

Pernicious treatment

Fred S. Rosen

Lorenzo's Oil. A film directed by George Miller. Written by Nick Enright and George Miller. Released by Universal: 1993.

In 1912, when the Tsarevich of Russia had a nearly fatal haemorrhage at the imperial hunting lodge at Spala, his royal and distraught parents summoned Rasputin for consolation. The Holy One wired back from Siberia to the Tsarina and advised her to discharge the doctors. At the time, that was probably good advice, for there was nothing that medicine had to offer in the treatment of haemophilia. There was only the dimmest notion of the X-linked inheritance of the disease, although the Tsarina certainly knew that her brother and her maternal uncle, the Duke of Albany, had died from this bleeding disorder and that her sister, the Princess of Prussia, had two affected sons.

Some 70 years later, the Odone, less royal, equally distraught and more intelligent and hysterical than the Romanovs, discovered that their only male child had a fatal X-linked disease, adrenoleukodystrophy (ALD), for which modern medicine had no therapy. It was known that the disease is caused by an accumulation of very-long-chain fatty acids, resulting in progressive demyelination of the central nervous system and adrenal insufficiency. Michaela and Augusto Odone set out to find a dietary cure for their son, who was neurologically deteriorating quickly, and this is the subject of *Lorenzo's Oil*, which opened in the United States last month and is released in the United Kingdom tomorrow. The film is brilliantly produced and the race for a 'cure' is acted out with extraordinary virtuosity. I haven't experienced such palpable suspense since Truman Capote's *In Cold Blood* appeared serially in *The New Yorker*. In the course of the film, the audience learns about X-linked autosomal recessive inheritance and fatty-acid metabolism in a graphic and comprehensible manner.

Unfortunately, this seductive film comes at a time when the anti-intellectual populism of Haider, LePen, Perot and others of their ilk has created a receptive audience for an anti-establishment diatribe. We learn in the course of two hours that nurses are heartless, physicians pompous fools and parent support groups as mindless as a herd of sheep. Michaela and Augusto Odone to the rescue! They go to the library and learn about fatty-acid metabolism, sponsor a scientific conference and come up with a solution when they

find that the fat-free diet recommended by the insouciant doctors is doing their child no good. First they pump in the triglyceride of oleic acid via a nasogastric tube to Joan Sutherland's rendition of *Casta diva* from *Norma* as background music. And later, when they find the true grail — erucic acid triglyceride from rapeseed oil — the childless, hetero-

symptoms does not seem convincingly to alter the onset of the disease. There is a complex array of phenotypes in ALD and the penetrance of the disease may result from so far unidentified autosomal genes. *Lorenzo's Oil* may be a cinematic triumph, but theatrical truth and scientific truth are not necessarily miscible.

Between the Romanovs and the Odone, concerned parents have often banded together to seek medical solutions for their afflicted children. Frequently they have acted effectively and expeditiously while the usual channels of the funding authorities have dragged their heels. The Muscular Dystrophy Association, which is capable of the



Slippery business — Nick Nolte as Augusto Odone in *Lorenzo's Oil*.

zygous maternal aunt of the propositus swallows a test meal of yet another triglyceride to the strains of *Una furtiva lagrima* from *L'Elisir d'Amore*. By the end of the film, when a chorus of children on the screen tell us they are all taking Lorenzo's oil, and a toll-free number is flashed up, you may be tempted to rush out and sprinkle your next green salad with this concoction. Before you do, beware.

The US Food and Drug Administration, roused by the Odone from its customary torpor, quickly approved Lorenzo's oil. Hugo Moser, one of the authors of the paper on page 726 of this issue, reporting the identification of a putative X-linked ALD gene (see also News and Views on page 682), will soon report that some 40 per cent of patients with ALD develop thrombocytopenia from this treatment, as the triglyceride disrupts the platelet membrane. Furthermore, feeding the stuff to boys with the ALD defect before the onset of

most flamboyant public relations, supported Dr Louis Kunkel in his successful effort to clone the dystrophin gene before the National Institutes of Health recognized the importance of his work. There are other compelling examples of this sort such as to encourage individual and group initiatives to seek solutions to biomedical problems. Indeed, the paper on page 726 cites such private funding sources in the quest for the ALD gene. A surprising answer to the underlying defect in ALD has been uncovered and it may in the long run provide a strategy for gene therapy in this distressing disorder. Augusto Odone, with his spoor of countless cigarette butts, and his monomaniacal wife, Michaela, have not set a good example for biomedical progress. That is why this entrancing film is, at base, pernicious. □

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