

Two Tales of Rice

Rice is the major source of calories for approximately half of the people on the planet. In much of Southeast Asia, people get more than half of their total calories from rice! In China, an average person consumes over 200 pounds of rice a year (in the United States the figure is only 20 pounds a year). In many of the regions where rice is the main food staple, there is also very high childhood mortality caused by malnutrition, diarrhea, and infections resulting from compromised immune systems.

In the United States, rice may not be as common a food source as wheat, but it still occupies an important role for producers/exporters, and for those who retain its cultural value. For many Americans, the subject of rice is only important when we are ordering take-out food and are asked “steamed rice for how many?” However, rice is at the heart of much controversy throughout the world.

Consider these two different tales involving rice and genetic modification.

Golden Rice

In the early 1990’s various publicly funded international scientists teamed to develop rice that would provide Vitamin A, which had been identified as one of the three main diet deficiencies in developing nations (the others were iron and iodine). The project proposed to genetically engineer genes from the pathway that creates beta-carotene in daffodils into rice endosperm. Beta-carotene is then converted by the body into Vitamin A. The process of trial and error took ten years. The potential product was called “golden rice” for its distinctive colored grains.

In 2000 the scientists announced their successful results. They had created transgenic rice plants that were capable of producing

the yellow-colored endosperm that contained Vitamin A and other related compounds of nutritional value. The July 2000 issue of *Time* magazine featured the most outspoken of the creators, Dr. Ingo Potrykus, Professor Emeritus of the Swiss Federal Institute of Technology, with the headline: “This Rice Could Save a Million Kids A Year,” which referred to the number of childhood deaths attributed to Vitamin A deficiency by the World Health Organization. At the time of that publication golden rice was considered a major breakthrough in biotechnology because the researchers had engineered an entire biosynthetic pathway. The scientific process for genetic engineering of rice had been a success, but the battle for acceptance was just beginning.

Golden rice has faced opposition primarily from environmental groups that are opposed to any use of biotechnology on the food supply, and view Genetically Modified Organisms (GMOs) as possibly leading to problems such as decreased biodiversity, human health and environmental risks, and the economic exploitation of subsistence farmers in developing countries. Golden rice 2 has now been developed, and provides 23 times more beta carotene than the original, but the rice is not yet available for human consumption in any part of the world.

Golden rice was developed with public funds and its creators carefully tried to keep their patent in the hands of a humanitarian organization so that its distribution could more readily serve their goal of meeting an urgent need. In the *Time* magazine article of 2000, golden rice was said to be “the first genetically modified crop that was inarguably beneficial.” Its methodology involves transgenics, moving genes from one species of plant to another. Vitamin A deficiency (VAD) has been associated

with one million childhood deaths per year; with up to 230 million children at risk of VAD, and 500,000 cases of blindness per year. Opponents state that there are other ways to alleviate Vitamin A deficiency.

Ventria's Rice

In May 2006 a company with sixteen employees, Ventria Biosciences, announced that they were developing a drug that would be used to fight diarrhea. According to the UNICEF report, "The State of the World's Children 1998," diarrhea ties with Acute Respiratory Infections as the cause of 18% of deaths in children under five in developing nations, worldwide. Deaths due to diarrhea are considered preventable, and it would seem that a drug to fight diarrhea would be welcome news. Instead the small company's announcement caused a furor among environmental groups, food corporations, and thousands of farmers. The reason involved their plan to grow the experimental drug in rice that had been genetically engineered by splicing human genes into the crop. The US Rice Producers Association has been particularly vocal in their criticism of Ventria's experimental work and the company had been forced to relocate from California to North Carolina, after rice customers in Japan refused to import California rice as long as Ventria was operating in that state.

The opposition to the experimental drug that is the proposed product of Ventria's genetically engineered rice stems from its use of the most controversial form of agricultural biotechnology, known as "biopharming." Biopharming involves splicing human genes into crops to produce proteins to be used for medicinal purposes. The proposed drug from Ventria would be a protein powder milled from the rice and would contain two human proteins that are commonly

found in a mother's milk, saliva, and tears. This protein powder is designed to help patients hydrate and may lessen the severity of serious diarrhea attacks (3.67 days versus 5.21 days in data presented at the Pediatric Academics Societies Meeting, San Francisco, 5/06).

Ventria's proposed product involves the use of human genes spliced with those of a crop, and grown as part of a for-profit endeavor. The company hopes that the resulting protein powder could be marketed as a "medical food" rather than a pharmaceutical and has applied to the Food and Drug Administration (FDA) for approval as such. If the protein powder is considered as a pharmaceutical it will be subject to human tests, resulting in a far lengthier process for approval. Diarrhea is considered a major childhood killer in developing countries. However the protein powder, while lessening the severity of attacks, does not have any preventive properties. Opponents also point out that other preventive measures are more useful in preventing diarrhea, along with educating health care providers and caregivers on the necessity of rehydration.

The arguments against the development of golden rice and Ventria's rice are similar, with opponents stating that growing genetically engineered crops will threaten the safety of conventional crops and decrease needed biodiversity. Trade groups and producers such as Riceland Foods Inc. (the world's largest rice miller) fear that nations that completely oppose GMO's, such as Japan, will refuse to buy US crops. Exports account for 50% of the rice industry's sales. The scientists involved with each GMO rice counter that rice is "self-pollinating" therefore it is virtually impossible for genetically engineered rice to cross breed with traditional crops.

Two Tales of Rice

To Think About

The case describes two different projects involving genetically engineered rice. Would you support one over the other? If only one type of rice could get approval, which rice would you choose?

Do you think that genetic engineering of foods is ever justified? If so when?

Does it make any difference in your decision-making process about who stands to profit?

Does biopharming using human genes seem more threatening than genetic engineering using plant genes? Why?

Could opposition to biopharming lead to a decrease in opposition to transgenic work such as golden rice?

Should golden rice be available for human consumption in developing nations? What about in the U.S.?

Do you think the FDA should consider Ventria's product as a "medical food" or a drug? What factors would you consider in deciding?

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Talk About Short

Zack knows the waiting room drill by heart. From the second the door opens he can sniff out new patients and how late the doctor is running on his appointment schedule. Pediatric Endocrinology. Zack used to wish that he'd never heard the words in his life. If he were a late night comedian there could be some very non-PC material in the waiting room. "How short were they?" the audience would shout. He could say, "The patients were so short that the fish tank was at floor level. They were so short that there were step stools so that they could climb onto the kindergarten size chairs..." But it's not really true. Short stature isn't the only metabolic disorder. Still, the waiting room always has a disproportionate number of boys, most of them still baby-faced. The first-timers usually have two parents with them. Everybody looks at one another but tries not to get caught doing so. Zack often wonders if the other patients are already taking recombinant growth hormone (rGH) or whether the family is in the early stages of trying to learn why "Johnny is so short."

Zack is aware that he's older than most of the others. He is getting dangerously close to puberty cut-off, when he may not even be a candidate for growth hormone. And at age thirteen, 4'11," what are the real chances that his own pituitary gland will kick start a growth spurt? There have been times that he wished that he were anywhere but in Dr. Bass's waiting room or at the Pediatric Clinic for tests. Zack does still wish that that he wasn't an on-line expert in growth hormone literature (diagnosis, prognosis, and ethical concerns!) and that he had never heard of "Idiopathic Short Stature". He laughs to himself when he thinks about this term. Maybe because his short stature is of unknown origin (his parents are of average height and his pituitary gland is apparently able to produce growth hormone) some people want to coin him an idiot for caring about his height when other people have "real problems."

He's the older of two boys. His younger brother Ben (he can't call him his 'little' brother any more), is four years younger. When Ben was as tall at five years old as Zack at nine, his parents seemed to freak out. First there was the family doctor for more measurements, then the referral to a specialist and since then there have been the

X-rays of his left wrist, the nutrition consultations, the sleep study, and mostly, the years of blood tests. It seems kind of funny that the specialists don't have one single test to determine what they really want to know, which is whether Zack's endocrine system is working properly to signal the pituitary gland to produce growth hormone and the other hormones that control his thyroid glands, adrenal glands, and sex glands. The hormone is produced in spurts, usually during deep sleep and so doctors have to look indirectly for the byproduct (somatomatin) in his bloodstream. The tests have showed that Zack is not completely deficient in growth hormone; his body makes it, but not enough to help him grow enough to be considered "normal." There's also a possibility that he's simply a male whose growth spurt is going to occur somewhat later than the average.

Anyway, the insurance company turned down the doctor's recommendation for growth hormone treatment when he was eleven years old and four feet tall. They said that since his body was producing growth hormone, and he was not at the crucial 2.5 deviations from the norm, that the treatment was not warranted based on medical need. That was fine with Zack when he was in fifth grade. His parents had tried to sound so gung-ho like it would be fun to mix up powder and water every day and inject it into himself. A powder, that he'd overheard a hundred times in his mother's crusade, which cost \$20,000 a year, up to \$40,000 if it was injected every day of the week. But the average gain in height with growth hormone is only 1-2 inches. Zack can see why the insurance company thinks that \$20,000 an inch is too expensive.

What's really strange is that Zack didn't ever think of himself having a problem until his parents got so concerned about his height. He had friends; sure they were each a bit taller than him but it hadn't been a big deal. No one had ever picked on him because of his height, maybe teased him about the bat being too big for him but it hadn't stopped him from hitting quite a few three-base hits.

When the specialist first confirmed that Zack's growth was not keeping up with the average it seems that his "problem" wasn't abnormal enough.

If his body wasn't producing any growth hormone then no problem, the insurance company would pay for treatments and he would be an old hand at self-injection by now. His mom had an entire stack of letters that she had exchanged with the insurance company as she waged a battle to get them to cover his treatment on the grounds that "early treatment works best" and that psychological damages would continue to mount. He tried to tell his parents that he thought he was going to have a late growth spurt, he didn't really feel "psychologically" damaged, but they were adamant that the world is very cruel for short people. They were going to battle the insurance company for his right to treatment. Zack didn't know how to feel about it; sometimes he was tempted to ask his mother, "Would you be fighting to get me growth hormone if they still had to extract it from corpses?"

Zack is sure that he and his mother are reading the same web sites, reviewing the latest articles cited on the Human Growth Foundation site and the links that he finds when he does a Google search. His mother as always seemed so sure about what they should do, but he's not as certain. When the FDA approved human growth hormone use for "short stature" in 2004, the review committee said they weren't convinced that short stature constituted a medical condition, but that the treatments didn't seem harmful. The possible side effects include headaches, bone aches, a diabetes-like condition, and potential effects later in life from having stimulated cell growth. He has read that boys are twice as likely to be referred to specialists as girls, but that once there, girls are the ones who usually have a diagnosable health problem. There's also a quote from Dr. Alan Rogol that appears on all the web sites against growth hormone therapy. The quote says, "Short stature became a disease when unlimited amounts of growth hormone became available."

Growth hormone therapy does not work overnight. Zack has read that many people think that small kids are like a seed that is ready to germinate if you add water, and Miracle-Gro. Meanwhile he has been rechecked, resized, his blood work updated, and he is getting his first injection today. After nine months of a plateau of 4'11," the insurance company has agreed to cover three injections a week for up to three years. For the first month he will receive the injections at Dr. Barr's office, to monitor and get him used to

proper mixing and injection techniques. After all the years of wishing that his parents wouldn't make such a big deal he is actually excited about trying the treatments. His friends have all shot up recently and he has that sense of being smaller than everyone else. At the library, the librarians eye his friends with skateboards under their arms like they are a dangerous menace, but their smiles at him seem to be saying, "Oh, isn't he cute?" Zack knows he is never going to be tall. If all goes well he'll be at least 5'3" since he could still have a natural growth spurt. He had always thought that it wasn't that bad being different from others, but that was before he felt so different. The girls have gotten so tall. Of all the couples that have suddenly developed in eighth grade, not one of the girls is taller than the guy. Maybe his parents had always been right to fight for this; they had known before he did that he was going to want to be more normal. It's strange because after his mom won the fight with the insurance company, she told him that the decision about whether to have the therapy was up to Zack. "I just always wanted you to have the choice," she told him. "Didn't you know that?"

One day there was a really pretty girl in the waiting room; she looked about his age. But she looked at Zack like she hated him. He'd seen a lot of short kids over the years, and could usually tell by their proportional bodies or chubby faces whether their short stature or size was a result of more severe endocrine malfunction. This girl was small all over and Zack had to admit that he found himself thinking how doll-like she was, like a magazine model but in miniature. She looked at him with loathing as though assuming (correctly) that he was thinking that she just looked "so darn cute." It was one time that he wished that he were shorter so she would look at him as an ally, instead of an enemy. But after that day he started noticing when people were looking at him as though he were cute and adorable. It made him feel angry too. He used to wonder why appearance seemed to be so important at school, in movies, everywhere. Now Zack has stopped wondering; it is a reality. He lives in a culture that prefers men to be tall; and a few headaches or bone aches don't seem like much of a price to pay. He can't wait to start the therapy and make up for all the lost years.

The inner door opens and the nurse announces, "Zack, we're ready for you."

Talk About Short

To Think About

Zack's family has health insurance and the treatments will be covered. If he was an uninsured male teenager, should he have the same right to treatment?

Do you think that Short Stature should be considered a medical condition? How would you define it?

If you were a short girl instead of a short boy, do you think it would make a difference?

What points would you make to convince Zack not to have the treatments?

What if Zack were against receiving Human Growth hormone but his parents insisted; at what age do you think a child should decide versus a parent?

If Short Stature is not considered physically dangerous, should potential psychological damages need to be proven before treatment is approved?

Should treatment criteria be different for treating an illness that is life-threatening or will be fatal in the long-term?

Pediatrician Alan D. Rogol has stated, "Short stature became a disease when unlimited amounts of growth hormone became available." Would it make a difference in considering treatment to think that the demand was due to pharmaceutical marketing instead of actual need?

If you had Idiopathic Short Stature, would you want to receive recombinant (biosynthetic) growth hormone? What if the growth hormone that was harvested from the pituitary glands of corpses was more effective and still available? Would you use it?

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Case written by Peggy Sturdivant

One Family's Dilemma

Kathleen knew that there was quite a bit of controversy regarding stem cell research in the news, but it didn't occur to her that it really affected her in any way. Then again, she had never thought the word 'infertility' would apply to her either. Kathleen and Tom were both raised in conservative religious households. She and Tom both came from large families; their parents now have 27 grandchildren. It wouldn't appear that there are any problems with reproduction. How could there be?

Kathleen and Tom made careful plans before their marriage so that they would be prepared for a family: researched career choices, accepted positions with growing software companies in the Seattle area, purchased a house in an area where the schools were highly recommended. Why couldn't she get pregnant? Two years passed, then three before they were able to bring themselves to discuss their apparent infertility and learn about the mind-boggling possibilities in fertility treatments, none of which they wanted to discuss with their seemingly problem-free siblings.

After a long journey through tests and research, Kathleen and Tom had two children through in vitro fertilization. The process was lengthy and expensive. After months of painful injections to boost her egg production, Kathleen underwent procedures to have 6-8 eggs removed. The eggs were then fertilized with her husband's sperm in a Petri dish, and the resulting embryos were incubated for several days in a carefully controlled environment.

Four blastocysts (embryos with about 150 cells) were implanted back into Kathleen. They were each smaller than a period at the end of a sentence, had no heartbeat and could not develop into a person without successfully

implanting in a womb. Statistically, one out of every four implanted embryos results in a full-term pregnancy, but the first time none of Kathleen's embryos developed into a fetus. They had to repeat the procedure two more times. There were six potentially good embryos remaining when Kathleen became officially pregnant. The extra embryos were frozen and stored in a special tank.

At holiday gatherings no one would ever know that Kathleen and Tom's children had been conceived any differently than any other cousin running around the back yard. Yet the path to parenthood had put them at odds with their faith, which does not approve of in vitro fertilization because of the risk to potential embryos and because of the use of technology for procreation. However Kathleen and Tom felt sure that they were meant to have children. Although there is more initial uncertainty with IVF than with a regular pregnancy (*What if the embryo doesn't implant? What if all four of them do?*), once the pregnancy is advanced it is no different than any other. Occasionally Kathleen and Tom remembered the extra embryos and were glad: if they decided to have a third child it would be possible. Then Kathleen learned that she was pregnant, after the years of fertility treatments she didn't even know to recognize the signs. Her doctor told her that it is not uncommon for women with infertility problems to be somewhat "cured" by having children. Their family is now complete. Their older children are five and three years old now, and the baby has just been born.

But they still have these extra embryos and the insurance company has notified them that the \$500/year storage fee is no longer covered. The notification letter came in the same mail with an invitation to yet another school fundraiser.

However, the insurance company also included a letter from a research institute citing a desperate need for embryos. That's when Kathleen learned that the debate over stem cell research involves her family, and also the family of her best friend.

The letter stated that there are potential medical breakthroughs that can be made on virtually every disease known if researchers are able to use stem cells in their research. According to the information (from Harvard's Stem Cell Center, no less) there are only about twenty-two stem cell lines available to researchers who use federal funding for their research. At the same time, an estimated 400,000 unused embryos are in storage tanks throughout the United States. Most stem cell lines have been grown on feeder cells derived from mice. The paper cites the need for more human embryonic stem cell lines. In the letter, one researcher wrote about his personal stake in creating more stem cell lines for research. His son and daughter have Type 1 diabetes and his son is insulin-dependent. He believes that scientists will be able to cure diabetes, perhaps using stem cells to grow insulin. Kathleen's best friend Clare has three children, and her oldest was diagnosed with diabetes when she was just two years old. Clare practically devotes her life to raising money for diabetes research, in addition to trying to make her daughter's life seem as normal as possible. Kathleen knows that if Clare had embryos to donate she would do it in a heartbeat.

Kathleen and Tom find time to sit down together to discuss their options. The embryos belong to them, but they do not plan to use them. The storage cost is \$500 per year, which would pay for a lot of new shoes. They hate the idea of their embryos, the embryos similar

to the ones that became Caitlin and Tom Jr., being discarded as medical waste. They believe those embryos have the possibility of life, even if they do not have heartbeats. The position of their religion is that these stem cells are sacred and should not be used for research. The Stem Cell Center states that due to the current government policy, they are not able to use any Federal dollars and must rely on private funding. The Center also notes that they will make the stem cell lines available to any scientist in the field. They estimate that from 350 donated embryos they could double the number of stem cell lines available for research.

Kathleen makes a list of possible actions to take, and then they read over the page again that gives specifics about research. It says that the embryos have been frozen for varying amounts of time; they do not always survive thawing. Those that survive may not develop into a blastocyst. The letter states that cells generated by the embryos cannot be identified with the donors. Kathleen and Tom talk about their own children and how they would feel if they were diagnosed with a disease. In the past they have talked about whether they would donate their organs if anything happened to them. They believe that life is sacred and that it begins at conception. Tom suggests that they pay the \$500 for another year, while they learn more, but Kathleen feels strongly that it is time for them to decide how they feel about stem cell research. Her children are like miracles, exhausting, but miracles. What research led to in vitro fertilization breakthroughs that allowed them to be born? She thinks to herself, "the embryos don't have heartbeats and they could help to save lives. But don't we have a duty to protect them? What should we do?"

One Family's Dilemma

To Think About

What are the options for Kathleen and Tom?

What do you think Kathleen and Tom should do with the extra fertilized eggs? Why?

Which bioethical principle is given the most weight in your solution?

Explain why you chose that ethical principle.

Please see NWABR's Stem Cell Curriculum, available online at www.nwabr.org, for a full classroom lesson based on this case.

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