Over a century ago, Koller first used cocaine to anaesthetise his eyes.

In 1865, Halsted used cocaine anaesthesia. Corning pioneered the epidural local anaesthetic block, whilst Bier reported on subarachnoid local anaesthetic in 1899. (Bier also reported the first spinal headache).

Lemmon in 1940, started using a continuous spinal technique; later intraoperative spinal anesthesia came into use; however, it wasn't until the 1990s that infusions of post-operative analgesia became widespread.([1])

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In recent correspondence with a Professor of Anaesthetics, I have established that the dangers of neurotoxic preservatives in anaesthetic agent preparations have been recognised for 50 years.

Indeed, it is common practice in the UK to use preservative-free preparations of agents such as bupivicaine.

Elsewhere, however, continued use of lidocaine occurs to this day. As I have mentioned in previous articles, the practice of combining steroid and local anaesthetic in ESIs remains a common one, and thus confers ?double jeopardy' on the unwitting patient.

CIRS, a Swiss-based website([2]) concerned with adverse incidents in anaesthesia, gives us a clear and sometimes uncomfortable insight into a specialty which is renowned for being 90% boredom, 10% panic.

On the CIRS site, there is the case of a 36 year old woman, for elective knee arthroscopy, a straightforward investigational procedure. She was given 4cc. of 2% lidocaine and immediately experienced problems, which later led to the necessity of an epidural blood patch to treat PDPH (post dural puncture headache).

This unfortunate lady went on to sustain cauda equina/conus medullaris damage and was subsequently diagnosed with arachnoiditis.

This is a clear-cut case of chemically-induced adhesive arachnoiditis (CIAA) without the typical cloudy picture seen in patients who have ongoing spinal pathology which complicates matters and obscures a single causative factor such as spinal anaesthesia.

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Quite large volumes of injectate appear to be used commonly by the anaesthetists who post to the site. Sometimes this entails isobaric preparations, at others, there may be a combination of isobaric and hyperbaric solutions.Hyperbaric solutions are those which contain glucose which tends to make the injected solution gravitate towards the lower end of the spinal canal. Hence there is a higher risk of cauda and conus damage.

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One case of a 65 year old woman for minor orthopaedic operation was commented on by an unknown contributor to the site:

"Spinal anaesthesia **IS NOT** harmless, and ist (sic) not the choice for peripheral procedures such as Hallux valgus.."

A further case in which 1.5cc of hyperbaric bupivicaine caused bradycardia and then asystole (which happily responded to treatment) prompted a remark on the ASA Closed Claims Study (undertaken more than 10 years ago) which reported several incidents of this type of problem associated with spinal anaesthesia: recommendation was made for the use of epinephrine.

An unknown contributor wrote:

"Practitioners still fail to recognise the physiological dangers associated with neuraxial blockade."

"Practitioners still fail to recognise the physiological dangers associated with neuraxial blockade."

(he/she went on to recommend the use of ephedrine).

Practitioners may also use epinephrine, a vasoconstrictor, which requires preservatives.

However, an anaesthetic contact in the UK has stated in private correspondence that the use of ephedrine or epinephrine seems unwise to say the least.

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As regards the safety of using hyperbaric solutions:

Verenko and Soosko (Ukraine) in 1993([3]), suggested that hyperbaric solutions permit a 2 to 3 fold decrease in the initial and total doses of anaesthetic required.

In 1996, Gallo et al ([4])compared the use of 1% and 0.5% hyperbaric bupivicaine adminstered intrathecally for Caesarean section. Patients were prehydrated as normal and the needle introduced at L2/3 or L3/4 (A 24G Sprotte's needle).

The authors reported little difference in the efficacy of the two concentrations and they remarked:

"In view of the possible relationship between the neurotoxicity of local anaesthetics and the concentration of the solution used for spinal anaesthesia, it is to be hoped that less concentrated solutions of hyperbaric bupivicaine will be introduced" (in Italy).

"In view of the possible relationship between the neurotoxicity of local anaesthetics and the concentration of the solution used for spinal anaesthesia, it is to be hoped that less concentrated solutions of hyperbaric bupivicaine will be introduced" (in Italy).As Malinovsky and Pinaud noted (also in 1996 [5]), neurotoxicity of anaesthetic agents can be due to:

- Reduced neuronal blood supply (note: will that be further worsened by ephedrine/epinephrine?)
- High concentrations
- Long duration of exposure
- The use of adjuvants.

They reported Cauda Equina Syndrome following continuous spinal anaesthesia using

hyperbaric lidocaine and tetracaine. The authors clearly recommended the use of preservative-free solutions.

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Meanwhile, Ganem et al ([6]) had studied the neurotoxicity of subarachnoid hyperbaric bupivicaine in dogs.

They found that

"Increasing doses of hyperbaric bupivicaine solutions increased the incidence of nerve tissue damage, which did not occur using hypobaric solutions."

Richardson et al, in 1998([7]), reported that

Richardson et al, in 1998([7]), reported that

"dextrose alters density of intrathecal bupivicaine solutions and is thought to influence sub-arachnoid distribution of the drug."

(whilst making no clinical difference to the quality of the anaesthesia).

Pollock et al in 1999 ([8]), looked at the dilution of spinal lidocaine, and the incidences of transient neurological symptoms following its use.

The incidences with 0.5%, 1.0% and 2.0% were all similar to the previously reported incidence for 5% lidocaine.

This concurred with Hampl et al who found a similar incidence of transient neurological symptoms with 2% and 5% lidocaine.

King et al, also in 1999([9]), compared isobaric and hyperbaric solutions for Caesarean section.

With hyperbaric tetracaine (2.0ml 0.5% tetracaine in 5% dextrose) the duration of anaesthesia and the sacral block longer than with the isobaric preparation (2.0ml 0.5% in CSF).

Ginther and Zamanian, in an Internet publication, "Toxicity, Local Anaesthetics from Emergency Medicine/toxicology" ([10])note:

Ginther and Zamanian, in an Internet publication, "Toxicity, Local Anaesthetics from Emergency Medicine/toxicology" ([10])note:"Very high doses of anesthetics can produce irreversible conduction block in less than 5 minutes. Peripheral neurotoxicity, such as prolonged sensory and motor deficits, has been documented. It is hypothesized that a combination of low pH and sodium bisulphite in the mixture can be partially responsible for these changes."

Reviewing various papers in the Canadian Journal of Anaesthesia (CJA), the Editor of the online Journal Club ([11]) raised the following important questions:

Reviewing various papers in the Canadian Journal of Anaesthesia (CJA), the Editor of the online Journal Club ([11]) raised the following important questions:

1. "Are we over-doing the dose of spinal bupivicaine?"
2. "Is spinal anaesthesia really safer than general anaesthesia?"

These comments were made in the February 2000 edition.

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He was prompted to these remarks by the paper of Bandi et al, published in CJA 1999([12]), in which the authors describe a worrying problem:

"in nearly a fifth of patients, the spinal block ascended 2 to 7 dermatomes from the level recorded at the start of surgery; there was a concomitant substantial hypotension in 10% of these patients."

The Editor also cited what he considered to be a ?landmark' study, published in the British Journal of Anaesthesia in 1995([13]).

The Editor also cited what he considered to be a ?landmark' study, published in the British Journal of Anaesthesia in 1995([13]).Tarkkila et al found that with 5% lidocaine, there was a 10% incidence of transient radicular irritation (not seen with bupivicaine).

He further cited Bernards([14]) who reported a lack of clinical superiority of epidural administration of fentanyl, over intravenous administration.

He further cited Bernards([14]) who reported a lack of clinical superiority of epidural administration of fentanyl, over intravenous administration.So whilst a British paper published in February 2001 ([15]) refutes the impact of epidural anaesthesia on long-term backache for up to a year post-procedure, there are questions that remain to be answered as to the risk of long-term neurological sequelae, which seem not to have been addressed as yet (studies to date concentrating on back pain but not necessarily on neurological problems).

More recently, Owen et al ([16]) described the use of low dose clonidine and neostigmine to prolong the duration of intrathecal bupivicaine and fentanyl for labour analgesia.

More recently, Owen et al ([16]) described the use of low dose clonidine and neostigmine to prolong the duration of intrathecal bupivicaine and fentanyl for labour analgesia.Their study involved comparing bupivicaine alone (B 2.5mg) B plus fentanyl 25microg (BF) BF plus clonidine 30microg (BFC) and BFC plus neostigmine 10 microg. (BNFC).

The authors conclude:

The authors conclude:"Although serious side effects were not observed in this study, safety must be further addressed before the routine use of multiple IT* drugs is advocated."
*IT= intrathecal.

Neostigmine has been found to cause profound nausea and vomiting, as well as sweating and distress, which may limit its use for post-operative analgesia([17]).

Neostigmine has been found to cause profound nausea and vomiting, as well as sweating and distress, which may limit its use for post-operative analgesia([17]).

Krukowski et al ([18]) looked at the use of intrathecally-administered 10-100 microg of neostigmine in a 1-mL solution of 5% glucose in normal saline followed by 2% epidural lidocaine, for post-caesarean section analgesia.

This demonstrates the accepted practice of trialling this technique in healthy young subjects. A recent study ([19]) looked at its use as a pre-emptive measure to improve post-operative analgesia.

Safety studies in animals have looked at the issue of the toxicity of both glucose (used to yield a hyperbaric solution) and the preservatives methyl- and propylparaben which are in the available neostigmine formulations.

However, the animals were only studied in the short term (14 days).

In Phase I clinical trials in 1997 (human volunteers) "no evidence of toxicity" was reported. The possibility of longer-term adverse effects has not been adequately addressed by these studies.

There are a number of other agents which are being studied. Ketamine, for example, a dissociative anaesthetic which has analgesic properties, has been used for about 4 years for post-herpetic neuralgia (PHN).

There are a number of other agents which are being studied. Ketamine, for example, a dissociative anaesthetic which has analgesic properties, has been used for about 4 years for post-herpetic neuralgia (PHN).

It has also gained a place in the repertoire of post-operative analgesia.

In the late 90s, it was used epidurally as a pre-emptive analgesic strategy for knee replacement surgery(Wong et al, 1997) and abdominal surgery, when it was administered pre-operatively, in conjunction with morphine.

Ketamine solutions commonly contain preservatives such as chlorobutanol, a derivative of chloroform, which has been implicated as causing neurotoxicity in animal studies when injected intrathecally.

Indeed Malinovskyt et al([20]) describe: "chlorobutanol (the preservative used in the ketamine solution) induced significant severe spinal cord lesions in both studies". (this was at concentrations of 0.05% chlorobutanol).

More recently, ketamine has also been combined with bupivicaine(). However, in a study in which transdermal ketamine was used after lidocaine epidural for minor abdominal surgery([21]);
it was found to be effective.

This is an important finding because it suggests that the non-invasive transdermal route is a viable and much safer alternative to spinally administered drugs.

This would have some bearing clinically-speaking on the use of ketamine in children.

A 1999 Scottish study ([22]) looked at 40 boys aged 1-5 years, undergoing orchidopexy, a relatively minor procedure, who underwent caudal epidural injection of bupivicaine + ketamine at 1ml.kg-1 of either 0.125% or 0.25% bupivicaine and 0.5 mg.kg-1 ketamine. Should we be trialling this drug in children?

Last year, Penn and Paice ([23]) reported on adverse effects associated with the intrathecal administration of ziconotide, made from sea-snail venom and aimed at reducing neuropathic pain.

They found cerebellar and other brain effects; whilst the drug solution disappeared quickly from the CSF, it remained bound to tissue and active for extended periods of time.

The authors concluded:

"Widespread use in general clinical conditions are likely to lead to an even greater prevalence of adverse side effects, with potentially more serious outcomes."

Other agents are also being studied: e.g. adenosine.

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[1] Source:Staats PS and Mitchell VD Future Directions in Intrathecal Therapies October 1997 Online Pain Journal http://www.pain.com/interventional/free_cme/in_art_pa_fdfit.cfm

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[11] Editor of The Worldwide Anaesthetist Journal Club 16 February 2000 Internet publication: http://www.anaesthetist.com/anaes/jnl/2000/2000fe16.htm

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