There are 2 principle ways in which the scar tissue of arachnoiditis causes pain at a local level. (Noting of course that there may well also be pre-existing or persisting underlying spinal pathology that contributes to the picture).

The first is mechanical: the physical effect of the scar on the tissue on which it impinges.

This is broadly similar to the effect of a prolapsed disc.

Nerve roots or dorsal root ganglia may be compressed. Nerve roots are commonly affected and the result will be sensory, causing pain and sensory disturbance, and motor, causing weakness and muscle spasms.

In rats, experimental compression of nerve roots by loose chromic gut ligatures induced prolonged thermal hyperalgesia (related to neuropathic pain), and initial transient motor dysfunction and mechanical hypoalgesia ([i]).

Compression causes different effects depending upon the level of pressure exerted upon the affected nerve root.

High pressure can directly deform nerve fibres and derange the integrity of the nerve structure, whereas low pressure causes impaired blood supply, reduced nutritional transport and intraneural (inside the nerve) oedema, which is associated with intraneural fibrosis([ii]).

Olmarker and Rydevik ([iii]) demonstrated that cauda equina blood supply is interrupted by

pressure equaling arterial blood pressure. 10mmHg applied pressure caused 20-30% reduction in nutrient transport to nerve roots.

Additionally, pressure can change the permeability of endoneural capillaries giving rise to oedema.

Dorsal root ganglia are highly sensitive to compression; normal, non-injured DRG respond to gentle pressure by producing prolonged repetitive firing. (Howe et al. 1977 [iv]).

Hanai et al. ([v]) more recently demonstrated that the DRG not the dorsal root, produced this response when either the root or the DRG were compressed.

Chatani et al. ([vi]) studying rats, found that DRG irritation generated thermal hyperalgesia. Sugawara et al. ([vii]) found that hypoxia (lack of oxygen) further increased sensitivity to mechanical stimuli and even provoked spontaneous firing.

As we have seen, adhesive arachnoiditis affects the flow of CSF and thus the provision of oxygen to nervous tissue within the affected area.

Thus a lack of oxygen may compound the physical compressive effects of the scar tissue.

Some authors (Lindblom & Rexed 1948 [viii] , Rydevik *et al*.1984 [ix]) have suggested that the DRG is the most likely site of compression by prolapsed disc material.

Kuslich et al. ([x]) demonstrated that sciatica is produced by stimulation of a swollen, stretched, restricted (by scar tissue) or compressed nerve root.

They concluded that the presence of scar tissue compounded pain associated with the nerve

root by fixing it in one position thereby increasing its susceptibility to tension or compression.

Secondly, arachnoiditis may involve inflammation and it may be that the inflammatory mediators involved exert a chemical effect upon the nervous tissue.

For instance, the inflammatory mediatorIL-1 plays an important role in experimental allergic radiculitis induced in rats, since IL-1 receptor antagonist ameliorated the symptoms (Wehling *et al* .
1996
[xi]
).

In fact, IL-1 and IFN act synergistically with TNF-alpha and are more or less neurotoxic (Chao *et al*
. 1995
[xii]
).

Peripheral nerve endings become sensitised by chemical mediators released during tissue damage and inflammation.

These include neurogenic mediators, such as substance P, and non-neurogenic mediators, such as bradykinin, histamine and prostaglandins ([xiii]).

Histological damage may occur without compression (Anderson [xiv]), largely as a result of exposure to chemical irritants from sources such as the nucleus pulposus of herniated disc material. (See above).

Inflammation renders the affected nociceptors more sensitive to mechanical stimulus such as that due to compression by scar tissue.

There may also be a third aspect of the effects arachnoiditis exerts both locally and more distantly.

This relates to the impact on CSF flow. Various authors have postulated impaired CSF flow in the development of syrinx secondary to arachnoiditis, and Jenik et al. described arachnoiditis symptoms as predominantly "syringomyelic" in nature ([xv]).

Warnke et al. ([xvi]) recently published a paper in which they reported on findings at thecaloscopy.

They noted that patients with a large thecal sac on MR and confirmed arachnoiditis at thecaloscopy had CSF under pressure.

They also commented on patients who experienced some relief of symptoms after lumbar puncture, conjecturing that this was due to temporary reduction in CSF pressure and "alteration of venous filling".

The authors noted that the subarachnoid space is not a single space but is divided by various arachnoid membranes, so that pressure levels may vary in different locations, and suggested:

"We assume that long term disturbances of CSF circulation with raised local CSF pressure may dilate the thecal sac...it is our opinion that further investigation should be concentrated on the solution of the problem of lumbar intrathecal CSF flow disturbances."

The disturbed CSF flow may cause local effects, but also potentially more distant effects and could account for unexplained upper body symptoms in patients who have lumbosacral arachnoiditis but no evidence of pathology in thoracic or cervical regions.
Aside from nervous tissue being affected, other anatomical structures in the vicinity may also be sources of pain.

These include prevertebral (intrinsic) muscles, ligaments (longitudinal, intertransverse etc.), joints (facet and zygopophyseal), dura, dural attachments, vertebral periosteum and epiradicular components.

Innervation of these structures (ventral and dorsal rami, sinuvertebral nerve) may be affected if the epidural space is compromised. Arachnoiditis is often accompanied by epidural fibrosis, so this may be a significant factor in generating pain.

In addition, sympathetic innervation may be affected (see below.)

Sensitisation of nociceptors in these tissues can, as we have seen, trigger a centralisation of the pain via the ?wind-up' process. This leads to a more widespread pain, which is commonly seen in arachnoiditis: central pain. (See below).

In addition, loss of input from impaired nerves may trigger a compensatory upregulation of central receptors. Again, this effects a central sensitisation.

SUMMARY: clearly the picture in adhesive arachnoiditis is somewhat complex, broadly comprising the effect of a combination of mechanical and chemical factors on various structures in and around the thecal sac.

These factors act somewhat synergistically to produce a sequence of events that are progressive and may lead on to centralisation of pain.

---

[i] Kawakami M, Weinstein JN, Chatani K, Spratt KF, Meller ST & Gebhart GF *Spine* 1994; 19: 1795-1802. Experimental lumbar radiculopathy. Behavioral and histologic changes in a model of radicular pain after spinal nerve root irritation with chromic gut ligatures in the rat.
[ii] Racz GB, Noe C, Heavner JE *Curr Rev Pain* 1999; 3: 333-341 Selective spinal injections for lower back pain.

[iii] Olmarker K, Rydevik B *Orthop Clin North Am* 1991; 22: 223-233 Pathophysiology of sciatica

[iv] Howe JF, Loeser JD & Calvin WH Pain 1977; 3: 25- 41.Mechanosensitivity of dorsal root ganglia and chronically injured axons: a physiological basis for the radicular pain of nerve root compression.   [v] Hanai F, Matsui N & Hongo N *Spine* 1996; 21: 1408-14.Changes in responses of wide dynamic range neurons in the
spinal dorsal horn after dorsal root or dorsal root ganglion compression.

[vi] Chatani K, Kawakami M, Weinstein JN, Meller ST & Gebhart GF *Spine* 1995; 20: 277-89. Characterization of thermal
hyperalgesia, c-fos expression, and alterations in neuropeptides after mechanical irritation of the dorsal root ganglion.

[vii] Sugawara O, Atsuta Y, Iwahara T, Muramoto T, Watakabe M & Takemitsu Y *Spine* 1996; 21: 2089-2094. The effects of
mechanical compression and hypoxia on nerve root and dorsal root ganglia. An analysis of ectopic
firing using an in vitro model.

[viii] Lindblom K & Rexed B *J Neurosurg* 1948; 5: 413-432. Spinal nerve injury in dorsolateral protrusions of lumbar disks.

[ix] Rydevik B, Brown MD & Lundborg G Spine 1984; 9: 7-15 Pathoanatomy and pathophysiology of nerve root compression.   [x] Kuslich SD, Ulstrom CL, Michael CJ *Orthop Clin North Am*
1991; 22: 181-187 The tissue origin of low back pain and sciatica: a report of pain response to tissue stimulation during operations on the lumbar spine using local anaesthesia.

[xi]
Wehling P, Cleveland SJ, Heininger K, Schulitz KP, Reinecke J & Evans CH
Spine
1996; 21: 931-935. Neurophysiologic changes in lumbar nerve root inflammation in the rat after treatment with cytokine inhibitors. Evidence for a role of interleukin-1.

[xii] Chao CC, Hu S, Ehrlich L & Peterson PK *Brain Behav Immun* 1995; 9: 355-365
Interleukin-1 and tumor necrosis factor-alpha synergistically mediate neurotoxicity: involvement of nitric oxide and of N-methyl-D-aspartate
receptors. [xiii] Cavanaugh JM Spine 1995; 20: 1804-1809 Neural mechanisms of lumbar pain.

[xiv]
Anderson SR
Current Review of Pain
2000; 4: 395-406 A Rationale for the Treatment Algorithm of Failed Back Surgery Syndrome

[xv]
Jenik F, Tekle-Haimanot R, Hamory BH
Paraplegia
1981; 19 (3): 14-54 Non-traumatic adhesive arachnoiditis as a cause for spinal cord syndromes.

[xvi] Warnke JP, Koppert H, Bensch-Schreiter B, Dzelzitis J, Tschabitscher M. *Minim Invasive Neurosurg*   .
2003 Apr; 46(2):94-9. Thecaloscopy part III: first clinical application.