There are a number of different research facilities investigating various aspects of scarring, and therapeutic agents to prevent or reduce scar tissue.

For instance, rat studies have looked at axon regeneration in CNS damage, which can be prevented by scar formation.

A resorbable polymer, Seprafilm has been piloted as a barrier to extrinsic scar formation and axon regeneration was improved.

Reports on CNS regeneration suggest that chondroitinase may play a role in reducing scar formation in the CNS and the PNS (peripheral nervous system). ([1])

FibroGen is an American company that developed a product based on prolyl hydroxylase inhibitors.

In 1998, the company reported on studies in which they "demonstrated a reduction in scar deposition with treatment and little or no recurrence of scarring after treatment was stopped.

In addition, increased apoptosis of the collagen-producing fibroblasts was observed in treated animals, which may explain why scarring did not recur after treatment ended."

They claimed that their product would be useful in all types of abnormal scarring, including,

"scarring after major surgeries such as laminectomies and discectomies."

In 1999, Llado et al. performed a dog study ([2]) to assess the use of expanded polytetrafluoroethylene (ePTFE) as a barrier to postoperative invasion of fibrous tissue into the laminectomy defect.

They looked at laminectomised dogs 12 weeks postoperatively.

They reported:

"We conclude that the ePTFE spinal membrane, when properly implanted, is an effective barrier to postsurgical fibrous invasion of the vertebral canal. Clinical studies of use of this material in spinal surgery are warranted."

In Israel in October 2002 ([3]), there was a report on Tempostatin™, which has been found to delay scar tissue formation by its effects on stroma cells which produce collagen.

"Tempostatin™ is actually the `circuit breaker' of the scar formation process," according to Dr. Bruce Bach, CEO of the U.S.-Israeli biotechnology company Collgard, which is currently developing the substance. Its method of activity is somewhat paradoxical, because it actually slows down the healing process.

The agent has already been tested for safety in patient populations and deemed acceptable for use in controlled clinical trials (currently underway in Europe), although its effectiveness has so far been proved only in animals.

Italian authors Bocchi et al. looked in 1995 ([4]) at the various factors in pathological scar

formation in burns. They outlined the treatment options available at that time, and suggested that

"Corticosteroids are the most successful agents in the non-surgical therapy of burn scars. A few mechanisms of their action are known: they decrease collagen synthesis, inhibit fibroblast migration into the wound, and affect the inflammatory and local immune response."

They included zinc oxide, hyaluronidase, retinoic acid and colchicines in their list of agents used to treat this type of problem. Hyaluronidase and colchicine have both been attempted in arachnoiditis, but there is no available data on the longer-term outcome.

Interestingly, the authors noted that vitamin E and zinc may be important factors:

"Vitamin E is a membrane stabilizer which inhibits the liberation of lysosomal contents, having an anti-inflammatory effect which decreases tissue repair. Zinc seems to inhibit fibroblast action, although there are reports of a stimulation of collagen synthesis."

Also in 1995, Hinton et al. ([5]) looked at the use of intraoperative steroid, (slow release) in animals and found that

"Dexamethasone acetate (Decadron...) significantly reduced the density of the scar tissue undermining the laminas. Steroids embedded in polymer did not change the scar formation in the back, but did decrease protein and DNA values in wound chamber tissues.

CONCLUSIONS. Long-term release of small amounts of steroid from the polymer poly-carboxy-phenoxypropane does not appear to reduce scar at laminectomy sites but does decrease the protein: DNA ratio in wound chambers. In contrast, Decadron does not significantly alter the biochemistry of wound chamber tissue but does reduce scar in the back."

However, the study only looked at the results 4 weeks after the laminectomy, so longer-term effects have yet to be evaluated.

A further study in 1995, by He et al. ([6]) used a rat model, and found that non-steroidal anti-inflammatory agents might offer a way of reducing post-operative scarring.

In 1999, Gerszten et al. ([7]) looked at rats 30 days after laminectomy to assess extent, density, and arachnoidal involvement by fibrosis.

They reported:

"Low-dose external beam radiation therapy administered before or after laminectomy in a rat model significantly decreases the extent, density, and arachnoidal involvement of peridural fibrosis. This technique may improve the outcome of patients who undergo reoperations for recurrent radicular and/or low back pain after successful lumbar discectomy in whom there is a significant amount of peridural fibrosis."

More recently a Turkish team ([8]) looked at an animal model for the use of external radiation in comparison with the use of a spinal membrane (as described above under treatment).

They found:

"This preliminary study showed that high-single-fraction/low-total-dose administered postoperatively can successfully inhibit postsurgical epidural fibrosis as effectively as applied spinal membrane."

In 2002, French authors Lui et al. ([9]) published the results of a rat study looking at the use of a collagen-based sealant, Gel Amidon Oxyde (GAO), in preventing the reformation of epidural scar adhesions in an adult rat model of laminectomy.

They stated:

"The authors found that GAO may be a safe and effective antiscarring adhesion biomaterial in vivo. When placed into the laminectomy site, GAO may prove beneficial in preventing the formation and reformation of epidural scar adhesions in humans."

This year, Lee et al. ([10]), in Germany, reported on the use of TachoComb?, an agent they compared with Spongostan?, and Tabotamp?. They found that in rats undergoing laminectomy, TachoComb reduced the amount of epidural fibrosis considerably, although the authors noted:

"However, complete prevention of scar tissue formation was not achieved."

In Manchester, Professor MWJ Ferguson (at the School of Biological Sciences) has been studying adult wound healing in relation to that in the embryo. There is known to be a substantial difference between them, mostly by virtue of the fact that the immune system in the embryo is still developing.

His team reduced the levels of growth factors present at high levels in the adult, but low levels in the embryo, e.g. Transforming Growth Factor Beta 1 and Beta 2 (TGFb1 and TGFb2) or elevated levels of growth factors present at high levels in an embryonic wound, but low levels in the adult wound (TGFb3). They reported in the prestigious journal *Nature* in 2002 ([11]):

"These experimental manipulations resulted in adult wounds that healed perfectly with no signs of scar formation."

It has been known for some time that transforming growth factors may have potential in minimising scar tissue formation. Choi et al. ([12]), in 1996, found that in animals,

"antisense TGF-beta 1 ODN could be used for ameliorating scar formation during wound healing."

The Children's Hospital in Boston, Massachusetts, has been investigating the use of topical mitomycin C, an antibiotic currently in use in chemotherapy ([13]). It is known to reduce collagen formation in vitro and has been used for some time in eye surgery ([14] , [15]), as well as otorhinolaryngology (ear, nose and throat) ([16]) and Chung et al. ([17]) found that it

"may reduce the incidence of postoperative adhesions"

after sinus surgery. The agent is applied to tissue prone to scarring, for 2-4 minutes at the end of an operation.

There are no published results from this study as yet, although a study has just been reported on the use of topical mitomycin in the prevention of scar tissue formation in the postsurgical external auditory canal, which failed to demonstrate any efficacy ([18]).

Mitomycin is an antimetabolite chemotherapy agent and as such carries a risk of severe adverse effects and is likely therefore be unsuitable for use in the subarachnoid space.

However, there is another potential treatment for use in eye surgery to reduce the incidence of scarring, amniotic membrane transplantation, which seems to perhaps be a little less effective than mitomycin C, but carries much less risk of the adverse effects.

This treatment is still at clinical trials stage. ([19])

We can see that over the past 15 years or so, a number of studies have been performed in an attempt to prevent scar formation. No doubt there are other initiatives underway to find

treatment options for scars in all parts of the body. I shall be attempting to keep abreast of any important developments.

As regards removal of established scar tissue, as we have seen (See Treatment), the problem of recurrence is the main stumbling block; therefore this is a vital area for research.

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[3] http://www.collgard.com/news/news5.html

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[13] http://www.tracheostomy.com/surgery/mitomycin.htm

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