The president has gone out on a very precarious limb to find the consensus necessary to effect change. He has promised Americans that they can have more security and peace of mind about their health care coverage, including improved benefits and a higher quality of care, simply by wringing savings out of the fat of the current system. This has led to charges from some quarters that the president is trying to get something for nothing. That assessment is too harsh. But it is true that the president is trying to convince the American people to sit still for fairly nasty surgery by promising that it will not hurt very much.

How much pain the "haves" in the current system believe reform will bring will determine the fate of Clinton's plan. Small businesses are already yelling loudly that a mandate to cover workers will cost jobs and lots of them. Although the tobacco industry is not what it once was, it is still a force to be reckoned with in American politics, and big increases in vice taxes will not sit well with them or their concerned and ready to lobby cousins in the alcohol, gambling, and food industries. Advocates for elderly people and the very poor will vigorously protest if their current entitlement programmes are targeted for more than minimal cuts. And, as eager as many Americans are for lower costs, many will wince over the notion of capping of the rate at which insurance premiums for the basic or baseline package of health care services can rise—a strategy that some fear will deny them access to the next generation of medical technology and breakthroughs.

Once the euphoria over the fact that the nation has finally managed to talk seriously about doing something about its flawed health care system wears off, four large potholes are likely to emerge on the road to legislation. Coverage for abortions is in the president's basic package, and this will trigger yet another round of finger pointing and screaming as the entrenched sides on this issue fight it out yet again. Rural Americans and their congressional representatives are likely to become nervous about reform built on the concept of managed competition when they realise that it does not guarantee that any health care plans will want to compete for the limited business that rural customers represent. Those who oppose change will point out that there is a danger that health care plans under managed competition will meet their payrolls by rationing services. Any talk of rationing could dry up middle and upper class support for change. And it will not be long before insured Americans realise that they will probably be getting less choice of provider than many now have. In autonomy mad America, loss of choice is politically lethal.

Still, punters would be wise to bet on change. While derailment is possible, exploding costs are pushing the Clinton engine down the track with enough momentum that a bill will most likely be signed by next summer.

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Asthma: what is there left to find out?

Firstly, why and how do people become asthmatic?

Despite the many recent advances in our understanding of asthma many questions remain unanswered.[1] Asthma has been rediscovered as an inflammatory disease, and the nature of the inflammatory reaction has been defined by applying modern immunohistological and molecular biological techniques to bronchial biopsy specimens and cells obtained by bronchoalveolar lavage.[2] Inflammation is found even in patients with the mildest asthma and is characterised by infiltration of eosinophils and activation of mast cells, T lymphocytes, and macrophages.

Activated inflammatory cells in asthmatic airways release a bewildering number of mediators, but the recent development of specific mediator antagonists has shed some light on their relative importance. Leukotriene D4 seems the most important mediator of bronchoconstriction, whereas various cytokines play a critical part in recruiting and activating inflammatory cells.[3,4] In addition to bronchoconstriction, evidence exists for exudation of plasma, vasodilatation, hypersecretion of mucus, and activation of sensory nerves—all contributing to the clinical features of asthma. Although acute inflammation has been emphasised, it is evident that asthma is a chronic inflammatory condition. Structural changes (subepithelial fibrosis, hyperplasia of airway smooth muscle, angiogenesis) may result, which may be irreversible.

So what uncertainties remain? The worldwide increases in morbidity caused by asthma and in mortality from the disease are largely unexplained.[5] The origins of asthma are obscure. Although atopy is by far the most important risk factor for the development of asthma, what determines whether an atopic person becomes asthmatic is uncertain. Several possible causes have been considered, including exposure to inhaled allergens (particularly house dust mite), viral infections, passive cigarette smoking, and air pollution. A critical period may exist in early childhood when asthmatic inflammation becomes established.

Perhaps the greatest mystery is why the underlying abnormalities of asthma persist (in most patients forever). The inflammatory response becomes chronic, and, although it may be controlled with steroids, it almost always recurs when steroids are stopped. This is best illustrated in occupational asthma due to exposure to chemical sensitisers, such as toluene di-isocyanate. Removal from industrial exposure usually results in the complete resolution of asthma if exposure was for less than six months, but with exposure for longer than six months asthmatic inflammation persists even after complete and prolonged avoidance of exposure.[6] This suggests that a mechanism exists for perpetuating the chronic inflammatory response even without a driving mechanism.

Recent observations on transplanted asthmatic lungs are instructive. Two non-asthmatic recipients of lungs obtained from known asthmatic donors developed features of asthma, with eosinophilic infiltration and the diurnal variation in airflow obstruction characteristic of asthma.[7] This suggests that the mechanism for the persistence of asthma is present in the lungs, possibly in the form of a permanent population of memory T cells which can orchestrate the typical asthmatic inflammation. Eradicating these lymphocytes may even offer the possibility of a cure for asthma in the future.

The debate about the relative roles of genes and the environment in the causation of asthma continues. While genetic influences are clearly important in atopy (although the existence of a single gene for atopy is debatable), the influence of genetic factors in asthma is less clear; most studies suggest that environmental influences are more important in converting an atopic person into an asthmatic patient.[5] The quest for a single "asthma gene" is unlikely to be rewarding as a complex interplay between many genes and several environmental factors is likely to exist. The role of environmental factors such as diet and viral infections in the causation of asthma is unknown, but air pollution is unlikely to be important.[8]

Recently, the management of asthma has changed substantially, and new national and international guidelines now recommend a stepwise approach to treatment.[9] Fundamental to management is the early introduction of anti-inflammatory treatment rather than reliance on bronchodilators.[10] Corticosteroids are by far the most effective anti-inflammatory treatment available and when inhaled are well tolerated. Inhaled steroids suppress the inflammation of asthma and effectively control symptoms in most patients. By contrast, inhaled β_2 agonists relieve symptoms in the short term but do not control the underlying inflammation. Indeed, it has been questioned whether excessive use of inhaled β_2 agonists may make asthma worse and contribute to the increased morbidity and mortality from the condition.[11] This important question needs to be resolved as the number of prescriptions for inhaled β_2 agonists is increasing worldwide to a greater extent than the number of prescriptions for other antiasthma drugs.

We still know little about the long term outcome of asthma, and prolonged trials of treatment are needed. Early treatment of asthma with inhaled steroids gives optimal long term control,[12,13] and preliminary evidence from children suggests that delaying the introduction of inhaled steroids may result in irreversible changes to the airways.[14] We need to know whether early control of asthma can "switch off" the disease; some data from adults with mild asthma suggest that this may be so.[15] Does better control of asthma in childhood reduce the risk of asthma recurring in adult life?

We need answers to these questions as asthma may account for 1-2% of the total health budget in industrialised countries. More research into basic mechanisms and careful evaluation of treatment with long term clinical trials should help to answer many of the remaining questions about this commonest of chronic diseases.

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Optimal pain relief in infants and children

Safe methods of analgesia and anaesthesia are now available

Until recently, infants and children commonly received insufficient pain relief.[1] In some cases infants were even denied anaesthesia during surgery either because of a belief that they would not feel or remember pain or because of valid concerns regarding the safety of anaesthetic agents in sick infants. For the most part these concerns are no longer valid. In 1987 LeDez and Lerman showed that premature neonates responded to painful stimuli and that anaesthetic agents blunted this response just as in adults.[2] Safe methods of analgesia and anaesthesia are now available for infants and children of all ages.

Recent research confirms that maturation of neuroanatomical, neurophysiological, and neurochemical development of the nociceptive pathways in the central nervous system of the fetus and newborn infant is such that even preterm neonates can mount behavioural and physiological responses to noxious stimuli.[3] The studies of Fitzgerald and colleagues indicate that repetitive noxious stimulation has persistent effects generating hyperalgesia with persistent increases in excitability of the spinal cord, which analgesia can prevent.[4]

Assessing pain in infants is difficult. In older patients we rely primarily on verbal reports, while in infants we are forced to use behavioural and physiological variables, which are imperfect measures. For example, an infant may cry or appear distressed not only because of pain but also because of the anticipation or expectation of pain, as well as from fear or hunger. Similarly, although tachycardia and other physiological alterations may reflect pain, other conditions such as hypovolaemia, hypoxaemia, or fever may be responsible. Sophisticated analyses of infant facial expression and crying have identified specific behaviours related to pain which have been used in trials of analgesics in newborn babies and young infants.[5]

Adequate pain control is important in the management of neonates and infants. Substantial humoral, metabolic, and cardiovascular responses to painful and stressful stimulation have been documented in paediatric patients of various ages during surgery and routine minor invasive or diagnostic procedures.[6-10] Such responses may increase the risk of morbidity or death.[9]

Over the past 10 years a series of studies has confirmed the safety and efficacy of providing pain relief for infants and children with both systemic analgesics and regional blockade