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 ozone²; 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 difficult 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

now outmoded, and both compressor driven and ultrasonic nebulisers are bulky and cumbersome. Dry powder inhalers may provide the answer; the original powder inhalers (Spinhaler and Rotahaler) have the inconvenience that a gelatine capsule containing the drug powder has to be loaded before use, but two new multidose powder inhalers (Diskhaler and Turbohaler) have recently been introduced. The Diskhaler contains eight doses of either salbutamol or beclomethasone dipropionate, while the Turbohaler (known as Turbuhaler in other countries) contains 200 metered doses of terbutaline sulphate in the manner of a metered dose inhaler but without additives of any kind.⁴ The topical corticosteroid budesonide is available from Turbuhaler in some European countries. Powder inhalers have the further merit that they are breath-

actuated and can be used satisfactorily by patients who cannot use a metered dose inhaler correctly. Turbohaler, Diskhaler, and other future multidose powder inhalers may provide one key to treating asthma in the coming decades.

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Depression and the menopause

Oestrogen may alleviate depressed mood but depressive disorder requires psychiatric treatment

Depression around the menopause poses three important questions. Is it more frequent than depression at other times of life? Has it special causes, notably lack of oestrogen? Does it need special treatment—that is, oestrogen replacement?

Research attempts to answer these questions have often been inconclusive because of three limitations of method. Firstly, the important distinction between depressed mood and depressive disorder has often been overlooked. Depressed mood is the feeling of sadness familiar to everyone. Depressive disorder is a syndrome that is less common but far more serious. It may include depressed mood; loss of interest, energy, and enjoyment; poor concentration; gloomy thoughts of guilt, worthlessness, hopelessness or suicide; disturbances of appetite, weight, sleep, and sex drive; and slow speech or movement.

The second limitation has been failure to use standardised measures of known reliability and validity to detect symptoms and to diagnose depressive disorder. The third has been inaccurate specification of the menopause. For example, menopausal state has sometimes been defined by age, although the menopause is not closely correlated with age. The best method is to use precise definitions of the terms premenopausal, menopausal, and postmenopausal based on the time since the last menstrual period.¹

Is the frequency of depression increased around the menopause? High rates of depression have been found among women attending menopause clinics² and among middle aged women attending gynaecology clinics.^{3,4} These findings are not surprising as psychiatric symptoms are increased among all hospital outpatients.⁵ If prevalence is to mean anything it must be assessed in representative samples of the general population. Postal surveys of general population samples have given conflicting results, probably because they are less sensitive than interviews.^{6,7} There have been interview surveys in four countries—Sweden,⁸ England,⁹ the United States,¹⁰ and Canada.¹¹ All four used large random samples, precise definitions, and standardised methods of case detection. They agreed in finding no excess of depressive disorder at the menopause.

Does perimenopausal depression have special causes, either psychological or physical? Psychologically, the menopause may induce depression in a woman if she regrets the loss of her fertility or thinks that she is losing her femininity. Research shows that such reactions are uncommon among women undergoing an “artificial” menopause as a result of

hysterectomy, with or without bilateral oophorectomy.¹² By inference, such reactions are unlikely to be common with the natural menopause. They occur in individual women, however, and should not be missed as causes of depression.

It is obvious but worth emphasising that a perimenopausal woman may be depressed for psychological reasons that are unrelated to the menopause. Her parents may be ill or dying; her children may leave home; her husband may be less attentive than previously. She may have the so called redundancy syndrome—the demoralisation resulting from the belief that there is no longer anything useful to do. This is not to say that the challenges and adversities of middle life are any more stressful than those of early parenthood or old age. Nevertheless, research has found that depressed mood and depressive disorder in middle aged women are related less to the menopause than to the vicissitudes of life.^{10,13}

As a physical agent lack of oestrogen may cause depression either directly as a biochemical effect or indirectly by causing physical symptoms, such as flushes or sweats, that induce depression. A direct biochemical effect has not been proved, but several possible mechanisms have been suggested. For example, lack of oestrogen might cause depressed mood by reducing plasma tryptophan concentration, and thereby brain 5-hydroxytryptamine function,^{14,15} or by influencing the action of monoamine oxidase,¹⁶ or by changing the sensitivity of monoamine receptors.¹⁷

An indirect effect through flushes and sweats is also unproved. Two postal surveys found that psychological symptoms such as depression peaked in frequency at an age before that at which vasomotor symptoms peaked.^{7,8} On the other hand, a community interview survey of over 500 middle aged women found a significant association between psychiatric symptoms and flushes and sweats⁹—though this does not prove a causal connection. Clinical experience suggests that vasomotor symptoms may be very distressing to some women.

Against this aetiological background an important practical question is whether oestrogen alleviates depression. For depressive disorder the evidence is scanty. In a study of women with severe depressive disorders that had not responded to standard antidepressant drugs the addition of high doses of oestrogen was more effective than placebo in reducing depressive symptoms in some women, though the overall reduction was small in the whole group.¹⁶ The main disadvantages of this approach are that potential responders