barrier providing further evidence of HIV infection within the central nervous system in patients infected with HIV.[5,6]

The neurological features of HIV infection may be classified as acute, subacute, and chronic. Three cases of acute encephalopathy,[7] one of acute meningitis,[4] and two of acute neuropathy[8] have been described—all when patients first developed antibodies to HIV. The three patients with acute encephalopathy had fever, general malaise, and changes of mood, and two had epileptiform seizures. But all these recovered almost completely within a week and have had no long term neurological sequelae. Both patients with acute neuropathy had facial palsy, which in one was bilateral and accompanied by sensory and motor impairment of the arms and legs. In each case gradual improvement took place over months.

The most common neurological syndrome has been called subacute encephalitis and occurs in about one third of patients with AIDS.[4,9,10] This condition is characterised in the early stages by subtle cognitive changes that may progress to serious dementia in several weeks or months. It may appear first as a confusional state together with fever or mild metabolic derangement. The cerebral dysfunction is accompanied by lethargy, loss of libido, and withdrawal that mimic psychological depression and may be difficult to distinguish from mood changes arising as a reaction to illness. Eventually patients may become bedridden and incontinent. Motor signs including generalised hyper-reflexia and increased tone may be seen, and an electroencephalogram commonly shows diffuse bilateral slowing.[11] Examination of the cerebrospinal fluid often shows a mild pleocytosis and a rise in protein concentration, a lowered glucose concentration, or both. Computed tomography usually shows dilated ventricles and prominent cortical sulci indicative of cerebral atrophy. Histopathological findings in advanced cases include ill defined pallor, multifocal perivascular rarefaction, and focal vacuolation of the white matter along with perivascular and parenchymal collections of macrophages and multinucleated giant cells.[10] A few affected individuals have disseminated cytomegalovirus infection of the brain. In the remaining cases no opportunistic infection is found to account for the changes, and the causative agent is believed to be HIV.

HIV has also been implicated as the cause of three mainly chronic or subacute neurological conditions—vacuolar myelopathy, peripheral neuropathy, and atypical aseptic meningitis. Vacuolar myelopathy was reported in 20 of 89 consecutive patients with AIDS on whom necropsies were performed.[12] Patients with this condition may complain of motor or sensory symptoms, or both. They may have bilateral or, less commonly, unilateral weakness of the legs, which may coincide with paraesthesiae. Seriously affected patients often have ataxia and incontinence. The peripheral neuropathy seen in patients with AIDs is a symmetrical sensorimotor neuropathy with painful dysaesthesiae and less commonly with weakness and distal atrophy.[13] It sometimes occurs before AIDS develops, but mononeuritis multiplex appears to be more common at this stage. Finally, an atypical aseptic meningitis may occur in people infected with HIV before AIDS develops.[13] They present with headache, fever, and meningeal signs but often also have atypical features such as recurrence, chronicity, cranial nerve involvement, and long tract signs. The fifth, seventh, and eighth cranial nerves are the most commonly affected. HIV has been isolated from the spinal cord, cerebrospinal fluid, and sural nerve of patients with AIDS suffering from these conditions.[4] Ho *et al* have also isolated the virus from the cerebrospinal fluid of two patients with chronic meningitis who had AIDS related complex rather than AIDS and from the cerebrospinal fluid of a previously healthy Haitian with dementia and psychosis.[4]

There is an urgent need to look out for, describe, and investigate the neurological aspects of infection with HIV. The average latent period of some types of HIV related neurological disease may be years. If so, neurological disease may be seen more often—even in patients who do not develop AIDS. The time consuming technique of psychometric testing may be necessary to pick up early and subtle changes, and such early recognition may prove vital so that, when it becomes available, antiviral treatment can be given. The number of people infected with HIV exceeds the number with AIDS by a factor of 50 to 100,[14] and these many people who are at risk of progressing to AIDS may also be at risk of developing HIV related neurological disease.

CHRISTOPHER A CARNE
Lecturer

MICHAEL W ADLER
Professor

Academic Department of Genitourinary Medicine,
Middlesex Hospital Medical School,
London W1 8AA

Correspondence to: Professor Adler.

1 Gajdusek DC, Amyx HL, Gibbs CJ, *et al*. Infection of chimpanzees by human T-lymphotropic retroviruses in brain and other tissues from AIDS patients. *Lancet* 1985;i:55-6.
2 Shaw GM, Harper ME, Hahn BH, *et al*. HTLV-III infection in brains of children and adults with AIDS encephalopathy. *Science* 1985;**227**:177-82.
3 Levy JA, Shimabukuro J, Hollander H, *et al*. Isolation of AIDS-associated retroviruses from cerebrospinal fluid and brain of patients with neurological symptoms. *Lancet* 1985;ii:586-8.
4 Ho DD, Rota TR, Schooley RT. Isolation of HTLV-III from cerebrospinal fluid and neural tissues of patients with neurologic syndromes related to the acquired immunodeficiency syndrome. *N Engl J Med* 1985;**313**:1493-7.
5 Resnick L, di Marzo-Veronese F, Schupback J, *et al*. Intra-blood-brain-barrier synthesis of HTLV-III specific IgG in patients with neurologic symptoms associated with AIDS or AIDS-related complex. *N Engl J Med* 1985;**313**:1498-504.
6 Goudsmit J, Wolters EC, Bakker M. Intrathecal synthesis of antibodies to HTLV-III in patients without AIDS or AIDS related complex. *Br Med J* 1986;**292**:1231-4.
7 Carne CA, Tedder RS, Smith A, *et al*. Acute encephalopathy coincident with seroconversion for anti-HTLV-III. *Lancet* 1985;ii:1206-8.
8 Piette AM, Tusseau F, Vignon D. Acute neuropathy coincident with seroconversion for anti LAV/HTLV III. *Lancet* 1986;i:852.
9 Snider WD, Simpson DM, Nielsen S. Neurological complications of acquired immune deficiency syndrome. Analysis of 50 patients. *Ann Neurol* 1983;**14**:403-18.
10 Price RW, Navia BA, Cho E-S. AIDS encephalopathy. *Neurologic Clinics* 1986;**4**:285-301.
11 Jordan BD, Navia BA, Petito C. Neurological syndromes complicating AIDS. *Front Radiat Ther Oncol* 1985;**19**:82-7.
12 Petito CK, Navia BA, Cho E-S, Jordan BD, George DC, Price RW. Vacuolar myelopathy pathologically resembling subacute combined degeneration in patients with the acquired immunodeficiency syndrome. *N Engl J Med* 1985;**312**:874-9.
13 Levy RM, Bredesen DE, Rosenblum ML. Neurological manifestations of the acquired immunodeficiency syndrome (AIDS): experience at UCSF and review of the literature. *J Neurosurg* 1985;**62**:474-95.
14 Curran JW, Meade Morgan W, Hardy AM, *et al*. The epidemiology of AIDS: current status and future prospects. *Science* 1985;**229**:1352-7.

Menière's syndrome: pathogenesis and treatment

Menière's syndrome consists of a combination of vertigo, fluctuating hearing loss, and tinnitus, often associated with a sensation of pressure or fullness in the ears. Deafness and tinnitus increase during episodes of vertigo with improvement afterwards, but hearing progressively declines. The disease is most common between 30 and 60 and rarely starts in childhood or old age.[1] Men and women are equally affected; three quarters of cases start unilaterally, but the numbers of bilateral cases gradually increase.[1,2]

The cause is endolymphatic hydrops—that is, an increase

Br Med J (Clin Res Ed): first published as 10.1136/bmj.293.6545.463 on 23 August 1986. Downloaded from http://www.bmj.com/ on 9 April 2024 by guest. Protected by copyright.

in the volume of the endolymph with distension of the membranous labyrinth.[3] Reisner's membrane may rupture leading to mixing of perilymph and endolymph.[3 4] Healing then occurs, but succeeding acute episodes are associated with further ruptures. The sensory elements of the ear atrophy.[3] These changes may be secondary to syphilis, Paget's disease of bone, or otosclerosis.[1 2] Delayed endolymphatic hydrops may follow a variety of insults to the inner ear.[5] The term Menière's disease should be reserved for idiopathic cases.

The hydrops results from disturbed endolymphatic homoeostasis, but how this happens is not clear. Some believe that abnormalities of the stria vascularis lead to overproduction of endolymph, while others blame blockage of the endolymphatic duct or disordered absorption in the endolymphatic sac. Alternatively, metabolites may accumulate in the endolymph causing an increase in its volume by osmosis. Blocking the endolymphatic duct or disrupting the sac in animals produces hydrops after a variable interval.[6-8] Some surgeons have reported during operations on the endolymphatic sac that its wall appears ischaemic in Menière's disease but not in other conditions.[9] Histological studies show perisacular fibrosis, reduced vascularity, and abnormalities of the epithelial elements of the sac.[3 9 10] Blockage of the endolymphatic duct has also been reported.[9 11]

About 5% of patients have a family history of the disease.[12] Vasomotor disturbances may be an underlying cause, a theory supported by the finding that a third of these patients also suffering from migraine.[12] Allergic problems have also been implicated, but, though food allergies are found in some patients, there is no overall increase in the prevalence of allergy in patients with Menière's disease compared with controls.[13] Viral infections and endocrine disturbances have also been suggested as causes.[1] Psychological factors may also be important: patients with the disease score highly for anxiety, obsessionality, and depression.

All treatments for Menière's disease are hard to assess because some patients experience long remissions whatever is done. Many patients may be managed medically. Surgery is usually reserved for those in whom medical treatment fails, but some surgeons advocate early conservative surgery to preserve hearing.[2] Vasodilators such as betahistine,[14] vestibular sedatives such as cinnarizine or prochlorperazine,[15] and diuretics such as hydrochlorothiazide[16] are all used, and medical "decompression" of the labyrinth may be attempted with a low salt diet. Vestibular function may be destroyed with streptomycin sulphate,[17] which may be particularly useful in bilateral Menière's disease as hearing may be preserved.[18]

The simplest surgical treatment practised is insertion of a ventilation tube into the tympanic membrane, but it is difficult to see why stabilisation of middle ear pressure should influence pathology in the inner ear.[1] Some surgical treatments that were once widely used—such as cervical sympathectomy[19] and destroying vestibular function with ultrasound[20]—have become less popular. Decompression of the endolymphatic sac is now one of the commonest surgical treatments.[21 22] It is an easy, safe operation that appears logical, but a trial against cortical mastoidectomy showed no difference in the results.[23]

Vertigo may be eliminated but hearing preserved by section of the vestibular nerve via either middle or posterior cranial fossa approaches.[24 25] These operations are effective, but risks and morbidity are greater than for other operations. Labyrinthectomy produces consistent improvement in vertigo but also complete deafness in the operated ear.[26] A translabyrinthine vestibular nerve section may also be performed.[2]

ROBERT MILLS

Senior Registrar,
Ear, Nose, and Throat Department,
King's College Hospital,
London SE5 9RS

1 Ludman H. Cochleovestibular diseases. In: Mawson SR, Ludman H. *Diseases of the ear*. London: Edward Arnold, 1979:490-8.
2 Morrison AW. Endolymphatic hydrops. In: *Management of sensorineural deafness*. London: Butterworths, 1975:145-74.
3 Hallpike CS, Cairns H. Observation of the pathology of Menière's syndrome. *Proceedings of the Royal Society of Medicine* 1938;**31**:1317-36.
4 Schuknecht HF. Pathophysiology of Menière's disease. *Am J Otol* 1984;5:526-7.
5 Schuknecht HF. Delayed endolymphatic hydrops. *Ann Otol Rhinol Laryngol* 1978;**87**:743-8.
6 Naito T. Experimental studies on Menière's disease. *Otorhinological Society of Japan (Tokyo)* 1970;**79**:754-6.
7 Kimura RS. Experimental blockage of the endolymphatic duct and sac and its effect on the inner ear of the Guinea pig. *Ann Otol Rhinol Laryngol* 1967;**76**:664-87.
8 Schuknecht HF, Norhtrop C, Igarashi M. Cochlear pathology after destruction of the endolymphatic sac in the cat. *Acta Otolaryngol (Stockh)* 1968;**65**:479-87.
9 Shambaugh GE, Clemis JP, Arenberg IK. Endolymphatic duct and sac in Menière's disease. *Arch Otolaryngol* 1969;**89**:816-25.
10 Arenberg IK, Marowitz WF, Shambaugh GE Jr. The role of the endolymphatic sac in the pathogenesis of endolymphatic hydrops in man. *Acta Otolaryngol (Stockh) (Suppl)* 1970;**275**: 1-49.
11 Schuknecht HF. Pathology of Menière's disease as it relates to sac and tac procedures. *Ann Otol Rhinol Laryngol* 1977;**86**:677-82.
12 Morrison AW. Menière's disease. *Journal of the Royal Society of Medicine* 1981;**74**:183-9.
13 Moffatt DA, Booth JB, Morrison AW. Metabolic investigations in Menière's disease. *J Laryngol Otol* 1979;**93**:545-56.
14 Wilmot TJ. The effect of betahistine hydrochloride in Menière's disease. *Acta Otolaryngol (Stockh) (Suppl)* 1970;**305**:18-21.
15 Hinchcliffe R. Review of treatment of Menière's disease. *Acta Otolaryngol (Stockh) (Suppl)* 1970;**305**:10-7.
16 Klockhoff I, Lindbaum U. Menière's disease and hydrochlorthiazide: a critical analysis of symptoms and therapeutic effects. *Acta Otolaryngol (Stockh)* 1967;**63**:347-65.
17 Schuknecht HF. Ablation therapy for Menière's disease. *Acta Otolaryngol (Stockh) (Suppl)* 1957;**32**:14-32.
18 Graham MD, Kemink JL. Titration streptomycin therapy for bilateral Menière's disease: a progress report. *Am J Otol* 1984;5:534-5.
19 Passe ERG, Seymour JS. Menière's syndrome: successful treatment by surgery on the sympathetic. *Br Med J* 1948;ii:812-6.
20 Angell-James J. Menière's disease: The present status of ultrasonic therapy. *Arch Otolaryngol* 1969;**89**:95-7.
21 Portmann G. Vertigo: Surgical treatment by opening the saccus endolymphaticus. *Arch Otolaryngol* 1927;**6**:309-19.
22 House WF. Subarachnoid shunt for drainage of hydrops: a preliminary report. *Laryngoscope* 1962;**72**:713-29.
23 Thomsen J, Bretlau P, Tos M, Johnsen NJ. Placebo effect of surgery in Menière's disease. *Arch Otolaryngol* 1981;**107**:271-81.
24 Fisch U. Vestibular and cochlear neurectomy. *Transactions of the American Academy of Ophthalmology and Otolaryngology* 1974;**78**:1450-501.
25 Silverstein H, Norell H. Retrolabyrinthine total vestibular neurectomy. *Otolaryngol Head Neck Surg* 1982;**90**:778-82.
26 Cawthorne T. Some recent work on the investigation and treatment of Menière's disease. *Proceedings of the Royal Society of Medicine* 1943;**36**:541-6.

Immunity and depression

There are good reasons for studying immunity in depression. Stress, which is closely associated with depression, affects immune responses, and its physiological consequences are now being defined more precisely.[1] Corticosteroids mediate some of the effects of stress on immune function, but other hormones and peptides synthesised by the central nervous system, such as β endorphin, are also important. In addition, lymphocyte responses to mitogen stimulation in vitro are depressed after bereavement, and similarly impaired responses and lymphopenia have been recorded in medical students during their examinations at Ohio State University, an institute not especially noted for academic harshness.[2 3]

More directly, physiological changes that might affect immune responses have been noted in depressed patients. The noradrenergic system seems to be abnormally activated, and this seems to induce excessive cortisol secretion. Rubin *et al* have shown that plasma concentrations of 3-methoxy-4-hydroxyphenylglycol are raised in depressed patients, sug-

Br Med J (Clin Res Ed): first published as 10.1136/bmj.293.6545.463 on 23 August 1986. Downloaded from http://www.bmj.com/ on 9 April 2024 by guest. Protected by copyright.