Lesson Plan – The Development of Lorenzo’s Oil, Strange Twists of Fate, and the Scientific Method

Objective: This lesson provides a mental exercise in applying the scientific method and developing hypotheses in an interesting real world situation. The lesson uses the fact that the effect of Lorenzo’s Oil on Lorenzo Odone was an anomaly that could not be consistently repeated in other boys with ALD. It was only by luck and perseverance that the Oil was found to be helpful to boys who were quite different than Lorenzo.

Grade Level: Grades 8 – 12.

Time: (Based on a 55 minute class period) This lesson plan can take between one and six class periods, depending upon how much is assigned to be done at home. The sections of this lesson plan are:

-- Lecture/introduction to the movie: 25 minutes; alternatively the Introductory Concepts Handout can be sent home to be read before seeing the film;
-- Watch the film: 135 minutes; alternatively the movie can be watched at home in groups, with families, or as a class event after school (or any combination);
-- Q and A based lecture: 80 minutes; (this is the core of the lesson plan);
-- Comprehension Test/Homework Assignment: 45 minutes if used as a test; no class time if used as a homework assignment or take home test.

TWM recommends: using one half class period to introduce (or review) the introductory concepts; have students watch the film as an event after school and, for students who cannot attend, a week to watch the film after school in groups or with their families; use one and one half class periods for the Q and A based lecture; and give the last assignment as homework or a take home test. In this way the unit will take only 2 class periods.

Curriculum Standards for the 11 most populous states:

California: Grade 8 – Standard 9; Grades 9 – 12: Investigation and Experimentation: 1.c, d, f & g.

Texas: Eighth Grade Science: §§ 112.24 (c) (2): (A), (C) & (D); (c) (3)(A); High School: §§ 112.42 – Integrated Physics and Chemistry: (c) (2): (A), (C) & (D); (c) (3)(A); 112.43 – Biology: (c) (2): (A), (C) & (D); (c) (3)(A) & (E); 112.44 – Environmental Systems: (c) (2): (A), (C) & (D); (c) (3)(A); 112.46 – Aquatic Science: (c)(2): (A), (C) & (D); (c) (3)(A);


Florida: The Nature of Science SC.H.1.4

Illinois: http://www.isbe.net/iils/science/standards.htm Goal 11: Middle/Jr. High School: 11.A.3a, 3d, 3e - 3g; 11.B.3a; 11; Early High School: 11.A.4a, 4e; Late High School: 11.A.5a; 11.A.5c;
Pennsylvania: Science and Technology: 3.2 Inquiry and Design: 3.2.10: (A) – (C); 3.2.12: (B) & (C);

Ohio: Grade: 10: Scientific Ways of Knowing; Grade 11: Scientific Ways of Knowing & Scientific Inquiry; Grade 12: Scientific Inquiry;

Michigan: Middle School: Strand I: Constructing New Scientific Knowledge: 1, 2 & 5; Strand II: Reflecting on Scientific Knowledge: 1, 2 & 3; High School: Strand I: Constructing New Scientific Knowledge: 1, 2 & 4, Strand II: Reflecting on Scientific Knowledge: 1;

New Jersey: Standard 5.1: Scientific Processes (A-C for all grades)

Georgia: 8th Grade Science: Habits of Mind: S8CS 1 & 5; The Nature of Science: S8CS 7 – 9; High School Biology: Habits of Mind: SCSh 1, 3, 5 & 6; The Nature of Science: SCSh 7 & 8;

North Carolina: Science Grade 8: Competency Goal 1: 1.01, 1.04, 1.05, 1.07 & 1.08; Grades 9 – 12: Biology: Competency Goal 1: Scientific Inquiry - 1.01 - 1.05; AP Biology: Competency Goal 1: Scientific Inquiry – 1.01 – 1.05.

Materials: The Introductory Concepts Handout, Neuron Sketch and Diagrams of Four Fatty Acids can be printed and given to the class before they see the film. Alternatively, they can be projected onto a screen and reviewed with the class. A black or white board will allow students to write the several hypotheses. A computer with a link to a projector on which the hypotheses can be typed will serve the same purpose. (For the hypotheses listed in a printable or viewable form see Possible Hypotheses in the Discovery of Lorenzo’s Oil.) Click here for a 45 minute test on these materials.

This lesson plan assumes that the class will watch the movie Lorenzo’s Oil and is familiar with the four step definition of the scientific method. A brief description of the scientific method can be found in the Helpful Background Section of the Learning Guide to “Lorenzo’s Oil.”

LESSON PLAN

Lecture Notes for Introductory Concepts -- 25 minutes
(An alternative to this lecture is to give students the Introductory Concepts Handout, Neuron Sketch and Diagrams of Four Fatty Acids to be read at home.)

Introduction:
-- We will be watching “Lorenzo’s Oil”;
-- about family with wonderful five year old by who gets ALD
-- rare genetic disease causes deterioration of myelin sheath;
-- myelin white matter of brain; insulation around nerve cells; See diagram.
-- no cure; no treatment;
-- parents go on a hunt to find a cure;
-- to help understand the movie, we need to understand a few concepts.

Saturated fats --
-- we’ve all heard of them;
-- same fats that cause plaque to build up and clog arteries; cause heart attacks;
-- top two in Diagrams of Four Fatty Acids;
-- hydrocarbon chain tail -- (H-C-H) links;
-- Carbon atoms need four electrons to complete outermost valence shell of 8;
-- Hydrogen need one electron to complete outermost valence shell of 2;
-- carbon atoms share one electron with each of the carbon atoms on either side in the chain and one with each of the two hydrogen atoms in their link.

Unsaturated fats
-- good fats; don’t clog arteries;
-- bottom two on Diagram;
-- have a double bond between carbon atoms in hydrocarbon chain;
-- double bond causes kinking in the chain; carbons share two electrons with other carbon atoms next to them in the chain; don’t need the electron from the hydrogen atom to fill their valence shell.

VLCSFAs
-- Very Long Chain Saturated Fatty Acids;
-- saturated fats with very long hydrocarbon chain in the tail, see Diagram;
-- children with ALD have high levels of VLCSFAs, Lignoceric Acid (C24:0) and Cerotic Acid (C26:0).

VLCUFAs
-- Very Long Chain Unsaturated Fatty Acids;
-- apparently not harmful.

Enzyme
-- biochemical catalyst produced by an organism;
-- causes a specific chemical reaction involving molecules of other substances without the enzyme itself being destroyed or changed;
-- Sometimes enzymes work in groups;
-- saliva contains enzymes, some convert complex carbohydrates like starch to simple sugars such as glucose.

The body gets VLCSFAs in two ways: food and it makes its own.

Biosynthesis
-- production of biological compounds by chemical reactions that occur within living cells;
**Endoplasmic reticulum**
-- highly convoluted membrane within cells;
-- biosynthesis of VLCSFAs and VLCUSFAs occurs here;
-- enzymes add carbohydrate links to chains of fatty acids.

**How the body regulates VLCSFA levels.**

**Peroxisomes**
-- are microbodies (organelles) within cells;
-- oxidize and break down various proteins and lipids;
-- peroxisomes in liver cells oxidize and degrade excess VLCSFAs.

**Adrenoleukodystrophy (ALD)**
-- rare recessive X linked genetic disease;
-- body does not make the protein that transports excess VLCSFAs into the peroxisomes to be degraded into harmless substances through oxidation;
-- VLCSFAs build up in the body.
-- only 35% of boys with ALD genetic defect develop the aggressive early childhood form of the disease; 65% of boys with ALD genetic defect develop usually milder symptoms later in life.

**Oleic acid** – See Diagrams of Four Fatty Acids
-- monounsaturated fatty acid found in olive oil, almonds, angelica, and other foods and herbs;
-- monounsaturated means one double bond between carbon atoms in tail;
-- oleic acid contains 18 carbon atoms.

**Erucic acid** -- See Diagrams of Four Fatty Acids
-- 22 carbon monounsaturated fatty acid;
-- present in rapeseed oil used as food in Orient;
-- causes plaque to build up in the arteries of rats and they die.

**Competitive inhibition**
-- biological process in which more than one substance is competing for the active sites of one enzyme; the substance that has a higher concentration will have more access to the enzyme sites and more of that substance will be modified by the enzyme;
-- resulting molecules are different because the molecules on which the changes were made were different;
-- example of 100 people in a line to get a limited number of vaccinations; some people are adults and others are children; if we bring in hundreds and thousands of children and they all line up together, then very few adults will be vaccinated;
-- If only a limited number of enzyme sites available, scientist could change how much of one compound is changed by giving the patient more of the other compound so that the first compound would be crowded out and less of it would...
get to the enzyme site. In effect the two types of molecules are in competition with each other.

**Hypothesis**
-- tentative explanation of a causal connection or of a fact in the natural world;
-- based on educated guesses;
-- must be able to be tested through experiment or observation;
-- often state a cause and effect relationship;
-- at the beginning of this movie scientists had made an educated guess that the enzyme that added hydrocarbon links to the chains in VLCSFAs in the endoplasmic reticulum worked only on saturated fats and that a separate enzyme added hydrocarbon links to unsaturated fats to make VLCUFAs;
-- if hypothesis true competitive inhibition would not work to limit biosynthesis of VLCFAs;
-- another example of a hypothesis: the reduction of VLCSFAs in a person’s diet will cause their VLCSFA level to decrease.

**Independent Variable/Dependent Variable**
-- in a hypothesis the variable changed by scientist = the independent variable;
-- variable the scientist does not change = dependent variable.
-- in our example, independent variable is diet with reduced VLCSFAs; dependent variable is the people on whom the experiment is conducted.

**Anomaly**
-- in scientific research, an unusual result which appears to be specific to only one or a few subjects;
-- if a person gets a unique and peculiar reaction to a medicine, he is said to be an anomaly.

**Anecdotal evidence**
-- evidence collected in circumstances in which there were no scientific controls present. Anecdotal evidence is of very limited value to scientists.

**Control group**
-- population which has not been changed in the experiment; in other words, the group for which the independent variable was not changed;
-- purpose: to make sure it was the change in the independent variable that caused any resulting change;
-- an example of a control group would be, in our hypothesis of testing whether lowering VLCSFAs in diet would reduce VLCSFA levels in the body, a control group would be a group of ALD patients whose diet was not changed.

**Symposium**
-- meeting in which the participants exchange information and theories.
-- hundreds every year where scientists travel to meet, present research findings and talk;
Clinical trial

-- medical research trying out new treatments on people;
-- strict ethical guidelines for clinical trials;
-- need to be careful not to hurt people;
-- ordinarily don’t try on people what hurts animals;
-- must be reviewed and approved by various committees of scientists before they can be started.

Question and Answer Based Lecture for
After the Class Has Seen the Movie – 80 Minutes

[The lecture should be stated in the teacher’s own words. What is contained here is a guide.]

[The lesson takes the form of questions to ask the class and teacher comments. Proposed answers describe the information to be elicited. If initial responses from the class are not complete, the teacher can prompt the class with further questions or simply state the information.]

Introduction from teacher to class: First, I’ll tell you a little about what’s true and not true in this movie. There are the usual Hollywood exaggerations to make things more dramatic. Michaela didn’t slap her husband or kick her sister out of the house. The people in the ALD Foundation were not unhelpful, as they are portrayed. Every film needs a villain, even a sympathetic one. The one real questionable area in this movie is the end when the movie claims that Lorenzo’s Oil is a good therapy for boys suffering from ALD. That’s not accurate and yet, in a strange twist of fate, it became true, in a sense, about ten years after the movie was made. Today, I’ll show you how that happened and we’ll also learn a lot about science.

Let’s look at how the steps taken by the Odones to develop Lorenzo’s Oil did or did not conform to the scientific method. We are at the point in the movie when both the restricted diet low in VLCSFAs and the immunosuppression trial has failed. Lorenzo’s symptoms are getting worse. The Odones realize that the doctors won’t have a cure until long after Lorenzo is dead. The Odones start on a journey to try to find some way to help their son.

Question #1: Can anyone describe the model of the sink with the plugged drain and what each of its four major components represents.
Scientists knew that elevated levels of VLCSFAs were a possible cause of ALD symptoms. However, even when VLCSFAs were eliminated from the diet of ALD patients, the level of VLCSFAs in their bodies, as measured by blood tests, stayed the same or continued to rise. The operative hypothesis was that the body itself created VLCSFAs. A model for the situation was a sink with two water taps and a defective drain.

\[
\begin{align*}
\text{level of water} & = \text{level of VLCSFAs} \\
\text{water taps} & = \text{sources of VLCSFAs – food and biosynthesis;} \\
\text{drain} & = \text{oxidizing enzymes in peroxisome} \\
\text{clog in drain} & = \text{lack of VLCSFA transporter enzyme}
\end{align*}
\]

Unless both taps were turned off water would continue to accumulate in the sink, i.e. the VLCSFAs in the body would increase to dangerous levels.

**Question #2:** What was the first step that the Odones took in their effort to find a therapy for their son and what was the first interesting thing that they found?

They researched the existing data. The Odones went to the library of the National Institutes of Health and read scientific papers relating to the metabolism of fatty acids. Michaela discovered an article written by scientists in Poland who had been working with rats. The scientists reported that for some unknown reason when rats were fed oleic acid the level of VLCSFAs in their blood went down. [*Teacher can note that research is step 1 of the scientific method.*]

**Question #3:** *Michaela said that it was just by chance that she had found the article from Poland. What did the Odones do to make sure they didn’t miss something?*

The Odones organized a symposium of scientists from all over the world who were doing research in areas that might apply to the development of a therapy for ALD.
Question #4: What did the Odone's learn at the symposium that was helpful in their quest to find a therapy for their son?

One of the scientists told them that oleic acid reduced the biosynthesis of VLCSFAs in fibroblasts (human skin cells) of ALD patients by more than 50%. This was the second important helpful fact that the Odone's had found. The scientist didn’t know why this happened, but he had observed it in experiments. Oleic acid in certain forms (as a triglyceride) was edible and safe, being the major ingredient in olive oil.

Teacher Comment to class: The discussion among the scientists and the Odone's was very helpful in finding a possible therapy. Symposia, where scientists get together, present papers, and talk about their research, are an important part of science. Every year there are hundreds of scientific symposia held all over the world. Scientists go to them and talk about their research. The scene in the film in which the scientist tells the Odone's about his research with skin cells of ALD patients is an excellent example of how symposia work to advance scientific knowledge.

Question #5: After the symposium the Odone's could have framed a hypothesis for the test they wanted to run on Lorenzo. How would you state that hypothesis?  [Have a student who gives a correct answer come to the board and write it high on the board. (Several other hypotheses will need to be placed below this hypothesis as the class progresses.) Alternatively, the teacher or a student can type it into a computer and project the image onto a screen. Put a “1” next to this hypothesis.]

[The hypothesis doesn't need to be worded exactly as set out below but it must have the same substance and be able to be tested by an experiment. Work with the class to make the hypothesis conform to these standards.]

Hypothesis #1. A diet rich oleic acid will cause VLCSFAs in children with ALD to drop to normal levels, stopping the progression of the disease.

Teacher Comment to class: We have now reached step 2 of the scientific method which requires us not only to state our hypothesis but also to set out our assumptions. The Odone's were making several assumptions. What are they? [Give the class a chance to tell you what the assumptions were. If they can't, tell them.]

Assumption #1: High VLCSFA levels cause the deterioration of the insulating myelin sheaths around nerves. At the time the Odone’s were scrambling to find
a therapy to save their son, no one knew if this was true. All they knew was that kids with ALD had elevated VLCSFA levels and deterioration of their myelin sheaths. It was very possible that the VLCSFAs had nothing to do with myelin deterioration or that they were only a by-product of that process. If so, reducing VLCSFA levels would have no effect on ALD symptoms.

**Assumption #2: If VLCSFA levels are brought down to normal, the progress of the disease will stop.** It could be that even if myelin deterioration is caused by high levels of VLCSFAs, the deterioration will continue even after VLCSFA levels are brought down to normal. This can occur, for instance, if ALD symptoms are caused by an inflammatory autoimmune response. An autoimmune response occurs when the body produces antibodies which attack its own tissues. Sometimes the autoimmune response continues long after the factor that caused the body to turn on itself has been removed.

**Assumption #3: The amount of oleic acid necessary to reduce VLCSFA levels would not harm people in some other way.**

**Question #6: When Lorenzo was fed oleic acid what were the results?**

The levels of VLCSFAs in his blood went down by 50% but they were still twice as high as they should have been. In addition, his symptoms continued to get worse. [Students or teacher should write these three findings on the board or display them on a screen beneath Hypothesis #1. Depending on class sophistication in working with the scientific method the teacher can note that this was step 3, experimentation or ask the class which step it was.]

**Teacher Comment to class:** These results are the conclusions described in step #4 of the scientific method.

**Question #7: Use the sink model to describe what was happening to Lorenzo’s VLCSFA levels when he was still on the diet restricted in VLCSFAs and when his parents fed him large amounts of oleic acid.**

The food intake faucet was turned off but the biosynthesis faucet was only partially turned off. The drain was still clogged and the water in the sink was still at a dangerous level.

**Question #8: What did this do to the Odones’ original hypothesis?**

The original hypothesis was shown to be false (falsified) or disproven.
Question #9: How do you state the results of the experiment on Lorenzo in terms of hypotheses? I’ll give you a hint. There are three. [A student or the teacher should write these or similar statements on the board or display them on a screen. See Possible Hypotheses in the Discovery of Lorenzo’s Oil.]

Hypothèse #2.A. A diet rich in oleic acid will cause a reduction in the VLCSFAs levels of a child suffering from ALD by 50%.

Hypothèse #2.B. A diet rich in oleic acid will cause a reduction in the VLCSFAs of a child suffering from ALD so that they will be only double the normal VLCSFA level.

Hypothèse #2.C. A diet rich in oleic acid will not cause the progression of ALD symptoms to stop.

Teacher comment to class: Quite frequently an experiment that leads to a rejection of a hypothesis results in several new hypotheses. Some of these could be provisionally confirmed and others would need more testing. What happened with Lorenzo and oleic acid is exactly what the scientific process is supposed to do: weed out incorrect hypotheses. Now the Odones had a question to answer. Why would an increase in unsaturated fats in the diet cause a reduction in the biosynthesis of VLCSFAs?

Question #10: What three criticisms would a scientist have of the first experiment by the Odones?

(1) The Odones tested only Lorenzo. In a scientifically designed experiment oleic acid would have been given to many ALD patients.
(2) There was no control group who received some substance other than oleic acid which was known to have no effect on VLCSFA levels.
(3) The Odones didn't follow the procedural steps required for clinical trials on human beings.

Question #11: Go back and read the three new hypotheses, were these any use to the Odones in their quest to find a therapy to save their son's life?

No. These provided no help in finding a therapy.

Question #12: What did the Odones have to do then? Which step in the scientific method does it correspond to?

They went back to step #1 of the scientific method. They started researching again. This is when Mr. Odone had the nightmare.
Question #13: When Mr. Odone was in the library doing research he had a nightmare. There was an idea in the nightmare. What was it and how was it different than what the scientists had thought was going on?

The idea was competitive inhibition.

Scientists "knew" (a hypothesis that had survived repeated experiments and observations) that VLCSFAs and VLCUFAs were made in the endoplasmic reticulum. They also "knew" that the endoplasmic reticulum had only a certain number of sites at which enzymes added hydrocarbon links (H-C-H) to fatty acids. They also "knew" that links were added to the hydrocarbon tails for both saturated fatty acids and unsaturated fatty acids. (The models for these were the chains of paper clips that Mr. Odone was making in the library.)

Scientists also had a working hypothesis that the enzyme that added hydrocarbon links to unsaturated fatty acid chains was different than the enzyme that added those links to saturated fats. The breakthrough came when Augusto Odone thought up with a different hypothesis. He solved the puzzle of why adding unsaturated fats would lower the level of saturated fats by proposing that hydrocarbon links were added to both saturated and unsaturated fatty acid chains by the same enzyme. If, in the endoplasmic reticula there were only a limited number of enzyme sites for this process, then adding unsaturated fats to the body might crowd out the saturated fats.

Teacher Comment to Class: Manipulating enzyme activity in this manner was not new. Scientists had used it in other situations and it had a name: "competitive inhibition." The character of Dr. Nikolais in the movie uses the term.

Question #14: Even if competitive inhibition was the reason that the oleic acid reduced the production of VLCSFAs, what did the Odones need to find to allow them to reduce Lorenzo's VLCSFAs to normal levels?

Another "competitive inhibitor" that was more powerful than oleic acid but still safe to give to human beings.

Question 15: What was the new ingredient and why did the Odones decide that it might to be helpful to Lorenzo?

The new ingredient was erucic acid. In selecting an ingredient to add to the oleic acid, the Odones made another educated guess. The fatty acids that they had to reduce were lignoceric acid (C24:0) and cerotic acid (C26:0). Oleic acid (C18:1) had only 18 carbon atoms. The Odones guessed that the most likely candidate to reduce Lorenzo's VLCSFA levels through competitive inhibition would be an unsaturated fatty acid which had more carbon atoms than oleic acid. The Odones settled on erucic acid (C:21:1) which had 21
carbon atoms and which was itself a long chain fatty acid, but was unsaturated.

**Teacher Comment to Class:** Educated guesses are the creative lifeblood of science.

**Question #16:** Frame a hypothesis that expresses the Odones’ new educated guess.

Hypothesis #3. In boys with ALD, a combination of oleic acid and erucic acid will cause a reduction in VLCSFAs to normal levels and stop the progression of ALD symptoms. *Have a student write this Hypothesis #2 on the board beneath or on the computer linked to the screen. The teacher might note, depending on the sophistication of the class, that we are now back to step 2 of the four step description of the scientific process.*

**Question: #17:** When the Odones first mentioned erucic acid to Dr. Nikolais, what was his reaction? What step was this in the scientific process?

It was step #3, part of designing the experiment. Dr. Nikolais told the Odones that erucic acid had caused heart disease and other ailments in laboratory animals.

**Question #18:** What did the Odones do in response to the concerns raised by Dr. Nikolais?

The Odones responded that erucic acid was a component of rapeseed oil which had been eaten in the Asia and India for centuries without ill effect. Seeing no alternative treatment for Lorenzo they decided to take the risk.

**Question #19:** How did the Odones decide on the proportion of oleic acid to erucic acid in the new therapy?

Dr. Nikolais gave them advice on how to do it. But he would help them only informally. Based on Dr. Nikolais’ advice, the Odones chose a 3 to 1 combination, three parts oleic acid to one part erucic acid.

**Question #20:** Why did Dr. Nikolais insist on helping the Odones with their experiment only on an informal basis?

The Odones again did not follow the procedural steps required for clinical trials on human beings. (Giving Lorenzo’s Oil to Deirdre for a month before giving it to Lorenzo was not an adequate test for the safety of erucic acid and did not satisfy the procedural requirements for a clinical trial.) But then again,
the Odones were not scientists and were facing the worst type of "deadline."

**Question #21:** After Dr. Nikolais had told the Odones that the proportion of oleic acid to erucic acid should be 3 to 1, state what the Odones were testing for in the form of a hypothetical.

Hypothesis #4. A combination of oleic acid and erucic acid in a 3 to 1 proportion will cause VLCSFA levels in boys with ALD to become normal, stopping the progression of the ALD symptoms.

**Teacher Comment to class:** The Odones were operating on at least eight assumptions:

1. **Assumption #1:** High VLCSFA levels cause the deterioration of the insulating myelin sheaths around nerves. [See Teacher Comment after Question #5.]
2. **Assumption #2:** If VLCSFA levels are brought down to normal, the progress of the disease will stop. [See Teacher Comment after Question #5.]
3. **Assumption #3:** The amount of oleic acid necessary to reduce VLCSFA levels would not harm people in some other way. [See Teacher Comment after Question #5.]
4. **Assumption #4:** There were a limited number of sites in the endoplasmic reticulum at which enzymes added hydrocarbon links to fatty acid hydrocarbon chains. (This had probably been verified in prior experiments and observations.)
5. **Assumption #5:** VLCSFAs and VLCUFAs were produced in the body by the same enzymes.
6. **Assumption #6:** If the body was flooded with unsaturated fats they would crowd out the saturated fats to a sufficient degree to reduce biosynthesis of VLCSFAs (in other words, competitive inhibition would work to reduce the biosynthesis of VLCSFAs).
7. **Assumption #7:** The increased VLCUFAs produced in the competitive inhibition process would not be harmful.
8. **Assumption #8:** Giving erucic acid as a triglyceride in pure form and in the quantities necessary to reduce VLCSFA levels would not cause a serious illness in a human being.

**Question #22:** When the Odones were able to get the erucic acid from Mr. Suddaby in England, and try it on Lorenzo (the experiment, step 3), what was the result?
Their hypothesis with its many assumptions appeared to be correct. Lorenzo's VLCSFA levels normalized and his condition stopped deteriorating. It even appeared that he regained some functions that he had lost. The Odones hoped that they had found a way to stop the progression of the disease in all ALD children.

**Question # 23:** In their at-home clinical trial on Lorenzo the Odones were again unable to comply with the requirements of the scientific method. Describe the ways in which they failed to comply.

1. The Odones didn't have a large enough test group. Their test group consisted of only Lorenzo and for a limited time Deirdre, Michaela's sister. A scientific test would not have relied on only one or two subjects.
2. There was no control group who received some substance other than Lorenzo's Oil, such as more oleic acid, which had a known effect on VLCSFA levels.
3. The Odones did not adequately test for the potential harmful effects of erucic acid before administering it to Lorenzo.

**Question #24:** What is an essential test of a scientific experiment?

Whether the results can be duplicated by other scientists.

**Teacher Comment to class:** No one could duplicate the Odones' results with Lorenzo's Oil. Scientists found that almost all children with ALD symptoms who were given Lorenzo’s Oil continued to deteriorate rapidly despite the fact that their VLCSFAs fell to normal levels. It turned out that Lorenzo was an anomaly. The oil apparently helped him but it didn't help others in his condition. It could have been that assumptions #s 1, 2, 5 or 6 were wrong. [Review them with the class.]

The movie let’s us assume that all children with the ALD genetic defect get the disease. In fact, only approximately 35% of boys with the ALD genetic defect develop the aggressive early childhood form of the disease. The kids shown at the end of the movie could have been among the 65% that wouldn’t develop symptoms, usually much milder symptoms, until later in life.

**Question #25:** Why didn’t the Odones’ experiment with Lorenzo disclose the anomaly that Lorenzo’s Oil would stop the progression of his symptoms but not those of other children with ALD symptoms?

The Odones could test the oil only on their own son. One subject is never enough for scientific research.

**Teacher Comment to class:** When scientists could not repeat the Odones’ test results, some doctors came to believe that Lorenzo's Oil had no benefit at all. Some suggested that the fact that Lorenzo had stopped deteriorating was due to
the superior nursing care given to him by his parents or to some unexplainable event. The results of the Odones' work appeared to be merely anecdotal.

Doctors also think that ALD symptoms are caused by an autoimmune response which, once it begins, can continue long after the VLCSFA levels are normalized. Thus, the second assumption made by the Odones when they tried to find a therapy for Lorenzo turned out not to be true for most people.

The filmmakers hadn't checked with the scientific experts in ALD before making the movie and they were heavily criticized as being irresponsible for not telling the truth. When the movie was released in theaters and for many years after that it was simply, scientifically, inaccurate.

The Odones and some other ALD parents still believed in Lorenzo's Oil and presented more anecdotal evidence of boys with the ALD genetic defect who took Lorenzo's Oil and didn't get sick. But still, these boys could have been among the 65% of boys with the ALD genetic defect that wouldn't develop symptoms until later in life.

Dr. Hugo Moser (presented in the movie as Dr. Nikolais) noted that there was one group of boys with the ALD genetic defect who might benefit from Lorenzo's Oil and who had not been fully tested in the existing scientific research. These were boys in a different situation than Lorenzo, boys who had not yet exhibited symptoms. Since Lorenzo's Oil did reduce levels of VLCSFAs to normal, it was certainly worth a try.

Dr. Moser embarked on a ten year study and in 2002, he published research that showed that Lorenzo's Oil was in fact effective for many children who had not yet developed symptoms. 76 per cent of the 68 boys who strictly adhered to a diet that limited VLCSFA consumption and took Lorenzo's Oil were still healthy and produced normal MRI scans of the brain. For the control group, 36 boys who did not take Lorenzo's Oil, no more than about one in three remained free of symptoms. (Lorenzo's Oil Finally Proven to Work, by David Concar, New Scientist News Service 26 September 2002)

Question # 26: What would have happened if Lorenzo’s reaction to the oil had not been an anomaly?

His symptoms would have continued to worsen, he would have died, and it was a substantial likelihood that no one would have given Lorenzo’s Oil much of a thought. It would simply have been a failed therapy.

Question # 27: What would have happened had Lorenzo’s Oil had been tried on many boys suffering from ALD symptoms?

The results would have shown that in a vast majority of the cases Lorenzo’s Oil had no impact.
Question # 28: This leads us to the most recent modification of the hypothesis, one which was provisionally confirmed by research completed ten years after the movie was released. What is it?

Hypothesis #5. Administration of Lorenzo’s Oil, a combination of oleic acid and erucic acid, will cause a substantial increase in the chances of boys with the ALD genetic defect but who have not yet developed neurological symptoms, to remain free of symptoms for extended periods of time.

[A 33 question, 50 minute test (or homework assignment) can be found at Test on the Scientific Method and the Development of Lorenzo’s Oil.]

[At TWM we are always interested in feedback. Tell us how this lesson plan worked with your class. Email jfrieden@teachwithmovies.com Put “Scientific Method Lesson Plan” in the subject line.]

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