greater wealth on health care—the United States now spends 15 times as much as Britain, though its population is only four times greater. McLachlan reiterates the basic economic facts: measured by per capita spending Britain has one of the cheapest health care systems in the world. And it is this highly effective system that is now to be transformed for reasons of ideology.

Should it not by now be obvious that the immediate prospect for the NHS is that it will be disrupted and disheartened over the next two years as its staff struggle to introduce new control and costing systems without the essential accounting infrastructure? Every health region is installing information systems and hiring accountants and computer programmers while closing beds and cutting down the numbers of outpatient clinics (including specialist clinics such as family planning clinics).[7] The NHS is steaming full ahead into an iceberg that will prove as devastating as the one that sank the Titanic. McLachlan is only the latest in a series of well informed and articulate commentators who have drawn attention to a forseeable disaster. Is there no one on the bridge prepared to order the engines to slow—or, even better, go full astern?

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Central pain

Much can be offered from a methodical approach

Central pain is the term used for pain arising from lesions confined to the central nervous system and of an intense unbearable nature. It is often associated with particularly unpleasant dysaesthesiae. It may be either diffuse or localised; it may be spontaneous or occur in response to minor stimulation, but it is usually associated with overreaction to stimulation. Sensory impairment or loss is invariable.

The definition of central pain is not, however, without some ambiguity. Some pain clearly has a mixture of a peripheral and a central cause—for example, the pain in arachnoiditis where peripheral lesions occur and where there is a central lesion as shown by the presence of long tract signs. Each year more research shows that peripheral mechanisms induce central changes, and the division between central and peripheral pain is necessarily becoming blurred. Nevertheless, Cline *et al* have shown in humans sensitisation of C nociceptors with low threshold and prolonged discharges after sensitisation (which would explain the abnormal quality of pain and exaggerated response in patients with chronic pain) but with no evidence of secondary dysfunction of the central nervous system or sympathetic disturbance.[1] There remain, therefore, considerable uncertainties about the mechanisms of both central and peripheral pain.

One of the best known categories of central pain is the thalamic syndrome, which is usually due to ischaemic or haemorrhagic vascular lesions or arteriovenous malformations. Less commonly it may follow trauma, including surgical lesions of thalamus, and relatively infrequently it may be due to a tumour. Bowsher *et al* have recently drawn attention to an important and often overlooked cause of central pain.[2] They described seven patients in whom subarachnoid haemorrhage (one from arteriovenous malformation) was followed by pain and discussed further cases after stroke other than intracranial haemorrhage. In most of the patients there was no evidence of delayed ischaemia and the central pain seemed to be due to primary neurological damage occurring at or soon after the haemorrhage. Their patients showed the classical features of central pain: it took time to develop, there was no tissue damage outside the central nervous system—as is the case in nociceptive (tissue damage) pain—and there was an associated sensory deficit. Furthermore, the patients showed allodynia—that is, the production of pain by a non-painful stimulus (pathognomonic of neurogenic pain), lower skin temperatures in the painful area with the frequent exacerbation of pain by temperature changes or emotional stress (suggesting autonomic activity), and resistance to analgesia with narcotic drugs.

Painful syndromes in the spinal cord may be due to vascular lesions or to trauma. In complete lesions phantom sensation or phantom pain occurs in a way similar to the description of phantom limb after amputation; it may be referred to any part of the body below the transection but is usually referred to the legs or the feet. In an incomplete lesion (such as a Brown-Séquard lesion) the pain is short lived on the side of the lesion but may persist for years on the contralateral side. Pain may occur with syringomyelia, and it may precede any other sign of the disease by many years. In patients with multiple sclerosis pain and dysaesthesia is not unusual, although frequently the patients do not report the pain unless questioned. Lhermitte's sign is usually associated with discomfort rather than pain.

The localised pain (sometimes of nerve root distribution) seen in patients with spinal tumours is not strictly pain of central origin. Painful dysaesthesia may, however, refer to areas below the level of the lesion and in rare cases pain may precede any other symptom or sign. Less common causes of central pain include myelitis and myelopathy due to cervical spondylosis.

Paradoxically, surgical lesions designed to alleviate pain, such as cordotomy and commissural myelotomy, may produce late unpleasant pain; this is often quite different from the original pain and is associated with dysaesthesia.

Suprathalamic lesions may give rise to pain that is similar to the pain of the thalamic syndrome.

Pathophysiology

The nociceptive system (nociceptive because it responds to noxious stimuli) has a complex and widespread organisation. As pain for most people is a minor event this system must either be concerned in other and perhaps more important aspects than signalling pain (for example, it may be concerned with inflammation or tissue repair) or it must be almost continuously suppressed in normal circumstances. Central

pain would then occur if the nociceptive system was "released"—as was suggested by many neurologists and neurophysiologists in the early part of the century. The gate control theory of Melzack and Wall, which has done so much to stimulate interest in and understanding of pain, proposed that nerve damage interfered with the constant inhibitory modulation of large diameter fibres and their connections.[3] Pain afferent fibres may be selectively inhibited at all levels of the central nervous system by both ascending and descending systems through presynaptic inhibition or by alteration of excitability of neurones. Nociception is mediated by the periventricular and periaqueduct grey matter, the nucleus raphe magnus of the medulla, and the dorsolateral funiculi of the spinal cord, with neurotransmission and modulation via enkephalins and endorphins, and by serotoninergic projections. Electrical stimulation of the brain stem structures[4] and of the spinal cord[5] partially blocks various clinical syndromes, possibly by activating the enkephalins and endorphins mediating analgesia system, but it may exacerbate pain occurring after central reorganisation after neurological damage.[6]

Partial or total interruption of afferent fibres results in the degeneration of presynaptic terminals and an alteration in function and structure. Denervated synaptic sites may be reinnervated by other axons (sprouting),[7-9] and previously ineffective synapses may become active (unmasking).[10] Excitation spreads to neighbouring areas and supersensitivity occurs, producing an abnormal firing pattern that may depend on stimulation or may occur spontaneously. This sequence of events explains many of the symptoms of central pain, including dysaesthesia (abnormal firing pattern), spontaneous shooting pain (paroxysmal burst discharges), evoked pain from non-painful stimuli, diffusion of the evoked abnormal sensation, and the long term failure of neurosurgical treatment.

Irritative lesions of sensory pathways may possibly produce hypersensitivity, and partial destruction results in the generation of new receptors. Although changes of these kinds have been shown to occur in the peripheral nervous system,[11] they have not been shown definitely in the central nervous system, and central pain may occur even after complete destruction of central sensory pathways. Damage to central sympathetic fibres (cerebrospinal sensory fibres) may possibly produce pain and hyperpathia. Experimental partial lesions of the posterolateral nucleus of the thalamus result in an alteration of the evoked response from the periphery and explain the presence of hyperpathia and dysaesthesia. Such partial lesions do not explain the symptoms in lesions below the thalamus unless they result in altered transmission characteristics in the spinothalamic and lemniscal systems so that the central pattern of impulses (spatial and temporal) is abnormal and wrongly interpreted or integrated.[12]

In summary, central pain may be due to abnormal hypersensitivity of damaged fibres, the generation of new receptors, alteration in the central pattern of impulses, alteration of inhibitory mechanisms—including the enkephalins and endorphins mediating analgesia system—and activation of secondary (polysynaptic) pathways.

The management of central pain

As in all cases of chronic pain the first step is an accurate diagnosis. This requires a careful neurological history and examination and, possibly, in some patients, complex neurophysiological and neuroradiological techniques to be performed. In the first instance the patient should be seen in a neurological pain clinic. An explanation of the diagnosis and discussion of the nature of intractable pain may have no effect on its severity, but these will make management much easier for both the doctor and the patient.

All classes of psychotropic drugs—including antidepressants, neuroleptics, and sedatives—have been reported to be beneficial in intractable pain. Most clinical studies, however, have been poorly designed, partly because of the serious problems imposed by the difficulty (or even impossibility) of measuring chronic pain objectively and partly because of the complex interaction of physical and psychological factors.

Stimulation of central grey matter may produce analgesia, and this has been linked with serotonin (5-hydroxytryptamine)—the neurotransmitter in pathways from the periaqueductal grey matter to the spinal cord. Anything that increases concentrations of serotonin is likely to increase analgesia and vice versa. Serotonin probably inhibits nociceptive neurones, which project to the spinal cord, and thus reduces pain transmission. Morphine analgesia is also linked with serotonin, and destruction of serotonin pathways blocks the analgesic action of morphine whereas stimulation of the dorsal raphe (connected to the periaqueductal gray matter) increases it. The concentrations of naturally occurring opioids increase after analgesia produced by stimulation. There is growing evidence linking serotonin, enkephalins, substance P, and opioids with analgesia produced by stimulation. Serotonin is one of the monoamine neurotransmitters (others are noradrenaline and dopamine) that are linked to the monoamine hypothesis of depression, which proposes that specific features of depression are the result of abnormalities of particular monoamines and antidepressant action depends on increasing the availability of these amines by producing a specific inhibition of reuptake at synaptic level.[13]

The clinical association between chronic pain and depression may, therefore, have a good pharmacological explanation—namely, reduction of serotonin concentration. Amitriptyline is regarded as the best antidepressant for its analgesic effect, and this assessment is supported by pharmacological evidence as serotonin seems to be more affected by drugs with a tertiary amine structure. It probably acts as a selective blocker of synaptic reuptake of serotonin, but it also ameliorates psychological stress and produces non-specific depression of arousal and thus may modify the central perception of pain. Intractable pain is associated with changes in personality, which regress with effective treatment of the pain, and it is perhaps necessary to document disturbance of the personality only as it affects the complaint of intractable pain rather than attempt to implicate such disturbance in the aetiology of the pain. About three fifths of patients with chronic illness also suffer from depression.[13] Conversely, pain is common in depressive illness. Depression and anxiety are influenced by insight, perception, and by the doctor's own perception of pain, and these factors must be included in the general management of chronic intractable pain.

The use of anticonvulsant drugs in intractable pain stems from the original trial of phenytoin in patients with trigeminal neuralgia.[14] Carbamazepine was introduced in 1962,[15] and since then anticonvulsant drugs have been used for a variety of paroxysmal lancinating pains and for central pain. Their mode of action is uncertain, but the anticonvulsant action is probably not relevant as antiepileptic barbiturate drugs have no effect in chronic pain. Phenytoin seems to stabilise hyperexcitability caused by low calcium concentrations and blocks post-tetanic potentiation. Carbamazepine also depresses post-tetanic potentiation and inhibits polysynaptic reflex activity.[16]

Peripheral nerve blocks, including section of nerve roots, have been attempted for treatment of central pain, but the results have been inconsistent. An anaesthetic block is worth attempting as temporary relief may occur. Sympathetic

block reduces the effect of sympathetic modulation on receptors and may be of short lived benefit.[17] Depletion of noradrenaline in postganglionic sympathetic terminals by a guanethidine block may be effective.[18]

Neurosurgical operations, including cordotomy and tractotomies, resection of sensory cortex, and stereotactic operations on the thalamus, have generally given disappointing results, as indicated earlier. Electrical stimulation is often effective in patients with pain of peripheral origin, but not usually in those with central pain. Spinal cord stimulation may be extremely effective in some patients, and the results are longer lasting and cause less disability than neurosurgery[19 20] but it is unlikely to help in pain due to spinal cord injury. Intracerebral stimulation (deep brain stimulation) is still considered a somewhat uncertain method of treatment because of the great variability in reported results.

In conclusion, the management of central pain is by no means settled, but it should not be considered a subject of therapeutic nihilism. Much can be done to help the patient—provided that a methodical approach is undertaken and that neurosurgery is considered only as a last resort.

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Aerosol inhalers

Environmentally friendly devices are becoming available

The pressurised metered dose inhaler, introduced in 1956, has stood the test of time as a popular and convenient form of treatment for asthma. Metered dose inhalers are powered by mixtures of two or three chlorofluorocarbon propellants ("Freons") chosen to give the desired vapour pressure and spray characteristics. These substances are gases under normal ambient conditions but may be liquefied by cooling or, as in the metered dose inhaler, by pressurisation. Chlorofluorocarbons make ideal propellants as they are non-toxic (unless greatly abused), non-flammable, and have suitable thermodynamic properties. This combination of desirable features cannot be found in alternative substances such as propane, isobutane, or compressed gases. I have recently reviewed these issues more fully in an editorial in the *European Respiratory Journal*.[1]

Not until 1974 did anyone realise that chlorofluorocarbons could cause severe environmental problems. In that year Molina and Rowland suggested that so called "hard" chlorofluorocarbons would diffuse into the stratosphere, where their degradation by ultraviolet radiation would lead to a build up of chlorine and hence to a depletion of stratospheric ozone[2]; it seems almost unbelievable that one atom of chlorine can destroy up to 100 000 atoms of ozone.

The urgency of dealing with the problem was appreciated only in the second half of the 1980s with the discovery by the British Antarctic Survey scientist Joe Farman of serious depletion in springtime ozone over the Antarctic, the so called ozone "hole."[3] This damage has been blamed on chlorine derived not only from chlorofluorocarbons but also from other chemicals, such as carbon tetrachloride, methyl chloroform, and bromine containing halons released from some fire extinguishers. Potential hazards to health from depletion of ozone include an increased incidence of malignant melanoma, non-malignant skin cancers, and cataracts; reductions in crop yields and disruptions to aquatic food chains are also foreseen. If only to compound the felony, chlorofluorocarbons are potent "greenhouse" gases and may contribute appreciably to the total man made greenhouse effect. Fortunately, there has been a rapid global response: in the Montreal Protocol of 1987 a cut of a half in chlorofluorocarbon consumption by 1998-9 was agreed, and when new data showed that this was inadequate representatives of over 80 nations meeting in Helsinki in 1989 agreed in principle to eliminate chlorofluorocarbons by the end of the century. A further meeting, organised by the United Nations Environmental Programme, will review the Montreal Protocol in London in June of this year.

Few people seem aware, however, that the use of chlorofluorocarbons in aerosols contributes only about a quarter of the total worldwide consumption of these compounds; their other main uses are for foam blowing, as refrigerants, and as solvents in the electronics industry. Medical aerosol inhalers use only 0·5% of the total consumption and hence make an insignificant contribution to the environmental problem. Nevertheless, the future proscription of chlorofluorocarbons will lead to difficulties in supply, and hence the pharmaceutical industry must look in other directions. The two obvious possibilities are, firstly, the development of alternative "ozone friendly" propellants not containing chlorine and, secondly, the use of alternative inhalers that do not use any propellants at all. It is dificult to find satisfactory alternative propellants; HFC134a (a hydrofluorocarbon) is a strong possibility but would only partly solve the problem as metered dose inhalers require at least two propellants with differing vapour pressures. Such alternatives will be required if metered dose inhalers are to survive into the next century.

"Wet" aerosols from nebulisers do not contain chlorofluorocarbons, but handheld squeeze-bulb nebulisers are