

The First Human Demonstration That Intrathecal Opiates

Produce Pain Relief

Peter Southorn, M.D.

In 1979, Anesthesiology's Drs. Josef Wang and Lee Nauss together with Dr. Juergen Thomas from Neurology first reported that morphine injected intrathecally relieved severe incapacitating pain secondary to cancer. The following is an account of the people involved and the events that led to this landmark study.

Lee and Joe joined the department in 1974, and with the encouragement and support of our then chair, Dr. Richard Theye, established the Pain Clinic. To permit Joe to pursue his interest in pain research, Dick Theye prevailed upon Dr. Frederick Kerr who directed Neurosurgical Research to provide Joe with laboratory space. In 1976 Drs. Tony Yaksh and Thomas Rudy in Madison, Wisconsin, reported that opioids injected intrathecally in rats produced pain relief with this being antagonized by naloxone. On a site visit to Madison in 1975, Fred Kerr learned about their studies, began trying to recruit Tony, and encouraged Joe to pursue their line of inquiry here at Mayo. Joe first confirmed their findings including their observation that the intrathecally applied morphine produced no adverse toxicological effect on the spinal cord. Given this, IRB permission was obtained in 1977 to study whether such intrathecally applied morphine could help patients with intractable pain secondary to malignancy involving the lumbosacral plexus. One of the reviewers of the proposed study was Dr. Sheila Muldoon. She was the first to suggest that preservative-free morphine be used for intrathecal injections to reduce the risk of spinal cord injury but such a preparation was unavailable at that time. Juergen Thomas's role in this study was to

examine each patient carefully to ensure that indeed no neurological injury occurred. Patients were enrolled, and they received on a double-blinded crossover basis either 0.5 or 1 mg of morphine intrathecally or a saline placebo control. With the morphine, each patient experienced dramatic pain relief with this lasting on average 20 hours in duration. Lee recalls that he administered the first dose of intrathecal morphine. Apparently, he immediately became unblinded as to the nature of the injection he had given when the patient began to cough vigorously once his pain, which had previously prevented him coughing, disappeared. Dr. Peter Wilson, a resident in the Pain Clinic at that time and still very active in the field, also remembers giving some of the intrathecal injections.

The paper* reporting these findings made the perceptive suggestion that the pain relief achieved by this means could be possibly sustained for long periods if the morphine were administered from a drug reservoir into an implanted intrathecal catheter. It also made the suggestion that the pain relief afforded by this means might find value in treating postoperative pain and that associated with childbirth. We can all be proud that this study emanated from our department. It and a study from Israel showing epidural morphine had a similar efficacious effect, also published in 1979, have had a profound impact on our practice. Of interest, Tony Yaksh did come here to work with Fred Kerr in 1977. While at the Clinic and then subsequently in San Diego, he has continued his groundbreaking basic science studies which have contributed so much to our understanding of the mechanisms of pain and its management.

**Anesthesiology* 50: 149-156, 1979.