### Table 1

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<th>Drug</th>
<th>IOP</th>
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<td>14.83 (S)</td>
<td>23.72 (S)</td>
<td>0.94 (S)</td>
</tr>
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<td>22.24</td>
<td>27.75</td>
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</table>


### Figure 1

A 5.5 mm. corneal button, re-excised, and sutured with 10-0 nylon suture within original 6.5 mm. graft.

One-half weeks after skin grafting eight of the remaining 16 rabbits had 5.5 mm. corneal buttons excised and resutured within the first graft. These grafts were all rejected 23 to 26 days after skin grafting. Of the eight grafts which were not excised, four remained clear and four were rejected 27 to 50 days after skin grafting. Without intervening skin grafts, all 10 re-excised corneal allografts remained clear. These results indicate that when afferent immune protection is short-circuited by sensitization with skin grafts some corneal grafts are protected from the efferent immune arc by corneal anatomy. When this anatomy is interrupted, efferent protection is abrogated, resulting in an increased graft rejection rate and decreased graft survival.

In rabbits and man, nonrejected penetrating corneal allografts (PKP's) do not sensitize the host. Therefore, a major factor protecting PKP's from immune rejection is a block in the afferent limb of the immune arc. In the present study, subsequent skin grafts from the same donor animals were used to sensitize the host and eliminate this afferent limb protection. We then studied the efferent limb of the immune arc in well-healed corneal transplants.

**Materials and methods.** Six and one-half millimeter penetrating corneal allografts were exchanged between pairs of virgin New Zealand white rabbits weighing 2.5 to 3.5 kilograms. The members of each pair were from two partially inbred strains. Continuous 8-0 silk suture was used, and topical antibiotics and dilating drops were applied daily until suture removal on Day 10.

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**Efferent limb protection of corneal allografts from immune rejection.** Stephen R. Waltman and Joel M. Engelstein.

Twenty-six rabbits with clear 6.5 mm. penetrating corneal allografts had skin grafts from the same donor eight weeks later. Ten animals rejected their corneas within 16 days. Two and
Twenty-six animals with clear corneal grafts had 12 mm. ear skin grafts exchanged between partners eight weeks postoperatively. Skin and corneal grafts were examined daily. Rejection was scored when the skin grafts were less than 10 per cent viable or when there was a definite ciliary flush leading to corneal graft clouding.1

Two and one-half weeks after skin grafting, the 16 animals with clear corneal grafts were randomly divided into two equal groups. In the experimental group, a 5.5 mm. corneal button, inside the original graft, was excised, rotated 180 degrees, and sutured in place with a continuous 10-0 nylon suture (Fig. 1). The corneal group was not operated (Fig. 2).

Nine rabbits with clear 6.5 mm. corneal autografts had 5.5 mm. buttons excised and sutured with 10-0 nylon. Ten additional rabbits had 6.5 mm. corneal allografts without subsequent skin grafts. Eight weeks postoperatively they had a 5.5 mm. central corneal button excised and resutured with 10-0 nylon. All animals were observed daily for three months.

Results. All 26 animals rejected their skin grafts within seven to fourteen days with a mean rejection time of 9.2 days. This is comparable to skin graft survival time in rabbits with clear corneal allografts.1

Ten of the animals rejected their corneal grafts during the first 16 days after skin grafting. Of the 16 remaining animals with clear grafts and noninflamed eyes, eight had corneal re-excisions (Fig. 2). All of these animals had clear grafts and quiet eyes within two days after this procedure. All went on to reject their resutured corneas between Day 23 and Day 26 following the initial skin graft (Fig. 3). The rejection began with a ciliary flush, and 24 to 48 hours later a line of keratitic precipitates could be seen advancing across the endothelium.

Of the eight control animals whose corneas were not re-excised, three rejected their grafts between Days 27 and 29, and one rejected at Day 50 (following trauma). Four animals retained clear grafts for the duration of the study. These results are shown in Table I. The survival times are significantly different for these two groups (p < 0.01). Furthermore, there are significantly more clear grafts in the control group (p < 0.025).

None of the nine re-excised autografts clouded. In the 10 animals without skin grafts, all of the ten re-excised corneal allografts remained clear for the three-month observation period (Fig. 4).

Discussion. The unique anatomy of the cornea allows corneal allografts to survive while other transplanted tissues are rejected. In previous experiments1,2 it has been shown that nonrejected corneal allografts do not lead to sensitization and second set rejection of subsequent skin grafts. Rejected corneal grafts, however, do sensitize the
Fig. 3. Rejection of re-excised 5.5 mm. corneal allograft in animal sensitized by a skin graft.

host and accelerate skin graft rejection. Stark and co-workers' reported that nonrejecting corneal transplants in humans did not lead to detectable lymphocytotoxic antibodies, but those patients with evidence of immune graft rejection did develop these antibodies. This indicates that unrejected corneal allografts do not sensitize the host, and a block in the afferent limb of the immune arc exists. Following skin grafting and rejection of the skin graft, however, the animal is sensitized, afferent protection is short-circuited, and the efferent limb can be studied.

In this study only 10 of 26 animals rejected their corneal allografts within 17 days when skin grafts were performed eight weeks later. This is in contrast to previous results where 75 per cent of corneas were rejected by this time using a different strain of rabbits, and is an example of strain variations. It emphasizes the difficulties in comparing experimental results between different groups of animals. When the corneal allograft was left unaltered, half of the rabbits retained clear grafts for the duration of the experiment. The other half had the onset of graft rejection delayed. In the sensitized host then, a well-healed corneal allograft is protected from immune rejection by the efferent limb of the immune arc. In some animals the protection was complete, in others only partial. This is in agreement with previous investigations.

When the efferent protection is eliminated by re-excising and re-stitching the corneal grafts, the rejection rate increases to 100 per cent in the sensitized host. All the re-excised grafts were clear and the eyes quiet three days postoperatively. They then went on to show typical signs of corneal rejection with endothelial precipitates. Since all the re-excised autografts and the allografts in nonsensitized hosts remained clear it is unlikely that the trauma of re-excision, per se, was responsible for the initiation of rejection. Induced uveitis can also lead to corneal graft clouding, but autografts are affected less often than homografts, and most grafts survive. Furthermore, there are often clinical differences between pure homograft rejection and uveitis-induced corneal clouding. Hence, the interruption in corneal anatomy resulting from a penetrating incision abrogates the protection from the efferent limb of the immune system allowing a sensitized host to reject a previously well-healed corneal graft.

These results are consistent with light and electron microscopic studies of graft rejection which indicate that the earliest morphologic changes in the rejecting grafts occur in areas of leukocytic infiltration at the corneal scar.

Fig. 4. Clear re-excised corneal allograft in animal without skin graft.

From the Department of Ophthalmology, Washington University School of Medicine, St. Louis, Mo., and the University of Florida College of Medicine, Gainesville, Fla. Supported in part by Grant EY-00004 from the National Eye Institute, Bethesda, Md. Submitted for publication Oct. 29, 1973. Reprint requests: Dr. Stephen Waltman, Department of Ophthalmology, Washington University School of Medicine, 660 S. Euclid Ave., St. Louis, Mo. 63110.

Key words: keratoplasty, corneal transplant, immune rejection, efferent limb, graft rejection.

REFERENCES
A viewer for correlation of fluorescein and color fundus photographs. ROBERT W. FLOWER AND ARNALL PATZ.*

A simple viewer for superposition of a fluorescein angiogram on a color fundus photograph without compromising the most desirable characteristics of either is described. The usefulness of this device is described as an aid in correlating an angiogram with the patient's retina, particularly in conjunction with a slit lamp photocoagulator.

The introduction of improved resolution photography for performing fluorescein angiography has permitted more precise studies of the retinal microcirculation. Also, new argon laser and Xenon arc slit lamp photocoagulation delivery systems now commercially available permit the photocoagulation of areas as small as 50 microns in diameter. These two innovations have introduced new concepts in the management of patients with macular disorders and with intravenous neovascularization emanating from the optic disc.

When photocoagulating lesions near the fovea, precise localization is required and even for less vital areas of the retina, precise localization in relationship to visible retinal landmarks seen through the fundus contact lens with a slit lamp photocoagulator is desirable. When studying the patient through a slit lamp photocoagulator, the fundus details are visible with approximately the same contrast and similar highlights as are seen in standard color fundus photography. However, much higher resolution of fine microvascular abnormalities and also more precise localization of leakage sites is possible with fluorescein angiograms. Therefore, when treating a patient with a slit lamp photocoagulator it is usually necessary to extrapolate from the much higher contrast fluorescein angiographic landmarks to the fundus view seen through the slit lamp. This extrapolation is frequently difficult, especially where details of the smaller branch vessels are concerned.

The difficulty of this extrapolation has been lessened in some instances by use of color fluorescein photography as suggested by Allen and Frazier and more recently advocated by Schatz and co-workers at Hopkins. Color fluorescein studies permit a greater degree of orientation with respect to retinal landmarks as seen by standard ophthalmoscopy. However, the resolution of the fluorescein fluorescence is definitely diminished by exchanging color film for the black-and-white film ordinarily used in fluorescein angiography.

This report describes a fairly simple viewer which permits superposition of a fluorescein angiogram on a color fundus photograph without compromising the most desirable characteristics of either. The only requirement for producing the two fundus photographs is that they both be made using identical fundus camera optics. This assures that the two images produced are of identical magnification.

The viewer consists of two slide holders oriented at right angles to each other with an independently variable light source behind each (Fig. 1, D and E). A 50 per cent beam splitter is located in such a way that it makes a 45° angle with each of the two slide holders (see Fig. 1). The reflecting surface of the beam splitter (Fig. 1, A) is centered at the intersection of two imaginary lines.