service to expand where it can; from looking seriously at why it has not expanded elsewhere; and from putting things right in time to attract potential new consultants when they become ready.

[1] Department of Health and Social Security, *Health Trends*, 1978, **10,** 61.
[2] Turner, J M, and McDowall, D G, *Anaesthesia*, 1973, **28,** 551.
[3] *Basic Medical Education in the British Isles, Report of GMC Survey.* London, Nuffield Provincial Hospitals Trust, 1977.
[4] Vickers, M D, and Rosen, M, *British Medical Journal*, 1978, **1,** 1491.
[5] Hunter, A R, *Anaesthesia*, 1978, **33,** 427.
[6] Royal Commission on the NHS, *Doctor Manpower 1975-2000: Alternative Forecasts and Their Resource Implications.* Research Paper No 4, p 37. London, HMSO, 1978.

Polypeptide hormones inside cells

The idea of polypeptide hormones entering cells seems revolutionary. The first stage in the action of a polypeptide hormone is binding to a specific receptor site on the surface of the target cell.[1] Until recently this interaction was thought to represent the limit of cell penetration by the hormone: all its effects were assumed to result from binding to the localised receptor on the plasma membrane. The belief that polypeptide hormones do not enter cells has now been challenged in a series of recent studies based on new techniques. Will this also revolutionise our ideas about cellular mechanisms?

One of the methods used in these investigations relies on electron microscopic autoradiography to localise ^{125}I-labelled hormones in target tissues. This technique has shown that insulin can enter intact liver cells[2] and cultured lymphocytes,[3 4] and that human chorionic gonadotrophin can enter ovarian cells.[5] Image intensification (with a highly sensitive light-amplifying television camera) has shown fluorescently labelled insulin and epidermal growth factor inside cultured fibroblasts.[6] These findings raise the possibility that certain actions of polypeptide hormones could be mediated through a direct effect inside the cell of the hormone itself, of the hormone-receptor complex, or of the degradation products rather than through events localised on the surface of the cell.

Exactly how polypeptide hormones—which have molecular weights ranging from a few thousand to nearly 40 000—penetrate cells remains unknown, but there is some evidence that they enter the cells as hormone-receptor complexes.[5] The surfaces of hormone target cells are probably turned over quite rapidly,[7] and this process is likely to cause plasma membrane components, including hormone receptors, to be taken into the cell and to be shed from it. Hormone bound to receptors might, then, be expected to pass into the cell as part of the process of the turnover of the cell surface. Alternatively, the movement into the cell could depend on specific endocytosis of hormone-receptor complexes,[8] particularly in the case of insulin, where such movement has been reported to occur fairly rapidly.[3 6] The eventual fate within the cell of hormone, hormone receptors, and other membrane components is probably in the lysosomes,[8] where they are broken down into amino-acids to be used again by the cell for the synthesis of macromolecules.

Though there is now substantial evidence that polypeptide hormones, particularly insulin, enter target cells there is nothing to show that this process is important in stimulating the cells. Among the possible roles that have been suggested for this passage into the cells are degradation of hormone and receptor and direct long-term actions on the nucleus. The intracellular effects of many polypeptide hormones (with the notable exception of insulin[1 9]) are, however, known to be mediated by a mechanism depending on adenylate cyclase-cyclic adenosine monophosphate (AMP), localised on the plasma membrane.[1 10] In this system, binding of the hormone to the receptor leads to activation of adenylate cyclase, and it is the resulting increases in cyclic AMP concentrations that mediate the hormone's various intracellular effects. Until some clear function for intracellular polypeptide hormones can be established, therefore, we should perhaps be cautious about assuming that the process has a general importance in physiological terms.

[1] Rees Smith, B, *Advances in Clinical Chemistry*, 1977, **19,** 91.
[2] Gorden, P, *et al*, *Science*, 1978, **200,** 782.
[3] *Science*, 1978, **202,** 260.
[4] Carpentier, J L, *et al*, *Journal of Clinical Investigation*, 1978, **61,** 1057.
[5] Conn, P M, *Nature*, 1978, **274,** 598.
[6] Schlessinger, J, *et al*, *Proceedings of the National Academy of Sciences of the United States of America*, 1978, **75,** 2659.
[7] Doljanski, F, and Kapeller, M, *Journal of Theoretical Biology*, 1976, **62,** 253.
[8] Silverstein, S C, Steinman, R M, and Cohn, Z A, *Annual Review of Biochemistry*, 1977, **46,** 669.
[9] Czech, M P, *Annual Review of Biochemistry*, 1977, **46,** 359.
[10] Pastan, I H, Johnson, G S, and Anderson, W B, *Annual Review of Biochemistry*, 1975, **44,** 491.

Prognosis of optic neuritis

Optic neuritis presents a characteristic clinical picture and has an excellent short-term prognosis with most patients recovering vision completely. The long-term prognosis is less certain, for the crucial question is the risk of developing multiple sclerosis. A recent paper in *Brain*[1] has highlighted some of the problems in estimating this possibility. The reported risk varies from a figure as low as 13% in a series from America[2] to as high as 87% in one from Australia.[3] In three large British studies[1 4 5] the risks were estimated to be 40%, 51%, and 78% respectively, the highest figure being the calculated probability of a patient developing multiple sclerosis within 15 years of an episode of optic neuritis. Indeed, the major factor in the variation of the figures quoted is the length of follow-up; for as McAlpine, Lumsden, and Acheson[6] wrote over ten years ago: "The longer the period of observation the higher will be the percentage of cases of retrobulbar neuritis which develop signs of multiple sclerosis."

In their review Compston and his colleagues[1] discussed some of the factors which might be useful in predicting this risk. Clinical factors—age, sex, degree of visual loss, and bilateral lesions—do not seem important, but recurrent attacks of optic neuritis and onset of symptoms in winter appear to be associated with an increased risk of developing multiple sclerosis. Until now investigation has proved unhelpful: surprisingly, a pleocytosis in the cerebrospinal fluid in optic neuritis does not necessarily indicate an increased risk of multiple sclerosis.[5] Nevertheless, the presence of oligoclonal immunoglobulins in the CSF may prove a useful predictor, and this warrants further study.[7] Another line of investigation which seems worth pursuing is the human leucocyte antigen (HLA) make-up of patients with optic neuritis. Compston *et al*[1] found that the risk of multiple sclerosis was higher in patients with optic neuritis who were

positive for the antigen BT101, and using an actuarial method of analysis they calculated that 73% of patients with optic neuritis who were BT101 positive would develop multiple sclerosis within eight years compared with only 34% of patients who were BT101 negative.

The problem remains that, despite a variety of claims to the contrary,[8 9] there is no reliable diagnostic test for multiple sclerosis. The diagnosis remains essentially clinical, based on the findings of dissemination of lesions in the central nervous system in both space and time. In a patient with apparently isolated optic neuritis any signs suggestive of more widespread lesions in the central nervous system must suggest multiple sclerosis, and in view of this perhaps all patients with optic neuritis should have a full neurological assessment. The techniques of auditory evoked responses[10] and somatosensory evoked responses[11] may be able to detect even preclinical disseminated lesions in either the brain stem or the spinal cord, and these may perhaps prove to be useful in the assessment of patients who appear to have isolated optic neuritis.

At present, however, our approach to a patient with isolated optic neuritis should be optimistic. The short-term prognosis is excellent and it is by no means certain that the patient will develop multiple sclerosis. The value of pursuing extensive complex and expensive investigations to give an exact prediction seems dubious. If the results of the tests are negative then the eventual outcome still remains uncertain. The fact that they are positive is of little practical help either to the physician or to the patient as, at present, there is no effective prophylaxis or treatment for multiple sclerosis.

[1] Compston, D A S, *et al*, *Brain*, 1978, **101**, 495.
[2] Kurland, L T, *et al*, *Acta Neurologica Scandinavica*, 1966, **42**, suppl **19**, 157.
[3] Rischbieth, R H C, *Proceedings of the Australian Association of Neurology*, 1968, **5**, 573.
[4] Bradley, W G, and Whitty, C W M, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1968, **31**, 10.
[5] Hutchinson, W M, *Journal of Neurology, Neurosurgery, and Psychiatry*, 1976, **39**, 283.
[6] McAlpine, D, Lumsden, C E, and Acheson, E F, *Multiple Sclerosis. A Reappraisal*. Edinburgh, Livingstone, 1965.
[7] Thompson, E J, *et al*, *British Medical Journal*, 1979, **1**, 16.
[8] Field, E J, Shenton, B K, and Joyce, G, *British Medical Journal*, 1974, **1**, 412.
[9] Field, E J, Joyce, G, and Smith, B M, *Journal of Neurology*, 1977, **214**, 113.
[10] Robinson, K, and Rudge, P, *Brain*, 1977, **100**, 19.
[11] Small, D G, Matthews, W B, and Small, M, *Journal of the Neurological Sciences*, 1978, **35**, 211.

Prevention of homicide

The medical profession has a long-standing interest in suicide and attempted suicide. Though few doctors these days are naive enough to believe that deliberate self-harm is an exclusively medical matter, equally few would deny that the study of the problem—and active intervention in appropriate cases—is a legitimate part of health care. Yet a related form of aggression, homicide and attempted homicide, is rarely considered in the same way. Casualty officers or general practitioners confronted with a patient threatening to murder his or her spouse, lover, or child are often at a loss as to what appropriate action they should take; sometimes they are even unsure how to determine whether the threat warrants medical (as opposed to other professional) attention.

A recent paper from Australia by Neville Parker[1] highlights this anomaly by showing—as other studies[2-5] have shown—that many people who kill or try to kill are emotionally disturbed at the time. Parker estimated that about 10% of the murderous assaults could have been prevented had the disturbed individuals had closer access to consultant psychiatric services, police forces, and other community agencies. How he arrived at this figure is not clear, but he quoted two vivid examples. The first was a woman whose husband was threatening to kill her; no one took any notice of her warnings and she was shot dead. The second, another woman, became (irrationally) convinced that her husband was a child killer and repeatedly told the police so. They did not intervene, and she shot him with his own rifle.

While the first man may or may not have been psychiatrically disturbed, the poor woman deserved more help than she received. The frequency and seriousness of incidents of this kind impressed itself on the recent British Parliamentary Select Committee on Violence in Marriage,[6] which made several recommendations for changing the law to protect women in such circumstances. The Select Committee also proposed setting up 24-hour advisory services for women needing urgent help, so echoing the broader proposal made by the Butler Committee, which looked at the mentally abnormal offender[7] and endorsed a BMA proposal for 24-hour multidisciplinary consultation and advisory services for patients with personality disorders.

A few organisations go some way to providing these facilities. The Inner London Probation and Aftercare Service has a special walk-in advisory service—but only on working daytime basis—and the Maudsley Hospital in South London provides a round-the-clock emergency clinic. One of the few set-ups aimed specifically at preventing homicide is the special violence clinic in Maryland, in the USA, organised by Lion and his colleagues,[8] which invites those feeling violent and out of control to seek professional advice.

Unfortunately, we do not know how effective this type of clinic will prove, nor what are the links between psychiatric disorder (including psychosis) and violence. Nevertheless, mentally abnormal offenders, especially violent ones, present such problems to the psychiatric services in Britain at present that the Government has set aside funds for the provision of security units to contain them. Surely prevention should be given more priority. It must be at least as important to follow up the findings reported from Australia with more detailed studies and to set up experimental services such as that developed in Maryland. Only then can doctors evaluate the place for their skills and the extent to which their intervention can be effective.

[1] Parker, N, *Medical Journal of Australia*, 1979, **1**, 36.
[2] Morris, N, and Hawkins, C, *The Honest Politician's Guide to Crime Control*. Chicago, University of Chicago Press, 1969.
[3] Wolfgang, M E, *Patterns in Criminal Homicide*. New York, Wiley, 1958.
[4] Gibson, E, and Klein, S, *Murder 1957-68*. London, HMSO, 1969.
[5] Morris, T, and Blom-Cooper, L A, *A Calendar of Murder: Criminal Homicide in England Since 1957*. London, Joseph, 1964.
[6] House of Commons, Parliamentary Papers, *Report from the Select Committee on Violence in Marriage Volume 2*. London, HMSO, 1975.
[7] Home Office, DHSS, *Report of the Committee on Mentally Abnormal Offenders*. London, HMSO, 1975.
[8] Lion, J R, in *Violence and Victims*, ed S A Pasternack, p 71. New York, Wiley, 1975.