



Eyes Without a Face: Stem Cell Research and Corneal Implants

Part I—"A Picturesque Day"

by

Kari Mergenhagen, University at Buffalo, State University of New York

A picturesque July day. Billowy clouds shaping stories in the blue sky ... a dusky spider lurching from a silken thread ... gulls' wingtips sailing through the air ... these were my last images.

At seven years old I was a curious, bored, and rambunctious girl. School had been out for several weeks but to me it felt like a year. I wanted to do something different and exciting ... something grownup.

"Mom, when's Dad coming home? When can we eat? I'm hungry."

"Honey, just be patient. When Dad gets home, we'll have dinner. He's going to barbeque tonight." She was cutting vegetables and seemed preoccupied.

"I can barbeque," I boasted. "I've seen Dad do it a hundred times. We don't have to wait for him. I can barbecue and it would be all ready for when he gets home. I know. I'll surprise him."

"Now, Lucy," Mom gave me a look that meant I was treading on thin ice. "You are much too young to barbeque without Dad and you know it. Wait until he gets home and you can help him. Now go back outside and play until supper is ready."

Frustrated, I banged through the back door. I would show my mom how helpful I could be. I went into the garage and dragged the grill onto the driveway. Then I scooped out pieces of charcoal from the bag in the corner of the garage. After several trips I was certain that I had filled the grill adequately. I climbed up on a stool and slid the charcoal fluid off the shelf. I squirted it on each square of ebony charcoal. I could only think of how proud my parents were going to be. Dad had always said the grill had to be really sizzling to cook the food. I added just a few more squirts. I wanted the fire to be especially hot.

I found the matches on the shelf in the garage. I knew just what Dad would do. After several attempts I was able to get the wooden stick to light. I threw it into the fire. The grill exploded into an inferno. I was knocked back several feet and sat in shock—screaming.

My life became utterly distorted. I survived, but I was blind. They told me my corneas were dysfunctional. But all I knew was that I would live my life in a characterless fuzzy world of light and dark. I carry a snapshot of that day in my mind. My psyche tells me I've aged, but my mind only recalls

my face as a young girl of seven. Every time I feel the warmth of the summer sun, I can see the vivid imagery, but the picture never changes—a picturesque July day, clouds, a spider

Questions:

1. What function does a cornea have in vision?
2. Can a cornea be repaired after sustaining damage? Explain.
3. What is a cornea transplant and how successful is the procedure?



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Part II—"New Hope"

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The next few years of my life were difficult, but I was determined to do more than just survive. I wanted to be independent, so I began the arduous process of learning how to function in an entirely new life. I had to learn how to dress, eat, play, and navigate the house. After several years I became proficient in reading and typing Braille. I acquired a Seeing Eye dog and a special "blind" cane, both of which acted as surrogate eyes. I developed a reliance on my other senses and once again started flourishing socially and in school.

Outwardly I was adjusting well, but inside I felt as though I were enveloped in a shroud of darkness. I intently focused on my other senses. These compensated to some extent. But I refused to admit I would never really see again. I enthusiastically pursued cornea transplants. When my third transplant failed, I realized it was time to move on.

After college, I married John, a kind, sensitive, and patient man. His only fault was a tendency to be overprotective. A daughter, Rose, blessed our lives several years later and with a little help I was able to gain the confidence needed to manage the job of motherhood.

When I caressed Rose's soft, pudgy cheeks, ran my fingers through her fine, silky hair, or heard her baby gibberish I would try to imagine her features in my mind. This surrogate image was something my other senses couldn't compensate for and I began to feel a huge void.

I longed for a true picture. I wanted to see her face when she pouted, giggled, when she was surprised. Conjectures of the mind were no longer acceptable to me, so I sought advice from Dr. Cooper, a friend and my ophthalmologist for the past 10 years. Incredibly, he informed me about a study being conducted at the University Medical Center that might help me to regain some sight.

"Lucy, this is a clinical study that is accepting patients in which conventional corneal transplants aren't effective. It involves the use of corneal stem cell implants. I believe you should look into it. You seem to fit all the criteria."

"I've had several unsuccessful transplants. What makes you think that this would be any different?" I was cautiously enthused, but didn't want to pursue a pipedream.

"Basically, the injury to your cornea was so severe that your stem cells were damaged. The stem cells are important because they provide a sort of clear surface over the cornea. In the normal eye the cells on this surface are constantly being knocked off by blinking or rubbing your eye and then they are replaced. In eyes in which the cornea has been severely impaired, like yours, the ability to do this is missing," Dr. Cooper explained. "I really think you should look into this. If you are interested, call this number and ask for Dr. Star. Tell him to contact me for your records."

I had a feeling of euphoria as Dr. Cooper placed the slip of paper in my hand. Soon I might actually be able to see my daughter. I couldn't wait to discuss the prospects with John. Unfortunately, John lacked my enthusiasm.

"Honey, I love you just the way you are. I want to do what's best for you, but you know how I feel about using stem cells." John tried to reason with me. "There has to be different way. I could never approve of killing a fetus to make our lives better. I would feel as though I was destroying a child, like Rose. I don't think we should support any research with stem cells."

"John, don't assume this procedure is like that." I could feel my voice rising as I tried to make my point. "I just want to look into the process. I promise if it seems unethical, I won't do it, but to have my sight... to see Rose's expressions... to watch her grow up.... It would be incredible. Please explore this with me," I begged.

"I just don't know" John shook his head. "Look at the disappointments you've endured in the past. I don't want to see you go through that again, and I can't stand for you to be used as a guinea pig," He could see how upset I was with his response. He put his arm around me. "Lucy, I'll look into it with you, but no promises."

Questions:

4. Why do some cornea transplants fail?
5. What is a stem cell?
 - a. What is the difference between a totipotent, pluripotent, multipotent and unipotent stem cell?
6. How do adult and embryonic stem cells differ?
7. What type of stem cell is used to reconstruct the cornea in this procedure, why are they important, and what problems have been encountered in using this type of stem cell?
8. How do stem cells normally function in the cornea?
9. What are some major concerns with adult stem cell use?



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Part III—"A Stem Cell Solution?"

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I was nervous about my visit to the University Medical Center. I could sense that even John had some reserved optimism. Dr. Star had reviewed my medical records before we arrived. He began by explaining why my past cornea implants had failed.

"In the normal eye the epithelial cells of a cornea wear away through ordinary eye movements and are replaced by stem cells located in the corneal limbus. Lucy, your eyes were extensively damaged by the heat generated in the accident that destroyed your vision. You lack the necessary stem cells to maintain a healthy cornea. This is the reason cornea implants have been unsuccessful for you."

"But I could see for a while after I had the implants, then I would return to blindness," I responded puzzled.

"Initially you may have regained some sight, but after several weeks or months the epithelial cells on the donor cornea would slough off. Without stem cells, aging epithelial cells cannot be replaced on the donor cornea," Dr. Star continued. "In your situation, Lucy, stem cells will be needed, preferably from a close relative."

"Lucy's gone through a lot emotionally with the failure of the past cornea transplants," John interjected. "Why do you think this will work if all of the past transplants failed?"

"Research has shown that traditional corneal implants can never be successful in patients lacking the limbus stem cells. With this approach there is a fifty percent or better chance that Lucy will have some degree of success; however, the longevity of the benefits and future side effects are not known," Dr. Star said. "This procedure also has a distinct advantage. The cultured stem cells can be frozen for use at a later time. If the transplant should fail, the banked stem cells could be used so there would be no need for another donor."

"So you just take the stem cells and stick them in my eye?"

"Not exactly, it's a bit more complicated," Dr. Star explained. "We get the stem cells from a donor using a device called a *Limbal Stem Cell Harvester*. It was developed by Dr. Roy Chuck, an eye surgeon at the UCI Medical Center. This device is a modified microkeratome, which is used in LASIK surgery. By using this method, more stem cells can be gathered quickly and easily. One of the reasons that

limbal stem cell transplants have failed in the past is the difficulty in identifying and obtaining an adequate amount of stem cells. To get enough of them we need to culture the stem cells on an amniotic membrane for about three to four weeks where they increase in number. Next, after the damaged corneal tissue from your eye is removed, the culture with the amniotic membrane is transplanted into your eye. This process will provide an epithelial cell layer with stem cells. Then about three months later a donor cornea is transplanted into your eye. With any luck it should restore a normal cornea surface on your eye."

"Dr. Star, these stem cells you're talking about culturing, do I understand you right; they don't come from an embryo?" John needed assurance that the procedure would be within his moral boundaries.

"Precisely, these are adult limbic stem cells. The exploration of adult stem cells is still in its infancy. The full potential, diversity, and problems associated with their use are only at the beginning stages of research, but early studies indicate great promise in this area," Dr. Star stated reassuringly.

John could sense how excited I was about this procedure. I just knew it would work. I would be able to see my daughter's smile and her pout. I would see the world again. We read over the literature that Dr. Star had given us and filled out the forms. As far as I was concerned, there was no down side. I was blind, so what did I have to lose?

Questions:

10. What is the limbus, where is it located and what impact does it have when it is damaged?
11. Where do the amniotic membranes come from, why are they used in culturing stem cells, and what problems could be encountered through their use?
12. What is the difference between a keratolimbal allograft and an autologous graft?
13. What advantage does the keratolimbal allograft procedure have over keratoplasties?