the other hand, a string of national bodies seems undesirable and perhaps even unnecessary. In 1991 the Dutch Ministry of Education initiated an educational review of all medical schools (carried out by the universities themselves). The reviewing committee, on which all schools were represented, was highly critical of the quality of education provided by several medical schools. What will happen if schools fail to comply with the recommendations remains to be seen—so far introduction of reviews has resulted in substantial voluntary initiatives for change in all Dutch medical schools.

Compared with other training programmes, medical education finds itself in relatively fortunate circumstances. Over recent decades many changes have taken place, considerable experience has accumulated, journals specifically for medical education have been published, and conferences devoted to medical education have been held. Courses and workshops on the topic are widely available. Much of what is needed to tackle the problems in medical education is already available—as Lowry’s series has made clear. We now know much more about designing curriculums and about methods of selecting, teaching, and assessing students than before. To progress, however, we need teachers and schools to become more conversant with the changes. In education we are overly inclined to rely on our own tradition and intuition and to overstate the uniqueness of our particular circumstances (think of the thousands of teachers with their own stock of test questions in their drawer). An open mind and a willingness to share are essential if we wish to tackle the current problems affecting medical education. Stella Lowry’s series should help.

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CEES VAN DER VLEUTEN


Pre-emptive analgesia

Local anaesthesia given before general anaesthesia may reduce the severity of postoperative pain

Might analgesia given before a painful stimulus somehow prevent or reduce the pain experienced later? Recent advances in our understanding of pain provide the background for this phenomenon of pre-emptive analgesia.

The nervous system does not modulate all pain in a fixed or "hardwired" manner. It responds to some stimuli by dynamic modification or "plasticity"; and once induced, this neuroplasticity may sustain and magnify the experience of pain.1 Experiments on decerebrate rats have shown that noxious stimulation may generate reflex hyperexcitability in the dorsal horn of the spinal cord.2 This central sensitisation prolongs and increases sensitivity to noxious stimuli over an expanded receptive field (hyperalgesia) and results in pain from previously innocuous stimuli (allodynia). Repetition of the noxious stimulus evokes a progressively escalating response in the cord, which further magnifies the pain—a phenomenon termed "wind up."1

In animals much smaller doses of morphine will prevent sensitisation of the nervous system to pain than are necessary to suppress it,1 indicating that pre-emptive analgesia might be worth while. Allodynia, hyperalgesia, and reflex hyperexcitability—presumably all caused by sensitisation of the nervous system—also occur in surgical patients,1 suggesting a potential for pre-emptive analgesia in humans.

Central sensitisation and wind up depend on the activity of N-methyl-D-aspartic acid (NMDA) receptors in the dorsal horn. Antagonism at this receptor can prevent and even abolish these changes, suggesting that antagonists have a place in preventing and treating this pathological pain.2 The only NMDA antagonist clinically available is the anaesthetic drug ketamine, but more useful agents with fewer undesirable effects on higher function are awaited with interest.

Peripheral sensitisation may also occur. Injury may sensitize nociceptors, causing hyperalgesia at the site of injury and in surrounding non-traumatised tissue. The mechanisms include the activity of chemical mediators from damaged tissue such as leukotrienes, bradykinin, histamine, and metabolites of arachidonic and sympathetic activity.3 In addition a recently identified group of pain afferents (usually functionally dormant and called "sleeping nociceptors") has been shown to be activated by inflammation and may contribute to peripheral sensitisation to pain after injury.4 Agents able to interrupt these two mechanisms should be able to bring about pre-emptive analgesia.

Pre-emptive analgesia has, indeed, been said to have been shown to occur in several clinical studies. Both premedication with opioids and local anaesthetic block before incision delayed the request for analgesia after orthopaedic surgery when used individually—and, more impressively, in combination.6 Various non-steroidal anti-inflammatory drugs given before surgery have been shown to have analgesic effects.7 Tverskoy et al reported that patients treated by infiltration of a local anaesthetic and then given general anaesthetic for herniorrhaphy experienced less pain, and for shorter duration, than patients who received general anaesthetic alone. Spinal blockade produced intermediate results.8 Pre-emptive analgesia may be relevant to the management of chronic pain; a Danish study showed a reduction of phantom limb pain for up to one year when ischaemic pain was treated effectively with epidural analgesia before amputation.9

McQuay pointed out that though such studies show clinical benefit from analgesic interventions before surgery the mechanism might not be pre-emptive analgesia because the study designs did not compare identical analgesic interventions after the surgical stimulus.10 Studies designed to compare identical analgesic interventions before and after injury have now been published. Pre-emptive local anaesthetic field block for inguinal herniorrhaphy resulted in reduced pain scores and a delay in requests for analgesia during the six hours studied by Ejlersen et al,12 but similar work detected no pre-emptive effect over a longer period.13 Katz et al found that patients given epidural fentanyl shortly before thoracotomy reported less pain and used less supplementary analgesic afterwards,14 while others found no equivalent effect of epidural bupivacaine and morphine before major abdominal surgery.15

These conflicting findings probably arise in part from differences in the effectiveness and time course of the afferent blockade of nociceptors by the different interventions. Furthermore, the sensitising effect of extensive nociceptive stimulation from surgery may prove much more difficult to block than the limited chemical or thermal stimuli used in
animal models of pain. Nor do we know how long afferent blockade must be continued during and after surgery to ensure that neuronal plasticity is prevented and not simply delayed. These considerations are important now that modern clinical anaesthesia uses low concentrations of volatile anaesthetics which abolish consciousness but may still allow sensitisation of the cord unless noiceptive input is otherwise reduced—a concern voiced 80 years ago by Crile. Perhaps general anaesthesia should be combined with pre-emptive local and regional anaesthetic blocks more often.

As is so often the case, more work needs to be done. Some encouraging laboratory and clinical studies suggest that pre-emptive analgesia does reduce pain after surgery, but the optimum choices of agents and timing required for a clinically useful effect remain to be established. The underlying mechanisms may also be relevant to some chronic neuropathic pain states.

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Select decontamination of the gut

Does not affect survival in intensive care units

Nosocomial infections are commonest in intensive care units, where prevalences of 18-36% have been reported. Rates of colonisation with potentially pathogenic micro-organisms are even higher, particularly in ventilated patients, and may exceed 80% in those staying in the intensive care unit for five or more days.

Potentially pathogenic micro-organisms are usually derived from the gastrointestinal tract and are mostly Gram negative bacilli, such as *Enterobacteriaceae* and *Pseudomonas* spp, but they also include yeasts, especially *Candida* spp. Patients requiring intensive care are at greater risk of nosocomial infection not only because their illness is severe but also because many therapeutic interventions actively promote colonisation or disable host defences. Various forms of instrumentation, including ventilation, inhibit the usual means of clearing organisms from normally sterile epithelial surfaces. Importantly, prophylaxis against stress ulcers with H₂ antagonists and antacids has been implicated in abnormal bacterial overgrowth in the stomach. Similarly, as the gut requires luminal nutritional support to prevent mucosal atrophy and subsequent bacterial translocation the use of parenteral rather than enteral nutrition may also increase the likelihood of infection. Vascular access may increase the risk of infection but cannulas are not usually colonised by organisms originating in the gut.

In the past decade attention has turned towards selective decontamination of the gut in an attempt to reduce these nosocomial infections. Various combinations of topical and non-absorbable antimicrobial agents have been used to reduce relative numbers of Gram negative bacilli and yeasts cultured from faeces and the oropharynx while maintaining normal anaerobic flora. Most regimens have included non-absorbable antibacterial and antifungal agents administered into the gastrointestinal tract by nasogastric tube as well as a topical preparation to the nasopharynx and hypopharynx. A variable period of intravenous antimicrobial prophylaxis (usually with cefotaxime) has also been used.

Selective decontamination of the gut was first performed in immunocompromised patients outside the intensive care unit and resulted in significant reductions in the rates of colonisation and infection. The first studies of patients in intensive care units began with investigations of multiply injured patients in the Netherlands, and these showed significantly fewer patients colonised with potentially pathogenic micro-organisms, particularly of the upper respiratory tract. Fewer infections occurred but without any effect on survival. Two recent prospective, double blind randomised trials have confirmed the absence of any improvement in overall mortality in the populations studied in intensive care units.

An earlier prospective study using a post hoc analysis, however, showed that selective decontamination of the gut was associated with a significant fall in mortality when patients with acute trauma were considered separately. While use of mortality as the sole criterion of therapeutic efficacy in intensive care units is open to debate, these studies have all failed to show any cost benefit; in one, selective decontamination of the gut doubled the total cost of antimicrobial drugs. Fears of the emergence of drug resistance in colonising bacteria in patients receiving selective decontamination of the gut have not been realised.

The lack of clearly defined benefit from selective decontamination of the gut in a heterogeneous population of patients led to a European consensus conference on the topic.

On the basis of published work (including the two recent large studies) the conference did not recommend the use of selective decontamination of the gut in any particular group of patients and, unsurprisingly, went on to suggest that further prospective controlled multicentre studies of sufficient statistical power should be done.

In our view, colonisation with potentially pathogenic micro-organisms can best be prevented by emphasising standard microbiological good practice. Poor hand hygiene by medical staff is particularly refractory to change and should be subject to constant observation and correction. Other simple measures include the avoidance of H₂ antagonists and antacids, regular changes of vascular access, and the use of enteral nutrition whenever possible. Obtaining regular and appropriate specimens for culture from potential sites

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