studying a single class depends on how these substances interact to impair behavior. If their adverse effects are additive, then eliminating even a single class should improve behavior measurably (but not normalize it). The effects of the substances might be redundant, however: any one class impairs behavior maximally whether or not others are also ingested, and only if all are removed does behavior improve. If so, we can explain the positive anecdotes: suspect substances sometimes do impair behavior, specifically when the other detrimental substances happen not to have been consumed recently. We can also explain the negative controlled studies of diet and challenge: eliminating a single class from the diet and reintroducing it has limited effect.

Whether nutrients can substantially influence behavior remains uncertain. But before discounting this possibility, one could investigate the redundancy model for multiple dietary sensitivities. One would begin with an elimination diet[4,5] and then reintroduce the suspect substances serially, using placebo as control. The findings to date from elimination diets[4,5] are sufficiently suggestive to justify such further research.

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MORE ON LORENZO'S OIL

To the Editor: The use of Lorenzo's oil in patients with adrenomyeloneuropathy, the form of adrenoleukodystrophy that occurs in adults, has recently been reported by Aubourg et al. (Sept. 9 issue),[1] with an editorial by Rizzo.[2] In contrast to rapidly progressive adrenoleukodystrophy in children, which affects the brain, adrenomyeloneuropathy develops at a slower rate and involves primarily the spinal cord and the peripheral nervous system. Although they present data on the inability of the oil to stop the progression of adrenomyeloneuropathy, Aubourg et al. make no reference to its potential for preventing the onset of adrenoleukodystrophy and, by implication, that of adrenomyeloneuropathy, nor does Rizzo mention this possibility. Indeed, the article and editorial portray Lorenzo's oil as a concoction totally useless in combating the adrenoleukodystrophy–adrenomyeloneuropathy complex. This portrayal is inaccurate.

There is a consensus among researchers studying adrenoleukodystrophy and adrenomyeloneuropathy that Lorenzo's oil almost invariably eliminates the abnormal accumulation of very-long-chain saturated fatty acids, the biochemical hallmark of adrenoleukodystrophy. As for its clinical effects, a world authority on adrenoleukodystrophy, Dr. Hugo Moser, believes that it either prevents the onset of the disease or greatly reduces its severity in boys who have the biochemical defect of adrenoleukodystrophy but are still neurologically intact.[3] If these boys are untreated, adrenoleukodystrophy will develop in 48 percent and adrenomyeloneuropathy in 25 percent; the remaining 27 percent will either have hybrid forms of the disease or, in some rare cases, escape it altogether.

A trial conducted by Moser et al. and sponsored by the National Institutes of Health and the Food and Drug Administration is now in its fourth year; it has studied 86 children with presymptomatic adrenoleukodystrophy, including 50 boys who have been treated for more than 12 months. During the period of the study, the rate of occurrence of adrenoleukodystrophy in this group of children has been strikingly lower than that suggested by trends among historical controls. Of the 50 boys, only 4 (8 percent) have had full-blown symptoms of cerebral childhood adrenoleukodystrophy.[3]

The indiscriminately negative account of the effects of Lorenzo's oil in a prestigious medical journal may induce parents not to start treatment with the oil in their children with presymptomatic adrenoleukodystrophy, or to stop the treatment if it has already begun. If this happens, symptoms will develop in children "destined" to have childhood adrenoleukodystrophy, and they will die. The "lucky" ones, who escape adrenoleukodystrophy, will have adrenomyeloneuropathy (or some hybrid form of the disease) and will be incapacitated for most of their adult lives. In sum, the misinformation engendered by the article and editorial has the potential to cause innumerable tragedies that could be averted by a simple change in dietary habit.

As for the negative conclusions of Aubourg et al. about the effects of Lorenzo's oil in patients who already have symptomatic adrenomyeloneuropathy, these are a bit perplexing. The authors' study was too short (two years) and involved too few patients (14 men) to provide reliable data. If, however, future, better-designed studies also conclude that Lorenzo's oil does not work after the symptoms have started, this would not be surprising. Most researchers believe that adrenoleukodystrophy has an autoimmune component, probably triggered by the abnormal accumulation of very-long-chain fatty acids. It is possible that the autoimmune response and accompanying inflammation persist even after Lorenzo's oil has eliminated this fatty-acid abnormality.

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1. Aubourg P, Adamsbaum C, Lavallard-Rousseau M-C, et al. A two-year trial of oleic and erucic acids ("Lorenzo's oil") as treatment for adrenomyeloneuropathy. N Engl J Med 1993;329:745-52.
2. Rizzo WB. Lorenzo's oil — hope and disappointment. N Engl J Med 1993;329:801-2.
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The authors reply:

To the Editor: We agree with Michaela and Augusto Odone, Lorenzo's parents, that no therapeutic efforts should be interrupted in patients with adrenoleukodystrophy as long as the treatment could still prove to have efficacy. Our report was not intended to discourage participation in well-designed clinical trials. We support additional studies of the potential preventive effects of the oil; we enrolled 21 patients with presymptomatic adrenoleukodystrophy in a trial of the oil four years ago. The long-term results, as well as those of the study by Moser et al., are eagerly awaited.

It is clear, however, that the dietary intervention has no

beneficial effects in patients with symptomatic adrenoleukodystrophy.[1,2] We need other approaches for these patients, who are prone to rapid deterioration of brain function. Allogeneic transplantation of hematopoietic cells can reverse or stabilize brain demyelination.[3] On the basis of these results and our recent cloning of the adrenoleukodystrophy gene,[4] gene transfer to the patient's own hematopoietic cells appears to be an approach with promise.

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To the Editor: The finding of Aubourg et al. that dietary therapy with monounsaturated fatty acids (Lorenzo's oil) fails to help patients with adrenomyeloneuropathy is supported by other reports of its clinical ineffectiveness in patients in whom neurologic symptoms have already developed.[1,2] To date, no study has yet demonstrated that Lorenzo's oil has unequivocal clinical efficacy in patients with childhood adrenoleukodystrophy or adrenomyeloneuropathy, despite its favorable biochemical effect of lowering plasma levels of very-long-chain fatty acids. The failure of Lorenzo's oil in patients with adrenoleukodystrophy is particularly disappointing, because these patients have milder neurologic symptoms and apparently lack the autoimmune reaction to myelin that is typically seen in childhood adrenoleukodystrophy.

The Odones raise an important issue, however, concerning the potential benefit of Lorenzo's oil in boys with presymptomatic adrenoleukodystrophy. As I mentioned in my editorial, clinical studies are in progress to determine whether dietary therapy will prevent or delay the onset of neurologic symptoms in these boys. The interim report by Moser et al.[3] of an open clinical trial of Lorenzo's oil is tentatively encouraging, but that study is ongoing and the results are not yet definitive with respect to efficacy. Nevertheless, because of the devastating nature of adrenoleukodystrophy and the relative safety of Lorenzo's oil, there is an overwhelming consensus in favor of recommending that this therapy be used in all male patients with presymptomatic adrenoleukodystrophy until clinical trials establish whether it is efficacious.

The failure of Lorenzo's oil against symptomatic adrenoleukodystrophy and adrenomyeloneuropathy does not negate the possibility that it could prevent or delay the onset of the disease in boys who do not yet have symptoms. There are other examples of inborn errors of metabolism, such as phenylketonuria, that respond to therapy only when it is started before the onset of symptoms. It is the hope of patients, their families, and all physicians that such will prove to be the case with adrenoleukodystrophy and that this tragic disease can be prevented.

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HIV-1 IN NEWBORNS

To the Editor: The study by Blanche et al. (Feb. 3 issue)[1] confirms the bimodal pattern of AIDS in newborns and shows a clear correlation between the survival of the infant and the severity of disease in the mother. The authors hypothesize that advanced maternal disease could result in transmission of a larger viral inoculum, increased pathogenicity of the viral strains, or earlier transmission in utero. However, none of these explain how infection of newborns with human immunodeficiency virus type 1 (HIV-1) can evolve into AIDS over a few months.

Analysis of HIV-1–specific T-cell responses of newborns shows that fetal T cells can be primed in utero to HIV-1 determinants.[2] HIV-1–infected children were, however, found only among those lacking HIV-1 *env*–specific T-cell activity, suggesting that HIV-1–specific immunity can be protective in newborns. Besides decreasing the risk of infection, T-cell immunity seems to reduce the spread or the pathogenicity of HIV-1. Rapidly progressive AIDS in newborns correlates with an absence of HIV-1–specific humoral[3] and cellular[4] immunity. In the patients described, virtually no HIV-1–specific antibodies and lymphocytes were detectable, and immune responses specific for other antigens were functional. This is in accordance with the hypothesis that HIV-1–specific immunologic tolerance may directly result in rapid progression of disease.[3]

Forty years ago, Billingham et al. showed that exposure to antigens during early embryonic life profoundly influences the immune system.[5] Antigens present in the fetal thymus during early development of the organ are regarded as self-antigens, and the naive immune system learns not to respond against them. This phenomenon is called (neonatal) immunologic tolerance.

Advanced maternal disease could result in early transmission in utero, possibly of a large inoculum or of more virulent strains able to infect the fetal thymus and subsequently induce specific immunologic tolerance to HIV-1 determinants. The condition of infants rendered unable to mount efficient HIV-1–specific immune responses may progress rapidly toward AIDS, whereas functional specific responses to HIV-1 antigens resulting from later in utero or perinatal contact with viral antigens may, by contrast, prevent or slow disease progression. Future applications of immune-based therapy require precise assessments of infants' immune responses to HIV-1 antigens. For the time being, antiviral therapy started early during gestation (in the first trimester) may be able to decrease the viral load in the mother and reduce the risk of very early transmission to the fetus.

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