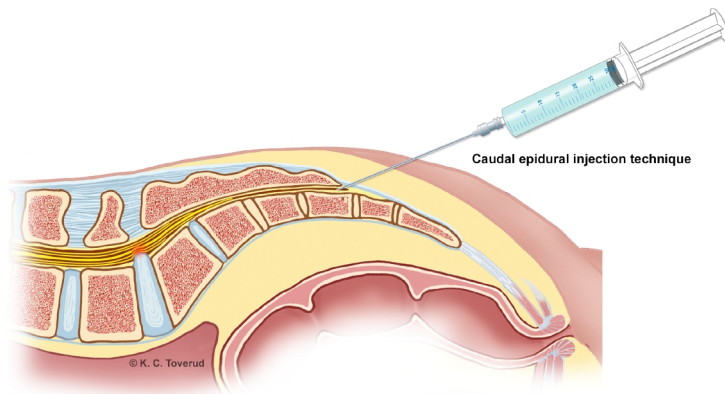


Figure 3. Caudal epidural injection technique against a disc herniation with nerve root displacement at level L5/S1.

## 6.12 Need for further research

Due to the significant increase in utilization of epidural steroid injections to treat lumbosacral radiculopathy in spite of lacking evidence for the efficacy of the method, further research is needed to clarify whether the method should be recommended or not. If the treatment can work, more research is needed to better refine selection criteria for epidural steroid injections, and to determine which approach, what dose, and how many injections are optimal (118).

A premise to select patients with suspected lumbosacral radiculopathy for either conservative or surgical treatment is correspondence between clinical and image findings. Further research is therefore needed to clarify the accuracy of the diagnostic tests to clarify the spinal level of lumbosacral radiculopathy due to disc herniation.

No specific predictors that can be used to modify the prognosis of lumbosacral radiculopathy have so far been identified. However, there is a strong association between elevated fear avoidance beliefs and chronic low back pain. Further research is needed to identify relevant predictors of the outcome of chronic lumbosacral radiculopathy. Information about risk factors and relevant predictors can be used for better selection of patients to avoid expensive and ineffective investigation and treatments and to inform patients about what benefit they can expect prior to treatment (shared decision-making).

### 6.13 Evidence-based medicine

According to Sackett, 'evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients' (127).

Incorporating the best evidence into clinical care requires a systematic approach in order to be manageable. The clinician must assess the patient and the problem to determine the pertinent issues, which may include a differential diagnosis, treatment decisions, or prognosis. From this evaluation the clinician must draw *a clear, answerable question to be pursued* from a range of appropriate sources. The quality of the evidence must be evaluated by its validity and reliability. Finally, the clinician must return to the patient and decide whether the evidence is applicable to the particular person at hand, appreciating their unique values and sociocultural setting.



The paramount objective in our research efforts has been to generate new knowledge to be used by clinicians in the evidence-based management of patients with lumbosacral radiculopathy.



## 7. RESEARCH QUESTIONS

### 7.1 Paper I

Are clinical tests accurate for the diagnosis and prediction of whether a lumbar nerve root is impinged or not by a disc herniation at a specific level in patients with chronic lumbosacral radiculopathy?

### 7.2 Paper II

Which prognostic factors predict persistent pain and disability in patients with chronic lumbar radiculopathy?

### 7.3 Paper III

Has treatment of chronic lumbosacral radiculopathy with caudal epidural injection of steroids or isotonic saline clinically important effects?



## 8. AIMS OF EACH PAPER

The aim of the thesis is to generate new knowledge in the research area of diagnostic accuracy, prediction and treatment efficacy of lumbosacral radiculopathy, so that the correct treatment can be given to the right patient more often. I will discuss the results presented in papers I, II and III in conjunction with the latest systematic reviews, meta-analyses and guidelines.

### 8.1 Paper I

The aims of this study were to investigate the association between findings at clinical examination and nerve root impingement, to evaluate the accuracy of clinical tests in a specialized care setting, and to see whether imaging clarifies the cause of clinically proven chronic lumbosacral radiculopathy. Patients were included when referred with symptoms of lumbar radiculopathy lasting more than 12 weeks and at least one positive clinical test. The tests were the SLR test, and tests for muscle strength, sensory loss, and reflex impairment.

### 8.2 Paper II

The aim of this study was to identify clinically relevant predictors of outcome of chronic lumbosacral radiculopathy at 52 weeks. We identified 15 clinically relevant baseline variables including demographic, psychosocial, clinical and imaging variables, and analysed them as predictors of outcome. The natural course of the disease was observed. Successful outcome at follow-up was set to  $\leq 17.5$  for visual analogue scale (VAS) leg pain,  $\leq 22.5$  for VAS back pain and  $\leq 20$  for the Oswestry Disability Index (ODI).

### 8.3 Paper III

The objective of the randomized controlled trial (RCT) was to evaluate the short- (6-week), intermediate- (12-week) and long-term (52-week) efficacy of caudal epidural steroid injections in the treatment of chronic (duration >12 weeks) lumbosacral radiculopathy. There were three intervention groups. Group 1 was given subcutaneous sham injections superficial to the sacral hiatus and not into the spinal canal, group 2 was given caudal epidural placebo injections of saline alone, and group 3 was given caudal epidural treatment injections of a combination of saline and triamcinolone acetonide. Each group received two injections over the course of 2 weeks. The primary outcome measure was the ODI, and the secondary outcome measures were the European quality of life (EuroQol) measure EQ-5D, VAS leg and back pain, and the Fear Avoidance Beliefs Questionnaire (FABQ).

## 9. STUDY DESIGN

### 9.1 Paper I

The aim of the STAndards for the Reporting of Diagnostic accuracy (STARD) studies initiative is to improve the accuracy and completeness of the reporting of studies of diagnostic accuracy by assessing potential for bias in the study (internal validity) and to evaluate its generalizability (external validity). The STARD statement consists of a checklist of 25 items and recommends the use of a flow diagram which describes the design of the study and the flow of patients (120, 121). We used the STARD guidelines in paper I.

### 9.2 Paper II

Cohort studies are a type of medical research used to establish links or associations between risk factors and health outcomes and are by definition prospective studies. The cohort is observed over a period to detect any changes in health in relation to predetermined risk factors or exposure(s). The cohort members are given questionnaires, and/or clinical examinations, and/or testing to determine exposure status. We used a cohort study design in paper II.

### 9.3 Paper III

The Consolidated Standards of Reporting Trials (CONSORT) statement is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT statement

comprises a 25-item checklist and a flow diagram. The checklist items focus on reporting how the trial was designed, analysed and interpreted; the flow diagram displays the progress of all participants through the trial (122). We used the CONSORT statement both in designing and reporting paper III.



## 10. MATERIAL AND METHODS

### 10.1 Referrals and eligibility

Patients with lumbosacral radiculopathy were referred from the catchment area (population 1,146,076) of the University Hospital of North Norway Tromsø (UNN), St Olavs University Hospital Trondheim, Levanger Hospital, Nordland Hospital Bodø, and Buskerud Hospital Drammen to the outpatient multidisciplinary back clinics at these five Norwegian hospitals. The general practitioners, neurosurgeons, orthopaedic surgeons, neurologists, manual physiotherapists, and chiropractors working in these areas were invited by letter to participate in the trial. Eligible patients between 20 and 60 years of age were consecutively assessed for inclusion. Written informed consent was obtained.

### 10.2 Inclusion criteria

The inclusion criteria were unilateral lumbosacral radiculopathy lasting for more than 12 weeks. The intensity of the leg pain, radiating from the back to below the knee, had to be comparable or worse than the back pain. There were no requests for a correspondence between demonstrated level of lumbosacral radiculopathy by clinical examination and findings on imaging.

### 10.3 Exclusion criteria

Patients presenting with a cauda-equina syndrome, severe paresis, severe pain, history of previous spinal injection or surgery, deformity, pregnancy, ongoing breastfeeding, warfarin therapy, ongoing treatment with NSAIDs not possible to cease, body mass

index >30, poorly controlled psychiatric conditions with possible secondary gains, or severe co-morbidity were excluded from the study. Patients with severe intraspinal pathology (large disc herniations occupying more than 50% of the spinal canal, spinal stenosis, tumours, bleeding, dural fistula, synovial cysts, or dysraphia) were excluded.

## 10.4 Study population

Between October 2005 and February 2009, 461 patients were assessed for inclusion. A total of 345 (74.8%) patients were excluded, and 116 (25.2%) patients with lumbar radiculopathy for more than 12 weeks were included in the study (Table 1).

Table 1. Study population.

<b>Excluded patients (n = 345) at baseline</b>	
Did not meet inclusion criteria, n (%)	97 (28.1)
Met exclusion criteria, n (%)	214 (62.0)
Declined to participate, n (%)	17 (4.9)
Substantial and rapid improvement after assessment, n (%)	17 (4.9)
<b>Characteristics of the included patients (n = 116) at baseline</b>	
<i>Sociodemographic variables</i>	
Age years, mean (SD)	42.0 (10.3)
Male gender, n (%)	68 (58.6)
Current smoker, n (%)	49 (42.2)
University or college education, n (%)	22 (19.0)
Working full-time, n (%)	43 (37.1)
<i>Low back pain/sciatica history</i>	
Low back pain weeks, mean (SD)	53.4 (110.0)
Leg pain weeks, mean (SD)	42.0 (99.0)
ODI score, mean (SD)	30.0 (13.2)
VAS score leg pain, mean (SD)	50.6 (24.7)
VAS score back pain, mean (SD)	47.6 (24.3)
EQ-5D, mean (SD)	0.51 (0.29)
FABQ-W, mean (SD)	12.8 (5.0)
FABQ-PA, mean (SD)	23.4 (10.2)
<i>Clinical examination</i>	
SLR <60°, n (%)	62 (53.4)
Muscle weakness, n (%)	94 (81.0)
Dermatomal sensory loss, n (%)	83 (71.6)
Reflex impairment, n (%)	55 (47.4)
Body mass index, mean (SD)	26.3 (3.8)
<i>Magnetic resonance or CT imaging</i>	
Concordance between nerve root impingement on MRI and clinical radiculopathy, n (%)	60 (51.7)
Disc herniation without nerve root impingement, n (%)	30 (25.9)
Normal or minor degenerative changes, n (%)	26 (22.4)
Modic type I and I/II, n (%)	66 (56.9)

Note: SD = standard deviation; FABQ-W = Fear Avoidance Beliefs Questionnaire for work; FABQ-PA = Fear Avoidance Beliefs Questionnaire for physical activity.

## 10.5 Clinical examination

The clinical examination followed a pre-prepared study procedure (Appendix 4) following the STARD initiative to decide whether the patient had a lumbosacral radiculopathy and to determine the most probable nerve root affected. The inclusion examination was done by trained neurologists or specialists in physical medicine and rehabilitation in cooperation with a physiotherapist.

## 10.6 Imaging

MRI in 109 (94.0%) patients or CT in 7 (6.0%) patients was performed. Experienced radiologists evaluated the images, and a written report from the radiologists was available for the clinicians to be able to exclude patients with severe intraspinal pathology obviously demanding surgery. All the MRI and CT scans were re-evaluated by two independent neuroradiologists using the Nordic Modic Classification (123) (Appendix 5). They were blinded regarding patient history and clinical findings. The locations of the disc herniation (Figures 4 and 5) were identified in the axial plane, and were categorized as being localized centrally or to the left or right in the spinal canal (124). In cases of disagreement, a consensus was reached emphasizing the conclusions of the most experienced neuroradiologist.



Figure 4. MRI longitudinal section showing normal disc, bulging degenerative disc and herniated disc.

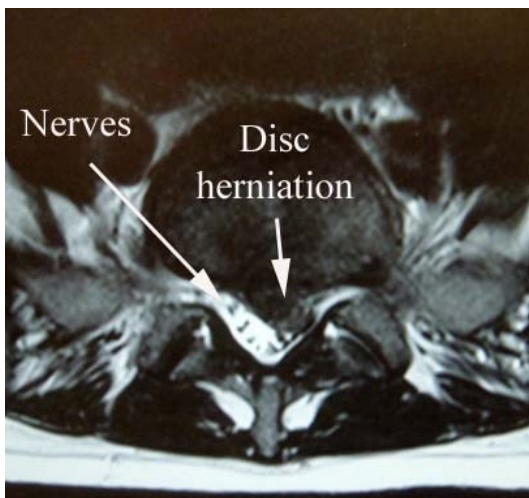


Figure 5. MRI transverse section showing herniated disc compressing the dura mater and nerve root.

## 10.7 Randomization

The randomization was done according to the CONSORT statement by the Clinical Research Centre at UNN. They used a computer generated block scheme for randomization, stratified according to intervention hospital.

## 10.8 Data collection

Each patient completed self-administered questionnaires, which were identical at baseline and follow-up (Appendix 6). The use of multidimensional patient reported outcome measures (PROMs) provides insight into how the impact of diseases and treatments are perceived by the patients. The PROMs in the study were the ODI, EQ-5D and FABQ (125). The questionnaires at baseline also contained questions about demographics, education, duration of pain, work status, medication, and lifestyle issues. Clinical signs of lumbosacral radiculopathy, need for physiotherapy or surgery during follow-up, patient perceived benefit of the intervention, and working capability were also monitored at each follow-up. A global question on a 4-point Likert scale was used to measure the benefit of the intervention at each follow-up (126).

## 10.9 Follow-up

All patients received standardized oral and written information about spine anatomy and function at baseline and follow-up. They were encouraged to engage in physical activity (127-130), and all patients received the brochure 'Worth knowing about bad backs. What experts agree on' (131). Patients using NSAIDs were told to cease this medication. The 6, 12 and 52-week follow-ups were conducted at the hospitals by a blinded physiotherapist and doctor. Use of physiotherapy was recorded during follow-up but was not routinely offered to the patients. During the study period, the need for surgical treatment among patients with increasing pain, or paresis, was evaluated by study-independent surgeons.

## 10.10 Outcome measures

The ODI was used as the primary outcome measure. The ODI questionnaire contains ten questions on limitations of activities to daily living. Each variable was rated on a 0–5 point scale, added up, and transferred into a percentage functional score ranging from 0 to 100 (0 = no disability) (132-134). Secondary outcome measures were evaluated by the EQ-5D, the VAS for low back pain and leg pain, and the FABQ. The EQ-5D measure is a generic and preference-weighted measure of health-related quality of life. It evaluates five dimensions: mobility, self-care, activities of daily life, pain, and anxiety and/or depression. For each dimension, the patient describes three possible levels of problems (no, mild to moderate, and severe). This descriptive system contains 243 combinations or index values for health states (135). We used the value set from the main survey of the EuroQol Group (136), which has been validated for patients with lumbar radiculopathy (137). Total score range is from –0.594 to 1, where 1 corresponds to perfect health and 0 to death. Negative values are considered to be worse than death (135). The intensity of leg pain and low back pain was indicated on a horizontal 100 mm VAS (0 = no pain) (137, 138). The FABQ is a questionnaire based on the Fear Avoidance Model of Exaggerated Pain Perception. The FABQ with the work (FABQ-W) and physical activity (FABQ-PA) subscales, measures patients' fear of pain and consequent avoidance of physical activity because of their fear. The questionnaire consists of 16 items, with each item scored from 0 to 6. The total possible score for the work subscale is 42 and for the physical activity subscale it is 24. Higher scores on the FABQ are indicative of greater fear and avoidance beliefs (38). The FABQ was used both as a continuous variable and was also dichotomized. We chose  $\geq 34$  as the cut-off for an elevated fear avoidance belief

for the FABQ-W (139) and  $\geq 15$  for the FABQ-PA (140). The FABQ subscale scores have been shown to have excellent test-retest reliability (intraclass correlation coefficient 0.77–0.90).

## 10.11 Statistical analysis

We calculated means and standard deviations (SDs) for continuous variables, and frequencies and proportions for categorical variables. Paired samples t-tests were used to test change scores between baseline and follow-up for patient reported outcomes. Analysis of variance (ANOVA) was used to compare mean differences between groups for continuous variables, and the Pearson chi-square test for categorical variables. All tests were two-sided using a significance level of 5%. All analyses were performed using the IBM SPSS Statistics software, versions 17, 19 and 22 (IBM Software, NY, USA), and in addition STATA 11.0 (Stata Corp®) was used for the mixed model analyses in paper III.

### 10.11.1 PAPER I

The prevalence of nerve root impingement based on the reference standard and the post-test probabilities for a positive and negative test were calculated. Diagnostic accuracy was quantified by calculating sensitivities, specificities, and positive and negative likelihood ratios (LRs), including 95% confidence intervals (CIs), for each clinical test. In a multivariable logistic regression model we included all index tests as independent variables. The estimated model was used to predict the probability of a positive MRI/CT for each patient. These probabilities were used to produce a receiver operating characteristic (ROC) curve and an estimate for the area under the curve (AUC).



### 10.11.2 PAPER II

We used univariable and stepwise backward (Wald) multivariable binary logistic regression to analyse associations between predictors and outcome measures.

Predictors with P value <0.20 from the univariable analysis were used in the multivariable analysis. In the analysis we adjusted for the baseline values. Odds ratios (ORs) with 95% CIs were calculated.

### 10.11.3 PAPER III

Linear mixed models were used to assess differences in time trends between the treatment groups for the primary and secondary outcome measures (141). We added time to the model as a categorical variable represented by dummy variables in order to analyse the differences between the groups at different time points. In all mixed model analyses, a crude adjustment was made for the baseline values of the particular outcome variable. In the secondary analysis, additional adjustments were performed for duration of back pain, duration of leg pain, and duration of sick leave prior to inclusion. The analyses for all outcome measures used all available data on an intention to treat basis.

## 10.12 Intervention and blinding

A standardized referral letter for the intervention contained information about the patient's cardiac and pulmonary status, medication and allergies but did not include information about back pain and radiculopathy (Appendix 6). There were three intervention groups (Appendix 7). Group 1 received subcutaneous sham injections of 2 ml 0.9% saline superficial to the sacral hiatus and not into the spinal canal. Group 2 received caudal epidural placebo injections of 30 mL 0.9% saline. Group 3 received

caudal epidural treatment injections of 40 mg triamcinolone acetonide in 29 mL 0.9% saline. All three intervention groups received two injections over the course of 2 weeks; the second injection was cancelled if spontaneous recovery had occurred between inclusion and the first intervention. An experienced anaesthesiologist gave the injections and followed a set procedure (142, 143) (Appendix 4). Anatomical landmarks were used to identify the sacral hiatus. In addition, use of an ultrasound machine (Honda Diagnostic Scanner HS-2000 Cine, Honda Electronics Co.) capable of examining musculoskeletal tissues with a 10 MHz real-time linear array ultrasound transducer increased the precision of the injections (144-146) (Appendix 4, Figure 6).

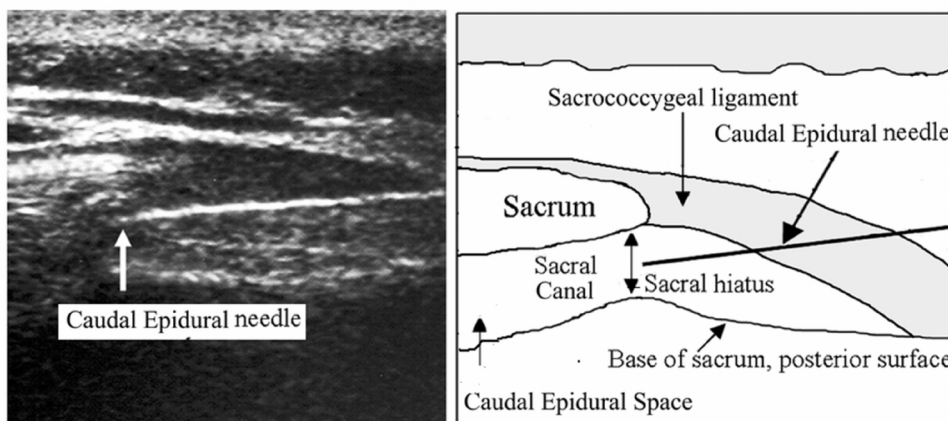


Figure 6. Ultrasound picture and diagram showing the epidural needle in the sacral hiatus entering the caudal epidural space (based on (145)).

We ensured that the patients, outcome assessors, and care providers were blinded during the study period; they were all unaware of the randomization and intervention given by the anaesthesiologists (Figure 7). The anaesthesiologists giving the injections were not blinded because inclusion of a subcutaneous sham group made this impossible (147). The injection products were concealed from the patients, and the

anaesthesiologists were instructed not to discuss the injection procedure or the products used with the patients.

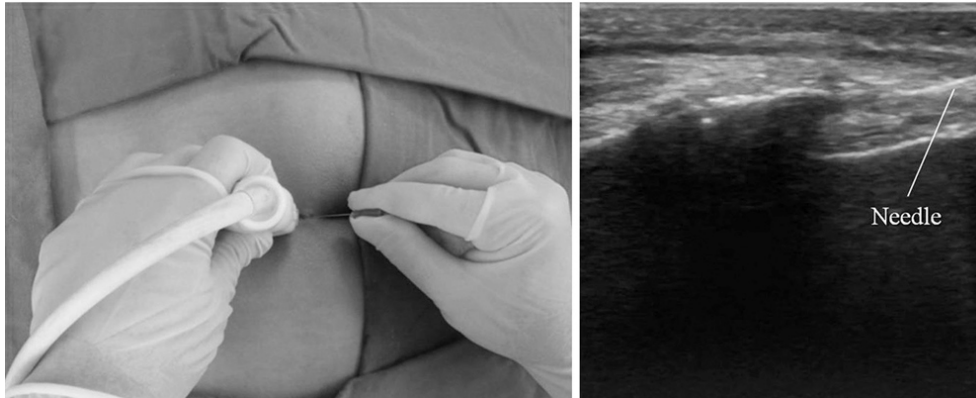


Figure 7. The caudal epidural injection technique with ultrasound guidance (145).

### 10.13 Placebo and sham procedure

We defined placebo intervention as administration of regular saline solution into the epidural space and sham intervention as administration of regular saline subcutaneously (148). In experimental studies, treatment is often compared with placebo or sham to determine whether or not treatment using an active medicine has any effect (149). In studies on the effect of epidural sacral injection, steroid treatment is often compared with placebo treatment using saline or local anaesthetic or with a sham injection. In some studies a positive effect has been recorded for epidural saline and local anaesthetic on its own. One possible interpretation of this could be that local anaesthetic results in a short-term suppression of pain transmission and that regular saline can have an effect via mechanisms other than purely pharmacological action, for example due to a volume or pressure effect. We wanted to clarify these mechanisms by comparing the effect of epidural injection of steroid (active treatment) and epidural

injection of regular saline (placebo injection) with non-epidural subcutaneous injection of regular saline (sham injection).

## 10.14 Ethics

The inclusion and randomization of patients with nerve root disease for epidural injection in a placebo and/or sham controlled study is associated with a number of ethical problems. The use of epidural injection is widespread and the procedure has been used both inside and outside hospitals to treat low back pain and radiculopathy. There is, however, no evidence that the method is effective. Since there is some uncertainty and lack of evidence associated with most methods for treating lower back pain and sciatica, testing the effect of epidural injection in a placebo and sham controlled study would be ethically defensible. Good patient information, informed consent, the principles of good clinical practice in clinical trials, the Declaration of Helsinki (150) and ethical approval are fundamental requirements followed in this study. Our study was registered in Current Controlled Trials with No 12574253 and the study protocol (Appendix 7) was approved by the ethics committee for Medical Research Region 5 Norway.

## 11. MAIN RESULTS

### 11.1 Paper I

We found a low correspondence between clinical findings and MRI proven disc herniation with relevant nerve root impingement. A correspondence was only present in 60 out of 116 patients (51.7%) in our study.

The diagnostic accuracy of individual index tests was low with no tests reaching positive LR  $>4.0$  or negative LR  $<0.4$ . The overall clinical evaluation was slightly more accurate, with a positive LR of 6.28 (95% CI 1.06–37.21) for L4, 1.74 (95% CI 1.04–2.93) for L5, and 1.29 (95% CI 0.97–1.72) for S1 nerve root impingement.

### 11.2 Paper II

At follow-up, 75 (64.7%) patients had reached a successful outcome with an ODI score  $\leq 20$ , 54 (46.6%) with a VAS leg pain score  $\leq 17.5$ , and 47 (40.5%) with a VAS back pain score  $\leq 22.5$ .

Lower age (OR 0.94 (CI 0.89–0.99) for each year increase in age) and FABQ-W  $\geq 34$  (OR 0.16 (CI 0.04–0.61)) were independent variables predicting a successful outcome on the ODI. Higher education (OR 5.77 (CI 1.46–22.87)) and working full-time (OR 2.70 (CI 1.02–7.18)) were statistically significant ( $P < 0.05$ ) independent predictors of successful outcome (VAS score  $\leq 17.5$ ) on the measure of leg pain. Lower age predicted success on the ODI (OR 0.94 (95% CI 0.89 to 0.99) for each year) and less back pain (OR 0.94 (0.90 to 0.99)), while higher education (OR 5.77 (1.46 to 22.87)), working full-time (OR 2.70 (1.02 to 7.18)) and muscle weakness at baseline (OR 4.11 (1.24 to 13.61) predicted less

leg pain, and reflex impairment at baseline predicted the contrary (OR 0.39 (0.15 to 0.97)).

### 11.3 Paper III

All groups improved following the interventions, but there were no statistical or clinical differences between the groups over time. The estimated change with 95% CI in the ODI from the adjusted baseline value for the sham group was  $-4.7$  ( $-0.6, -8.8$ ) at the 6-week follow-up,  $-11.4$  ( $-6.3, -14.5$ ) at the 12-week follow-up, and  $-14.3$  ( $-10.0, -18.7$ ) at the 52-week follow-up. The differences in outcome for the epidural saline intervention group compared to the sham intervention group were  $-0.5$  ( $-6.3, 5.4$ ) at the 6-week follow-up,  $1.4$  ( $-4.5, 7.2$ ) at the 12-week follow-up, and  $-1.9$  ( $-8.0, 4.3$ ) at the 52-week follow-up. The differences in outcome for the epidural steroid intervention group compared to the sham intervention group were  $-2.9$  ( $-8.7, 3.0$ ) at the 6-week follow-up,  $4.0$  ( $-1.9, 9.9$ ) at the 12-week follow-up, and  $1.9$  ( $-4.2, 8.0$ ) at the 52-week follow-up. Analysis adjusted for duration of leg pain, back pain, and sick leave did not change this trend.

## 12. DISCUSSION OF THE RESEARCH QUESTIONS

### 12.1 Paper I

Are individual clinical tests accurate for the diagnosis and prediction of whether a lumbar nerve root is impinged or not by a disc herniation at a specific level in patients with chronic lumbosacral radiculopathy?

Our main finding in paper I was that individual clinical tests lack diagnostic accuracy for predicting whether a lumbar nerve root is impinged or not at a specific level in patients with chronic lumbosacral radiculopathy, when the specialist was unaware of the radiological findings.

In 2014, the North American Spine Society (NASS) published clinical guidelines for the diagnosis of lumbar disc herniation with lumbosacral radiculopathy (151). The work group consisted of multidisciplinary spine care specialists trained in the principles of evidence-based analysis. They recommended the usual clinical tests for muscle power, sensibility and the SLR test but not to use tendon reflexes for diagnosing lumbosacral radiculopathy. In patients with a history consistent with physical examination findings, MRI was recommended as an appropriate non-invasive diagnostic test to confirm the presence of lumbosacral disc herniation.

In a systematic review from 2013 (152), Nezari examined the diagnostic accuracy of the standard neurological examination in detecting disc herniation with suspected lumbosacral radiculopathy using MRI as a reference standard. This meta-analysis including 14 studies showed that all the clinical tests had low sensitivity, moderate

specificity, and limited diagnostic accuracy. The pooled sensitivity was low for sensory testing (0.32), motor testing (0.40) and reflex testing (0.25). The corresponding pooled specificity values were high, 0.72, 0.62 and 0.75, respectively. The pooled positive LR for all neurological examination components were low, ranging from 1.02 to 1.26. Nezari argues that insufficient standardization of the testing procedures, variation in use of reference standard, and the complexity of the pathology associated with disc herniation can explain the low diagnostic accuracy. He called for studies that evaluate the accuracy of the neurological tests to detect disc herniation at specific spine levels.

In paper I, on the accuracy of physical examination for chronic lumbar radiculopathy, we obtained identical findings concerning the sensitivity and specificity tests that Nezari found in his pooled analysis. We also addressed the issue of the accuracy of the tests at specific spine levels, which were low.

An MRI can with a high degree of precision show which level and side the herniated disc is localized and whether the nerve root is likely to be impinged. For a surgeon, a correspondence between clinical and MRI findings is crucial. In accordance with previous studies (151, 152) we found that this correspondence between clinical findings and the level and side of disc herniation with nerve root impingement on MRI was low, only 51.5% (paper I).

In 2014, Verwoerd (153) examined the diagnostic accuracy of patient reported symptoms and signs to detect lumbosacral nerve root impingement on MRI among 395 patients with lumbosacral radiculopathy. Age, gender, pain worse in leg than in back, subjective sensory loss, subjective muscle weakness, and more pain on



coughing/sneezing/straining were used as predictors. Verwoerd found poor accuracy for all predictors, with sensitivity values ranging from 0.53 to 0.89 and specificity values ranging from 0.18 to 0.59.

The diagnosis of lumbosacral radiculopathy is inaccurate. Information from history, clinical examination and imaging separately gives conflicting results. Clinical skills and practise improves the diagnostic accuracy, but further research is necessary to develop evidence-based knowledge to be able to select the most efficient diagnostic methods and to minimize dependency on imaging to reach a valid diagnosis.

## 12.2 Paper II

Which prognostic factors predict persistent pain and disability in patients with chronic lumbar radiculopathy?

In paper II, we identified that lower age and low FABQ-W predicted a better functional outcome and less back pain at the 52-week follow-up, while higher education and working full-time predicted less leg pain at the 52-week follow-up.

Most prognostic estimates of lumbosacral radiculopathy are based on individual studies examining a range of predictors measured and quantified differently. Results have therefore been difficult to reproduce in more comprehensive studies, but the prognosis seems generally to be most influenced by an individual's expectations and beliefs regarding pain and disability (154).

Fritz (139) found that a FABQ-W score >34 identified patients at risk of not returning to work 4 weeks after an incident of acute low back pain. In a prospective cohort study of

49 patients with lumbosacral radiculopathy treated with physiotherapy they found at long-term follow-up that the FABQ-PA score had improved by 4.5 points, from 20.5 at baseline (155). A clinically important change in beliefs has occurred, but a clinically relevant change value has, however, not yet been established (139). For patients treated with disc prosthesis, long duration of back pain and high FABQ-W score at baseline have been shown to significantly be associated with a worse outcome at the 2-year follow-up as assessed by the ODI (156). Cognitive behavioural therapy and graded exposure to physical activity can reduce back pain in patients with high fear avoidance measured by the FABQ (157-159). Recent studies also show that high fear avoidance can be reduced by cognitive intervention with the prospect of improved outcomes (160-163). This indicates that high fear avoidance is a modifiable risk factor that is clinically relevant.

Our findings are further partially consistent with the findings of a study by Suri (154), that being in full-time employment appears to predict a lower leg pain level. In a study of surgically and conservatively treated patients with lumbosacral radiculopathy due to disc herniation (164), most patients who were receiving workers' compensation had significantly worse outcome than patients not initially receiving workers' compensation.

In a systematic review of bio-psychosocial risk factors for an unfavourable outcome after lumbar disc surgery (165), den Boer found positive evidence that a lower level of education predicts an unfavourable outcome. This is in line with the findings of our paper II that higher education predicted less leg pain at 52-week follow-up. Research conducted among chronic pain patients demonstrates that a low social economic status is a risk factor for various chronic pain conditions. The specific nature of this

relationship is not entirely clear, and could be caused by various factors, such as physical work conditions, less access to health services, and/or less healthy behaviours.

Patient reported outcomes after conservative treatment of lumbosacral radiculopathy due to disc herniation are diverse. Many patients experience a spontaneous recovery, while others experience a more protracted course. Treatment failure after conservative treatment is often defined as lack of recovery or the need for subsequent surgery. Early identification of patients with a poor prognosis is important and can prevent initiation of ineffective conservative treatment and prolonged sick leave.

In a recently published systematic review of prognostic factors for non-surgically treated patients with lumbosacral radiculopathy (166), Verwoerd found that higher baseline leg pain intensity was the only independent predictor of treatment failure. However, in 2014, Suri was unable to reproduce this finding (154). This reflects a large problem in the research on prognostic factors, namely the inability to find risk factors that are clinically relevant and can be modified to improve treatment and prognosis of lumbosacral radiculopathy. As highlighted by Suri, focus has to be put on risk factors for unsuccessful outcomes, where the potential for improvements is greatest. Furthermore, identification of independent risk factors needs to be reproduced in subsequent studies to gain credibility in the scientific community. Suri defined four main groups of predictors of treatment failure – subsequent surgery, persistent leg pain, persistent disability, and patient reported lack of recovery (Table 2).

Table 2. Candidate predictors of treatment failure of conservative treatment for lumbosacral radiculopathy leading to subsequent surgery, persistent leg pain, persistent disability and patient reported lack of recovery (154).

<b>Subsequent surgery</b>	<b>Persistent disability</b>
High initial leg pain intensity	<i>High initial disability</i>
High initial disability	High initial back pain intensity
Long duration of symptoms	<i>Female gender</i>
<i>Prior low back pain</i>	Long duration of symptoms
<i>Positive SLR</i>	Current smoking
Positive crossed SLR	Medical comorbidities
Positive femoral stretch test	Prior low back pain
	Sick leave
	Herniated extruded disc
	Abnormal tendon reflexes
<b>Persistent leg pain</b>	<b>Patient reported lack of recovery</b>
High initial leg pain intensity	High age
High initial back pain intensity	<i>Female gender</i>
Female gender	Long duration of symptoms
Long duration of symptoms	Current smoking
Current smoking	Sick leave
Medical comorbidities	Positive SLR
<i>Sick leave</i>	Positive femoral stretch test
Muscle weakness	Foraminal disc herniation
Herniated extruded disc	<i>High initial disability</i>

Suri identified *prior low back pain* and *positive SLR* as predictors of subsequent surgery, *sick leave* for persistent leg pain, and *high initial disability* and *female gender* for persistent disability and patient reported lack of recovery.

Searching for an evidence-based answer to a common clinical question such as ‘What is the prognosis for recovery with conservative care for a 43-year-old man with lumbar disc herniation and lumbosacral radiculopathy?’, Emary (167) found only two relevant systematic reviews to base his answer to the patient on (50, 168). Unfortunately, both were unable to give an adequate answer to his question. However, two individual cohort studies by Suri (93, 169) made it possible for Emary to estimate a likely outcome for his patient, indicating a 72–90% chance of recovering from leg pain within 6 months, but with a 15–35% chance of recurrent leg pain within a year, regardless of type of conservative treatment chosen (87).

Reviews show that most previous studies suffer from methodological weaknesses, which may explain why no consistent predictors have been identified (166, 168). Appropriate methodology implies a careful cohort study design and use of multivariable analysis to determine adjusted and independent risk factors for different outcomes.

Identification of prognostic factors predicting persistent pain and disability is important for better understanding of the clinical course – information that can be provided to patients and physicians – and better decision-making in the treatment and guidance of patients with radiculopathy.

## 12.3 Paper III

Has treatment of chronic lumbosacral radiculopathy using caudal epidural injection of steroids or isotonic saline clinically important effects?

In paper III, 39 patients received caudal epidural injection of saline and 37 received caudal epidural injection of saline plus steroid. At both short- and long-term follow-up there was a significant within-group difference for both groups compared with the baseline values for pain and function, but there were no between-group differences.

Parr (116) and Manchikanti (170) have, in two systematic reviews on the effect of epidural steroid injection from 2012 and 2014 respectively, analysed four key RCTs of high methodological quality (171-176) treating lumbosacral radiculopathy. They compared these four studies with our study in paper III and found similar results.

In the included study by Dashfield in 2005 (171), 60 patients with an average 10-month history of sciatica were included. Patients were randomized into groups to receive either caudal epidural injection of steroids and local anaesthetic, or to receive targeted epidural local anaesthetic and steroid placement with a spinal endoscope. The follow-up period was 6 months. No significant differences were found between the groups for pain scores, but there were significant improvements within both groups compared with pretreatment values.

In the included study by Ackerman in 2007 (172), 90 patients with a prolapse in level L5/S1 and an average case history of 1 month were randomized to receive caudal epidural injection, interlaminar epidural injection or transforaminal injection of steroids and saline. The follow-up period was 6 months. Pain improved within all groups but was

significantly greater with the transforaminal approach. Improvements in disability scores were equal for the three groups. The reason why more patients specified pain freedom after the transforaminal epidural injection technique was attributed to the placement of the steroids in the ventral epidural space, theoretically providing a better anti-inflammatory effect compared with the two other injection techniques.

The third included study was conducted by Manchikanti. Preliminary results were published in 2008 (173), 1-year follow-up results in 2011 (174) and the 2-year follow-up results in 2012 (175). In this study, 120 patients were randomized to receive caudal epidural injection of steroids and local anaesthetic or only local anaesthetic. All patients had chronic lumbosacral radiculopathy and MRI-verified disc herniation with nerve root impingement. Both groups had significant improvement in pain and disability.

The fourth study, by Murakibhavi in 2011 (176), included 100 patients with chronic lumbosacral radiculopathy due to disc herniation. The patients were randomized to physiotherapy and pain killing medication or caudal epidural steroid injection in combination with saline and local anaesthetic. The patients were followed for 6 months. A within-group effect in the injection group was shown, but no between-group effect.

Parr (116) concludes that the evidence is considered good for short- and long-term relief of pain from treatment with epidural steroid injections and local anaesthetics injections. Manchikanti (170) concludes that the available evidence suggests that epidural steroid injections offer improvement in pain and function in well-selected patients with lumbar disc herniation.

These conclusions are only based on effects within the treatment groups. None of the studies have shown better results in the intervention groups compared to controls and none have shown any long-term effects. The conclusion from the systematic reviews by Parr and Manchikanti, that epidural steroid injections are an effective treatment for lumbosacral radiculopathy caused by disc herniation, is therefore likely to be flawed.

Our study, which concludes that epidural steroid injections are not efficacious, has been criticized for being methodologically weak, i.e. in design, selection criteria and inclusion criteria, and for not including injection of local anaesthetic. In the systematic reviews of Parr and Manchikanti, paper III therefore received only a moderate method score (3 on a scale from 0 to 8). However, another systematic review (177) gave it a strong method score of 7. This illustrates that scoring of methodological quality is not solely based on objective criteria, but also on subjective judgement.

When summarizing our results with those of the other four studies one can conclude that the patients improve regardless of injection technique and type of drug use, but that there are no between-group treatment effects when comparing epidural steroid injections with epidural local anaesthetic or saline injections.

### **12.3.1 IS THERE A BETWEEN-GROUP DIFFERENCE WHEN EPIDURAL STEROID INJECTIONS ARE COMPARED WITH PLACEBO INJECTIONS?**

In 2013, Pinto published a systematic review to determine the efficacy of epidural steroid injections for lumbosacral radiculopathy compared with placebo epidural injections of saline or local anaesthetics (177) via the caudal, transforaminal and interlaminar route. For the caudal technique he compared our paper III with two other



similar studies (174, 178). Pinto argues that an important limitation for interpreting the results of many clinical trials is that the comparator is often another active drug of unknown effectiveness (local anaesthetics) rather than an inert epidural placebo injection of saline (177, 179-180). Manchikanti (170) argues that even an epidural injection of saline into the epidural space cannot be regarded as placebo, but an effective treatment to relieve pain and improve function. The physiological mechanisms involved for such a proposed effect are still unexplained, but studies indicate that epidural injection of saline alone may have a positive effect by diluting inflammatory cytokines or lysing of scar tissue (173, 181, 182).

In a study by Bush in 1991 (178), 23 patients were randomized into groups to receive caudal epidural injections of steroids and local anaesthetic or to receive caudal epidural injections of saline only used as placebo. At 1-year follow-up, both groups demonstrated a statistically significant reduction in pain score, but there were no differences in outcome between the treatment arms.

The second study was conducted by Manchikanti in 2011 (174). In this study, 120 patients with MRI-confirmed disc herniation with nerve root impingement were randomized into groups to receive caudal epidural injections of steroids and local anaesthetic or epidural injections of only local anaesthetic as a placebo. There was a significant improvement in pain and function in both groups.

A meta-analysis of the included studies for all injection techniques (lumbar, transforaminal and caudal) to estimate the short- and long-term efficacy showed

significant short-term effect favouring epidural steroids but non-significant results at long-term follow-up compared to placebo (177).

Table 3 shows the weighted mean difference (WMD) for short- and long-term efficacy for leg pain and disability for the caudal epidural steroid injections compared to placebo.

Table 3. Short- and long-term WMD for leg pain and disability for caudal epidural injections (177).

Author (Reference)	Steroids		Placebo		WMD (95% CI)
Leg Pain	Patients <i>n</i>	Mean Pain Score (SD)	Patients <i>n</i>	Mean Pain Score (SD)	
<b>Short-term follow-up</b>					
Bush (178)	12	-	11	-	
Iversen (Paper III)	37	37.6 (23.6)	35	42.4 (25.0)	
Manchikanti (174)	60	34.0 (17.0)	60	41.0 (18.0)	
<b>Long-term follow-up</b>					
Bush (178)	12	-	11	-	
Iversen (Paper III)	34	21.2 (23.6)	33	27.1 (25.0)	
Manchikanti (174)	60	35.0 (19.0)	60	41.0 (18.0)	
<b>Disability</b>					
		Mean Disability Score (SD)		Mean Disability Score (SD)	
<b>Short-term follow-up</b>					
Iversen (Paper III)	37	22.9 (12.1)	35	24.7 (14.3)	
Manchikanti (174)	60	27.2 (13.0)	60	33.0 (14.4)	
<b>Long-term follow-up</b>					
Iversen (Paper III)	34	18.8 (12.1)	33	14.1 (14.7)	
Manchikanti (174)	60	26.2 (14.0)	60	31.0 (15.5)	

The small effects observed in the review by Pinto were less than the proposed thresholds for minimal clinically important difference (177), which is in accordance with the conclusion in paper III. Table 4 shows the WMDs (95% CI) calculated by Pinto for the caudal epidural injection of steroids and placebo. Including all trials in the meta-analysis, the effect size (WMD (95% CI)) for leg pain at short-term follow-up was -6.2(-9.4 to -3.0) and -4.8(-10.2 to 0.7) at long-term follow-up. The respective values for disability were -3.1(-5.0 to -1.2) at short-term follow-up and -2.7(-6.8 to 1.3) at long-term follow-up. Negative values favoured the epidural corticosteroid group.

Pinto concludes that the low between-group effects for pain and disability were too small to be judged as clinically meaningful by patients and clinicians.

Table 4. Effect sizes for short- and long-term leg pain and disability for caudal epidural injections (177).

Study, Year (Reference)	Outcome Measure -ment Scale	Mean (SD or ± SE)* Data Extracted from the Published Report. Groups:		Mean (SD)* Data Converted to 0-100 Scale. Groups:		Steroid Group, n	Placebo Group, n	Mean Difference (95% CI)
		Steroid	Placebo	Steroid	Placebo			
<b>Short-term follow-up for leg pain</b>								
Bush (178)	VAS	NA‡	NA‡	NA‡	NA‡	12	11	-26.9 (-49.2 to -0.6)
Iversen (Paper III)	VAS	NA§	NA§	37.1 (24.2)	42.4 (25.0)	37	35	-4.7 (-15.9 to 6.5)
Manchikanti (174)	NRS	3.4 (1.7)	4.1 (1.8)	34.0 (17.0)	41.0 (18.0)	60	60	-7.0 (-13.3 to -0.7)
<b>Long-term follow-up for leg pain</b>								
Bush (178)	VAS	NA‡	NA‡	NA‡	NA‡	12	11	-13.0 (-42.3 to 16.3)
Iversen (Paper III)	VAS	NA§	NA§	21.2 (23.6)	27.1 (25.0)	34	33	-5.9 (-17.5 to 5.7)
Manchikanti (174)	NRS	3.5 (1.9)	4.1 (1.8)	35.0 (19.0)	41.0 (18.0)	60	60	-6.0 (-12.6 to 0.6)
<b>Short-term follow-up for disability</b>								
Iversen (Paper III)	ODI	NA§	NA§	22.9 (12.1)	24.7 (14.3)	37	35	-1.8 (-7.9 to 4.3)
Manchikanti (174)	ODI	13.6 (6.5)	16.5 (7.2)	27.2 (13.0)	33.0 (14.4)	60	60	-5.8 (-10.7 to -0.9)
<b>Long-term follow-up for disability</b>								
Iversen (Paper III)	ODI	NA§	NA§	18.8 (12.1)	14.1 (14.3)	34	33	4.7 (-1.6 to 11.0)
Manchikanti (174)	ODI	13.1 (7.0)	15.5 (7.74)	26.2 (14.0)	31.0 (15.5)	60	60	-4.8 (-10.1 to 0.5)

Note: NA = not applicable; NRS = numeric rating scale; SE = standard error.

\* Positive mean values are post-intervention scores.

‡ Data for all patients were available in the published report; mean difference was calculated using analysis of covariance (ANCOVA) adjusted for baseline.

§ Mean was calculated from graphs.

|| SD calculated from the CI of the baseline data and sample size.

||| Authors report the ODI without multiplying the final score by a factor of 2.

### 12.3.2 DO EPIDURAL PLACEBO INJECTIONS CONSTITUTE A TREATMENT IN COMPARISON WITH SHAM INJECTIONS?

So far we have seen that epidural steroid injections, and epidural injections of saline or local anaesthetic could have some effects, but no significant differences in outcome between the treatment alternatives have been found. The effect of epidural steroid injections compared to epidural placebo injections (saline and local anaesthetic) has been found to be too small to be considered clinically relevant, but research has found that epidural injection of saline or local anaesthetic may be regarded as active treatment rather than a placebo.

In 2013, a review by Bicket therefore evaluated whether epidural steroid injections, or epidural injection of saline or local anaesthetic could have a treatment effect compared with sham injections (181).

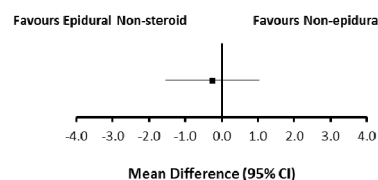
In our study in paper III, which was included in the review, a non-significant tendency favouring both epidural steroid injections (treatment) and saline injections (placebo) over subcutaneous saline injections (sham) was demonstrated using the caudal route. Table 5 shows these results in comparison with the other three studies using the caudal route from the systematic review of Bicket.

The main conclusion of Bicket from analyses based on 28 different studies including all administration routes (caudal, interlaminar and transforaminal) was no significant differences in pain reduction when comparing the epidural placebo injections with epidural steroid injections and sham injections. Both of these conclusions were entirely consistent with the findings in our study in paper III.

Table 5. Forest plots comparing pain score reduction versus injection for epidural steroid injections, epidural non-steroid (placebo) injections and non-epidural (sham) injections (181).

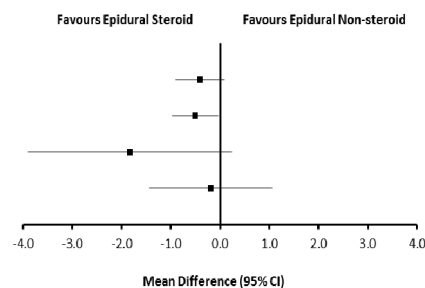
**Direct comparison of epidural non-steroid (placebo) to non-epidural (sham) injections**

Study	Epidural Non-steroid Injection			Non-epidural Injection		
	Mean	SD	Total	Mean	SD	Total
Iversen (Paper III)	-1.34	2.96	39	-1.09	2.89	40



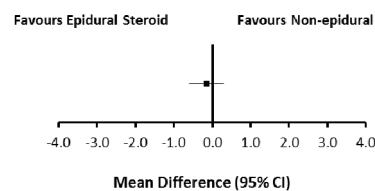
**Direct comparison of epidural steroid to epidural non-steroid (placebo) injections**

Study	Epidural Steroid Injection			Epidural Non-steroid Injection		
	Mean	SD	Total	Mean	SD	Total
Manchikanti (175)	-4.40	1.36	60	-4.00	1.42	60
Manchikanti (174)	-4.30	1.22	60	-3.80	1.40	60
Bush (178)	-2.25	1.95	12	-0.42	2.96	11
Iversen (Paper III)	-1.53	2.61	37	-1.34	2.96	39



**Direct comparison of epidural steroid to non-epidural (sham) injections**

Study	Epidural Steroid Injection			Non-epidural Injection		
	Mean	SD	Total	Mean	SD	Total
Iversen (Paper III)	-1.53	2.61	37	-1.09	2.89	40



### 12.3.3 ARE THERE DIFFERENCES IN EFFECT SIZE BETWEEN EPIDURAL STEROID INJECTIONS AND SHAM INJECTIONS?

In a systematic review and meta-analysis by Høltedahl from 2015 (183), paper III is evaluated along with three other key RCTs regarding the effect of epidural steroid injections compared with a sham procedure (184-186).

In this review, the effect size for both the active and the sham treatments were calculated. An effect size of 0.8 or more was assumed to be large, while an effect size of 0.5–0.8 was considered moderate (see Figure 8).

In the included study by Valat from 2003 (184), 85 patients with lumbosacral radiculopathy were randomized into groups to receive lumbar epidural steroid injections of 2 ml saline (defined as sham by Høltedahl). At 35-day follow-up, there was no difference in pain scores and disability scores between the groups: 48.3% in the steroid group and 47.6% in the sham group had experienced good recovery.

In a randomized study by Arden (185) from 2005, 228 patients with lumbosacral radiculopathy lasting less than 18 months received lumbar epidural steroid injections of 2 ml saline in the interspinous ligament. At 52-week follow-up there were no statistically significant differences in recovery of leg pain and disability between the groups.

In a study by Cohen (186) in 2012, 84 patients with lumbosacral radiculopathy with a history of less than 6 months were included. They were randomized to transforaminal epidural injection of steroids, the tumour necrosis factor alfa (TNFA) inhibitor etanercept, or saline (defined as sham by Høltedahl). All groups were given additional



local anaesthetic. The patients were followed for 12 weeks and no differences were found between the groups in reduction of leg pain or disability. Figure 8 shows the effect sizes (Cohen's d) calculated by Høltedahl for the four epidural steroid injection studies in comparison with the sham procedure. The effect size was calculated by subtracting the average score after treatment from the average score before treatment and dividing the result by the average of the SDs before and after treatment.

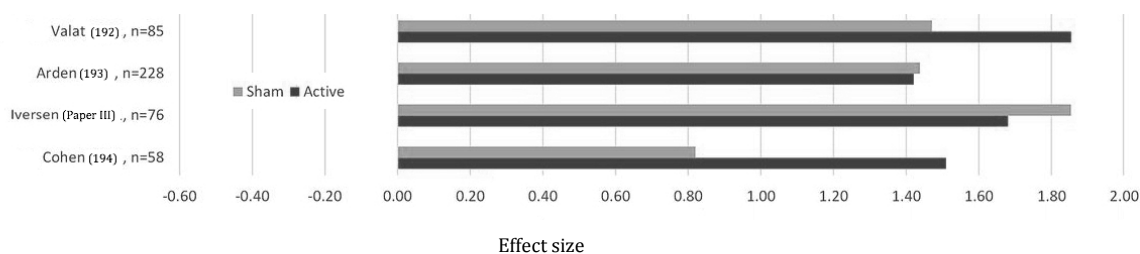


Figure 8. Effect sizes of epidural steroid injections (active treatment) and sham injections on the primary outcome pain and disability (183).

None of the studies showed a large difference in effect size between active treatment and sham groups on primary outcomes. Høltedahl concludes that 'a large part of the reported outcomes in the active treatment groups are due to placebo effects, statistical regression to the mean or the natural course of the condition' (183).

#### 12.3.4 DO EPIDURAL STEROID INJECTIONS HAVE A SURGERY-SPARING EFFECT?

In paper III, referral to surgery was a secondary outcome measure. At 1 year, 1 out of 37 (2.7%) patients in the epidural steroid group had received surgery versus 14 out of 79 (17.7%) in the epidural saline (placebo) and subcutaneous saline (sham) groups.

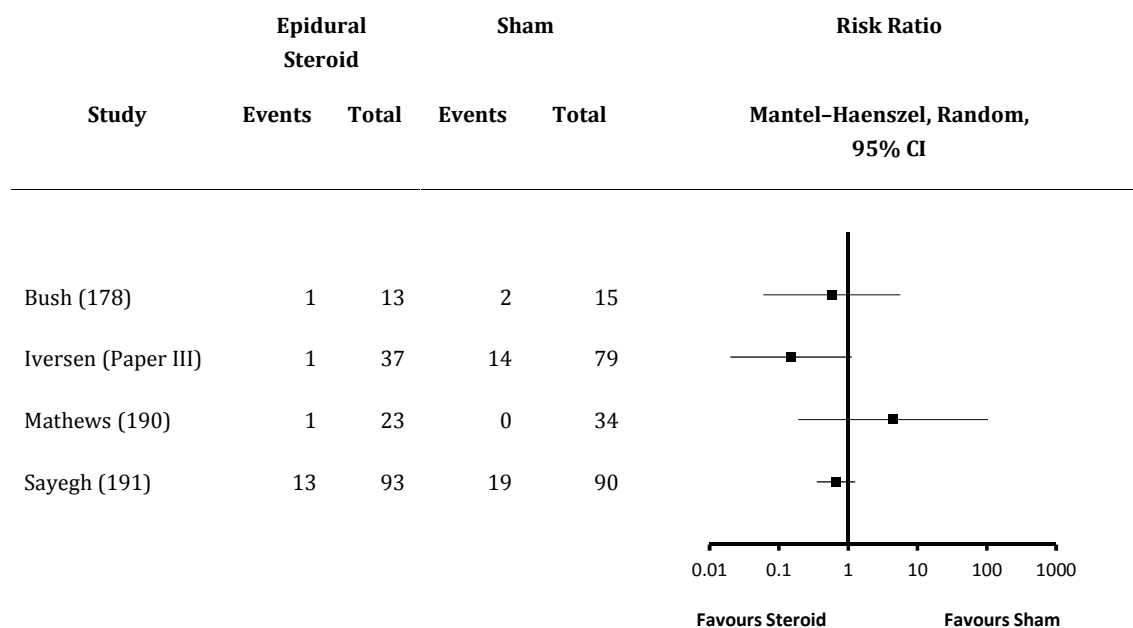
There is only one RCT available to date which has used surgery prevention as the primary outcome after epidural steroid injections (187, 188). This study from 2000 included 55 patients with indication for prolapse surgery and nerve root impingement confirmed on MRI. They were randomized into two equal groups which were given treatment with transforaminal injection of steroids plus local anaesthesia, or treatment with transforaminal injection of local anaesthetic alone. They found that 29% of patients in the steroid group had had surgery, versus 67% in the control group at 1-year follow-up, and very few further patients had to be operated up to the 5-year follow-up.

In studies where the surgery-sparing effect of epidural steroid injection is used as a secondary outcome measure, the results are more complex, and meta-analyses of the RCTs have failed to demonstrate a surgery-sparing effect (189).

In a systematic review of 21 studies from 2015 (189), Bicket investigated whether epidural steroid injections could be cost-effective by preventing costly spinal surgery. We are in this context interested to see what effect the caudal epidural injection technique has on this outcome measure. Our study in paper III is compared in the meta-analysis with three other RCTs (178, 190-191).

This meta-analysis showed no differences in surgery rates among patients treated with epidural steroid injections and the control groups. Table 6 shows the risk ratio for need of surgery for the individual studies applying the caudal epidural injection technique.

Table 6. Forest plot of the effect of caudal epidural steroid injections compared to sham injections on need for surgery in the long-term ( $\geq 1$  year) outcome (189).



Risk ratio left of the midline favours caudal epidural steroid injection. Risk ratio right of the midline favours sham injection. If the horizontal lines (95% CI) touch the midline, the risk reduction for needing surgery is not statistically significant, i.e. it is comparable for the two treatment alternatives. To increase statistical power, Bicket merged the data from all the studies, but the overall surgery-sparing effect showed the same non-significant trend towards the benefit of epidural steroid injections, with 17.2% needing surgery in the steroid group versus 38.9% in the sham group. Given the previous discussion, the only surgery-sparing effect of epidural injections would be the natural course of lumbosacral radiculopathy, possibly modified by placebo (150).

### 12.3.5 IS THERE EVIDENCE TO SUPPORT THE USE OF EPIDURAL STEROID INJECTIONS?

In 2009, an expert group from the US Food and Drug Administration (FDA) (192) evaluated the safety and indications for epidural steroid injections after several reports about serious complications such as infections and nerve injury following interlaminar and transforaminal epidural steroid injections (193). The expert group developed 17 safeguard statements to prevent neurological complications, but despite this, further neurological complications were reported. In 2014, the FDA therefore announced that the use of epidural steroids was 'off-label' and not recommended (194).

In a detailed review of the effect mechanism of steroids on nerve root inflammation due to disc herniation, Balague concluded as early as 2012 (1) that steroid injection is neither clinically effective nor cost-effective, despite a strong biologically anti-inflammatory effect. In this context he refers to paper III. Balague claims that 'the proponents of epidural injection therapy always will find potential flaws in previous studies to justify starting new clinical trials and continuing this kind of treatment, despite safety concerns and striking scientific evidence against any benefits for the patients' (1).

Still there has been an increase in all injection procedures in the USA from the year 2000 to the year 2011 (see Figure 9) (195).

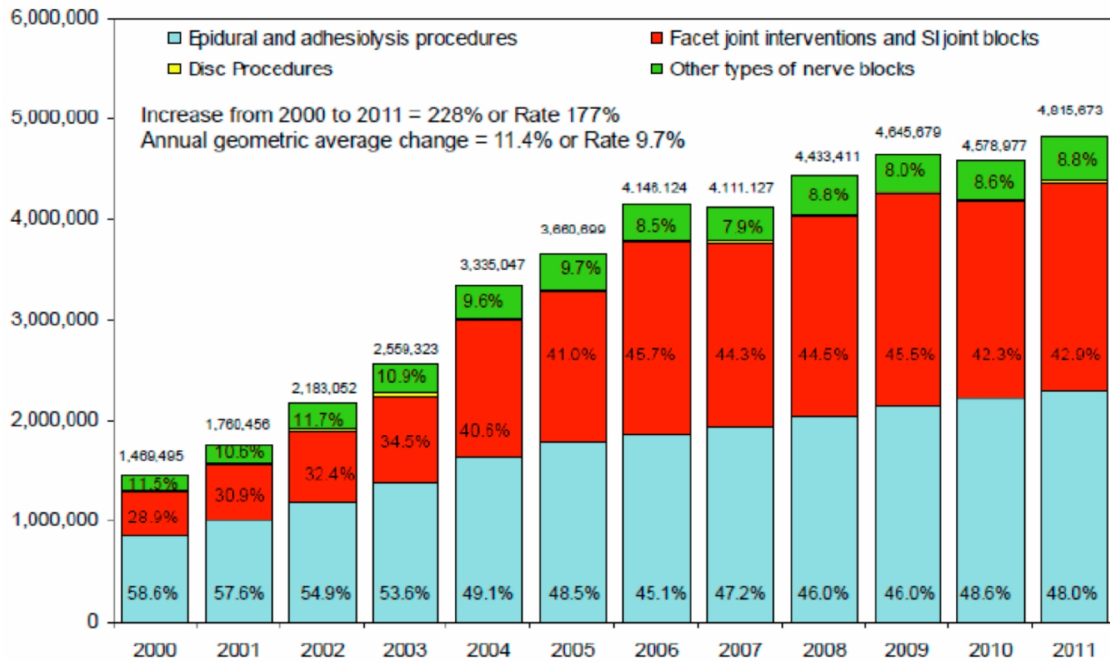


Figure 9. Distribution of procedural characteristics by type of procedures from 2000 to 2011 (195). SI = sacroiliaca.

The Centers for Medicare & Medicaid Services (CMS) proposed in 2013 cuts in reimbursements for epidural injections amounting to 49%. As a consequence (195), many pain management physicians will be struggling to keep their practice open and survive into the future despite high skills, and extensive and expensive training. On the other hand, time consuming and costly procedures, that are stressful and risky for the patients, can be spared.



## 13. LIMITATIONS

### 13.1 Paper I

The present study has weaknesses. We did not register inter-tester variability for the clinical tests and image interpretations. However, all clinicians were trained to perform the tests in a standardized manner, and agreement should thus be superior to that achieved between clinicians in daily practice. MRI was substituted with CT in 7 (6.0%) of the study subjects. A few cases of nerve root impingement may have been missed, but this is unlikely to have influenced the results significantly. Further, the duration of symptoms (average 42 weeks) was relatively long. Development of chronic centralized pain followed by regression of nerve root impingement may have occurred in some patients, and our results may not be generalizable to situations with shorter symptom duration.

Finally, it must be emphasized that the index tests work differently when applied in other settings. In unselected primary care populations, the proportion of false positives will be lower and the specificity of the tests higher. Accordingly, the tests may be useful in primary care to reduce the post-test likelihood of lumbar radiculopathy and thereby restrict unnecessary referrals for imaging and specialized care. On the other hand, when applied in a highly selected surgical patient population with shorter duration of symptoms and a large disc herniation obviously corresponding with the symptoms, the proportion of true positives will be high and the proportion of false positives low, resulting in high sensitivity and specificity. The results from the present study should

therefore not be generalized to unselected patient populations in primary care nor to even more selected surgical populations.

## 13.2 Paper II

Our study is limited by a relatively small number of patients, which precluded explorative analysis of the effect of different combinations of predictors. We chose to analyse 15 possible predictors, and thereby exceeded the generally accepted recommendation of a minimum of 10 events per tested predictor. In our multivariable analyses, only 5–8 predictors were included. It is a weakness that this approach entails a risk of type 1 error occurring.

Many previous prognostic studies of chronic radiculopathy have focused on patients encountered in primary care or at the surgical units. The present study deals with patients referred to outpatient multidisciplinary back clinics. Our results should not be generalized to surgical patient populations or to patients from unselected primary care.

## 13.3 Paper III

Our power calculation required inclusion of 41 patients in each group. Due to rapid improvement in 17 patients between inclusion and randomization we did not reach this goal. The study is therefore slightly underpowered, missing 4 patients in the epidural steroid group, 2 patients in the epidural saline group, and 1 in the sham group. The number of 41 patients in each group considered necessary to detect a 10-point between-group difference for the main outcome measure was not reached. On the other hand, the study showed no trend towards any group difference after 12 months. We therefore



consider it highly unlikely that a larger study population would have influenced the results.

The patients in our study had long-lasting symptoms of radiculopathy (26–57 weeks), and our results may be less relevant for patients with radiculopathy of shorter duration.

Low efficacy of the selected active substance, under-dosage of the substance, and a dilution effect of the steroid due to high injected volumes could have influenced the effect of the caudal epidural steroid injections in our study.



## 14. NEW AREAS OF RESEARCH

### 14.1 Modic changes

Are Modic changes clinically relevant MRI abnormalities, and is the presence of Modic changes an important predictor of outcome in lumbar disc herniation patients?

Modic marrow changes are common in disc herniation patients with a prevalence of 25–49% in patients with acute and chronic lumbosacral radiculopathy (196). In particular, Modic type I (197) but also Modic type II (198) have been linked to increased risk of pain, but how Modic changes affect recovery of pain is unclear (199).

In a systematic review in 2011 (200), it was not possible to draw firm conclusions regarding whether or not Modic changes were associated with treatment outcomes for low back pain.

In paper II, a total of 66 (56.9%) out of 116 patients had Modic type I and type I/II changes at baseline. They were not found to be significant predictors for outcome for either pain or disability. This may be due to lack of statistical power (type II error).

Further studies are needed to clarify the relevance of Modic changes for the prognosis of lumbosacral radiculopathy, and possible treatment options for this condition.

In 2014, Peterson (201) performed a cohort study of 346 patients with lumbosacral radiculopathy and MRI-confirmed disc herniation treated with transforaminal epidural steroid injections. Peterson's study found no association between the chance of Modic type I and II being present and reduction in pain after transforaminal epidural steroid injections. In a study in 2014 (202), 243 patients with lumbosacral radiculopathy were

followed for 1 year. There were no differences in VAS back pain or VAS leg pain scores at follow-up. The authors concluded that Modic type I changes delayed the recovery of lumbosacral radiculopathy, but the prognosis was still good.

In a 2-year follow-up study (203), there was found a significant positive association between decrease of Modic type I change at follow-up and improvement of low back pain and disability measured by the ODI.

To date, there is no evidence-based treatment for Modic changes. Two randomized trials have evaluated the efficacy of medication for low back pain due to Modic changes. In a Danish study (204), amoxicillin-clavulanate treatment for 3 months was effective compared to placebo among patients with Modic type I and verified disc herniation. In another study (205), zoledronic acid, a long-acting bisphosphonate, was effective in reducing the intensity of low back pain in the short term and in reducing the use of NSAIDs at 1-year follow-up among patients with chronic low back pain and Modic changes. Although these results are promising, the authors conclude that more research should be carried out to verify their results.

## 14.2 Pro-inflammatory interleukins

We showed in paper II that a high level of fear avoidance is an important predictor of more pain and poor function among patients with chronic lumbosacral radiculopathy. There may well be a connection between high fear avoidance, negative emotions and high levels of serum IL-6, which can intensify central sensitization and development of chronic pain.

Pedersen (206) investigated 127 patients with at least a 1-month case history and clinical findings indicating lumbosacral radiculopathy due to MRI-verified disc herniation. During follow-up, 46 patients were operated and 81 patients received cognitive therapy and physiotherapy. Serum levels of interleukin IL-6 and IL-8 were measured at inclusion and after 12 months and compared to leg pain. All the patients had a drop in serum level of IL-6 and IL-8 during the first 6 weeks. At 12 months there were statistically significant higher levels of IL-6 and IL-8 in patients with more VAS leg pain. The author concluded that high levels of interleukins may be associated with persistent pain either by local inflammatory processes or as part of a central pain sensitization. These findings are very interesting because they shed light on the complexity of the development and maintenance of radicular pain following disc herniation. Much of the treatment has been directed against the local inflammation or unblocking of the impinged nerve root by surgery. The understanding of how central sensitization and development of chronic pain are communicated through pro-inflammatory interleukins may open up new and more effective treatment strategies.

High levels of interleukins can be seen in chronic anxiety and depression. In 2015, Stellar (207) examined how positive emotions affect the level of pro-inflammatory cytokines (interleukin IL-6). The hypothesis was that high levels of interleukins can cause negative health effects through increased activity in the hypothalamic–pituitary–adrenal axis. Conversely, positive emotions could lower the serum levels of interleukins. Therefore, they examined a total of 223 students, measuring concentration of interleukin IL-6 and the extent of positive emotions (the latter by the use of questionnaires). A high score on positive emotions was associated with low values of IL-

6, but no causal relationship could be drawn. However, this study may be a step towards a biological understanding of the relationship between positive attitudes and good health.

In 2013, Miyamoto (208) investigated how negative emotions can predict high levels of interleukin IL-6. He included 1,044 patients in the USA and 382 patients in Japan. In the US population there was a significant relationship between negative emotions and high levels of serum IL-6, but not in the Japanese population. Miyamoto postulated that this may be related to cultural differences, and that negative emotions can be more accepted in Japan than in the USA.

If a biological explanation for the association between chronic pain and personality profile can be shown, new treatment strategies for chronic lumbosacral radiculopathy can be found. To investigate whether cognitive therapy or medication can lower the serum level of IL-6 to stimulate positive emotions and reduce pain, complex interventional studies have to be performed.

### **14.3 Tumour necrosis factor alfa**

In 1993, Olmarker (209) was the first to show that the material from animal nucleus pulposus induces histological and neurophysiological changes in non-impinged spinal nerves. In 2000, Igarashi (210) showed that application of TNFA produced similar effects. In 2001, Olmarker (211) showed that TNFA inhibitor reversed inflammation and nerve conduction deficits induced by nucleus pulposus material. TNFA may therefore be an inflammatory factor involved in nerve swelling and neuropathic pain induced by a disc herniation.

The first studies of the effect of transforaminal epidural injection of TNFA inhibitor etanercept were carried out by Cohen in 2009 (147) and 2012 (186). In the first study, no dose–response relationship between etanercept and improvement of pain and disability was found. In the second study, Cohen found no difference in improvement of pain and disability between patients with lumbosacral radiculopathy randomized to transforaminal epidural injection of either a steroid or an etanercept.

In a systematic review from 2014 of the effect of treatment of lumbosacral radiculopathy with TNFA inhibitors, Wang (212) found that the TNFA inhibitor could reduce the risk of surgery at medium-term follow-up but neither provided additional pain relief nor improved function compared to placebo or steroids. He attributed the surgery-sparing effect of TNFA inhibitors to a possible neuroprotective effect, and concluded that the mechanisms underlying nociceptive and neuropathic pain still remain unclear (213). In a state-of-the-art review from 2014 (103) concerning the mechanisms and clinical implications of neuropathic pain, Cohen concluded that ‘there is a considerable overlap between neuropathic and nociceptive pain both concerning pathophysiological mechanisms and response to treatment, but that the affective component of chronic pain makes neuropathic pain notoriously refractory to treatment’.

#### **14.4 Pain neurobiology and glial activation**

The cytokines are thought to play an essential role in the pathogenesis of chronic pain, inducing central sensitization and enhancing pain conditions. In a study by Loggia in 2015 (214), 19 patients with chronic low back pain were compared with 25 healthy subjects to map levels of glial activation. The hypothesis was that chronic pain activates

microglia and astrocytes, causing neuro-inflammation in the central nervous system resulting in the production of pro-inflammatory cytokines (TNFA and the interleukins IL-1B and IL-6). The participants completed integrated positron emission tomography (PET)/MRI to assess signs of neuro-inflammation in key regions of the brain, and inflammatory cytokines from blood samples were analysed. Loggia found that glial activation was correlated with high levels of serum interleukin IL-6 in patients with chronic low back pain. He concluded that 'glial activation might be an early marker for the alterations that have been shown to occur in the brains of chronic pain patients and that this might allow early identification of individuals at risk of developing chronic pain'. More recent studies indicate that anti-inflammatory drugs that inhibit glial cells may be beneficial for chronic pain patients (215). This finding is interesting because it might help to explain the difference in treatment response we see in patients with acute and chronic lumbosacral radiculopathy. As we have seen, some patients can respond to local anti-inflammatory treatment with epidural steroid injections in the acute phase, but this effect seems to decrease as symptoms prolong and central sensitization occurs. If effective drugs that can reduce glial activation are found, one can hope that development of chronic lumbosacral radiculopathy can be prevented.



## 15. TRANSLATING EVIDENCE-BASED CLINICAL GUIDELINES FOR EPIDURAL STEROID INJECTIONS INTO PRACTICE – CURRENT RECOMMENDATIONS

### 15.1 Same trials, different conclusions in clinical guidelines

The first systematic review of the effect of caudal epidural steroid injections was performed by Kepes in 1985 (216). He concluded that there was no scientific basis for supporting the use of epidural steroid injections. However, in 1986, Benzon (217), utilizing the same studies, concluded that nerve root irritation may respond to epidural steroid injections.

In 1995, Watts and Koes published two systematic reviews of the effect of epidural steroid injection in the treatment of patients with lumbosacral radiculopathy due to disc herniation (218-219). Watts included 13 studies in his meta-analysis, while Koes included 12 studies. Nine of the studies were the same in the two meta-analyses, but the conclusions were different. Watts concluded that 'epidural administration of steroids is effective in management of lumbosacral radicular pain', while Koes concluded that 'the efficacy of epidural steroid injections has not yet been established'. Hopayian (220) therefore advised clinicians to read reviews critically.

In 2007, the American Academy of Neurology (221, 222) stated that epidural steroid injections could not be recommended to treat radiculopathy.

Manchikanti (223), on behalf of the American Society of Interventional Pain Physicians (ASIPP), presented a set of 'comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain' in 2009 and concluded that there is 'level I evidence for caudal epidural steroid injections in managing disc herniation'. In the same year, the American Pain Society (APS) published evidence-based clinical practice guidelines for interventional therapies for low back pain (224-225) and concluded that epidural steroid injection is moderately effective for short-term, but not long-term, symptom relief. Hence, different understanding and interpretation of study design was crucial in how the two pain groups came to different conclusions in the two sets of guidelines. Levin (226) claims that an active control trial intends to show that a new treatment is equivalent or superior to the standard treatment. He claimed that ASIPP drew incorrect conclusions by overestimating treatment effects in active control studies, assuming that the control groups had received known effective injection treatments. Levin claims that such an assumption cannot be made, because no accepted effective treatment of lumbosacral radiculopathy that new treatments can be compared with exists.

A review by Cohen in 2013 (227) showed that reviews performed by interventionists are approximately three times more likely to find that epidural steroid injections are effective compared with reviews conducted by non-interventionist physicians.

Chou (228) summarizes the discussion of clinical guidelines with different recommendations and claims that 'professional societies should support the training of members in systematic review and guideline development methodology'. Chou argues further that 'when the evidence is weak for an intervention and the trade-offs between

benefits and harms is close, the perspectives and values of the guideline development group tend to have a great effect on how the evidence is interpreted'. In response, Manchikanti argues (229) that 'knowing the tools of evidence-based practice methodology is necessary, but not sufficient, for delivering the highest quality patient care. The clinical guidelines panel must incorporate not only the methodologists, but also the clinicians who actually practice medicine and are experts in the technique being reviewed'.

In 2014, NASS provided updated evidence-based clinical guidelines for the diagnosis and treatment of lumbar disc herniation with radiculopathy (151). NASS summarizes the evidence for epidural steroid treatment in the following way: there is insufficient evidence to make a recommendation for the use of one injection approach over another (interlaminar, transforaminal, caudal). Transforaminal epidural steroid injection is recommended to provide short-term (2 to 4-week) pain relief, but there is insufficient evidence to make a recommendation for long-term (52-week) efficacy. Referring to two Finnish studies by Karppinen from 2001 (22, 230), NASS recommend transforaminal epidural steroid injections when there is a so-called 'contained disc herniation' but not when there is a 'disc extrusion'. When MRI proves a contained disc herniation, NASS refer to 'savings at 1 year of \$12,666 per responder', as opposed to an extruded disc herniation where the use of transforaminal epidural steroid injections can increase the rate of surgery.

## 15.2 Guidelines for epidural steroid injections in the Nordic countries

The Swedish, Norwegian and Danish national guidelines agree that the evidence for the use of epidural steroid injections for acute and chronic lumbosacral radiculopathy due to disc herniation is weak, level C (231-237). The Swedish guidelines do not give any specific advice about when injections can be tried, and the Norwegian and Danish guidelines give conflicting advice. In the Norwegian guidelines, it is recommended that epidural steroid injections can be tried while waiting for surgery, while the Danish guidelines recommend trying epidural steroid injections only in those patients with long-lasting symptoms where there is no indication for surgery.

## 15.3 Implementation and change of practice

In a follow-up study in 2005 (238) after presenting the Norwegian national guidelines for the diagnosis and treatment of acute low back pain, it was concluded that the guidelines may have contributed to better cooperation between different professions, that they were an important reference frame for education and communication, and that they made health workers more confident in their communication with the individual patient. The leader of the national spinal network claimed that the guidelines also may have contributed to a more realistic attitude towards back pain in the general population.

In May 2015, the Norwegian Knowledge Centre for the Health Services published a report on the effect of interventions for implementing clinical practice guidelines. They included 19 systematic reviews which addressed different guideline implementation

strategies. The transfer of research into clinical practice is a difficult and slow process, and even in the face of evidence it may be difficult to change long-held beliefs and practices (239).



## 16. MAIN CONCLUSIONS

### 16.1 Paper I

The accuracy of individual clinical index tests used to predict imaging findings of nerve root impingement in patients with chronic lumbar radiculopathy is low when applied in specialized care, but clinicians' overall evaluation improves diagnostic accuracy slightly. The tests are not very helpful in clarifying the cause of radicular pain, and are therefore inaccurate for guidance in the diagnostic workup of the patients. Further studies on diagnostic accuracy are needed.

### 16.2 Paper II

Lower age, higher education, working full-time and low fear avoidance beliefs each predict a better outcome of chronic unilateral lumbar radiculopathy. Specifically, lower age and low fear avoidance predict a better functional outcome and less back pain, while higher education and working full-time predict less leg pain. Fear avoidance may be a modifiable risk factor. These results should be validated in further studies before being used to inform patients.

### 16.3 Paper III

Treating chronic lumbar radiculopathy with either caudal epidural steroid injection or epidural saline cannot be recommended. Compared to a sham procedure, we found no evidence of any clinically important treatment effect of caudal epidural steroid or saline injections in patients with chronic lumbar radiculopathy.





## 17. REFERENCE LIST

1. Balague F, Pigué V, Dudler J. Steroids for LBP - from rationale to inconvenient truth. *Swiss Med Wkly*. 2012;142:w13566.
2. Manchikanti L, Singh V, Falco FJ, Benyamin RM, Hirsch JA. Epidemiology of low back pain in adults. *Neuromodulation*. 2014;17 Suppl 2:3-10.
3. Elders LA, Burdorf A. Prevalence, incidence, and recurrence of low back pain in scaffolders during a 3-year follow-up study. *Spine (Phila Pa 1976)*. 2004;29(6):E101-6.
4. Natvig B, Bruusgaard D, Eriksen W. Localized low back pain and low back pain as part of widespread musculoskeletal pain: two different disorders? A cross-sectional population study. *J Rehabil Med*. 2001;33(1):21-5.
5. Schoenfeld AJ, Weiner BK. Treatment of lumbar disc herniation: Evidence-based practice. *Int J Gen Med*. 2010;3:209-14.
6. Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Hanscom B, Skinner JS, et al. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA*. 2006;296(20):2441-50.
7. Atlas SJ, Keller RB, Wu YA, Deyo RA, Singer DE. Long-term outcomes of surgical and nonsurgical management of sciatica secondary to a lumbar disc herniation: 10 year results from the maine lumbar spine study. *Spine (Phila Pa 1976 )*. 2005;30(8):927-35.
8. Weinstein JN, Lurie JD, Tosteson TD, Tosteson AN, Blood EA, Abdu WA, et al. Surgical versus nonoperative treatment for lumbar disc herniation: four-year results for the Spine Patient Outcomes Research Trial (SPORT). *Spine (Phila Pa 1976)*. 2008;33(25):2789-800.
9. Heliovaara M, Impivaara O, Sievers K, Melkas T, Knekt P, Korpi J, et al. Lumbar disc syndrome in Finland. *J Epidemiol Community Health*. 1987;41(3):251-8.
10. Konstantinou K, Dunn KM. Sciatica: review of epidemiological studies and prevalence estimates. *Spine (Phila Pa 1976 )*. 2008;33(22):2464-72.
11. Palmer KT, Griffin MJ, Syddall HE, Pannett B, Cooper C, Coggon D. The relative importance of whole body vibration and occupational lifting as risk factors for low-back pain. *Occup Environ Med*. 2003;60(10):715-21.
12. Younes M, Bejia I, Aguir Z, Letaief M, Hassen-Zrour S, Touzi M, et al. Prevalence and risk factors of disk-related sciatica in an urban population in Tunisia. *Joint Bone Spine*. 2006;73(5):538-42.
13. Rhee JM, Schaufele M, Abdu WA. Radiculopathy and the herniated lumbar disc. Controversies regarding pathophysiology and management. *J Bone Joint Surg Am*. 2006;88(9):2070-80.
14. Deyo RA, Tsui-Wu YJ. Descriptive epidemiology of low-back pain and its related medical care in the United States. *Spine (Phila Pa 1976)*. 1987;12(3):264-8.
15. Manek NJ, MacGregor AJ. Epidemiology of back disorders: prevalence, risk factors, and prognosis. *Curr Opin Rheumatol*. 2005;17(2):134-40.

16. Stafford MA, Peng P, Hill DA. Sciatica: a review of history, epidemiology, pathogenesis, and the role of epidural steroid injection in management. *Br J Anaesth*. 2007;99(4):461-73.
17. Koes BW, van Tulder MW, Peul WC. Diagnosis and treatment of sciatica. *BMJ*. 2007;334(7607):1313-7.
18. Valat JP, Genevay S, Marty M, Rozenberg S, Koes B. Sciatica. *Best Pract Res Clin Rheumatol*. 2010;24(2):241-52.
19. Legrand E, Bouvard B, Audran M, Fournier D, Valat JP. Sciatica from disk herniation: Medical treatment or surgery? *Joint Bone Spine*. 2007;74(6):530-5.
20. Vroomen PC, de Krom MC, Slofstra PD, Knottnerus JA. Conservative treatment of sciatica: a systematic review. *J Spinal Disord*. 2000;13(6):463-9.
21. Weber H, Holme I, Amlie E. The natural course of acute sciatica with nerve root symptoms in a double-blind placebo-controlled trial evaluating the effect of piroxicam. *Spine (Phila Pa 1976)*. 1993;18(11):1433-8.
22. Karppinen J, Ohinmaa A, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimäki T, et al. Cost effectiveness of periradicular infiltration for sciatica: subgroup analysis of a randomized controlled trial. *Spine (Phila Pa 1976)*. 2001;26(23):2587-95.
23. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. *Spine (Phila Pa 1976)*. 2002;27(1):11-6.
24. Bush K, Cowan N, Katz DE, Gishen P. The natural history of sciatica associated with disc pathology. A prospective study with clinical and independent radiologic follow-up. *Spine (Phila Pa 1976)*. 1992;17(10):1205-12.
25. Tubach F, Beaute J, Leclerc A. Natural history and prognostic indicators of sciatica. *J Clin Epidemiol*. 2004;57(2):174-9.
26. Selim AJ, Ren XS, Fincke G, Deyo RA, Rogers W, Miller D, et al. The importance of radiating leg pain in assessing health outcomes among patients with low back pain. Results from the Veterans Health Study. *Spine (Phila Pa 1976)*. 1998;23(4):470-4.
27. Jensen OK, Nielsen CV, Stengaard-Pedersen K. One-year prognosis in sick-listed low back pain patients with and without radiculopathy. Prognostic factors influencing pain and disability. *Spine J*. 2010;10(8):659-75.
28. Kostova V, Koleva M. Back disorders (low back pain, cervicobrachial and lumbosacral radicular syndromes) and some related risk factors. *J Neurol Sci*. 2001;192(1-2):17-25.
29. Kalichman L, Hunter DJ. The genetics of intervertebral disc degeneration. Familial predisposition and heritability estimation. *Joint Bone Spine*. 2008;75(4):383-7.
30. Kelsey JL. An epidemiological study of the relationship between occupations and acute herniated lumbar intervertebral discs. *Int J Epidemiol*. 1975;4(3):197-205.
31. Brage S, Ihlebaek C, Natvig B, Bruusgaard D. [Musculoskeletal disorders as causes of sick leave and disability benefits]. *Tidsskr Nor Laegeforen*. 2010;130(23):2369-70.
32. Hilliard PE. Functional Pain Syndromes: Presentation and Pathophysiology. *Anesthesiology*. 2010;112(5):1298.
33. Bogduk N. On the definitions and physiology of back pain, referred pain, and radicular pain. *Pain*. 2009;147(1-3):17-9.
34. Gibson JN, Waddell G. Surgical interventions for lumbar disc prolapse: updated Cochrane Review. *Spine (Phila Pa 1976)*. 2007;32(16):1735-47.

35. Tarulli AW, Raynor EM. Lumbosacral radiculopathy. *Neurol Clin.* 2007;25(2):387-405.
36. van TM, Peul W, Koes B. Sciatica: what the rheumatologist needs to know. *Nat Rev Rheumatol.* 2010;6(3):139-45.
37. Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. *Health Technol Assess.* 2005;9(33):1-58, iii.
38. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. *Pain.* 1993;52(2):157-68.
39. Fairbank JC. Sciatic: An archaic term. *BMJ.* 2007;335(7611):112.
40. Vroomen PC, de Krom MC, Knottnerus JA. Diagnostic value of history and physical examination in patients suspected of sciatica due to disc herniation: a systematic review. *J Neurol.* 1999;246(10):899-906.
41. Albeck MJ. A critical assessment of clinical diagnosis of disc herniation in patients with monoradicular sciatica. *Acta Neurochir (Wien).* 1996;138(1):40-4.
42. Vroomen PC, de Krom MC, Wilmlink JT, Kester AD, Knottnerus JA. Diagnostic value of history and physical examination in patients suspected of lumbosacral nerve root compression. *J Neurol Neurosurg Psychiatry.* 2002;72(5):630-4.
43. Knutsson B. Comparative value of electromyographic, myelographic and clinical-neurological examinations in diagnosis of lumbar root compression syndrome. *Acta Orthop Scand Suppl.* 1961;49:1-135.
44. Scaia V, Baxter D, Cook C. The pain provocation-based straight leg raise test for diagnosis of lumbar disc herniation, lumbar radiculopathy, and/or sciatica: a systematic review of clinical utility. *J Back Musculoskelet Rehabil.* 2012;25(4):215-23.
45. van der Windt DA, Simons E, Riphagen II, Ammendolia C, Verhagen AP, Laslett M, et al. Physical examination for lumbar radiculopathy due to disc herniation in patients with low-back pain. *Cochrane Database Syst Rev.* 2010(2):CD007431.
46. Borenstein DG, O'Mara JW, Jr., Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects : a seven-year follow-up study. *J Bone Joint Surg Am.* 2001;83-A(9):1306-11.
47. Vroomen PC, de Krom MC, Knottnerus JA. Consistency of history taking and physical examination in patients with suspected lumbar nerve root involvement. *Spine (Phila Pa 1976).* 2000;25(1):91-6.
48. McCarthy CJ, Gittins M, Roberts C, Oldham JA. The reliability of the clinical tests and questions recommended in international guidelines for low back pain. *Spine (Phila Pa 1976).* 2007;32(8):921-6.
49. Bertilson BC, Bring J, Sjoblom A, Sundell K, Strender LE. Inter-examiner reliability in the assessment of low back pain (LBP) using the Kirkaldy-Willis classification (KWC). *Eur Spine J.* 2006;15(11):1695-703.
50. Pengel LH, Herbert RD, Maher CG, Refshauge KM. Acute low back pain: systematic review of its prognosis. *BMJ.* 2003;327(7410):323.
51. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. *Eur Spine J.* 2003;12(2):149-65.

52. Brauholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a "trial effect". *J Clin Epidemiol.* 2001;54(3):217-24.
53. Vist GE, Hagen KB, Devereaux PJ, Bryant D, Kristoffersen DT, Oxman AD. Systematic review to determine whether participation in a trial influences outcome. *BMJ.* 2005;330(7501):1175.
54. Benedetti F, Pollo A, Lopiano L, Lanotte M, Vighetti S, Rainero I. Conscious expectation and unconscious conditioning in analgesic, motor, and hormonal placebo/nocebo responses. *J Neurosci.* 2003;23(10):4315-23.
55. Benedetti F, Mayberg HS, Wager TD, Stohler CS, Zubieta JK. Neurobiological mechanisms of the placebo effect. *J Neurosci.* 2005;25(45):10390-402.
56. Kaptchuk TJ, Kelley JM, Conboy LA, Davis RB, Kerr CE, Jacobson EE, et al. Components of placebo effect: randomised controlled trial in patients with irritable bowel syndrome. *BMJ.* 2008;336(7651):999-1003.
57. Cotugno D. The first description of the spinal fluid. By Domenico Cotugno, 1775. *Clin Orthop Relat Res.* 1988;227:6-9.
58. Robinson JS. Sciatica and the lumbar disk syndrome: a historic perspective. *South Med J.* 1983;76(2):232-8.
59. Mixer WJ. Rupture of the lumbar intervertebral disk: An etiologic factor for so-called "sciatic" pain. *Ann Surg.* 1937;106(4):777-87.
60. Mixer WJ. Rupture of the intervertebral disk; a short history of this evolution as a syndrome of importance to the surgeon. *J Am Med Assoc.* 1949;140(3):278-82.
61. Boos N, Rieder R, Schade V, Spratt KF, Semmer N, Aebi M. 1995 Volvo Award in clinical sciences. The diagnostic accuracy of magnetic resonance imaging, work perception, and psychosocial factors in identifying symptomatic disc herniations. *Spine (Phila Pa 1976).* 1995;20(24):2613-25.
62. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med.* 1994;331(2):69-73.
63. Modic MT, Obuchowski NA, Ross JS, Brant-Zawadzki MN, Grooff PN, Mazanec DJ, et al. Acute low back pain and radiculopathy: MR imaging findings and their prognostic role and effect on outcome. *Radiology.* 2005;237(2):597-604.
64. Modic MT, Ross JS, Obuchowski NA, Browning KH, Cianflocco AJ, Mazanec DJ. Contrast-enhanced MR imaging in acute lumbar radiculopathy: a pilot study of the natural history. *Radiology.* 1995;195(2):429-35.
65. Andrade P, Visser-Vandewalle V, Philippens M, Daemen MA, Steinbusch HW, Buurman WA, et al. Tumor necrosis factor-alpha levels correlate with postoperative pain severity in lumbar disc hernia patients: opposite clinical effects between tumor necrosis factor receptor 1 and 2. *Pain.* 2011;152(11):2645-52.
66. Chen C, Cavanaugh JM, Ozaktay AC, Kallakuri S, King AI. Effects of phospholipase A2 on lumbar nerve root structure and function. *Spine (Phila Pa 1976).* 1997;22(10):1057-64.
67. Deyo RA. Real help and red herrings in spinal imaging. *N Engl J Med.* 2013;368(11):1056-8.
68. Saifuddin A, Mitchell R, Taylor BA. Extradural inflammation associated with annular tears: demonstration with gadolinium-enhanced lumbar spine MRI. *Eur Spine J.* 1999;8(1):34-9.

69. Lauder TD, Dillingham TR, Andary M, Kumar S, Pezzin LE, Stephens RT, et al. Effect of history and exam in predicting electrodiagnostic outcome among patients with suspected lumbosacral radiculopathy. *Am J Phys Med Rehabil.* 2000;79(1):60-8.
70. De Luigi AJ, Fitzpatrick KF. Physical examination in radiculopathy. *Phys Med Rehabil Clin N Am.* 2011;22(1):7-40.
71. Levin KH. Electrodiagnostic approach to the patient with suspected radiculopathy. *Neurol Clin.* 2002;20(2):397-421, vi.
72. McCarron RF, Wimpee MW, Hudkins PG, Laros GS. The inflammatory effect of nucleus pulposus. A possible element in the pathogenesis of low-back pain. *Spine (Phila Pa 1976).* 1987;12(8):760-4.
73. Laupacis A, Evans W. Diagnostic imaging in Canada. *Healthc Pap.* 2005;6(1):8-15.
74. Boden SD, McCowin PR, Davis DO, Dina TS, Mark AS, Wiesel S. Abnormal magnetic-resonance scans of the cervical spine in asymptomatic subjects. A prospective investigation. *J Bone Joint Surg Am.* 1990;72(8):1178-84.
75. Jensen MC, Brant-Zawadzki MN, Obuchowski N, Modic MT, Malkasian D, Ross JS. Magnetic resonance imaging of the lumbar spine in people without back pain. *N Engl J Med.* 1994;331(2):69-73.
76. Suri P, Hunter DJ, Katz JN, Li L, Rainville J. Bias in the physical examination of patients with lumbar radiculopathy. *BMC Musculoskelet Disord.* 2010;11:275.
77. Ransohoff DF, Feinstein AR. Problems of spectrum and bias in evaluating the efficacy of diagnostic tests. *N Engl J Med.* 1978;299(17):926-30.
78. Suri P, Boyko EJ, Goldberg J, Forsberg CW, Jarvik JG. Longitudinal associations between incident lumbar spine MRI findings and chronic low back pain or radicular symptoms: retrospective analysis of data from the longitudinal assessment of imaging and disability of the back (LAIDBACK). *BMC Musculoskelet Disord.* 2014;15:152.
79. Gopalakrishnan N, Nadhamuni K, Karthikeyan T. Categorization of Pathology Causing Low Back Pain using Magnetic Resonance Imaging (MRI). *J Clin Diagn Res.* 2015;9(1):TC17-TC20.
80. Pinto RZ, Maher CG, Ferreira ML, Ferreira PH, Hancock M, Oliveira VC, et al. Drugs for relief of pain in patients with sciatica: systematic review and meta-analysis. *BMJ.* 2012;344:e497.
81. Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol.* 2015;14(2):162-73.
82. Dworkin RH, O'Connor AB, Audette J, Baron R, Gourlay GK, Haanpaa ML, et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc.* 2010;85(3 Suppl):S3-14.
83. Okoro T, Tafazal SI, Longworth S, Sell PJ. Tumor necrosis alpha-blocking agent (etanercept): a triple blind randomized controlled trial of its use in treatment of sciatica. *J Spinal Disord Tech.* 2010;23(1):74-7.
84. Cohen SP, Hanling S, Bicket MC, White RL, Veizi E, Kurihara C, et al. Epidural steroid injections compared with gabapentin for lumbosacral radicular pain: multicenter randomized double blind comparative efficacy study. *BMJ.* 2015;350:h1748.
85. Clarke J, van Tulder M, Blomberg S, de Vet H, van der Heijden G, Bronfort G. Traction for low back pain with or without sciatica: an updated systematic review within

- the framework of the Cochrane collaboration. *Spine (Phila Pa 1976)*. 2006;31(14):1591-9.
86. Luijsterburg PA, Verhagen AP, Ostelo RW, van den Hoogen HJ, Peul WC, Avezaat CJ, et al. Physical therapy plus general practitioners' care versus general practitioners' care alone for sciatica: a randomised clinical trial with a 12-month follow-up. *Eur Spine J*. 2008;17(4):509-17.
87. Luijsterburg PA, Verhagen AP, Ostelo RW, van Os TA, Peul WC, Koes BW. Effectiveness of conservative treatments for the lumbosacral radicular syndrome: a systematic review. *Eur Spine J*. 2007;16(7):881-99.
88. Jacobs WC, van TM, Arts M, Rubinstein SM, van MM, Ostelo R, et al. Surgery versus conservative management of sciatica due to a lumbar herniated disc: a systematic review. *Eur Spine J*. 2011;20(4):513-22.
89. Manchikanti L, Singh V, Pampati V, Falco FJ, Hirsch JA. Comparison of the efficacy of caudal, interlaminar, and transforaminal epidural injections in managing lumbar disc herniation: is one method superior to the other? *Korean J Pain*. 2015;28(1):11-21.
90. Manchikanti L, Pampati V, Falco FJ, Hirsch JA. Growth of spinal interventional pain management techniques: analysis of utilization trends and Medicare expenditures 2000 to 2008. *Spine (Phila Pa 1976)*. 2013;38(2):157-68.
91. Rajae SS, Bae HW, Kanim LE, Delamarter RB. Spinal fusion in the United States: analysis of trends from 1998 to 2008. *Spine (Phila Pa 1976)*. 2012;37(1):67-76.
92. Gregory DS, Seto CK, Wortley GC, Shugart CM. Acute lumbar disk pain: navigating evaluation and treatment choices. *Am Fam Physician*. 2008;78(7):835-42.
93. Suri P, Rainville J, Hunter DJ, Li L, Katz JN. Recurrence of radicular pain or back pain after nonsurgical treatment of symptomatic lumbar disk herniation. *Arch Phys Med Rehabil*. 2012;93(4):690-5.
94. Freburger JK, Holmes GM, Agans RP, Jackman AM, Darter JD, Wallace AS, et al. The rising prevalence of chronic low back pain. *Arch Intern Med*. 2009;169(3):251-8.
95. Keller RB, Atlas SJ, Soule DN, Singer DE, Deyo RA. Relationship between rates and outcomes of operative treatment for lumbar disc herniation and spinal stenosis. *J Bone Joint Surg Am*. 1999;81(6):752-62.
96. Friedly J, Chan L, Deyo R. Geographic variation in epidural steroid injection use in medicare patients. *J Bone Joint Surg Am*. 2008;90(8):1730-7.
97. Manchikanti L, Helm I S, Singh V, Hirsch JA. Accountable interventional pain management: a collaboration among practitioners, patients, payers, and government. *Pain Physician*. 2013;16(6):E635-70.
98. Manchikanti L, Falco FJ, Pampati V, Cash KA, Benyamin RM, Hirsch JA. Cost utility analysis of caudal epidural injections in the treatment of lumbar disc herniation, axial or discogenic low back pain, central spinal stenosis, and post lumbar surgery syndrome. *Pain Physician*. 2013;16(3):E129-43.
99. Centre HaSCI. Hospital Episodes Statistics (HESonline). Total procedures and interventions. [www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=210](http://www.hesonline.nhs.uk/Ease/servlet/ContentServer?siteID=1937&categoryID=210) on 7 August 2012.
100. Olmarker K, Blomquist J, Stromberg J, Nannmark U, Thomsen P, Rydevik B. Inflammatory properties of nucleus pulposus. *Spine (Phila Pa 1976)*. 1995;20(6):665-9.

101. Schaible HG, Schmidt RF. Effects of an experimental arthritis on the sensory properties of fine articular afferent units. *J Neurophysiol.* 1985;54(5):1109-22.
102. Edgar MA. The nerve supply of the lumbar intervertebral disc. *J Bone Joint Surg Br.* 2007;89(9):1135-9.
103. Cohen SP, Mao J. Neuropathic pain: mechanisms and their clinical implications. *BMJ.* 2014;348:f7656.
104. Lievre JA. [Treatment of lumbago]. *Gaz Med Fr.* 1953;60(6):359-65.
105. Tonkovich-Quaranta LA, Winkler SR. Use of epidural corticosteroids in low back pain. *Ann Pharmacother.* 2000;34(10):1165-72.
106. Rang HP. *Pharmacology.* 5 ed. London: Churchill Livingstone; 2003.
107. Hogan QH. Lumbar epidural anatomy. A new look by cryomicrotome section. *Anesthesiology.* 1991;75(5):767-75.
108. Parkin IG, Harrison GR. The topographical anatomy of the lumbar epidural space. *J Anat.* 1985;141:211-7.
109. Brockstein B, Johns L, Gewertz BL. Blood supply to the spinal cord: anatomic and physiologic correlations. *Ann Vasc Surg.* 1994;8(4):394-9.
110. Bernards CM, Shen DD, Sterling ES, Adkins JE, Risler L, Phillips B, et al. Epidural, cerebrospinal fluid, and plasma pharmacokinetics of epidural opioids (part 1): differences among opioids. *Anesthesiology.* 2003;99(2):455-65.
111. Kerber CW, Newton TH. The macro and microvasculature of the dura mater. *Neuroradiology.* 1973;6(4):175-9.
112. Fyneface-Ogan S. *Anatomy and Clinical Importance of the Epidural Space, Epidural Analgesia-Current views and approaches 2012.*
113. Gilchrist RV, Isaac Z, Bhat AL. Innervation of the anterior spinal canal: an update. *Pain Physician.* 2002;5(2):167-71.
114. Kumar R, Berger RJ, Dunsker SB, Keller JT. Innervation of the spinal dura. Myth or reality? *Spine (Phila Pa 1976).* 1996;21(1):18-26.
115. Groen GJ, Baljet B, Drukker J. The innervation of the spinal dura mater: anatomy and clinical implications. *Acta Neurochir (Wien).* 1988;92(1-4):39-46.
116. Parr AT, Manchikanti L, Hameed H, Conn A, Manchikanti KN, Benyamin RM, et al. Caudal epidural injections in the management of chronic low back pain: a systematic appraisal of the literature. *Pain Physician.* 2012;15(3):E159-98.
117. Nelson DA, Landau WM. Intraspinous steroids: history, efficacy, accidentality, and controversy with review of United States Food and Drug Administration reports. *J Neurol Neurosurg Psychiatry.* 2001;70(4):433-43.
118. Wilkinson I, Cohen SP. Epidural steroids for spinal pain and radiculopathy: a narrative, evidence-based review. *Curr Opin Anaesthesiol.* 2013.
119. Sackett DL. *Evidence-Based Medicine: how to practice and teach EBM.* Edinburgh: Churchill Livingstone; 2000.
120. Simel DL, Rennie D, Bossuyt PM. The STARD statement for reporting diagnostic accuracy studies: application to the history and physical examination. *J Gen Intern Med.* 2008;23(6):768-74.
121. Whiting P, Rutjes AW, Reitsma JB, Glas AS, Bossuyt PM, Kleijnen J. Sources of variation and bias in studies of diagnostic accuracy: a systematic review. *Ann Intern Med.* 2004;140(3):189-202.

122. Artus M, van der Windt D, Jordan KP, Croft PR. The clinical course of low back pain: a meta-analysis comparing outcomes in randomised clinical trials (RCTs) and observational studies. *BMC Musculoskelet Disord.* 2014;15:68.
123. Jensen TS, Sorensen JS, Kjaer P. Intra- and interobserver reproducibility of vertebral endplate signal (modic) changes in the lumbar spine: the Nordic Modic Consensus Group classification. *Acta Radiol.* 2007;48(7):748-54.
124. Summers B, Malhan K, Cassar-Pullicino V. Low back pain on passive straight leg raising: the anterior theca as a source of pain. *Spine (Phila Pa 1976).* 2005;30(3):342-5.
125. Grotle M, Brox JI, Vollestad NK. Reliability, validity and responsiveness of the fear-avoidance beliefs questionnaire: methodological aspects of the Norwegian version. *J Rehabil Med.* 2006;38(6):346-53.
126. Peul WC, van den Hout WB, Brand R, Thomeer RT, Koes BW. Prolonged conservative care versus early surgery in patients with sciatica caused by lumbar disc herniation: two year results of a randomised controlled trial. *BMJ.* 2008;336(7657):1355-8.
127. Hagen EM, Odelien KH, Lie SA, Eriksen HR. Adding a physical exercise programme to brief intervention for low back pain patients did not increase return to work. *Scand J Public Health,* 2010;38:731-738.
128. Storheim K, Brox JI, Holm I, Koller AK, Bo K. Intensive group training versus cognitive intervention in sub-acute low back pain: short-term results of a single-blind randomized controlled trial. *J Rehabil Med.* 2003;35(3):132-40.
129. Skouen JS, Grasdahl AL, Haldorsen EM, Ursin H. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. *Spine (Phila Pa 1976 ).* 2002;27(9):901-9.
130. Brox JI, Sorensen R, Friis A, Nygaard O, Indahl A, Keller A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. *Spine (Phila Pa 1976 ).* 2003;28(17):1913-21.
131. Laerum E, Indahl A, Skouen JS. What is "the good back-consultation"? A combined qualitative and quantitative study of chronic low back pain patients' interaction with and perceptions of consultations with specialists. *J Rehabil Med.* 2006;38(4):255-62.
132. Grotle M, Brox JI, Vollestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. *J Rehabil Med.* 2003;35(5):241-7.
133. Roland M, Fairbank J. The Roland-Morris Disability Questionnaire and the Oswestry Disability Questionnaire. *Spine (Phila Pa 1976 ).* 2000;25(24):3115-24.
134. Hagg O, Fritzell P, Nordwall A. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J.* 2003;12(1):12-20.
135. EuroQol--a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy.* 1990;16(3):199-208.
136. Dolan P. Modeling valuations for EuroQol health states. *Med Care.* 1997;35(11):1095-108.
137. Solberg TK, Olsen JA, Ingebrigtsen T, Hofoss D, Nygaard OP. Health-related quality of life assessment by the EuroQol-5D can provide cost-utility data in the field of low-back surgery. *Eur Spine J.* 2005;14(10):1000-7.



138. Giraudeau B, Rozenberg S, Valat JP. Assessment of the clinically relevant change in pain for patients with sciatica. *Ann Rheum Dis.* 2004;63(9):1180-1.
139. Fritz JM, George SZ. Identifying psychosocial variables in patients with acute work-related low back pain: the importance of fear-avoidance beliefs. *Phys Ther.* 2002;82(10):973-83.
140. Crombez G, Vlaeyen JW, Heuts PH, Lysens R. Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability. *Pain.* 1999;80(1-2):329-39.
141. Twisk JW, de VW. The analysis of randomised controlled trial data with more than one follow-up measurement. A comparison between different approaches. *Eur J Epidemiol.* 2008;23(10):655-60.
142. Stitz MY, Sommer HM. Accuracy of blind versus fluoroscopically guided caudal epidural injection. *Spine (Phila Pa 1976 ).* 1999;24(13):1371-6.
143. Anaesthetists TRCo. Recommendations on the use of epidural injections for the treatment of back pain and leg pain of spinal origin. *Bulletin 14 ed2002.*
144. Chen CP, Tang SF, Hsu TC, Tsai WC, Liu HP, Chen MJ, et al. Ultrasound guidance in caudal epidural needle placement. *Anesthesiology.* 2004;101(1):181-4.
145. Chen CP, Wong AM, Hsu CC, Tsai WC, Chang CN, Lin SC, et al. Ultrasound as a screening tool for proceeding with caudal epidural injections. *Arch Phys Med Rehabil.* 2010;91(3):358-63.
146. Klocke R, Jenkinson T, Glew D. Sonographically guided caudal epidural steroid injections. *J Ultrasound Med.* 2003;22(11):1229-32.
147. Cohen SP, Bogduk N, Dragovich A, Buckenmaier CC, III, Griffith S, Kurihara C, et al. Randomized, double-blind, placebo-controlled, dose-response, and preclinical safety study of transforaminal epidural etanercept for the treatment of sciatica. *Anesthesiology.* 2009;110(5):1116-26.
148. Finnis DG, Kaptchuk TJ, Miller F, Benedetti F. Biological, clinical, and ethical advances of placebo effects. *Lancet.* 2010;375(9715):686-95.
149. Spiegel D. Placebos in practice. *BMJ.* 2004;329(7472):927-8.
150. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects 64th WMA General Assembly, Fortaleza, Brazil, October 2013.
151. Kreiner DS, Hwang SW, Easa JE, Resnick DK, Baisden JL, Bess S, et al. An evidence-based clinical guideline for the diagnosis and treatment of lumbar disc herniation with radiculopathy. *Spine J.* 2014;14(1):180-91.
152. Al Nezari NH, Schneiders AG, Hendrick PA. Neurological examination of the peripheral nervous system to diagnose lumbar spinal disc herniation with suspected radiculopathy: a systematic review and meta-analysis. *Spine J.* 2013;13(6):657-74.
153. Verwoerd AJ, Peul WC, Willemsen SP, Koes BW, Vleggeert-Lankamp CL, el BA, et al. Diagnostic accuracy of history taking to assess lumbosacral nerve root compression. *Spine J.* 2014;14(9):2028-37.
154. Suri P, Carlson MJ, Rainville J. Nonoperative treatment for lumbosacral radiculopathy: what factors predict treatment failure? *Clin Orthop Relat Res.* 2015;473(6):1931-9.
155. Murphy DR, Hurwitz EL, McGovern EE. A nonsurgical approach to the management of patients with lumbar radiculopathy secondary to herniated disk: a

- prospective observational cohort study with follow-up. *J Manipulative Physiol Ther.* 2009;32(9):723-33.
156. Hellum C, Johnsen LG, Gjertsen O, Berg L, Neckelmann G, Grundnes O, et al. Predictors of outcome after surgery with disc prosthesis and rehabilitation in patients with chronic low back pain and degenerative disc: 2-year follow-up. *Eur Spine J.* 2012;21(4):681-90.
157. Waddell G. 1987 Volvo award in clinical sciences. A new clinical model for the treatment of low-back pain. *Spine (Phila Pa 1976 ).* 1987;12(7):632-44.
158. George SZ, Fritz JM, McNeil DW. Fear-avoidance beliefs as measured by the fear-avoidance beliefs questionnaire: change in fear-avoidance beliefs questionnaire is predictive of change in self-report of disability and pain intensity for patients with acute low back pain. *Clin J Pain.* 2006;22(2):197-203.
159. Wertli MM, Rasmussen-Barr E, Held U, Weiser S, Bachmann LM, Brunner F. Fear-avoidance beliefs-a moderator of treatment efficacy in patients with low back pain: a systematic review. *Spine J.* 2014;14(11):2658-78.
160. Rainville J, Smeets RJ, Bendix T, Tveito TH, Poiraudreau S, Indahl AJ. Fear-avoidance beliefs and pain avoidance in low back pain--translating research into clinical practice. *Spine J.* 2011;11(9):895-903.
161. Dederig A, Borjesson T. Assessing fear-avoidance beliefs in patients with cervical radiculopathy. *Physiother Res Int.* 2013;18(4):193-202.
162. Cleland JA, Fritz JM, Brennan GP. Predictive validity of initial fear avoidance beliefs in patients with low back pain receiving physical therapy: is the FABQ a useful screening tool for identifying patients at risk for a poor recovery? *Eur Spine J.* 2008;17(1):70-9.
163. George SZ, Fritz JM, Childs JD. Investigation of elevated fear-avoidance beliefs for patients with low back pain: a secondary analysis involving patients enrolled in physical therapy clinical trials. *J Orthop Sports Phys Ther.* 2008;38(2):50-8.
164. Atlas SJ, Chang Y, Keller RB, Singer DE, Wu YA, Deyo RA. The impact of disability compensation on long-term treatment outcomes of patients with sciatica due to a lumbar disc herniation. *Spine (Phila Pa 1976 ).* 2006;31(26):3061-9.
165. den Boer JJ, Oostendorp RA, Beems T, Munneke M, Oerlemans M, Evers AW. A systematic review of bio-psychosocial risk factors for an unfavourable outcome after lumbar disc surgery. *Eur Spine J.* 2006;15(5):527-36.
166. Verwoerd AJ, Luijsterburg PA, Lin CW, Jacobs WC, Koes BW, Verhagen AP. Systematic review of prognostic factors predicting outcome in non-surgically treated patients with sciatica. *Eur J Pain.* 2013;17(8):1126-37.
167. Emary PC. Evidence-based prognostication in a case of sciatica. *J Can Chiropr Assoc.* 2015;59(1):24-9.
168. Ashworth J, Konstantinou K, Dunn KM. Prognostic factors in non-surgically treated sciatica: a systematic review. *BMC Musculoskelet Disord.* 2011;12:208.
169. Suri P, Rainville J, Gellhorn A. Predictors of patient-reported recovery from motor or sensory deficits two years after acute symptomatic lumbar disk herniation. *PM R.* 2012;4(12):936-44 e1.
170. Manchikanti L, Benyamin RM, Falco FJ, Kaye AD, Hirsch JA. Do Epidural Injections Provide Short- and Long-term Relief for Lumbar Disc Herniation? A Systematic Review. *Clin Orthop Relat Res.* 2015;473(6):1940-56.

171. Dashfield AK, Taylor MB, Cleaver JS, Farrow D. Comparison of caudal steroid epidural with targeted steroid placement during spinal endoscopy for chronic sciatica: a prospective, randomized, double-blind trial. *Br J Anaesth.* 2005;94(4):514-9.
172. Ackerman WE, III, Ahmad M. The efficacy of lumbar epidural steroid injections in patients with lumbar disc herniations. *Anesth Analg.* 2007;104(5):1217-22, tables.
173. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. Preliminary results of a randomized, equivalence trial of fluoroscopic caudal epidural injections in managing chronic low back pain: Part 2--Disc herniation and radiculitis. *Pain Physician.* 2008;11(6):801-15.
174. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. A randomized, controlled, double-blind trial of fluoroscopic caudal epidural injections in the treatment of lumbar disc herniation and radiculitis. *Spine (Phila Pa 1976).* 2011;36(23):1897-905.
175. Manchikanti L, Singh V, Cash KA, Pampati V, Damron KS, Boswell MV. Effect of fluoroscopically guided caudal epidural steroid or local anesthetic injections in the treatment of lumbar disc herniation and radiculitis: a randomized, controlled, double blind trial with a two-year follow-up. *Pain Physician.* 2012;15(4):273-86.
176. Murakibhavi VG, Khemka AG. Caudal epidural steroid injection: a randomized controlled trial. *Evid Based Spine Care J.* 2011;2(4):19-26.
177. Pinto RZ, Maher CG, Ferreira ML, Hancock M, Oliveira VC, McLachlan AJ, et al. Epidural corticosteroid injections in the management of sciatica: a systematic review and meta-analysis. *Ann Intern Med.* 2012;157(12):865-77.
178. Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. *Spine (Phila Pa 1976 ).* 1991;16(5):572-5.
179. Hrobjartsson A, Gotzsche PC. Placebo interventions for all clinical conditions. *Cochrane Database Syst Rev.* 2010(1):CD003974.
180. Howick J, Bishop FL, Heneghan C, Wolstenholme J, Stevens S, Hobbs FD, et al. Placebo use in the United kingdom: results from a national survey of primary care practitioners. *PLoS One.* 2013;8(3):e58247.
181. Bicket MC, Gupta A, Brown CH, Cohen SP. Epidural injections for spinal pain: a systematic review and meta-analysis evaluating the "control" injections in randomized controlled trials. *Anesthesiology.* 2013;119(4):907-31.
182. Rabinovitch DL, Peliowski A, Furlan AD. Influence of lumbar epidural injection volume on pain relief for radicular leg pain and/or low back pain. *Spine J.* 2009;9(6):509-17.
183. Holtedahl R, Brox JI, Tjomsland O. Placebo effects in trials evaluating 12 selected minimally invasive interventions: a systematic review and meta-analysis. *BMJ Open.* 2015;5(1):e007331.
184. Valat JP, Giraudeau B, Rozenberg S, Goupille P, Bourgeois P, Micheau-Beaugendre V, et al. Epidural corticosteroid injections for sciatica: a randomised, double blind, controlled clinical trial. *Ann Rheum Dis.* 2003;62(7):639-43.
185. Arden NK, Price C, Reading I, Stubbing J, Hazelgrove J, Dunne C, et al. A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: the WEST study. *Rheumatology (Oxford).* 2005;44(11):1399-406.

186. Cohen SP, White RL, Kurihara C, Larkin TM, Chang A, Griffith SR, et al. Epidural steroids, etanercept, or saline in subacute sciatica: a multicenter, randomized trial. *Ann Intern Med.* 2012;156(8):551-9.
187. Riew KD, Yin Y, Gilula L, Bridwell KH, Lenke LG, Laurusson C, et al. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. *J Bone Joint Surg Am.* 2000;82-A(11):1589-93.
188. Riew KD, Park JB, Cho YS, Gilula L, Patel A, Lenke LG, et al. Nerve root blocks in the treatment of lumbar radicular pain. A minimum five-year follow-up. *J Bone Joint Surg Am.* 2006;88(8):1722-5.
189. Bicket MC, Horowitz JM, Benzon HT, Cohen SP. Epidural injections in prevention of surgery for spinal pain: systematic review and meta-analysis of randomized controlled trials. *Spine J.* 2015;15(2):348-62.
190. Mathews JA, Mills SB, Jenkins VM, Grimes SM, Morkel MJ, Mathews W, et al. Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections. *Br J Rheumatol.* 1987;26(6):416-23.
191. Sayegh FE, Kenanidis EI, Papavasiliou KA, Potoupnis ME, Kirkos JM, Kapetanios GA. Efficacy of steroid and nonsteroid caudal epidural injections for low back pain and sciatica: a prospective, randomized, double-blind clinical trial. *Spine (Phila Pa 1976).* 2009;34(14):1441-7.
192. FDA Drug Safety Communication: FDA requires label changes to warn of rare but serious neurologic problems after epidural corticosteroid injections for pain 4-23-2014.
193. Rathmell JP, Benzon HT, Dreyfuss P, Huntoon M, Wallace M, Baker R, et al. Safeguards to prevent neurologic complications after epidural steroid injections: consensus opinions from a multidisciplinary working group and national organizations. *Anesthesiology.* 2015;122(5):974-84.
194. Bateman BT, Brenner GJ. An important step forward in the safe use of epidural steroid injections. *Anesthesiology.* 2015;122(5):964-6.
195. Manchikanti L, Benyamin RM, Hansen H, Swicegood JR, Hirsch JA. Reversal of epidural cuts in 2015 physician payment schedule: two steps forward, one step back. *Pain Physician.* 2014;17(5):E565-E73.
196. Albert HB, Manniche C. Modic changes following lumbar disc herniation. *Eur Spine J.* 2007;16(7):977-82.
197. Jensen RK, Leboeuf-Yde C, Wedderkopp N, Sorensen JS, Jensen TS, Manniche C. Is the development of Modic changes associated with clinical symptoms? A 14-month cohort study with MRI. *Eur Spine J.* 2012;21(11):2271-9.
198. Weishaupt D, Zanetti M, Hodler J, Boos N. MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. *Radiology.* 1998;209(3):661-6.
199. Keller A, Boyle E, Skog TA, Cassidy JD, Bautz-Holter E. Are Modic changes prognostic for recovery in a cohort of patients with non-specific low back pain? *Eur Spine J.* 2012;21(3):418-24.
200. Jensen RK, Leboeuf-Yde C. Is the presence of modic changes associated with the outcomes of different treatments? A systematic critical review. *BMC Musculoskeletal Disord.* 2011;12:183.

201. Peterson CK, Pfirrmann CW, Hodler J. Are Modic changes related to outcomes in lumbar disc herniation patients treated with imaging-guided lumbar nerve root blocks? *Eur J Radiol.* 2014;83(10):1786-92.
202. Schistad EI, Espeland A, Rygh LJ, Roe C, Gjerstad J. The association between Modic changes and pain during 1-year follow-up in patients with lumbar radicular pain. *Skeletal Radiol.* 2014;43(9):1271-9.
203. Jarvinen J, Karppinen J, Niinimäki J, Haapea M, Gronblad M, Luoma K, et al. Association between changes in lumbar Modic changes and low back symptoms over a two-year period. *BMC Musculoskelet Disord.* 2015;16:98.
204. Albert HB, Sorensen JS, Christensen BS, Manniche C. Antibiotic treatment in patients with chronic low back pain and vertebral bone edema (Modic type 1 changes): a double-blind randomized clinical controlled trial of efficacy. *Eur Spine J.* 2013;22(4):697-707.
205. Koivisto K, Kyllonen E, Haapea M, Niinimäki J, Sundqvist K, Pehkonen T, et al. Efficacy of zoledronic acid for chronic low back pain associated with Modic changes in magnetic resonance imaging. *BMC Musculoskelet Disord.* 2014;15:64.
206. Pedersen LM, Schistad E, Jacobsen LM, Roe C, Gjerstad J. Serum levels of the pro-inflammatory interleukins 6 (IL-6) and -8 (IL-8) in patients with lumbar radicular pain due to disc herniation: A 12-month prospective study. *Brain Behav Immun.* 2015;46:132-6.
207. Stellar JE, John-Henderson N, Anderson CL, Gordon AM, McNeil GD, Keltner D. Positive Affect and Markers of Inflammation: Discrete Positive Emotions Predict Lower Levels of Inflammatory Cytokines. *Emotion.* 2015.
208. Miyamoto Y, Boylan JM, Coe CL, Curhan KB, Levine CS, Markus HR, et al. Negative emotions predict elevated interleukin-6 in the United States but not in Japan. *Brain Behav Immun.* 2013;34:79-85.
209. Olmarker K, Rydevik B, Nordborg C. Autologous nucleus pulposus induces neurophysiologic and histologic changes in porcine cauda equina nerve roots. *Spine (Phila Pa 1976).* 1993;18(11):1425-32.
210. Igarashi T, Kikuchi S, Shubayev V, Myers RR. 2000 Volvo Award winner in basic science studies: Exogenous tumor necrosis factor- $\alpha$  mimics nucleus pulposus-induced neuropathology. Molecular, histologic, and behavioral comparisons in rats. *Spine (Phila Pa 1976).* 2000;25(23):2975-80.
211. Olmarker K, Rydevik B. Selective inhibition of tumor necrosis factor- $\alpha$  prevents nucleus pulposus-induced thrombus formation, intraneural edema, and reduction of nerve conduction velocity: possible implications for future pharmacologic treatment strategies of sciatica. *Spine (Phila Pa 1976).* 2001;26(8):863-9.
212. Wang YF, Chen PY, Chang W, Zhu FQ, Xu LL, Wang SL, et al. Clinical significance of tumor necrosis factor- $\alpha$  inhibitors in the treatment of sciatica: a systematic review and meta-analysis. *PLoS One.* 2014;9(7):e103147.
213. Liang C, Li H, Tao Y, Shen C, Li F, Shi Z, et al. New hypothesis of chronic back pain: low pH promotes nerve ingrowth into damaged intervertebral disks. *Acta Anaesthesiol Scand.* 2013;57(3):271-7.
214. Loggia ML, Chonde DB, Akeju O, Arabasz G, Catana C, Edwards RR, et al. Evidence for brain glial activation in chronic pain patients. *Brain.* 2015;138(Pt 3):604-15.

215. Younger J, Parkitny L, McLain D. The use of low-dose naltrexone (LDN) as a novel anti-inflammatory treatment for chronic pain. *Clin Rheumatol*. 2014;33(4):451-9.
216. Kepes ER, Duncalf D. Treatment of backache with spinal injections of local anesthetics, spinal and systemic steroids. A review. *Pain*. 1985;22(1):33-47.
217. Benzon HT. Epidural steroid injections for low back pain and lumbosacral radiculopathy. *Pain*. 1986;24(3):277-95.
218. Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesth Intensive Care*. 1995;23(5):564-9.
219. Koes BW, Scholten RJ, Mens JM, Bouter LM. Efficacy of epidural steroid injections for low-back pain and sciatica: a systematic review of randomized clinical trials. *Pain*. 1995;63(3):279-88.
220. Hopayian K. The need for caution in interpreting high quality systematic reviews. *BMJ*. 2001;323(7314):681-4.
221. Armon C, Argoff CE, Samuels J, Backonja MM. Assessment: use of epidural steroid injections to treat radicular lumbosacral pain: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2007;68(10):723-9.
222. Armon C, Argoff CE, Backonja MM. Assessment: use of epidural steroid injections to treat radicular lumbosacral pain: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. 2007;69(6):614; author reply -5.
223. Manchikanti L, Boswell MV, Singh V, Benyamin RM, Fellows B, Abdi S, et al. Comprehensive evidence-based guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician*. 2009;12(4):699-802.
224. Chou R, Loeser JD, Owens DK, Rosenquist RW, Atlas SJ, Baisden J, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: an evidence-based clinical practice guideline from the American Pain Society. *Spine (Phila Pa 1976)*. 2009;34(10):1066-77.
225. Chou R, Atlas SJ, Stanos SP, Rosenquist RW. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. *Spine (Phila Pa 1976)*. 2009;34(10):1078-93.
226. Levin JH. Prospective, double-blind, randomized placebo-controlled trials in interventional spine: what the highest quality literature tells us. *Spine J*. 2009;9(8):690-703.
227. Cohen SP, Bicket MC, Jamison D, Wilkinson I, Rathmell JP. Epidural steroids: a comprehensive, evidence-based review. *Reg Anesth Pain Med*. 2013;38(3):175-200.
228. Chou R, Atlas SJ, Loeser JD, Rosenquist RW, Stanos SP. Guideline warfare over interventional therapies for low back pain: can we raise the level of discourse? *J Pain*. 2011;12(8):833-9.
229. Manchikanti L, Benyamin RM, Falco FJ, Caraway DL, Datta S, Hirsch JA. Guidelines warfare over interventional techniques: is there a lack of discourse or straw man? *Pain Physician*. 2012;15(1):E1-E26.
230. Karppinen J, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimäki T, Nieminen P, et al. Periradicular infiltration for sciatica: a randomized controlled trial. *Spine (Phila Pa 1976)*. 2001;26(9):1059-67.

231. Johansson BH. [The SBU report "Back pain, neck pain" critically illuminated]. *Lakartidningen*. 2001;98(9):983-4, 7.
232. Reports from the Swedish Council on Technology Assessment in Health Care. Back pain. *Int J Technol Assess Health Care*. 2000;16(3):929-43.
233. Andersson HI, Leden I. [The SBU report on back pain and neck pain. An ambitious survey of a big problem]. *Lakartidningen*. 2000;97(44):4952-4.
234. Laerum E, Storheim K, Brox JI. [New clinical guidelines for low back pain]. *Tidsskr Nor Laegeforen*. 2007;127(20):2706.
235. DSAM Klinisk vejledning. Diagnostik og behandling af lændesmerter i almen praksis. Dansk selskab for almen medicin-2006.
236. Nasjonalt Ryggnettverk, Formidlingsenheten. Akutte korsryggsmerter. Tverrfaglige, kliniske retningslinjer. Oslo: Nasjonalt Ryggnettverk; 2002.
237. Formidlingsenheten for muskel- og skjelettlidelser (FORMI). Lærum E (Hovedredatør). Nasjonale kliniske retningslinjer. Korsryggsmerter med og uten nerverotaffeksjon. Oslo: Sosial og helsedirektoratet; 2007.
238. Ihlebaek C, Eriksen HR. Myths and perceptions of back pain in the Norwegian population, before and after the introduction of guidelines for acute back pain. *Scand J Public Health*. 2005;33(5):401-6.
239. Hofstede SN, Marang-van de Mheen PJ, Wentink MM, Stiggelbout AM, Vleggeert-Lankamp CL, Vliet Vlieland TP, et al. Barriers and facilitators to implement shared decision making in multidisciplinary sciatica care: a qualitative study. *Implement Sci*. 2013;8:95.





## APPENDICES

Appendix 1 Paper I

Appendix 2 Paper II

Appendix 3 Paper III

Appendix 4 Investigator's brochure

Appendix 5 Template for radiological evaluation of magnetic resonance or CT images

Appendix 6 Form book

Appendix 7 Study protocol

## Appendix 4 Investigator's brochure



# PROSEDYREBOK

Epidural sacral injection study.

Effect of volume and triamcinolone on chronic  
lumbosacral radiculopathy?

Double blind multicentre randomised placebo-controlled trial.

Prosjektleder:

Trond Iversen

Avd for fys med og rehabilitering, UNN

Institutt for samfunnsmedisin (ISM), Universitetet i Tromsø

Mobilnummer 95 18 69 88

Epost [trondiv@online.no](mailto:trondiv@online.no)

**Epidural sacral injection study**

**Prosedyrebok**

**Ryggundersøkelse**

## **Selection and withdrawal of subjects.**

### Inclusion criteria based on medical history and clinical examination.

1. Patients aged 20 – 60 years old, of both sexes.
2. Duration of radicular symptoms  $\geq$  12 weeks (chronic pain).
3. Clinically proven radiculopathy at nerve root L3, L4, L5 or S1. The radiculopathy may be unilateral/bilateral on the same level, or unilateral/bilateral on one or more levels at the same time.
4. Body Mass Index (BMI)  $<$  30.

### Exclusion criteria based on medical history and clinical examination.

1. Indication of acute back surgery at the time of inclusion. To determine whether acute surgery is indicated, the guidelines drawn up by the Neurosurgery Department, UNN are followed (Solberg, 2000).
2. Previous back surgery.
3. Previous epidural or nerve root injection for low back pain or sciatica.
4. Red Flags (Rheumatic inflammatory disease, Malignant disease, Diabetes mellitus, Severe and uncompensated cardiovascular disease, Known autoimmune disease, Currently known infection, Haemophilia, Some other type of disease that affects the coagulation system)
5. Yellow Flags (Known severe mental disease, Known problems with alcohol or substance abuse)
6. The patient must not have noticed an improvement in symptoms for the previous two weeks before inclusion.

The person investigating the patient for the first time asks the following question:

## Epidural sacral injection study, Inklusjons- og eksklusjonskriterier

*“Have you got better over the past two weeks?” (Yes/No)*

If the patient answers *Yes* to this question, the individual in question is excluded.

7. Nor must the patient have experienced centralisation of the pain, i.e. the pain has moved from the lower extremity towards the middle of the back, as this is regarded as a clinical sign of an already ongoing spontaneous improvement in the patient's condition (Lisi, 2001).

The person investigating the patient for the first time asks the following question:

*“Over the past two weeks, have you experienced a shift in the pain from severe leg pain to severe pain in your back?” (Yes/No).*

If the patient answers *Yes* to this question, the individual in question is excluded.

8. Women of childbearing age are asked about pregnancy and breast feeding.

HCG in urine are tested.

The person investigating the patient for the first time asks the following question:

*“Are you pregnant or giving breast feeding?” (Yes/No)*

If the patient answers *Yes* to this question, the individual in question is excluded.

9. Anticlotting therapy.

The person investigating the patient for the first time asks the following question:

*“Are you taking Warfarin (Marevan)?” (Yes/No)*

If the patient answers *Yes* to this question, the person in question is excluded.

Use of ASA is not an exclusion criterion (Horlocker et al 2002).

10. Ongoing drug treatment with Non-Steroidal-Anti-Inflammatory-Drug (NSAID).

The person investigating the patient for the first time asks the following question:

*“Can you come off the NSAID?” (Yes/No)*

If the patient answers *No* to this question, the individual in question is excluded.

## Epidural sacral injection study, Inklusjons- og eksklusjonskriterier

### Exclusion criteria based on MR findings.

The physician who conducts the inclusion check must, after the clinical examination is completed, assess the MR response provided by the radiologist for the patient. If, based on the radiologist's description, a *Yes* answer is given to one or more of the findings listed below, the patient must be excluded. If the MR description does not provide a basis for answering *Yes* or *No* to the questions, the radiologist who has described the scans must be contacted and asked to clarify his description.

- Lateral recess stenosis of osteogenic aetiology (Yes/No?)
- Tumour (Yes/No?).
- Bleeding (Yes/No?).
- Dural fistula (Yes/No?).
- Synovial cyst (Yes/No?).
- Dysraphia conditions (Yes/No?).

### Written informed consent.

The patients in question, who are demonstrated as having a lumbosacral radiculopathy and fulfill the inclusion criteria and no exclusion criteria, provide written informed consent if they wish to take part in the study (Written informed consent).

### Back information for patients included. The good back consultation.

All patients included who have given written informed consent to take part in the study are given a standardised oral information on back anatomy and back function with the emphasis on management and encouragement to engage in activity (Hagen et al 2003, Storheim et al 2003, Skouen et al 2002, Brox et al 2003, Mayo Clinic Health Information 2004). The



## Epidural sacral injection study, Inklusjons- og eksklusjonskriterier

information are given by the doctor and physiotherapist conducting the inclusion check. A recently published study shows that back information alone can be just as effective in treating low back pain as standard physiotherapy treatment (Frost et al, 2004). In the back consultation that the doctor conducts with the patient, the Norwegian national guidelines as set out in “Acute low back pain. Interdisciplinary, clinical guidelines” (The Norwegian Back Pain Network, The Communication Unit, 2002a) and the European Guidelines for the management of chronic non-specific low back pain (COST B13 Working Group on Guidelines for Chronic Low Back pain 2004) are followed, with a special focus on the recommendations concerning “The good back consultation”. All patients included also receive the brochure “Worth knowing about bad backs. What experts agree on” (The Norwegian Back Pain Network, The Communication Unit, 2002b) after the inclusion check and back consultation have been conducted.

### Recording use of medication.

1. The patient records his consumption of medication over one week before the first injection is performed. The names of the medicinal products, their strength and the number of tablets taken are recorded by the patient.
2. After the second injection is administered, the patient is asked to record his consumption of pain-killing medication in the same way over one week before the agreed checkups.
3. The consumption of each drug will be calculated with defined daily doses as a measurement unit and classified and presented by therapeutic group according to the anatomical therapeutic chemical system (Brox et al, 2003).

## **Kliniske undersøkelsen for å bestemme nivå nerverotaffeksjon**

1. Forekomst av nevrologiske utfall registreres, og det utføres en klinisk diagnostikk hvor det bestemmes hvilket skivenivå nerverotaffeksjonen utgår fra. I undersøkelsene følges prinsippene for nivådiagnostikk i Conesa og Argote (1976), Hoppenfeld (1997) og Ombregt et al (2003).
2. Ved undersøkelsene utføres SLR (Strait Leg Raise) (Deville et al 2000, Thelander et al 1992, Kosteljanetz 1988, Xin et al 1987), og gradtall for eventuell positiv test (der pasienten angir smerteutstråling distalt for knehasen) registreres. L3 nervestrekktest utføres med pasienten i mageleie og fleksjon i kneleddet, smerteutstråling noteres.
3. Muskelkraften graderes fra 0-5 der 0 = total paralyse, 3 = at muskelen kan bevege leddet mot tyngdekraften, men ikke mot ekstra motstand, 5 = normal kraft.
4. De myotatiske refleksene graderes fra 0 - +++++, der + er moderat svekket refleks, ++ indikerer normalt refleksutslag, +++ forøket refleks og +++++ klonisk refleks.
5. Overfladisk sensibilitet undersøkes med henblikk på berøringssans, smerte – og temperatursans. Forekomst av eventuelt radikulært sensibilitetsutfall registreres.
6. ”Registreringsskjema for pasienter som injiseres i ryggen” (Modifisert etter Nevrokirurgisk avdeling, UNN) fylles ut før injeksjonsbehandlingen.
7. ”Registreringsskjema ved kontroll etter rygginjeksjon” (Modifisert etter Nevrokirurgisk avdeling, UNN) fylles ut ved kontrollene.
8. Disse skjemaene inneholder opplysninger om alder, kjønn, sykehistorie, symptomvarighet, kliniske funn, eventuelle komplikasjoner, sosioøkonomisk status, sykmelding og trygdeforhold.
9. Pasientene svarer ved inklusjon og ved hver oppfølgingsundersøkelse på et livskvalitetsskjema EuroQol-5D (EQ-5D) (Luo et al 2003, Hurst et al 1997, Burstrom et al 2001) og et symptom- og funksjonskåreskjema (Oswestry Low Back Pain

Disability Questionnaire) (Hagg et al 2003, Niskanen 2002, Little 1994) og de avgir på tre ulike VAS (Visual Analog Scale) grad av smerter i rygg og hofte (VAS rygg), grad av smerter i ben (VAS ben) og nåværende helsetilstand (VAS generell helse) (Carragee, 2001). Waddells Fear-Avoidance Beliefs Questionnaire (FABQ) fylles ut ved inklusjon og ved oppfølgingsundersøkelsene. Det avsettes tid på poliklinikken for pasientene til å fylle ut disse skjemaene. Dersom de trenger hjelp til å forstå spørsmålene får de råd og veiledning.

10. Livskvalitetskjemaet (EQ-5D), symptom- og funksjonskåreskjemaet (ODI) og VAS skalaene inngår i et spesialdesignet spørreskjema som er validert for bruk i Norge. Skjemaet vi bruker i studien er modifisert etter ”Spørreskjema for pasienter som skal opereres i ryggen” og ”Spørreskjema for pasienter etter ryggoperasjon”, Nevrokirurgisk avdeling, UNN.
11. Pasienter som ikke møter til etterkontroll får tilsendt et tilpasset spørreskjema i posten hvor både EQ-5D, ODI og VAS rygg/hofte, ben og generell helse inngår (Modifisert etter ”Spørreskjema for pasienter etter ryggoperasjon, Besvares per brev av pasienten”, Nevrokirurgisk avdeling UNN).
12. I forbindelse med oppfølgingsundersøkelsene får pasientene anledning til å gi uttrykk for misnøye eller fornøydhet med behandlingen.
13. Pasientene svarer også ved hver undersøkelse på følgende spørsmål;  
”Får du for tiden noen annen type behandling for dine ryggplager?” (Ja/Nei)
14. De pasientene som svarer Ja på spørsmålet i punkt 13 blir anmodet om å angi type behandling eventuelt medikament type og dose.
15. De pasienter som etter at injeksjonene er utført har vedvarende sterke smerter og/eller neurologiske utfall, henvises tilbake til den legen som inkluderte pasienten som i sin

Epidural sacral injection study, Klinisk undersøkelse beskrevet

tur eventuelt viderehenviser til ortoped eller nevrokirurg for å avklare om det foreligger indikasjon for ryggoperasjon (Borenstein et al 2001, Komori et al 2002).

16. Pasienter som eventuelt blir ryggoperert fortsetter oppfølgingen i studien (intention to treat).

**Deville, WL ; van der Windt, DA ; Dzaferagic, A ; Bezemer, PD ; Bouter, LM (2000)** The test of Lasegue: systematic review of the accuracy in diagnosing herniated discs. *Spine May 1;25(9):1140-7*

**Thelander, U ; Fagerlund, M ; Friberg, S ; Larsson, S (1992)** Straight leg raising test versus radiologic size, shape, and position of lumbar disc hernias. *Spine Apr;17(4):395-9*

**Kosteljanetz, M ; Bang, F ; Schmidt-Olsen, S (1988)** The significance of straight-leg raising (Lasegue's sign) in the diagnosis of prolapsed lumbar disc. Interobserver variation and correlation with surgical finding. *Spine Apr;13(4):393-5*

**Xin, SQ ; Zhang, QZ ; Fan, DH (1987)** Significance of the straight-leg-raising test in the diagnosis and clinical evaluation of lower lumbar intervertebral-disc protrusion. *J Bone Joint Surg Am Apr;69(4):517-22*

**Conesa, SH ; Argote, ML (1976)** A visual aid to the examination of nerve roots. Bailliere Tindall.

**Hoppenfeld, S (1997)** Orthopaedic Neurology. A Diagnostic Guide to Neurologic Levels. Lippincott Williams & Wilkins

**Ombregt, L ; Bisschop, P ; ter Veer, HJ (2003)** A system of Orthopaedic Medicine. Churchill Livingstone.

Epidural sacral injection study, Klinisk undersøkelse beskrevet

**Luo, N ; Chew, LH ; Fong, KY ; Koh, DR ; Ng, S C ; Yoon, KH ; Vasoo, S ; Li, SC ;**

**Thumboo, J (2003)** A comparison of the EuroQol-5D and the Health Utilities Index Mark 3 in patients with rheumatic disease. *J Rheumatol Oct;30(10):2268-74*

**Hurst, NP ; Kind, P ; Ruta, D ; Hunter, M ; Stubbings, A (1997)** Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Br J Rheumatol May;36(5):551-9*

**Burstrom, K ; Johannesson, M ; Diderichsen, F (2001)** Swedish population health-related quality of life results using the EQ-5D. *Qual Life Res 10(7):621-35*

**Hagg, O ; Fritzell, P ; Nordwall, A (2003)** The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J Feb;12(1):12-20*

**Niskanen, RO (2002)** The Oswestry Low Back Pain Disability Questionnaire, a two-year follow-up of spine surgery patients. *Scand J Surg 91(2):208-11*

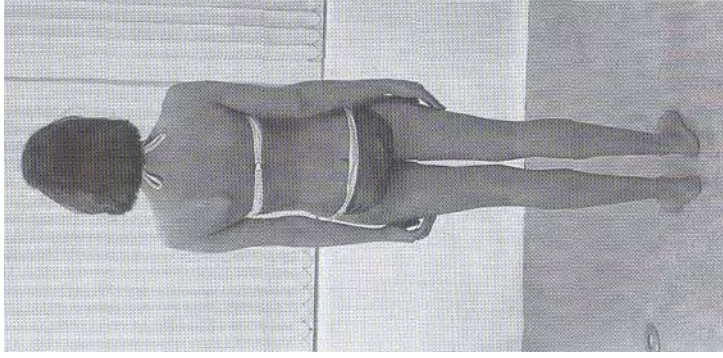
**Little, DG ; MacDonald, D (1994)** The use of the percentage change in Oswestry Disability Index score as an outcome measure in lumbar spinal surgery. *Spine Oct 1;19(19):2139-43*

**Carragee, EJ (2001)** Psychological and functional profiles in select subjects with low back pain. *Spine May-Jun;1(3):198-204*

**Borenstein, DG ; O'Mara, JW Jr ; Boden, SD ; Lauerma, WC ; Jacobson, A ;**

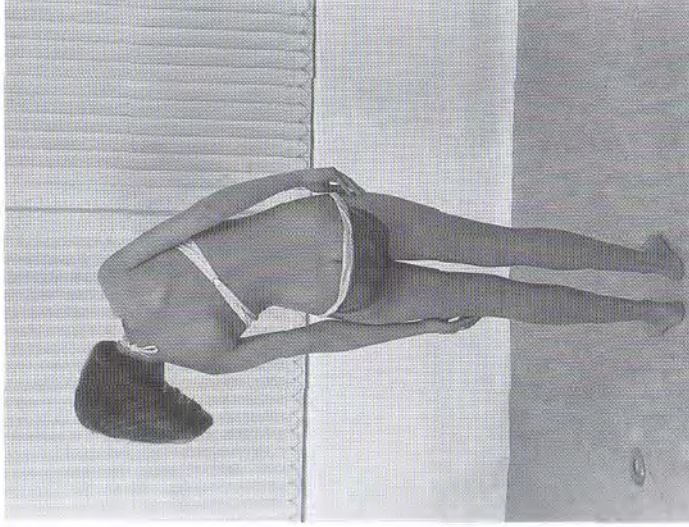
**Platenberg, C ; Schellinger, D ; Wiesel, SW (2001)** The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects: a seven-year follow-up study. *J Bone Joint Surg Am Sep;83-A(9):1306-11*

**Komori, H ; Okawa, A ; Haro, H ; Shinomiya, K(2002)** Factors predicting the prognosis of lumbar radiculopathy due to disc herniation. *J Orthop Sci 7(1):56-61*



## **EXTENSION**

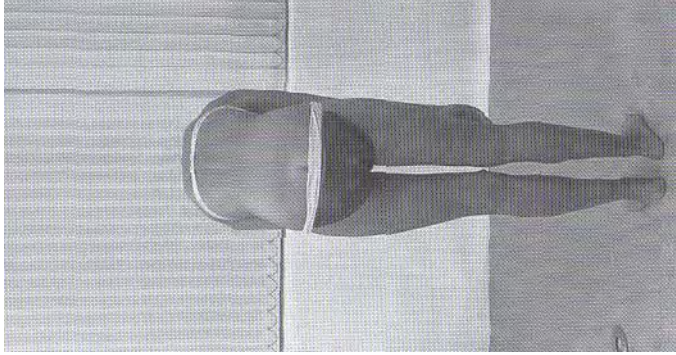
- Painful limitation: Large protrusion, Small protrusion+spondylosis, Spinal stenosis+spondylosis, Serious disease
- Painless limitation: Spondylosis, Long-standing ankylosing spondylitis, Vertebral hyperostosis
- Pain at full range: Small protrusion, Ligamentous lesion, Capsular lesion, Sacroiliac joint lesion, Hip joint lesion
- Deviation: Strong suggestion of disc protrusion



## **SIDE FLEXION**

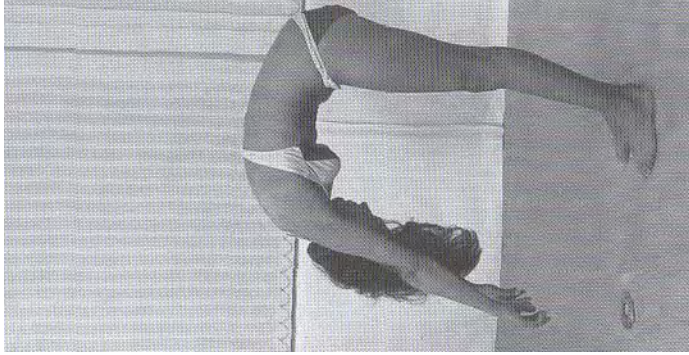
- Painful limitation of both side flexion movements: Serious disease, Ankylosing spondylitis
- Painless limitation of both side flexion movements: Spondylosis, Advance osteoporosis, Osteitis deformans
- Painful limitation of one side flexion movement: Large disc protrusion L4, Serious extra-articular lesion
- Pain at full range: Small disc protrusion, Minor fracture, Sprained ligament, Capsular lesion, Muscular lesion
- Painful arc: Disc lesion



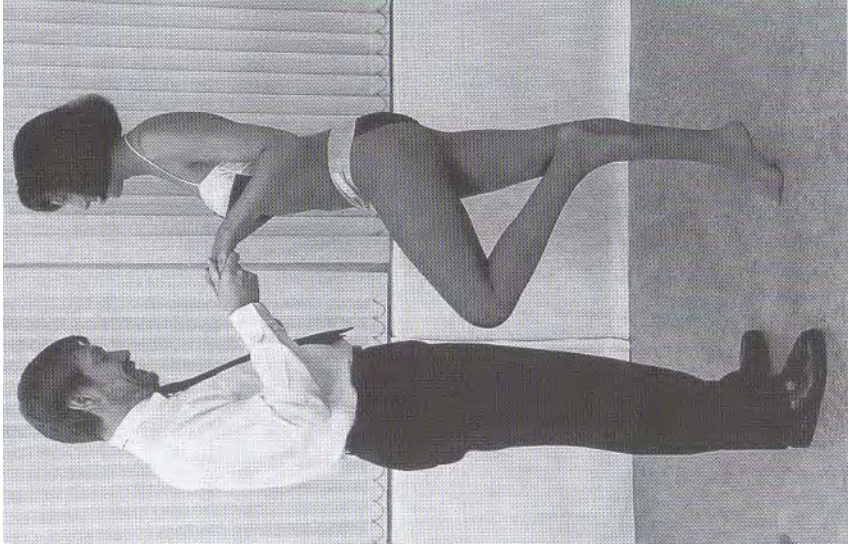


## **FLEXION**

- Painful limitation: Large disc protrusion, Serious disease (+ limitation of both side bending movements), Major lesion at the buttock
- Painless limitation: Spondylosis
- Pain at full range: Small disc protrusion, Sprained ligament, Capsular lesion, Injured muscle, Sacroiliac joint lesion, Minor lesion at the buttock, Hip joint lesion
- Painful arc: Disc protrusion
- Deviation: Large disc protrusion, Large intraspinal lesion







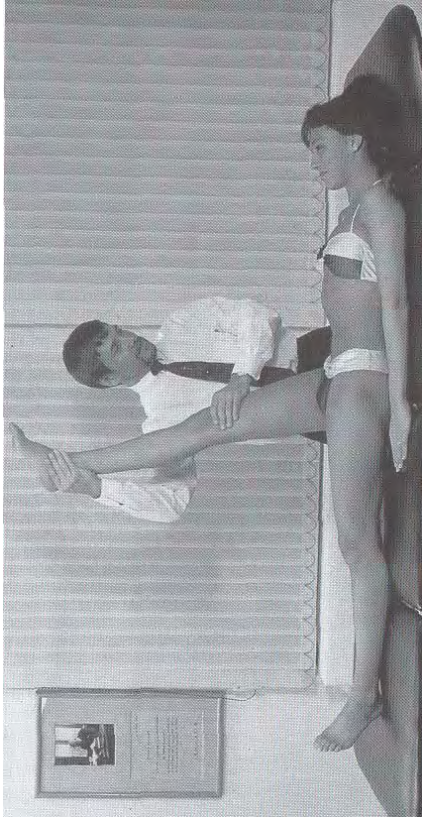
## **RISING ON TIPTOE**

Examines the strength of the calf muscles and thus the integrity of the S1/S2 segment



## **SACROILLIAC JOINT**

Distraction test: In a positive test, a deep-seated unilateral ache is evoked at the gluteal and/or posterior crural area



## **POSITIVE STRAIGHT LEG RAISING (SLR/LASEGUE)**

Intraspinal lesions: Discogenic (Protrusion),  
Non-discogenic (tumor,neuroma)

Extraspinal lesions: Sacroiliac joint lesions,  
major lesions at the buttock, major lesions at the  
hip joint, lesions of the hamstring muscle belly,  
non-organic disorders



## **STAGES IN THE SLR (L4-S2)**

Full and painless

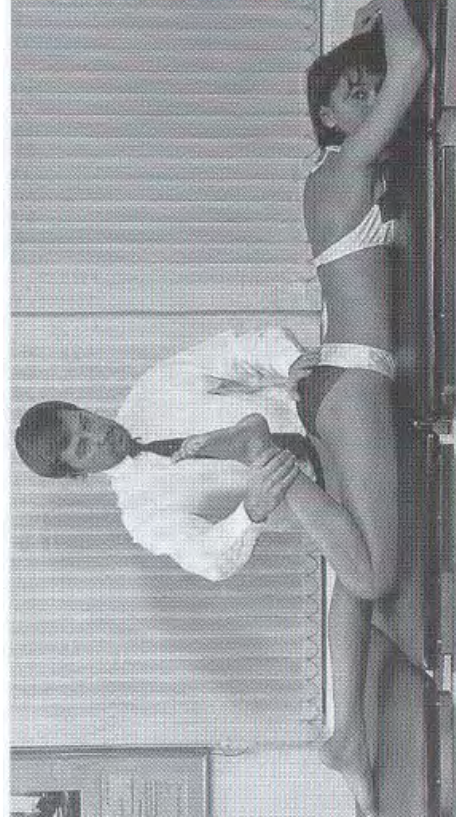
Pain on full range

Painful arc

Painful and limited without neurological deficit

Painful and limited with neurological deficit

Full and painless with neurological deficit



## **PASSIVE KNEE FLEXION**

Test the mobility of the third lumbar nerve root.  
Pain is felt in the back and/or the anterior part of the  
upper leg, depending on whether the test provokes a  
Discordural or a discoradicular interaction.

## **SIX STAGES IN THE SLR CAN BE DISTINGUISHED AND EACH USED AS A CRITERION TO ASCERTAIN THE SIZE OF THE PROTRUSION**

Full and painless: This does not exclude disc protrusions. In the supine position these may be too small to make contact with the dura or the dural sleeve and thus these structures can move freely.

Pain on full range: A small protrusion is likely.

Painful arc: Suggestive of a small protrusion. The dura or nerve root slips over the protrusion.

Painful and limited without neurological deficit: The protrusion is larger, limiting the mobility of the dura or the dural sleeve of one of the lower lumbar or upper sacral nerve roots.

Painful and limited with neurological deficit: A large posterolateral protrusion is compressing a nerve root, impairing mobility and conduction. The severity of the palsy takes over from SLR as the criterion of the degree of interference.

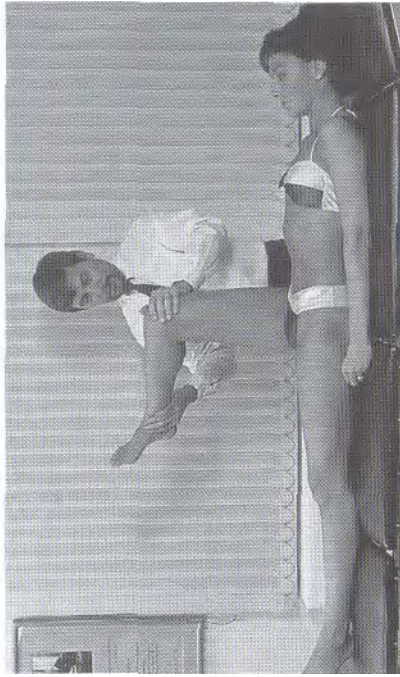
Full and painless with neurological deficit: A large posterolateral protrusion has become maximal, compressing the Nerve root so intensively that it has become ischaemic and atrophies.

## **FLEXION**



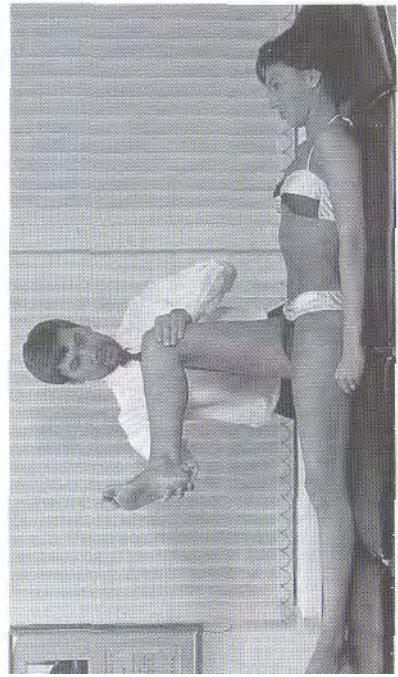
(a)

## **MEDIAL ROTATION**



(b)

## **LATERAL ROTATION**



(c)

## RESISTED FLEXION OF THE HIP JOINT

L2  
L3



## RESISTED DORSIFLEXION OF FOOT

L4





## **RESISTED DORSIFLEXION OF THE BIG TOE**

L4  
L5

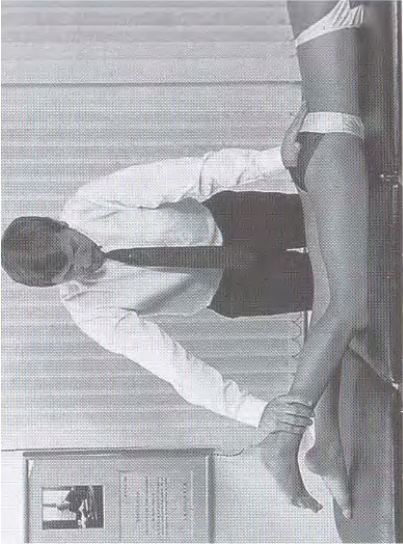


## **RESISTED EVERSION OF THE FOOT**

L5  
S1

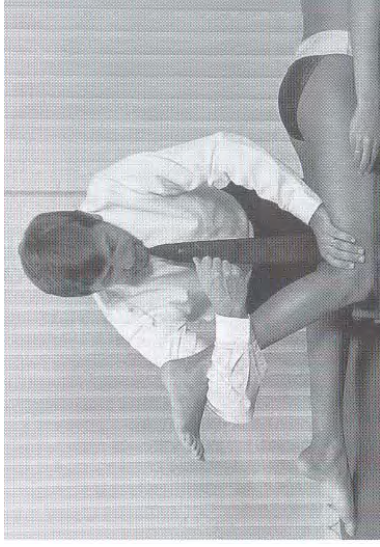
## RESISTED FLEXION OF THE KNEE

S1  
S2



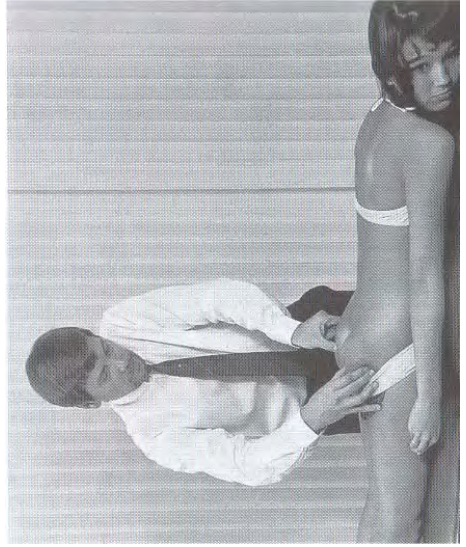
## RESISTED EXTENSION OF THE KNEE

L3



## CONTRACTION OF BUTTOCK MUSCLES

S1  
S2





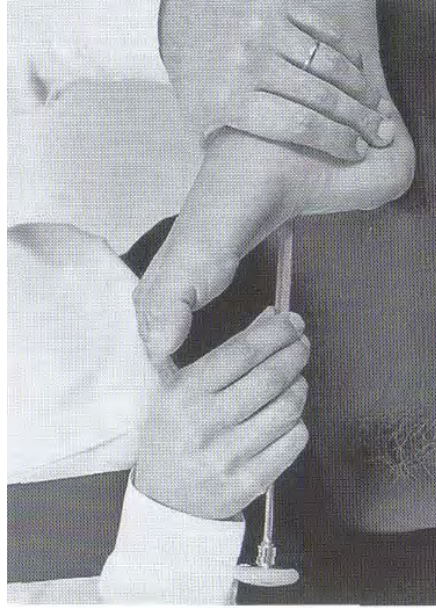
## **KNEE REFLEX**

L3



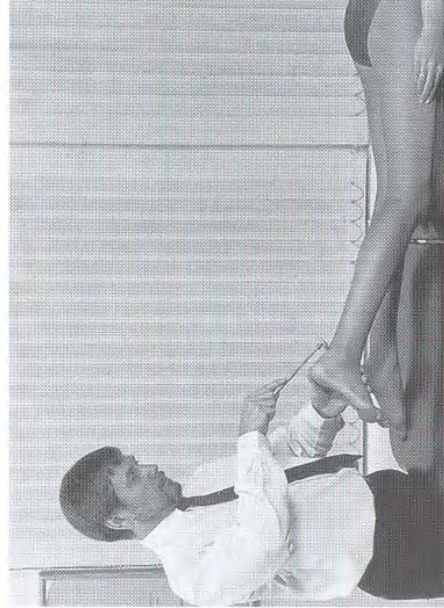
## **PLANTAR REFLEX**

Spinal cord



## **ANKLE REFLEX**

L5  
S1  
S2



Ombregt (2003)



## **TESTING FOR SENSORY CONDUCTION**

L2: Front of the thigh.

L3: Front and inner side of lower leg to just above the foot.

L4: Big toe alone.

L5: Big toe and two adjacent toes.

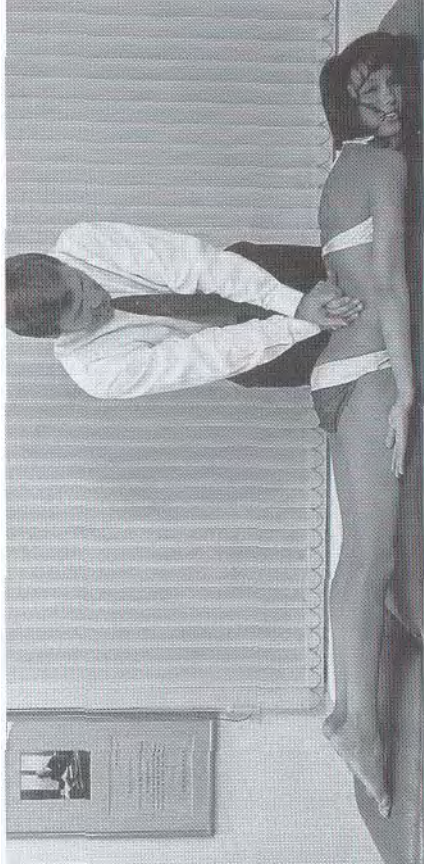
S1: Outer border of the foot, together with the two outer toes.

S2: Sole of the heel.



## **PALPATION**

Lumbar spinous processes to detect irregularities or a shelf between L4-L5 (indicating spondylolisthesis)



## **EXTENSION PRESSURE**

To detect the level of the lesion, note at which level pain and muscle guarding are most provoked and the end-feel (normal elastic, hard in ankylosing spondylitis)

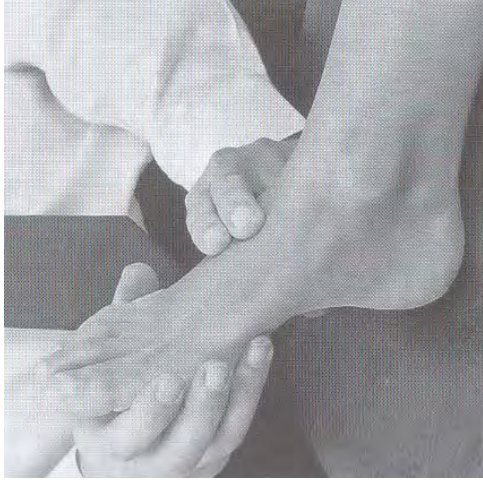
## **FEMORAL ARTERY**



## **POSTERIOR TIBIAL ARTERY**



## **DORSALIS PEDIS ARTERY**

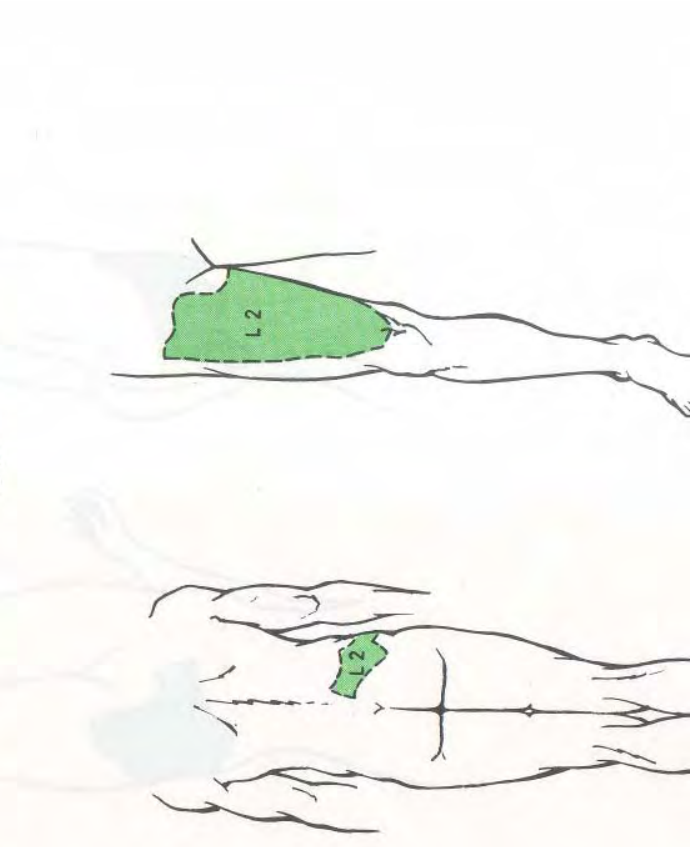


Ombregt (2003)



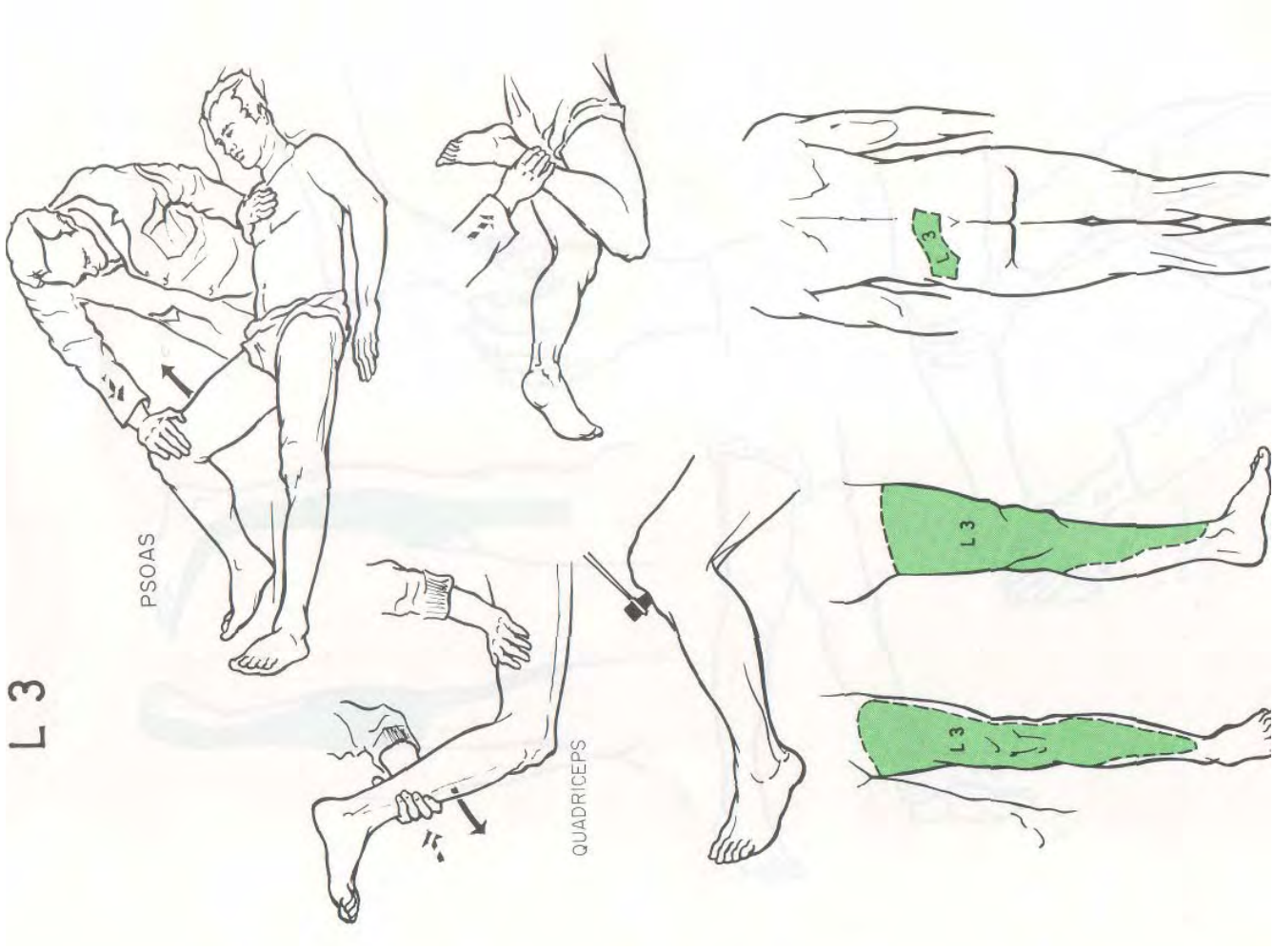
Conesa (1976)

L 2



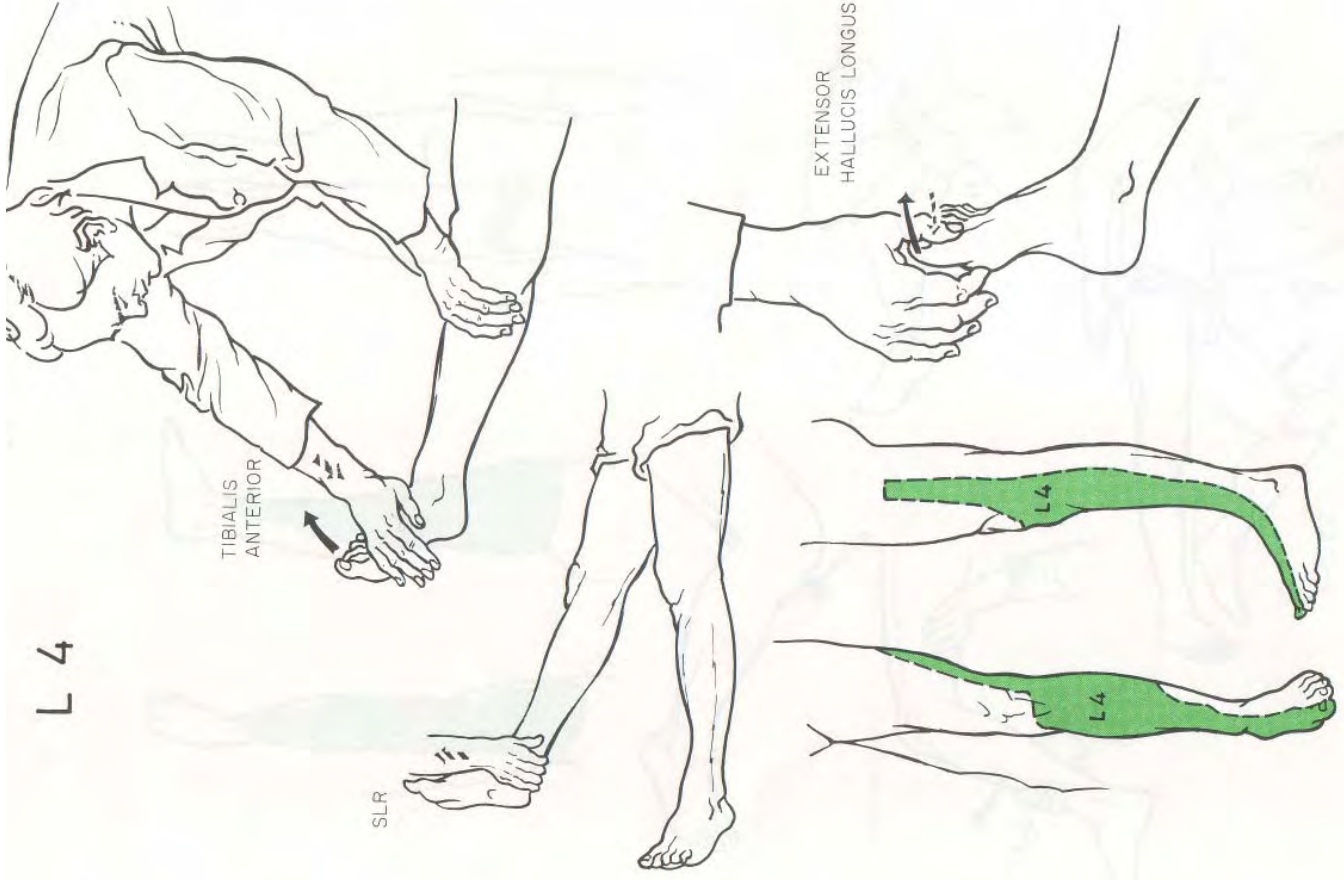
Conesa (1976)

L 3



Conesa (1976)

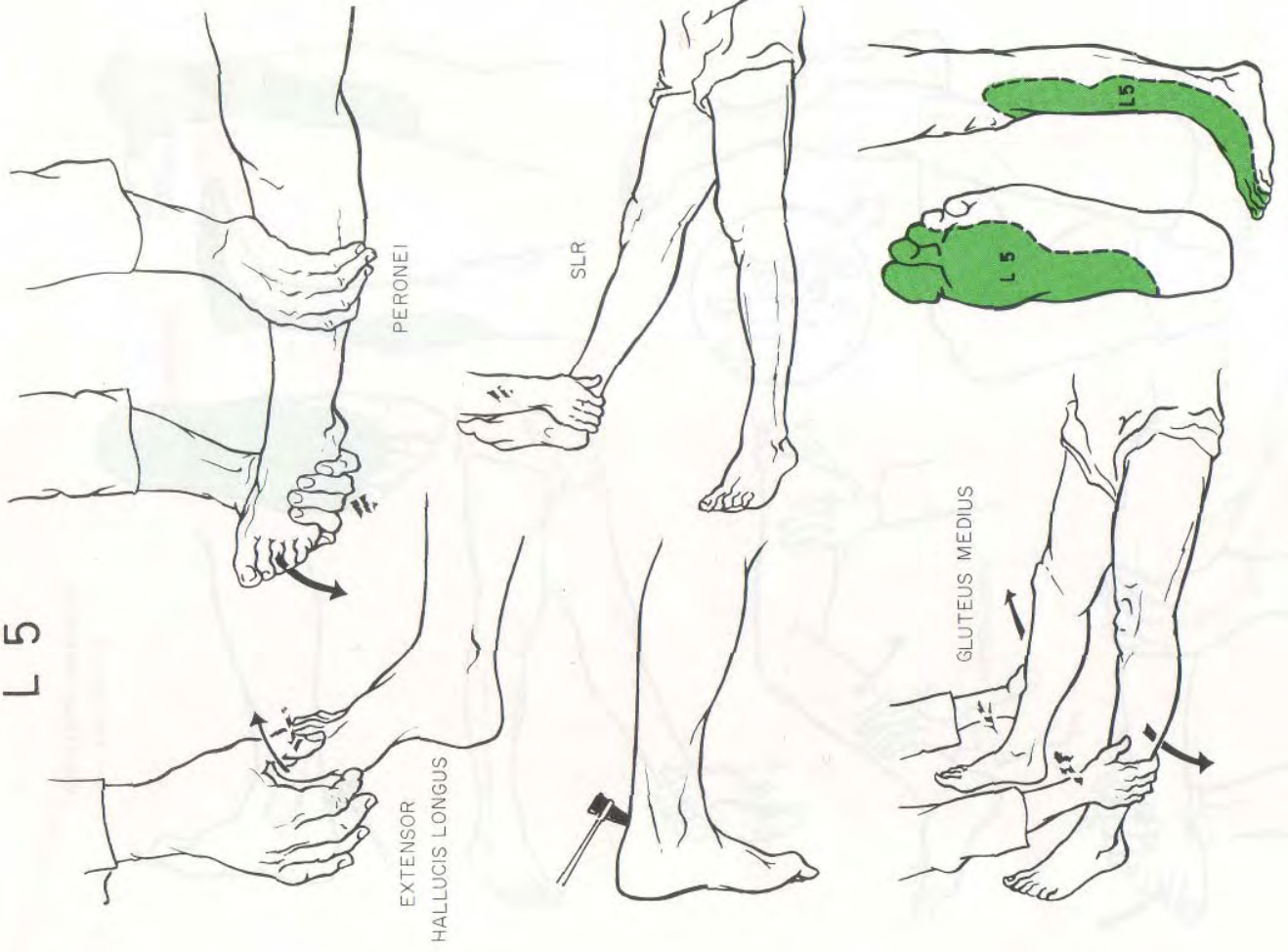
L 4



Conesa (1976)

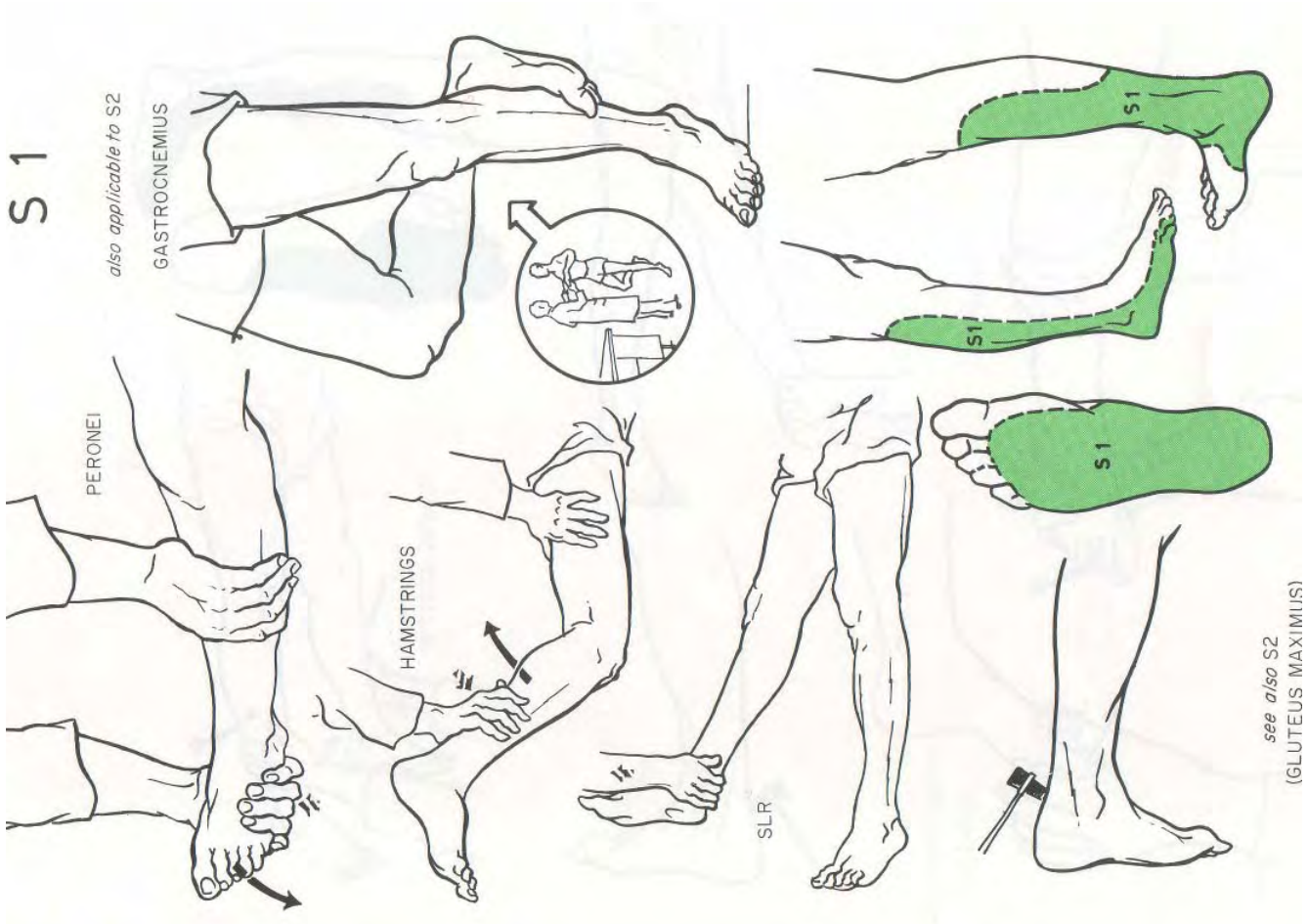


L 5



Conesa (1976)

S1



also applicable to S2

GASTROCNEMIUS

PERONEI

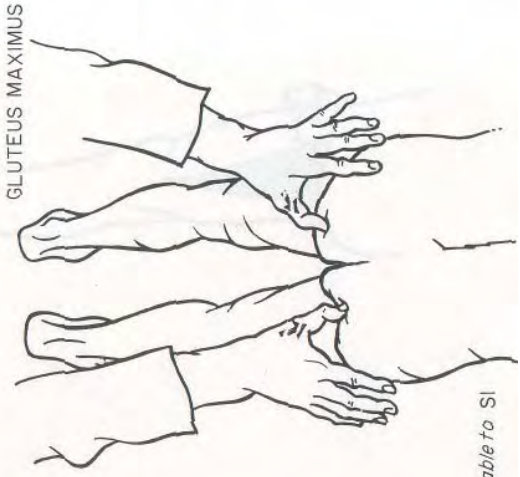
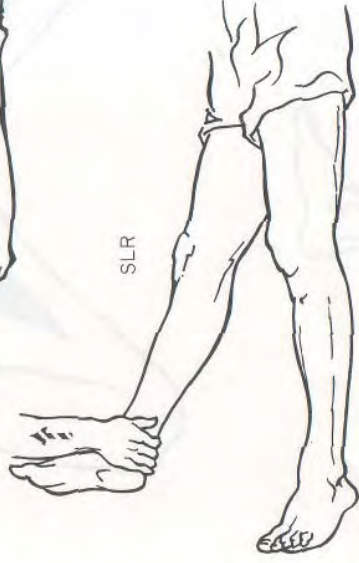
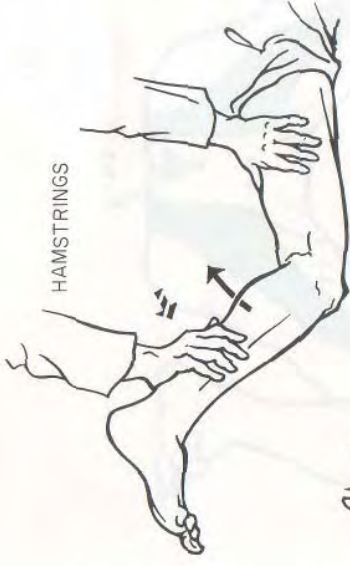
HAMSTRINGS

SLR

see also S2  
(GLUTEUS MAXIMUS)

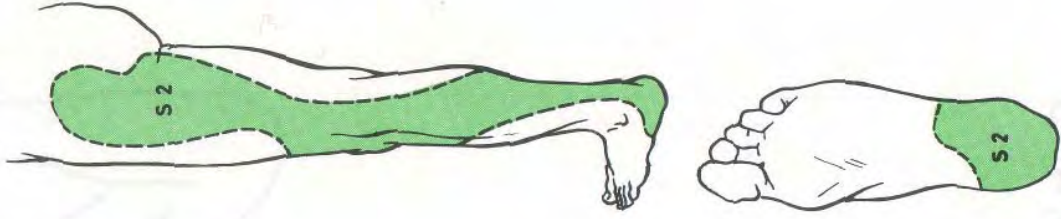
Conesa (1976)

S 2



*also applicable to SI*

(GASTROCNEMIUS)  
*see also SI*

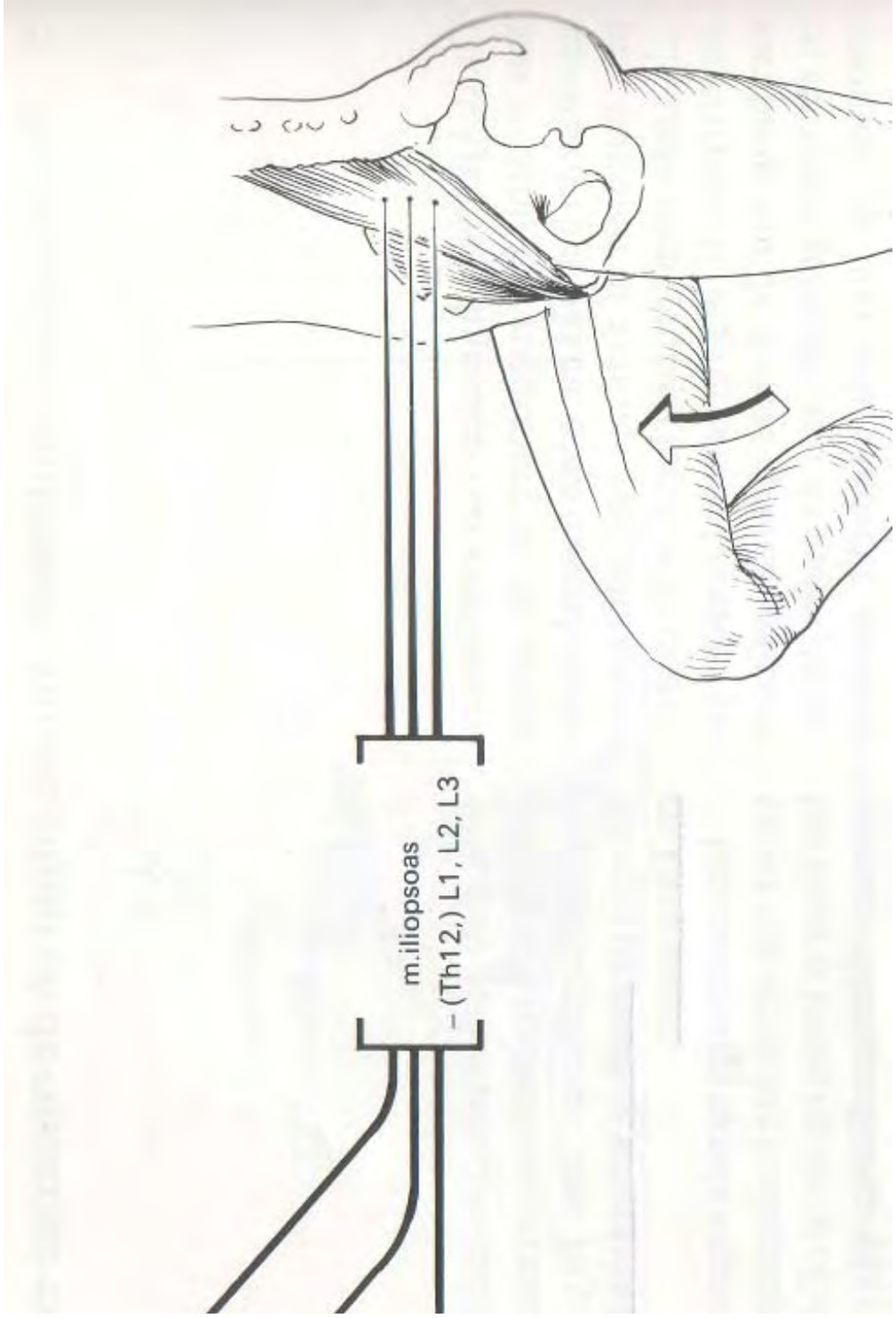


Conesa (1976)

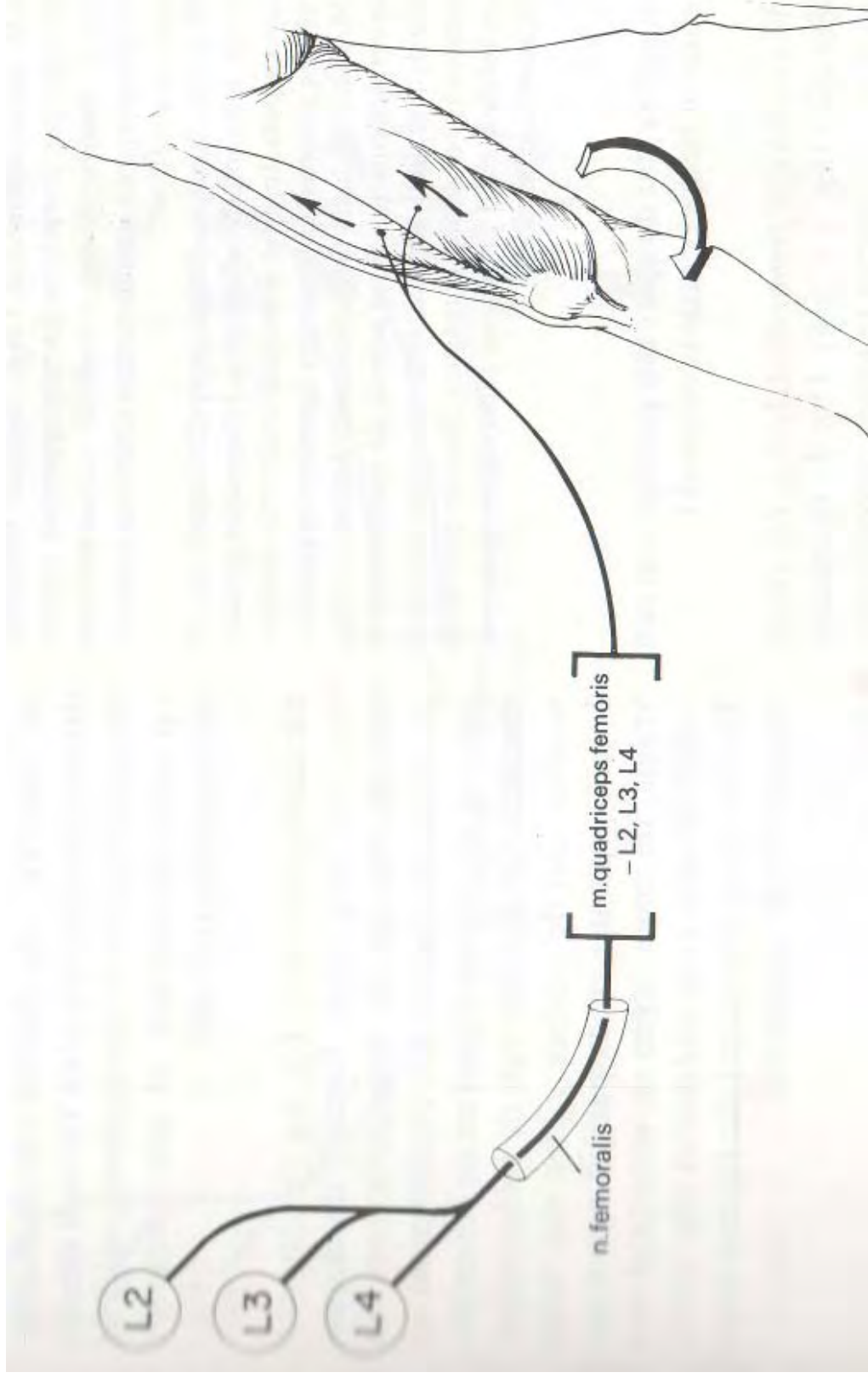
S 3,4, 5



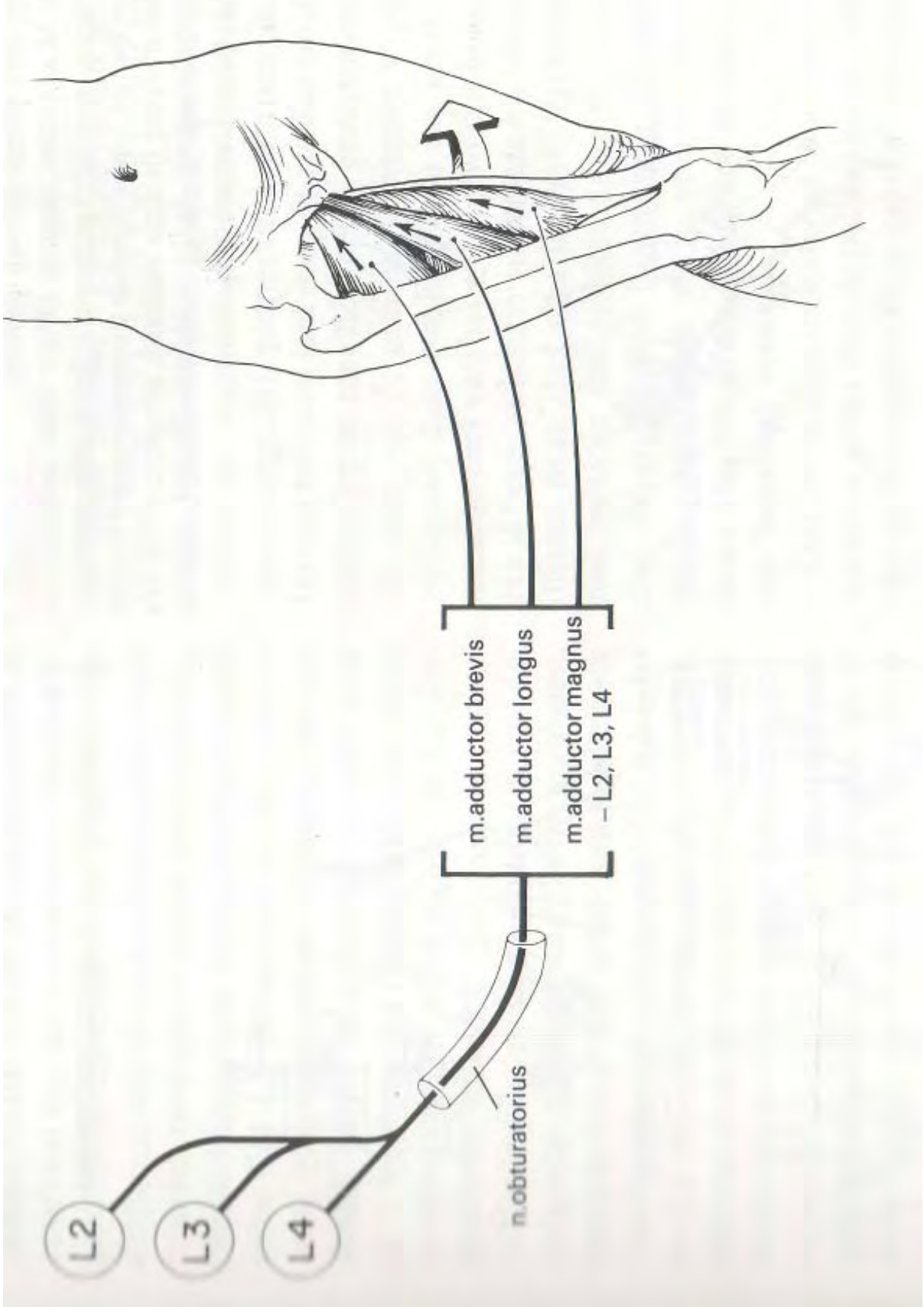
Conesa (1976)



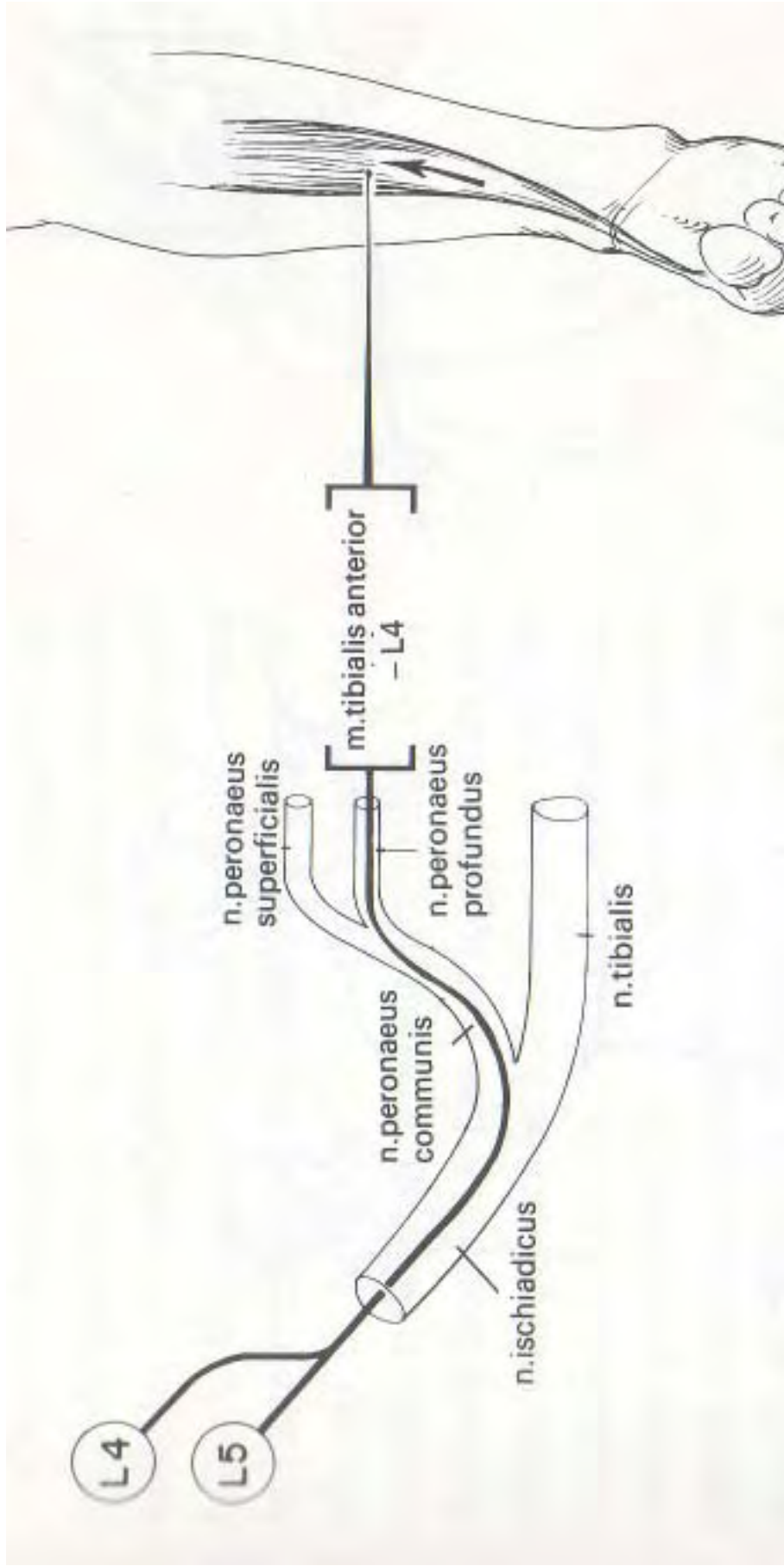
Hoppenfeld (1997)



Hoppenfeld (1997)

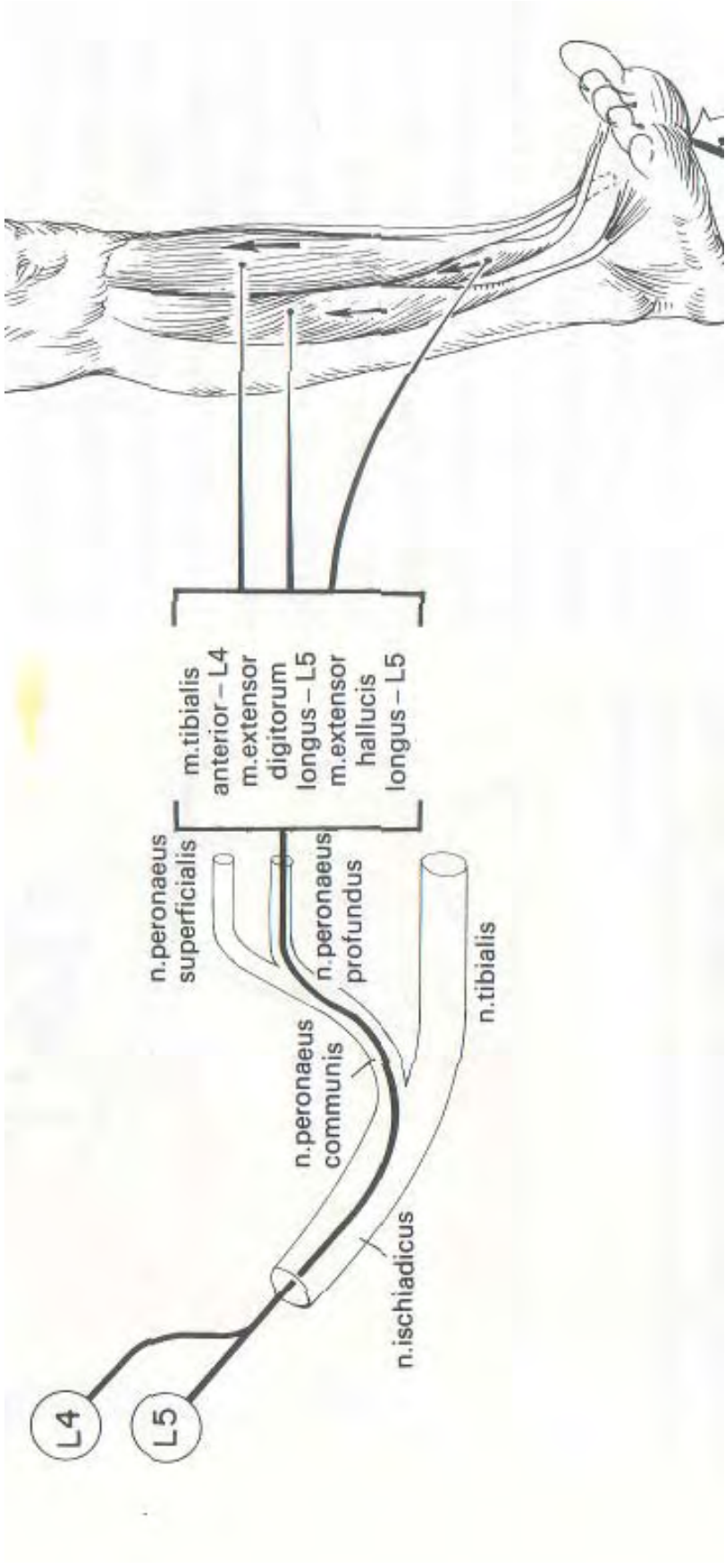


Hoppenfeld (1997)

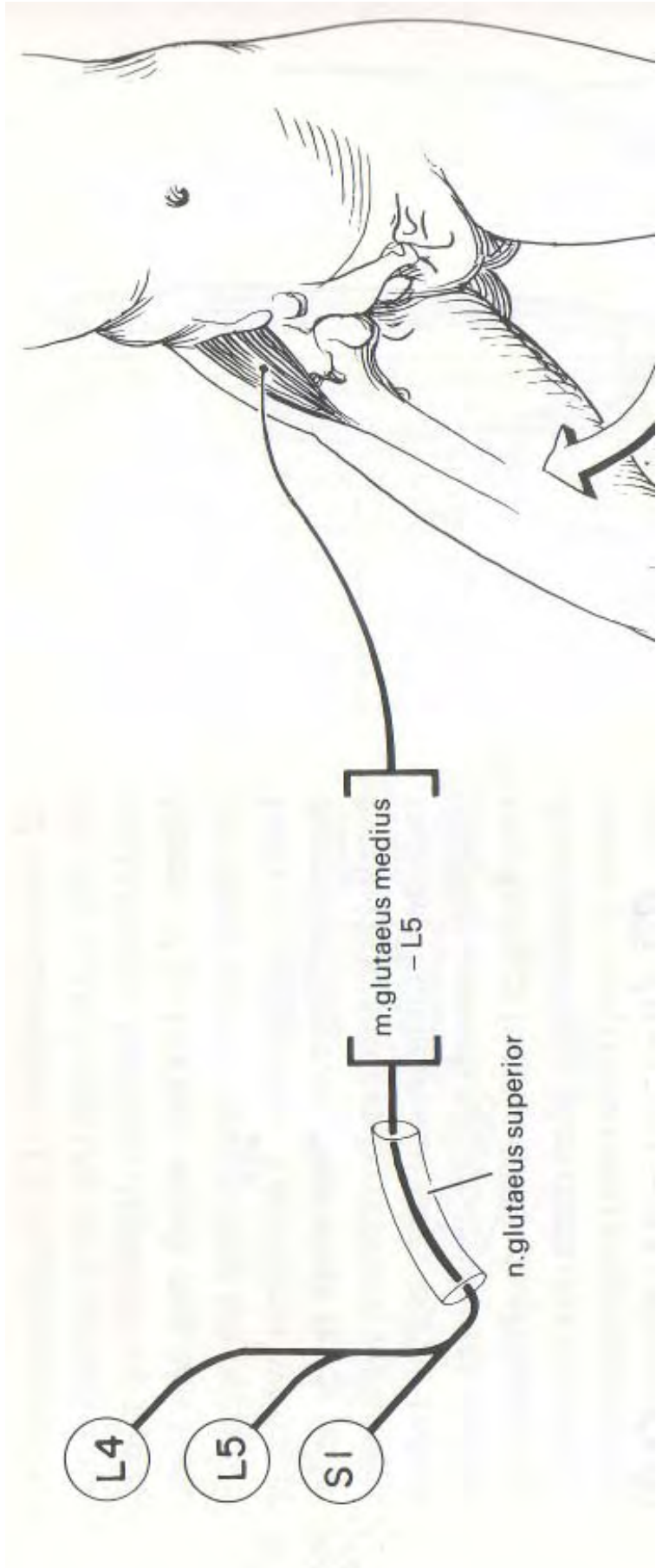


Hoppenfeld (1997)

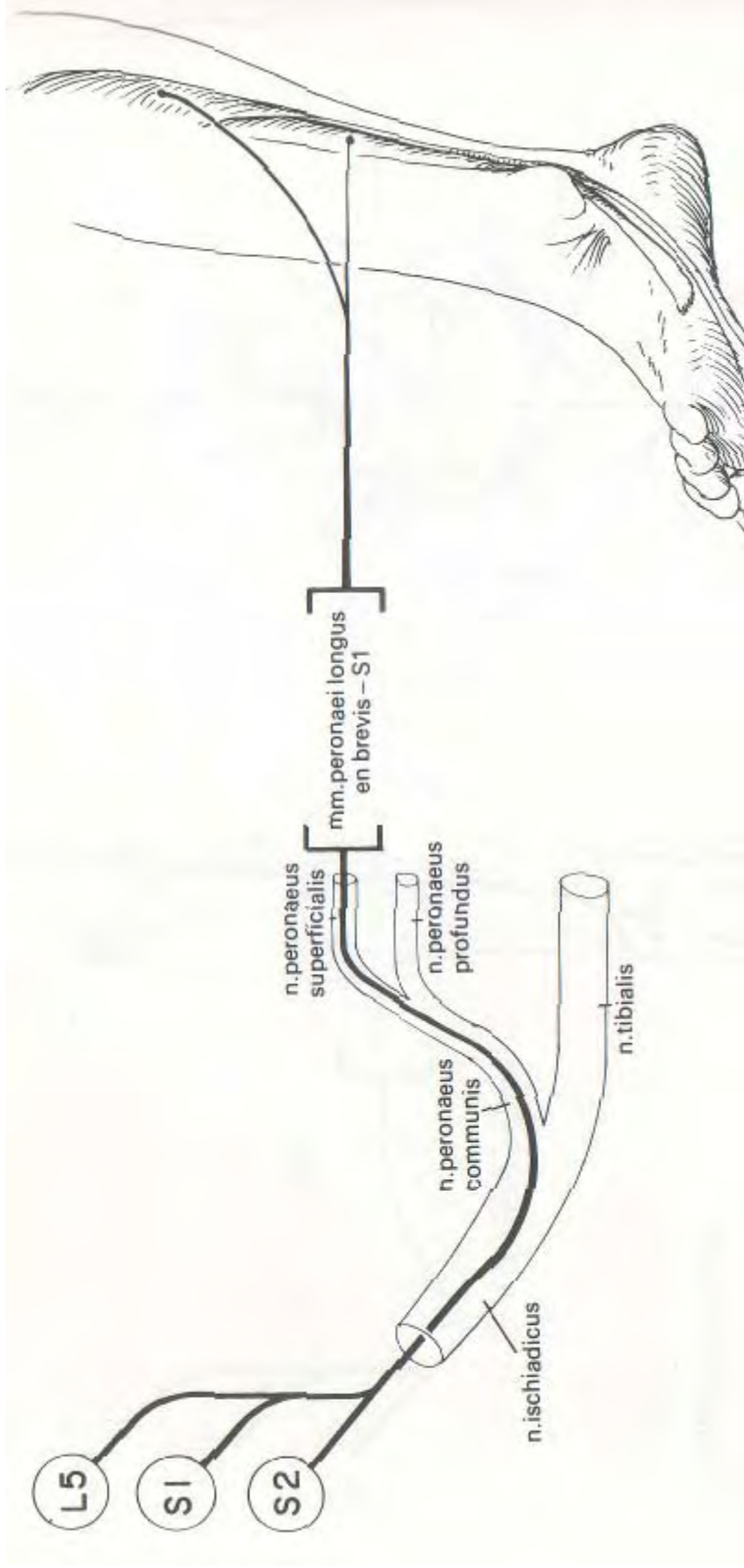


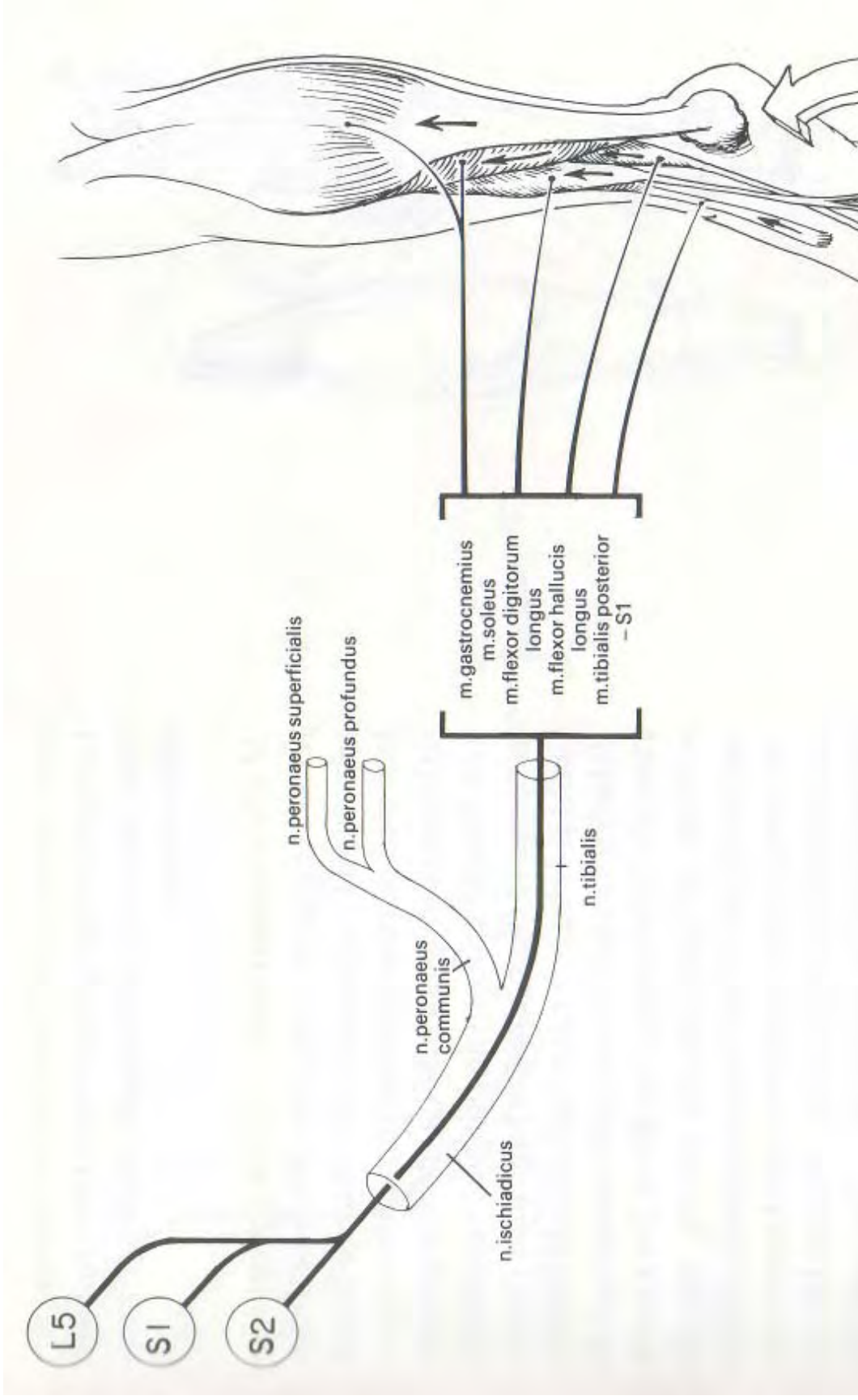


Hoppenfeld (1997)

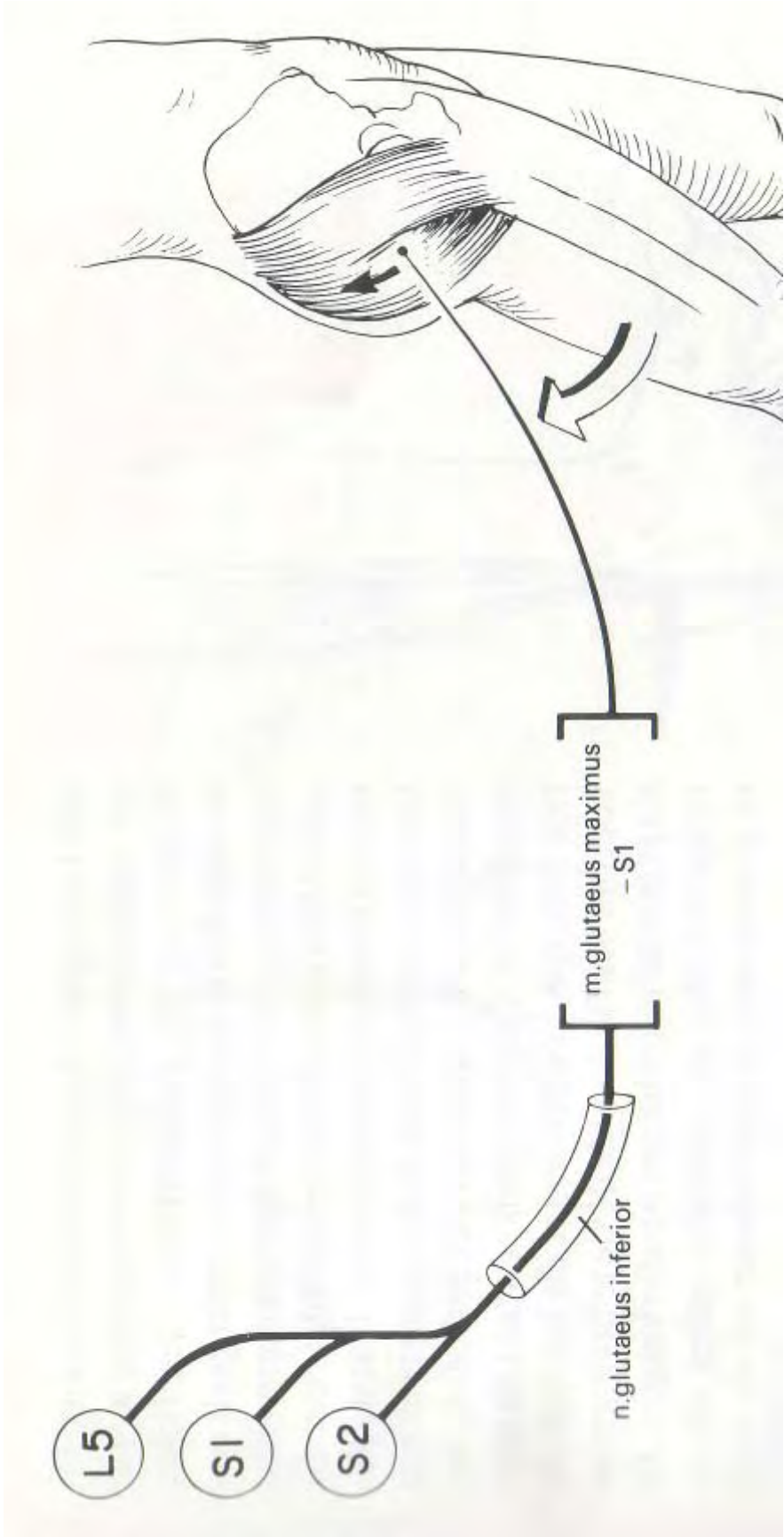


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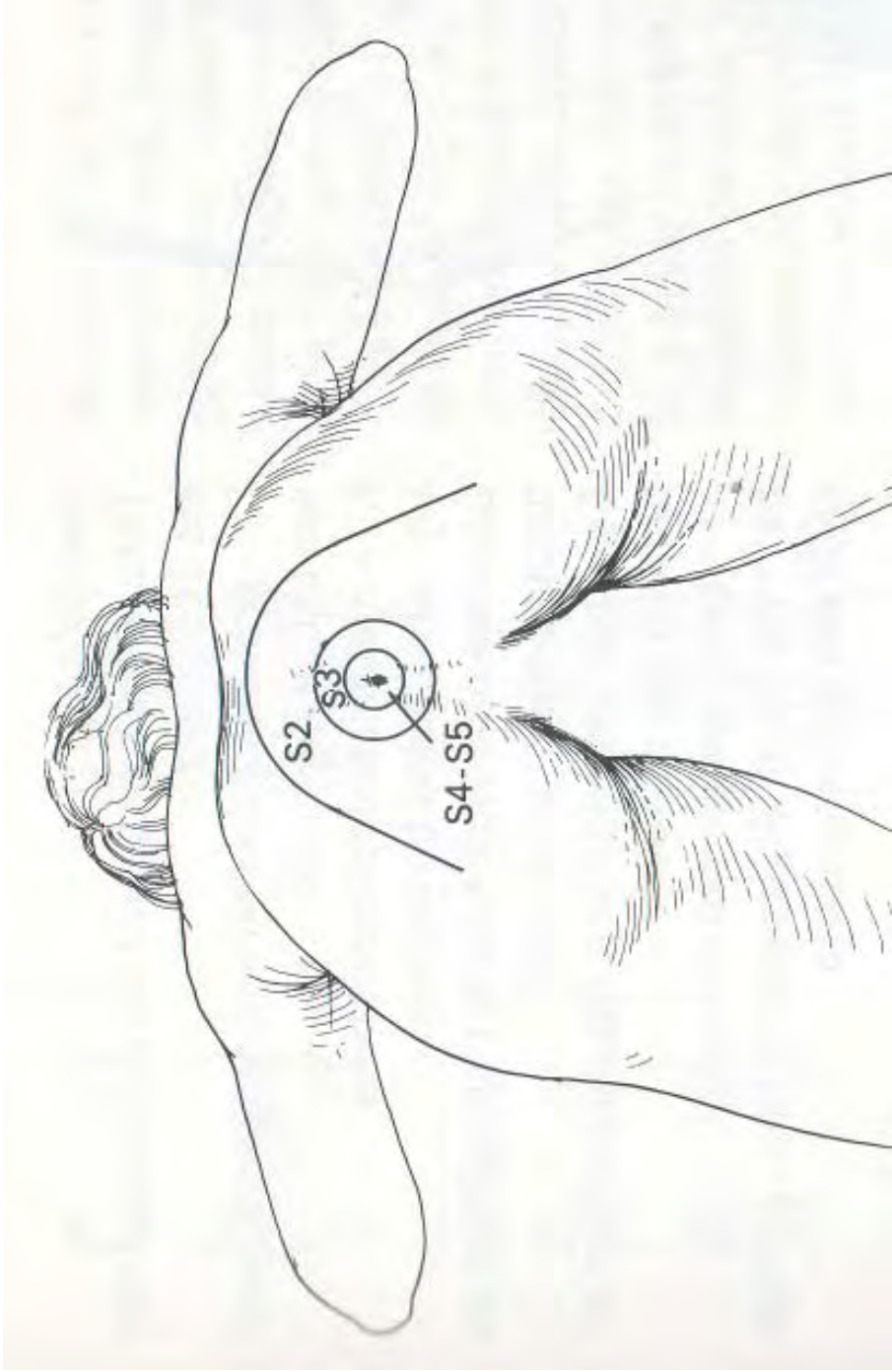




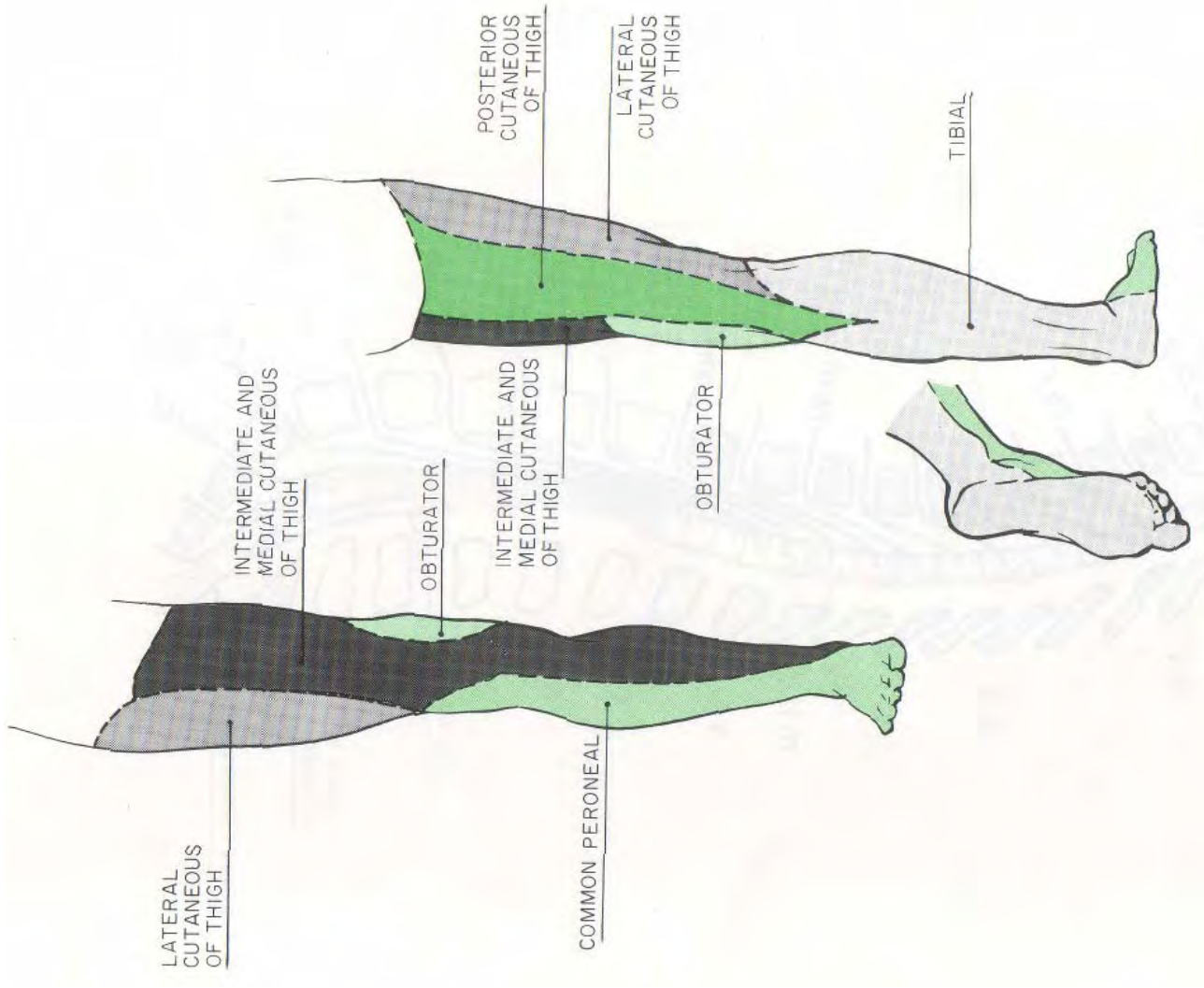
Hoppenfeld (1997)



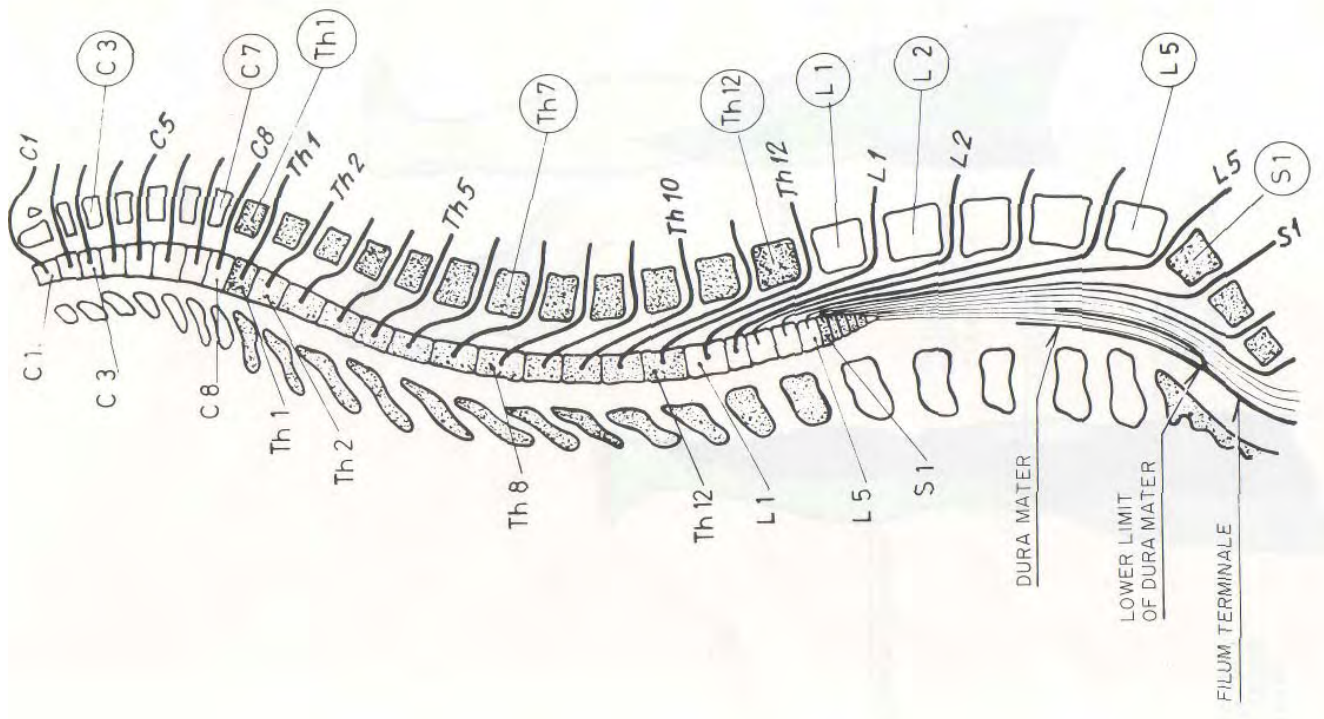
Hoppenfeld (1997)



Hoppenfeld (1997)



Conesa (1976)



Conesa (1976)



# Criteria for the Classification of Fibromyalgia<sup>a</sup>

## 1. History of widespread pain

*Definition.* Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine or anterior chest or thoracic spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.

## 2. Pain in 11 of 18 tender point sites on digital palpation.<sup>†</sup>

*Definition.* Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:

*Occiput:* bilateral, at the suboccipital muscle insertions.

*Low cervical:* bilateral, at the anterior aspects of the intertransverse spaces at C5-C7.

*Trapezius:* bilateral, at the midpoint of the upper border.

*Supraspinatus:* bilateral, at origins, above the scapula spine near the medial border.

*Second rib:* bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.

*Lateral epicondyle:* bilateral, 2 cm distal to the epicondyles.

*Gluteal:* bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.

*Greater trochanter:* bilateral, posterior to the trochanteric prominence.

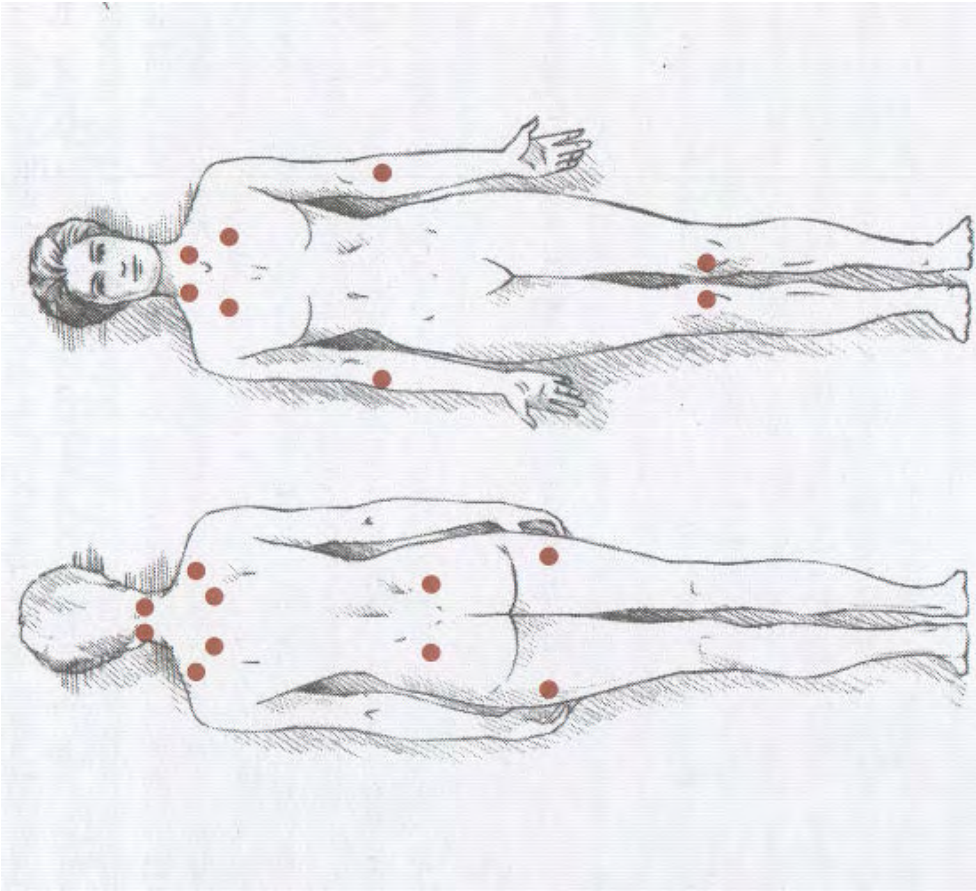
*Knee:* bilateral, at the medial fat pad proximal to the joint line.

**a) For classification purposes, patients will be said to have fibromyalgia if both criteria are Satisfied. Widespread pain must have been present at least 3 months. The presence of a second Clinical disorder does not exclude the diagnosis of fibromyalgia.**

Adapted from Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the multicenter criteria committee. *Arthritis Rheum* 1990;33:160-172, with Permission of the American College of Rheumatology.

**The location of the nine paired tender points that comprise the 1990 American College of Rheumatology criteria for fibromyalgia**

Digital palpation should be performed with an approximate force of 4 kg. For a tender point to be considered "positive", the subject must state that the palpation was painful. "Tender" is not to be considered "painful".



## Den gode ryggsamtalen

### Generelt

God klinisk kommunikasjon med pasienten (her kalt ”Den gode ryggsamtalen”) har generelt signifikant innvirkning på pasienttilfredshet, placeboeffekt, pasientens egenmestring, pasientens etterlevelse med hensyn til råd og behandling, prognose og klagesaker.

Det er vist at pasientens opplevelse av hva som er en god konsultasjon er knyttet til at behandleren viser empati, interesse og forståelse for pasientens plager og problemer inklusiv psykososiale aspekter (pasienten blir trodd og tatt på alvor). I tillegg til å bli lyttet til, er det viktig at pasienten får god og forståelig informasjon. Undersøkelser har også vist at psykiske og sosiale faktorer kan være viktigere enn organisk betingete smerteårsaker i ryggen når det gjelder fare for langvarige plager og uførhet.

### Vær pasientsentrert

Forskning har i tråd med dette vist at det i samtalen er viktig å få fram de tanker, følelser og forventninger pasienten selv har om prognose, årsaker, hvorfor det gjør vondt, tiltak for å bli bra og rask tilbakevending til jobb. Ryggpasienter som er langvarig plaget sier ofte at de kan leve med smertene, men ikke med usikkerheten forbundet med ryggtilstanden. Usikkerheten dreier seg om hva som feiler dem, hvorfor det gjør vondt, hvordan dette vil gå og hva som er den beste måten å bli bedre på. Tre norske undersøkelser hvor disse elementene er en del av behandlingsopplegget dokumenterer effekt på tilbakevending til jobb.

Hensikten med å fokusere på psykososiale faktorer bør være å stimulere pasienten selv til å oppdage og erkjenne mulige sammenhenger og interaksjoner mellom kropp, psyke og livssituasjon. Vi vil imidlertid også her sterkt understreke at å drøfte psykiske og sosiale faktorer ikke må bære bud om bagatellisering av smertene og/eller at biomekaniske forhold ikke er av betydning. Signaler om at den vonde ryggen ”bare er psykisk” eller ”bare skyldes en vanskelig livssituasjon” (negativ psykologisering av plagene) har ingen plass i god pasientkommunikasjon. Eventuelle tiltak bør diskuteres ut fra en omforent og ikke behandler-diktert forståelse. En forklaring som er forståelig for pasienten ( gjerne med bruk av modeller) på hvorfor det gjør vondt er også generelt et positivt kommunikasjonsmoment.

Det er viktig å få fram hva andre behandlere har fortalt er galt med ryggen og hva de har sagt er riktig behandling, og eventuelt få fram pasientens forklaring på hva tidligere røntgenfunn har vist. Pasientene har ofte hørt ulike versjoner fra ulike behandlere. Dette kan bidra til usikkerhet og manglende tro på at noe kan gjøres.

### Avdramatisering og trygghetsskapende informasjon

Det er også viktig å avdramatisere og si direkte (hvis det er belegg for det) at ryggsmertene ikke er farlige, og at det ikke finnes holdepunkter for at annen sykdom ligger bak (ingen ”røde flagg”). Det beste for ryggen er å være i normal aktivitet, og at en viss smerteforverring er naturlig i begynnelsen. Videre er det viktig å klargjøre at smerter kan fortsette i ryggen selv om det ikke lenger foreligger tegn til skade eller sykdom. Økt følsomhet i mellomvirvelskiver, ledd og stramme muskler kan vedlikeholde smertene en tid. Til å begynne med bør pasientene oppfordres til å øke funksjonsnivået til de krav hverdagen stiller. Først når dette er oppnådd, vil ofte smertene gradvis avta.

”Den gode ryggsamtalen” er trygghetsskapende for pasienten og bør lede til at pasienten skjønner hvorfor det gjør vondt og at det ikke er noe farlig.

### **Ved langvarig forløp/fare for kronisitet ("gule flagg")**

Initialt i forløpet vil det ofte være naturlig med hovedfokus på biomekaniske forhold. Hvis forløpet trekker ut (mer enn 4-6 uker uten tilfredsstillende bedring) bør det rettes mer oppmerksomhet mot potensielle betydningsfulle psykososiale faktorer. Imidlertid må det understrekes at det ennå mangler gode RCTs og systematiske oversikter (med enkelte unntak ) på betydningen av intervensjoner rettet mot "gule flagg".

Psykososiale risikofaktorer kan være:

- Fortsatt engstelse for at ryggplagene er noe farlig
- Psykiske plager før ryggsmertene
- Påvisbar angst og depresjon (eventuelt maskert depresjon), somatisering
- Sosiale belastninger i familie eller trivselsproblemer på jobb
- Engstelse for å øke aktivitetsnivået
- Manglende tro på bedring og videre arbeidsevne
- Dårlig fysisk form, manglende fysisk aktivitet/trening

For hver måned pasienten er sykmeldt, jo mindre er sjansen for tilbakeføring til arbeid. (Etter 8 uker med sykefravær er sannsynlighet for tilbakevending til jobb redusert med 50%. Hvor hyppig den enkelte pasient må følges opp er ikke dokumentert, og bør være opp til behandlerens vurdering.

Til slutt: Gi pasienten brosjyren "Verdt å vite om vond rygg. Hva fagfolkene er enige om".



Original Article:

<http://www.mayoclinic.com/invoke.cfm?id=DS00516&dsection=8>

## Sciatica

### Treatment

For most people, sciatica responds well to self-care measures. You'll heal more quickly if you continue with your usual activities but avoid what may have triggered the pain in the first place. Although resting for a day or so may provide some relief, prolonged bed rest isn't a good idea. In the long run, inactivity will make your symptoms worse.

Here are conservative measures that you can take or that your doctor may suggest:

**Cold packs.** Initially, your doctor may suggest using cold packs to reduce inflammation and relieve discomfort. Wrap an ice pack or a package of frozen peas in a clean towel and apply to the painful areas for 15 to 20 minutes at least four times a day.

**Hot packs.** After 48 hours, apply heat to the areas that hurt. Use warm packs, a heat lamp or a heating pad on the lowest setting. If you continue to have pain, try alternating warm and cold packs.

**Stretching.** Initially, passive stretching exercises can help you feel better and may relieve compression, but avoid jerking, bouncing or twisting.

**Over-the-counter medications.** Pain relievers (analgesics) fall into two categories — those that reduce pain and inflammation and those that only treat pain. Nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen (Motrin, Advil, others) which help alleviate both discomfort and inflammation, are the most helpful for sciatica. Although they can provide real relief, NSAIDs have a "ceiling effect" — that is, there's a limit to how much pain they can control. If you have moderate to severe pain, exceeding the recommended dosage won't provide additional benefits. What's more, NSAIDs can cause side effects such as nausea, stomach bleeding or ulcers. If you take these medications, talk to your doctor so that you can be monitored for problems. In addition, periodically re-evaluate whether you still need NSAIDs. Exercise, stretching, massage and other nondrug treatments can often provide the same benefits without side effects.

**Prescription drugs.** In some cases, your doctor may prescribe an anti-inflammatory medication along with a muscle relaxant. Tricyclic antidepressants, such as nortriptyline (Aventyl, Pamelor) or amitriptyline (Elavil) and anticonvulsant drugs, such as gabapentin (Neurontin), also may be prescribed for chronic pain. They may help by blocking pain messages to the brain or by enhancing the production of endorphins, your body's natural painkillers.

**Physical therapy.** If you have a herniated disk, physical therapy can play a vital role in your recovery. Once acute pain improves, your doctor or a physical therapist can design a rehabilitation program to help prevent recurrent injuries. Rehabilitation typically

includes exercises to help correct your posture, strengthen the muscles supporting your back and improve your flexibility. Your doctor will have you start physical therapy, exercise or both as early as possible. It's the cornerstone of your treatment program and should become part of your permanent routine at home.

**Regular exercise.** It may seem counterintuitive to exercise when you're in pain, but the fact is that regular exercise is one of the best ways to combat chronic discomfort. Exercise prompts your body to release endorphins — chemicals that prevent pain signals from reaching your brain. Endorphins also help alleviate anxiety and depression, conditions that can make your pain more difficult to control. What's more, combining aerobics with strength training and exercises that maintain or improve flexibility can help prevent age-related degenerative changes in your back. If you're new to exercise, start out slowly and progress to at least 30 minutes most days. To prevent injury, consider learning proper weight lifting techniques from a certified personal trainer, fitness specialist or physical therapist.

When conservative measures don't alleviate your pain within a few months, one of the following may be an option:

**Epidural steroid injections.** In some cases, your doctor may inject a corticosteroid medication into the affected area. Corticosteroids mimic the effects of the hormones cortisone and hydrocortisone, which are made by the outer layer (cortex) of your adrenal glands. When prescribed in doses that exceed your natural levels, corticosteroids suppress inflammation, thereby relieving pressure and pain. Their usefulness in treating sciatica is a matter of debate, however, and they seem most effective when used in conjunction with a rehabilitation program. In addition, corticosteroids can cause serious side effects, so the number of injections you can receive is limited — usually no more than three in one year.

**Surgery.** This is usually reserved for times when the compressed nerve causes significant weakness or you have pain that gets progressively worse or doesn't improve with other therapies. Surgery is most often performed to remove a portion of a herniated disk that's pressing on a nerve, a procedure called discectomy. Ideally, most of the disk is left intact to preserve as much of the normal anatomy as possible. Sometimes a surgeon will perform this operation through a small incision while looking through a microscope (microdiscectomy). Success rates of standard discectomy and microdiscectomy are about equal, but you're likely to have less pain and to recover more quickly with microdiscectomy. Possible complications for either type of disk surgery include bleeding, infection, injury to the nerves or spinal cord, scarring and the risks of anesthesia. What's more, although you may experience immediate results from disk surgery, it doesn't stop degenerative changes and your pain may recur in time.

By Mayo Clinic staff

DS00516

April 21, 2004

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## LUMBALT SKIVEPROLAPS

### Undersøkelser:

- Rtg. LS kolumna
- CT. LS kolumna
- Radikulografi
- MR. LS kolumna

### Operasjonsvurdering:

1. Konservativ behandling i 4-8 uker gir ingen/liten effekt. Alvorlig invalidiserende smerte distalt for knenivå i definert nerverot område. Positiv Laseque med eller uten nevrologisk funn. Smerteutstråling ved testing samsvarer med beskrevet radikulopathi. Utredningsfunn (CT/MR/Radikulografi) samsvarer med kliniske funn.
2. Tidligere intervensjon kreves ved økende intens isjias-smerter under den konservative behandlingsperioden. Rask behandling kreves ved pareseutvikling i underekstremitetene.
3. Akutt intervensjon ved Cauda Equina syndrom, dvs. ved nedsatt sensibilitet perianalt, vannlatningsforstyrrelser, sphinkterparese og rask utvikling av pareser i underekstremitetene.

### Operasjonsprosedyre (Mikroteknikk):

- Peroperativ AB med Keflin 2g iv ved innledning av anestesi.
- Intubasjonsnarkose. Kne-albue leie.
- Preoperativ markering av nivå med gjennomlysning.
- Lokalbedøvelse i hud med adrenalin.
- 3 cm hudsnitt på aktuell side.
- Lumbodorsal fascie åpnes bueformet og hængles medialt. M. Multifidus løses fra prosessus spinosi.
- Caspar haker i såret. Mikroskop innstilles.
- Lig. Flavum insidieres med kniv og ekstirperes ved hjelp av stansetang.
- Partiell arcotomi utføres om nødvendig.
- Nerverot mobiliseres medialt.
- Frie prolaps ekstirperes med prolapsstang. Skiven sonderes og tømmes dersom det fortsatt er skivebukning eller løse fragmenter igjen i skiven.
- Subligamentære prolaps ekstirperes og skiven tømmes.
- Nerveroten skal nå forløpe fritt i rotkanalen. Rotkanalen bites opp hvis det foreligger sideleddsartrose og recesstenose i tillegg til prolapsset.
- Såret skylles med NaCl
- Såret lukkes lagvis, dren er sjelden nødvendig.

### Komplikasjoner:

Peroperative: Blødning. Durarift. Nerveskade.

Postoperative: Hematom. Sårinfeksjon. Diskitt.

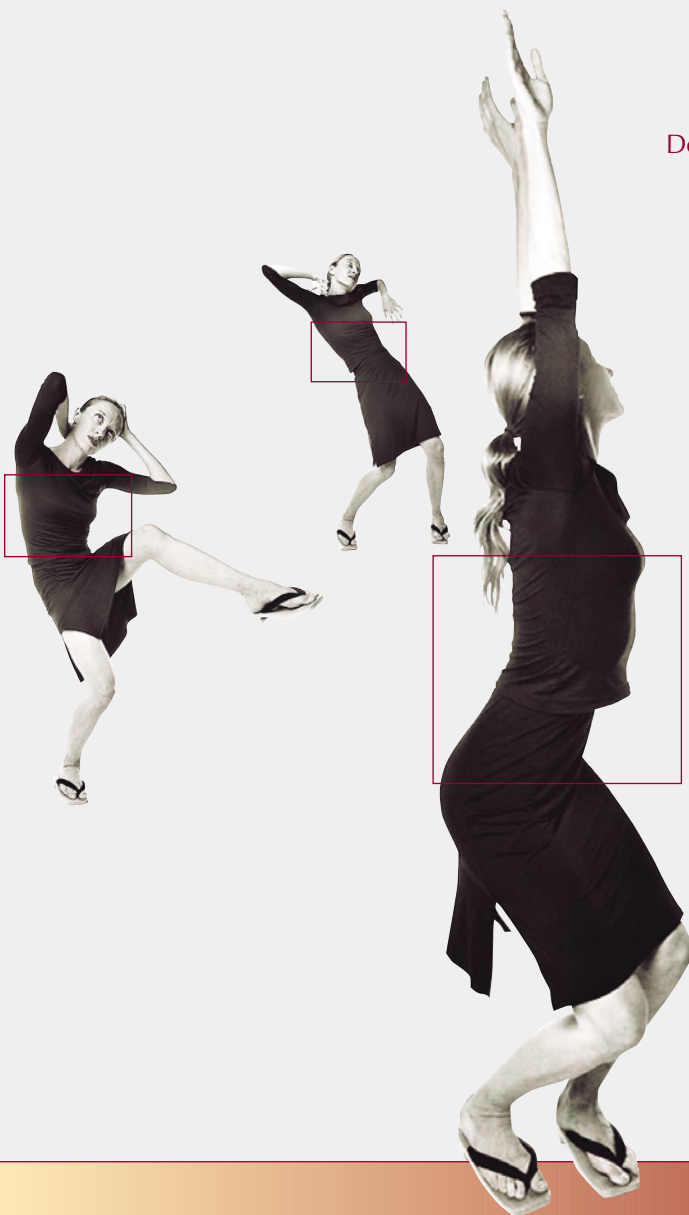
### Oppfølging:

Mobilisering 1. postoperative dag ved hjelp av fysioterapeut. Utskrives 1.-3. postoperative dag. Ryggskole 4-6 uker postoperativt. Poliklinisk kontroll etter 3 måneder.

# Verdt å vite om **vond rygg**

## Hva fagfolk er enige om

Denne brosjyren er laget for deg som har akutte ryggplager.



- Forekomst
- Hvordan ryggen er bygget opp
- Årsaker og hvorfor det gjør vondt
- Hva du kan gjøre selv
- Når oppsøke hjelp
- Hva behandlerne kan bidra med
- Utsiktene til å bli bra igjen

Brosjyren bygger på oppdatert kunnskap fra forskning og hva fagfolk er enige om. Ansvarlig for brosjyren er Nasjonalt ryggnettverk - Formidlingsenheten.

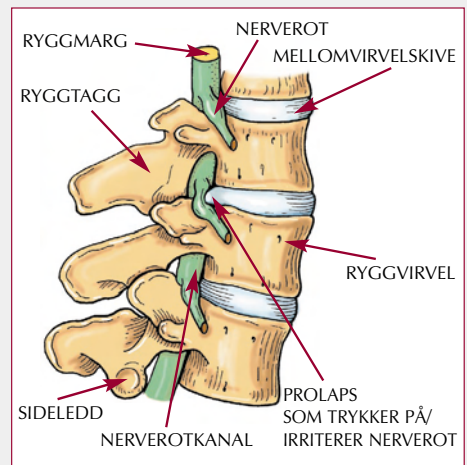


## Hvor utbredt er ryggplager?

Smerter i ryggen er svært vanlig. 60-80% av befolkningen får ryggsmarter en eller flere ganger. Over en 12 måneders periode har ca. 50% hatt plager og til enhver tid angir 8-15% at de har vondt i ryggen. Dette er altså en folkeplage. Ryggplager kan være akutte eller kroniske. Akutt betyr at smertene varer i mindre enn tre måneder, og mange opplever flere episoder med akutte ryggsmarter i løpet av livet. Denne brosjyren handler om slike ryggplager.

## Hvordan er rygg søylen bygget opp, og hvilke forandringer skjer med årene?

Ryggen er i utgangspunktet sterk og tåler mye. Den gjør at vi kan bevege oss oppreist og beskytter nervefibrene i ryggmargen. Den består av 7 virvler i nakken, 12 i brystdelen og 5 i korsryggen. Mellom virvlene er det bruskskiver med et mykt materiale i midten som fungerer som en "støtpute". Mellom hver virvel finnes sideledd ("styringsledd") som tillater bevegelser og sørger for stabilitet. Flere lag muskler er viktig for stabilitet og bevegelighet. Med årene skjer det normale aldersforandringer, særlig i bruskskivene. De blir lavere og kan få sprekker. I blant kan innholdet i midten av bruskskivene presses ut gjennom slike sprekker og trykke på en eller flere nerve-røtter i rygg- eller nervekanalen. Utpresset skiveinnhold kalles prolaps. Opptil 35% av oss har imidlertid prolaps uten at det gjør vondt.



## Hva er årsakene?

Oftest vet vi ikke med sikkerhet hvorfor den enkelte får ryggplager. Følgende kan være av betydning (men vanligvis er sammenhengene svake): tunge løft og vridninger eller ensidig kroppslig arbeid; dårlig fysisk form og inaktivitet over tid; mistrivsel og problemer på jobb eller hjemme, og arvelig disponering. Ofte er det en kombinasjon av flere årsaker.

## Hvordan oppstår smertene?

Vi kan i de fleste tilfeller ikke slå fast nøyaktig hvor smertene kommer fra. Som oftest dreier det seg om helt ufarlige tilstander, ofte kalt lumbago eller hekseskudd. Det kan imidlertid gjøre svært vondt. I noen tilfeller kan rifter eller sprekker i mellomvirvelskiven irritere små nerveender i ytterkant av skiven. Det kan også være prolaps, med trykk på og irritasjon av en nerverot. I en for trang nerverotkanal kan nerveroten komme i klem på grunn av slitasje og aldersforandringer (særlig rundt sideleddene). Ofte vil musklene "knyte seg" og bli vonde.

I sjeldne tilfeller kan det være annen (og mulig alvorlig) sykdom som ligger bak, f.eks. brudd i ryggen, svulster eller infeksjoner/revmatisk betennelse. Dette omfatter bare noen få prosent.

Ut fra dette kan vi dele inn ryggplager på følgende måte:

1. Vanlige (uspesifikke) ryggsmarter eller lumbago (80-90%).
2. Nerverotsmerter med utstråling nedenfor kneet, oftest på grunn av prolaps eller trang nerverotkanal (10%).  
(Isjias er bare en betegnelse på smerter med utstråling langs hovednerven ned i foten.)
3. Mulig annen og sjelden sykdom (svulst, brudd, revmatisk sykdom) (1-5%).



## Hva kan du gjøre selv?

Følgende råd er basert på oppdatert forskning:

- 1.** Ryggens tilhelning stimuleres best ved å være mest mulig i normal aktivitet. Dagligdags aktivitet og jobb bør derfor gjenopptas så fort som mulig. Kanskje kan delvis eller aktiv sykmelding være en løsning. Det er ikke skadelig eller farlig om det gjør noe vondt når du er i aktivitet.
- 2.** Du bør ligge minst mulig. I blant kan smertene være så sterke at det er nødvendig å ligge (særlig ved nerverotsmerter), men pass da på at sengeleiet ikke blir langvarig. Sengeleie er i seg selv ikke behandling, og ryggen helbredes ikke av å ligge.
- 3.** Plagene kan ofte lindres effektivt med reseptfrie medisiner. Hvis du tar smertestillende midler bør disse tas med jevne mellomrom, f.eks. 3-4 ganger daglig.
- 4.** Prøv å ha en optimistisk holdning til at dette kommer til å gå bra og at det ikke er farlig. Sammen med fysisk aktivitet stimulerer det kroppens evne til å lege seg selv.

## Når oppsøke hjelp?

Selv om smertene er sterke er de sjelden uttrykk for noe alvorlig. Du bør imidlertid søke hjelp hvis:

- Du føler deg utrygg på hva det kan være
- Smertene er sterke og du ikke får nok hjelp av smertestillende tablettar eller ved avlastning av ryggen
- Du trenger sykmelding eller smertene ikke raskt blir bedre
- Du merker nedsatt muskelkraft
- Du får problemer med vannlatingen eller blir nummen i skrittet (dette kan skyldes stort prolaps som må opereres innen 24 timer)
- Du har hatt ufrivillig vekttap eller føler deg generelt syk

## Hva kan legen eller annen behandler gjøre?

Punktene nedenfor tilpasses individuelt:

- Undersøke deg for å finne ut om du har "vanlige ryggsmarter" eller nerverotsmerter på grunn av prolaps eller trange forhold i ryggen. Det må også utelukkes at du hører til den sjeldne gruppen med mulig alvorlig sykdom.
- I noen tilfeller er det nødvendig å ta blodprøver og henvise til røntgen. Men røntgen er ikke rutinemessig nødvendig, bortsett fra når smertene er nesten uforandret etter 4-6 uker. Dette gjelder både vanlig ryggvondt og nerverotsmerter/mistanke om prolaps. Røntgen kan bare påvise årsaker til ryggsmarter hos et mindretall. Dessuten skal du ikke utsettes for unødvendig røntgenstråling.
- Forklare hva slags tilstand du har og gi deg råd om hva du kan gjøre selv.
- Foreskrive tilstrekkelig smertestillende medisiner hvis vanlig paracetamol ikke er nok.
- Vurdere om du greier å være på jobben eller tilrettelegge den i samarbeid med arbeidsgiver. Delvis eller aktiv sykmelding kan være aktuelt. De som klarer å være i vanlig aktivitet, inklusiv jobb, blir fortere bra.



- Vurdere om du kan ha nytte av manipulasjonsbehandling hvis du ikke blir bedre etter ca. 1-2 uker. Slik behandling gis av kiropraktor eller fysioterapeut med spesialutdanning i manuell terapi. Behandlingen kan lindre smerte og gjøre at du fungerer bedre.
- Vurdere om det er nødvendig med operasjon hvis du har nerverotsmerter. Det gjelder bare noen få prosent, de fleste blir raskt bedre og har ikke behov for operasjon.
- Vurdere om det etter hvert (ca. 4-6 uker) blir nødvendig med øvelses- eller aktivitetsprogram hos fysioterapeut eller annen behandler.
- Følge opp med kontroller for å se at det går rett vei. Hvis du ikke klarer å gjenoppta vanlige aktiviteter, kan det bli aktuelt å ta opp livssituasjonen din. Kanskje noe utover ryggsmertene plager deg og er med å hindre at du blir frisk.
- Dersom du har betydelige, langvarige plager (mer enn 8-12 uker), kan det være aktuelt å henvise deg til ryggpoliklinikk eller spesialist.

## **Blir du bra igjen?**

De aller fleste med akutte ryggmerter vil, med eller uten behandling, være bra eller betydelig bedre etter få uker.

Har du nerverotsmerter tar det ofte lengre tid, kanskje flere måneder. Endel får tilbakefall i løpet av 1-2 år. Mange har litt vondt innimellom, uten at det betyr noe farlig eller unormalt. Kunsten er å lære seg å mestre plagene.

## Kan plagene forebygges?

Det er umulig å gi råd som passer for alle. Det finnes lite forskning på forebyggingstiltak. En del anbefalinger er likevel vanlige å gi, og kan oppleves nyttige for mange, særlig for å hindre tilbakefall:

- Prøv å hold deg i form gjennom lystbetont mosjon og variert aktivitet. Gjør noe som passer for deg. Ryggen er konstruert for å være i bevegelse, er i utgangspunktet sterk og tåler mye.
- Det er bra med 20-30 minutters daglig aktivitet som gange, sykling eller svømming.
- Unngå langvarig sitting, særlig når du har vondt.
- Mange har glede av øvelsesprogram med tøyninger og variert muskelaktivitet.
- Løft og bær bare det du vet du kan klare. Bær nært inntil kroppen.
- Prøv å gjør noe med en eventuell vanskelig arbeids- eller livssituasjon.
- Og husk: Trivsel og glede gjør også godt for ryggen!

## For deg som vil vite mer

Pasientinformasjonsbasen [www.rygginfo.no](http://www.rygginfo.no), som drives av Statens folkehelseinstitutt og pasientforeningen Ryggforeningen i Norge.

Nasjonalt ryggnettverks hjemmesider [www.ryggnett.no](http://www.ryggnett.no).

Den danske boka "Kort og klart om rygsmerter" av M. Jayson, Nyt Nordisk Forlag.

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Kommunenes Sentralforbund,

Norges teknisk-naturvitenskapelige universitet,

Norsk Ergoterapeutforbund, Norsk Forening

for Ryggforskning, Norsk Kiropraktorforening,

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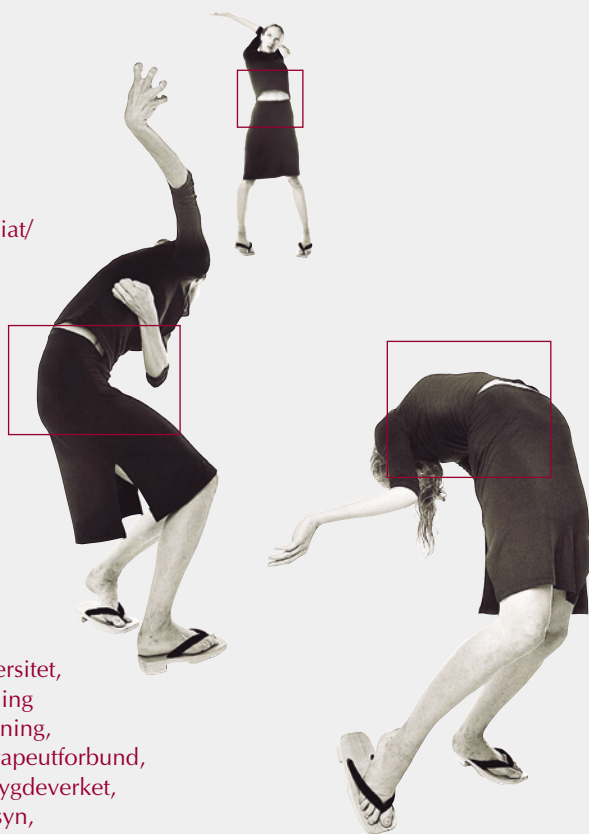
Næringslivets Hovedorganisasjon, Rikstrygdeverket,

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gruppen for Nasjonalt ryggnettverk, samt flere framtreddende  
ryggeksperter i Norge, Storbritannia og Nederland.



**Epidural sacral injection study**

**Prosedyrebok**

**Epiduralinjeksjon**



### **Guidance for the sacral epidural injection technique.**

1. The patient is given either two epidural sacral injections of 30 ml NaCl 0.9 % (volume), two epidural sacral injections of 29 ml NaCl 0.9 % + Kenacort 40 mg/ml 1 ml (volume+steroid) or 1 ml NaCl 0.9 % subcutaneously (placebo).
2. The patients are prone while they are given the injection. If necessary, a small cushion can be put beneath their abdomens to raise the pelvis slightly so that the anatomical structures are easier to identify (Sekiguchi et al, 2004). The injection is given via the sacral hiatus. An aseptic technique is used, and the area is washed thoroughly using Chlorhexidine 5 % before the injection is administered.
3. The recommendations given in “Recommendations on the use of epidural injections for the treatment of back pain and leg pain of spinal origin” (The Royal College of Anaesthetists and Pain Society, 2002) are adhered to in order to ensure the quality of the epidural injections.
4. 0.5 ml local anaesthetic (lidocaine hydrochloride 20 mg/ml) is first administered using a 1 ml syringe and a blue needle (23G 0.6 x 0.25 mm) in the area around the sacral hiatus. Five minutes after the skin anaesthetic, a Spinocan spinal needle (22G 0.73 x 88 mm) is inserted via the sacral hiatus and no more than 2 cm up into the epidural space. Following insertion of the needle, the stylet is removed to see if there is any spinal fluid present in the needle. Aspiration is carried out as a precaution to check for the presence of blood. If any spinal fluid is found, the procedure is discontinued. Another attempt can be made after two days. If aspiration shows the presence of any blood, the position of the needle is adjusted slightly and a new aspiration is carried out. If there is no blood, the procedure can continue, otherwise it is stopped. It can then be repeated after two days.

## Epidural sacral injection, Technique explained

5. A 30 ml syringe is used (Braun Omnifix Luer Lock), which is connected to the spinal needle. The injection is administered slowly over 10 minutes (3 ml/minute). There is continuous digital palpatory inspection over the sacrum to check that the injection is not being administered subcutaneously. If this palpatory check reveals that fluid is entering the subcutaneous region, the injection must be stopped. Careful aspiration is carried out regularly throughout the injection process. If there is any blood in the aspirate, and changing the position of the needle does not help, the injection must be stopped. Once the injection is completed, the spinal needle is removed and a plaster is applied to on the injection site.
6. During the injection procedure the patient might feel some pressure over the lumbar region and in the pelvic region. Occasionally there may also be some pain radiating out into the legs. If these pains become too intense, and the patient says that he or she cannot tolerate them despite a slow injection technique, the injection must be stopped.
7. After the injection, the patient continues lying in a prone position for ten minutes, and then for 15 minutes in a supine position. Before the patient leaves the treatment room, the anaesthetist must make sure there are no signs of acute complications and that the patient feels fine.
8. Verbal and written information is provided on what the patient should and should not do following the injection.

**Sekiguchi, M ; Yabuki, S ; Satoh, K ; Kikuchi, S (2004)** An anatomic study of the sacral hiatus: a basis for successful caudal epidural block.. *Clin J Pain Jan-Feb; 20(1):51-4*

**The Royal College of Anaesthetists (2002)** Recommendations on the use of epidural injections for the treatment of back pain and leg pain of spinal origin. *Bulletin 14, July 2002:695-97*

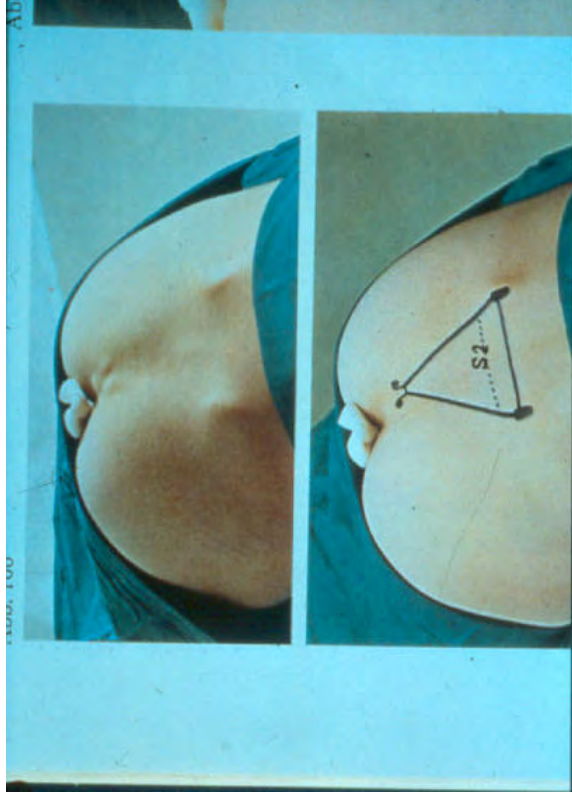
# Anatomy of the epidural space

- Virtual space in between to cylinders
- Inner cylinder = dura mater + dural sleeves
- Outer cylinder = spinal canal
- Closed by intercornual ligament
- Venous plexus



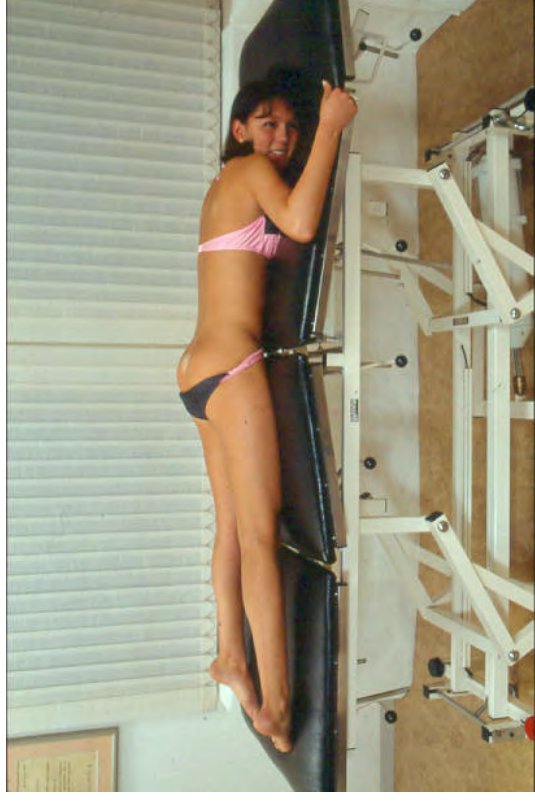
# Injection technique

- Points of references:
  - cornua sacralia
  - intercornual ligament



# Injection technique

- Positioning of the patient:
  - in kyphosis



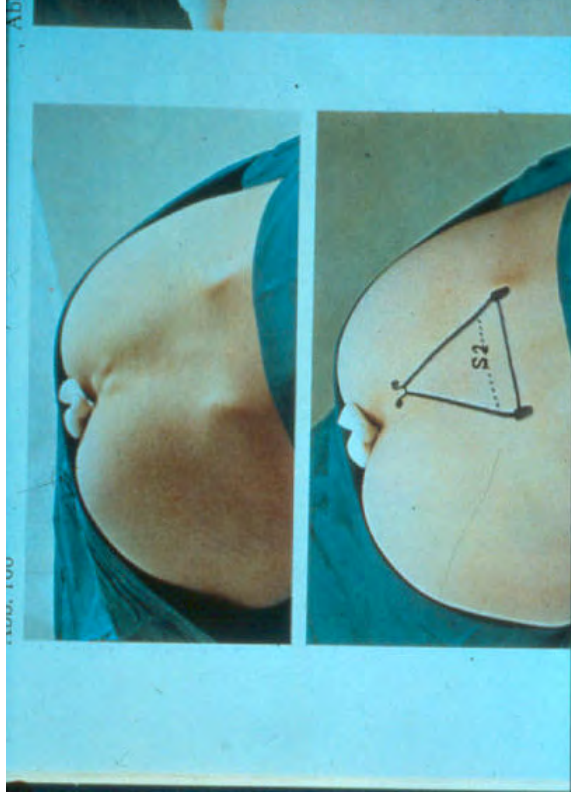
# Injection technique

- Positioning of the patient:
  - in kyphosis
  - hips in internal rotation



# Injection technique

- Positioning of the patient:
  - in kyphosis
  - hips in internal rotation
  - identifying points of reference



# Injection technique

- Positioning of the patient:
  - in kyphosis
  - hips in internal rotation
  - identifying points of reference





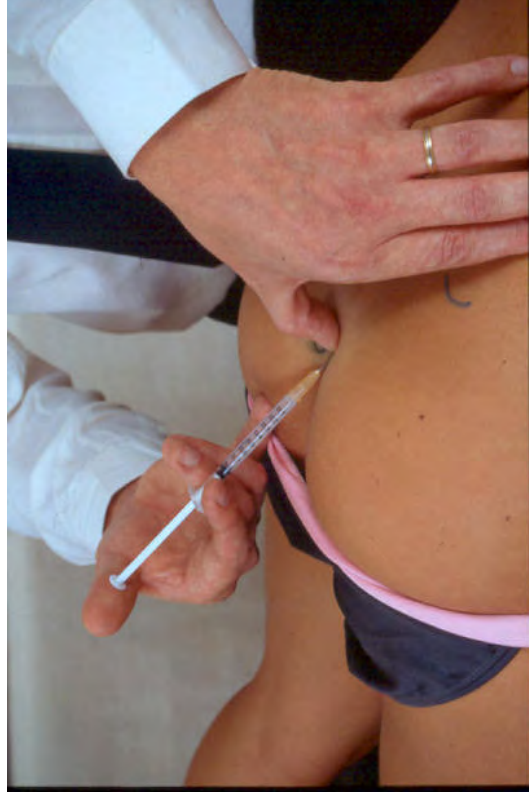
# Injection technique

- Positioning of the patient:
  - in kyphosis
  - hips in internal rotation
  - identifying points of reference



# Injection technique

- Shaving of the skin
- Desinfection of the skin
- Local anaesthesia of the skin and the intercornual ligament



# Injection technique

- Introduction of the spinal needle



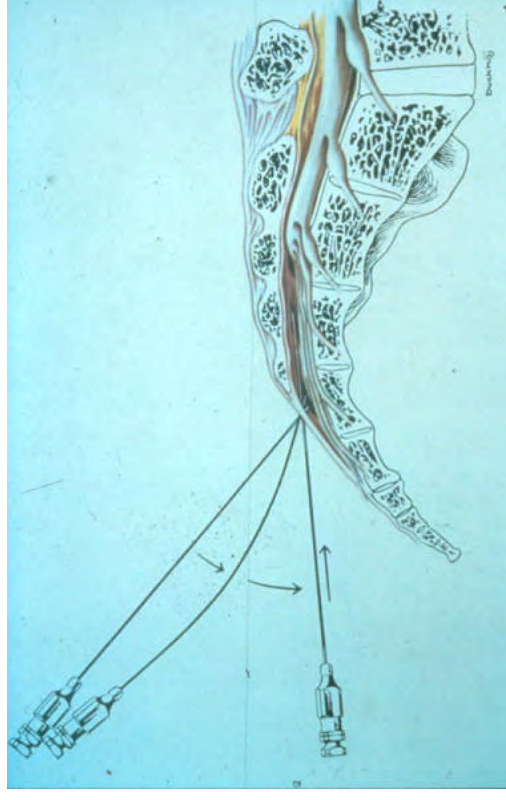
# Injection technique

- Introduction of the spinal needle
- Between the cornua



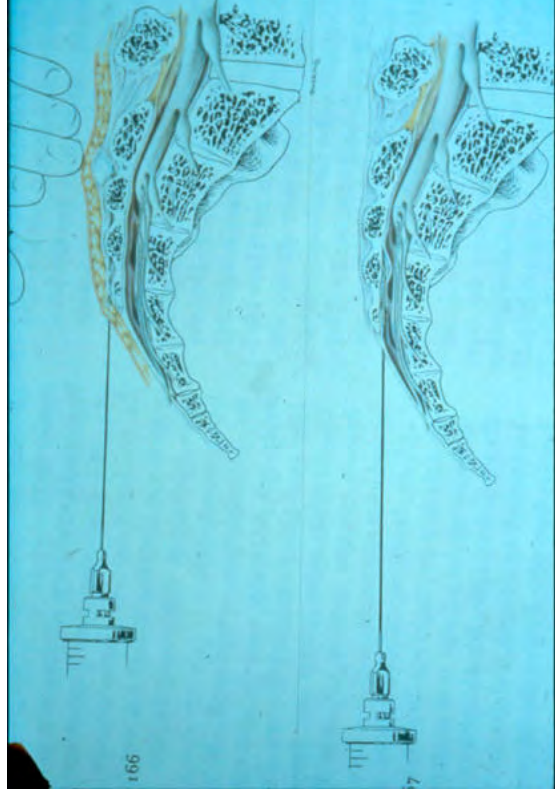
# Injection technique

- Introduction of the spinal needle
- Between the cornua
- Adapt direction to shape of sacrum



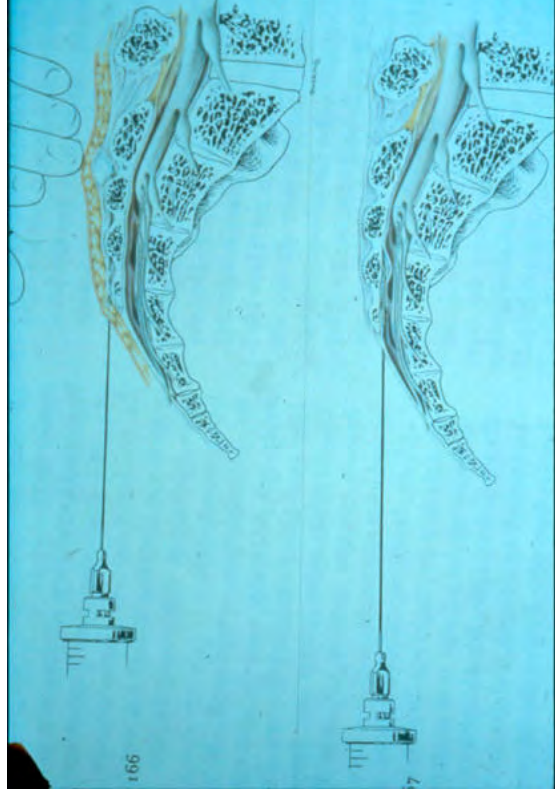
# Injection technique

- Introduction of the spinal needle
- Between the cornua
- Adapt direction to shape of sacrum
- Technical problems



# Injection technique

- Introduction of the spinal needle
- Between the cornua
- Adapt direction to shape of sacrum
- Removal of stylet:
  - blood ?
  - cerebrospinal fluid ?



# Injection technique

- Injection:
  - slowly
  - verbal contact
  - palpation of sacrum
  - regular aspiration
  - after injection: rest







# THE ROYAL COLLEGE OF ANAESTHETISTS AND THE PAIN SOCIETY

## Recommendations on the use of epidural injections for the treatment of back pain and leg pain of spinal origin (March 2002)

### Disclaimer

These recommendations are concerned with the competencies of doctors who perform epidural injections for the treatment of back pain and leg pain of spinal origin and with the clinical environment in which such injections are performed. The recommendations do not endorse or recommend the use of any particular medication or product for epidural injection. The choice of medication or product for epidural injection is the responsibility of the individual practitioner. The organisations involved in the preparation of these recommendations, including the Royal College of Anaesthetists and The Pain Society, take no responsibility legal or otherwise for the choice by an individual practitioner of a medication or product used for epidural injection.

### Introduction

- 1 The General Medical Council advises doctors that they must 'make the care of your patient your first concern.' General Medical Council *Good Medical Practice* May 2001.
- 2 The desire to improve safety for patients receiving epidural injections reflects the evolution of professional standards in all areas of medical practice. Doctors must strive to provide the best possible care and safest treatment for all patients by reducing risk to an absolute minimum.
- 3 Historical precedent and tradition can no longer be regarded as justification for practices that are perceived to fall below the standards acceptable to a responsible body of doctors. If one patient is harmed by sub-standard practice then that is one too many.
- 4 The Royal College of Anaesthetists always encourages safe practice. It is the desire of the College to have safe practice adopted by all doctors who perform invasive treatment near the spinal cord and near potential sources of infection. This includes the anus and perineum in addition to obvious skin lesions.
- 5 The recommendations refer to 'single-shot' epidural injections that are performed by either the lumbar or caudal routes. The risks are similar with the two routes. There may be an increased risk of infection with the caudal approach because it is closer to potential sources of infection.
- 6 The recommendations do not refer to the insertion of indwelling epidural catheters.
- 7 The injection of local anaesthetic (whether amide or ester) is associated with specific risks. Additional precautions are necessary for patients who receive epidural local anaesthetic injections. In some techniques relatively large volumes of local anaesthetic are injected thereby delivering a large dose of the active drug even though the concentration is low.
- 8 The use of local anaesthetic for epidural injection is associated with the risk of inadvertent intrathecal injection leading to a 'total spinal' or of inadvertent intravenous injection resulting in local anaesthetic toxicity. These serious untoward incidents may occur during either lumbar or caudal injection. Both clinical situations are life threatening and require immediate resuscitation.
- 9 The recommendations do not address any issues concerning the evidence for effectiveness of epidural injections (including epidural steroid injections) in the management of back and leg pain. For an analysis of the evidence, and of long term safety, see:
  - a National Health and Medical Research Council of Australia. Epidural use of steroids in the management of back pain and sciatica of spinal origin. Canberra, NHMRC, 1994.
  - b Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesthesia and Intensive Care* 1995;23:564-569.
  - c Koes BW, Scholten RJ, Mens JM, Bouter LM. Efficacy of epidural steroid injections for low-back pain and sciatica: a systematic review of randomised clinical trials. *Pain* 1995;63:279-288.
  - d Abram SE, O'Connor TC. Complications associated with epidural steroid injections. *Regional Anesthesia* 1996;21:149-162.
  - e McQuay H, Moore A. An evidence-based resource for pain relief. Oxford: Oxford University Press, 1998:216-218.
  - f van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic non-specific low back pain. *Spine* 1997;22:2128-2156.

## Recommendations

- 1** Doctors in training should possess defined competencies before performing epidural injections unsupervised (see Explanatory note **a**).
- 2** Established practitioners in non-training grades must ensure that they possess the competencies defined for trainees if they wish to perform epidural injections and/or train others (see Explanatory note **b**).
- 3** Any doctor who performs epidural injections at the request of another doctor must be aware that the doctor who performs the injections will be held wholly or jointly responsible for any adverse outcomes of the injections. The doctor who undertakes the procedure must possess the defined competencies or receive appropriate supervision. The doctor who undertakes the procedure must be satisfied that the indications for the injection are appropriate and that there are no contraindications to epidural injection.
- 4** All doctors who perform epidural injections must be competent in resuscitation (see Explanatory note **c**).
- 5** The process of obtaining consent from the patient before an epidural injection is performed must comply with the current guidance published by the General Medical Council and the Department of Health. The doctor who obtains consent, if he or she is not the person who carries out the epidural injection, must be suitably trained and qualified, must have sufficient knowledge of the proposed treatment, and must understand the risks involved. It is the responsibility of the doctor, or doctors, who prescribe and perform the injection to decide what to explain to the patient if any drug is being used for an indication and by a route that is not recommended in the product information sheet or drug licence.
- 6** Epidural injections must be performed using an aseptic technique. This should include: hand washing, sterile gloves, hat, mask, skin preparation and sterile drapes around the injection site. Normally a sterile gown should be included as a part of the aseptic technique.
- 7** Epidural injections must be performed in a setting that provides appropriate monitoring and resuscitation facilities. If local anaesthetic is to be injected there must be immediate availability of full resuscitation equipment and the presence of a skilled assistant for the operator. Minimum monitoring during the performance of an injection containing local anaesthetic should include regular measurement of blood pressure and pulse oximetry (see Explanatory note **d**).
- 8** Epidural injections for the treatment of back pain and leg pain of spinal origin should not be performed without good reason on a *patient whose conscious level is depressed (as a result of anaesthesia or sedation)*, or a patient who cannot communicate (as a result of mental health problems or language difficulties).
- 9** If local anaesthetic has been injected into the epidural space the minimum monitoring after injection should include regular measurement of pulse rate and blood pressure every five minutes for the first 30 minutes. Oxygen saturation should be monitored during recovery if sedation has been used during the procedure. If local anaesthetic has been injected into the epidural space there should be assessment of lower limb motor power and of ability to pass urine before discharging the patient (see Explanatory note **e**).
- 10** There must be contemporaneous records of the consent for the procedure, of the technique used and of the physiological monitoring before, during and after the procedure.
- 11** Following discharge the patient must be able to contact a member of the team should a problem arise in the immediate post-injection period.
- 12** Follow-up should be arranged with the person who performed the injection or with another member of the team who has responsibility for the patient's ongoing care and has access to the patient's records. The timing of this follow-up will depend upon clinical circumstances but normally should occur no later than six weeks after the injection.

### Explanatory notes

- a** Competence describes possession of the knowledge, skills and attitudes required to undertake safe clinical practice at a level commensurate with the grade of the doctor. For epidural injections the following competencies apply:

#### *Knowledge*

Applied anatomy, pathology and clinical characteristics of acute and chronic spinal pain and radicular pain, interpretation of investigations such as CT and MRI scans, pharmacology of drugs injected into the epidural space, indications, contraindications (including coagulopathies, anticoagulant medication and local infection at the proposed site of injection), evidence of benefit, potential risks and complications.

## ii Skills

Performance of caudal epidural injection, performance of lumbar epidural injection. (Some practitioners may confine their skills to caudal epidural injection.)

Identification of the epidural space. Recognition of incorrect needle placement. Recognition of dural puncture. Perioperative management of patient. Management of complications.

## iii Attitudes

Ability to select appropriate patients. Ability to communicate with patients and to offer appropriate information. Gentle handling of patient throughout treatment.

It is important to note the standards set by CNST (Clinical Negligence Scheme for Trusts). From 1 October 1999 the CNST requires that all medical staff in training when taking up a new post are given by their supervisor a list of the technical skills they are expected to be able to perform. The trainees must indicate their competence to perform the specified tasks. A supervised training programme must rectify any deficiencies in initial, or continuing, competence.

- b** This is a matter of responsibility for the individual practitioner and also for the institution in which that practitioner performs epidural injections.
- c** Resuscitation skills must be appropriate for the type of epidural injection. The injection of local anaesthetic carries the risk of inadvertent intrathecal or intravascular injection. Both these situations require an advanced level of resuscitation skills. Competence in resuscitation includes:

## i Knowledge

Resuscitation guidelines of Resuscitation Council (UK). Causes of cardiac arrest during epidural injections. Clinical features of local anaesthetic toxicity. The factors relating to brain injury at cardiac arrest. Factors influencing the effectiveness of cardiac compression. Drugs used during cardiopulmonary resuscitation (CPR) (adrenaline, atropine, lignocaine, calcium, magnesium, sodium bicarbonate). The ethics of CPR. Record keeping at CPR.

## ii Skills

Able to recognise total spinal, local anaesthetic toxicity, cardiac and respiratory arrest. Able to perform cardiac compression. Able to manage the airway during CPR: using expired air breathing, bag and mask, laryngeal mask and endotracheal intubation. Able to perform CPR either single-handed or as a member of a team. Able to use a defibrillator. Able to interpret arrhythmias causing and associated with cardiac arrest. Able to perform resuscitation sequences for ventricular tachycardia, ventricular fibrillation, asystole, EMD (electromechanical dissociation). Able to move a patient into the recovery position.

## iii Attitudes

Desire to offer the best possible chance of survival. Able to organise ongoing care after resuscitation.

- d** The use of local anaesthetic for epidural injection is associated with the risk of inadvertent intrathecal injection leading to a 'total spinal' or of inadvertent intravenous injection resulting in local anaesthetic toxicity. Both clinical situations are life threatening and require immediate resuscitation. The skilled assistant should be a doctor, nurse or operating department assistant who has undergone training in resuscitation and has kept up to date in resuscitation skills appropriate for the potential clinical situation.
- e** The introduction of minimal monitoring during anaesthesia represented a major advance in patient safety. Even though adverse events are relatively uncommon, if one patient is harmed by the absence of monitoring, then that is one too many.

# An Anatomic Study of the Sacral Hiatus: A Basis for Successful Caudal Epidural Block

Miho Sekiguchi, MD, Shoji Yabuki, MD, Koichiro Satoh, MD, and Shinichi Kikuchi, MD

**Study Design:** An anatomic study of the sacral hiatus using isolated sacra.

**Objectives:** To clarify the anatomic variations of the sacral hiatus using the bony landmarks of the sacrum for improving the reliability of caudal epidural block (CEB).

**Background Data:** The CEB has been widely used for the diagnosis and treatment of lumbar spinal disorders. The reliability of CEB is 70%–80% in the literatures. The cause of failure of CEB may depend on anatomic basis.

**Methods:** A total of 92 isolated sacra were used in this study. The bony landmarks were sacral hiatus and sacral cornua. Morphologic types of the sacral hiatus were classified using these landmarks. Also, location of the apex of sacral hiatus, diameter of the sacral canal at the apex of sacral hiatus, and the distance between bilateral cornua were measured. Two orthopedic surgeons performed measurements independently.

**Results:** Forty-two percent of the cases have both hiatus and cornu. Four percent of the cases showed the absent hiatus. The apex of sacral hiatus existed at the level of S4 vertebrae in 64% of the cases. The average diameter of the sacral canal was  $6.0 \pm 1.9$  mm. The average distance of bilateral sacral cornua was  $10.2 \pm 0.35$  mm. There were closed hiatus in 3% of cases.

**Conclusions:** The sacral hiatus has anatomic variations. Understanding of these variations may improve the reliability of CEB.

**Key Words:** caudal epidural block, sacral hiatus

(*Clin J Pain* 2004;20:51–54)

Caudal epidural block (CEB) has been widely used for the diagnosis and treatment of lumbar spinal disorders in the orthopedic field.<sup>1–5</sup> In clinical studies, the success rate of CEB

has been reported to be about 70–80%.<sup>5–7</sup> White and colleagues reported that 82% of patients with lumbar pain had pain relief 1 day after CEB.<sup>5–8</sup> Stitz and colleagues showed that there was a successful injection without using fluoroscopic view in 74% of the cases.<sup>7</sup> It has been reported that one of the anatomic reasons of CEB failure was caused by an absent hiatus and the frequency of absent hiatus was 7.7%.<sup>9</sup> One of the important key factors of successful CEB may be a clear understanding of the normal anatomy of the sacral hiatus and the surrounding structures. The sacral hiatus is located at the caudal end of the sacrum and bordered laterally by two sacral cornua. Only skin, subcutaneous fat tissue, and the sacrococcygeal ligament cover the hiatus. When the needle has passed through the sacrococcygeal ligament, the hiatus communicates with the epidural space directly.

The purpose of the present study was to clarify the anatomic variations of the sacral hiatus using the bony landmarks of the sacrum for improving the reliability of CEB.

## MATERIALS AND METHODS

The sacra in this study are from Fukushima Medical University and Nagoya University School of Medicine. Thirty-four were male, 13 were female, and 45 were unknown. The average age was 61.9 years old (range of age: 20–82 years old) in 46 of the 92 sacra (50% of the cases). In the other 46 of 92 sacra (50% of the cases), the age was unknown. A total of 92 cadaveric human sacra were stripped of all soft tissue in this study. All of them were Japanese. The bony landmarks used in this study were the sacral hiatus, the sacral cornua, and the median sacral crest (Fig. 1).

## Macroscopic Observation

### The Ratio of Existence or Absence of the Sacral Hiatus

The ratio of the existence or absence of the sacral hiatus and the sacral cornu was observed. The sacral hiatus were classified into two types, existence and absence. An absent hiatus means that no dimple exists at the posterior wall of the sacrum.

### The Ratio of Existence or Absence of the Sacral Cornu

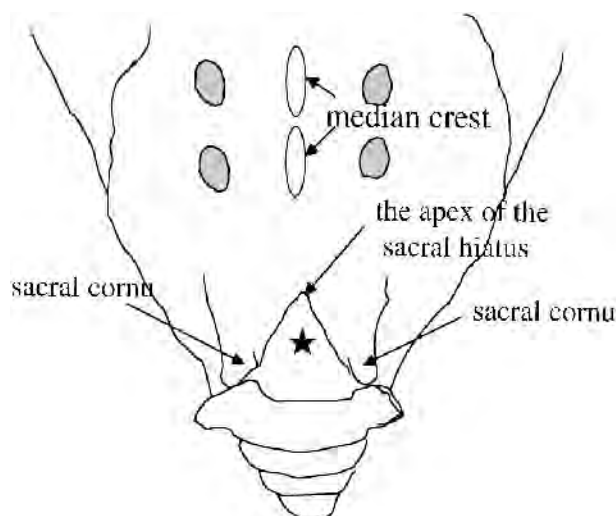
The sacral cornua were classified into three types: bilateral cornua, unilateral cornu, and absent cornu. An absent sa-

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**FIGURE 1.** The bony landmarks. The sacral hiatus (★), the sacral cornua, and the median sacral crest.

cral cornu means that the height of the bony protrusion is less than 3 mm.

#### Morphologic Types of the Sacral Hiatus

Various morphologic types of sacral hiatus were classified into 4 types according to the existence or absence of two landmarks. Type A has both hiatus and cornua; Type B has hiatus, but absence of cornua; Type C has cornua, but absence of hiatus; and Type D has no hiatus or cornua.

#### Location of the Apex of the Sacral Hiatus

Location of the apex of sacral hiatus was determined by the level of the sacral vertebrae from S1 to S5.

#### Measurements

##### Diameter of the Sacral Canal at the Apex of Hiatus

The distance between anterior wall and posterior wall of the hiatus was measured at the apex (Fig. 2A).

##### Distance Between Bilateral Cornua

The distance between the apex of the bilateral sacral cornu was measured (Fig. 2B). When the height of the bony protrusion is less than 3 mm, the distance between the mcenter of the bilateral cornu was measured.

##### Distance Between the Caudal End of the Median Sacral Crest and the Apex of the Hiatus

The distance between the caudal edge of the median sacral crest and the apex of the hiatus was measured (Fig. 2B).

All of the measurements were performed independently by two orthopedic surgeons using a pair of calipers.

#### Statistical Analysis

Intra-observer reproducibility and inter-observer reliability were analyzed using Kappa coefficient.

### RESULTS

#### Macroscopic Observation

##### The Ratio of Existence or Absence of the Sacral Hiatus

Sacral hiatus occurred in 88 of 92 sacra (96%). Absent hiatus occurred in 4 of 92 sacra (4%).

##### The Ratio of Existence or Absence of the Sacral Cornu

Sacral cornu occurred in 42 of 92 sacra (46%), and absent cornua occurred in 50 of 92 sacra (54%). Bilateral sacral cornua occurred in 19 of 42 sacra (45%), and unilateral cornu occurred in 23 of 42 sacra (55%).

#### Morphologic Types of the Sacral Hiatus

The incidences of each morphologic type of sacral hiatus were Type A: 39 of 92 sacra (42%); Type B: 49 of 92 sacra (53%); Type C: 3 of 92 sacra (3%); and Type D: 1 of 92 sacra (1%) (Fig. 3).

#### Location of the Apex of the Sacral Hiatus

The incidences of the apex of sacral hiatus located at the level of S1 to S5 vertebrae were: S1: 1 of 92 sacra (1%); S2: 4 of 92 sacra (4%); S3: 13 of 92 sacra (15%); S4: 60 of 92 sacra (65%); and S5: 14 of 92 sacra (15%). The apex of the sacral hiatus at the S4 or S5 level was 80% of the cases. The apex of the hiatus lies lower than the middle of the S5 vertebra in 3 of 92 sacra (3%).

#### Measurements

Intra-observer reproducibility was 0.86, and inter-observer reliability was 0.81 in this study.

##### Diameter of the Sacral Canal at the Apex of the Sacral Hiatus

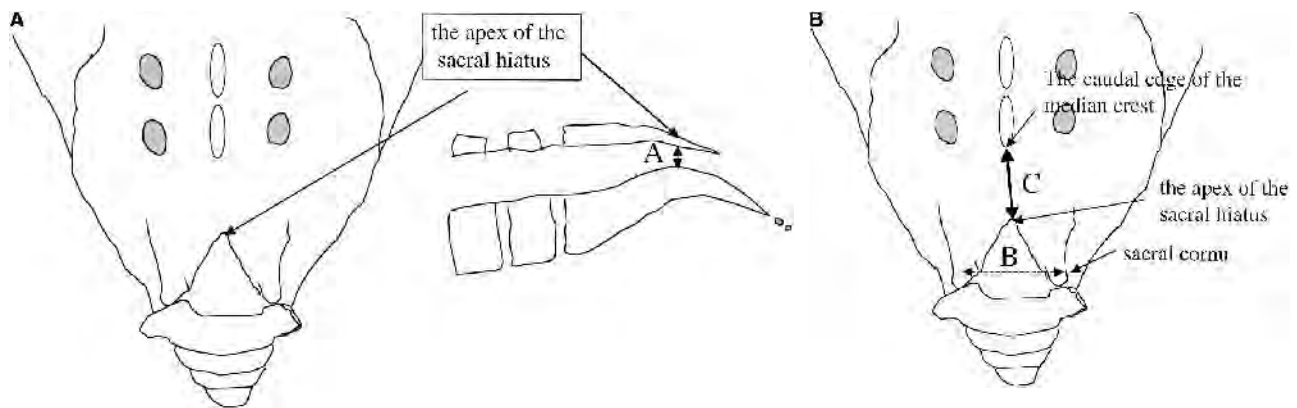
The range of the diameter of the sacral canal was from 1.9 mm to 11.4 mm. The average diameter  $\pm$  standard deviation (SD) of the sacral canal was  $6.0 \pm 1.9$  mm. The diameter of sacral canal at the apex of the hiatus was less than 2 mm in 1 of 92 sacra (1%).

##### Distance Between Bilateral Cornua

The range of the distance between the bilateral cornua was from 2.2 mm to 18.4 mm. The average distance  $\pm$  SD of bilateral sacral cornua was  $10.2 \pm 0.35$  mm. In 5 of 92 sacra (5%), the distance between the bilateral cornua was less than 5 mm.

##### Distance Between the Caudal End of the Median Sacral Crest and Apex of the Hiatus

In 92 sacra, the distance was less than 5 mm in 34 cases (37%), more than 5 mm, but less than 10 mm in 12 cases



**FIGURE 2.** Measurements. Diameter of the sacral canal at the apex of hiatus (A), distance between the apex of the bilateral cornua (B), and distance between the caudal edge of the median sacral crest and the apex of the hiatus (C).

(13%), and more than 10 mm in 44 cases (49%). There was a wide range of distance variations in this series.

**Anatomic Abnormalities of Sacrum**

Anatomic abnormalities of the sacral hiatus were absent hiatus (4%), bony septum (2%), and complete agenesis which means that sacrum has no posterior wall (1%) (Fig. 4). A closed sacral canal occurred in 3 of 92 sacra (3%); however, two of them had sacral hiatus.

**DISCUSSION**

There are closed sacral canals in 3% of the cases. In 7% of the cases there are some anatomic abnormalities of sacral hiatus such as absent hiatus (4%), bony septum (2%), and com-





plete agenesis (1%). The diameter of sacral canal was less than 2 mm in 1% of the cases. Both sacral hiatus and cornua existed in only 42% of the cases. The cornua was absent in 54% of the cases.

One of the factors of CEB failure is anatomic variation. The sacral hiatus is the most important bony landmark for CEB since the apex of the sacral hiatus shows the existence of a sacral canal. Clinicians sometimes experience difficulties to palpate the sacral hiatus and other bony landmarks. Therefore, it is important to clarify the anatomic variations of the sacral hiatus without soft tissue.

In the current study, closed sacral canals make CEB impossible anatomically in 3% of the cases because the needle cannot be inserted into the sacral canal. When the location of the sacral canal is not identified, it is difficult to insert the needle through the canal. Cases of the absence of hiatus (absent hiatus), bony septum at sacral hiatus, and complete agenesis make it difficult to locate the sacral canal opening. These factors might cause CEB failure in 7% of the cases. Also, in a narrow canal it may be difficult to insert the needle into the sacral canal. The 22gauge needle is used for CEB. The diameter of sacral canals less than 2 mm might cause CEB failure in 1% of the cases. In our study, the apex of the hiatus was located higher than the S3 vertebra in 20% of the cases. The sacral spinal canal contains the terminal part of the dural sac, which is usually located at the S2 vertebral level.<sup>10</sup> Therefore, 20% of the cases have a risk of puncturing the dural sac.

One may assume that palpation of the median sacral crest toward caudal direction may also indicate the location of the sacral hiatus. However, 44 of 92 sacra (49%) showed a distance of more than 10 mm between the distal end of median sacral crest and the apex of hiatus. This means that the median crest cannot be a landmark to detect the sacral canal.

Black has shown that the incidence of absent hiatus, which causes CEB failure, is 7.7%.<sup>9</sup> Stitz and colleagues have reported that patients with successful CEB using the fluoro-

	(+) sacral cornua	(-) sacral cornua
(+) sacral hiatus	Type A: 42% 	Type B: 53% 
(-) sacral hiatus	Type C: 3% 	Type D: 1% 

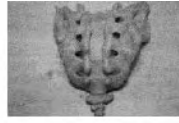
**FIGURE 3.** The incidences of morphologic types of sacral hiatus.



Absent hiatus  
4/92 (4%)



bony septum  
2/92 (2%)



complete agenesis  
1/92 (1%)

**FIGURE 4.** Anatomic variations of the sacral hiatus. Absent hiatus: 4/92 (4%), bony septum 2/92 (2%), and complete agenesis 1/92 (1%).

scopic view are approximately 94%.<sup>7</sup> The CEB failure occurs even if the fluoroscopic view is used. The present study showed that CEB failure might occur in 3–11% of patients because of anatomic abnormalities. Black showed that the rate of normal sacral cornua is 52% and unilateral cornu is 17%.<sup>9</sup> The current study showed that the rate of normal sacral cornua was only 21% and absent cornua was more than 50%. The rate of absent cornua was quite different from Black's study, since we defined it as an absent cornua when the sacral cornu was less than 3 mm in height. In human patients, connective and fatty tissues existed between the hiatus and the skin. These factors may influence the palpation of the hiatus.

In conclusion, there are anatomic variations in the sacral hiatus, which may relate to the failure of CEB. The rate of impossible CEB is 3% since the sacral canal was closed. There are bony anatomic abnormalities: absent hiatus (4%), bony septum (2%), complete agenesis (1%), and narrow sacral space (1%). These anatomic abnormalities may be a factor to cause CEB failure. We should pay attention to anatomic variations of sacral hiatus when performing CEB. When the operator notices an abnormality of the hiatus, he should choose lumbar

epidural block or other treatments to avoid the risk of the soft tissue injury and the toxicity of local anesthetics.

#### REFERENCES

1. Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. *Spine*. 1991;16:572–575.
2. Cuckler JM, Bernini PA, Wiesel SW. The use of epidural steroid in the treatment of radicular pain. *J Bone Joint Surg*. 1985;67:63–66.
3. Daly P. Caudal epidural anesthesia in lumbosacral pain. *Anaesthesia*. 1970;25:346–348.
4. El-Khoury G, Ehara S, Weinstein JN. Epidural steroid injection: a procedure ideally performed with fluoroscopic control. *Radiology*. 1988;168:554–557.
5. White AH, Derby R, Wynne GAR. Epidural injections for the diagnosis and treatment of low-back pain. *Spine*. 1980;5:78–86.
6. Price CM, Rogers PD, Prosser AJS. Comparison of the caudal and lumbar approaches to the epidural space. *Ann Rheum Dis*. 2000;59:879–882.
7. Stitz MY, Sommer HM. Accuracy of blind versus fluoroscopically guided caudal epidural injection. *Spine*. 1999;24:1371–1376.
8. White AH. Injection techniques for the diagnosis and treatment of low back pain. *Orthop Clin North Am*. 1983;14:553–567.
9. Black MG. Anatomic reasons for caudal anesthesia failure. *Anesth. Analg (Cleve.)* 1949;28:33–39.
10. Willis RJ. Caudal epidural blockade. In: Cousins MJ, ed. *Neural Blockade in Clinical Anesthesia and Management of Pain*. 3rd ed. Philadelphia: Lippincott-Raven Publishers; 1998:323–342.

# Ultrasound Guidance in Caudal Epidural Needle Placement

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**Background:** This study was conducted to investigate the feasibility of using ultrasound as an image tool to locate the sacral hiatus accurately for caudal epidural injections.

**Methods:** Between August 2002 and July 2003, 70 patients (39 male and 31 female patients) with low back pain and sciatica were studied. Soft tissue ultrasonography was performed to locate the sacral hiatus. A 21-gauge caudal epidural needle was inserted and guided by ultrasound to the sacral hiatus and into the caudal epidural space. Proper needle placement was confirmed by fluoroscopy.

**Results:** In all the recruited patients, the sacral hiatus was located accurately by ultrasound, and the caudal epidural needle was guided successfully to the sacral hiatus and into the caudal epidural space. There was 100% accuracy in caudal epidural needle placement into the caudal epidural space under ultrasound guidance as confirmed by contrast dye fluoroscopy.

**Conclusions:** Ultrasound is radiation free, is easy to use, and can provide real-time images in guiding the caudal epidural needle into the caudal epidural space. Ultrasound may therefore be used as an adjuvant tool in caudal needle placement.

*CAUDAL epidural anesthesia* is the injection of medications into the epidural space *via* the sacral hiatus. It is useful when anesthesia of the lumbar and sacral dermatomes is needed.<sup>1</sup> Successful caudal anesthesia relies on the proper placement of a needle in the epidural space. The most common method to identify the caudal epidural space is detecting the characteristic “give” or “pop” when the sacrococcygeal ligament is penetrated.<sup>1,2</sup> Even with experienced physicians, the failure rate of the placement of needles into the caudal epidural space can be up to 25%.<sup>1,3</sup>

In clinical practice, the “whoosh” test,<sup>3</sup> nerve stimulation,<sup>1</sup> and fluoroscopy are the three methods that can be used to identify the caudal space before the injection of medications. The application of ultrasonography to locate the sacral hiatus for caudal epidural injections has not been described. The purpose of this study was to examine the practicality of using ultrasound guidance in the placement of a caudal needle into the caudal epidural space.

## Materials and Methods

Seventy patients with low back pain and sciatica were studied. This study was approved by the local medical ethics and the human clinical trial committee (Chang Gung Memorial Hospital, Tao-Yuan County, Taiwan). All of the recruited subjects signed the informed consent and agreed to receive caudal injections.

The SONOS 4500 (Philips Medical Systems, Andover, MA) ultrasound machine was used in this study. The selected transducer was the S12 5-12 MHz real-time linear-array ultrasound transducer (Philips Medical Systems).

### Design

Patients were placed in the prone position. The assistant's arms were placed horizontally, out of the physician's way, to hold the gluteal masses apart to achieve a flatter skin surface at the sacral hiatus area for the placement of ultrasound transducer. The examined area was prepared and draped in the usual sterile fashion. The transducer was covered with sterile plastic.

The transducer was first placed transversely at the midline to obtain the sonographic transverse view of the sacral hiatus. The following findings were observed (fig. 1):

1. The two hyperechoic reversed U-shaped structures were the two bony prominences of sacral cornua.
2. Between the two cornua, there were two hyperechoic band-like structures. The band-like structure on top was the sacrococcygeal ligament. The band-like structure at the bottom was the dorsal bony surface of the sacrum.
3. The sacral hiatus was the hypoechoic region observed between the two hyperechoic band-like structures.

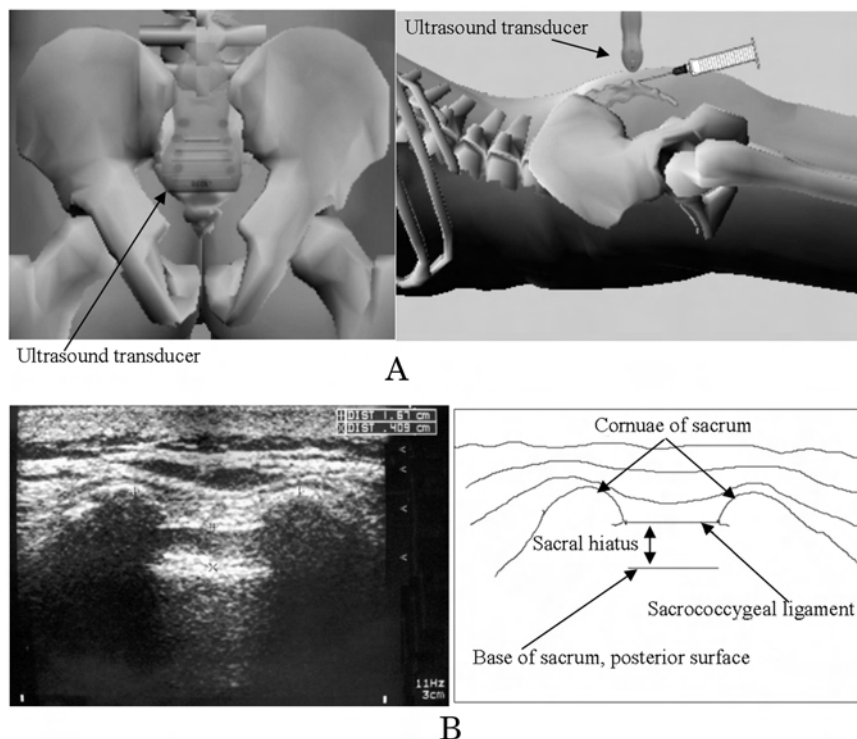
The transducer was then rotated 90° to examine the sonographic longitudinal view of the sacral hiatus. Anatomically, the transducer then rested between the two cornua. A 21-gauge caudal epidural needle was inserted and advanced under the sonographic longitudinal view of the sacral hiatus. The caudal epidural needle appeared as a hyperechoic structure under sonography (fig. 2). The advancement of the caudal epidural needle between the two cornua to the sacral hiatus and into the caudal epidural space was observed as continuous and real-time sonographic images. As the caudal epidural needle pierced through the sacrococcygeal ligament, the portion of the needle inside the caudal epidural space was no longer observed under sonography (fig. 2).

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**Fig. 1. (A) Transverse plane placement of the ultrasound transducer. (B) Sonographic transverse view of the sacral hiatus.**

The ultrasound transducer was then adjusted in transverse and longitudinal views to make sure the spinal needle was inserted correctly into the caudal epidural space. Under the transverse view, the spinal needle appeared as a small circular hyperechoic structure, resting between the two hyperechoic cornua, and within the two hyperechoic band-like structures (fig. 3). Finally, contrast dye fluoroscopy was used to confirm the location of the caudal epidural needle (fig. 4). To prevent bias, the ultrasound-guided caudal needle insertions and the interpretation of fluoroscopy images were performed by different physicians.

## Results

Seventy patients with low back pain and sciatica were recruited for this study. There were a total of 39 male and 31 female patients. The average age was  $38 \pm 5.6$  yr. The average body height was  $168 \pm 8.9$  cm for the male patients and  $160 \pm 4.3$  cm for the female patients.

In all the recruited patients, the sacral hiatus was located correctly by ultrasonography in both the transverse and longitudinal views. The advancing motion of the hyperechoic caudal epidural needle to the sacral hiatus and into the caudal epidural space was observed as continuous and real-time images under the sonographic longitudinal view. The portion of the caudal epidural needle inside the caudal epidural space could not be observed under sonography (fig. 2). In all the cases, the characteristic “give” or “pop” was detected when the sacrococcygeal ligament was penetrated.

The average time span from locating the sacral hiatus to the insertion of the caudal epidural needle into the caudal epidural space was less than 2 min. Under ultrasound guidance, only one attempt was needed in guiding the caudal epidural needle into the caudal epidural space.

Fluoroscopy was then used to confirm the location of the caudal epidural needle. The caudal epidural needle was correctly placed into the caudal epidural space in all of the recruited patients as confirmed by contrast dye fluoroscopy. Christmas tree-like appearance resembling contrast dye distribution was observed in all of the patients (fig. 4).

Therefore, after fluoroscopic confirmation, the accuracy of ultrasound guidance in locating the sacral hiatus for proper placement of the caudal epidural needle into the caudal epidural space was 100%.

## Discussion

Epidural injections of local anesthetic agents and corticosteroids are widely used to provide symptomatic relief in patients with low back disorders.<sup>3</sup> Epidural steroid injections have been used since 1952.<sup>4</sup> These injections can be approached by translaminar,<sup>5</sup> transforaminal,<sup>4</sup> and caudal routes.<sup>5</sup> The caudal entry into the epidural space is preferred by many practitioners because accidental puncture of the dural sac and subsequent risk of intrathecal injection of medication is rare.<sup>1,3</sup> However, even with experienced physicians, up to 25% of the injections using the caudal route do not

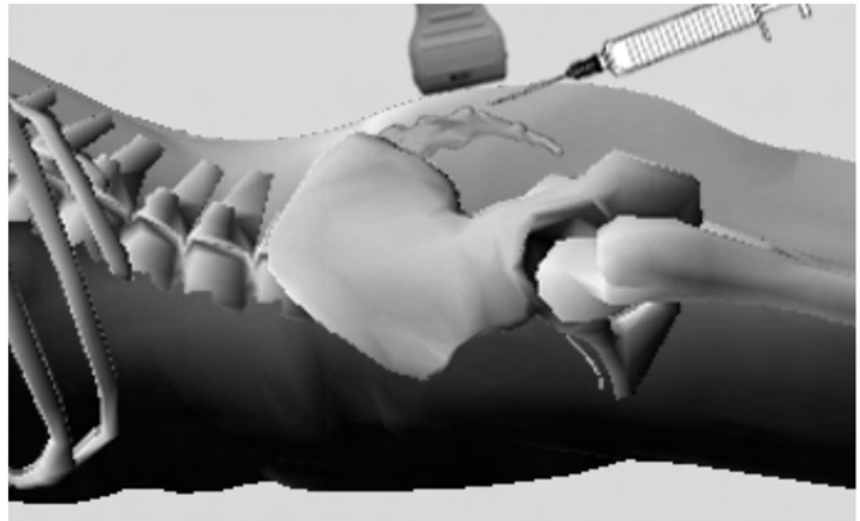
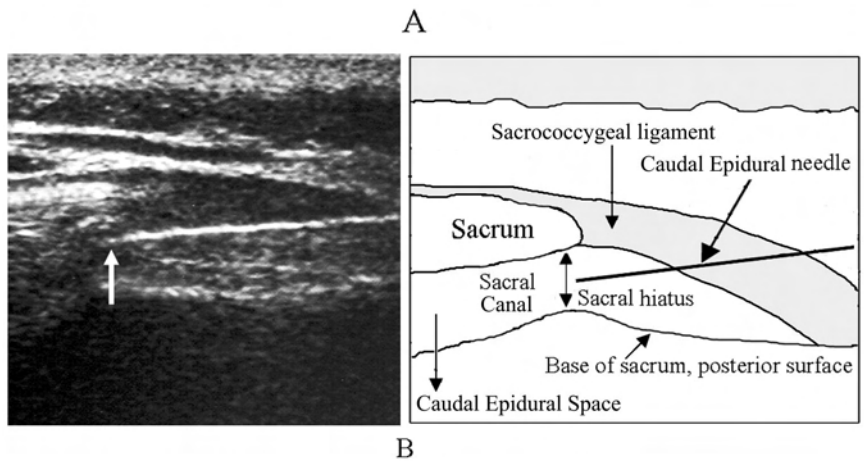


Fig. 2. (A) Longitudinal plane placement of the ultrasound transducer. (B) Caudal epidural needle is observed as a hyper-echoic structure under sonography. The portion of the needle inside the caudal epidural space cannot be observed under ultrasonography.



enter the epidural space.<sup>1,3</sup> As a result, the development of an easy and reliable objective method that enables rapid confirmation of proper caudal needle placement is desirable.<sup>1</sup>

There are several ways to identify the caudal epidural

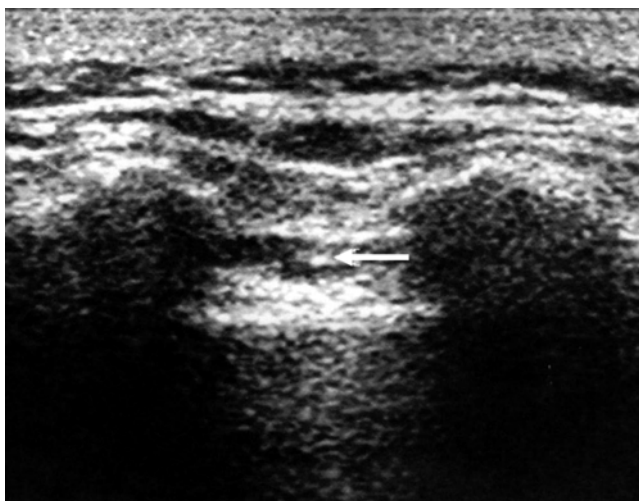
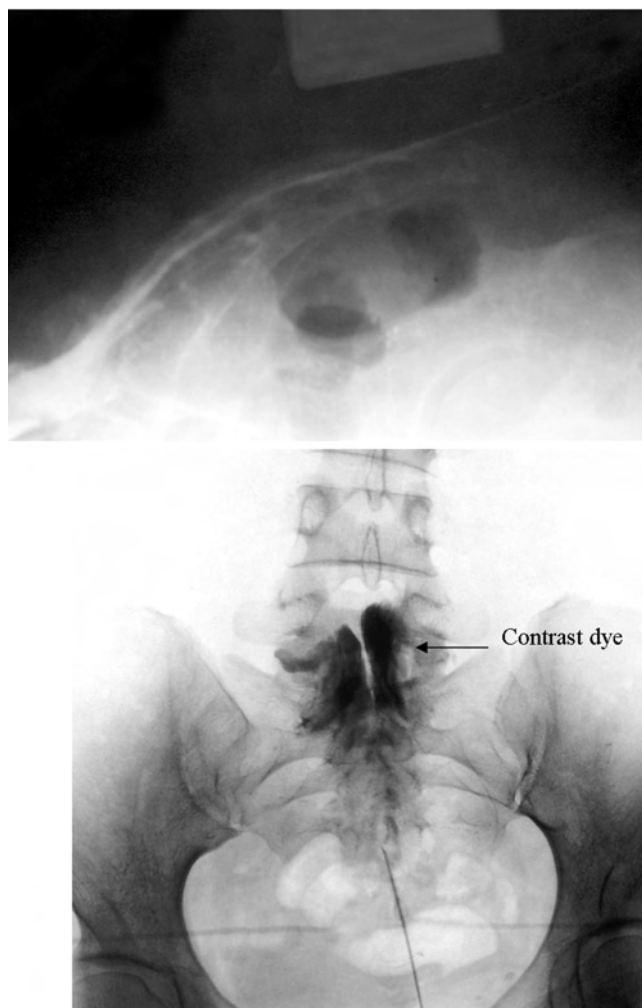


Fig. 3. The ultrasound transverse view. Arrow indicates caudal epidural needle.

space. The most common one is the detection of the characteristic “give” or “pop” on penetration of the sacrococcygeal ligament.<sup>1</sup> However, final confirmation of the proper needle placement can be made only after observing the clinical effect of the injected medication.<sup>1</sup> The lack of subcutaneous bulging or resistance on injection of local anesthetic are also important signs of proper needle placement.<sup>1</sup> The “whoosh” test was claimed to be more reliable than the “give” or “pop” of the sacrococcygeal ligament.<sup>6</sup> However, eliciting the “whoosh” may cause venous air embolism after injection of 2.5 ml air.<sup>1,2</sup> The nerve stimulation test is the other method to confirm caudal needle placement.<sup>1,7</sup> The needle is classified as correctly or incorrectly placed depending on the presence or absence of anal sphincter contraction to electrical stimulation.<sup>1</sup>

Fluoroscopy is most commonly used in interventional spine procedures<sup>4</sup> and is frequently used in confirming the location of caudal epidural needle. It has been advocated that caudal epidural needle placement should be confirmed by fluoroscopy alone or by epidurography.<sup>3</sup> Radiation exposure is the major concern when obtaining fluoroscopic images. Botwin *et al.*<sup>4</sup> stated that spinal



**Fig. 4. Fluoroscopy confirmation with contrast dye. Christmas tree-like appearance can be observed as the contrast dye bathes the external aspect of the dura mater and nerve roots.**

interventionalists should adhere to simple rules of radiation safety to minimize the cumulative radiation exposures. These rules included increasing the distance between the interventionalist and the radiation source; decreasing the overall time of exposure; shielding susceptible areas with leaded aprons, thyroid shields, leaded glasses, and leaded gloves; and being proficient in

guiding needles under the fluoroscope.<sup>4</sup> Fluoroscopy can also provide real-time and continuous images, but this increases the overall time of exposure. Currently, pulsed imaging is preferred during fluoroscopy because it can reduce overall exposure by 20–75%.<sup>4</sup>

In this study, ultrasonography proved to be an effective tool, with 100% accuracy in locating the sacral hiatus and in guiding the caudal epidural needle into the caudal epidural space. The advantages of ultrasound are that it is easy to use, it is radiation-free, and can be used in virtually any clinical setting.<sup>8</sup> Most significantly, ultrasonography can provide real-time and continuous needle-guiding images without radiation exposure. It takes approximately 2 h of training for an inexperienced physician to learn the ultrasound-guided caudal epidural injection technique. Physicians must be acquainted with skills in manipulating the ultrasound probe and interpreting the sonograms.

Perhaps the only disadvantage with ultrasound is the fact that it cannot provide us with the image information as to the depth of the inserted needle. Ultrasound waves cannot penetrate the sacral bone to observe the hyperechoic caudal epidural needle inside the caudal epidural space. Therefore, checking for the escape of cerebrospinal fluid for possible dura tear is critical before steroid injection can be pursued.

## References

1. Tsui BC, Tarkkila P, Gupta S, Kearney R: Confirmation of caudal needle placement using nerve stimulation. *ANESTHESIOLOGY* 1999; 91:374–8
2. Guinard JP, Borboen M: Probable venous air embolism during caudal anesthesia in a child. *Anesth Analg* 1993; 76:1134–5
3. Lewis MPN, Thomas P, Wilson LF, Mulholland RC: The “whoosh” test: A clinical test to confirm correct needle placement in caudal epidural injections. *Anaesthesia* 1992; 47:57–8
4. Botwin KP, Thomas S, Gruber RD, Torres FM, Bouchlas CC, Rittenberg JJ, Rao S: Radiation exposure of the spinal interventionalist performing fluoroscopically guided lumbar transforaminal epidural steroid injections. *Arch Phys Med Rehabil* 2002; 83:697–701
5. Lippert JA, McGraw JK: Spine interventions. *Sem Roentgenol* 2002; 37:266–81
6. Chan SY, Tay HBD, Thomas E: “Whoosh” test as a teaching aid in caudal block. *Anaesth Intensive Care* 1993; 21:414–5
7. Singh M, Khan RM: Use of a peripheral nerve stimulator for predicting caudal epidural analgesia. *Anaesthesia* 2000; 55:830–1
8. Van Holsbeeck M, Introcaso JH: Musculoskeletal ultrasonography. *Radiol Clin North Am* 1992; 30:907–25

# Sonographically Guided Caudal Epidural Steroid Injections

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**Objective.** Caudal epidural steroid injections are used for the symptomatic treatment of radicular lumbosacral pain syndromes, but incorrect injection placement has been recognized as a common problem with the routinely used unguided technique. We aimed to explore the use of sonography to facilitate this procedure. **Methods.** In patients with clinically unreliable anatomic landmarks, high-resolution real-time sonography was used to identify those landmarks and to assist in correct needle placement. **Results.** Sonography enabled localization of the sacral hiatus landmarks. We found this method particularly useful for guiding needle placement in patients with moderate obesity. **Conclusions.** Real-time sonography can facilitate caudal epidural steroid injections. **Key words:** caudal epidural injection; interventional sonography; sciatica.

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**E**pidural steroid injections can be helpful in the symptomatic treatment of pain due to lumbosacral root compression, such as sciatica and lumbar spinal canal stenosis.<sup>1,2</sup> The caudal approach to the epidural space via the sacral hiatus is often preferred by nonanesthetists because it carries a lower risk of inadvertent thecal sac puncture and intrathecal injection. The sacral hiatus is a triangular aperture at the base of the sacrum bordered by 2 bony prominences, the sacral cornua (Fig. 1). The clinical procedure depends on the correct identification of these anatomic landmarks by palpation. However, in the technique of fluoroscopic control with contrast agent injection after unaided insertion, incorrect needle placement has been reported to occur in 25% to 38% of cases,<sup>3-5</sup> even in the hands of experienced operators. Furthermore, even when operators were confident, incorrect placement was seen in about 1 per 7 procedures. An incorrect needle position leads predominantly to deep subcutaneous injection.<sup>5</sup> Factors associated

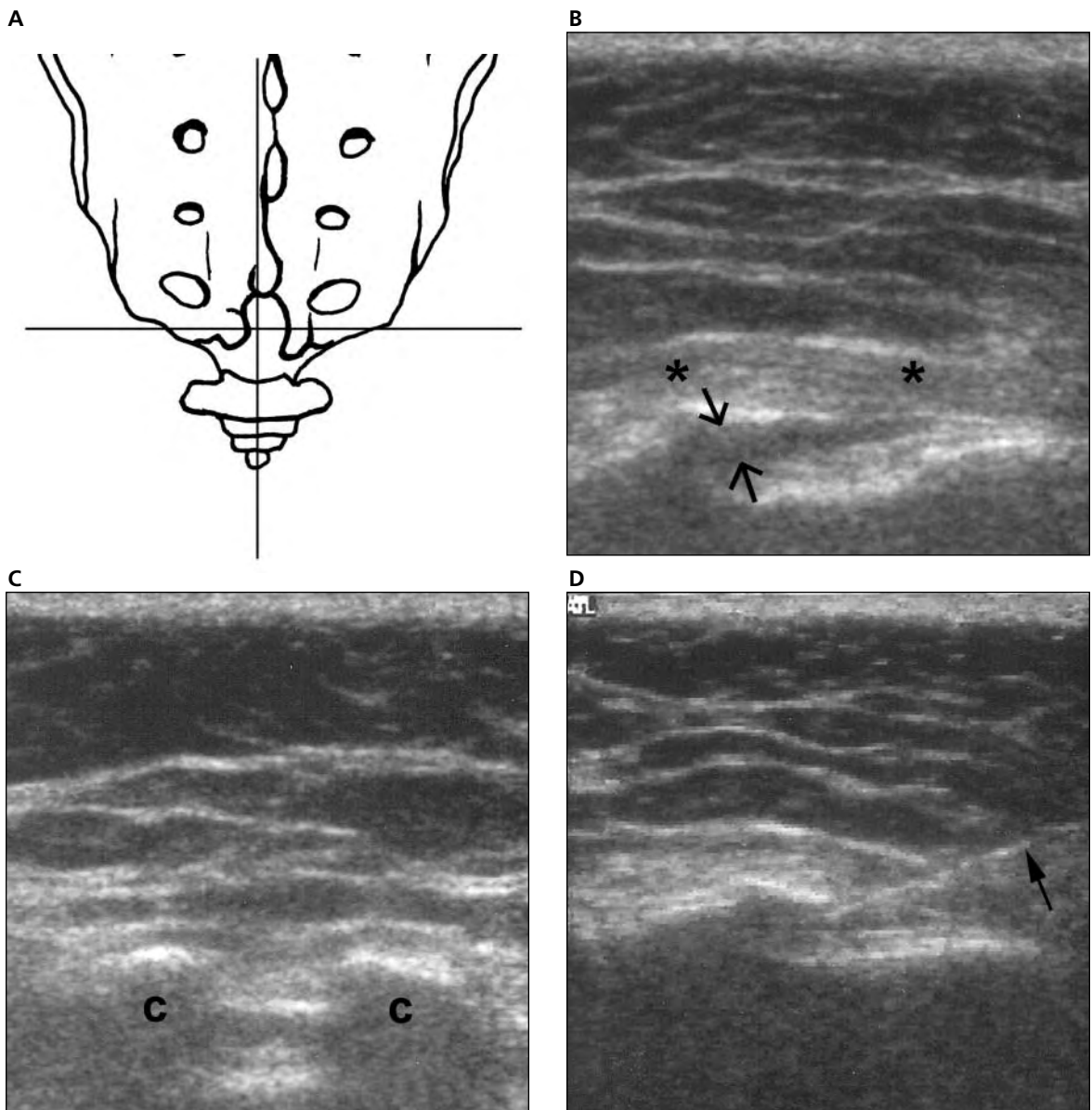
with incorrect placement include obesity, presumably because it causes impairment of correct clinical identification of the anatomic landmarks of the sacral hiatus. Finally, it has to be remembered that all aspects of the sacral canal anatomic characteristics, including the palpable landmarks, may vary.<sup>6</sup>

The authors of the fluoroscopically controlled studies concluded that all caudal epidural steroid injections should be performed under fluoro-

scopic guidance with contrast agent injection.<sup>3-5</sup> Fluoroscopy, however, involves ionizing radiation close to the gonadal area, which will require careful consideration, particularly in patients of reproductive age.

We used high-resolution sonography to identify the anatomic landmarks of the sacral hiatus and then to guide the injection needle into the epidural space.

**Figure 1.** **A**, Schematic drawing of the posterior aspect of the bony sacral hiatus. The vertical and horizontal axes indicate the imaging planes of the sonographic images taken in case 1 (**B** and **C**, respectively). **B**, Longitudinal sonogram showing the sacrococcygeal ligament (asterisks) and the epidural space in the sacral canal (arrows). **C**, Transverse image showing the sacral cornua (c). **D**, Still image from a video recording showing the injection needle (arrow) correctly positioned in the epidural space in case 1.



## Materials and Methods

Patients attending the Royal National Hospital for Rheumatic Diseases for sciatica or lumbar spinal canal stenosis who had been routinely referred for therapeutic caudal epidural steroid injections were assessed by diagnostic sonography when anatomic landmarks were unreliable by palpation.

We used an HDI 5000 sonography system (Philips Medical Systems, Bothell, WA), with a 5- to 12-MHz, 38-mm-footprint linear array transducer. The patient was usually in a prone position with the pelvis supported by a pillow. After skin disinfection and application of a sterile transducer sheath and gel, the following structures were identified: the 2 sacral cornua, the apex of the sacral hiatus, and the sacrococcygeal ligament that stretches across the sacral hiatus and separates the subcutaneous tissue layer from the epidural space underneath (Fig. 1, A–C). In obese patients, it was sometimes necessary to use a 2- to 5-MHz curvilinear array transducer to achieve adequate penetration of deeper subcutaneous tissues. A 5- to 10-MHz, small-footprint “hockey stick” transducer was used occasionally when close proximity of the needle and transducer was required, for example, in thin individuals.

After skin anesthesia with 1% lignocaine, the sacral hiatus was visualized longitudinally, and a 20-gauge (0.9 × 90-mm) spinal needle was inserted and advanced under sonographic guidance through the sacrococcygeal ligament into the epidural space of the sacral canal (Fig. 1D). Slow injection of about 2 mL of air was used as a final check of correct needle placement; in the case of the epidural needle position, no air would emerge outside the sacrococcygeal ligament as judged by real-time sonography. Forty milligrams of triamcinolone acetonide in 15 to 20 mL of 0.9% sodium chloride was then injected slowly.

## Results

In our experience, the anatomic landmarks and the sacrococcygeal ligament could be readily visualized, except in cases of extreme obesity. We used and found this procedure particularly helpful in the following clinical situations.

### Case 1

A 65-year-old obese woman (body mass index, 33.8 kg/m<sup>2</sup>) with sciatica underwent sonography because anatomic landmarks of the sacral hiatus were impalpable. Figure 1 shows the longitudinal and transverse sonographic sections of her sacral hiatus (Fig. 1, B and C). The injection needle was then successfully guided through the sacrococcygeal ligament into the epidural space (Fig. 1D).

### Case 2

A 70-year-old woman with sciatica was unable to lie in a prone or lateral decubitus position because of coexistent advanced rheumatoid arthritis. Successful sonographically guided epidural steroid injection was achieved with the patient in an oblique lateral position.

### Case 3

In a 60-year-old woman with sciatica and psoriatic spondyloarthropathy, sonography was used to guide the needle into the sacral hiatus, avoiding psoriatic skin plaques in the sacral area, which may have posed an increased risk of a septic complication from the procedure.

## Discussion

Here we describe the use of sonography to facilitate correct caudal epidural injection. In addition to the examples presented above (unreliable landmarks due to obesity, unusual patient positions, and individual local factors), this method would appear to be a safer alternative to the standard method of fluoroscopic guidance in patients of reproductive age. Given the above-mentioned relative lack of agreement between operator confidence in correct needle positioning and successful epidural injection placement, one could further argue for the routine use of sonography to verify sacral hiatus landmarks before all caudal epidural injections.

There is an important limitation to this method. Inadvertent intravenous injection, which has been reported to occur in about 5% to 9% of procedures,<sup>3–5</sup> cannot be avoided with this technique. This is particularly important because aspiration or return of blood does not appear to be very sensitive or specific for intravenous positioning of the needle.<sup>4</sup> A local anesthetic is preferred by some operators as the diluent for the epidural steroid preparation.

However, toxic plasma concentrations of a local anesthetic may occur upon inadvertent injection into an epidural vein. Because we use 0.9% sodium chloride instead, the adverse risks associated with accidental intravenous injection become negligible.

In conclusion, we have described a sonographic method for identifying the sacral hiatus landmarks to facilitate real-time guidance of steroid injections into the caudal epidural space. This method may be a good alternative to the current standard of fluoroscopic guidance.

### References

1. Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesth Intensive Care* 1995; 23:564–569.
2. Carette S, Leclaire R, Marcoux S, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med* 1997; 336:1634–1640.
3. White AH, Derby R, Wynne G. Epidural injections for the treatment of low-back pain. *Spine* 1980; 5:78–86.
4. Renfrew DL, Moore TE, Kathol MH, el-Khoury G, Lemke JH, Walker CW. Correct placement of epidural steroid injections: fluoroscopic guidance and contrast administration. *AJNR Am J Neuroradiol* 1991; 12:1003–1007.
5. Price CM, Rogers PD, Prosser AS, Arden NK. Comparison and lumbar approaches to the epidural space. *Ann Rheum Dis* 2000; 59:879–882.
6. Trotter M. Variations of the sacral canal: their significance in the administration of caudal analgesia. *Anesth Analg* 1947; 26:192–202.

# Melding om bivirkninger ved bruk av legemidler (inkl. naturlegemidler)

# ?RELIS

Statens legemiddelverk  
Norwegian Medicines Agency



Skjemaet er på to (2) sider.  
Utfyllt skjema sendes til RELIS i din helseregion. Se baksiden for adresser.

Unntatt offentlighet jf. Offl. § 5a, jf fvl. § 13 første ledd nr. 1

## PASIENTOPPLYSNINGER

Navn: \_\_\_\_\_

Kjønn: \_\_\_\_\_

Fødselsdato: \_\_\_\_\_

Vedlagt:  Epikrise  Obduksjonsrapport  
 Labjournal  Annet  
 Journalnotat

<b>Årsak til meldingen:</b> <input type="checkbox"/> Resulterte i død <input type="checkbox"/> Livstruende <input type="checkbox"/> Sykehusinnleggelse/forlenget opphold <input type="checkbox"/> Vedvarende uførhet/nedsatt funksjons evne <input type="checkbox"/> Anomali/fødselsdefekt <input type="checkbox"/> Ikke beskrevet i preparatomtalen <input type="checkbox"/> Bivirkning(er) ved generisk bytte <input type="checkbox"/> Bivirkning(er) ved bruk av reseptfritt legemiddel/naturlegemiddel <input type="checkbox"/> Bivirkning(er) av legemidler under særlig overvåking (se liste <a href="http://www.legemiddelverket.no">www.legemiddelverket.no</a> ) <input type="checkbox"/> Annet _____	<b>Konsekvenser for pasienten</b> <input type="checkbox"/> Restituert uten ettervirkninger <input type="checkbox"/> I bedring, men ikke fullstendig restituert <input type="checkbox"/> Restituert, men med ettervirkninger <input type="checkbox"/> Ingen bedring <input type="checkbox"/> Død
--	--

## LEGEMIDLER

Navn, styrke, legemiddelform Produsentnavn - generisk bytte	Dosering	Indikasjon	Startdato evt varighet av behandling	Stoppdato	Seponert (x)
<b>Mistenkte legemidler*</b>					
<b>Andre legemidler</b> Ingen andre legemidler <input type="checkbox"/>					

Mistanke om interaksjon  Hvilke legemidler? \_\_\_\_\_

Reeksponeering av mistenkte legemidler  Ja  Nei Evt resultat \_\_\_\_\_

## BIVIRKNINGER

Bivirkningsdiagnose(r) evt symptomer	Startdato (evt varighet)	Stoppdato
--------------------------------------	-----------------------------	-----------

\* For biologiske produkt og vaksiner bør batchnr/lotnr oppgis



# RELEVANTE OPPLYSNINGER (kan erstattes av vedlegg)

Beskrivelse av forløpet:

Pasientens sykehistorie:

Resultater av tester (inkl datoer):

## Melders navn og adresse

Tlf: \_\_\_\_\_

E-post: \_\_\_\_\_

Lege

Tannlege

Farmasøyt

Annet helsepersonell

Melders dato: \_\_\_\_\_

Melders underskrift: \_\_\_\_\_

Utfylt skjema sendes til RELIS i din region:

**Helseregion Sør (Vest-Agder, Aust-Agder, Telemark, Vestfold og Buskerud samt Det norske radiumhospital HF, Rikshospitalet HF og Spesialsykehuset for epilepsi HF):**

**RELIS Sør**  
Rikshospitalet  
0027 Oslo  
tlf. 23 07 53 80  
[relis@rikshospitalet.no](mailto:relis@rikshospitalet.no)

**Helseregion Vest (Rogaland, Hordaland og Sogn og Fjordane):**

**RELIS Vest**  
LKB  
Haukeland Universitetssykehus  
Postboks 1  
5021 Bergen  
Tlf. 55 97 53 46/60/61  
[relis@haukeland.no](mailto:relis@haukeland.no)

**Helseregion Nord (Nordland, Troms og Finnmark):**

**RELIS Nord-Norge**  
Universitetssykehuset i Nord-Norge HF  
Postboks 79  
9038 Tromsø  
Tlf. 77 64 58 89/90/91  
[relis@unn.no](mailto:relis@unn.no)

**Helseregion Øst (Østfold, Akershus, Oslo, Oppland og Hedmark):**

**RELIS Øst**  
Ullevål universitetssykehus  
0407 Oslo  
tlf. 23 01 64 11/12/13  
[postmaster@relis.ullevaal.no](mailto:postmaster@relis.ullevaal.no)

**Helseregion Midt-Norge (Møre og Romsdal, Sør-Trøndelag og Nord-Trøndelag):**

**RELIS Midt-Norge**  
Avdeling for legemidler  
St. Olavs Hospital HF  
7006 Trondheim  
Tlf. 73 55 01 58/59/62/63  
[relis@legemidler.no](mailto:relis@legemidler.no)

Andre nyttige adresser:

**Statens legemiddelverk**  
Sven Oftedals vei 8  
0950 Oslo  
Tlf. 22 89 77 00  
[www.legemiddelverket.no](http://www.legemiddelverket.no)

**Regionalt legemiddelinformasjonscenter (RELIS) – felles vevside**  
[www.relis.no](http://www.relis.no)

Skjema kan bestilles fra de enkelte RELIS eller Statens legemiddelverk eller hentes på [www.relis.no](http://www.relis.no) eller [www.legemiddelverket.no/bivirk/bivirkninger.htm](http://www.legemiddelverket.no/bivirk/bivirkninger.htm)

### Hva skal meldes?

Følgende bivirkninger er meldepliktige:

- Dødelige og livstruende bivirkninger
- Bivirkninger som har gitt varige alvorlige følger
- Nye eller uventede bivirkninger

Statens legemiddelverk anser det også som nyttig å få meldinger om:

- Alle bivirkninger av nye legemidler
- Alle bivirkninger av legemidler under særlig overvåking (se [www.legemiddelverket.no](http://www.legemiddelverket.no) eller «Nytt om legemidler»)
- Problemer ved seponering av legemidler
- Reaksjoner på grunn av overdosering eller feilbruk av reseptfrie legemidler
- Bivirkninger av naturlegemidler og ved generisk bytte

Mistanke om bivirkning er tilstrekkelig for å melde. Meldinger som blir vurdert å ha en årsakssammenheng blir lagt inn i den nasjonale databasen for at opplysningene skal kunne formidles videre til Verdens helseorganisasjon (WHO) og de europeiske legemiddelmyndighetene, samt brukes senere. Klassifiseringen innebærer ikke at årsakssammenheng er bevist. Vedlegg av epikriser, journalnotater eller obduksjonsrapporter gir oss verdifull tilleggsinformasjon.

### Hvem skal melde?

Blir pasienten lagt inn på sykehus, bør meldingen skrives av den sykehuslege som har behandlet eller utredet pasienten. Utenfor sykehus bør meldingen sendes av legen/tannlegen som diagnostiserer reaksjonen. Apotekfarmasøyer med pasientkontakt oppfordres til å melde bivirkninger de får kunnskap om gjennom sitt arbeid.

### Personvern

Alle pasientopplysninger blir behandlet strengt konfidensielt av RELIS og Statens legemiddelverk. Alle persondata blir anonymisert ved innleggelse i bivirkningsdatabasen. Identifiserbare data blir ikke gitt videre i noe tilfelle.

## Tables

Causes of acute lower back pain (Modified according to Eriksen and Brage, 2000)

Divided into the three main diagnostic groups

<b>Non-specific back pain</b> , rarely any definite or proven relation to the diagnosis
Muscle injury
Myalgia
Spondylosis
Degenerative changes
Pelvic loosening
Osteoarthritis
Scheuermann's disease
Spondylolisthesis
Scoliosis
Kyphosis
Deformities
<b>Radiculopathy</b>
Disc prolapse
Recess stenosis (lateral spinal stenosis)
Spinal stenosis (medial spinal stenosis)
Benign tumour in the nerve root
Synovial cysts
<b>Systemic/visceral/possible severe pathology</b>
Fracture/injury
Osteoporosis
Growths (Myeloma, Metastasis, Spinal tumour)
Inflammatory disease (Ankylosing spondylitis, Polymyalgia rheumatica, Reiter's disease, psoriasis, Intestinal disease)
Metabolic bone disease (Paget's disease)
Pancreatitis
Perforated ulcer
Pyelonephritis
Prostatitis
Kidney stone
Herpes zoster
Endometriosis
Aortic aneurysm



Appendix 5 Template for radiological  
evaluation of magnetic resonance or CT  
images



# Template for radiological evaluation of MR and CT images

Date: Us:\_\_\_\_\_ Investigation:\_\_\_\_\_

Pasient: Initials:\_\_\_\_\_ B.date:\_\_\_\_\_ Pa.no:\_\_\_\_\_ Rand.no:\_\_\_\_\_

Radiologist:\_\_\_\_\_ MR Seq.\_\_\_\_\_

## Disc L3/L4:

Modic: I  II  III  Mixed type I/II  II/III   
\_\_\_\_\_ % of end plate Max Depth \_\_\_\_\_ mm

Facettjoint: Degeneration: No  Slight  Severe   
Assymmetry: No  Yes

Spinal stenosis: Central: 0  1  2  Foraminal: 0  1  2

Discus: Signal intensity: 0  1  2  3

Disc height: \_\_\_\_\_ % of normal disc above

HIZ (High Intensity Zone): Not present  Present

Disc contour: 0  1  2  3  4  5

Herniation Size:\_\_\_\_\_ Location:\_\_\_\_\_

Nerve root: 0  1  2  3  Thickening \_\_\_\_\_

Anterolisthesis: Not present  Present  \_\_\_mm +Spondylolysis

Retrolisthesis: Not present  Present  \_\_\_mm

## Disc L4/L5:

Modic: I  II  III  Mixed type I/II  II/III   
\_\_\_\_\_ % of end plate Max Depth \_\_\_\_\_ mm

Facettjoint: Degeneration: No  Slight  Severe   
Assymmetry: No  Yes

Spinal stenosis: Central: 0  1  2  Foraminal: 0  1  2

Discus: Signal intensity: 0  1  2  3

Disc height: \_\_\_\_\_% of normal disc above

HIZ (High Intensity Zone): Not present  Present

Disc contour: 0  1  2  3  4  5

Herniation Size: \_\_\_\_\_ Location: \_\_\_\_\_

Nerve root: 0  1  2  3  Thickening \_\_\_\_\_

Anterolisthesis: Not present  Present  \_\_mm +Spondylolysis

Retrolisthesis: Not present  Present  \_\_mm

### Disc L5/S1:

Modic: I  II  III  Mixed type I/II  II/III

\_\_\_\_\_ % of end plate Max Depth \_\_\_\_\_ mm

Facettjoint: Degeneration: No  Slight  Severe

Assymetry: No  Yes

Spinal stenosis: Central: 0  1  2  Foraminal: 0  1  2

Discus: Signal intensity: 0  1  2  3

Disc height: \_\_\_\_\_% of the disc above

HIZ (High Intensity Zone): Not present  Present

Disc contour: 0  1  2  3  4  5

Herniation Size: \_\_\_\_\_ Location: \_\_\_\_\_

Nerve root: 0  1  2  3  Thickening \_\_\_\_\_

Anterolisthesis: Not present  Present  \_\_mm +Spondylolysis

Retrolisthesis: Not present  Present  \_\_mm

### Modic changes in other levels:

L1/L2: \_\_\_\_\_

L2/L3: \_\_\_\_\_

Signal intensity: 0: hyperintense homogeneous  
 1: hyperintense with visible intranuclear cleft  
 2: intermediate  
 3: hypointense

Disc height is measured in percent of the height of the nearest normal disc above the disc we are evaluating.

Disc contour:	0: normal	Herniation Size:	0: no
	1: bulging		1: <1/3
	2: focal protrusion		2: 1/3-2/3
	3: broad based protrusion		3: >2/3
	4: extrusion		of spinal
	5: sequestration		canal (axial)

Location in axial plane:

0:	left extraforaminal
1:	left foraminal
2:	left recess
3:	left central
4:	central
5:	right central
6:	right recess
7:	right foraminal
8:	right extraforaminal

Nerve root:	0: no contact	Thickening of nerve root is defined as thicker than the contralateral one in the same level
	1: in contact	
	2: dislocation	
	3: compression	

Central spinal stenosis:

0:	normal
1:	relative
2:	severe

Foraminal spinal stenosis:

0:	normal
1:	reduced fat around the nerve root
2:	no visible fat around the nerve root

### References:

- 1) Modic, Steinberg, Ross, Masaryk, Carter. Degenerative disk disease: assessment of changes in vertebral body marrow with MR imaging. Radiology 1988.
- 2) Weishaupt et al. MR imaging and CT in osteoarthritis of the lumbar facet joints. Skeletal Radiology 1999.
- 3) Weishaupt et al. Positional MR imaging of the lumbar spine: does it demonstrate nerve root compromise not visible at conventional MR imaging? Radiology 2000.
- 4) Weishaupt et al. MR imaging of the lumbar spine: prevalence of intervertebral disk extrusion and sequestration, nerve root compression, end plate abnormalities, and osteoarthritis of the facet joints in asymptomatic volunteers. Radiology 1998.
- 5) Raininko et al. Observer variability in the assessment of disc degeneration on magnetic resonance images of the lumbar and thoracic spine. Spine 1995.
- 6) Roberts et al. MRI analysis of lumbar intervertebral disc height in young and older populations. Magn Reson Imaging 1997.
- 7) Aprill et al. High-intensity zone: a diagnostic sign of painful lumbar disc on magnetic resonance imaging. Br J Radiol 1992.
- 8) Fardon et al. Nomenclature and classification of lumbar disc pathology. Recommendations of the Combined task Forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology. Spine 2001.
- 9) Boos et al. The diagnostic accuracy of magnetic resonance imaging, work perception, and psychosocial factors in identifying symptomatic disc herniations. Spine 1995.
- 10) Yochum, Barry. Diagnostic imaging of the musculoskeletal system. Essentials of Skeletal Radiology 1996.





## Appendix 6 Form book



Pasientnr. 

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Fødselsnr. 

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Sykehus

- Sykehuset Levanger (420)
- Universitetssykehuset Nord-Norge (500)
- Nordlandssykehuset Bodø (510)
- Sykehuset Buskerud (230)
- St. Olavs Hospital (400)

# SKJEMABOK

Versjon 3

## Epidural sacral injection study

Effect of volume and triamcinolone on chronic  
lumbosacral radiculopathy?

Double blind multicentre randomised  
placebo-controlled trial.

Pasientens navn/mobilnr \_\_\_\_\_

Denne skjemabok skal følge pasientens journal

Prosjektleder:

Trond Iversen

Avd. for fys med og rehabilitering, UNN

Institutt for samfunnsmedisin (ISM), Universitetet i Tromsø

Mobilnummer 95 18 69 88

Epost trondiv@online.no

# OVERSIKT SKJEMA

Dato for innsending  
av skjema

Signatur

Pasientinformasjon (sendes til pasienten med innkallingen)

Skriftelig informert samtykke

\_\_\_\_\_

Skjema 1 - inklusjon - uke 0

\_\_\_\_\_

Skjema 2 - inklusjon - uke 0

\_\_\_\_\_

Medikamentforbruk før injeksjon

Henvisning anestesilege vedlagt

- Randomisering og injeksjon
- Pasientinformasjon etter injeksjon
- Medikamentforbruk før etterundersøkelse
- Ultralydundersøkelse
- Årsaker til at epiduralinjeksjon nr 2 ikke blir gitt

Henvisning nevrofysiologi

Svar fra nevrofysiologi

Skjema 3 - 1. etterundersøkelse - uke 6

\_\_\_\_\_

Skjema 4 - 1. etterundersøkelse - uke 6

\_\_\_\_\_

Skjema 3 - 2. etterundersøkelse - uke 12

\_\_\_\_\_

Skjema 4 - 2. etterundersøkelse - uke 12

\_\_\_\_\_

Skjema 3 - 3. etterundersøkelse - uke 52

\_\_\_\_\_

Skjema 4 - 3. etterundersøkelse - uke 52

\_\_\_\_\_

Epidural sacral injection study. Protocol Code Number 2137. EudraCT Number 2004-004585-32. ISRCTN Number 12574253. **Pasientinformasjon og Skriftlig informert samtykke.** 2007-10-15.

Sendes til pasienten sammen med innkallingen til poliklinikken.

### **Forespørsel om deltagelse i forskningsprosjekt.**

Du har fått time for ryggundersøkelse ved poliklinikken. I den forbindelse ønsker vi å informere deg om et pågående forskningsprosjekt ved poliklinikken vedrørende rygginjeksjoner, såkalt sakral epidural injeksjon. Dersom dine ryggplager, etter grundig forundersøkelse, viser seg å være egnet for rygginjeksjon vil du bli spurt om deltagelse i forskningsprosjektet. Gravide kvinner, og kvinner som ammer, er utelukket fra deltagelse. Ikke-gravide kvinner i fertil alder som ønsker å delta i forskningsprosjektet må benytte sikker prevensjon.

Ryggsmerter og isjias er et vanlig forekommende problem. Vi regner med at om lag 80 % av alle mennesker opplever ryggsmerter en eller flere ganger i løpet av livet. For de pasientene som får kroniske smerter, ofte med utstråling i benet, kan det være vanskelig å finne en egnet behandlingsmetode. Mange har prøvd ulike typer medikamenter, fysioterapi og kiropraktorbehandling uten varig bedring. Bare et lite antall av alle ryggpasienter egner seg for operasjon.

Helt fra begynnelsen av 1900 tallet har det vært anvendt såkalt sakral epidural injeksjon (sprøyte) mot ryggsmerter. Sakral epidural injeksjon betyr en rygginjeksjon (sprøyte i ryggen). Injeksjonen settes i en naturlig åpning like over halebenet. Området hvor injeksjonen settes bedøves først, og selve injeksjonen oppleves vanligvis ikke som smertefull. Selve injeksjonen tar om lag 10 minutter, og utføres av anestesilege som er vant med denne typen behandling og derfor ivaretar sikkerheten ved behandlingen på en faglig forsvarlig måte. Til tross for at metoden har vært brukt i snart 100 år finnes det bare et fåtall gode vitenskapelige studier som dokumenterer at denne behandlingsmetoden hjelper. Dersom det i vår undersøkelse kan bevises at injeksjonen hjelper mot ryggsmerter og isjias, slik at de som plages kan få en smertefri hverdag og komme raskere tilbake i jobb, vil behandlingsmetoden kanskje kunne få en større utbredelse.

Forskningsprosjektet utføres som et samarbeidsprosjekt mellom Universitetet i Nord-Norge, Nordlandssykehuset i Bodø, Sykehuset Levanger, St. Olavs Hospital og Sykehuset Buskerud. Pasienter som henvises fra fastlegene til ryggundersøkelse ved et av disse sykehusene er aktuelle for deltagelse i studien. Hovedhensikten med forskningsprosjektet er å finne ut om medikamentet Kenacort® (steroidpreparatet triamcinolon) kan redusere smerte og bedre ryggfunksjon.

De som ønsker å være med på denne undersøkelsen vil få to rygginjeksjoner med to ukers mellomrom. Før injeksjonen skal alle pasientene ha tatt MR undersøkelse av ryggen. I tillegg vil alle pasientene som deltar få ryggundervisning og instruksjon i ryggøvelse av fysioterapeut og lege. Dersom du ikke ønsker å delta i forskningsstudien vil du allikevel få det beste tilbudet poliklinikken kan tilby enten i form av medikamenter eller fysikalsk behandling. Dersom du ønsker å delta, men senere trekker deg fra studien, vil du selvsagt få det til enhver tid beste behandlingstilbud poliklinikken kan tilby.

Når det gjelder injeksjonene vil de pasientene som deltar bli tilfeldig fordelt til enten sprøyte med aktivt medikament eller sprøyte med ikke-aktivt medikament (såkalt placebo). I vår

Epidural sacral injection study. Protocol Code Number 2137. EudraCT Number 2004-004585-32. ISRCTN Number 12574253. **Pasientinformasjon og Skriftlig informert samtykke.** 2007-10-15.

studie brukes saltvann som placebomedikament. Det er registrert få alvorlige bivirkninger ved bruk av medikamentet Kenacort®. De fleste vil etter injeksjonen kunne kjenne et lett press i korsryggen det første døgnet. Noen pasienter kan oppleve varmfølelse og forbigående rødhet i huden et par dager etter injeksjonen. Når medikamentet brukes til rygginjeksjon kan det i sjeldne tilfeller oppstå en irritasjon i den nervehinnen som omslutter nervene (araknoidea) som i sin tur kan gi opphav til kroniske smerter (araknoiditt). Selve rygginjeksjonen kan i sjeldne tilfeller føre til infeksjon eller blødning i epiduralrommet. Dette kan være en alvorlig komplikasjon som må behandles på sykehus. Rygginjeksjonen kan også gi punksjon av nervehinnen dura mater med lekkasje av spinalvæske som følge. Spinalvæskelekkasje kan gi hodepine (spinal hodepine). Medikamentet Kenacort® brukes daglig av leger ved sykehus og på allmennlegekontor for å behandle smerte- og betennelsestilstander i ledd og sener. Faren for skade, infeksjon eller forverring av tilstanden er minimal. Det vil etter at injeksjonene er satt ikke være spesielle restriksjoner hva gjelder hvilke medikamenter din fastlege kan bruke for å behandle dine rygg smerter.

Alle pasienter som deltar i undersøkelsen vil bli bedt om å svare på spørreskjema som kartlegger ryggplagene. Når injeksjonene er satt vil det bli oppfølgende kontroller av lege og fysioterapeut etter 6, 12 og 52 uker. Dersom det skulle vise seg at du i løpet av oppfølgningstiden får så sterke ryggplager at du vil trenge ryggoperasjon vil du få tilbud om dette.

Alle opplysninger om deg blir behandlet konfidensielt, og data blir oppbevart i aidentifisert form. Deltagelse i forskningsprosjektet er frivillig, og du vil på ethvert tidspunkt ha anledning til å trekke deg fra undersøkelsen. Allerede innsamlede data vil da ikke bli slettet og informasjonen som er samlet inn om deg kan fortsatt brukes i forbindelse med studien. Du har imidlertid rett til å få vite hva slags informasjon som fortsatt vil bli oppbevart. Data fra studien vil bli oppbevart i din sykehusjournal i minst 15 år etter at prosjektet er avsluttet. Vi gjør også oppmerksom på at statlige kontrollmyndigheter vil kunne ha behov for å sjekke at opplysninger gitt i studien stemmer med opplysninger i din journal for å kontrollere studiens kvalitet. Alle som deltar i studien vil ha full tilgang til prosjektets konklusjoner når disse foreligger i form av publiserte vitenskapelige artikler. Prosjektleder vil også etter avsluttet prosjekt utarbeide en oppsummering av resultatene som vil bli tilsendt alle som har deltatt i studien.

Når du er undersøkt ved sykehuset vil legen orientere deg om forskningsprosjektet. Dersom du etter å ha mottatt informasjon om studien ønsker å delta vil du bli bedt om å fylle ut en samtykkeerklæring. Vi håper at dette ikke vil legge unødig press på deg, og understreker at det selvsagt er frivillig å delta.

Prosjektet finansieres med Regionale forskningsmidler fra Helse-Nord. Prosjektet er vurdert av Regional komité for medisinsk forskningsetikk (REK NORD), av Personvernombudet i Norsk Samfunnsvitenskapelig datatjeneste (NSD) og godkjent av Statens Legemiddelverk. Forsøkspersonene er forsikret mot skade som skyldes deltagelse i studien etter reglene i Lov om produktansvar (Legemiddelforsikringen).

Dersom du har spørsmål om forskningsprosjektet kan du ta kontakt med sykehuset og den legen som du har fått time til ved poliklinikken.

Epidural sacral injection study. Protocol Code Number 2137. EudraCT Number 2004-004585-32. ISRCTN Number 12574253. **Pasientinformasjon og Skriftlig informert samtykke.** 2007-10-15.

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### **Forespørsel om deltagelse i forskningsprosjekt.**

Du har fått time for ryggundersøkelse ved poliklinikken. I den forbindelse ønsker vi å informere deg om et pågående forskningsprosjekt ved poliklinikken vedrørende rygginjeksjoner, såkalt sakral epidural injeksjon. Dersom dine ryggplager, etter grundig forundersøkelse, viser seg å være egnet for rygginjeksjon vil du bli spurt om deltagelse i forskningsprosjektet. Gravide kvinner, og kvinner som ammer, er utelukket fra deltagelse. Ikke-gravide kvinner i fertil alder som ønsker å delta i forskningsprosjektet må benytte sikker prevensjon.

Ryggsmerter og isjias er et vanlig forekommende problem. Vi regner med at om lag 80 % av alle mennesker opplever ryggsmerter en eller flere ganger i løpet av livet. For de pasientene som får kroniske smerter, ofte med utstråling i benet, kan det være vanskelig å finne en egnet behandlingsmetode. Mange har prøvd ulike typer medikamenter, fysioterapi og kiropraktorbehandling uten varig bedring. Bare et lite antall av alle ryggpasienter egner seg for operasjon.

Helt fra begynnelsen av 1900 tallet har det vært anvendt såkalt sakral epidural injeksjon (sprøyte) mot ryggsmerter. Sakral epidural injeksjon betyr en rygginjeksjon (sprøyte i ryggen). Injeksjonen settes i en naturlig åpning like over halebenet. Området hvor injeksjonen settes bedøves først, og selve injeksjonen oppleves vanligvis ikke som smertefull. Selve injeksjonen tar om lag 10 minutter, og utføres av anestesilege som er vant med denne typen behandling og derfor ivaretar sikkerheten ved behandlingen på en faglig forsvarlig måte. Til tross for at metoden har vært brukt i snart 100 år finnes det bare et fåtall gode vitenskapelige studier som dokumenterer at denne behandlingsmetoden hjelper. Dersom det i vår undersøkelse kan bevises at injeksjonen hjelper mot ryggsmerter og isjias, slik at de som plages kan få en smertefri hverdag og komme raskere tilbake i jobb, vil behandlingsmetoden kanskje kunne få en større utbredelse.

Forskningsprosjektet utføres som et samarbeidsprosjekt mellom Universitetet i Nord-Norge, Nordlandssykehuset i Bodø, Sykehuset Levanger, St. Olavs Hospital og Sykehuset Buskerud. Pasienter som henvises fra fastlegene til ryggundersøkelse ved et av disse sykehusene er aktuelle for deltagelse i studien. Hovedhensikten med forskningsprosjektet er å finne ut om medikamentet Kenacort® (steroidpreparatet triamcinolon) kan redusere smerte og bedre ryggfunksjon.

De som ønsker å være med på denne undersøkelsen vil få to rygginjeksjoner med to ukers mellomrom. Før injeksjonen skal alle pasientene ha tatt MR undersøkelse av ryggen. I tillegg vil alle pasientene som deltar få ryggundervisning og instruksjon i ryggøvelse av fysioterapeut og lege. Dersom du ikke ønsker å delta i forskningsstudien vil du allikevel få det beste tilbudet poliklinikken kan tilby enten i form av medikamenter eller fysikalsk behandling. Dersom du ønsker å delta, men senere trekker deg fra studien, vil du selvsagt få det til enhver tid beste behandlingstilbud poliklinikken kan tilby.

Når det gjelder injeksjonene vil de pasientene som deltar bli tilfeldig fordelt til enten sprøyte med aktivt medikament eller sprøyte med ikke-aktivt medikament (såkalt placebo). I vår



Epidural sacral injection study. Protocol Code Number 2137. EudraCT Number 2004-004585-32. ISRCTN Number 12574253. **Pasientinformasjon og Skriftlig informert samtykke.** 2007-10-15.

studie brukes saltvann som placebomedikament. Det er registrert få alvorlige bivirkninger ved bruk av medikamentet Kenacort®. De fleste vil etter injeksjonen kunne kjenne et lett press i korsryggen det første døgnet. Noen pasienter kan oppleve varmfølelse og forbigående rødhet i huden et par dager etter injeksjonen. Når medikamentet brukes til rygginjeksjon kan det i sjeldne tilfeller oppstå en irritasjon i den nervehinnen som omslutter nervene (araknoidea) som i sin tur kan gi opphav til kroniske smerter (araknoiditt). Selve rygginjeksjonen kan i sjeldne tilfeller føre til infeksjon eller blødning i epiduralrommet. Dette kan være en alvorlig komplikasjon som må behandles på sykehus. Rygginjeksjonen kan også gi punksjon av nervehinnen dura mater med lekkasje av spinalvæske som følge. Spinalvæskelekkasje kan gi hodepine (spinal hodepine). Medikamentet Kenacort® brukes daglig av leger ved sykehus og på allmennlegekontor for å behandle smerte- og betennelsestilstander i ledd og sener. Faren for skade, infeksjon eller forverring av tilstanden er minimal. Det vil etter at injeksjonene er satt ikke være spesielle restriksjoner hva gjelder hvilke medikamenter din fastlege kan bruke for å behandle dine rygg smerter.

Alle pasienter som deltar i undersøkelsen vil bli bedt om å svare på spørreskjema som kartlegger ryggplagene. Når injeksjonene er satt vil det bli oppfølgende kontroller av lege og fysioterapeut etter 6, 12 og 52 uker. Dersom det skulle vise seg at du i løpet av oppfølgningstiden får så sterke ryggplager at du vil trenge ryggoperasjon vil du få tilbud om dette.

Alle opplysninger om deg blir behandlet konfidensielt, og data blir oppbevart i aidentifisert form. Deltagelse i forskningsprosjektet er frivillig, og du vil på ethvert tidspunkt ha anledning til å trekke deg fra undersøkelsen. Allerede innsamlede data vil da ikke bli slettet og informasjonen som er samlet inn om deg kan fortsatt brukes i forbindelse med studien. Du har imidlertid rett til å få vite hva slags informasjon som fortsatt vil bli oppbevart. Data fra studien vil bli oppbevart i din sykehusjournal i minst 15 år etter at prosjektet er avsluttet. Vi gjør også oppmerksom på at statlige kontrollmyndigheter vil kunne ha behov for å sjekke at opplysninger gitt i studien stemmer med opplysninger i din journal for å kontrollere studiens kvalitet. Alle som deltar i studien vil ha full tilgang til prosjektets konklusjoner når disse foreligger i form av publiserte vitenskapelige artikler. Prosjektleder vil også etter avsluttet prosjekt utarbeide en oppsummering av resultatene som vil bli tilsendt alle som har deltatt i studien.

Når du er undersøkt ved sykehuset vil legen orientere deg om forskningsprosjektet. Dersom du etter å ha mottatt informasjon om studien ønsker å delta vil du bli bedt om å fylle ut en samtykkeerklæring. Vi håper at dette ikke vil legge unødig press på deg, og understreker at det selvsagt er frivillig å delta.

Prosjektet finansieres med Regionale forskningsmidler fra Helse-Nord. Prosjektet er vurdert av Regional komité for medisinsk forskningsetikk (REK NORD), av Personvernombudet i Norsk Samfunnsvitenskapelig datatjeneste (NSD) og godkjent av Statens Legemiddelverk. Forsøkspersonene er forsikret mot skade som skyldes deltagelse i studien etter reglene i Lov om produktansvar (Legemiddelforsikringen).

Dersom du har spørsmål om forskningsprosjektet kan du ta kontakt med sykehuset og den legen som du har fått time til ved poliklinikken.

Epidural sacral injection study. Protocol Code Number 2137. EudraCT Number 2004-004585-32. ISRCTN Number 12574253. **Pasientinformasjon og Skriftlig informert samtykke.** 2007-10-15.

Fylles ut når pasienten oppfyller inklusjonskriteriene og samtykker til deltagelse i studien.

### **Skriftlig informert samtykke.**

Informasjon om studien er gitt skriftlig og muntlig og pasienten har lest pasientinformasjonen om studien.

Dato:

Signatur:

Tittel:

Jeg har lest pasientinformasjonen og samtykker med dette i å delta i studien hvor effekten av sakral epidural rygginjeksjon med steroider sammenlignes med sakral epidural rygginjeksjon med placebo (saltvann).

Dato:

Pasientsignatur:

Din kontaktperson på sykehuset er:

Telefon:

Originalen beholdes i skjemaboken (Pasientens journal)

Kopi 1 er pasientens eksemplar

Kopi 2 sendes til: Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge, 9030 Tromsø, merket "Epiduralstudien".

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# Spørreskjema for pasienter som skal injiseres i ryggen

Skjema 1 Pasient nr. Sykehus nr. 

Pasientdata	
Navn	
Fødselsnr. (11 siffer) <input type="text"/>	
Adresse	
Alder (år) <input type="text"/>	
Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne	

Formålet med dette spørreskjemaet er å gi leger, sykepleiere og fysioterapeuter bedre forståelse av ryggpasienters plager og å vurdere effekter av behandling. Din utfylling av skjemaet vil være til stor nytte for å kunne gi et best mulig behandlingstilbud til ryggpasienter i fremtiden.

Spørreskjemaet har fire deler. Første del omhandler ulike sider ved din utdanning og familie samt dine smerter og plager. De neste delene består av tre ulike sett spørsmål for måling av din nåværende helse. Det første av disse (kalt Oswestryskåre) måler hvordan ryggplagene påvirker dine dagligdagse gjøremål. Det andre (kalt EQ-5D) måler din helserelaterte livskvalitet. Den siste delen er en skala der du skal merke av hvor god eller dårlig din helsetilstand er.

Dato for utfylling	<input type="text"/>	.	<input type="text"/>	.	<input type="text"/>
	Dag		Måned		År

Røyker du?	<input type="checkbox"/> Ja	<input type="checkbox"/> Nei
------------	-----------------------------	------------------------------

## Høyde og vekt

1. Hvor mye veier du?  kg2. Hvor høy er du?  cm

## Utdanning og yrke

1. Hva er din høyeste fullførte utdanning? (Sett ett kryss)

- Grunnskole 7-10 år, framhaldsskole eller folkehøyskole
- Yrkesfaglig videregående skole, yrkesskole eller realskole
- Allmennfaglig videregående skole eller gymnas
- Høyskole eller universitet (mindre enn 4 år)
- Høyskole eller universitet (4 år eller mer)

2. Hvilket yrke har du, eller hadde du tidligere (før du eventuelt ble arbeidsledig, permittert, trygdet eller pensjonert)

## Familie og barn

1. Sivilstatus (sett ett kryss)

- Gift
- Samboende
- Enslig

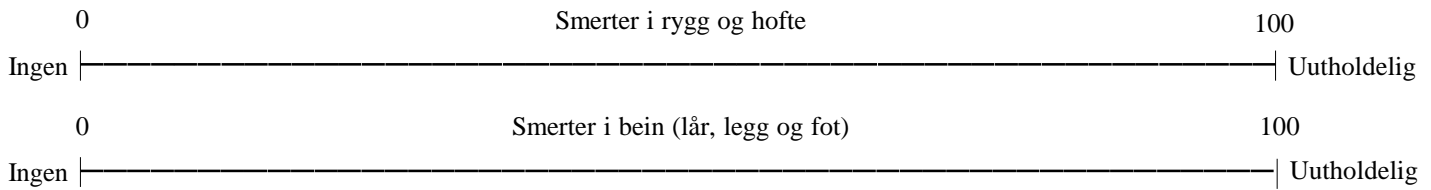
2. Hvor mange barn har du?  stk

## Morsmål

- Norsk
- Samisk
- Annet, angi hvilket

### Hvor sterke smerter har du nå

De vannrette linjene nedenfor viser en skala fra 0 til 100 for smertestyrke. Den begrenses på venstre side av ingen smerte (0) og på høyre side av uutholdelig smerte (100). Sett en strek på tvers av linjene svarende til din største smerte nå for tiden (den siste uken).



### Funksjonsscore (Oswestry)

Disse spørsmålene er utarbeidet for å gi oss informasjon om hvordan dine smerter har påvirket dine muligheter til å klare dagliglivet ditt. Vær så snill å besvare spørsmålene ved å sette kryss (kun ett kryss for hvert avsnitt) i de rutene som passer best for deg.

#### 1. Smerte

- Jeg har ingen smerter for øyeblikket
- Smertene er veldig svake for øyeblikket
- Smertene er moderate for øyeblikket
- Smertene er temmelig sterke for øyeblikket
- Smertene er veldig sterke for øyeblikket
- Smertene er det verste jeg kan tenke meg for øyeblikket

#### 2. Personlig stell

- Jeg kan stelle meg selv på valig måte uten at det forårsaker ekstra smerter
- Jeg kan stelle meg selv på vanlig måte, men det er veldig smertefult
- Det er smertefult å stelle seg selv, og jeg gjør det langsomt og forsiktig
- Jeg trenger noe hjelp, men klarer det meste av mitt personlige stell
- Jeg trenger hjelp hver dag til det meste av eget stell
- Jeg kler ikke på meg, har vanskeligheter med å vaske meg og holder sengen

#### 4. Å gå

- Smerter hindrer meg ikke i å gå i det hele tatt
- Smerter hindrer meg i å gå mer enn 1 1/2 km
- Smerter hindrer meg i å gå mer enn 3/4 km
- Smerter hindrer meg i å gå mer enn 100 m
- Jeg kan bare gå med stokk eller krykker
- Jeg ligger for det meste i sengen, og jeg må krabbe til toalettet

#### 5. Å sitte

- Jeg kan sitte så lenge jeg vil i en hvilken som helst stol
- Jeg kan sitte så lenge jeg vil i min favorittstol
- Smerter hindrer meg i å sitte mer enn en time
- Smerter hindrer meg i å sitte mer enn en halv time
- Smerter hindrer meg i å sitte mer enn ti minutter
- Smerter hindrer meg i å sitte i det hele tatt

#### 3. Å løfte

- Jeg kan løfte tunge ting uten å få mer smerter
- Jeg kan løfte tunge ting, men får smerter
- Smertene hindrer meg i å løfte tunge ting opp fra gulvet, men jeg greier det hvis det som skal løftes er gunstig plassert, for eksempel på et bord
- Smertene hindrer meg i å løfte tunge ting, men jeg klarer lette og middels tunge ting, hvis det er gunstig plassert
- Jeg kan bare løfte noe som er veldig lett
- Jeg kan ikke løfte eller bære noe i det hele tatt

#### 6. Å stå

- Jeg kan stå så lenge jeg vil uten å få smerter
- Jeg kan stå så lenge jeg vil, men får mer smerter
- Smerter hindrer meg i å stå mer enn en time
- Smerter hindrer meg i å stå mer enn en halv time
- Smerter hindrer meg i å stå mer enn ti minutter
- Smerter hindrer meg i å stå i det hele tatt



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**7. Å sove**

- Søvnens min forstyrres aldri av smerter
- Søvnens min forstyrres av og til av smerter
- På grunn av smerter får jeg mindre enn seks timers søvn
- På grunn av smerter får jeg mindre en fire timers søvn
- På grunn av smerter får jeg mindre enn to timers søvn
- Smerter hindrer all søvn

**8. Seksualliv**

- Seksuallivet mitt er normalt og forårsaker ikke mer smerter
- Seksuallivet mitt er normalt, men forårsaker noe mer smerter
- Seksuallivet mitt er normalt, men svært smertefullt
- Seksuallivet mitt er svært begrenset av smerter
- Seksuallivet mitt er nesten borte på grunn av smerter
- Smerter forhindrer alt seksualliv

**9. Sosialt liv (omgang med venner og bekjente)**

- Det sosiale livet mitt er normalt og forårsaker ikke mer smerter
- Det sosiale livet mitt er normalt, men øker graden av smerter
- Smerter har ingen betydelig innvirkning på mitt sosiale liv, bortsett fra at de begrenser mine mer fysiske aktive sider, som sport osv.
- Smerter har begrenset mitt sosiale liv, og jeg går ikke så ofte ut
- Smerter har begrenset mitt sosiale liv til hjemmet
- På grunn av smerter har jeg ikke noe sosialt liv

**10. Å reise**

- Jeg kan reise hvor som helst uten smerter
- Jeg kan reise hvor som helst, men det gir mer smerter
- Smertene er ille, men jeg klarer reiser på to timer
- Smerter begrenser meg til korte reiser på under en time
- Smerter begrenser meg til korte, nødvendige reiser på under 30 minutter
- Smerter forhindrer meg fra å reise, unntatt for å få behandling

**Beskrivelse av helsetilstand (EQ-5D)**

Vis hvilke utsagn som passer på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av dimensjonene nedenfor.

**1. Gange**

- Jeg har ingen problemer med å gå omkring
- Jeg har litt problemer med å gå omkring
- Jeg er sengeliggende

**2. Personlig stell**

- Jeg har ingen problemer med personlig stell
- Jeg har litt problemer med å vaske meg eller kle meg
- Jeg er ute av stand til å vaske meg eller kle meg

**3. Vanlige gjøremål** (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- Jeg har ingen problemer med å utføre mine vanlige gjøremål
- Jeg har litt problemer med å utføre mine vanlige gjøremål
- Jeg er ute av stand til å utføre mine vanlige gjøremål

**4. Smerte og ubehag**

- Jeg har verken smerte eller ubehag
- Jeg har moderat smerte og ubehag
- Jeg har sterk smerte og ubehag

**5. Angst og depresjon**

- Jeg er hverken engstelig eller depriment
- Jeg er noe engstelig og depriment
- Jeg er svært engstelig og depriment

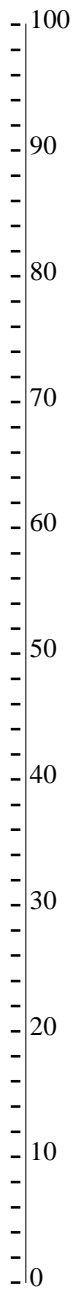
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## Helsetilstand

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0.

Vi ber deg om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.

Best tenkelige  
helsetilstand



Nåværende  
helsetilstand

Verst tenkelige  
helsetilstand

## Har du søkt om uføretrygd?

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget

## Har du søkt om erstatning fra forsikringsselskap eller folketrygden (evt. yrkesskadeerstatning)?

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget



# SMERTE, FYSISK AKTIVITET OG JOBB

(Fear-Avoidance Beliefs Questionnaire,  
Waddell et al 1993)

Her er noe av det som andre har fortalt oss om ryggsmertene sine. Kryss av for ett tall fra 0 (helt uenig) til 6 (helt enig) for hvert utsagn for å si hvor mye fysiske aktiviteter som å bøye seg, løfte, gå eller kjøre vil påvirke ryggen din.

		HELT UENIG		USIKKER			HELT ENIG		
		0	1	2	3	4	5	6	
1	Smertene mine ble forårsaket av fysisk aktivitet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2	Fysisk aktivitet forverrer smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3	Fysisk aktivitet kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4	Jeg burde ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5	Jeg kan ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Følgende utsagn handler om hvordan det vanlige arbeidet ditt påvirker eller kan påvirke ryggsmertene dine.

		HELT UENIG		USIKKER			HELT ENIG		
		0	1	2	3	4	5	6	
6	Smertene mine ble forårsaket av arbeidet mitt eller et uhell på jobben	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7	Arbeidet mitt forverret smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8	Jeg har framsatt erstatningskrav for smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9	Arbeidet mitt er for tungt for meg	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10	Arbeidet mitt forverrer eller kan forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11	Arbeidet mitt kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12	Jeg burde ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
13	Jeg kan ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
14	Jeg kan ikke utføre det vanlige arbeidet mitt før smertene er behandlet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15	Jeg tror ikke jeg vil være tilbake på det vanlige arbeidet mitt innen tre måneder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
16	Jeg tror ikke jeg noen gang vil være i stand til å komme tilbake til det arbeidet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	





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# Registrerings skjema for pasienter som injiseres i ryggen

<p><b>Pasientdata</b></p> <p>Navn</p> <p>Fødselsnr. (11 siffer) <table border="1"><tr><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td><td> </td></tr></table></p> <p>Adresse</p> <p>Alder (år) <table border="1"><tr><td> </td><td> </td></tr></table></p> <p>Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne</p> <p>Dato for utfylling <table border="1"><tr><td> </td><td> </td><td>.</td><td> </td><td> </td><td>.</td><td> </td><td> </td></tr><tr><td colspan="2">Dag</td><td></td><td colspan="2">Måned</td><td></td><td colspan="2">År</td></tr></table></p> <p><b>Arbeidsstatus</b></p> <p><input type="checkbox"/> I arbeid <input type="checkbox"/> Student/skoleelev</p> <p><input type="checkbox"/> Sykemeldt <input type="checkbox"/> Pensjonist</p> <p><input type="checkbox"/> Aktiv sykemeldt <input type="checkbox"/> Arbeidsledig</p> <p><input type="checkbox"/> Delvis sykemeldt <input type="checkbox"/> Attføring/rehabilitering</p> <p><table border="1"><tr><td> </td><td> </td></tr></table> % sykemeldt <input type="checkbox"/> Uføretrygdet</p> <p><input type="checkbox"/> Hjemneværende</p> <p><b>Symptomvarighet</b></p> <p>Ryggsmerter <table border="1"><tr><td> </td><td> </td><td> </td></tr></table> (uker)</p> <p>Utrålende smerter <table border="1"><tr><td> </td><td> </td><td> </td></tr></table> (uker)</p> <p>Varighet sykemelding og/eller attføring pga. disse smertene <table border="1"><tr><td> </td><td> </td><td> </td></tr></table> (uker)</p>																.			.			Dag			Måned			År													<p><b>Radiologisk vurdering</b> (Kryss av for flere alternativer når det er aktuelt)</p> <p>1. Undersøkelse</p> <p><input type="checkbox"/> MR Dato <table border="1"><tr><td> </td><td> </td><td>.</td><td> </td><td> </td><td>.</td><td> </td><td> </td></tr><tr><td colspan="2">Dag</td><td></td><td colspan="2">Måned</td><td></td><td colspan="2">År</td></tr></table></p> <p>Sykehus/institutt.....</p> <p>2. Funn</p> <p><input type="checkbox"/> Normal</p> <p><input type="checkbox"/> Signalforandringer</p> <p><input type="checkbox"/> Skive bukning/dekket prolaps</p> <p><input type="checkbox"/> Fritt/Sekvestrert prolaps</p> <p><input type="checkbox"/> Fortykket nerverot</p> <p><input type="checkbox"/> Lateral resesstenose med dislosert nerverot</p>			.			.			Dag			Måned			År	
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Dag			Måned			År																																																			



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**Kliniske funn**
**1. SLR**

 Gradtall positiv test 

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 Hø  Ve

 2. Omvendt Lasegue positiv  
(sett kryss)  Hø  Ve

**3. Muskelkraft (tall 0-5)**

 Tågåing  Hø  Ve

 Fleksjon, hofte  Hø  Ve

 Abduksjon, hofte  Hø  Ve

 Dorsalfleksjon, ankel  Hø  Ve

 Dorsalfleksjon , stortå  Hø  Ve

 Eversjon ankel  Hø  Ve

 Fleksjon kne  Hø  Ve

 Ekstensjon kne  Hø  Ve

 Kontraksjon rompeballer  Hø  Ve

**4. Reflekser**

(sett kryss)

 Kne Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

 Plantar Hø  Normal  Invertert  
 Ve  Normal  Invertert

 Achilles Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

**5. Sensibilitetstap**

(sett kryss)

 L3  Hø  Ve

 L4  Hø  Ve

 L5  Hø  Ve

 S1  Hø  Ve

**Nerverotsutfall og side(r).**  
**Konklusjon basert på klinisk us.**  
 (Sett om nødvendig flere kryss)

 L3  Hø.  Ve.

 L4  Hø.  Ve.

 L5  Hø.  Ve.

 S1  Hø.  Ve.

 Flere nivåer, spesifiser:
 

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# Medikamentbruk før injeksjon

Pasient nr.

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Sykehus nr.

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## Pasientdata

Navn

Fødselsnr. (11 siffer)

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Du deltar i en studie for å undersøke effekten av rygginjeksjon ved isjias.

Det er svært viktig for oss å vite hvor mye medikamenter/tabletter du tener for å dempe smerter.

Vi ber deg om å registrere (navn, antall) på alle medikamenter du bruker i en uke før den første rygginjeksjonen skal gies.

Bruk dette arket til å notere ned ditt medikamentforbruk.

Ta med notatene dine til sykehuset og lever det til den legen som skal sette injeksjonen. Legen vil videresende ditt skjema til Klinisk forskningssenter.

Medisin	Mandag	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag	Søndag

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

Epidural sacral injection study, Henvisning anestesilege

## **Til anestesilege**

Olaf Sivertsen og/eller Just Thoner, UNN

Jørgen Hansen, Nordlandssykehuset Bodø

Gunnar Engesnes, Sykehuset Levanger

Tarjei Rygnestad, St. Olavs Hospital

Niels Becker, Sykehuset Buskerud

Vedr pasient (Navn/Adresse/Telefon):

Dato henvist:

### **HENVISNING FOR INKLUSJON I EPIDURALSTUDIEN OG INJEKSJON**

Pasienten er inkludert i epiduralstudien. Det foreligger ingen kontraindikasjoner mot injeksjon.

Pasienten henvises med dette til to injeksjoner ut fra resultat av randomisering.

Med vennlig hilsen

Henvisende lege

## Randomisation and Treatment of subjects.

Pasient nr.

Sykehus nr.

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

After the inclusion check, back consultation and MR investigation have been performed, the doctor refers the patient to the anaesthesiologist for random allocation and injections according to the randomisation outcome. The referral to the anaesthesiologist is standardised, and include important information on cardiac and pulmonary status, medication and any allergies (Referral for injection). The referrals do not include information on the patient's clinical back details at the time of inclusion. As a rule, no more than 2 weeks should elapse between the inclusion check and randomisation to intervention.

The patients included are given either two epidural sacral injections (ESI) with volume plus steroid (Group I) or volume alone (Group II), or two placebo saline subcutaneous (SC) injections (Group III). The two injections are administrated at two-week intervals. Tick the result of randomisation in the table, note the date for injection 1 and 2 estimate technical success of injections on VAS scale where 0 (= failure) - 100(=success).

Group	Inervention with two injections	Randomisation Tick and date	Date Inj. 1 Success 0 -100	Date Inj. 2 Success 0 -100
I Volume + Steroid ESI	1 ml Triamcinolone 40 mg/ml + 29 ml NaCl 0.9 %			
II Volume ESI	30 ml NaCl 0.9 %			
III Placebo SC	2 ml NaCl 0.9 %			

For randomisering vennligst ring til Klinisk forskningscenter  
Tlf 77 66 91 17 eller Fax 77 66 90 74

Skjema sendes til:

Klinisk forskningscenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

## Ultrasound examination technique.

Pasient nr.	<input type="text"/>	<input type="text"/>	<input type="text"/>
Sykehus nr.	<input type="text"/>	<input type="text"/>	<input type="text"/>

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	<input type="text"/>

The injection technique is checked before and after the procedure by means of an ultrasound scan of the sacrum (Klocke et al, 2003, Chen et al 2004). The anaesthetists who are to administer the injections are trained in this standardised examination (longitudinal and transverse sections over the sacrum). All examinations are recorded with images. The anaesthetists at the various hospitals have access to ultrasound equipment. If the ultrasound examination reveals the presence of fluid over the sacrum, indication that the injection was given subcutaneously without this having been detected by palpatory inspection, this is recorded as a complication of the procedure. Subcutaneous injection is considered a non-hazardous complication and the patient is not excluded from the study if there is a complication of this kind with one or more of the injections.

Injection number	Ultrasound sacrum Subcutaneously fluid? Yes/No
1	
2	

Chen, CP ; Tang, SF ; Hsu, TC ; Tsai, WC ; Liu, HP ; Chen, MJ ; Date, E ; Lew, HL (2004) Ultrasound guidance in caudal epidural needle placement. *Anesthesiology*. Jul; 101(1):181-4

Klocke, R ; Jenkinson, T ; Glew, D (2003) Sonographically guided caudal epidural steroid injections. *J Ultrasound Med*. Nov; 22(11) : 1229-32

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

## **Pasientinformasjon etter injeksjon.**

Injeksjonen settes inn via det såkalte hiatus sakralis, en liten åpning i ryggraden like over halebeinet. Injeksjonen tar vanligvis 10-15 minutter. Medikamentet legger seg i det såkalte epiduralrommet som er det rommet som ligger rundt nervene i ryggen. Du vil under injeksjonen kunne kjenne et press over lenderyggen og noen ganger nedover i benet.

Etter injeksjonen ligger du 10 minutter på magen og deretter 15 minutter på ryggen. Det blir gjort en kontrollundersøkelse før du forlater legekantoret for å påse at det ikke har oppstått noen komplikasjoner.

Det første døgnet etter injeksjonen anbefales sengeleie, og du bør unngå langvarig sittende stilling. De fleste vil oppleve en bedring i ryggsmertene etter injeksjonen, men noen vil kunne kjenne en forbigående forverring i smertene to tre dager etter at injeksjonen er gitt. Etter et par dager kan du gjenoppta vanlig aktivitet.

Den første uka etter injeksjonen ber vi deg være spesielt oppmerksom på følgende plager; Sterk lokal smerte der sprøyten er satt, feber og sykdomsfølelse. Dersom du merker slike plager må du ta kontakt med din fastlege, legevakta i din kommune eller ta direkte kontakt med det sykehuset hvor du fikk injeksjonen.

# Medikamentbruk før etterundersøkelse

Pasient nr.

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Sykehus nr.

--	--	--

## Pasientdata

Navn

Fødselsnr. (11 siffer)

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Du deltar i en studie for å undersøke effekten av rygginjeksjon ved isjias.

Det er svært viktig for oss å vite hvor mye medikamenter/tabletter du tener for å dempe smerter.

Vi ber deg om å registrere (navn, antall) på alle medikamenter du bruker i en uke før den første etterkontrollen.

Bruk dette arket til å notere ned ditt medikamentforbruk.

Ta med notatene dine til sykehuset og lever det til den legen som skal utfører etterundersøkelsen.

Legen vil videresende ditt skjema til Klinisk forskningssenter.

Medisin	Mandag	Tirsdag	Onsdag	Torsdag	Fredag	Lørdag	Søndag

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"



# Årsak til at epiduralinjeksjon nr 2 ikke blir gitt

Pasient nr.

Sykehus nr.

Pasientdata
Navn
Fødselsnr. (11 siffer) <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

Erkjent eller mistenkt infeksjon

Pasienten ønsker ikke ny injeksjon

Betydelig bedring etter første injeksjon

Mye smerter i forb. med første injeksjon

Andre årsaker

Angi grunn .....

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

2784



## Epidural sacral injection study, Henvisning nevrofysiologi

Til neurolog/nevrofysiologisk undersøkelse

UNN

Nordlandssykehuset Bodø

Sykehuset Levanger

St. Olavs Hospital

Buskerud sykehus

Vedr pasient (Navn/Adresse/Telefon)

Dato henvist:

### HENVISNING TIL NEVROFYSIOLOGISK UNDERSØKELSE

Pasienten er inkludert i epiduralstudien. Det er påvist kliniske tegn til nerverotaffeksjon med kraftsvikt ved isometriske tester. Det er ønskelig med nevrofysiologisk undersøkelse for å kartlegge om det er objektive nevrologiske tegn til svekket funksjon i aktuelle muskel/muskelgruppe.

Isometrisk muskeltest	Hø (0-5 muskelkraft)	Ve (0-5 muskelkraft)
Tågang		
Fleksjon hofte		
Abduksjon hofte		
Dorsalfleksjon ankel		
Dorsalfleksjon stortå		
Eversjon ankel		
Fleksjon kne		
Ekstensjon kne		
Kontraksjon rompeballer		

Med vennlig hilsen

Henvisende lege

# Svar på EMG undersøkelse ved klinisk påvist kraftsvikt i muskulatur

Pasient nr.

Sykehus nr.

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

Muskel	EMG resultat			
1. Gastrocnemius (tågang):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
2. Psoas (fleksjon hofte):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
3. Gluteus medius (abduksjon hofte):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
4. Tibialis anterior (dorsalfleksjon ankel):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
5. Ext hallucis longus (dorsalfleksjon stortå):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
6. Peroneus (eversjon ankel):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
7. Hamstrings (fleksjon kne):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
8. Quadriceps (ekstensjon kne):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet
9. Gluteus maximus (kontraksjon rompeballer):	<input type="checkbox"/> Normalt	<input type="checkbox"/> Nevrogenombygning	<input type="checkbox"/> Denervasjon	<input type="checkbox"/> Annet



# Spørreskjema for pasienter etter rygginjeksjon

Skjema 3

Pasient nr.




Sykehus nr.




Etterkontroll nr

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	
Adresse	
Alder (år)	
Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne	

Formålet med dette spørreskjemaet er å gi leger, sykepleiere og fysioterapeuter bedre forståelse av ryggpasienters plager og å vurdere effekter av behandling. Din utfylling av skjemaet vil være til stor nytte for å kunne gi et best mulig behandlings-tilbud til ryggpasienter i fremtiden.

Spørreskjemaet har fem deler. Første del omhandler ulike sider ved din utdanning og familie samt dine smerter og plager. De neste delene består av tre ulike sett spørsmål for måling av din nåværende helse. Det første av disse (kalt Oswestryskåre) måler hvordan ryggplagene påvirker dine dagligdage gjøremål. Det andre (kalt EQ-5D) måler din helserelaterte livskvalitet. Den siste delen er en skala der du skal merke av hvor god eller dårlig din helsetilstand er.

Dato for utfylling	<input type="text"/>	<input type="text"/>	.	<input type="text"/>	<input type="text"/>	.	<input type="text"/>	<input type="text"/>
	Dag			Måned			År	
Tidspunkt etter injeksjon	<input type="text"/>	<input type="text"/>	(måned)					

Er skjemaet besvart per brev?

 Ja Nei

Hvor stor nytte mener du at du har hatt av injeksjon?

- Stor nytte
- Litt nytte
- Ingen nytte
- Er blitt verre

Hvor fornøyd er du med behandlingen du har fått på sykehuset?

- Fornøyd
- Litt fornøyd
- Hverken fornøyd eller misfornøyd
- Litt misfornøyd
- Misfornøyd

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

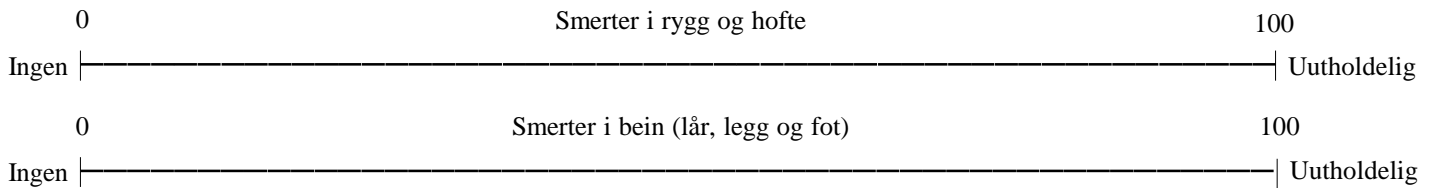
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### Hvor sterke smerter har du nå

De vannrette linjene nedenfor viser en skala fra 0 til 100 for smertestyrke. Den begrenses på venstre side av ingen smerte (0) og på høyre side av uutholdelig smerte (100). Sett en strek på tvers av linjene svarende til din største smerte nå for tiden (den siste uken).



### Funksjonsscore (Oswestry)

Disse spørsmålene er utarbeidet for å gi oss informasjon om hvordan dine smerter har påvirket dine muligheter til å klare dagliglivet ditt. Vær så snill å besvare spørsmålene ved å sette kryss (kun ett kryss for hvert avsnitt) i de rutene som passer best for deg.

#### 1. Smerte

- Jeg har ingen smerter for øyeblikket
- Smertene er veldig svake for øyeblikket
- Smertene er moderate for øyeblikket
- Smertene er temmelig sterke for øyeblikket
- Smertene er veldig sterke for øyeblikket
- Smertene er det verste jeg kan tenke meg for øyeblikket

#### 2. Personlig stell

- Jeg kan stelle meg selv på valig måte uten at det forårsaker ekstra smerter
- Jeg kan stelle meg selv på vanlig måte, men det er veldig smertefult
- Det er smertefult å stelle seg selv, og jeg gjør det langsomt og forsiktig
- Jeg trenger noe hjelp, men klarer det meste av mitt personlige stell
- Jeg trenger hjelp hver dag til det meste av eget stell
- Jeg kler ikke på meg, har vanskeligheter med å vaske meg og holder sengen

#### 3. Å løfte

- Jeg kan løfte tunge ting uten å få mer smerter
- Jeg kan løfte tunge ting, men får smerter
- Smertene hindrer meg i å løfte tunge ting opp fra gulvet, men jeg greier det hvis det som skal løftes er gunstig plassert, for eksempel på et bord
- Smertene hindrer meg i å løfte tunge ting, men jeg klarer lette og middels tunge ting, hvis det er gunstig plassert
- Jeg kan bare løfte noe som er veldig lett
- Jeg kan ikke løfte eller bære noe i det hele tatt

#### 4. Å gå

- Smerter hindrer meg ikke i å gå i det hele tatt
- Smerter hindrer meg i å gå mer enn 1 1/2 km
- Smerter hindrer meg i å gå mer enn 3/4 km
- Smerter hindrer meg i å gå mer enn 100 m
- Jeg kan bare gå med stokk eller krykker
- Jeg ligger for det meste i sengen, og jeg må krabbe til toalettet

#### 5. Å sitte

- Jeg kan sitte så lenge jeg vil i en hvilken som helst stol
- Jeg kan sitte så lenge jeg vil i min favorittstol
- Smerter hindrer meg i å sitte mer enn en time
- Smerter hindrer meg i å sitte mer enn en halv time
- Smerter hindrer meg i å sitte mer enn ti minutter
- Smerter hindrer meg i å sitte i det hele tatt

#### 6. Å stå

- Jeg kan stå så lenge jeg vil uten å få smerter
- Jeg kan stå så lenge jeg vil, men får mer smerter
- Smerter hindrer meg i å stå mer enn en time
- Smerter hindrer meg i å stå mer enn en halv time
- Smerter hindrer meg i å stå mer enn ti minutter
- Smerter hindrer meg i å stå i det hele tatt



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**7. Å sove**

- Søvnens min forstyrres aldri av smerter
- Søvnens min forstyrres av og til av smerter
- På grunn av smerter får jeg mindre enn seks timers søvn
- På grunn av smerter får jeg mindre en fire timers søvn
- På grunn av smerter får jeg mindre enn to timers søvn
- Smerter hindre all søvn

**Beskrivelse av helsetilstand (EQ-5D)**

Vis hvilke utsagn som passer på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av dimensjonene nedenfor.

**1. Gange**

- Jeg har ingen problemer med å gå omkring
- Jeg har litt problemer med å gå omkring
- Jeg er sengeliggende

**8. Seksualliv**

- Seksuallivet mitt er normalt og forårsaker ikke mer smerter
- Seksuallivet mitt er normalt, men forårsaker noe mer smerter
- Seksuallivet mitt er normalt, men svært smertefullt
- Seksuallivet mitt er svært begrenset av smerter
- Seksuallivet mitt er nesten borte på grunn av smerter
- Smerter forhindrer alt seksualliv

**2. Personlig stell**

- Jeg har ingen problemer med personlig stell
- Jeg har litt problemer med å vaske meg eller kle meg
- Jeg er ute av stand til å vaske meg eller kle meg

**9. Sosialt liv (omgang med venner og bekjente)**

- Det sosiale livet mitt er normalt og forårsaker ikke mer smerter
- Det sosiale livet mitt er normalt, men øker graden av smerter
- Smerter har ingen betydelig innvirkning på mitt sosiale liv, bortsett fra at de begrenser mine mer fysiske aktive sider, som sport osv.
- Smerter har begrenset mitt sosiale liv, og jeg går ikke så ofte ut
- Smerter har begrenset mitt sosiale liv til hjemmet
- På grunn av smerter har jeg ikke noe sosialt liv

**3. Vanlige gjøremål** (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- Jeg har ingen problemer med å utføre mine vanlige gjøremål
- Jeg har litt problemer med å utføre mine vanlige gjøremål
- Jeg er ute av stand til å utføre mine vanlige gjøremål

**4. Smerte og ubehag**

- Jeg har verken smerte eller ubehag
- Jeg har moderat smerte og ubehag
- Jeg har sterk smerte og ubehag

**5. Angst og depresjon**

- Jeg er hverken engstelig eller deprimeret
- Jeg er noe engstelig og deprimeret
- Jeg er svært engstelig og deprimeret

**10. Å reise**

- Jeg kan reise hvor som helst uten smerter
- Jeg kan reise hvor som helst, men det gir mer smerter
- Smertene er ille, men jeg klarer reiser på to timer
- Smerter begrenser meg til korte reiser på under en time
- Smerter begrenser meg til korte, nødvendige reiser på under 30 minutter
- Smerter forhindrer meg fra å reise, unntatt for å få behandling



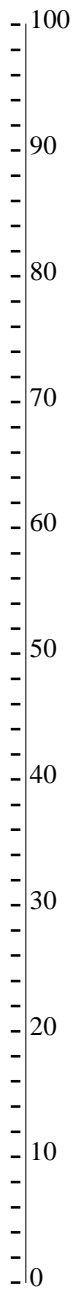
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**Helsetilstand**

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0.

Vi ber deg om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.

Best tenkelige  
helsetilstand



Nåværende  
helsetilstand

Verst tenkelige  
helsetilstand

**Arbeidsstatus**

(Fylles ut hvis besvarelsen er per brev)

- |   |   |
|---|---|
| <input type="checkbox"/> I arbeid         | <input type="checkbox"/> Student/skoleelev        |
| <input type="checkbox"/> Sykemeldt        | <input type="checkbox"/> Pensjonist               |
| <input type="checkbox"/> Aktiv sykemeldt  | <input type="checkbox"/> Arbeidsledig             |
| <input type="checkbox"/> Delvis sykemeldt | <input type="checkbox"/> Attføring/rehabilitering |
| <input type="checkbox"/> % sykemeldt      | <input type="checkbox"/> Uføretrygdet             |
| <input type="checkbox"/> Hjemmeværende    |   |

**Friskmeldt?**

(Fylles ut hvis besvarelsen er per brev)

Hvis ja, angi dato

Dag		Måned		År	

Varighet av sykemelding etter injeksjon

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 (uker)
**Komplikasjoner til injeksjon?**

(Fylles ut hvis besvarelsen er per brev)

- Uventet skade
- Blødning
- Infeksjon i huden etter injeksjon
- Allergiske reaksjoner
- Annet (spesifiser)

**Har du søkt om uføretrygd?**

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget

**Har du søkt om erstatning fra forsikrings-selskap eller folketrygden (evt. yrkesskadeerstatning)?**

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget



# SMERTE, FYSISK AKTIVITET OG JOBB

(Fear-Avoidance Beliefs Questionnaire,  
Waddell et al 1993)

Her er noe av det som andre har fortalt oss om ryggsmertene sine. Kryss av for ett tall fra 0 (helt uenig) til 6 (helt enig) for hvert utsagn for å si hvor mye fysiske aktiviteter som å bøye seg, løfte, gå eller kjøre vil påvirke ryggen din.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
1	Smertene mine ble forårsaket av fysisk aktivitet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2	Fysisk aktivitet forverrer smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3	Fysisk aktivitet kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4	Jeg burde ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5	Jeg kan ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Følgende utsagn handler om hvordan det vanlige arbeidet ditt påvirker eller kan påvirke ryggsmertene dine.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
6	Smertene mine ble forårsaket av arbeidet mitt eller et uhell på jobben	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7	Arbeidet mitt forverret smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8	Jeg har framsatt erstatningskrav for smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9	Arbeidet mitt er for tungt for meg	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10	Arbeidet mitt forverrer eller kan forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11	Arbeidet mitt kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12	Jeg burde ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
13	Jeg kan ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
14	Jeg kan ikke utføre det vanlige arbeidet mitt før smertene er behandlet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15	Jeg tror ikke jeg vil være tilbake på det vanlige arbeidet mitt innen tre måneder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
16	Jeg tror ikke jeg noen gang vil være i stand til å komme tilbake til det arbeidet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	





# Registrerings skjema ved kontroll etter rygginjeksjon

<b>Pasientdata</b>	<b>Friskmeldt?</b>
Navn	Hvis ja, angi dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År
Fødselsnr. (11 siffer)	Varighet av sykemelding etter injeksjon <input type="text"/> <input type="text"/> <input type="text"/> (uker)
Adresse	<b>Komplikasjoner til injeksjonen?</b>
Alder (år) <input type="text"/> <input type="text"/>	<input type="checkbox"/> Nerveskade, spesifiser
Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne	-----
Etterundersøkelse dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År	<input type="checkbox"/> Blødning
Tidspunkt etter injeksjon <input type="text"/> <input type="text"/> (måneder)	<input type="checkbox"/> Infeksjon <input type="checkbox"/> Overfladisk sårinfeksjon
<b>Har pasienten møtt personlig til etterkontroll?</b>	<input type="checkbox"/> Dyp sårinfeksjon/spondylitt
<input type="checkbox"/> Ja	<input type="checkbox"/> Allergisk reaksjon
<input type="checkbox"/> Nei	<input type="checkbox"/> Durapunksjon
Hvis nei, er skjemaet besvart per brev?	<input type="checkbox"/> Annet (spesifiser)
<input type="checkbox"/> Ja	-----
<input type="checkbox"/> Nei	<b>Får du for tiden annen behandling for ryggplager</b>
<b>Arbeidsstatus</b>	<input type="checkbox"/> Fysioterapi
<input type="checkbox"/> I arbeid <input type="checkbox"/> Student/skoleelev	<input type="checkbox"/> Kiropraktor
<input type="checkbox"/> Sykemeldt <input type="checkbox"/> Pensjonist	<input type="checkbox"/> Annen type behandling
<input type="checkbox"/> Aktiv sykemeldt <input type="checkbox"/> Arbeidsledig	Ja, spesifiser.....
<input type="checkbox"/> Delvis sykemeldt <input type="checkbox"/> Attføring/rehabilitering	<b>Andre relevante sykdommer, skader eller plager</b>
<input type="text"/> <input type="text"/> % sykemeldt <input type="checkbox"/> Uføretrygdet	<input type="checkbox"/> Nei
<input type="checkbox"/> Hjemmeværende	<input type="checkbox"/> Ja, spesifiser
	-----



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**Kliniske funn**
**1. SLR**

 Gradtall positiv test 

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 Hø  Ve

 2. Omvendt Lasegue positiv (sett kryss)  Hø  Ve

**3. Muskelkraft (tall 0-5)**

Tågåing	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Fleksjon, hofte	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Abduksjon, hofte	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Dorsalfleksjon, ankel	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Dorsalfleksjon , stortå	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Eversjon ankel	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Fleksjon kne	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Ekstensjon kne	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Kontraksjon rompeballer	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve

**4. Reflekser**

(sett kryss)

 Kne Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

 Plantar Hø  Normal  Invertert  
 Ve  Normal  Invertert

 Achilles Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

**5. Sensibilitetstap**

(sett kryss)

L3	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
L4	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
L5	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
S1	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve

**Nerverotsutfall og side(r).**
**Konklusjon basert på klinisk us.**

(Sett om nødvendig flere kryss)

<input type="checkbox"/> L3	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> L4	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> L5	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> S1	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.

Flere nivåer, spesifiser:

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# Spørreskjema for pasienter etter rygginjeksjon

Skjema 3

Pasient nr.




Sykehus nr.




Etterkontroll nr

2

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	
Adresse	
Alder (år)	<input type="text"/> <input type="text"/>
Kjønn	<input type="checkbox"/> Mann <input type="checkbox"/> Kvinne

Formålet med dette spørreskjemaet er å gi leger, sykepleiere og fysioterapeuter bedre forståelse av ryggpasienters plager og å vurdere effekter av behandling. Din utfylling av skjemaet vil være til stor nytte for å kunne gi et best mulig behandlingstilbud til ryggpasienter i fremtiden.

Spørreskjemaet har fem deler. Første del omhandler ulike sider ved din utdanning og familie samt dine smerter og plager. De neste delene består av tre ulike sett spørsmål for måling av din nåværende helse. Det første av disse (kalt Oswestryskåre) måler hvordan ryggplagene påvirker dine dagligdagse gjøremål. Det andre (kalt EQ-5D) måler din helserelaterte livskvalitet. Den siste delen er en skala der du skal merke av hvor god eller dårlig din helsetilstand er.

Dato for utfylling	<input type="text"/> <input type="text"/>	.	<input type="text"/> <input type="text"/>	.	<input type="text"/> <input type="text"/>
	Dag		Måned		År
Tidspunkt etter injeksjon	<input type="text"/> <input type="text"/>	(måned)			

Er skjemaet besvart per brev?

 Ja Nei

Hvor stor nytte mener du at du har hatt av injeksjon?

- Stor nytte
- Litt nytte
- Ingen nytte
- Er blitt verre

Hvor fornøyd er du med behandlingen du har fått på sykehuset?

- Fornøyd
- Litt fornøyd
- Hverken fornøyd eller misfornøyd
- Litt misfornøyd
- Misfornøyd

Skjema sendes til:

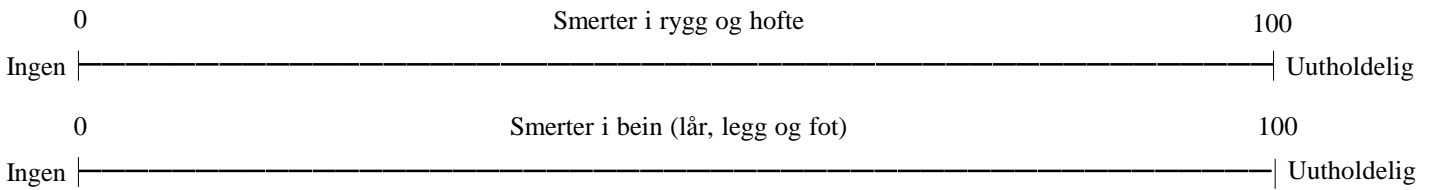
Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

24684



**Hvor sterke smerter har du nå**

De vannrette linjene nedenfor viser en skala fra 0 til 100 for smertestyrke. Den begrenses på venstre side av ingen smerte (0) og på høyre side av uutholdelig smerte (100). Sett en strek på tvers av linjene svarende til din største smerte nå for tiden (den siste uken).

**Funksjonsscore (Oswestry)**

Disse spørsmålene er utarbeidet for å gi oss informasjon om hvordan dine smerter har påvirket dine muligheter til å klare dagliglivet ditt. Vær så snill å besvare spørsmålene ved å sette kryss (kun ett kryss for hvert avsnitt) i de rutene som passer best for deg.

**1. Smerte**

- Jeg har ingen smerter for øyeblikket
- Smertene er veldig svake for øyeblikket
- Smertene er moderate for øyeblikket
- Smertene er temmelig sterke for øyeblikket
- Smertene er veldig sterke for øyeblikket
- Smertene er det verste jeg kan tenke meg for øyeblikket

**2. Personlig stell**

- Jeg kan stelle meg selv på valig måte uten at det forårsaker ekstra smerter
- Jeg kan stelle meg selv på vanlig måte, men det er veldig smertefult
- Det er smertefult å stelle seg selv, og jeg gjør det langsomt og forsiktig
- Jeg trenger noe hjelp, men klarer det meste av mitt personlige stell
- Jeg trenger hjelp hver dag til det meste av eget stell
- Jeg kler ikke på meg, har vanskeligheter med å vaske meg og holder sengen

**3. Å løfte**

- Jeg kan løfte tunge ting uten å få mer smerter
- Jeg kan løfte tunge ting, men får smerter
- Smertene hindrer meg i å løfte tunge ting opp fra gulvet, men jeg greier det hvis det som skal løftes er gunstig plassert, for eksempel på et bord
- Smertene hindrer meg i å løfte tunge ting, men jeg klarer lette og middels tunge ting, hvis det er gunstig plassert
- Jeg kan bare løfte noe som er veldig lett
- Jeg kan ikke løfte eller bære noe i det hele tatt

**4. Å gå**

- Smerter hindrer meg ikke i å gå i det hele tatt
- Smerter hindrer meg i å gå mer enn 1 1/2 km
- Smerter hindrer meg i å gå mer enn 3/4 km
- Smerter hindrer meg i å gå mer enn 100 m
- Jeg kan bare gå med stokk eller krykker
- Jeg ligger for det meste i sengen, og jeg må krabbe til toalettet

**5. Å sitte**

- Jeg kan sitte så lenge jeg vil i en hvilken som helst stol
- Jeg kan sitte så lenge jeg vil i min favorittstol
- Smerter hindrer meg i å sitte mer enn en time
- Smerter hindrer meg i å sitte mer enn en halv time
- Smerter hindrer meg i å sitte mer enn ti minutter
- Smerter hindrer meg i å sitte i det hele tatt

**6. Å stå**

- Jeg kan stå så lenge jeg vil uten å få smerter
- Jeg kan stå så lenge jeg vil, men får mer smerter
- Smerter hindrer meg i å stå mer enn en time
- Smerter hindrer meg i å stå mer enn en halv time
- Smerter hindrer meg i å stå mer enn ti minutter
- Smerter hindrer meg i å stå i det hele tatt



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**7. Å sove**

- Søvnens min forstyrres aldri av smerter
- Søvnens min forstyrres av og til av smerter
- På grunn av smerter får jeg mindre enn seks timers søvn
- På grunn av smerter får jeg mindre en fire timers søvn
- På grunn av smerter får jeg mindre enn to timers søvn
- Smerter hindre all søvn

**Beskrivelse av helsetilstand (EQ-5D)**

Vis hvilke utsagn som passer på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av dimensjonene nedenfor.

**1. Gange**

- Jeg har ingen problemer med å gå omkring
- Jeg har litt problemer med å gå omkring
- Jeg er sengeliggende

**8. Seksualliv**

- Seksuallivet mitt er normalt og forårsaker ikke mer smerter
- Seksuallivet mitt er normalt, men forårsaker noe mer smerter
- Seksuallivet mitt er normalt, men svært smertefullt
- Seksuallivet mitt er svært begrenset av smerter
- Seksuallivet mitt er nesten borte på grunn av smerter
- Smerter forhindrer alt seksualliv

**2. Personlig stell**

- Jeg har ingen problemer med personlig stell
- Jeg har litt problemer med å vaske meg eller kle meg
- Jeg er ute av stand til å vaske meg eller kle meg

**9. Sosialt liv (omgang med venner og bekjente)**

- Det sosiale livet mitt er normalt og forårsaker ikke mer smerter
- Det sosiale livet mitt er normalt, men øker graden av smerter
- Smerter har ingen betydelig innvirkning på mitt sosiale liv, bortsett fra at de begrenser mine mer fysiske aktive sider, som sport osv.
- Smerter har begrenset mitt sosiale liv, og jeg går ikke så ofte ut
- Smerter har begrenset mitt sosiale liv til hjemmet
- På grunn av smerter har jeg ikke noe sosialt liv

**3. Vanlige gjøremål** (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- Jeg har ingen problemer med å utføre mine vanlige gjøremål
- Jeg har litt problemer med å utføre mine vanlige gjøremål
- Jeg er ute av stand til å utføre mine vanlige gjøremål

**4. Smerte og ubehag**

- Jeg har verken smerte eller ubehag
- Jeg har moderat smerte og ubehag
- Jeg har sterk smerte og ubehag

**5. Angst og depresjon**

- Jeg er hverken engstelig eller depriment
- Jeg er noe engstelig og depriment
- Jeg er svært engstelig og depriment

**10. Å reise**

- Jeg kan reise hvor som helst uten smerter
- Jeg kan reise hvor som helst, men det gir mer smerter
- Smertene er ille, men jeg klarer reiser på to timer
- Smerter begrenser meg til korte reiser på under en time
- Smerter begrenser meg til korte, nødvendige reiser på under 30 minutter
- Smerter forhindrer meg fra å reise, unntatt for å få behandling



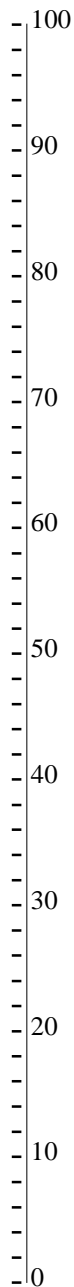
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### Helsetilstand

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0.

Vi ber deg om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.

Best tenkelige  
helsetilstand



Nåværende  
helsetilstand

Verst tenkelige  
helsetilstand

### Arbeidsstatus (Fylles ut hvis besvarelsen er per brev)

- |  |   |
|--|---|
| <input type="checkbox"/> I arbeid  | <input type="checkbox"/> Student/skoleelev        |
| <input type="checkbox"/> Sykemeldt   | <input type="checkbox"/> Pensjonist               |
| <input type="checkbox"/> Aktiv sykemeldt   | <input type="checkbox"/> Arbeidsledig             |
| <input type="checkbox"/> Delvis sykemeldt  | <input type="checkbox"/> Attføring/rehabilitering |
| <table border="1" style="display: inline-table; width: 30px; height: 20px;"></table> % sykemeldt | <input type="checkbox"/> Uføretrygdet             |
| <input type="checkbox"/> Hjemmeværende   |   |

### Friskmeldt? (Fylles ut hvis besvarelsen er per brev)

Hvis ja, angi dato 



 . 



 . 



  
Dag Måned År

Varighet av sykemelding etter injeksjon 



 (uker)

### Komplikasjoner til injeksjon? (Fylles ut hvis besvarelsen er per brev)

- Uventet skade
- Blødning
- Infeksjon i huden etter injeksjon
- Allergiske reaksjoner
- Annet (spesifiser)

### Har du søkt om uføretrygd?

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget

### Har du søkt om erstatning fra forsikrings-selskap eller folketrygden (evt. yrkesskadeerstatning)?

- Ja
- Nei
- Planlegger å søke
- Er allerede innvilget



# SMERTE, FYSISK AKTIVITET OG JOBB

(Fear-Avoidance Beliefs Questionnaire,  
Waddell et al 1993)

Her er noe av det som andre har fortalt oss om ryggsmertene sine. Kryss av for ett tall fra 0 (helt uenig) til 6 (helt enig) for hvert utsagn for å si hvor mye fysiske aktiviteter som å bøye seg, løfte, gå eller kjøre vil påvirke ryggen din.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
1	Smertene mine ble forårsaket av fysisk aktivitet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2	Fysisk aktivitet forverrer smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3	Fysisk aktivitet kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4	Jeg burde ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5	Jeg kan ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Følgende utsagn handler om hvordan det vanlige arbeidet ditt påvirker eller kan påvirke ryggsmertene dine.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
6	Smertene mine ble forårsaket av arbeidet mitt eller et uhell på jobben	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7	Arbeidet mitt forverret smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8	Jeg har framsatt erstatningskrav for smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9	Arbeidet mitt er for tungt for meg	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10	Arbeidet mitt forverrer eller kan forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11	Arbeidet mitt kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12	Jeg burde ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
13	Jeg kan ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
14	Jeg kan ikke utføre det vanlige arbeidet mitt før smertene er behandlet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15	Jeg tror ikke jeg vil være tilbake på det vanlige arbeidet mitt innen tre måneder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
16	Jeg tror ikke jeg noen gang vil være i stand til å komme tilbake til det arbeidet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	



# Registrerings skjema ved kontroll etter rygginjeksjon

<b>Pasientdata</b>	<b>Friskmeldt?</b>
Navn	Hvis ja, angi dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År
Fødselsnr. (11 siffer)	Varighet av sykemelding etter injeksjon <input type="text"/> <input type="text"/> <input type="text"/> (uker)
Adresse	<b>Komplikasjoner til injeksjonen?</b>
Alder (år) <input type="text"/> <input type="text"/>	<input type="checkbox"/> Nerveskade, spesifiser
Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne	-----
Etterundersøkelse dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År	<input type="checkbox"/> Blødning
Tidspunkt etter injeksjon <input type="text"/> <input type="text"/> (måneder)	<input type="checkbox"/> Infeksjon <input type="checkbox"/> Overfladisk sårinfeksjon
<b>Har pasienten møtt personlig til etterkontroll?</b>	<input type="checkbox"/> Dyp sårinfeksjon/spondylitt
<input type="checkbox"/> Ja	<input type="checkbox"/> Allergisk reaksjon
<input type="checkbox"/> Nei	<input type="checkbox"/> Durapunksjon
Hvis nei, er skjemaet besvart per brev?	<input type="checkbox"/> Annet (spesifiser)
<input type="checkbox"/> Ja	-----
<input type="checkbox"/> Nei	<b>Får du for tiden annen behandling for ryggplager</b>
<b>Arbeidsstatus</b>	<input type="checkbox"/> Fysioterapi
<input type="checkbox"/> I arbeid <input type="checkbox"/> Student/skoleelev	<input type="checkbox"/> Kiropraktor
<input type="checkbox"/> Sykemeldt <input type="checkbox"/> Pensjonist	<input type="checkbox"/> Annen type behandling
<input type="checkbox"/> Aktiv sykemeldt <input type="checkbox"/> Arbeidsledig	Ja, spesifiser.....
<input type="checkbox"/> Delvis sykemeldt <input type="checkbox"/> Attføring/rehabilitering	<b>Andre relevante sykdommer, skader eller plager</b>
<input type="text"/> <input type="text"/> % sykemeldt <input type="checkbox"/> Uføretrygdet	<input type="checkbox"/> Nei
<input type="checkbox"/> Hjemmeværende	<input type="checkbox"/> Ja, spesifiser
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**Kliniske funn**
**1. SLR**

 Gradtall positiv test 

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 Hø  Ve

 2. Omvendt Lasegue positiv (sett kryss)  Hø  Ve

**3. Muskelkraft (tall 0-5)**

Tågåing	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Fleksjon, hofte	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Abduksjon, hofte	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Dorsalfleksjon, ankel	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Dorsalfleksjon , stortå	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Eversjon ankel	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Fleksjon kne	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Ekstensjon kne	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
Kontraksjon rompeballer	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve

**4. Reflekser**

(sett kryss)

 Kne Hø  0  +  ++  +++  +++++  
 Ve  0  +  ++  +++  +++++

 Plantar Hø  Normal  Invertert  
 Ve  Normal  Invertert

 Achilles Hø  0  +  ++  +++  +++++  
 Ve  0  +  ++  +++  +++++

**5. Sensibilitetstap**

(sett kryss)

L3	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
L4	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
L5	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve
S1	<input type="checkbox"/>	Hø	<input type="checkbox"/>	Ve

**Nerverotsutfall og side(r).**
**Konklusjon basert på klinisk us.**

(Sett om nødvendig flere kryss)

<input type="checkbox"/> L3	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> L4	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> L5	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.
<input type="checkbox"/> S1	<input type="checkbox"/> Hø.	<input type="checkbox"/> Ve.

Flere nivåer, spesifiser:

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# Spørreskjema for pasienter etter rygginjeksjon

Skjema 3

Pasient nr.




Sykehus nr.




Etterkontroll nr

3

Pasientdata	
Navn	
Fødselsnr. (11 siffer)	
Adresse	
Alder (år)	<input type="text"/> <input type="text"/>
Kjønn	<input type="checkbox"/> Mann <input type="checkbox"/> Kvinne

Formålet med dette spørreskjemaet er å gi leger, sykepleiere og fysioterapeuter bedre forståelse av ryggpasienters plager og å vurdere effekter av behandling. Din utfylling av skjemaet vil være til stor nytte for å kunne gi et best mulig behandlingstilbud til ryggpasienter i fremtiden.

Spørreskjemaet har fem deler. Første del omhandler ulike sider ved din utdanning og familie samt dine smerter og plager. De neste delene består av tre ulike sett spørsmål for måling av din nåværende helse. Det første av disse (kalt Oswestryskåre) måler hvordan ryggplagene påvirker dine dagligdage gjøremål. Det andre (kalt EQ-5D) måler din helserelaterte livskvalitet. Den siste delen er en skala der du skal merke av hvor god eller dårlig din helsetilstand er.

Dato for utfylling	<input type="text"/> <input type="text"/>	.	<input type="text"/> <input type="text"/>	.	<input type="text"/> <input type="text"/>
	Dag		Måned		År
Tidspunkt etter injeksjon	<input type="text"/> <input type="text"/>	(måned)			

Er skjemaet besvart per brev?

 Ja Nei

Hvor stor nytte mener du at du har hatt av injeksjon?

- Stor nytte
- Litt nytte
- Ingen nytte
- Er blitt verre

Hvor fornøyd er du med behandlingen du har fått på sykehuset?

- Fornøyd
- Litt fornøyd
- Hverken fornøyd eller misfornøyd
- Litt misfornøyd
- Misfornøyd

Skjema sendes til:

Klinisk forskningssenter, Postboks 78, Universitetssykehuset Nord-Norge,  
9038 Tromsø, merket "Epidural studien"

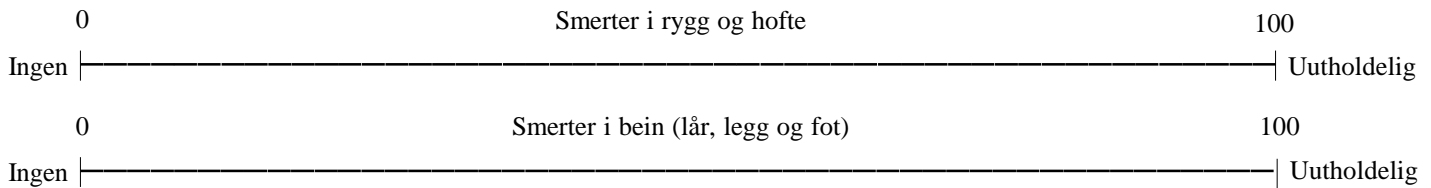
18444



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### Hvor sterke smerter har du nå

De vannrette linjene nedenfor viser en skala fra 0 til 100 for smertestyrke. Den begrenses på venstre side av ingen smerte (0) og på høyre side av uutholdelig smerte (100). Sett en strek på tvers av linjene svarende til din største smerte nå for tiden (den siste uken).



### Funksjonsscore (Oswestry)

Disse spørsmålene er utarbeidet for å gi oss informasjon om hvordan dine smerter har påvirket dine muligheter til å klare dagliglivet ditt. Vær så snill å besvare spørsmålene ved å sette kryss (kun ett kryss for hvert avsnitt) i de rutene som passer best for deg.

#### 1. Smerte

- Jeg har ingen smerter for øyeblikket
- Smertene er veldig svake for øyeblikket
- Smertene er moderate for øyeblikket
- Smertene er temmelig sterke for øyeblikket
- Smertene er veldig sterke for øyeblikket
- Smertene er det verste jeg kan tenke meg for øyeblikket

#### 2. Personlig stell

- Jeg kan stelle meg selv på valig måte uten at det forårsaker ekstra smerter
- Jeg kan stelle meg selv på vanlig måte, men det er veldig smertefult
- Det er smertefult å stelle seg selv, og jeg gjør det langsomt og forsiktig
- Jeg trenger noe hjelp, men klarer det meste av mitt personlige stell
- Jeg trenger hjelp hver dag til det meste av eget stell
- Jeg kler ikke på meg, har vanskeligheter med å vaske meg og holder sengen

#### 4. Å gå

- Smerter hindrer meg ikke i å gå i det hele tatt
- Smerter hindrer meg i å gå mer enn 1 1/2 km
- Smerter hindrer meg i å gå mer enn 3/4 km
- Smerter hindrer meg i å gå mer enn 100 m
- Jeg kan bare gå med stokk eller krykker
- Jeg ligger for det meste i sengen, og jeg må krabbe til toalettet

#### 5. Å sitte

- Jeg kan sitte så lenge jeg vil i en hvilken som helst stol
- Jeg kan sitte så lenge jeg vil i min favorittstol
- Smerter hindrer meg i å sitte mer enn en time
- Smerter hindrer meg i å sitte mer enn en halv time
- Smerter hindrer meg i å sitte mer enn ti minutter
- Smerter hindrer meg i å sitte i det hele tatt

#### 3. Å løfte

- Jeg kan løfte tunge ting uten å få mer smerter
- Jeg kan løfte tunge ting, men får smerter
- Smertene hindrer meg i å løfte tunge ting opp fra gulvet, men jeg greier det hvis det som skal løftes er gunstig plassert, for eksempel på et bord
- Smertene hindrer meg i å løfte tunge ting, men jeg klarer lette og middels tunge ting, hvis det er gunstig plassert
- Jeg kan bare løfte noe som er veldig lett
- Jeg kan ikke løfte eller bære noe i det hele tatt

#### 6. Å stå

- Jeg kan stå så lenge jeg vil uten å få smerter
- Jeg kan stå så lenge jeg vil, men får mer smerter
- Smerter hindrer meg i å stå mer enn en time
- Smerter hindrer meg i å stå mer enn en halv time
- Smerter hindrer meg i å stå mer enn ti minutter
- Smerter hindrer meg i å stå i det hele tatt



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**7. Å sove**

- Søvnens min forstyrres aldri av smerter
- Søvnens min forstyrres av og til av smerter
- På grunn av smerter får jeg mindre enn seks timers søvn
- På grunn av smerter får jeg mindre en fire timers søvn
- På grunn av smerter får jeg mindre enn to timers søvn
- Smerter hindre all søvn

**8. Seksualliv**

- Seksuallivet mitt er normalt og forårsaker ikke mer smerter
- Seksuallivet mitt er normalt, men forårsaker noe mer smerter
- Seksuallivet mitt er normalt, men svært smertefullt
- Seksuallivet mitt er svært begrenset av smerter
- Seksuallivet mitt er nesten borte på grunn av smerter
- Smerter forhindrer alt seksualliv

**9. Sosialt liv (omgang med venner og bekjente)**

- Det sosiale livet mitt er normalt og forårsaker ikke mer smerter
- Det sosiale livet mitt er normalt, men øker graden av smerter
- Smerter har ingen betydelig innvirkning på mitt sosiale liv, bortsett fra at de begrenser mine mer fysiske aktive sider, som sport osv.
- Smerter har begrenset mitt sosiale liv, og jeg går ikke så ofte ut
- Smerter har begrenset mitt sosiale liv til hjemmet
- På grunn av smerter har jeg ikke noe sosialt liv

**10. Å reise**

- Jeg kan reise hvor som helst uten smerter
- Jeg kan reise hvor som helst, men det gir mer smerter
- Smertene er ille, men jeg klarer reiser på to timer
- Smerter begrenser meg til korte reiser på under en time
- Smerter begrenser meg til korte, nødvendige reiser på under 30 minutter
- Smerter forhindrer meg fra å reise, unntatt for å få behandling

**Beskrivelse av helsetilstand (EQ-5D)**

Vis hvilke utsagn som passer på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av dimensjonene nedenfor.

**1. Gange**

- Jeg har ingen problemer med å gå omkring
- Jeg har litt problemer med å gå omkring
- Jeg er sengeliggende

**2. Personlig stell**

- Jeg har ingen problemer med personlig stell
- Jeg har litt problemer med å vaske meg eller kle meg
- Jeg er ute av stand til å vaske meg eller kle meg

**3. Vanlige gjøremål** (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- Jeg har ingen problemer med å utføre mine vanlige gjøremål
- Jeg har litt problemer med å utføre mine vanlige gjøremål
- Jeg er ute av stand til å utføre mine vanlige gjøremål

**4. Smerte og ubehag**

- Jeg har verken smerte eller ubehag
- Jeg har moderat smerte og ubehag
- Jeg har sterk smerte og ubehag

**5. Angst og depresjon**

- Jeg er hverken engstelig eller deprimert
- Jeg er noe engstelig og deprimert
- Jeg er svært engstelig og deprimert

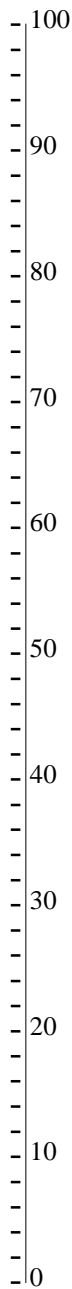


**Helsetilstand**

For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0.

Vi ber deg om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.

Best tenkelige  
helsetilstand



Nåværende  
helsetilstand

Verst tenkelige  
helsetilstand

**Arbeidsstatus** (Fylles ut hvis besvarelsen er per brev)

- I arbeid  Student/skoleelev  
 Sykemeldt  Pensjonist  
 Aktiv sykemeldt  Arbeidsledig  
 Delvis sykemeldt  Attføring/rehabilitering  
  % sykemeldt  Uføretrygdet  
 Hjemmeværende

**Friskmeldt?** (Fylles ut hvis besvarelsen er per brev)

Hvis ja, angi dato   .   .    
Dag Måned År

Varighet av sykemelding etter injeksjon  (uker)

**Komplikasjoner til injeksjon?** (Fylles ut hvis besvarelsen er per brev)

- Uventet skade  
 Blødning  
 Infeksjon i huden etter injeksjon  
 Allergiske reaksjoner  
 Annet (spesifiser)

**Har du søkt om uføretrygd?**

- Ja  
 Nei  
 Planlegger å søke  
 Er allerede innvilget

**Har du søkt om erstatning fra forsikringselskap eller folketrygden (evt. yrkesskadeerstatning)?**

- Ja  
 Nei  
 Planlegger å søke  
 Er allerede innvilget



**SMERTE, FYSISK AKTIVITET OG JOBB**

(Fear-Avoidance Beliefs Questionnaire,  
Waddell et al 1993)

Her er noe av det som andre har fortalt oss om ryggsmertene sine. Kryss av for ett tall fra 0 (helt uenig) til 6 (helt enig) for hvert utsagn for å si hvor mye fysiske aktiviteter som å bøye seg, løfte, gå eller kjøre vil påvirke ryggen din.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
1	Smertene mine ble forårsaket av fysisk aktivitet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2	Fysisk aktivitet forverrer smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3	Fysisk aktivitet kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4	Jeg burde ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5	Jeg kan ikke utføre fysiske aktiviteter som (kan) forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Følgende utsagn handler om hvordan det vanlige arbeidet ditt påvirker eller kan påvirke ryggsmertene dine.

		HELT UENIG		USIKKER				HELT ENIG	
		0	1	2	3	4	5	6	
6	Smertene mine ble forårsaket av arbeidet mitt eller et uhell på jobben	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7	Arbeidet mitt forverret smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8	Jeg har framsatt erstatningskrav for smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9	Arbeidet mitt er for tungt for meg	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10	Arbeidet mitt forverrer eller kan forverre smertene mine	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11	Arbeidet mitt kan skade ryggen min	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12	Jeg burde ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
13	Jeg kan ikke utføre det vanlige arbeidet mitt med mine nåværende smerter	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
14	Jeg kan ikke utføre det vanlige arbeidet mitt før smertene er behandlet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15	Jeg tror ikke jeg vil være tilbake på det vanlige arbeidet mitt innen tre måneder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
16	Jeg tror ikke jeg noen gang vil være i stand til å komme tilbake til det arbeidet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	



# Registrerings skjema ved kontroll etter rygginjeksjon

<b>Pasientdata</b>	<b>Friskmeldt?</b>
Navn	Hvis ja, angi dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År
Fødselsnr. (11 siffer)	Varighet av sykemelding etter injeksjon <input type="text"/> <input type="text"/> <input type="text"/> (uker)
Adresse	<b>Komplikasjoner til injeksjonen?</b>
Alder (år) <input type="text"/> <input type="text"/>	<input type="checkbox"/> Nerveskade, spesifiser
Kjønn <input type="checkbox"/> Mann <input type="checkbox"/> Kvinne	-----
Etterundersøkelse dato <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> . <input type="text"/> <input type="text"/> Dag Måned År	<input type="checkbox"/> Blødning
Tidspunkt etter injeksjon <input type="text"/> <input type="text"/> (måned)	<input type="checkbox"/> Infeksjon <input type="checkbox"/> Overfladisk sårinfeksjon
<b>Har pasienten møtt personlig til etterkontroll?</b>	<input type="checkbox"/> Dyp sårinfeksjon/spondylitt
<input type="checkbox"/> Ja	<input type="checkbox"/> Allergisk reaksjon
<input type="checkbox"/> Nei	<input type="checkbox"/> Durapunksjon
Hvis nei, er skjemaet besvart per brev?	<input type="checkbox"/> Annet (spesifiser)
<input type="checkbox"/> Ja	-----
<input type="checkbox"/> Nei	<b>Får du for tiden annen behandling for ryggplager</b>
<b>Arbeidsstatus</b>	<input type="checkbox"/> Fysioterapi
<input type="checkbox"/> I arbeid <input type="checkbox"/> Student/skoleelev	<input type="checkbox"/> Kiropraktor
<input type="checkbox"/> Sykemeldt <input type="checkbox"/> Pensjonist	<input type="checkbox"/> Annen type behandling
<input type="checkbox"/> Aktiv sykemeldt <input type="checkbox"/> Arbeidsledig	Ja, spesifiser.....
<input type="checkbox"/> Delvis sykemeldt <input type="checkbox"/> Attføring/rehabilitering	<b>Andre relevante sykdommer, skader eller plager</b>
<input type="text"/> <input type="text"/> % sykemeldt <input type="checkbox"/> Uføretrygdet	<input type="checkbox"/> Nei
<input type="checkbox"/> Hjemmeværende	<input type="checkbox"/> Ja, spesifiser
	-----

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**Kliniske funn**
**1. SLR**

Gradtall positiv test

--	--

Hø

Ve

**2. Omvendt Lasegue positiv  
(sett kryss)**


Hø

Ve

**3. Muskelkraft (tall 0-5)**

Tågåing

Hø

Ve

Fleksjon, hofte

Hø

Ve

Abduksjon, hofte

Hø

Ve

Dorsalfleksjon, ankel

Hø

Ve

Dorsalfleksjon, stortå

Hø

Ve

Eversjon ankel

Hø

Ve

Fleksjon kne

Hø

Ve

Ekstensjon kne

Hø

Ve

Kontraksjon rompeballer

Hø

Ve

**4. Reflekser**

(sett kryss)

 Kne Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

 Plantar Hø  Normal  Invertert  
 Ve  Normal  Invertert

 Achilles Hø  0  +  ++  +++  ++++  
 Ve  0  +  ++  +++  ++++

**5. Sensibilitetstap**

(sett kryss)

 L3  Hø  Ve

 L4  Hø  Ve

 L5  Hø  Ve

 S1  Hø  Ve

**Nerverotsutfall og side(r).**
**Konklusjon basert på klinisk us.**

(Sett om nødvendig flere kryss)

L3

Hø.

Ve.

L4

Hø.

Ve.

L5

Hø.

Ve.

S1

Hø.

Ve.

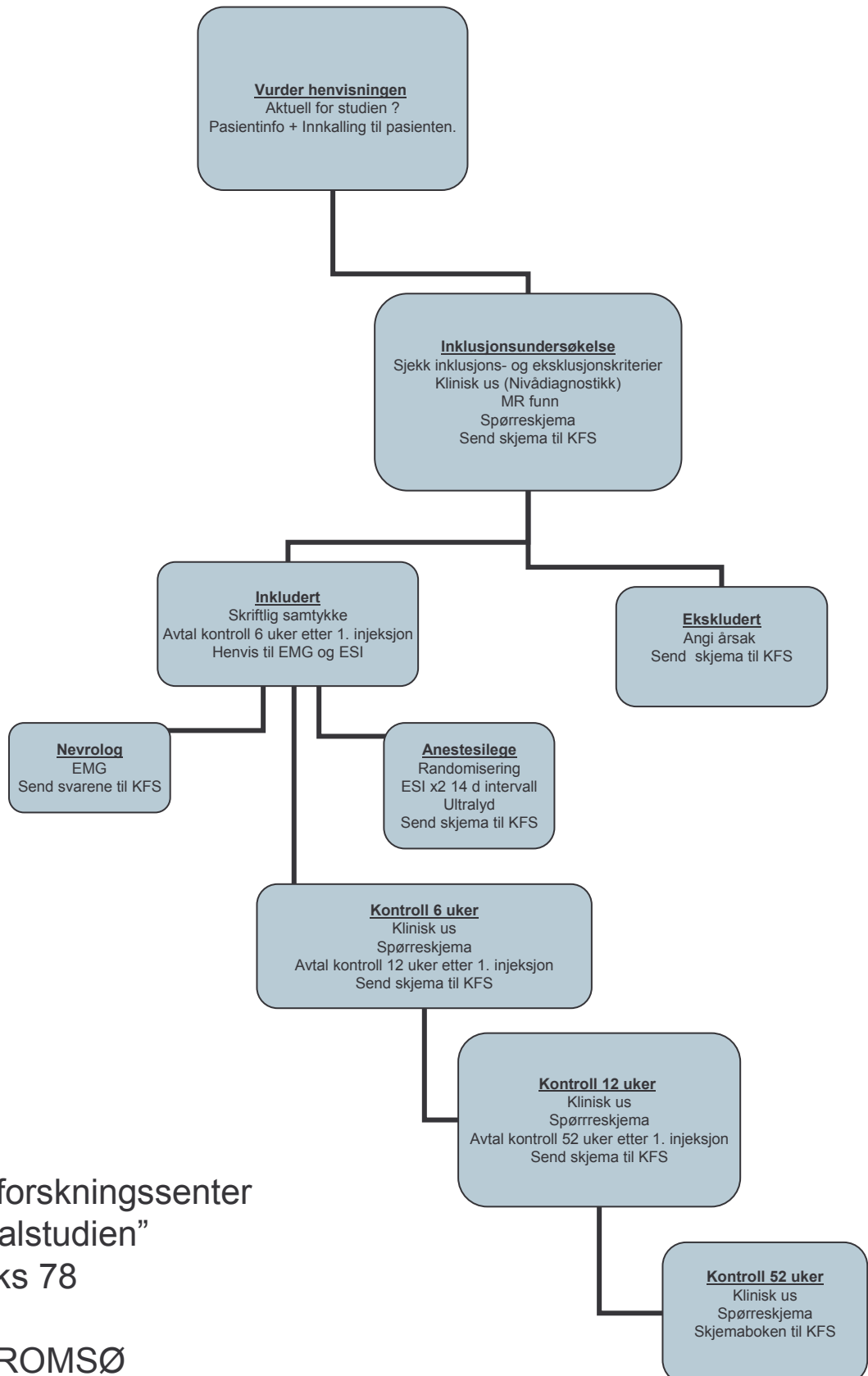
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# Epidural sacral injection study



KFS =  
Klinisk forskningscenter  
"Epiduralstudien"  
Postboks 78  
UNN  
9038 TROMSØ

**Inklusjonskriterier**

1. 20 - 60 år
2. Smertevarighet  $\geq 12$  uker
3. Nerverotaffeksjon/radikulopati L3, L4, L5, S1
4. Body mass index  $\leq 30$

**Eksklusjonskriterier**

1. Tidligere ryggoperert
2. Tidligere rygginjisert
3. Røde flagg
4. Gule flagg
5. Gravide
6. Marevanbruker
7. Amming



## Appendix 7 Study protocol



**Epidural steroid injection. Effect of saline solution and triamcinolone  
acetonide (Kenacort-T<sup>®</sup>) on chronic lumbosacral radiculopathy. Blinded  
multicentre randomized placebo-controlled trial.**

Protocol Code Number 2137

EudraCT Number 2004-004585-32

ISRCTN Number 12574253

Recommendation of trial amendments by the Norwegian Medicines Agency 20 January 2009

Trial amendments approved by the Privacy Issues Unit, Norwegian Social Science Data Services (NSD)

4 May 2007 and Privacy Issues Unit, University Hospital of North Norway, 16 January 2009

Recommendation of trial amendments issued by the Regional Committee for Medical and Health

Research Ethics, North Norway (REK nord) 18 December 2003, 1 April 2005, 9 May 2007 and 19

December 2008

St. Olavs Hospital, Trondheim University Hospital. New centre from 8 May 2007

Approved as a Clinical Trial by the Norwegian Medicines Agency 20 June 2005

Approved by the Privacy Issues Unit, NSD 26 November 2003

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## Principles and guidelines for this study protocol

The content of this trial protocol follows the principles and guidelines in these documents

- The European Union Directive 2001/20/EC, April 2001 (The Clinical Trials Directive).
- Note for Guidance on Good Clinical Practice, September 1997 (CPMP/ICH/135/95).
- Detailed Guidelines on the principles of good clinical practice in the conduct in the EU of clinical trials on medicinal products for human use, July 2002 (ENTR/6416/01).
- Detailed guidance on the European database of Suspected Unexpected Serious Adverse Reactions (Eudravigilance-Clinical Trial Module), April 2004 (ENTR/CT 4).
- Detailed guidance on the collection, verification and presentation of adverse reaction reports arising from clinical trials on medicinal products for human use, April 2004 (ENTR/CT 3).
- The rules governing medicinal products in the European Union, volume 4 – Medicinal products for human and veterinary use: Good manufacturing practices, Annex 13 – Manufacture of investigational medicinal products, July 2003 (2003/94/EC 6).
- Declaration of Helsinki, 2000 version with note of clarification on paragraph 29 of the World Medical Association (WMA) on placebo-controlled trial.

- Statens legemiddelverk (Norwegian Medicines Agency) Melding om bivirkninger ved bruk av legemidler (inkl. naturlegemidler), September 2004.
- Forskrift om klinisk utprøving av legemidler til mennesker (FOR 2003-09-24 nr 1202).

## **Name, title and addresses of the investigators who are responsible for conducting the trial**

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Responsible for epidural injections: Olaf Sivertsen (Senior Physician, Anaesthesiology Department) and Just Thoner (Senior Physician, Anaesthesiology Department).

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### The Coordinating Committee

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Trond Iversen (Coordinating Investigator), (Senior Registrar, Senior Physician, Department of Physical Medicine and Rehabilitation).

### The Independent Data-Monitoring Committee

Tom Wilsgaard (Chairman), Senior Researcher (Dr Scient.), Institute of Community Medicine, University of Tromsø.

Holger Ursin (Professor, The Norwegian Back Pain Network, The Research Unit, Bergen).

Inger B Scheel (Senior Researcher (Dr Philos.), The Norwegian Back Pain Network, The Communication Unit, Oslo).

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### Radiologists for independent assessment of magnetic resonance scans

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### Sponsors

Tor Ingebrigtsen, Professor, Neurosurgery Department, University Hospital of North Norway.

Audny Anke, Departmental Senior Physician, Department of Physical Medicine and Rehabilitation, University Hospital of North Norway.

Toralf Hasvold, Professor, Institute of Community Medicine, University of Tromsø.

## **Abstract**

### **Background**

Epidural steroid injection for lumbar radiculopathy has been used since 1953. Along with mechanical compression of nerve roots, lumbar radiculopathy can be triggered by different pro-inflammatory chemical agents, causing ectopic neuron firing. It has been hypothesized that steroids injected into the epidural space or around the affected nerve root inhibit these inflammatory mediators. However, there is conflicting evidence for a potential benefit of epidural steroid injections. Some studies have shown a moderate short-term benefit, while others show no difference between epidural steroid and placebo injections. Studies of epidural steroid injections compared to epidural saline or local anaesthetic injections show less benefit from steroids than studies comparing epidural steroid injections with sham or soft tissue injections. Furthermore, recent studies conclude that epidural local anaesthetics or saline alone may have a positive effect by themselves.

## Methods/Design

The objective is to evaluate the short (6-week), intermediate (12-week), and long-term (52-week) efficacy of caudal epidural steroid and caudal epidural saline injection in the treatment of chronic (duration >12 weeks) lumbar radiculopathy.

The study is designed as a multicentre blinded randomized controlled trial.

The setting is outpatient multidisciplinary back clinics of five Norwegian hospitals.

Inclusion of patients with lumbar radiculopathy for more than 12 weeks.

There are three intervention groups. Each group receives two injections with a 2-week interval. Group one is given subcutaneous sham injections superficial to the sacral hiatus and not into the spinal canal, Group two is given caudal epidural injections with saline alone, and Group three is given caudal epidural injections with a combination of saline and triamcinolone acetonide (Kenacort-T<sup>®</sup>). There are three follow-up measurements: 6, 12 and 52 weeks after the intervention.

The primary outcome measure is the Oswestry Disability Index. The secondary outcome measures are the European Quality of Life measure, the visual analogue scale score for low back pain, and the visual analogue scale score for leg pain.

## Discussion

This randomized controlled trial will compare caudal epidural steroid injections and caudal epidural saline injections with subcutaneous sham injections. The null hypothesis is that treatment of chronic lumbar radiculopathy with caudal epidural injection with steroids or isotonic saline has no clinically important effect.

## Trial registration

Current Controlled Trials ISRCTN12574253. Registered 18 May 2005.

## Keywords

Back pain; Epidural steroid; European Quality of Life; Leg pain; Lumbar nerve root impingement; Lumbar radiculopathy; Oswestry Disability Index; Physical examination; Randomized controlled trial; Sciatica

## Background

### Back pain, social costs

The risk of developing back pain in the course of one's life is put at about 60–80% [1-3]. Every year, one-third of all adults are afflicted by severe back pain [4]. Back pain causes considerable suffering, and the social costs are high [5]. Among Norwegians in their forties, about 6% report that their capacity for work is reduced to a greater or lesser extent by back pain [6]. Two per cent of Norwegians of working age, about 50,000 people, have such a reduced work capacity owing to back pain that they report sick, retrain or take early retirement [1]. The duration that they are off sick (more than 2 weeks) depends on whether or not the back complaints are associated with radiating pain. Hagen and Thune (1998) found that the median duration was 59 days for those with radiating pain, and 38 days for those without radiating pain [7]. Low levels of physical activity, a lack of energy, work involving heavy loads on the back, and low expectations of getting back into work are shown to

be predictors for not being back at work one year after taking time off sick for low back complaints [8]. The total cost associated with bad backs in Norway is between 13 and 15 billion Norwegian kroner per annum. In 2002, 14.1% of all disabled people were diagnosed as having a back disorder, and this diagnosis accounted for 15.7% of all new disabled pensioners in the same year [9].

### **Back pain, classification based on type of disease**

Low back pain can roughly be divided into three types [10]. The largest group (80–90%) is ‘Non-specific low back pain’. Patients experience the spread of pain in their lower backs, buttocks and thighs. They experience variable pain intensity, are in good general health and experience an improvement at rest. The patient group with ‘Nerve root disease’ accounts for around 5–10% of all low back pain sufferers. In this group, the pain is radiating in nature, and there can be a variable degree of neurological effects in the form of loss of sensitivity, strength or reflexes. Usually, the radiation of pain is reproduced by Lasegue’s test. A spontaneous improvement in this type of back pain usually occurs within 8–12 months in about 70% of patients [11,12]. The last group is made up of patients with ‘Possibly severe underlying disease’. Around 1–5% of all patients with low back pain can prove to have fractures/damage, cancer or inflammation. The typical feature of this patient group is that patients experience constant pain, pain at rest and often a general sensation of illness. The multidisciplinary guidelines for the treatment of acute low back pain [10] describe the causes of acute low back pain based on these three main diagnostic groups [13].

### **Back pain, classification based on duration of symptoms**

Bogduk and McGuirk (2002) and Ihlebæk and Lærum (2004) classify low back pain, regardless of cause, as acute (<6 weeks), subacute (6–12 weeks) and chronic pain (duration >12 weeks) [3,14].

## **Back pain, traditional treatment**

Traditionally, low back pain is treated by reporting sick, resting, taking painkilling medication and receiving physiotherapy [15]. The treatment of lumbago and sciatica is a controversial issue [16]. Many guidelines have been issued for treating back pain [17-19]. The main message is that physical exercise and activity help [20]. In many cases, a combination of expensive painkilling and anti-inflammatory drugs are often used. These therapeutic approaches are not shown to have a proven effect [21]. The prospects of improvement for patients with inoperable low back pain, and who have tried various types of conservative treatment to no effect, are poor [22]. Traction therapy [23,24], bed rest [25] and non-steroidal anti-inflammatory drugs (NSAIDs) [26] have not been shown to have any effect on chronic lumbar back pain. NSAIDs can have a symptomatic effect on acute back pain [27]. There is some evidence that electrotherapy [28], cognitive therapy [29], McKenzie exercises [30] and physical exercise [31] can have an effect, but randomized clinical studies are needed [15].

## **Back pain, surgery**

Major disc prolapses with neurological deficits and pain are usually treated by surgery. The results of microdiscectomy and macrodiscectomy are good [32,33]. Most clinics operating on back patients have clear guidelines for when surgical treatment is indicated [34]. A lot of patients with sciatica are offered an operation. This treatment is considered a 'gold-standard'. However, the long-term results following operation for sciatica are not convincing, with a high frequency of recurrence [35]. It will, for these reasons, also be important to investigate whether epidural sacral injection (ESI) can postpone or reduce the frequency of back operations. However, the steroid ESI treatment has yet to be established as an effective method compared to placebo.

## **Methods/Design**

ESI is a method of treating low back pain and radiculopathy that is the subject of considerable discussion [36]. Although the method with steroid epidural injection has been in use from 1953, there are only a few good randomized controlled studies [37,38]. In Nelemans et al (2000), evidence for the method is given as weak, and studies of a high scientific quality are sought [39]. Randomized controlled studies are needed to clarify the effect of the volume of the epidural injection and steroids versus placebo. Many patients with chronic low back pain and sciatica feel that they have few therapeutic options besides surgery. Only a few patients with sciatica are suitable for surgical treatment. The surgeon needs a correspondence between the clinical level of radiculopathy and magnetic resonance (MR) diagnosis of disc protrusion [40]. Many patients lack this correspondence. We therefore want to conduct the study on patients with clinical signs of lumbosacral radiculopathy, where the pain has lasted for more than 12 weeks (chronic) and where surgical treatment is not indicated at the time of inclusion due either to lack of correspondence between clinical and MR finding or low Oswestry Disability Index (ODI). In our study, we wish to use a corticosteroid preparation with a weak anti-inflammatory effect. Triamcinolone acetonide (Kenacort-T<sup>®</sup>) in a strength of 40 mg/ml and a quantity of 1 ml diluted with 29 ml NaCl 0.9% in the epidural space meets this requirement. The effect is to be compared with placebo/sham injection (2 ml NaCl 0.9% subcutaneously) and 30 ml NaCl 0.9% without steroid in the epidural space. In many studies, injections have been used with a small volume (<10 ml). We will use a volume of 30 ml to be sure that the medicinal product is distributed throughout the epidural space in the lumbosacral column up to level L2.

If our study can demonstrate a significant therapeutic effect for ESI of steroid, the method could become an important tool in the treatment of patients with low back pain and radiculopathy. We could also clarify in the study whether there are special subgroups of patients with radiculopathy (e.g. signal changes in the disc; covered prolapse; free prolapse; thickened nerve root; disclosed nerve root) that respond better to steroid injection. If the method can also be proven to be easy to perform, and is associated with few serious complications and adverse drug reactions (ADRs), it could



become useful in both the treatment and rehabilitation of sciatica patients. At present, we do not know enough about the risk associated with use of the method, the incidence of side effects, and what should be regarded as adequate follow-up of patients. Hopefully, a study could yield valuable information on this. Given a good effect from the treatment and a low incidence of side effects, we will probably be able to substantiate a positive gain in the form of reduced suffering for the individual in addition to a socioeconomic gain from patients recovering their health and being able to return to work more quickly.

## **Trial design**

The study can be classified as a blinded, placebo-controlled, explanatory, effectiveness, multicentre, randomized controlled trial (RCT) [41]. Blinding is ensured by keeping the subjects and investigators responsible for the follow-ups at the different hospitals unaware of the treatment assignment. The study is a placebo-controlled explanatory trial because it addresses whether or not the intervention with steroid has a better effect compared to placebo injections [41]. The effectiveness of the intervention is measured on primary and secondary outcome measures.

## **Randomized controlled trial, patient selection**

Patients with clinically suspected lumbosacral radiculopathy who are referred in the course of 2005–2008 from the general practitioners to the Outpatient Back Department at the University Hospital of North Norway (UNN) in Tromsø, the Outpatient Neurology Department at Nordland Hospital in Bodø, the Outpatient Back Department at Levanger Hospital and to the Outpatient Back Department at Buskerud Hospital in Drammen will be continuously assessed for possible inclusion in the study (Figure 1). Referred patients who may be suitable for inclusion in the study are given, together with the invitation to a consultation at the appropriate outpatient department, an information letter on

the study indicating that, if they meet special criteria in terms of their back complaints, they will be invited to take part in the study (Figure 2).

### **Inclusion, clinical examination**

The inclusion examination and follow-up is conducted by a physician on an outpatient basis. The examination follows a study template that has been drawn up, and the aim is to decide whether the patient clinically suffers from a lumbosacral radiculopathy and at which level (Figure 3). Based on the standardized clinical back examination, the doctor must determine which of the levels from L3 to S1 the radiculopathy affects.

### **Definition of the term 'lumbosacral radiculopathy'**

The term 'lumbosacral radiculopathy' should be understood to mean that a patient with or without low back pain has either radicular radiating pain in the leg below the knee joint, reduced strength, impaired sensitivity or attenuated tendon reflexes, or possibly a combination of several clinical findings of this kind.

### **Magnetic resonance diagnosis. Investigation procedure and assessment**

All patients included must have undergone an MR scan of their lumbosacral column. The scans are taken and described at the time of inclusion at the MR departments at UNN, Nordland Hospital in Bodø, Levanger Hospital or at Buskerud Hospital. Scans taken and described at other hospitals or private radiography bodies are accepted. The scans should as a rule be taken within 8 weeks before the inclusion check. An important condition for the use of scans taken before the time of inclusion is that the patient's clinical findings have not changed from when the MR scans were taken. The MR

scans are taken in accordance with a standardized protocol (Sagittal T1/T2, Axial T1/T2) with a view to prolapse diagnosis.

### **Magnetic resonance diagnosis, based on Modic [42]**

Based on the radiologist's MR description of the individual patient, it must be recorded whether one or more of the specified findings are present and their level and side.

- Normal
- Signal changes/Degenerative changes in the disc (Yes/No?, Level/Side?)
- Disc bending/Covered prolapse (Yes/No?, Level/Side?)
- Free/Sequestered prolapse (Yes/No?, Level/Side?)
- Thickened nerve root (Yes/No?, Level/Side?)
- Lateral recess stenosis with disclosed nerve root (Yes/No?, Level/Side?)

Each patient's scans are stored on CD-ROM. This is labelled with the patient ID and sent to the Clinical Research Centre, the Unit for Research Methodology, UNN. The CD-ROMs are then later sent for review by two independent experienced radiologists.

### **Treatment groups**

1. We want to investigate whether ESI with 30 ml saline (Volume intervention group), has a positive effect on patients with clinical signs of chronic lumbosacral radiculopathy.
2. We want to investigate whether the use of ESI with 29 ml saline plus 1 ml 40 mg triamcinolone (Volume plus Steroid intervention group) has a positive additional effect

compared to volume alone on patients with clinical signs of chronic lumbosacral radiculopathy.

3. We want to investigate whether a possible effect of volume or triamcinolone depends on which subgroups of patients with chronic lumbosacral radiculopathy we treat [43].

Subgroups are classified on the basis of the clinical level of the radiculopathy, and what MR diagnosis the patient is given.

### **Blinding of treatment**

The patient being given the injection is not informed whether ESI treatment or placebo is being given. The anaesthesiologist and the patient do not discuss the patient's medical history. The anaesthesiologist does not inform the doctor or physiotherapist who included the patient as to which injection has been given.

### **Randomization process**

1. The randomization process is performed at a central randomization unit (Clinical research centre, Unit for Research Methodology, UNN) by personnel who have nothing to do with the patients.
2. Patients included are randomized ('Random Allocation') to receive placebo or one of the two treatments. Stratified block randomization is used. As this is a multicentre RCT, the hospital where the treatment is administered forms a stratification factor [44]. The anaesthesiologist, who is to administer the injection, telephones the randomization unit. He is told to which group (steroid, volume or placebo) the patient has been randomized.

3. The anaesthesiologist administering the injection has nothing to do with the study, nor does he find out about the patient's medical history or clinical findings made during the inclusion check.

## Selection and withdrawal of subjects

### Inclusion criteria based on medical history and clinical examination

1. Patients aged 20–60 years old, of both sexes.
2. Duration of radicular symptoms  $\geq 12$  weeks (chronic pain).
3. Clinically proven radiculopathy at nerve root L3, L4, L5 or S1. The radiculopathy may be unilateral/bilateral on the same level, or unilateral/bilateral on one or more levels at the same time.

### Exclusion criteria based on medical history and clinical examination

1. Indication of acute back surgery at the time of inclusion. To determine whether acute surgery is indicated, the guidelines drawn up by the Neurosurgery Department, UNN, are followed [34].
2. Previous back surgery.
3. Previous epidural or nerve root injection for low back pain or sciatica.
4. Body mass index (BMI)  $>30$ .
5. Red flags (rheumatic inflammatory disease; malignant disease; diabetes mellitus; severe and uncompensated cardiovascular disease; known autoimmune disease; currently known infection; haemophilia; some other type of disease that affects the coagulation system).

6. Yellow flags (known severe mental disease; known problems with alcohol or substance abuse).
7. The patient must not have noticed an improvement in symptoms for the previous 2 weeks before inclusion. The person investigating the patient for the first time asks the following question:  
*Have you got better over the past 2 weeks? (Yes/No)*  
If the patient answers *Yes* to this question, the individual is excluded.
8. Nor must the patient have experienced centralization of the pain, i.e. the pain has moved from the lower extremity towards the middle of the back, as this is regarded as a clinical sign of an already ongoing spontaneous improvement in the patient's condition [45]. The person investigating the patient for the first time asks the following question:  
*Over the past 2 weeks, have you experienced a shift in the pain from severe leg pain to severe pain in your back? (Yes/No)*  
If the patient answers *Yes* to this question, the individual in question is excluded.
9. Women of childbearing age are asked about pregnancy. The person investigating the patient for the first time asks the following question:  
*Are you pregnant? (Yes/No)*  
If the patient answers *Yes* to this question, the individual in question is excluded. All women of childbearing age are tested for HCG in urine.
10. Women who are breastfeeding.
11. Anticlotting therapy. The person investigating the patient for the first time asks the following question:  
*Are you taking warfarin (Marevan)? (Yes/No)*

If the patient answers *Yes* to this question, the person is excluded. Use of Acetyl Salicylic Acid is not an exclusion criterion [46].

12. Ongoing drug treatment with NSAID. The person investigating the patient for the first time asks the following question:

*Can you come off the NSAID? (Yes/No)*

If the patient answers *No* to this question, the individual in question is excluded.

### Exclusion criteria based on magnetic resonance findings

The physician who conducts the inclusion check must, after the clinical examination is completed, assess the MR response provided by the radiologist for the patient. If, based on the radiologist's description, a *Yes* answer is given to one or more of the findings listed below, the patient must be excluded. If the MR description does not provide a basis for answering *Yes* or *No* to the questions, the radiologist who has described the scans must be contacted and asked to clarify his description.

- Lateral recess stenosis of osteogenic aetiology (Yes/No?)
  
- Tumour (Yes/No?)
  
- Bleeding (Yes/No?)
  
- Dural fistula (Yes/No?)
  
- Synovial cyst (Yes/No?)
  
- Dysraphia conditions (Yes/No?)

## **Written informed consent**

The patients in question, who it is demonstrated have a lumbosacral radiculopathy and fulfil the inclusion criteria and no exclusion criteria, provide written informed consent if they wish to take part in the study (Figure 4).

## **Back information for patients included. The good back consultation**

All patients included who have given written informed consent to take part in the study are given standardized oral information on back anatomy and back function with the emphasis on management and encouragement to engage in activity [47-52]. The information is given by the doctor and physiotherapist conducting the inclusion check. A recently published study shows that back information alone can be just as effective in treating low back pain as standard physiotherapy treatment [53]. In the back consultation that the doctor conducts with the patient, the Norwegian national guidelines as set out in 'Acute low back pain. Interdisciplinary clinical guidelines' [10] and the 'European guidelines for the management of chronic nonspecific low back pain' [19] are followed, with a special focus on the recommendations concerning 'The good back consultation'. All patients included also receive the brochure 'Worth knowing about bad backs. What experts agree on' [10] after the inclusion check and back consultation have been conducted.

## **Recording use of medication**

1. The patient records his consumption of medication over one week before the first injection is performed. The names of the medicinal products, their strength and the number of tablets taken are recorded by the patient.



2. After the second injection is administered, the patient is asked to record his consumption of painkilling medication in the same way over one week before the agreed check-ups.
3. The consumption of each drug will be calculated with defined daily doses as a measurement unit and classified and presented by therapeutic group according to the anatomical therapeutic chemical system [50].

## **Treatment of subjects**

After the inclusion check, back consultation and MR investigation have been performed, the doctor refers the patient to the anaesthesiologist for random allocation and injections according to the randomization outcome. The referral to the anaesthesiologist is standardized, and includes important information on cardiac and pulmonary status, medication and any allergies (Figure 5). The referrals do not include information on the patient's clinical back details at the time of inclusion. As a rule, no more than 2 weeks should elapse between the inclusion check and randomization to intervention.

## **The intervention**

The patients included are given either two ESIs with volume plus steroid (Group I) or volume alone (Group II), or two placebo saline subcutaneous injections (Group III). The two injections are administered at 2-week intervals. The injections are administered by an anaesthesiologist with competence in spine injections. The injections follow a set template for injections of this kind (Figure 6). Ultrasound is used to localize the hiatus sacralis and increase the precision of the ESI.

## Intervention groups

The following three intervention groups are established.

Group	Intervention with two injections
I Volume + Steroid ESI	1 ml triamcinolone 40 mg/ml + 29 ml NaCl 0.9%
II Volume ESI	30 ml NaCl 0.9%
III Placebo subcutaneous	2 ml NaCl 0.9%

## Assessment of efficacy

The patients are examined by a physician at the time of inclusion and after 6 weeks. The follow-up checks by a physiotherapist are done after 12 and 52 weeks. The inclusion and follow-up checks include completing the standardized registration form and questionnaire and a clinical examination with focus on radicular pain, muscle power, sensibility and reflexes [54-58].

## Primary outcome

### Oswestry Disability Index

The ODI measure consists of 10 questions about pain, pain-related disability in daily life, and social participation [59,60]. The total score ranges from 0 (no pain or disability) to 100 (worst possible pain

and disability). The Norwegian version of the original ODI (version 2.0) will be used in this study. The Norwegian version of the ODI has been found to be reliable and valid for Norwegian patients with low back pain [61,62]. The scores (0–5) from all 10 sections are summarized, divided by the number of sections answered and multiplied by 20% [63].

## Secondary outcomes

European Quality of Life measure

Fear-Avoidance Beliefs Questionnaire

Visual analogue scale back pain, leg pain and general health

Number of patients referred to all types of back surgery during follow-up

European Quality of Life measure (EQ-5D) is a generic (aims to capture physical, mental, and social functioning) measure of health-related quality of life (HRQL) in which health status is defined in terms of five dimensions: Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression [64,65]. Each dimension has three qualifying levels of response roughly corresponding to ‘no problems’, ‘some difficulties/problems’ and ‘extreme difficulties’. Information collected using EQ-5D can be reported in terms of its individual dimensions and as a single index score (EQ-5D) [66,67].

Fear-avoidance beliefs are measured by the Fear-Avoidance Beliefs Questionnaire (FABQ) [68]. The FABQ consists of 16 items and is divided into two subscales: fear-avoidance beliefs for work (FABQ-Work) and fear-avoidance beliefs for physical activity (FABQ-PA). The items are scored from 0 to 6, with higher numbers indicating increased levels of fear-avoidance beliefs. According to the paper by Waddell et al [68], seven of the 11 items in the FABQ-Work and four of the five items in the FABQ-PA are summarized in one score. The FABQ-Work scores range from 0 to 42, and the FABQ-PA from 0 to 24. Previous studies have found the FABQ to be a reliable and valid instrument [69].

The patients score their current pain intensity in the lower back and lower limb on visual analogue scale back pain and leg pain (VAS<sub>BP</sub>, VAS<sub>LP</sub>) ranging from 0 to 100, where 0 reflects no pain and 100 the worst possible pain. In addition, the patients are invited to state how good or bad their general health state is on visual analogue scale general health (VAS<sub>GH</sub>), in which the best state is marked by 100 and the worst state that they can imagine is marked by 0.

The last of the secondary outcome measurements, need for back surgery, is registered as type of surgery done in the follow-up period.

### **Assessment of safety**

No harmful effects have been demonstrated on the dura mater or nerve tissue after a series of steroid ESIs [70,71]. Following reported cases of arachnoiditis after epidural injection of the steroid preparation Depo-Medrol, the indications for the use of this medicinal product were restricted, and the manufacturer stated in its product information in 1981 that 'we would advise against the epidural/extradural routes of administration because of possible adverse reactions'. This warning was removed from later product information [72].

Nelson and Landau (2001) have also reviewed the complications and adverse reactions following epidural injections (both lumbar and sacral) reported to the US Food and Drug Administration (FDA) in the period 1930 to 1994 [72]. Their aim was to clarify effectiveness, side effects, complications and what information should be given to patients who are given epidural steroid injections. They conclude as follows: (1) Intraspinal steroid therapy is not effective therapy for back pain or radicular syndromes because steroid formulations, placebos, and sham injections have similar outcomes. (2) When injected, epidural medications may not remain confined to the epidural space and some inaccuracies of placement approach 40% [73-75]. (3) The additives of steroid formulations – polyethylene glycol, benzyl alcohol, and benzalkonium chloride – can be neurotoxic when injected

intrathecally. Further research may disclose that the steroid formulations and mixtures themselves may be neurotoxic because of high osmolalities. (4) Epidural steroid infusion may result in increased pain, early or late. There may also be serious complications of arachnoiditis, spinal infection [76-79], or permanent neurological deficits [80,81]. (5) Patients should be informed that there is no evidence that epidural steroid injections provide permanent relief of pain. Serious permanent complications to the spinal cord, nerve roots, or peripheral nerves are a rare but certain risk [82,83].

Despite this negative evaluation of what we know so far concerning problems associated with steroid ESI primarily on the lumbar level, not the sacral/caudal level, a search is being started for good randomized placebo-controlled studies in order to get some answers to many of the questions and uncertainties relating to this form of treatment [84]. Most recently, in an editorial in the *BMJ* dated June 2004 [85], it was claimed that 'a need exists for well-designed trials of adequate size to determine the effectiveness of epidural injection in back pain'. Epidural injection therapy may provide a useful adjunct to recovery in patients whose symptoms have extended beyond 3 months in the absence of recognized indicators of chronicity ('yellow flags') and who may have radicular symptoms. In a review article about steroid ESI, Ogoke (2000) concludes that it is 'essential that further meticulously controlled, randomized studies are conducted to prove the rational and unequivocal efficiency of steroid ESI' [86].

### **The intervention, safety rules**

1. In the interests of patient safety, the anaesthesiologist who is to administer the injections is not blinded for the injections given.
2. The sacral route (ESI) is used.
3. If serious complications arise from the injection, every patient must be treated as if there has been given active treatment (steroid). The anaesthesiologist records every injection given,

and this record with information concerning medication and batch number may be opened if necessary.

4. Use of ultrasound to enhance ESI safety and precision.

## **Serious complications ('Serious adverse events'). Procedure for recording and notification**

1. The patients are given a list of which serious complications may arise after the injections, and which call for immediate contact with the doctor. Patients are told to contact the duty medical officer in their place of residence if suspected serious complications arise (Figure 7).
2. Doctors who are invited to refer patients to the study are informed in a separate letter about the study, possible serious complications after the injections, and about recommended therapeutic measures (Figure 8). If a serious complication arises before the two planned injections are administered, the patient will not receive the injections, but will be followed up as planned ('intention to treat').
3. The risk of serious complications as a result of sacral epidural injection is generally low. *Infection, haemorrhage, nerve damage and dural puncture* are possible serious complications.
  - *Infection* is characterized by high temperature, discomfort and significant local pain, possibly in combination with redness, heat and swelling at the injection site on the sacrum. The estimated incidence of infection is 0.01 to 0.1%. Most frequently this involves superficial skin infection, and very rarely epidural abscesses.
  - *Haemorrhaging* is a very rare complication of the sacral epidural injection technique. During the procedure, aspiration is regularly performed to check for the effusion of

blood. Superficial bleeding from the skin at the injection site may occur, but the risk is reduced by light compression of the injection site when the needle is removed.

- *Nerve damage and dural puncture* are very rare in connection with sacral epidural injection. Normally there is around 6 cm from the sacral hiatus to the lower limit of the dura (the lower limit is at S2 level). In the injection technique, the needle is inserted about 2 cm from the sacral hiatus and is consequently about 4 cm from the dura. Anomalies can, however, arise from the lower limit of the dura being nearer the sacral hiatus than normal. During the injection, particular attention is therefore paid to preventing the presence of spinal fluid in the spinal needle before the injection starts. In the case of dural puncture, what is known as a 'spinal headache' can arise. Most individuals who experience a complication of this kind spontaneously get better after a few days. In isolated cases of persistent headache, treatment with so-called 'blood patches' can be necessary. Spinal nerves at level S2 to S5 start, in normal anatomy, at a level cranially before the upper limit of the spinal needle. The sacral epidural technique is therefore associated with very little danger of direct damage to spinal nerves.

4. In the event of a serious complication (infection, haemorrhage, nerve damage, dural puncture) from an injection, this is recorded and reported by the coordinating investigator to the chairman of the Independent Data-Monitoring Committee (IDMC). Based on an overall assessment of the individual event, it will then be decided whether the event is of such a nature and severity that the study should be discontinued.

## Adverse drug reactions ('Minor adverse events'). Procedure for recording and notification

1. Corticosteroids administered orally, used for local injection or for spinal injection, may induce a range of side effects of variable severity in the patient. If the side effects are significant, and are considered to be harmful to health, the doctor refers the patient to the doctor who included the patient at the hospital in question. The case is assessed and discussed by the Coordinating Committee, and a decision will be taken on whether the patient should drop out of the study owing to the side effects.
2. The assumed frequency of ADRs from the use of corticosteroids for injections is about 2%, and the commonest ADRs are:
  - Transient flushing and heat in the skin
  - Menstruation-like bleeding
  - Fluid retention
  - Weight gain. Increased appetite
  - Increased blood pressure
  - Mood swings
  - Irritability
  - Anxiety
  - Sleeping problems
  - Elevated blood sugar
  - Transient impairment of immune defence



- In long-term use (dose-dependent), corticosteroids can contribute to the development of cataracts, avascular osteonecrosis and osteoporosis
3. Corticosteroid side effects reported by the patient or doctor are recorded and reported by the coordinating investigator to the chairman of the IDMC if the side effect is considered to be abnormally marked or if it has resulted in damage to health. It will then be decided whether the side effect is of such a nature and severity that the study must be discontinued.

### **Notification to the Norwegian Medicines Agency**

All serious complications, ADRs and serious unexpected severe adverse reactions (SUSARs) are reported to the Norwegian Medicines Agency, regionale legemiddelinformasjonssentre (RELIS) and the Regional Committee for Medical and Health Research Ethics, Nordland, Troms og Finnmark (North Norway) (REK nord / REKNOR) in accordance with defined procedures.

All SUSARs will also be electronically reported to the European Medicines Agency's (EMA's) EudraVigilance database.

### **Independent Data-Monitoring Committee, interim analysis**

The main functions of the IDMC are to perform continuous monitoring during the study for the occurrence of serious complications ('Serious adverse events'), serious ADRs ('Minor adverse events') or unexpected serious side effects ('Serious unexpected events'), and for the occurrence of statistically significant more serious side effects in the treatment group. We adopt a sequential design in which we assume five interim analyses in the course of the study. The difference in the proportion of serious adverse events between the groups is tested at a total significance level of 5%. The interim analyses are performed with the aid of the program EaSt-2000. The advantage of a sequential design is that we can monitor the study for early termination on ethical grounds. If

significantly ( $P < 0.05$ ) more serious complications or significant side effects that are harmful to health are recorded in the treatment group (the corticosteroid group), the Coordinating Committee must be immediately informed. As the disease that is being studied in this study is not a life-threatening one, and as a rule spontaneously improves over time, a statistically significant greater therapeutic effect in the group receiving active treatment than with the group receiving placebo alone will in itself not be a reason to terminate the study. Any decision to terminate the study must be taken by the Coordinating Committee on the advice of the IDMC.

## Data analysis

1. Analysis is performed by the 'intention to treat' method.
2. Change in the primary outcome variable (ODI) and the secondary outcome variables (EQ-5D, VAS leg and back pain) will be calculated.
3. The results of the MR investigation and clinical examination will cover the following subgroups (in different combinations) of patients with nerve root disease.
  - MR signal changes in the disc (Yes/No)
  - MR covered prolapse (Yes/No)
  - MR free prolapse (Yes/No)
  - MR thickened nerve root (Yes/No)
  - MR disclosed nerve root (Yes/No)
  - CLINICAL L3 root radiculopathy (Yes/No)
  - CLINICAL L4 root radiculopathy (Yes/No)

- CLINICAL L5 root radiculopathy (Yes/No)
- CLINICAL S1 root radiculopathy (Yes/No)

An important part of the study is comparison of the effect of sacral epidural injection on these different combinations of clinical and MR findings. A one-way ANOVA (for normally distributed data) or Kruskal-Wallis test (for non-normally distributed data) are used here.

4. The statistical program SPSS is used to analyse the results. The statistical analyses are performed at the Institutt for Samfunns Medisin (ISM), Universitetet i Tromsø, by personnel who do not know the patients' clinical details or which patients have received placebo or treatment.

### Calculation of sample size

Many studies have been conducted that can provide a basis for calculating the sample size of the trial. In the case of the primary outcome measure, the ODI, a clinically significant difference between the groups can be set at  $\Delta = 10$  [50]. Based on this, and by using a quantitative method where  $f(\alpha = 0.05, \beta = 0.10) = 10.5$  [87], we can calculate the necessary sample size for each randomization group:  $n = 69 \{n = 2 (\sigma/\Delta)^2 \times f(\alpha, \beta)\}$  patients in each group if the standard deviation ( $\sigma$ ) = 18, strength ( $\beta$ ) = 90% and significance level ( $\alpha$ ) = 5%. With three groups we therefore need a total of 207 patients included in the study. We want to have five interim analyses performed during the study, and therefore need to increase the number of patients to 72 in each group. If we add a few more to take account of lost-to-follow-up, non-compliance, etc., we will probably have to increase the size of the groups to 80 patients. Based on this, we aim to include a total of 240 patients.

## Direct access to source data/documents

All data from the standardized questionnaires are input in anonymized form in a database established at the Clinical Research Centre, the Unit for Research Methodology, UNN. Data input is carried out by optical scanning of the questionnaires.

## Quality control and quality assurance

Monitoring of the quality of data recording and record keeping may be performed unannounced by personnel from the Clinical Research Centre, the Unit for Research Methodology, UNN.

## The Coordinating Committee

The Coordinating Committee's tasks are, via its members, to ensure that the study progresses and that it is performed as intended at each hospital. The Coordinating Committee must also take a view on serious complications and ADRs recorded and, in consultation with the IDMC, decide to terminate the study if appropriate.

## Ethics

Placebo is traditionally regarded as inactive treatment. In experimental studies, treatment is often compared with placebo to determine whether or not treatment using an active medicine has any effect [88]. In studies on the effect of ESI, steroid treatment is often compared with placebo treatment using saline. The reason for this is that so far there is still no standard treatment for ESI for back pain. In some studies a positive effect has been recorded for epidural saline on its own. One possible interpretation of this could be that an inactive substance can have an effect via mechanisms other than the purely pharmacological action, for example due to a volume or pressure effect. The

inclusion and randomization of patients with nerve root disease for ESI is basically associated with a number of ethical problems. The use of ESI is widespread. This method has been used both inside and outside hospitals. There is, however, no evidence that the method is effective. It is therefore important that a high-quality randomized controlled study is carried out in order to document any effect of steroid and volume versus placebo in patients with chronic lumbosacral radiculopathy. Since there is some uncertainty and lack of evidence associated with most methods for treating lower back pain and sciatica, testing the effect of ESI would be ethically defensible. Good patient information, informed consent, the principles of good clinical practice in clinical trials, the Declaration of Helsinki and ethical approval are fundamental requirements for conducting a study of this kind.

## **Data handling**

All questionnaires and clinical record forms in the study are collected in a dedicated 'Form book' that tracks the patient until the study has been completed (Figure 9). All procedures and recorded information about the patients will be saved and accessible at each involved clinical trial hospital (in the electronic patient journal) for at least 15 years after the study report has been completed.

## **Insurance**

Section 3 of the Product Liability Act no. 104 of 23 December 1988 contains special rules governing liability for compensation in respect of harm caused by medicinal products. Under these rules, manufacturers, importers and testers of medicinal products must take out special insurance known as Medicinal Product Insurance. This insurance will, under the detailed rules of the Act, compensate any injured party in an objective manner, i.e. regardless of whether blame is established. The Product Liability Act requires manufacturers, importers and testers to take out insurance via membership of a

special association known as the Drug Liability Association. The epidural project is insured under the Medicinal Product Insurance scheme via membership of the Drug Liability Association.

## **Own risk**

The project covers health insurance for the patients for the inclusion check, two injections and three follow-up check-ups.

## **Trial plan**

- Start of trial: October 2005.
- End of study: December 2009 (or when inclusion of 240 patients is completed).
- Actual inclusion rate from 2005 to 2007: 2 per month.
- Estimated inclusion rate all hospitals at start of RCT was 16 per month. This gap between expected and current inclusion rate has initiated a rerun of the information letter concerning the study to the doctors, chiropractors and physiotherapists referring patients to the study and stronger internal logistics in coadjutant hospitals. All departments will give priority to the RCT and increase the inclusion rate. By the end of 2007 it is estimated that 100 patients are included, by the end of 2008, 170 patients, and by the end of 2009, 240 patients.
- Presentation of results: 2010.

## **Discussion**

## **Back pain, injections**

Ever since the beginning of the 20th century, ESI has been used as a method of treating lumbago and sciatica [89]. Clinical findings for sacral epidural injection for back pain were reported as long ago as 1925 [90]. In one clinical study from 1930, full and permanent improvement was reported for 61% of a group of sciatica patients who were treated with ESI of the local anaesthetic procaine [91]. The English physician James Cyriax used ESI regularly in the treatment of his back patients. Over the period 1937–1980, he probably used more than 50,000 such injections [92].

Bogduk (2004) has in a clinical update concerning management of chronic low back pain argued in defence of a so-called reductionism [93]. Reductionism describes the pursuit of a pathoanatomical diagnosis for chronic low back pain with the view to implementing a target-specific treatment. Bogduk describes diagnostic joint blocks, discography, intradiscal electrothermal therapy as examples of target-specific treatment. It is possible that the use of ESI can be classified as both reductionism and target-specific treatment.

## **Back injections, evidence from Cochrane**

ESI for low back pain was described as a potentially effective method of treatment in a Cochrane report [39] dealing with evidence for injection treatment for back pain. Injections, according to this systematic review, should not be seen as an alternative to the surgical treatment of sciatica, but more as a supplement. Injections can in some cases have the effect of postponing surgery and in this way enable the patient to train his or her back muscles in a pain-free period before any subsequent surgery. In some cases, the injections can provide an effective therapeutic option for the large group of back patients for whom surgery is not indicated and for whom exercise and other conservative treatment has been unsuccessful [21,85]. Some American clinics are increasingly using ESI preoperatively, both as a diagnostic aid and for treatment purposes [94]. Used in this way, the injections may perhaps also postpone, or prevent, surgery [95-98].

## **Back injections, effect on radiculopathy**

The effect of ESI is not well elucidated [70,99-102]. The use of ESI in disc prolapse with radiculopathy is based on the hypothesis that inflammation develops as a result of compression either against the dura or against the nerve root [103]. Compression against the dura gives rise to multisegmental pain via an effect on sensory nerve fibres in the dura, or segmental pain on compression against the nerve root [104]. In theory, it is conceivable that the volume used in ESI may be important for the painkilling effect in multisegmental pain, either via a pressure effect on the dura in which the dura is pressed away from the disc, or via a tensile effect in which the fluid breaks or loosens inflammatory-induced adhesions between the disc and dura [105-107]. In two recently published studies [108,109], it has been documented in animal experiments that material from the pulpy nucleus that comes into contact with nerve tissue can trigger pain without there being mechanical pressure against the nerve. This may help explain how significant problems with back pain and sciatica can be experienced even if a definitely free prolapse with an effect on the dura mater or nerve root cannot be demonstrated by MR diagnosis [110-112]. In a study using gadolinium-enhanced lumbar spine MRI, Saifuddin et al (1999) found that patients with annular tears may experience low back pain with radiation into the lower limb in the absence of nerve root compression [113]. Inflammation of nerve roots from leak of degenerative nuclear material through full-thickness annular tears was the proposed mechanism for such leg pain.

## **Back injections, effect of volume in the epidural space**

Variable volumes have been used for ESI in various studies. Cuckler et al (1985) used 7 ml [114], Klenerman et al (1984) 20 ml [115], Beliveau (1971) 42 ml [116] and Evans (1930) 98 ml [91]. Klenerman et al (1984) injected a volume of 20 ml for three different treatment groups [115]. One group received corticosteroid and saline, another group received only saline and the third was given



only local anaesthetic. Klenerman recorded an effect from the injections on pain but was unable to establish a significant difference between the treatment groups. One possible interpretation of this result is that neither corticosteroid nor local anaesthesia has an effect. Another possible interpretation of this result is that the injected volume of 20 ml has an effect in itself [117]. Fluoroscopic studies of ESI have shown that, by using a volume of 8 ml, it is possible to reach disc level L4/L5. Epidural injections of preparations show that a volume of 30 ml reaches L2 level, and is distributed throughout the epidural space (Professor in anatomy University of Oslo, Norway, Eric Rinvik, personal communication from 2003). A study published by Valat et al (2003) reports that ESI of 2 ml saline alone yields a reduction in pain, but no additional effect from the injection of 2 ml prednisolone acetate (50 mg) was demonstrable [118].

### **Back injections, evidence from clinical studies, systematic reviews and randomized controlled trials**

ESI has been used as treatment for lumbago and sciatica for many years, but the method is still not established as good clinical practice. It is documented in one review that ESI was recommended to as many as 12.6% of all patients with lumbago and sciatica [119]. Despite this, there are few randomized controlled studies documenting the therapeutic effect [120]. The weakness of the studies that exist in this field is that they have generally been conducted on small patient populations, often without the use of control groups [102,121-127]. In addition, inclusion criteria and diagnosis groups have been poorly explained [128].

Two of the studies mentioned above [122,123] comprise more than 200 patients, but the studies lack control groups. The findings therefore become difficult to interpret. Variable results have been reported for ESI with a one-year success rate ranging from 25% [129] to 65% [122]. In other studies with patient populations comprising 30–70 patients and with control groups, no statistically significant improvement is reported after epidural injection [114,115,130-134]. Many of these

studies conclude that ESI of corticosteroids has no effect either on relieving symptoms or on the duration of disease in the case of sciatica [131,133]. In one of the studies, epidural injection of corticosteroid was compared with NSAID, without any significant difference in reduction of symptoms and duration of disease being demonstrable [130]. In four of the studies, corticosteroids are compared with local anaesthesia and saline, without it having been possible to demonstrate significant differences in therapeutic effect [114,115,132,134].

In five randomized controlled studies, improvement in back complaints has been documented following ESI of corticosteroids. Breivik et al (1976) report a significant improvement in pain and objective neurological signs after injection of corticosteroid and bupivacaine compared with injection of saline and bupivacaine [135]. Mathews et al (1987) and Bush and Hillier (1991) report significantly more pain-free patients, and an improvement in Lasegue's test, 3 months after ESI of corticosteroid and procaine compared with saline [136,137]. Ridley et al (1988) found that the effect of epidural injection of corticosteroid was better than placebo injection of saline in the spinous ligament [138]. Carrette et al (1997) found that epidural injection of corticosteroid and saline yielded better results on pain than injection of saline alone [139].

Some of the randomized controlled studies in this area lend support to the use of ESI for low back pain and sciatica [140,141], whereas others reject the method [142]. This uncertainty concerning the findings of the studies that have been conducted means that evidence for use of the method is weak [143]. The method has therefore not been generally accepted as good clinical practice. However, the method is inexpensive, easy to use and has few reported side effects [144,145].

### **Accuracy of the method**

There are a number of more recent reports indicating that accuracy of the ESI method is lower than previously assumed [146-151]. It is indicated in one study that clinical perception of a properly

performed technique has a sensitivity rate of 94%, and a specificity rate of 20% [152]. In another study, in which 304 ESIs were administered by experienced clinicians, it turned out that 25% of the injections were performed incorrectly [153]. Another important aspect of not using fluoroscopic guided epidural injection is the uncertainty concerning the likelihood of placing the injection intravasally in the venous plexus in the epidural space. Sensitivity when using aspiration for sacral epidural injection has not been described in the literature.

### **Side effects**

In around 15% of patients, less serious side effects can be experienced from epidural injection. Sleeping problems, headache, flushing and temporarily increased back pain have been reported for the first 24 hours after the injection has been administered [154]. There is no systematic summary of the incidence of side effects and complications associated with corticosteroid ESI.

### **Need for further investigations**

There are currently no studies that have systematically investigated the importance of mechanical volume effects in the epidural space as a result of ESI. We also lack evidence-based knowledge of which patient groups with lumbar back pain may benefit from sacral epidural injection. It is assumed that patients with an element of local inflammation, for example in association with radiculopathy as a result of disc prolapse or radiculitis of different aetiology, may respond best to steroid injection [39].

## The anti-inflammatory effects of steroids in the epidural space

The body's own steroids are produced in the reticular region of the adrenal cortex. Steroids affect protein metabolism (nitrogen catabolism) and glucose metabolism (increasing gluconeogenesis) [155]. Corticosteroids for joint injection have been used since 1951 [156]. Caudal epidural hydrocortisone therapy gained wide popularity after Lievre et al (1953) reported improvement in five of 20 patients with sciatica [157]. The mechanisms of action and local effect in inflammatory tissue have still not been fully elucidated [158]. The anti-inflammatory effect of steroids (the glucocorticoid effect) is first and foremost regarded as being mediated via a reduction in prostaglandin synthesis [155]. The mechanism behind this is not fully understood, but most probably glucocorticosteroids work intracellularly and bind to specific receptor proteins in the cell nucleus [155]. This steroid receptor complex is thought to affect the transcription of genes, inhibiting formation of the enzyme cyclo-oxygenase 2 (cox-2). This enzyme is responsible for formation of the prostaglandins involved in the inflammation process [155]. Corticosteroids also suppress the immunological response to lymphocytes, reduce oedema formation in inflammatory tissue and stimulate production of the anti-inflammatory mediator lipocortin [155].

The medicinal product triamcinolone has a relative anti-inflammatory effect of 4 (by way of comparison, hydrocortisone = cortisol has an anti-inflammatory effect = 1 in a dosage of 20 mg). The biological action time of triamcinolone is estimated to be between 15 and 48 hours; the local effect in tissue is more uncertain, but may probably be up to 14 days. The reason for this long local action time is thought to be that steroid preparations are barely soluble, and are therefore absorbed slowly in the systemic circulation for metabolization [159]. Steroids have for many years been used for spinal injections [160,161], but clinical documentation concerning the action and effect of the medicinal product on nerve tissue is limited [162]. More recent studies indicate that corticosteroids can have a direct impact on pain via an effect on the pain mediator, substance P [163]. Nygaard et al (1997) found that inflammatory mechanisms are involved in sciatica and that different types of disc herniation have different inflammatory properties [164]. Muramoto et al (1997) found that

triamcinolone suppressed the firing induced by prostaglandin suggesting that steroids may be effective in the treatment of root symptoms [165]. In the studies conducted, corticosteroid preparations of differing anti-inflammatory effect have been used. There is therefore uncertainty as to whether the effect depends on which corticosteroid preparation is used. In a comparative study of the effect of epidural injections on low back pain, triamcinolone has been found to be more efficacious than betamethasone [166]. Triamcinolone is regarded as a safe preparation in spinal injections. A regression of the hernia disc material following corticosteroid ESI has been reported in one paper [167]. The mechanisms behind the spontaneous regression of pulpy nucleus prolapse are still not fully understood [168-170].

### **What this study emphasizes**

- Use of strict inclusion and exclusion criteria, template for clinical back examination and high level of competence on the part of physicians and physiotherapists investigating the patients ensuring a homogeneous patient population (lumbosacral nerve root disease).
- Study design as a blinded RCT with good randomization and calculation of strength.
- Multicentre study.
- The treatment consists of two injections at 14-day intervals, which conforms to good clinical practice.
- Use of a volume of 30 ml for the epidurals, which ensures that the entire epidural space in the lumbosacral column is covered up to level L2.
- The injections are performed by well-qualified personnel with the same technical background (anaesthesiologists).

- To follow internationally accepted and validated outcome measures (ODI, EQ-5D, VAS leg and back pain), which means that the results from the study can be compared with other back research.
- Use of MRI makes it possible to identify subgroups of the disease and compare clinical findings and MRI findings.
- Use of diagnostic ultrasound to increase the accuracy of the epidural injections.

## **Planned publications based on this study**

- Placebo-controlled study of the effect of sacral epidural injection with triamcinolone versus volume on patients with lumbosacral radiculopathy in which ODI is the primary outcome variable and EQ-5D, VAS low back pain and VAS leg pain are the secondary outcome variables.
- Appraisal of whether the effect differs in patients with clinical radiculopathy and whether MR showed either signal changes in the disc, covered prolapse, free prolapse, thickened nerve root or disclosed nerve root.
- Description of the relationship between clinical findings of the level and side of the radiculopathy in connection with back examination and corresponding MR findings.
- Description of the correspondence between clinical finding, MR and electromyography (EMG) in those cases where there is clinical loss of muscle strength.
- The benefit of ultrasound in identifying sacral hiatus and thus improving the accuracy of sacral epidural injection.

## List of abbreviations

ADR	adverse drug reaction
BMI	Body mass index
EMA	European Medicines Agency
EMG	Electromyography
EQ-5D	European Quality of Life measure
ESI	Epidural Steroid Injection
FABQ	Fear-Avoidance Beliefs Questionnaire
FABQ-Work	Fear-Avoidance Beliefs Questionnaire for work
FABQ-PA	Fear-Avoidance Beliefs Questionnaire for physical activity
FDA	Food and Drug Administration
HRQL	Health-related quality of life
ISM	Institutt for Samfunns Medisin
MR	Magnetic resonance
MRI	Magnetic resonance imaging
NSAID	Non-steroidal anti-inflammatory drug
NSD	Norwegian Social Science Data Services
RCT	Randomized controlled trial
REK nord / REKNOR	Regionale komiteer for medisinsk og helsefaglig forskningsetikk Nordland, Troms og Finnmark

RELIS	Regionale legemiddelinformasjonssentre
SUSAR	Serious unexpected severe adverse reaction
UNN	University Hospital of North Norway
VAS <sub>BP</sub>	Visual analogue scale back pain
VAS <sub>LP</sub>	Visual analogue scale leg pain
VAS <sub>GH</sub>	Visual analogue scale general health
WMA	World Medical Association

## **Competing interests**

The author declare that they have no competing interests.

## **Authors' contributions**

The author contributed to the study design and writing of the manuscript.

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## **References**

1. Brage S, Lærum E. Ryggglidelser i Norge – en epidemiologisk beskrivelse. Tidsskr Nor Lægeforen. 1999; 119:161-23.
2. Linton SJ, Hellsing AL, Hallden K. A population-based study of spinal pain among 35-45-year-old individuals: prevalence, sick leave, and health care use. Spine. 1998;23(13):1457-63.

3. Ihlebæk C, Lærum E. Plager flest – koster mest – muskel og skjelettlidelser i Norge. Rapport nr. 1. Oslo: Nasjonalt Ryggnettverk; 2004.
4. Indahl A. Når ryggen krangler. Oslo: Valdisholm Forlag; 2003.
5. Hafstad A. Dårlig ryggbehandling koster dyrt. Aftenposten Helse 27 Jul 2001.
6. Hoddevik G, Selmer R. Kroniske korsryggsmerter hos 40-åringer i 12 norske fylker. Tidsskr Nor Lægeforen. 1999;119:2224-8.
7. Hagen KB, Thune O. Work incapacity from low back pain in the general population. Spine. 1998;23(19): 2091-5.
8. Haldorsen EMH, Kronholm K, Skouen JS, Ursin H. Predictors for outcome of a multi-modal cognitive behavioural treatment program for low back pain patients — a 12-month follow-up study. European Journal of Pain. 1998;2(4):293-307.
9. Kristoffersen AP. Utviklingen på uførepensjonsområdet. RTV-rapport nr. 7-1999. 23 Nov 1999. <https://www.nav.no/no/NAV+og+samfunn/Kunnskap/Analyser/NAV+rapportserie/NAV+rappporter/Utviklingen+p%C3%A5+uf%C3%B8repensjonsomr%C3%A5det.355549.cms>. Accessed 19 Feb 2015.
10. The Norwegian Back Pain Network, The Communication Unit (Nasjonalt Ryggnettverk, Formidlingsenheten). Acute low back pain. Interdisciplinary clinical guidelines (Akutte korsryggsmerter. Tverrfaglige, kliniske retningslinjer). Oslo: The Norwegian Back Pain Network (Nasjonalt Ryggnettverk); 2002.
11. Weber H, Holme I, Amlie E. The natural course of acute sciatica with nerve root symptoms in a double-blind placebo-controlled trial evaluating the effect of piroxicam. Spine. 1993;18(11):1433-8.
12. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. Eur Spine J. 2003;12(2):149-65.

13. Lærum E, Brox JI, Storheim K, Espeland A, Haldorsen E, Munch-Ellingsen J, et al. Korsryggsmerter – med og uten nerverotaffeksjon. Nasjonale Kliniske Retningslinjer. Formidlingsenheten for muskel- og skjelettlidelser (Formi). 2002. [http://www.formi.no/Helsepersonell/id/kliniske\\_retningslinjer/](http://www.formi.no/Helsepersonell/id/kliniske_retningslinjer/). Accessed 18 Feb 2015.
14. Bogduk N, McGuirk B. Medical management of acute and chronic low back pain: an evidence-based approach. London: Elsevier; 2002.
15. Magnæs B, Kjønniksen I, Dullerud R, Grundnes O, Haagensen Ø, Indahl A, et al. Metodevurdering av behandling ved lumbalt skiveprolaps med rotaffeksjon. Tidsskr Nor Lægeforen Nr 7. 2002;122:718-20. <http://tidsskriftet.no/article/508784>. Accessed 18 Feb 2015.
16. Ursin H. Prognose ved ryggliedelser. Tidsskr Nor Lægeforen. 1999;119:1909-12.
17. Waddell G, McIntosh A, Hutchinson A, Feder G, Lewis M. Low back pain evidence review. 2nd ed. London: Royal College of General Practitioners; 1999.
18. Koes BW, van Tulder MW, Ostelo R, Kim Burton A, Waddell G. Clinical guidelines for the management of low back pain in primary care: an international comparison. Spine. 2001;26(22):2504-13; discussion 2513-4.
19. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, et al. on behalf of the COST B13 Working Group on Guidelines for Chronic Low Back Pain. Chapter 4. European guidelines for the management of chronic nonspecific low back pain. Eur Spine J. 2006;15(Suppl 2):S192-300.
20. Gustavsen T. Knuser myter om rygger som krangler. Aftenposten 21 Sep 2003.
21. Samanta A, Beardsley J. Sciatica: which intervention? BMJ. 1999;319(7205):302-3.
22. Seferlis T, Nemeth G, Carlsson AM, Gillstrom P. Conservative treatment in patients sick-listed for acute low-back pain: a prospective randomised study with 12 months' follow-up. Eur Spine J. 1998; 7(6):461-70.

23. Ljunggren AE, Weber H, Larsen S. Autotrraction versus manual traction in patients with prolapsed lumbar intervertebral discs. *Scd J Rehabil Med.* 1984;16(3):117-24.
24. Weber H, Ljunggren AE, Walker L. Traction therapy in patients with herniated lumbar intervertebral discs. *J Oslo City Hosp.* 1984;34(7-8):61-70.
25. Vroomen PC, de Krom MC, Wilmink JT, Kester AD, Knottnerus JA. Lack of effectiveness of bed rest for sciatica. *N Engl J Med.* 1999;340(6):418-23.
26. Koes BW, Scholten RJ, Mens JM, Bouter LM. Efficacy of non-steroidal anti-inflammatory drugs for low back pain: a systematic review of randomised clinical trials. *Ann Rheum Dis.* 1997;56(4):214-23.
27. van Tulder MW, Scholten RJ, Koes BW, Deyo RA. Non-steroidal anti-inflammatory drugs for low back pain. *Cochrane Database Syst Rev (2):CD000396.* 2000.
28. Nwuga VC. Ultrasound in treatment of back pain resulting from prolapsed intervertebral disc. *Arch Phys Med Rehabil.* 1983;64(2):88-9.
29. Hasenbring M, Ulrich HW, Hartmann M, Soyka D. The efficacy of a risk factor-based cognitive behavioral intervention and electromyographic biofeedback in patients with acute sciatic pain. An attempt to prevent chronicity. *Spine.* 1999;24(23):2525-35.
30. Nwuga VC. Relationship between low back pain and life-stressing events among Nigerian patients. *J Trop Med Hyg.* 1985;88(1):17-20.
31. van Tulder MW, Malmivaara A, Esmail R, Koes BW. Exercise therapy for low back pain. *Cochrane Database Syst Rev (2):CD000335.* 2000.
32. Tullberg T, Isacson J, Weidenhielm L. Does microscopic removal of lumbar disc herniation lead to better results than the standard procedure? Results of a one-year randomized study. *Spine.* 1993;18(1):24-7.

33. Henriksen L, Schmidt K, Eskesen V, Jantzen E. A controlled study of microsurgical versus standard lumbar discectomy. *Br J Neurosurg.* 1996;10(3):289-93.
34. Solberg T. Rutiner for henvisning av ryggpasienter til nevrokirurgisk poliklinikk, RiTØ. Nevrokirurgisk avdeling; 2000.
35. Vik A, Zwart JA, Hulleberg G, Nygaard OP. Eight year outcome after surgery for lumbar disc herniation: a comparison of reoperated and not reoperated patients. *Acta Neurochir (Wien).* 2001;143(6):607-610; discussion 610-11.
36. Wright MG. Clinical use of procaine. *Br J Hosp Med.* 1995;53(6):296.
37. Cyriax J. Epidural anaesthesia and bed rest in sciatica. *BMJ.* 1961;1(5223):428.
38. Manchikanti L, Boswell MV, Raj PP, Racz GB. Evolution of interventional pain management. *Pain Physician.* 2003;6(4):485-94.
39. Nelemans PJ, deBie RA, deVet HC, Sturmans F. Injection therapy for subacute and chronic benign low back pain. *Cochrane Database Syst Rev.* 2:CD001824. 2000.
40. Borenstein DG, O'Mara JW Jr, Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The value of magnetic resonance imaging of the lumbar spine to predict low-back pain in asymptomatic subjects: a seven-year follow-up study. *J Bone Joint Surg Am.* 2001;83-A(9):1306-11.
41. Jadad AR, Rennie D. The randomized controlled trial gets a middle-aged checkup. *JAMA.* 1998;279(4):319-20.
42. Jensen TS, Sorensen JS, Kjaer P. Intra- and interobserver reproducibility of vertebral endplate signal (modic) changes in the lumbar spine: the Nordic Modic Consensus Group classification. *Acta Radiol.* 2007;48:748-54.

43. Karppinen J, Malmivaara A, Tervonen O, Pääkkö E, Kurunlahti M, Syrjälä P, et al. Severity of symptoms and signs in relation to magnetic resonance imaging findings among sciatic patients. *Spine*. 2001;26(7):E149-54.
44. Altman, DG. *Practical statistics for medical research*. London: Chapman and Hall; 1991.
45. Lisi AJ. The centralization phenomenon in chiropractic spinal manipulation of discogenic low back pain and sciatica. *J Manipulative Physiol Ther*. 2001;24(9):596-602.
46. Horlocker TT, Bajwa ZH, Ashraf Z, Khan S, Wilson JL, Sami N, et al. Risk assessment of hemorrhagic complications associated with nonsteroidal antiinflammatory medications in ambulatory pain clinic patients undergoing epidural steroid injection. *Anesth Analg*. 2002;95(6):1691-7.
47. Hagen KB, Hilde G, Jamtvedt G, Winnem MF. The cochrane review of advice to stay active as a single treatment for low back pain and sciatica. *Spine*. 2002;27(16):1736-41.
48. Storheim K, Brox JI, Holm I, Koller AK, Bø K. Intensive group training versus cognitive intervention in sub-acute low back pain: short-term results of a single-blind randomized controlled trial. *J Rehabil Med*. 2003;35(3):132-40.
49. Skouen JS, Grasdal AL, Haldorsen EMH, Ursin H. Relative cost-effectiveness of extensive and light multidisciplinary treatment programs versus treatment as usual for patients with chronic low back pain on long-term sick leave: randomized controlled study. *Spine*. 2002;27(9):901-9; discussion 909-10.
50. Brox JI, Sørensen R, Friis A, Nygaard Ø, Indahl A, Keller A, et al. Randomized clinical trial of lumbar instrumented fusion and cognitive intervention and exercises in patients with chronic low back pain and disc degeneration. *Spine*. 2003;28(17):1913-21.

51. Mayo Clinic Health Information. Diseases and conditions: sciatica. 2004.  
<http://www.mayoclinic.org/diseases-conditions/sciatica/basics/definition/con-20026478>. Accessed 18 Feb 2015.
52. Spine-health. What you need to know about sciatica. <http://www.spine-health.com/conditions/sciatica/what-you-need-know-about-sciatica>. Accessed 17 Feb 2015.
53. Frost H, Lamb SE, Doll HA, Carver PT, Stewart-Brown S. Randomised controlled trial of physiotherapy compared with advice for low back pain. *BMJ*. 2004;329:708.
54. Deville WL, van der Windt DA, Dzaferagic A, Bezemer PD, Bouter LM. The test of Lasegue: systematic review of the accuracy in diagnosing herniated discs. *Spine*. 2000;25(9):1140-7.
55. Kosteljanetz M, Bang F, Schmidt-Olsen S. The clinical significance of straight-leg raising (Lasegue's sign) in the diagnosis of prolapsed lumbar disc. Interobserver variation and correlation with surgical finding. *Spine*. 1988;13(4):393-5.
56. Xin SQ, Zhang QZ, Fan DH. Significance of the straight-leg-raising test in the diagnosis and clinical evaluation of lower lumbar intervertebral-disc protrusion. *J Bone Joint Surg Am*. 1987;69(4):517-22.
57. Cyriax J. Textbook of orthopaedic medicine, Vol. I Diagnosis of soft tissue lesions. 8th ed. London: Bailliere Tindall; 1982.
58. Ombregt L, Bisschop P, ter Veer HJ. A system of orthopaedic medicine. London: Churchill Livingstone; 2003.
59. Little DG, MacDonald D. The use of the percentage change in Oswestry Disability Index score as an outcome measure in lumbar spinal surgery. *Spine*. 1994;19(19):2139-43.
60. Niskanen RO. The Oswestry Low Back Pain Disability Questionnaire, a two-year follow-up of spine surgery patients. *Scand J Surg*. 2002;91(2):208-11.

61. Grotle M, Brox JI, Vøllestad NK. Cross-cultural adaptation of the Norwegian versions of the Roland-Morris Disability Questionnaire and the Oswestry Disability Index. *J Rehabil Med*. 2003;35(5):241-7.
62. Holm I, Friis A, Storheim K, Brox JI. Measuring self-reported functional status and pain in patients with chronic low back pain by postal questionnaires: a reliability study. *Spine*. 2003;28(8):828-33.
63. Hagg O, Fritzell P, Nordwall A. The clinical importance of changes in outcome scores after treatment for chronic low back pain. *Eur Spine J*. 2003;12(1):12-20.
64. Burstrom K, Johannesson M, Diderichsen F. Swedish population health-related quality of life results using the EQ-5D. *Qual Life Res*. 2001;10(7):621-35.
65. Hurst NP, Kind P, Ruta D, Hunter M, Stubbings A. Measuring health-related quality of life in rheumatoid arthritis: validity, responsiveness and reliability of EuroQol (EQ-5D). *Br J Rheumatol*. 1997;36(5):551-9.
66. Sapin C, Fantino B, Nowicki ML, Kind P. Usefulness of EQ-5D in assessing health status in primary care patients with major depressive disorder. *Health Qual Life Outcomes*. 2004;2:20.
67. Luo N, Chew LH, Fong KY, Koh DR, Ng SC, Yoon KH, et al. A comparison of the EuroQol-5D and the Health Utilities Index mark 3 in patients with rheumatic disease. *J Rheumatol*. 2003;30(10):2268-74.
68. Waddell G, Newton M, Henderson I, Somerville D, Main CJ. A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability. *Pain*. 1993;52(2):157-68.
69. Grotle M, Vøllestad NK, Veierød MB, Brox JI. Fear-avoidance beliefs and distress in relation to disability in acute and chronic low back pain. *Pain*. 2004;112(3):343-52.
70. Slucky AV, Sacks MS, Pallares VS, Malinin TI, Eismont FJ. Effects of epidural steroids on lumbar dura material properties. *J Spinal Disord*. 1999;12(4):331-40.



71. Delaney TJ, Rowlingson JC, Carron H, Butler A. Epidural steroid effects on nerves and meninges. *Anesth Analg*. 1980;59(8):610-4.
72. Nelson DA, Landau WM. Intraspinal steroids: history, efficacy, accidentality, and controversy with review of United States Food and Drug Administration reports. *J Neurol Neurosurg Psychiatry*. 2001;70(4):433-43.
73. Young WF. Transient blindness after lumbar epidural steroid injection: a case report and literature review. *Spine*. 2002;27(21):E476-7.
74. Sullivan WJ, Willick SE, Chira-Adisai W, Zuhosky J, Tyburski M, Dreyfuss P, et al. Incidence of intravascular uptake in lumbar spinal injection procedures. *Spine*. 2000;25(4):481-6.
75. Ward A, Watson J, Wood P, Dunne C, Kerr D. Glucocorticoid epidural for sciatica: metabolic and endocrine sequelae. *Rheumatology (Oxford)*. 2002;41(1):68-71.
76. Cooper AB, Sharpe MD. Bacterial meningitis and cauda equina syndrome after epidural steroid injections. *Can J Anaesth*. 1996;43(5 Pt 1):471-4.
77. Lowell TD, Errico TJ, Eskenazi MS. Use of epidural steroids after discectomy may predispose to infection. *Spine*. 2000;25(4):516-9.
78. Koka VK, Potti A. Spinal epidural abscess after corticosteroid injections. *South Med J*. 2002;95(7):772-4.
79. Trautmann M, Lepper PM, Schmitz FJ. Three cases of bacterial meningitis after spinal and epidural anesthesia. *Eur J Clin Microbiol Infect Dis*. 2002;21(1):43-5.
80. McLain RF, Fry M, Hecht ST. Transient paralysis associated with epidural steroid injection. *J Spinal Disord*. 1997;10(5):441-4.

81. Slipman CW, Chow DW, Lenrow DA, Blaugrund JE, Chou LH. Dysphonia associated with epidural steroid injection: a case report. *Arch Phys Med Rehabil.* 2002;83(9):1309-10.
82. Furman MB, O'Brien EM, Zgleszewski TM. Incidence of intravascular penetration in transforaminal lumbosacral epidural steroid injections. *Spine.* 2000;25(20):2628-32.
83. McCullen GM, Spurling GR, Webster JS. Epidural lipomatosis complicating lumbar steroid injections. *J Spinal Disord.* 1999;12(6):526-9.
84. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. *Spine.* 2002;27(1):11-16.
85. Samanta A, Samanta J. Is epidural injection of steroids effective for low back pain? *BMJ.* 2004;328(7455):1509-10.
86. Ogoke BA. Caudal epidural steroid injections. *Pain Physician.* 2000;3(3):305-12.
87. Pocock SJ. *Clinical trials: a practical approach.* New York: Wiley; 1983.
88. Spiegel D. Placebos in practice. *BMJ.* 2004;329(7472):927-8.
89. Caussade G, Queste P. Traitement de la neuralgie sciatique par la méthode de Sicard. Résultats favorables même dans les cas chroniques par la cocaïne à doses élevées et répétées à intervalles rapprochés. *Bull Soc Med Hosp.* 1909;28:865.
90. Viner N. Intractable sciatica: sacral epidural injection. *Can Med Assoc J.* 1925;15:630.
91. Evans W. Intracanal epidural injection in the treatment of sciatica. *Lancet.* 1930;1225-9.
92. Cyriax JH, Cyriax PJ. *Cyriax's illustrated manual of orthopaedic medicine.* 2nd ed. London: Butterworth-Heinemann Ltd; 1993.
93. Bogduk N. Management of chronic low back pain. *Med J Aust.* 2004;180(2):79-83.

94. Cannon DT, Aprill CN. Lumbosacral epidural steroid injections. *Arch Phys Med Rehabil*. 2000;81(3 Suppl 1):S87-98.
95. Gupta AK, Singh RC, Shukla RK, Nath R. Role of epidural medication in the treatment of resistant low back pain. *J Indian Med Assoc*. 1996;94(6):224-6.
96. Riew KD, Yin Y, Gilula L, Bridwell KH, Lenke LG, Laurysen C, et al. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. A prospective, randomized, controlled, double-blind study. *J Bone Joint Surg Am*. 2000;82-A(11):1589-93.
97. Rydevik BL, Cohen DB, Kostuik JP. Spine epidural steroids for patients with lumbar spinal stenosis. *Spine*. 1997;22(19):2313-17.
98. Woodman R, Balavender H, Froeb R. Relief of low back pain by epidural injection. A case report. *Phys Ther*. 1987;67(11):1712-14.
99. Weinstein SM, Herring SA, Derby R. Contemporary concepts in spine care. Epidural steroid injections. *Spine*. 1995;20(16):1842-6.
100. Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. *Clin J Pain*. 1998;14(2):148-51.
101. Rivest C, Katz JN, Ferrante FM, Jamison RN. Effects of epidural steroid injection on pain due to lumbar spinal stenosis or herniated disks: a prospective study. *Arthritis Care Res*. 1998;11(4):291-7.
102. Berman AT, Garbarino JL Jr, Fisher SM, Bosacco SJ. The effects of epidural injection of local anesthetics and corticosteroids on patients with lumbosciatic pain. *Clin Orthop*. 1984;188:144-51.
103. Cyriax JH. The mechanism of dural pain. *Lancet*. 1945;ii:427.
104. Slipman CW, Chow DW. Therapeutic spinal corticosteroid injections for the management of radiculopathies. *Phys Med Rehabil Clin N Am*. 2002;13(3):697-711.

105. Lipetz JS. Pathophysiology of inflammatory, degenerative, and compressive radiculopathies. *Phys Med Rehabil Clin N Am.* 2002;13(3):439-49.
106. Dunbar SA, Manikantan P, Philip J. Epidural infusion pressure in degenerative spinal disease before and after epidural steroid therapy. *Anesth Analg.* 2002;94(2):417-20.
107. Fukushige T, Kano T, Sano T, Irie M. Computed tomographic epidurography: an aid to understanding deformation of the lumbar dural sac by epidural injections. *Eur J Anaesthesiol.* 1999;16(9):628-33.
108. Anzai H, Hamba M, Onda A, Konno S, Kikuchi S. Epidural application of nucleus pulposus enhances nociceptor responses of rat dorsal horn neurons. *Spine.* 2002;27(3):E50-5.
109. Igarashi T, Kikuchi S, Shubayev V, Myers RR. 2000 Volvo Award Winner in Basic Science Studies: Exogenous tumor necrosis factor- $\alpha$  mimics nucleus pulposus-induced neuropathology: molecular, histologic, and behavioral comparisons in rats. *Spine.* 2000;25(23):2975-80.
110. Harrington JF, Messier AA, Bereiter D, Barnes B, Epstein MH. Herniated lumbar disc material as a source of free glutamate available to affect pain signals through the dorsal root ganglion. *Spine.* 2000;25(8):929-36.
111. Kawakami M, Matsumoto T, Tamaki T. Roles of thromboxane A<sub>2</sub> and leukotriene B<sub>4</sub> in radicular pain induced by herniated nucleus pulposus. *J Orthop Res.* 2001;19(3):472-7.
112. McCall IW. Lumbar herniated disks. *Radiol Clin North Am.* 2000;38(6):1293-309.
113. Saifuddin A, Mitchell R, Taylor BA. Extradural inflammation associated with annular tears: demonstration with gadolinium-enhanced lumbar spine MRI. *Eur Spine J.* 1999;8(1):34-9.
114. Cuckler JM, Bernini PA, Wiesel SW, Booth RE Jr, Rothman RH, Pickens GT. The use of epidural steroids in the treatment of lumbar radicular pain. A prospective, randomized, double-blind study. *J Bone Joint Surg Am.* 1985;67(1):63-6.

115. Klenerman L, Greenwood R, Davenport HT, White DC, Peskett S. Lumbar epidural injections in the treatment of Sciatica. *Br J Rheumatol*. 1984;23(1):35-8.
116. Beliveau P. A comparison between epidural anaesthesia with and without corticosteroid in the treatment of sciatica. *Rheumatol Phys Med*. 1971;11(1):40-3.
117. Takahashi K, Shima I, Porter RW. Nerve root pressure in lumbar disc herniation. *Spine*. 1999;24(19):2003-6.
118. Valat J-P, Giraudeau B, Rozenberg S, Goupille P, Bourgeois P, Micheau-Beaugendre V, et al. Epidural corticosteroid injections for sciatica: a randomised, double blind, controlled clinical trial. *Ann Rheum Dis*. 2003;62(7):639-43.
119. Fanciullo GJ, Hanscom B, Seville J, Ball PA, Rose RJ. An observational study of the frequency and pattern of use of epidural steroid injection in 25,479 patients with spinal and radicular pain. *Reg Anesth Pain Med*. 2001;26(1):5-11.
120. Ringsdal VS, Nielsen NA, Slot O, Kryger P. Epidural glucocorticoid injection in lumbago sciatica. *Ugeskr Laeger*. 1997;159(38):5653-7.
121. Hauswirth R, Michot F. Sacral epidural anesthesia in the treatment of lumbosacral backache. *Schweiz Med Wochenschr*. 1982;112(7):222-5.
122. Mam MK. Results of epidural injection of local anaesthetic and corticosteroid in patients with lumbosciatic pain. *J Indian Med Assoc*. 1995;93(1):17-18,24.
123. Sharma PK. Indications, technique and results of caudal epidural injection for lumbar disc retropulsion. *Postgrad Med J*. 1977;53(615):1-6.
124. Papagelopoulos PJ, Petrou HG, Triantafyllidis PG, Vlamis JA, Psomas-Pasalis M, Korres DS, et al. Treatment of lumbosacral radicular pain with epidural steroid injections. *Orthopedics*. 2001;24(2):145-9.

125. Heyse-Moore GH. A rational approach to the use of epidural medication in the treatment of sciatic pain. *Acta Orthop Scan.* 1978;49(4):366-70.
126. Hickey RF. Outpatient epidural steroid injections for low back pain and lumbosacral radiculopathy. *N Z Med J.* 1987;100(832):594-6.
127. Wang JC, Lin E, Brodke DS, Youssef JA. Epidural injections for the treatment of symptomatic lumbar herniated discs. *J Spinal Disord Tech.* 2002;15(4):269-72.
128. Komori H, Okawa A, Haro H, Shinomiya K. Factors predicting the prognosis of lumbar radiculopathy due to disc herniation. *J Orthop Sci.* 2002;7(1):56-61.
129. Rosen CD, Kahanovitz N, Bernstein R, Viola K. A retrospective analysis of the efficacy of epidural steroid injections. *Clin Orthop.* 1988;228:270-2.
130. Lafuma A, Bouvenot G, Cohen C, Eschwege E, Fagnani F, Vignon E. A pragmatic cost-effectiveness study of routine epidural corticosteroid injections for lumbosacral syndrome requiring in-hospital management. *Rev Rhum (Engl Ed).* 1997;64(10):549-55.
131. Buchner M, Zeifang F, Brocai DR, Schiltenwolf M. Epidural corticosteroid injection in the conservative management of sciatica. *Clin Orthop.* 2000;375:149-56.
132. Apathy A, Penczner G, Licker E, Eiben A, Balint G, Genti G, et al. Caudal epidural injection in the management of lumbosacral nerve pain syndromes. *Orv Hetil.* 1999;140(19):1055-8.
133. Matyjek J, Lubinski I. Treatment of sciatica with injection of hydrocortisone into the sacral hiatus. *Neurol Neurochir Pol.* 1986;20(3):218-21.
134. Stanley D, Stockley I, Davies GK, Getty CJ. A prospective study of diagnostic epidural blockade in the assessment of chronic back and leg pain. *J Spinal Disord.* 1993;6(3):208-11.

135. Breivik H, Hesla PE, Molnar I, Lind B. Treatment of chronic low back pain and sciatica: comparison of caudal epidural injections of bupivacaine followed by saline. *Advances in Pain Research and Therapy*. 1976;1:927-32.
136. Mathews JA, Mills SB, Jenkins VM, Grimes SM, Morkel MJ, Mathews W, et al. Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections. *Br J Rheumatol*. 1987;26(6):416-23.
137. Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. *Spine*. 1991;16(5):572-5.
138. Ridley MG, Kingsley GH, Gibson T, Grahame R. Outpatient lumbar epidural corticosteroid injection in the management of sciatica. *Br J Rheumatol*. 1988;27(4):295-9.
139. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, et al. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med*. 1997;336(23):1634-40.
140. Koes BW, Scholten RJ, Mens JM, Bouter LM. Efficacy of epidural steroid injections for low-back pain and sciatica: a systematic review of randomized clinical trials. *Pain*. 1995;63(3):279-88.
141. Rozenberg S, Dubourg G, Khalifa P, Paolozzi L, Maheu E, Ravaud P. Efficacy of epidural steroids in low back pain and sciatica. A critical appraisal by a French Task Force of randomized trials. *Critical Analysis Group of the French Society for Rheumatology. Rev Rhum (Engl Ed)*. 1999;66(2):79-85.
142. Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesth Intensive Care*. 1995;23(5):564-9.
143. Spaccarelli KC. Lumbar and caudal epidural corticosteroid injections. *Mayo Clin Proc*. 1996;71(2):169-78.
144. Abram SE, O'Connor TC. Complications associated with epidural steroid injections. *Reg Anesth*. 1996;21(2):149-62.

145. Loy TT. Epidural steroid injection for sciatica: an analysis of 526 consecutive cases with measurements and the whistle test. *J Orthop Surg (Hong Kong)*. 2000;8(1):39-44.
146. Fredman B, Nun MB, Zohar E, Iraqi G, Shapiro M, Gepstein R, et al. Epidural steroids for treating 'failed back surgery syndrome': is fluoroscopy really necessary? *Anesth Analg*. 1999;88(2):367-72.
147. Price CM, Rogers PD, Prosser AS, Arden NK. Comparison of the caudal and lumbar approaches to the epidural space. *Ann Rheum Dis*. 2000;59(11):879-82.
148. Stitz MY, Sommer HM. Accuracy of blind versus fluoroscopically guided caudal epidural injection. *Spine*. 1999;24(13):1371-6.
149. Bogduk N. Epidural steroids. *Spine*. 1995;20(7):845-8.
150. Watanabe AT, Nishimura E, Garris J. Image-guided epidural steroid injections. *Tech Vasc Interv Radiol*. 2002;5(4):186-93.
151. Johnson BA, Schellhas KP, Pollei SR. Epidurography and therapeutic epidural injections: technical considerations and experience with 5334 cases. *AJNR Am J Neuroradiol*. 1999;20(4):697-705.
152. Eastwood D, Williams C, Buchan I. Caudal epidurals: the whoosh test. *Anaesthesia*. 1998;53(3):305-7.
153. White AH, Derby R, Wynne G. Epidural injections for the diagnosis and treatment of low-back pain. *Spine*. 1980;5(1):78-86.
154. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Hanna A, Rittenberg J, et al. Complications of fluoroscopically guided caudal epidural injections. *Am J Phys Med Rehabil*. 2001;80(6):416-24.
155. Rang HP, Dale MM, Ritter JM, Moore PK. *Pharmacology*. 5th ed. London: Churchill Livingstone; 2003.



156. Hollander JL, Brown EM, Jessar RA, Brown CY. Hydrocortisone and cortisone injected into arthritic joints; comparative effects of and use of hydrocortisone as a local antiarthritic agent. *Journal of the American Medical Association*. 1951;147(17):1629-35.
157. Lievre JA, Bloch-Michel H, Pean G, Uro J. L'hydrocortisone en injection locale. *Rev Rhum Mal Osteoartic*. 1953;20:310-11.
158. Kesson M, Atkins E, Davies I. *Musculoskeletal injection skills*. London: Butterworth-Heinemann; 2002.
159. Maillefert JF, Aho S, Huguenin MC, Chatard C, Peere T, Marquignon MF, et al. Systemic effects of epidural dexamethasone injections. *Rev Rhum (Engl Ed)*. 1995;62(6):429-32.
160. Karppinen J, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimäki T, Nieminen P, et al. Periradicular infiltration for sciatica: a randomized controlled trial. *Spine*. 2001;26(9):1059-67.
161. Karppinen J, Ohinmaa A, Malmivaara A, Kurunlahti M, Kyllönen E, Pienimäki T, et al. Cost effectiveness of periradicular infiltration for sciatica: subgroup analysis of a randomized controlled trial. *Spine*. 2001;26(23):2587-95.
162. Tonkovich-Quaranta LA, Winkler SR. Use of epidural corticosteroids in low back pain. *Ann Pharmacother*. 2000;34(10):1165-72.
163. Wong HK, Tan KJ. Effects of corticosteroids on nerve root recovery after spinal nerve root compression. *Clin Orthop*. 2002;403:248-52.
164. Nygaard ØP, Mellgren SI, Østerud B. The inflammatory properties of contained and noncontained lumbar disc herniation. *Spine*. 1997;22(21):2484-8.
165. Muramoto T, Atsuta Y, Iwahara T, Sato M, Takemitsu Y. The action of prostaglandin E2 and triamcinolone acetonide on the firing activity of lumbar nerve roots. *Int Orthop*. 1997;21(3):172-5.

166. Stanczak J, Blankenbaker DG, De Smet AA, Fine J. Efficacy of epidural injections of Kenalog and Celestone in the treatment of lower back pain. *AJR Am J Roentgenol*. 2003;181(5):1255-8.
167. Buttermann GR. Lumbar disc herniation regression after successful epidural steroid injection. *J Spinal Disord Tech*. 2002;15(6):469-76.
168. Slavin KV, Raja A, Thornton J, Wagner FC Jr. Spontaneous regression of a large lumbar disc herniation: report of an illustrative case. *Surg Neurol*. 2001;56(5):333-6; discussion 337.
169. Ito T, Takano Y, Yuasa N. Types of lumbar herniated disc and clinical course. *Spine*. 2001;26(6):648-51.
170. Lebkowski WJ, Dzieciol, J. Degenerated lumbar intervertebral disc. A morphological study. *Pol J Pathol*. 2002;53(2):83-6.

Figure 1 Flow diagram of the study (p. 46 in Epidural Skjemabok v3)

Figure 2 Information letter to patients concerning the study (p. 3-4 in Epidural Skjemabok v3)

Figure 3 Template for clinical examination (p. 11-47 in Prosedyrebok)

Figure 4 Written informed consent (p. 5 in Epidural Skjemabok v3)

Figure 5 Referral for injection (p. 17 in Epidural Skjemabok v3)

Figure 6 Template for ESI (p. 18-19 in Epidural Skjemabok v3)

Figure 7 Patient information after sacral epidural injection (p. 20 in Epidural Skjemabok v3)

Figure 8 Information for doctors concerning the study

Figure 9 Form book

