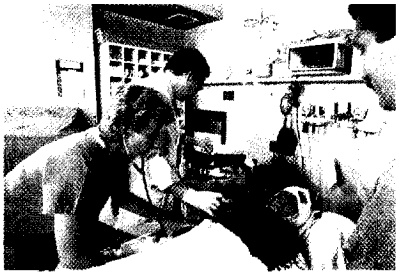
Cannabinoid is neuroprotective in head trauma

The leading cause of death among young men in the western world—sequelae of severe head trauma—has no approved treatment. But clinical results from Israel indicate that dexanabinol (HU-211), a non-psychotropic cannabinoid analogue, may be "the most promising neuroprotective agent seen to date", says Lawrence Marshall (University of California, San Diego, CA, USA), an authority on head trauma. Phase II clinical trials provide strong evidence that the analogue can reduce intracranial pressure and significantly improve outcome in severe head injury, he adds. Other treatments, in phase III clinical trials, are yet to show definitive human benefit.

Dexanabinol is "distinguished from earlier failed drugs by its triple mechanism of action", explains neuropharmcologist Anat Biegon (Pharmos, Rehovot, Israel). Dexanabinol's neuroinhibitory effect on NMDA receptors was discovered 10 years ago by Tel Aviv University biochemists Mordechai Sokolovsky and Yoel Kloog. Pharmos licensed dexanabinol in 1991 for development as a drug. Biegon then directed work in Israel and the USA that revealed dexanabinol's potent anti-inflammatory and antioxidant activities.

2 years ago, Pharmos began phase II double-blind, randomised, placebo-controlled clinical trials in six Israeli trauma centres (*Lancet* 1996, **348:** 1436). Of 67 unconscious patients, mostly young men injured in road accidents, 30 were given dexanabinol and 37 received placebo intravenously within 6 hours of injury (mean time 5 hours).



Science Photo Library

Improving the chance of a good outcome

"The significant reduction in intracranial pressure below the 'damage threshold' of 25 mm Hg—a key predictor of neurological outcome—without jeopardising blood pressure was quite impressive", says Marshall. Mortality was reduced by 26% and neurological outcome was improved. "Recovery was accelerated in the treated group" and "return to normal life among most severely injured patients was outstanding", says lead investigator Nachshon Knoller (Sheba Medical Center, Tel Hashomer, Israel), who reported the results at the National Neurotrauma Society in Los Angeles, CA, USA on Nov 5. Phase III trials on dexanabinol are due to start in 1999.

Rachelle H B Fishman

News in brief

Flying with sildenafil An article in the autumn issue of *The Federal Air Surgeon's Medical Bulletin* warns pilots not to take sildenafil less than 6 hours before a flight. The pilot's attention could be distracted by the effects of the drug, and the blue-green colour disturbance reported by some men after taking the drug could be dangerous during night flights (http://www.cami.jccbi.gov/AAM400A/fasmb.html).

Hyperplastic polyps and *H pylori* In a trial, 35 patients with hyperplastic gastric polyps and *Helicobacter pylori* infection received either a drug to eradicate *H pylori* (n=17) or no treatment. Polyps disappeared in 12 of the 15 treated patients in whom *H pylori* was eradicated, but in controls there were no changes in infection or polyps. The authors say that for patients similar to those they studied, *H pylori* eradication should be tried before endoscopic polyp removal (*Ann Intern Med* 1998; **129:** 712–15).

Ovarian cancer therapy A survey released on Oct 29 by the charity CancerBACUP shows that of 60 UK health authorities, only 12 were committed to giving women with ovarian cancer paclitaxel and platinum as recommended by the Joint Council of Clinical Oncology.

Discovery of dividing neurons in human brains excites researchers

Scientists report that neurons in the adult human brain can, after all, divide. This finding "flies in the face of what most people believed in the past", and could have implications for the treatment of neurodegenerative diseases and trauma, says Fred Gage (Salk Institute, La Jolla, CA, USA).

Gage and co-workers examined necropsy tissue from five patients who had had cancer and who had received an intravenous injection of bromodeoxyuridine (BrdU) to check for tumour proliferation. BrdU is incorporated into the DNA of dividing cells and can be easily detected. The team found BrdU-labelled cells in the dentate gyrus of all the patients. The labelled cells were neurons (*Nat Med* 1998; **4:** 1313–17).

"Seeing the first cells was pretty amazing", admits Gage. "None of us were confident they were going to be there, which is why we waited for five patients. We wanted to make sure it was real."

Proliferating neurons may not always be good news, he warns. In one animal model of epilepsy, for example, newly generated but incorrectly wired neurons may have made the disease worse. However, information now being gathered about cellular mechanisms "could eventually be used to direct endogenous cells to migrate and differentiate in areas where neurodegenerative diseases and trauma occur". Gage's finding also puts animal studies of neurogenesis in a new perspective. "It allows us to at least begin thinking about relating some of the information from lower vertebrates to people", explains Gage.

Marilynn Larkin

Mutated α-synuclein fibrils important in Parkinson's disease
In familial Parkinson's disease, mutated α-synuclein protein rapidly forms insoluble fibrils in vitro, and this could explain the early disease onset, say US researchers (Harvard Medical School, Boston, MA, USA). Fibrils are linked to neuronal degeneration in Parkinson's, Huntington's, and Alzheimer's diseases, says principal investigator Peter Lansbury. He suspects the fibrils are the "end product" of a cellular pathway "that is itself toxic in some way". He is now trying to find "the step that comes before the bad step", since a drug that acts before fibrils begin to form might prevent disease (*Nat Med* 1998; **4:** 1318–20).