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Bicentennial of keratoplasty: thus spoke the pioneers

Dvestota godišnjica keratoplastike: tako su govorili začetnici

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Introduction

Two hundred years ago, Franz Reisinger [1], a German professor of surgery, obstetrics, and ophthalmology, coined the term “keratoplasty” for a new corneal procedure promoted by his experiments on a rabbit eye six years earlier. The bicentennial of the appearance of this term used in his paper, as well as of a novel, revolutionary surgical attempt at curing blindness, is the opportunity to shed light on Reisinger’s landmark achievement.

Yet another jubilee celebrated in 2024 is the 190th anniversary of the introduction of “corneal transplantation” (CT) as a new term that was to become a widely used synonym for “keratoplasty.” Therefore, the current year is the right time to revisit the site of its origin – Wilhelm Thomé’s [2] inaugural dissertation, using a recent translation.

These first attempts at corneal grafting have often been used as an introduction to many texts on transplantation in ophthalmology. With a few remarkable exceptions, the tendency of using secondary sources has led to a multiplication of inaccurate presentations of Reisinger’s [1] experiment, such as stating that he had sutured a graft from one animal to the other, using hundreds of rabbits and chickens, all without success. On the other hand, Thomé’s [2] significant work has been reduced to a mere date when the term CT appeared in literature and was overshadowed by more attractive experiments performed by his follower Samuel Bigger [3]. The best way to rectify this injustice is to consult primary sources and let these pioneers of keratoplasty speak for themselves.

Reisinger’s ipsilateral autokeratoplasty

In a paper published in 1824 under the title “Keratoplasty, a search for the broadening of ophthalmology”, Reisinger [1] wrote: “In February 1818, I separated the cornea of a young rabbit close to the sclera, up to the line (2.18 mm, author’s remark), using a cataract knife and a pair of scissors subsequently. Now, this almost totally excised cornea was spread over the iris again, and the lids were closed with an appropriate bandage, which was taken off by the animal two and a half days later; the cornea was almost white and opaque, but more than its half became clear after it had reunited. The second operation was done on the same eye of this rabbit on June 6, 1818. I performed a complete corneal separation, but not quite close to the sclera, which was left with a narrow remnant of the cornea. This completely separated cornea was put back in its place, and the lids were closed with an appropriate bandage.”. Forty days later, gross edema had been resolved, revealing the attached cornea with only a small, convex, and opaque dot at its mid-periphery [1].

Reisinger’s [1] idea was to check if a completely excised corneal button would create an “organic connection” with the remaining cornea and retain its transparency after having been put back into its place. The result can be described in modern terms as an ipsilateral autokeratoplasty, a neat experiment devoid of rough sutures and foreign tissue – no more, no less.

The promise of “a special treatise on this matter, to my best knowledge unmentioned before, with a presentation of my investigation and proposals, is soon to be published” [1] seems not to have been fulfilled. The burden of being an editor of Bavarian Annals, the journal in which his paper was

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published, as well as a professor of surgery, ophthalmology, and obstetrics, might be an adequate explanation for the lack of time.

In the words of a contemporary, it was inevitable that Reisinger's [1] essay would cause a general commotion and various controversies.

Thome's allografts and the use of direct suturing

The answer to some of these controversies was offered by Wilhelm Thomé [2] in his inaugural dissertation "*De Corneae Transplantatione*", published in 1834. He performed six experiments in which he sutured cornea from one rabbit to the other; in one of these, the recipient cornea was made opaque with the use of sulfuric acid. The additional two experiments included corneal grafting between a rabbit and a dog.

His first task was to construct a cage for holding unanesthetized animals during surgery. After having excised the donor cornea with a cataract knife and a pair of scissors, he fixed it with a suture: "For that purpose, a manufacturer of surgical instruments supplied me with the adequate needles, unknown to the medical theory, very fine, 2/3 circle curved, made from English steel, with a red wax coated thread intended to be recognizable within the pus. The edge of the corneal button was stabbed with one needle and pulled out until the middle of the thread reached the canal, while the opposite edge was stabbed with the other needle. Next, these sutures were pulled through the recipient cornea in the horizontal diameter, and the knots were tied." [2]. The follow-up was eight weeks, except for two rabbits with a fatal outcome after one and three weeks, respectively. The results were only partially successful, as shown in beautiful lithographs: five transplants coalesced with the recipient's corneoscleral rim, of which two were completely transparent, while three were semitransparent and vascularized. There were two cases of lens expulsion and one complete failure with a retracted opaque graft. Even so, we believe that Thomé [2] was the first to introduce direct corneal sutures and to show that allografts and xenografts of the cornea were possible, even in a traumatized recipient tissue.

His work immediately gave a strong impetus to further experiments with keratoplasty. Sadly, it was consigned to oblivion in decades to come due to Thomé's [2] untimely death. Furthermore, the use of Latin has limited the interest in his dissertation to collectors and dealers of antique books. A recent German translation of this text may help Thomé in retrieving his place in the history of keratoplasty [2].

Bigger's optic keratoplasty and veterinary ocular surgery

One of those who "tried to faithfully follow the plan laid out by Thomé" [2] was Dr. Samuel Bigger [3]. His lecture on keratoplasty was published in 1837, "with the permission of the author, from the notes taken by Mr. Swift". This article stood out in that issue of the Dublin Journal of Medical Science as the only one written in the third person. It enabled the author to get "the highest credit on the ingenuity, patience, and manual dexterity" in his own paper. Although his experiments on rabbits are not substantially different from those performed by Thomé [2], this master of presentation fires the imagination of a reader with his sight-saving act of the corneal allotransplantation in which a mortally wounded gazelle was the donor and a pet gazelle the recipient; this scene took place in 1835, during the surgeon's captivity in the Egyptian desert, at the moment of an outbreak of plague in a country shaken by a rebellion. Back in Dublin, the good doctor repeated the procedure on a dog with a corneal scar, with a dead wolf as the donor. The dog ran away to a forest two days after surgery, only to return with the excellent function of the operated eye.

Our opinion is that these two transplantations might be considered the first optic keratoplasties and unique attempts at sight-saving surgical procedures in animals. As an author who published in English, the lingua franca of the future, Bigger [3] was able to convey the ideas and surgical techniques of his two predecessors to the New World and later communicate them globally.

Immediately, these ideas influenced Richard Kissam [4], a surgeon from New York who used a piglet as a donor and performed the first human xenograft in 1838. This premature attempt ended with a complete graft melting, as Kissam [4] seemingly failed to follow Bigger's [3] advice and "give this matter his attentive consideration."

Lamellar versus penetrating keratoplasty

Although the technique introduced by Reisinger [1] and developed by Thomé [2] and Bigger [3] was occasionally used almost unchanged even a century later [5, 6], and throughout the whole twentieth century as a modified procedure called penetrating keratoplasty, the history of CT took a sharp turn in 1840, when Franz Mühlbauer [7] published his inaugural dissertation with a lithograph which illustrated his triangular lamellar corneal grafts fixed to the recipient rabbit eyes with one or two direct sutures. From that moment to the present day, the approach to CT has been oscillating from lamellar to penetrating keratoplasty and back.

Almost half a century had passed until Arthur von Hippel [8] invented a motor-driven trephine and performed the first successful CT in a patient by placing a small-diameter, full-thickness rabbit corneal button into a young woman's lamellar bed.

His technique was immediately accepted except for the use of the lamellar xenograft. On the contrary, it was penetrating keratoplasty using a human donor that made a comeback after the publication of Eduard Zirm's [9] famous case in 1905. As both von Hippel's [8] and Zirm's [9] patients had similar postoperative visual acuity, the result of the competition between the two methods was still a draw. It was Anton Elschnig's [10] twenty years long work and his epochal series of 174 patients with a 22 percent overall success and about three-quarters of clear grafts in the eyes with interstitial keratitis that confirmed the leading role of penetrating keratoplasty.

A giant step further was made when Vladimir Petrovich Filatov [11, 12] presented his success with a modified André Magitot's procedure [13] for storage and transplantation of cadaver donor corneas on a large scale. Closely followed by Zdravko Nižetić [14, 15], Filatov [12] was instrumental in paving the way for the establishment of the first eye bank. Established in 1944 as a result of a combined effort invested by Townley Paton [16], John MacLean, and Aida de Acosta Brackinridge, this institution was soon joined by a web of similar ones and enabled piling of still larger series of keratoplasties mounting to several thousand cases in the hands of masters like Ramon Castroviejo [17].

A short and promising revival of lamellar keratoplasty in 1948, created by Paufique et al. [18], was overcome by a tide of visually more successful penetrating keratoplasties enabled by the introduction of corticosteroids and microsurgery. From the sixties to the end of the twentieth century, penetrating keratoplasty ruled the scene, and a few generations of corneal surgeons kept this "gold standard" serenely. Yet, there were those like José Barraquer [19] in the fifties and Gerrit Melles [20] in the nineties who could not comply with the drawbacks of this standard, mainly the unpredictable high and often irregular astigmatism, as well as its open sky technique. These surgeons invented some new approaches. José Barraquer [19] came up with refractive corneal surgery, while Gerrit Melles [20] invented selective lamellar transplantation, crowned with Descemet stripping endothelial keratoplasty (DSEK) and Descemet membrane endothelial keratoplasty (DMEK). Refractive corneal surgery can correct most of the refractive errors, while DSEK and DMEK do not create significant errors at all, thanks to a small limbal opening for the transplantation of endothelium on a thin carrier and its sutureless fixation with air.

Future trends in corneal transplantation

History of science teaches us that the seeds of breakthroughs in physics, chemistry, and biology, unknown to us at present, become future game changers in medicine. The history of keratoplasty reveals that such seeds grow silently even, or shall we say, especially during the stagnant periods of a particular surgical discipline. It was Pasteur's [21] proof of germ theory of diseases, Lister's [22] introduction of antiseptic methods in surgery, Morton's application of general anesthesia [23], and Koller's [24] announcement of local anesthesia that happened during those forty years between Mühlbauer's [7] and von Hippel's [8] achievements, a period of a stand-still in CT. These discoveries saved more eyes and lives and helped both patients and surgeons more than any innovation in the technique of keratoplasty.

Likewise, the greatest discoveries of the twentieth century, quantum mechanics [25] and the structure of deoxyribonucleic acid [26] led to quantum electronics, the invention of lasers, and genetic engineering, respectively. First of these changed the approach to surgery and imaging procedures, while the ability to change genes could eliminate some indications for transplantation. Further, the discovery of immunity [27] has brought corticosteroids to the scene, lowered graft rejection, and saved more transplants than any microsurgical device, while the knowledge of the role of corneal endothelium enabled DSEK and DMEK.

Finally, polymer chemistry [28] and tissue culture [29] led to the development of tissue engineering, helped the construction of a more tolerable keratoprosthesis, and offered hope for the creation of either an artificial cornea or a method of replacing a part of the cornea with cultured cells arranged on a polymer scaffold.

Conclusion

The moral of these stories from the two previous centuries can be summarized in the following way: there are more things happening in the basic sciences of the twenty-first century than are dreamt of in our clinically oriented minds; therefore, it will be prudent to restrain from any prediction of their influence on corneal transplantation in the future.

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