controls. Antibodies to the relevant peptide sequence in the bovine serum albumin also identified the p69 antigen from islets on immunoblots. Karjalainen and colleagues have hypothesised that one route to type I diabetes is through molecular mimicry between the islet antigen p69 and bovine serum albumin in cows' milk.[14] Early sensitisation to bovine serum albumin through bottle feeding in infancy leaves memory T cells which destroy β cells expressing p69. The p69 antigen is inducible by interferon γ released intermittently during childhood infections, so that the process of destruction of β cells is protracted, variable, and uncertain. Only a subset of the population—those with a genetic make up that was able to present the critical sequence of bovine serum albumin to the immune system—would be susceptible to the mimicry.

It therefore seems conceivable that susceptibility to both type I and type II diabetes is determined during gestation or infancy in response to nutrition, and research should respond with a new focus on early events. But the similarity between the two of an early influence of nutrition may not stop there. Diabetes results when the insulin reserve no longer meets demand. If the stress on β cells that leads to type II diabetes is a progressively increasing demand (insulin resistance), the stress that leads to type I diabetes is arguably a progressively diminishing reserve (insulitis). In either case the outcome is likely to be influenced by the peak β cell mass. Perhaps the genetic linkage that has recently been described between type I and type II diabetes[15] is a determinant of the β cell proliferative compartment and its response to early nutrition.

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Improving medical education

Educators need to develop an open mind and a willingness to share

Stella Lowry's analysis of the problems affecting medical education (which ends this week, p 320[1]) holds for countries other than Britain. For example, we in the Netherlands are also struggling with medical curriculums overloaded with factual information, often of little clinical relevance, which risk turning our students into passive consumers, their creativity and curiosity stifled. We assume that competent doctors emerge at the end of an obstacle course of traditional examinations based on facts.

Little place exists in many of our curriculums for other important opportunities for learning, such as use of simulated patients and early clinical contact, or for developing skills in self directed learning and communication. As in Britain, changes in health care are only haphazardly incorporated into the educational programme.

If we all agree that change is required then why is it so difficult to implement? Two impediments come to mind. The first is the attitude of teachers. Typically, tradition weighs heavily on us: curriculums are organised and taught in the way that we have always done it. We have all gone through the same system (which seems not to have harmed us), and it is difficult to accept that current students should be taught differently. Interestingly, this attitude contrasts starkly with how people conduct their clinical practice or academic research. Here, a highly rational approach is the norm. In clinical practice we try to keep up with the scientific literature and adapt our actions accordingly. In academic research we submit our findings to rigorous peer review. Regrettably, this attitude does not extend to our educational activities.

The reward system in our universities is the second impediment to change. Just as examinations define students' academic success, so the academic success of university staff is defined by excellence outside education: higher status is mainly attained through outstanding research or excellence in clinical work rather than educational achievements. Spending too much time on education may actually endanger one's career as less time is available for more effective ways of achieving success. As long as this biased reward system persists, motivating teaching staff to improve the training of medical students will be difficult.

Starting from scratch has a certain attraction but is hardly an option in countries, such as Britain, which have long established medical schools. So how could change be achieved in existing medical schools? In her article Stella Lowry provides several examples. Firstly, we need to convince our colleagues that problems exist and that there are better ways of doing things. As well as persuasion, however, some external pressure, both from within and from outside schools, is needed to produce change. Some central control is required over medical education to ensure that rational decisions are being taken and that the quality of education is monitored.

Individual departments in most medical schools have nearly unrestricted autonomy as far as their teaching is concerned. We can therefore hardly expect change from individual departments: they lack an appreciation of the curriculum as a whole and are inherently inclined to defend their own interests.

Outside pressure is another indispensable force to achieve change. In Britain institutions like the General Medical Council and the King's Fund could provide it yet they apparently lack the power to enforce recommendations. On

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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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,[3] 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,[4] 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.[5] 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 sensitise 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.[1] 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.[6] 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.[7] Various non-steroidal anti-inflammatory drugs given before surgery have been shown to have analgesic effects.[8] 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.[9] 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.[10]

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.[11] 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