impairments of memory and concentration, along with mental slowing. This cognitive decline, which is often accompanied by motor disorders, has been termed AIDS dementia complex (ADC), or more recently HIV-1-associated cognitive/motor complex. Most patients with ADC are severely immunosuppressed and have already been diagnosed with AIDS. Although the pathogenesis of the syndrome is only partly understood, a large body of evidence points to a central role of HIV-1 itself. This notion is also supported by the clinical efficacy of antiretroviral treatment.

Shortly after the introduction of zidovudine in the late 1980s, there was a major decline in the incidence of ADC; ADC has become a rare disease in patients on continued zidovudine treatment. In addition to its prophylactic efficacy, zidovudine has therapeutic efficacy in patients with ADC. CSF-markers of central nervous system HIV-1 infection may decline with zidovudine use, and the frequency of HIV-1-related neuropathological abnormalities has been reduced by zidovudine. An increase in frequency of ADC has lately been observed in a group of HIV-1-infected individuals in London, among whom the number of patients taking zidovudine diminished in the past few years (J Catalan, personal communication). From all these data one can conclude that zidovudine is a central nervous system protective drug in the treatment of HIV-1.

What about the neuroprotective efficacy of other nucleoside analogues? Didanosine improved neurocognitive functioning in a small group of children with AIDS, but it did not prevent the development of ADC in adults with advanced HIV-1 infection. Clinical neurological data on patients receiving zalcitabine, lamivudine, stavudine, and protease-inhibitors are not available yet. CSF penetration of these drugs varies widely, with CSF/plasma ratios of 0.06 for zidovudine, 0.2 for didanosine and zalcitabine, 0.06 for lamivudine, and 0.4 for stavudine. Although CSF penetration cannot be equated with clinical efficacy, drugs that do not penetrate into the CNS are unlikely to be very effective in preventing neurological deterioration.

Additional neuroprotection might be achieved by drugs that do not inhibit viral replication but interfere with other steps in the pathogenesis of ADC. Thus pentoxifylline inhibits production and effects of TNF-α, memantine blocks the action of toxins acting at the N-methyl-D-aspartate receptor, nimodipine is a calcium-channel blocker, and peptide-T is a neurotrophic peptide. Several of these drugs are on the point of entering clinical trials. A small unpublished study (ACTG Clinical Trial Group [ACTG] 162) with nimodipine failed to show clinical efficacy.

Based on preliminary analyses of ACTG 175 and Delta, presented recently in San Francisco and Copenhagen, respectively, one could envisage combined regimens becoming standard treatment in HIV-1 infection. To prevent the development of ADC, combination regimens should include at least one neuroprotective drug. All the evidence strongly favours the use of zidovudine for this purpose. However, zidovudine-resistant CSF and brain isolates have already been reported, and some patients are zidovudine intolerant. Consequently, more drugs are needed, preferably both antiretrovirals and adjunctive secondary treatments. Effort should be put into the development of these drugs, followed by early CSF-pharmacokinetic studies and clinical trials with potential neuroprotective compounds in patients with ADC. Neurological monitoring for early signs of ADC in patients participating in ongoing and future clinical trials with antiretrovirals will provide us with crucial clinical data as well. In this way, we remain able to treat and prevent one of the most distressing complications of HIV-1 infection.

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Exit trans fatty acids

From now on Dutch margarine manufacturers will state the trans fatty acid content of their products on the label. In addition, the trans content of margarines and spreads will be reduced to less than 5%, and for many products it may drop below 1% within the next year. These innovations will affect other countries as well, although it is not yet clear what will happen in the USA. Certain US manufacturers sell effectively trans-free spreads and some product reformulation is occurring; however, the majority view of the US industry is that allegations against trans fats are exaggerated.
Small amounts of trans fatty acids are present in butter and cheese and in the body fat of ruminants but most of the trans content of foods arises during the hardening of oils. This hardening process has been a mainstay of the edible fats industry ever since it started to produce margarine as a replacement for butter. Butter consists largely of saturated fatty acids, which are hard; the replacement thus needed to be firm, but the oils available were mostly rich in cis-unsaturated fatty acids and fluid. The solution was found in partial hardening or hydrogenation; this converts part of the cis-unsaturates into higher melting point saturated and trans-unsaturated fatty acids. Partial hydrogenation spurred the growth of an industry which now provides much of the visible and invisible fats that we eat, including those in many baked goods and fast foods.

Although health effects of trans fatty acids were occasionally questioned, extensive toxicological testing uncovered no adverse effects. Discussion started in 1990 when trans fatty acids were reported to raise serum low-density lipoprotein (LDL) and lower high-density lipoprotein (HDL) cholesterol concentrations in volunteers. Subsequent studies confirmed the effect on LDL and, though less consistently, on HDL. Trans fatty acids also raise plasma triglyceride and lipoprotein(a) concentrations, a hereditary risk factor for cardiovascular disease that is otherwise little affected by diet. Prospective studies also showed associations between trans fatty acid intake and subsequent coronary disease. In such studies a high intake of trans could be merely an indicator of an unhealthy lifestyle; however, the rise in LDL and fall in HDL cholesterol seen in metabolic trials make a cause-and-effect relation credible. Some epidemiological studies found no association, but confidence intervals were wide enough to embrace the increase in coronary risk seen in the US investigations.

As a result of the changes in the composition of food fats now underway, the average Dutchman will be eating 4 g less of trans fatty acids per day than he or she did 10–15 years ago. These 4 g will be replaced by 2 g of saturated fat, 1 g of stearic acid (also saturated, but with little effect on LDL), and 1 g of cis-unsaturated fat. Together this should produce a fall in LDL cholesterol of about 0.05 mmol/L, which should lower coronary risk by 2% or so. In addition, HDL should rise by 0.02 mmol/L, so the total fall in coronary disease incidence could reach 5% even without counting the effect on lipoprotein(a).

Lifestyle changes tend to benefit the well-educated and wealthy more than the poor, and to widen the health gap between the social classes; this one, however, may especially benefit the poor because they may be major consumers of cheap fats and fast foods. Producers of fats and oils may be in for some turmoil, but consumers should be the winners; they may gain a modest rise in HDL and drop in LDL without having to lift a finger.


Learning from stories—The Lancet’s Case Reports

Clinicians learn from anecdotes—stories they heard at medical school, stories they tell each other, and stories their patients tell them. This is an efficient way to grasp new knowledge—even the most obscure hints and warnings can be made memorable if tagged to real people and actual events. This week we start a section of peer-reviewed Case Reports, an opportunity for clinicians to relay the sort of clinical anecdote they might tell colleagues during a morning coffee break. We expect younger clinicians, whose daily involvement with patient care is greater than that of their chiefs, to be an especially fertile source of good stories.

There are, however, several rules to be observed. The report occupies one page, has a table or figure, and has no more than five references. This leaves about 600 words of text, to be in three paragraphs: case presentation; investigations, treatment, and outcome; and discussion. There should be no more than four authors, one of whom was in clinical charge of the patient when the events took place.

Potential authors must ask themselves: why do we wish to tell Lancet readers about this case? Our answer is that your report must have a striking message: a description of a new treatment, adverse effect of medication, evidence that might suggest a new mechanism for a disease process, or a new intervention. The message may not be new but it should be of sufficient practical importance to bear repeating. Case Reports are designed to provide readers concerned more with patient care than laboratory research an opportunity to display the rich variety of clinical medicine. We look forward to your response.

John Bignall, Richard Horton
The Lancet, London, UK