In 1955, Hurst conducted studies on monkeys ([i]), which demonstrated that a wide range of chemicals, when introduced into the CSF, produced an immediate pathological response, which "proceeds steadily to its termination".

The early stages are asymptomatic, but after a latent period, the clinical picture is then one of "severe and progressive signs and symptoms".

This is similar to the picture in arachnoiditis, and therefore all short-term studies (which make up the majority of the evidence concerning safety of ESI) will fail to address the issue of arachnoiditis, which tends to occur after an indeterminate interval following exposure.

In 1975, Kelly et al ([ii]) wrote a paper describing the neuropathological effects of intrathecal water.

They concluded that infusion of distilled water intrathecally could cause distinctive lesions of spinal roots and cord.

It follows therefore, that if a substance as inert as water can cause damage, that more complex preparations are likely to carry some risk also.

As early as 1954, Moore ([iii]) advised that local anaesthetic administered epidurally should be free of preservatives. Malinovsky ([iv]) suggests that "neurotoxicity can result from ...the use of adjuvants."

Some authors suggest that arachnoiditis occurs as a result of the vasoconstrictive component of the anaesthetic, whilst others say that contaminants ([v]) or preservative agents are

responsible.

It must be stressed that ANY drug preparation injected in to the spine, may contain preservatives such as benzyl alcohol, polyethylene glycol, and chlorobutanol (a derivative of chloroform) and that these carry a risk of neurotoxic effects.

Another preservative that can cause reaction is sodium bisulfate, which may trigger a severe allergic reaction if the patient is susceptible (and it is unclear how many of the general population may be susceptible).

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

Indeed Malinovsky et al ([vi]) describe "significant severe spinal cord lesions" at concentrations of 0.05% chlorobutanol.

Usually the injectable form of morphine sulfate contains 0.5% chlorobutanol and not more than 1% sodium bisulfate in every ml of morphine sulfate injection USP.

An animal study in 1993 showed that 0.05% chlorobutanol injected intrathecally

"induced significant severe spinal cord lesions" ([vii])

It is therefore vital to ensure that preservative-free solution is used. Chlorobutanol toxicity may cause increased somnolence, alterations in speech patterns, dysarthria and haemodynamic changes. ([viii])

Hetherington and Dooley ([ix]) noted in 2000 that the intrathecal route of administration "reduces systemic adverse effects, but can increase the risk of local adverse effects such as arachnoiditis."

They also remarked

"It is accepted practice that any spinal injection should not contain any preservatives (such as benzyl alcohol and parabens-containing compounds). The intrathecal administration of solutions preserved with benzyl alcohol has been shown in case studies to increase the risk of adverse neurological events... Steps should be taken to ensure that preservative-free products are used."

Recently in America, a journalist reported ([x]) on adverse events due to implanted morphine pumps: 8 of 13 patients at a Memphis, Tennessee pain clinic suffered severe neurological problems after a pharmacist apparently made faulty batches of morphine from bulk ingredients to refill their pumps.

Three of the eight required surgery and are now partially paralysed. An investigation by the Tennessee Board of Pharmacy found two jars of compounded solution containing a mixture of morphine and methadone but labelled as morphine.

Contaminants ethanol and methanol were also found in poor quality morphine powder. Compounded preparations used for refills from bulk, unsterile powders may carry a risk of contamination not only from processing chemicals, but also from organic debris that can slip through filters designed to strain out bacteria.

Pharmacist Sarah Sellers, who is a consultant to an FDA advisory committee on pharmacy compounding, is highly critical of using compounded drugs to fill implantable pumps.

This again demonstrates the dangers of impure preparations when placed into the spinal fluid.

Radiologists in Minneapolis, when faced in 2001 with a shortage of Celestone Soluspan, a preservative-free steroid preparation, which they used for epidural injections, issued a statement to all referring physicians:

"As you may know, the inadvertent injection of Depo-Medrol and other members of the steroid family into the thecal sac can cause arachnoiditis. This is a risk and complication which we feel is unacceptable and will therefore not use Depo-Medrol as a substitute."

By doing so, this group (Consulting Radiologists Ltd.) demonstrated their commitment to avoiding the use of preservatives.

This example should be followed by physicians throughout the world.

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