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CORNEAL TRANSPLANTATION YESTERDAY AND TODAY[1]

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When Dr. Farge a week ago invited me to speak on this subject, my impulse was to decline with thanks. I felt unprepared, the notice too short, and I felt too old. I remembered that John Adams, one of the founding fathers of the United States, eloquent revolutionary in the cause of democratic government, had declined at 37, an invitation to speak in Boston because, he said, "he was too old to make declamations." People lived shorter lives and aged earlier in those days. Similarly, people lost their vision earlier forever in those and in much more recent yesterdays. But then I remembered that I had experienced those more recent yesterdays. Indeed, while I respectfully invoke my rights against self incrimination under the fifth amendment of the constitution of the United States in declining to comment on my memory of recent events, my memory of distant events is clear and sharp. I remembered that I was a bit player in the continuing drama of ocular surgery, and played a larger although forgotten role in the act about corneal transplantation. And so, wrapping myself in quotations-as a beggar would enfold himself in the clothes of an emperor, in order to express to you my deep feelings, I did accept Dr. Farge's kind invitation to speak on the subject of corneal transplantation yesterday and today.

"Speak we now of famous men, men of little showing, for their work continueth, broad and wide continueth, far beyond their knowing." In the beginning their was von Hippel, but he was past even my memory. Then I remember there was Filatov in Odessa. He, like Castroviejo in New York,

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operated at great risk under primitive conditions with large sutures (6-0), large and dull needles, without antibiotics, corticosteroids, most of the paraphernalia that make corneal surgery so predictable and gratifyingly successful now. With the materials available to them, a suture could not be passed into graft without damaging it and making the operation potentially even more disastrous than it was. So, they used a cable of sutures fixed at the limbus and overlying the graft like a spider's web, pressing the graft down into place. This obviously insecure method of fixation required that the patient postoperatively restrict his activities severely. Both of his eyes were bandaged, he was put on his back for a week, and endured pain from the large sutures and large exposed knots scratching the inside of this eyelids. The pain caused by the large sutures and knots were in some cases reduced by laying a strip of the amniotic membrane of a hard boiled chicken's egg over the cornea and graft at the end of the operation, but it usually rolled up and was displaced by the time of the first change of dressing one or two days later. The inflammatory response to the suture not only caused pain, but caused blood vessels to grow from the limbus into the patient's cornea toward the graft. If the sutures were not removed in about two weeks the blood vessels would invade the graft, bringing with them cells and chemicals. An immune homograft reaction and clouding of the graft would follow. To reduce the likelihood of this, grafts were made small-about 5 mm. in diameter, so that the edge of the graft would be as far as possible from the source of the new blood vessels, and yet be large enough to provide good vision if the operation was otherwise successful. If the patient strained at stool, coughed, sneezed or horror or horrors vomited the graft might extrude, like a cork popping out of a bottle and with the gush of the aqueous out of the anterior chamber would come some of the iris. Severe inflammation, or even infection, or secondary glaucoma or cataract, and enucleation of the entire eye or at least an opaque white graft would result. For that patient's eye darkness would continue to lie upon the face of the deep. This sequence of postoperative events occurred so frequently yesterday that very few ophthalmic surgeons chose to perform corneal transplantation. Today almost every ophthalmic surgeon routinely does so.

Then came Hinch and Kendall at the Mayo Clinic with their synthesizing of cortisone, and Gordon at Cornell who showed that its topical application to the eye suppressed inflammation, and Maumanee at Stanford who demonstrated in rats that the immune response caused vascularization and opacification of corneal grafts, and most important José Barraquer, then of Barcelona, and I was his prophet-at least in the English language, as well-I affirm-as my own.

Barraquer's major contribution to corneal surgery, and he has made many in my opinion was made so long ago that many younger ophthalmologists who

know his innovations in refractive surgery are unaware that he is the father of corneal transplantation as it is performed today universally. Universally, that is, except in Russia.

Before briefly summarizing the technic of corneal transplantation as performed today, which is more or less uniform everywhere else, let me tell you how it is done today, or at least was done as recently as five years ago at the Filatov Eye Institute in Odessa. Briefly, the method used there was unchanged form that used by Filatov in the 1930s, that is the use of a cable of overlying sutures to hold the graft in place, combined with bed rest. The grafts used were still 5 mm. in size. A surgeon on the staff said that they had tried Barraquer's technic but did not like it! To prepare the host for receiving the graft when the surrounding cornea was in such condition that the chance of the graft stavyng clear was not good, they administered a preparation devised by Filatov made from placental tissue, primordial mud and aloes. This they asserted was good for a variety of other ailments including disorders of the kidneyx, heart, skin, and rheumatic diseases. Their displays and promotion of these packaged medicines to a group of Texas ophthalmologists, me included, reminded me of a medicine man's pitch for a nostrum that was good for everything form womans complaint to baldness that I saw as a child at Fort Davis in west Texas. The Russian preparation is injected subconjunctivally repeatedly. They call this tissue therapy. To be fair to the Russian ophthalmologists, our conversations with them were through a Russian interpreter, who might have been in the security apparatus of the Soviet government or of the Communist party. The Russian doctors may have been fearful that their statements might endanger their positions. Otherwise, why should one of them in response to a question assert vehemently that at the Filatov Institute they NEVER had post operative iris prolapse, an obvious lie, believable only to one who would believe that an otodolaringologist never had post operative hemorrhage after tonsillectomies. The word "never" in medicine and surgery is a dangerous word, harming both the teller and the listener. All this was at the largest center for corneal transplantation in the world. Over four hundred transplantation had been done in one section of the Filatov Eye Institute in the past year alone, we were told, the patients having been sent there from all over the Soviet Union. The surgeons were using 7-0 silk sutures and removing them early. Steroids were used in selected cases along with the tissue therapy. So much for surgery today in Russia. Perhaps, with the new freedon permitted by Michael Gorbachov, Barraquer's method has finally found acceptance, and the Russian doctors are not afraid to tell the truth.

Old ophthalmologists never die, they just fade away reading their reprints. One of mine of which I am most fond, was published in 1953, the firts report in

English of the successful use of Barraquer's technic of corneal transplantation. It was also the firts publication advocating the routine use of topical corticosteroid medication in corneal transplantation to reduce the incidence of allergic homograft reaction, which can cause clouding of the graft. The use of this medicine in this way for this purpose is now universal, I believe. Barraquer's technic was basically what is used today-the suturing of the graft directly to the cornea of the host. In order to accomplish this, much sharper needles were necessary. Barraquer had the Swiss instrument house of Grieshaber make very small (4 mm.), sharp needles to which the surgeon threaded the smallest suture available in the early 1950s-6-0 silk. Unfortunately the problems created by this large suture and knots still existed. The patients had to be taken back to opeerating room two or three weeks postoperatively, given an injection of a local anesthetic and paralyzing agent into the facial muscles surrounding the eye in order to prevent squeezing. Then the sutures were removed very carefully in order to avoid wound rupture with its terrible sequellae. The use of cortisone ointment reduced the interval of time before vascularization of the surrounding cornea began, but I soon found that it also delayed healing, and that removal of the sutures two or three weeks postoperatively allowed the incision to open. Delaying the removal of sutures to six weeks was possible without undue vascularization of the surrounding cornea when cortisone ointment was used.

Cortisone also reversed allergic homograft reactions when it, occurred at any time after surgery if used soon after the onset of the reaction, a major advance in postoperative management, and future care of corneal grafts, since the homograft reaction may occur years postoperatively. The Barraquer technic combined with cortisone or its derivatives truly revolutionized corneal grafting.

Significan refinements in his technic have occurred over the succeeding thirty-five years. The introduction of a balanced salt solution as a substitute for normal saline for irrigation during surgery helped to protect the graft from develping intraoperative edema. Finer suture were devised. Barraquer had made first a suture of "virgin silk" made of seven strands of silk, then of only two strands. The latter was manufactured only in Columbia. I obtained it from him and used it for over ten years for all cataract and corneal surgery. It had to be threaded on to a Swiss needle. I forgot to mention that the operating microscope was not ye invented. The best magnification obtainable with loupes wor over eyeglasses was about 2# The very fine virgin silk broke easily and the needle had to be rethreaded sometimes four or five times during the operation. About 1966, Harms of Tubingen starte the use of 10—0 nylon. This created another minor revolution in corneal transplantation. This suture excites almost no foreign body reaction in the tissues surrounding it. It can be left in place for years. Some

diseases formerly considered un favorable for corneal grafting do well with the use of this inert suture, ie. apahakic bullous keraopapthy, and Fuchs's corneal to dystrophy. It can be used as a running or multiple interrupted suture, buryng the knots either way. At first the nylon suture had to be threaded into the eye of a Swiss needle, but like all other sutures it is now swaged onto extremely sharp needles, making suturing easy and atraumatic. This very fine suture can be placed best using the operating microscope.

The microscope enables the surgeon to see detail formerly impossible, to perform safely and precisely maneuvers otherwise risky, and to so secure the incision that when closed properly with nylon sutures, corneal transplantation now is done routinely as an outpatient procedure, requiring only the facilities of the hospital's operating room for a couple of hours, and an hour of monitoring postoperatively in the holding area before discharging the patient. The eye can be unbandaged permitting vision and increasing comfort twenty-four to ninety-six hours postoperatively.

Another major advance making corneal grafting safer is the recent introduction of viscoelastic substances to coat the endothelial cells on the inner surface of the graft and protect them from damage that can be caused by their contact with any other solid material. Damage to the endothelial cells can result in permanent edema and clouding of the graft. Other advances include the use of osmotic agents to reduce the intraocular pressure at the time of surgery such as intravenous acetazolamide, and mannitol, the use of sophisticated instruments to perform vitrectomy, at the time of corneal transplantation for aphakia, the use of broad spectrum antibiotics at the time of surgery to reduce the incidence of infection, and very important, improvements in eyebanking.

In 1950, the only eyebank that would ship eyes to Houston, Texas, was the Eye Bank for Sight Restoration at the New York Eye and Ear Infirmary in New York City. Whole freshly enucleated eyes were placed on a strip of gauze soaked in sterile saline in small sterile glass jars. The jar was placed in a thermos bottle with ice around it and sent by propellor driven aircraft. Eastern Airline gave special priority to the shipment of these eyes. Usually they were shipped at about 2 p.m. and arrived at about 10 p.m. in Houston. Someone had to be at the airport in the beginning, usually myself, to meet the plane. I took the eye directly to the hospital at first and operated at night. This was very tiring, even to a young and eager surgeon. Later, the thermos was put in an outer container and was surrounded by dry ice. I arranged for the airline to deliver the container to a taxi driver who for his usual tarriff, brought it my home where I removed the glass jar containing the eye and placed it in the ice box overnight. Early next morning I

replaced the glass jar in the thermos replacing the melted ice with ice cubes and went directly to surgery. Nearly all of the eyes showed some clouding of the cornea which cleared withing four or five days after grafting. If the clouding was severe the operation had to be postponed until another eye became available and this might be several weeks or even months.

The demand for corneas in the early fifties was not great in as much as only a few surgeons grafted corneas. Although my report of a hig rate of success using Barraquer's technic in six cases? received skeptical review at first, within a few years Castroviejo and nearly all other surgeons had adopted it. The reported high rate of success, with it encouraged other surgeons to perform corneal grafting, and the demand for eyes far exceeded the supply. Not until Dr. Farge became director of the Lion's Eye Bank in Houston did the availability of eyes become plentiful under his energetic and innovative management. This eye bank, I believe is now one of the world's largest and sends eyes everywhere. I and all surgeons can schedule a corneal graft and be almost certain that the tissue will be available at the scheduled time.

That the surgery can now be done as a scheduled procedure is not entirely due to the devotion and energy and innovation of Dr. Farge. In the 1960's Drs. McCavey and Kaufman devised a media in which corneal tissue might remain suitable for grafting for several days. Formerly corneas from cold whole eyes were grafted within 24 hours after death. Some surgeons have found that a more recently formulated media-K-sol-permits successful grafting even after seven days of preservation.

While eyebanking has made corneas plentiful, unforeseen problems have arisen recently with the recognition of ther danger of transmitting fatal diseases through corneal transplantation. Eyebanks have met these new problems forthrightly. Now, all donors are tested for antibodies to hepatitis. AIDS and Jacob Kreutzfeld disease. Unfortunately, one cornea from a patient with the latter dreaded neurological, dementing disorder has been transplanted. Whether the recipient will be harmed by this slow virus is not yet known. No known transmission of AIDS by corneal grafting has been reported, but the probablility that someday a patien who has received a corneal graft will develop AIDS is causing medico-legal concern among those responsible for supervising eye banking procedures.

To conclude: Yesterday I was young; today I am old, but the seventh age of man has not yet come upon me. The I knew and was a part of all that I had met; now, still I strive to seek, to find, and not to yield. How dull it is to pause, to make an end, to rust unburnished, not to shine in use.

All the world's a stage and all the people in it merely players. In turn we strut and play our parts, and then are heard no more. How fortunate am I to have lived when such great advances have taken place in restoring vision to those who lost it, and to have contributed in a small way to this advance. How fortunate am I and my ophthalmic colleaguess to have been able to help others to see again. But without the help of many others, without the dedication and skill of those who direct and work in the Lions Eye Bank, much of our knowledge and skill would have been as souding brass or a tinkling cymbal.