Corneal Vascularization in a Group of Soft Contact Lens Wearers: Prevalence, Magnitude, Type and Related Factors

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Abstract

Groups of 827 soft contact lens wearers and 900 non-contact lens wearers were examined for corneal vascularization by means of biomicroscopy. Slit-lamp photographs were taken to record cases of vascularization and to permit measurements of the magnitude of the vascular response. The prevalence of corneal vascularization in the soft contact lens group was 33.9% compared to 2.0% in the non-contact lens group; a highly significant difference [X^2=304.12, df=1, $p<0.005$]. Of the soft contact lens related vascular responses, 98.6% were located in the superficial stroma, indicating that the conjunctival circulation is most often involved in corneal vascular responses to soft contact lenses. Vascular penetration radially into the cornea from the limbus did not exceed 4.5 mm in either the study or control groups; 96.8% of the vascular responses being 1.5 mm or less in the soft contact lens group. Age and sex of the patients were not significantly related to the observed frequency of corneal vascularization in either the study or control groups. However, refractive error, daily wearing time and the total length of time soft contact lenses had been worn were significantly related to the observed frequency of corneal vascularization in the soft contact lens group.

Even though sampling error and bias affect this type of study, it appears that corneal vascularization is a frequent ocular response in patients who are wearing daily-wear and extended-wear soft contact lenses. This study supports the recommendation that all soft contact lens patients, including those who may be asymptomatic, should be carefully examined at regular intervals for signs of adverse ocular responses such as corneal vascularization.

Introduction

Corneal vascularization is an adverse ocular response to contact lenses. Both PMMA and hydrophilic soft contact lenses have been implicated in the development of superficial and/or deep stromal corneal vascularization in humans as well as in experimental animals.[1-11] In most cases, the zone of vascularization is limited to the peripheral cornea,[12] while in more severe cases, blood vessels and granualation tissue extend to the central optic zone of the cornea.[13]

The physical, physiological, biochemical, neurological and associated factors which are involved in the pathogenesis of corneal vascularization are still incompletely understood. Nevertheless, several factors have been shown to be common to both corneal vascularization and contact lens wear: corneal hypoxia, corneal edema, limbal injection, increased peripheral corneal lactate concentration and immunological responses.[14]

In a study of steep, tight-fitting hard and soft contact lenses, Tomlinson and Haas[15] discovered a direct relationship between the degree of central corneal edema and the degree of limbal vessel injection when corneal edema exceeded 6%. This correlation was noted for hard and soft contact lenses alike, although the former did not impinge physically upon the limbal vessels. It was accordingly suggested that the limbal vascular injection resulted from tissue hypoxia and ensuing corneal edema rather than from mechanical or physical lens factors.

Comparing the limbal vascular responses related to hard and soft contact lenses, McMonnies, Chapman-Davies and Holden[16] reported that soft contact lens wearers had significantly more limbal vascular injection than hard contact lens wearers, even though the average number of years of wear was only 3.8 years for soft lens wearers and 11.6 years for hard lens wearers. They voiced concern that the limbal injection of soft contact lens wearers might ultimately result in corneal vascularization.

McMonnies[17] reviewed anatomical criteria and clinical methods of examining the limbal vasculature for signs of abnormalities prior to contact lens wear in

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order to permit an accurate assessment of the vascular response to the contact lenses later. He stressed the importance of monitoring the limbal vascular response at regular intervals after prescribing contact lenses in order to gain an overall indication of the contact lens tolerance, as well as to allow improved lens fittings to be made before corneal vascularization could develop.

The examination of the zone of capillary end-loops to diagnose corneal vascularization demands careful observation and attention to anatomical detail. Duke-Elder[18] writes:

> "These capillary end-loops do not normally extend beyond the serrated rim of the normal limbal opacity but lie along the line where the limbal curve changes to the corneal. . . . If they transgress the limit of the limbus as a further series of vascular loops, the vascularization is pathological."

McMonnies, Chapman-Davies and Holden[16] stressed the importance of distinguishing between the translucent limbal tissue surrounding the cornea and the transparent corneal tissue by means of retro-illumination techniques when evaluating the limbal capillaries with the biomicroscope. It is known that this zone of translucent limbal tissue is most prominent superiorly and is quite variable in width from person to person, ranging from zero to approximately 2.5 mm from the margin of the opaque sclera. Normal limbal capillary loops are routinely observed within this variable-width translucent limbal zone (Fig. 1), whereas abnormal corneal vessels are observed more axially in clear corneal tissue (Fig. 2). The morphological structure of the limbal loops is also helpful in the early diagnosis of corneal vascularization, for it is known that vascular "spiking" occurs in the initial stages of superficial corneal vascularization[17] (Fig. 3). As the vessels continue to grow into the superficial corneal stroma, they become increasingly tortuous, bifurcate and often become dendritic in appearance (Fig. 4). The diagnosis of deep stromal corneal vascularization is simpler to make since these vessels emerge from deep within the corneal stroma, are straighter than superficial vessels and are discontinuous with the conjunctival circulation (Fig. 5).

The prevalence of corneal vascularization in the population of soft contact lens wearers is unknown and may be impossible to discover exactly because of the difficulties inherent in studying such a large, diverse group. Nevertheless, examining a sample of this population would produce statistical estimates within the limits of sampling error and bias. In addition, data could also be gathered indicating the frequency and type of corneal vascular responses (superficial or deep stromal), the magnitude of vascular infiltration into the cornea, and the relationship of other likely correlated clinical factors such as age, sex, refractive error, daily wearing time and total contact lens wearing time.

Purpose

The purpose of this investigation is:

Part I:
to compare the prevalence, magnitude and type of corneal vascularization in a group of soft contact lens wearers with that of a control group of non-contact lens wearers, and

Part II:
to determine if a correlation exists in soft contact lens wearers between corneal vascularization frequency and the following factors: age, sex, refractive error, daily wearing time and total wearing time.

Method

The study group was comprised of soft contact lens patients who had been

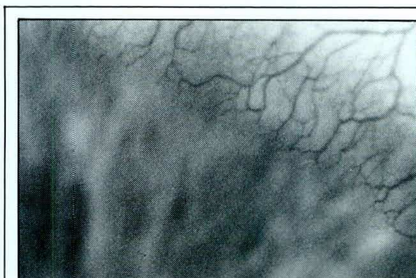

Figure 1
Normal limbal vessels within the variable-width translucent limbal zone surrounding clear corneal tissue (96×)

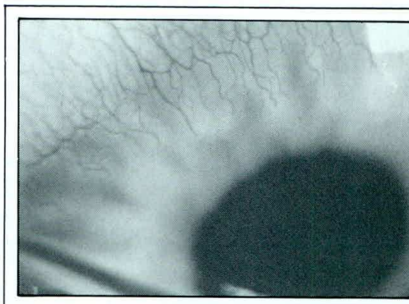

Figure 2
Abnormal corneal vessels outside the zone of normal limbal translucency in clear corneal tissue (96×).

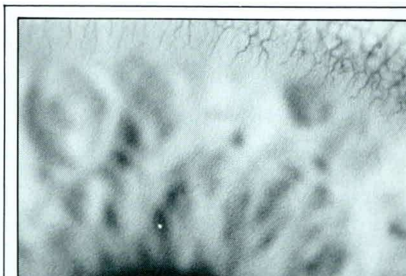

Figure 3
Early stage of superficial stromal corneal vascularization showing vascular "spiking" (96×).

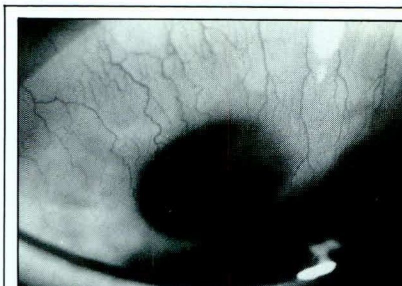

Figure 4
Late stage of superficial stromal corneal vascularization showing increased tortuosity, bifurcation and dendritic appearance (96×).

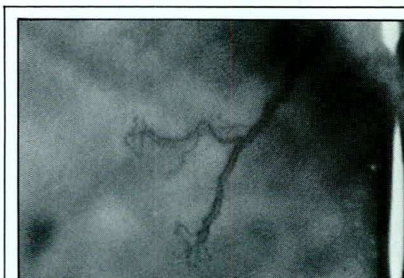

Figure 5
Deep stromal corneal vascularization showing straighter appearance of vessels emerging from deep within the corneal stroma (96×).

wearing daily-wear or extended-wear lenses on a regular basis for at least one year. Soft lens wearers who had previously worn hard contact lenses were exluded from the study. There were 262 males and 565 females in the study group, for a total of 827 soft lens wearers. Lenses were worn on a daily-wear basis by 784 patients while 43 patients were extended-wear.

The control group was made up of patients who had never worn contact lenses. There were 374 males and 526 females in the control group, for a total of 900 non-contact lens wearing patients. Figs. 6-7 and Table 1 show the patient frequency distributions for the study and control groups. The study group ranged in age from 4-75 years with a mean of 28.9 years and a standard deviation of 8.9 years. The control group ranged in age from 8-78 years with a mean of 34.2 and a standard deviation of 16.3 years (Table 2).

The age frequency distributions of the study and control groups are shown in Figs. 8-9 and Tables 3-4. As might be expected of a group of contact lens wearers, the majority (756/827 or 91.4%) were less than 40 years of age. In the control group, only 580/900 or 64.4% were under the age of 40 years.

The study and control groups consisted of patients who were examined on a daily basis from the patient population of the authors' practice. It was consequently impossible to conceal from the examiners the identity of the group, either study or control, to which the patients belonged.

Prior to the clinical examination, a questionnaire was completed by the soft contact lens wearers which documented their age, sex, refractive error, average daily contact lens wearing time and the total number of years soft contact lenses had been worn. Patients in the study group who had received their contact lenses outside the authors' practice were often unfamiliar with the manufacturer-type, design-type or water content of the soft lenses they were wearing; nor was it always possible for the examiners to determine this information. For these reasons, it was not possible to examine the connection between the frequency of corneal vascularization and manufacturer-type, design-type or water content of the soft contact lenses which the study patients were wearing.

Biomicroscopic examination of the limbal vessels in each of the four quadrants of both eyes was performed using direct and indirect retro-illumination

TABLE 1
Patient Frequency Distributions

Group	Males	Females	Totals
Study	262 (31.7%)	565 (68.3%)	827 (100.0%)
Control	374 (41.6%)	526 (58.4%)	900 (100.0%)

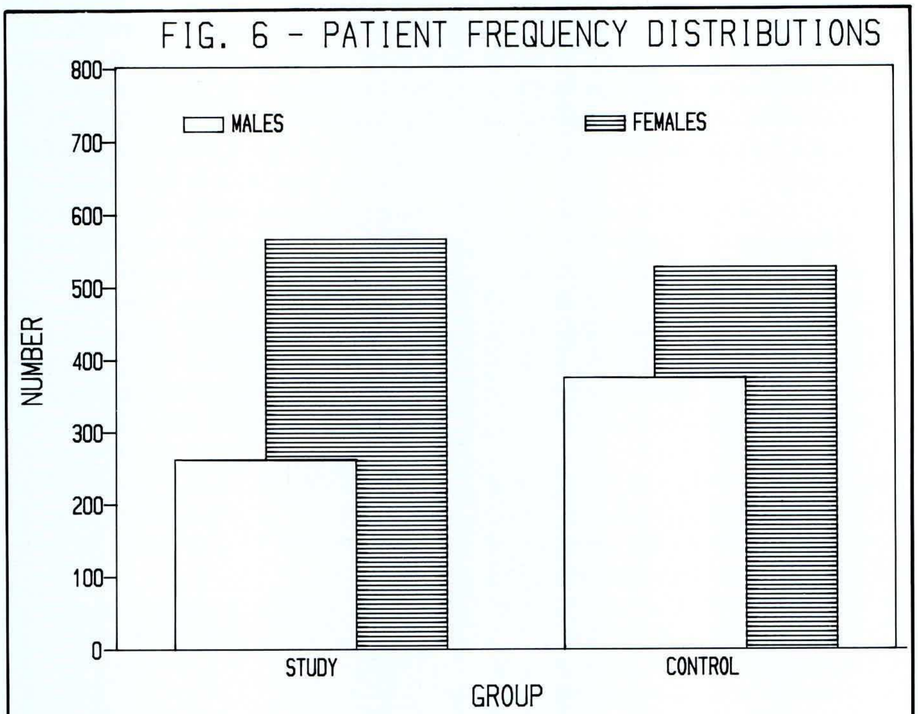

Figure 6
Number of patients in the soft contact lens (study) group and the non-contact lens (control) group by sex.

TABLE 2
Patient Age Statistics
(Years)

Group	Range	Mean	Std. Dev.
Study	4-75	28.9	8.9
Control	8-78	34.2	16.3

TABLE 3
Age Frequency Distribution
(Study Group N=827)

Age Group	Males	Females	Totals
0-9	0 (0.0%)	1 (0.1%)	1 (0.1%)
10-19	44 (5.3%)	80 (9.7%)	124 (15.0%)
20-29	126 (15.2%)	251 (30.4%)	377 (45.6%)
30-39	70 (8.5%)	184 (22.2%)	254 (30.7%)
40-49	17 (2.1%)	36 (4.4%)	53 (6.4%)
50-59	3 (0.4%)	10 (1.2%)	13 (1.6%)
60-69	1 (0.1%)	2 (0.2%)	3 (0.4%)
70-79	1 (0.1%)	1 (0.1%)	2 (0.2%)
	262 (31.7%)	565 (68.3%)	827 (100.0%)

TABLE 4
Age Frequency Distribution
(Control Group N=900)

Age Group	Males	Females	Totals
0-9	1 (0.1%)	2 (0.2%)	3 (0.3%)
10-19	79 (8.8%)	109 (12.1%)	188 (20.9%)
20-29	63 (7.0%)	95 (10.6%)	158 (17.6%)
30-39	87 (9.7%)	144 (16.0%)	231 (25.7%)
40-49	89 (9.9%)	111 (12.3%)	200 (22.2%)
50-59	43 (4.8%)	45 (5.0%)	88 (9.8%)
60-69	9 (1.0%)	17 (1.9%)	26 (2.9%)
70-79	3 (0.3%)	3 (0.3%)	6 (0.6%)
	374 (41.6%)	526 (58.4%)	900 (100.0%)

TABLE 5
Prevalence of Corneal Vascularization For Each Group
(Study Group N=827) (Control Group N=900)

Group	Males	Females	Totals
Study	97/262 (37.0%)	183/565 (32.4%)	280/827 (33.9%)
Control	7/374 (1.9%)	11/526 (2.1%)	18/900 (2.0%)

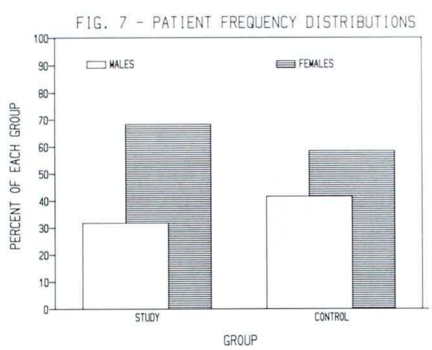

Figure 7
Percentage of patients in the soft contact lens (study) group and the non-contact lens (control) group by sex.

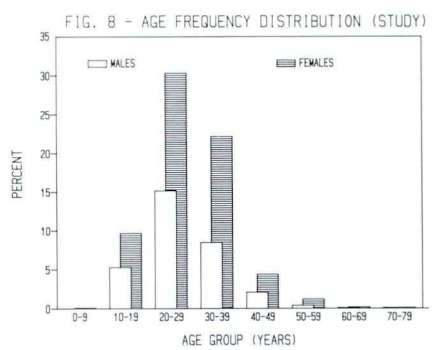

Figure 8
Percentage of patients in the soft contact lens (study) group by age and sex.

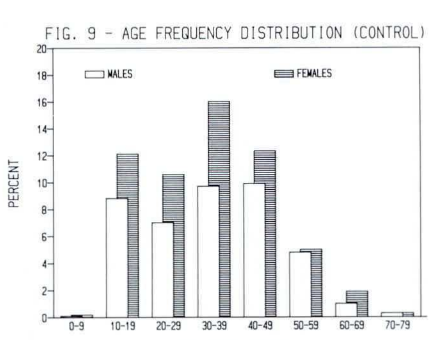

Figure 9
Percentage of patients in the non-contact lens (control) group by age and sex.

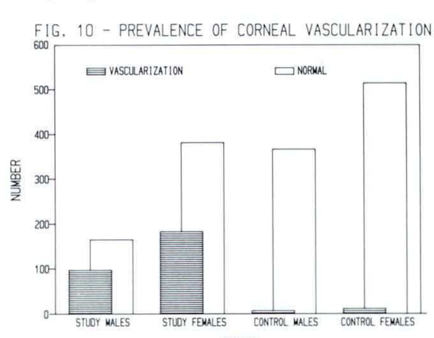

Figure 10
Number of patients by sex in the soft contact lens (study) group and the non-contact lens (control) control group with and without corneal vascularization.

methods. Slit-lamp magnifications ranging from 15–40× were used in conjunction with white and red-free illumination to examine the zone of limbal translucency and the capillary end-loops. Vessels which were observed to extend inward from the edge of the normal zone of limbal translucency into clear corneal tissue were classified as abnormal. In cases where there was no apparent translucent zone, vessels which were observed in clear corneal tissue against the background of the iris were considered abnormal.

Corneas in which vascularization was observed were photographed using a Topcon SL-5D photo slit-lamp and Kodachrome ASA 64 color transparency film. The maximum vessel penetration distance into the cornea from the limbus (the magnitude of the vascular response) was determined later by analyzing projected enlargements of the transparencies; using a comparator to make measurements to the nearest 0.1 mm. The inner margin of the translucent limbal zone, when present, or the periphery of the visible iris was used as the standard reference point for all measurements. Slide analysis magnifications varied from 15–96×.

The type of vascularization, superficial and/or deep stromal, was predetermined at the time of the clinical examination by evaluating the depth of the vessels within the corneal stroma using the usual optic section technique.

Results

Part I: Prevalence, Magnitude and Type of Corneal Vascularization Prevalence

The prevalence of corneal vascularization, as shown in Figs. 10–11 and Table 5, was 33.9% in the soft contact lens group and 2.0% in the control group of non-contact lens wearers. Chi-square analysis showed this difference to be highly significant [$X^2=304.12$, df=1, $p<0.0005$].

Of the 18 cases of corneal vascularization in the control group, 7 resulted from previous corneal infections, 3 from past ocular injuries and 8 were of unknown causes.

Magnitude

The extent of vessel penetration distance into the cornea from the limbus did not exceed 4.5 mm in either the study or control groups (Tables 6–7). However, a difference was noted in the frequency distributions of the two groups (Figs. 12–13). Whereas 96.8% of soft contact lens wearers had vessel growth within 1.5 mm of the limbus, only 44.4% of the control group were within this region, all of the latter being of unknown causes. Of the known causes of corneal pathology in the control group, (7 keratitis and 3 ocular injuries) all had vessel penetrations 2.0 mm or greater into the cornea. The soft contact lens wearers had vascularization frequencies which appeared to decrease in an exponential manner as a function of vessel penetration distance from the limbus, in contrast to the non-contact lens wearers who had an essentially constant vascularization frequency.

Type

Corneal vascularization was observed in the superficial and deep stromal layers in both groups (Fig. 14; Table 8). Most vascular responses were located in the superficial corneal stroma for soft lens wearers and non-contact lens wearers alike; 98.6% vs 66.7% respectively. Although Chi-square analysis could not be employed because of low expected frequencies (E<5), Fig. 14 does show an obvious preponderance of superficial stromal vascularization in the study group.

Part II: Corneal Vascularization vs Age, Sex, Refractive Error, Daily Wearing Time and Total Wearing Time

Age

Fig. 15 shows the age frequency distribution of the study group by number. Plotting corneal vascularization frequency as a percentage of each age group results in the histogram shown in Fig. 16 and summarized in Table 9. The sample sizes in the 0–9, 60–69 and 70–79 age groups are small (N<5), so vascularization frequencies for these age groups must be interpreted accordingly or disregarded altogether. Because the small observed frequencies in these age groups resulted in expected frequencies of less than 5, Chi-square analysis again could not be applied. Disregarding these age groups then and considering only the remaining age groups which were sufficiently large for statistical comparison, Chi-square analysis showed no significant difference in the frequency of vascularization as a function of age in the soft contact lens group.

The prevalence of vascularization for the control group is shown as a function

TABLE 6
Magnitude of Corneal Vascular Growth From Limbus
(Study Group N=280)

Distance (mm)	Males	Females	Totals
0.5	56 (20.0%)	120 (42.9%)	176 (62.9%)
1.0	32 (11.4%)	52 (18.6%)	84 (30.0%)
1.5	5 (1.8%)	6 (2.1%)	11 (3.9%)
2.0	3 (1.1%)	1 (0.4%)	4 (1.4%)
2.5	1 (0.4%)	3 (1.1%)	4 (1.4%)
3.0	0 (0.0%)	0 (0.0%)	0 (0.0%)
3.5	0 (0.0%)	0 (0.0%)	0 (0.0%)
4.0	0 (0.0%)	1 (0.4%)	1 (0.4%)
4.5	0 (0.0%)	0 (0.0%)	0 (0.0%)
	97 (34.6%)	183 (65.4%)	280 (100.0%)

TABLE 7
Magnitude Of Corneal Vascular Growth From Limbus
(Control Group N=18)

Distance (mm)	Males	Females	Totals
0.5	2 (11.1%)	0 (0.0%)	2 (11.1%)
1.0	3 (16.7%)	1 (5.6%)	4 (22.2%)
1.5	0 (0.0%)	2 (11.1%)	2 (11.1%)
2.0	1 (5.6%)	3 (16.7%)	4 (22.2%)
2.5	1 (5.6%)	2 (11.1%)	3 (16.7%)
3.0	0 (0.0%)	2 (11.1%)	2 (11.1%)
3.5	0 (0.0%)	0 (0.0%)	0 (0.0%)
4.0	0 (0.0%)	0 (0.0%)	0 (0.0%)
4.5	0 (0.0%)	1 (5.6%)	1 (5.6%)
	7 (38.9%)	11 (61.1%)	18 (100.0%)

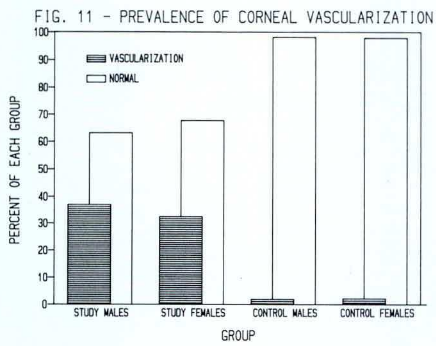

Figure 11
Prevalence of normal and vascularized corneas in the soft contact lens (study) group and the non-contact lens (control) group by sex.

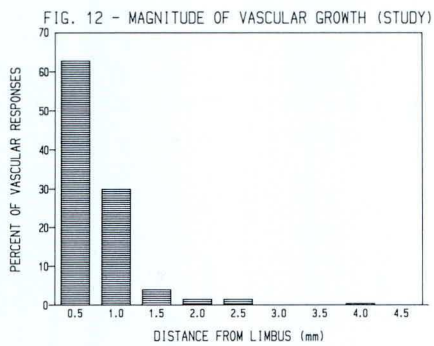

Figure 12
Extent of vessel penetration into the cornea from the edge of the translucent limbal zone for the soft contact lens (study) group.

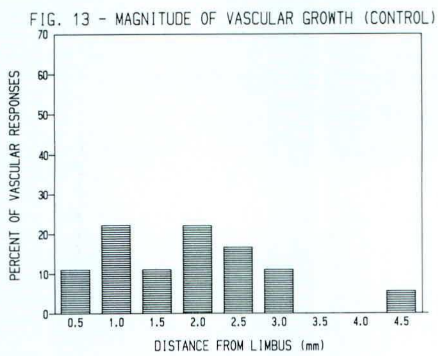

Figure 13
Extent of vessel penetration into the cornea from the edge of the translucent limbal zone for the non-contact lens (control) group.

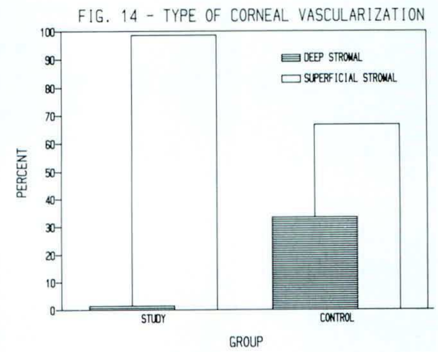

Figure 14
Prevalence of superficial and deep stromal corneal vascularization in the soft contact lens (study) group and the non-contact lens (control) group.

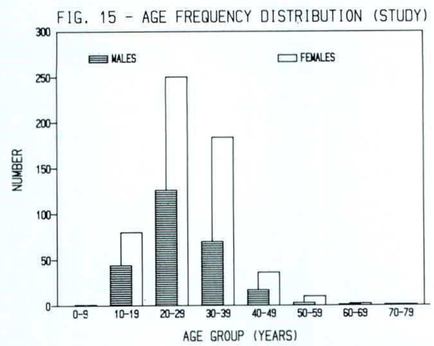

Figure 15
Number of patients in the soft contact lens (study) group by age and sex.

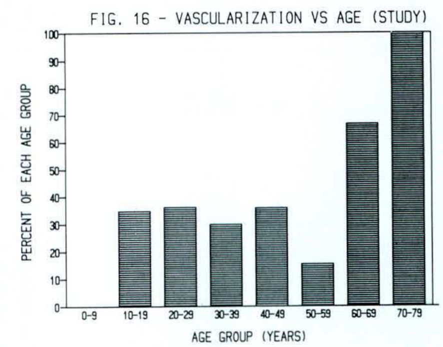

Figure 16
Prevalence of corneal vascularization in the soft contact lens (study) group by age.

TABLE 8
Classification Type Of Corneal Vascular Responses (Study Group N=280) (Control Group N=18)

Group	Superficial Stromal	Deep Stromal
Study	276/280 (98.6%)	4/280 (1.4%)
Control	12/18 (66.7%)	6/18 (33.3%)

TABLE 9
Prevalence Of Vascularization For Each Age Group (Study Group N=827)

Age Group	Males	Females	Totals
0-9	0/0 (0.0%)	0/1 (0.0%)	0/1 (0.0%)
10-19	13/44 (29.5%)	30/80 (37.5%)	43/124 (34.7%)
20-29	48/126 (38.1%)	88/251 (35.1%)	136/377 (36.1%)
30-39	28/70 (40.0%)	48/184 (26.1%)	76/254 (29.9%)
40-49	7/17 (41.2%)	12/36 (33.3%)	19/53 (53.8%)
50-59	0/3 (0.0%)	2/10 (20.0%)	2/13 (15.4%)
60-69	0/1 (0.0%)	2/2 (100.0%)	2/3 (66.7%)
70-79	1/1 (100.0%)	1/1 (100.0%)	2/2 (100.0%)
	97/262 (37.0%)	183/565 (32.4%)	280/827 (33.9%)

of age in Figs. 17–18 and Table 10. Once again, the small number of patients with vascularization in the control group precluded Chi-square analysis with the study group or between age groups within the control group itself. In the control group, the age groups 0–9 years and 70–79 years were comprised of small samples ($N<10$), so vascularization frequencies for these age groups must also be interpreted with care or disregarded totally as with the study group. Visual inspection of Fig. 18, disregarding the age groups 0–9 years and 70–79 years, shows a slight increase in vascularization frequency with age in the control group, although whether this is statistically significant is uncertain. Since most cases of vascularization in the control group were due to acute causes, such as keratitis and ocular injuries which would be expected to occur randomly throughout life, one might expect to see fewer of these cases in younger patients, which indeed is the situation here.

Sex

The data shown in Figs. 10–11 and Table 5, when tested by Chi-square analysis, showed no significant difference at the 0.01 level in the prevalence of corneal vascularization for either males or females in the study group [$X^2=1.52$, df=1] or the control group [$X^2=0.00$, df=1].

Refractive Error

The distribution of refractive errors for the study group is shown in Fig. 19 and Table 11. The greatest number of refractive errors were in the −4.00 D to 0.00 D range (70.2%), followed by the −8.00 D to −4.00 D range (23.0%), for a cumulative frequency of 93.2% of refractive errors within the −8.00 D to 0.00 D range.

The distribution in Fig. 20 and Table 12, shows the prevalence of corneal vascularization as a function of refractive error. Chi-square tests of significance of each refractive error group with every other refractive error group did not produce valid results in every case because of expected frequencies less than 5. Of the data which could be compared however, it was discovered that patients wearing soft lenses in the power range of −8.00 D to −4.00 D had significantly more corneal vascularization at the 0.01 level than patients in the −4.00 D to 0.00 D range. No significant difference in corneal vascularization frequency was found for patients in the −8.00 D to −4.00 D range with those in the 0.00 D to +4.00 D and +4.00 D to +8.00 D ranges.

Daily Wearing Time

Fig. 21 and Table 13 show the frequency distribution of daily wearing times for the study group. The majority of soft contact lens wearers (75.1%) were found to wear their lenses between 8 and 16 hours per day. There were 5.2% of patients who wore their soft lenses on an extended-wear basis. Fig. 22 and Table 14 show a smooth increase in frequency of vascularization as a function of daily wearing time until the 20–24 hour range at which point a slight drop in vascularization frequency is noted. Statistically, patients who wore their lenses 12–20 hours per day had significantly more corneal vascularization than patients who wore their lenses less than 12 hours per day ($p<0.01$). Patients wearing soft lenses on an extended-wear basis had no significant difference in vascularization frequency from patients who wore daily-wear soft lenses 12 hours per day or less ($p<0.01$). There was also no significant difference in vascularization frequency between groups who wore their lenses less than 12 hours per day ($p<0.01$).

Total Wearing Time

Fig. 23 and Table 15 show the frequency distribution of total wearing times for the soft contact lens group. The majority (72.5%) of soft contact lens wearers had been wearing lenses five years or less. Only 27.5% of the study group had been wearing soft contact lenses more than five years.

Fig. 24 and Table 16 show vascularization frequency versus total soft contact lens wearing time in years. The prevalence of vascularization shown in Fig. 24 for the 11 and 12 year groups should be disregarded because of the small sample sizes ($N<10$).

Chi-square analysis of each total wearing time period with every other total wearing time period established that patients who had been wearing soft contact lenses two years or less had significantly less corneal vascularization frequencies than those who had been wearing soft lenses three years or more ($p<0.01$). After three years of soft contact lens wear, there was no significant increase in vascularization frequency as the total number of years of contact lens wear increased ($p<0.01$).

TABLE 10
Prevalence Of Vascularization For Each Age Group
(Control Group N=900)

Age Group	Males	Females	Totals
0-9	0/1 (0.0%)	0/2 (0.0%)	0/3 (0.0%)
10-19	0/79 (0.0%)	0/109 (0.0%)	0/188 (0.0%)
20-29	0/63 (0.0%)	3/95 (3.2%)	3/158 (1.9%)
30-39	1/87 (1.1%)	4/144 (2.8%)	5/231 (2.2%)
40-49	2/89 (2.2%)	3/111 (2.7%)	5/200 (2.5%)
50-59	3/43 (7.0%)	0/45 (0.0%)	3/88 (3.4%)
60-69	1/9 (11.1%)	0/17 (0.0%)	1/26 (3.8%)
70-79	0/3 (0.0%)	1/3 (33.3%)	1/6 (16.7%)
	7/374 (1.9%)	11/526 (2.1%)	18/900 (2.0%)

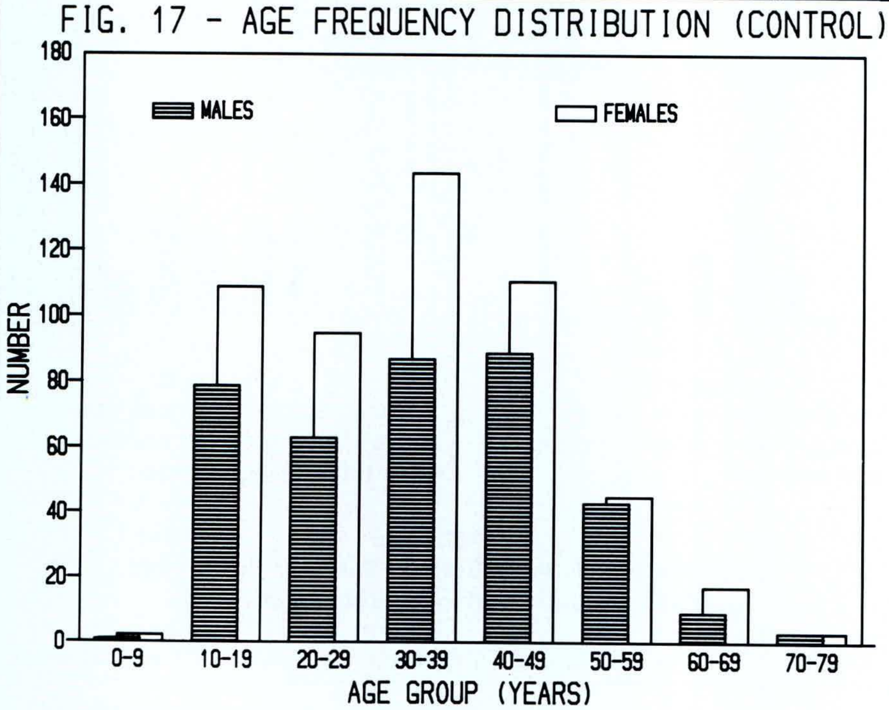

Figure 17
Number of patients in the non-contact lens (control) group by age and sex.

TABLE 11
Refractive Error Group Distribution
(Study Group N=732)

Rx Range (D)	Males	Females	Totals
−16−12	1 (0.1%)	2 (0.3%)	3 (0.4%)
−12−8	5 (0.7%)	10 (1.4%)	15 (2.0%)
−8−4	56 (7.7%)	112 (15.3%)	168 (23.0%)
−4−0	154 (21.0%)	360 (49.2%)	514 (70.2%)
0+4	5 (0.7%)	11 (1.5%)	16 (2.2%)
+4+8	4 (0.5%)	9 (1.2%)	13 (1.8%)
+8+12	2 (0.3%)	0 (0.0%)	2 (0.3%)
+12+16	0 (0.0%)	1 (0.1%)	1 (0.1%)
	227 (31.0%)	505 (69.0%)	732 (100.0%)

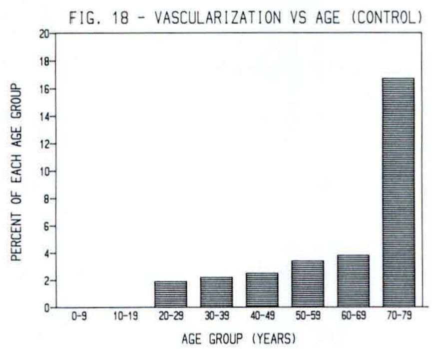

Figure 18
Prevalence of corneal vascularization in the non-contact lens (control) group by age.

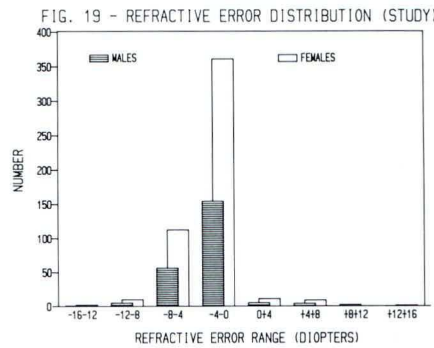

Figure 19
Number of patients in the soft contact lens (study) group by refractive error.

TABLE 12
Prevalence of Vascularization For Each Refractive Error Group (Study Group N=732)

Rx Group (D)	Males	Females	Totals
−16−12	0/1 (0.0%)	1/2 (50.0%)	1/3 (33.3%)
−12−8	3/5 (60.0%)	2/10 (20.0%)	5/15 (33.3%)
−8−4	28/56 (50.0%)	45/112 (40.2%)	73/168 (43.5%)
−4−0	47/154 (30.5%)	101/360 (28.1%)	148/514 (28.8%)
0+4	2/5 (40.0%)	1111 (9.1%)	3/16 (18.8%)
+4+8	2/4 (50.0%)	2/9 (22.2%)	4113 (30.8%)
+8+12	1/2 (50.0%)	0/0 (0.0%)	1/2 (50.0%)
+12+16	0/0 (0.0%)	1/1 (100.0%)	1/1 (100.0%)
	83/227 (36.6%)	153/505 (30.3%)	236/732 (32.2%)

TABLE 13
Daily Wearing Time Frequency Distribution (Study Group N=827)

D.W.T. (Hr)	Males	Females	Totals
0-4	10 (1.2%)	12 (1.5%)	22 (2.7%)
4-8	34 (4.1%)	77 (9.3%)	111 (13.4%)
8-12	75 (9.1%)	200 (24.2%)	275 (33.3%)
12-16	111 (13.4%)	235 (28.4%)	346 (41.8%)
16-20	20 (2.4%)	10 (1.2%)	30 (3.6%)
20-24	12 (1.5%)	31 (3.7%)	43 (5.2%)
	262 (31.7%)	565 (68.3%)	827 (100.0%)

Discussion

McMonnies et al[16] were concerned about the high frequency of limbal vascular engorgement which they found only in soft contact lens wearers. Their concern was that these patients may be predisposed, by virtue of their limbal vascular engorgement, to develop corneal vascularization at some later date. The results of this study would seem to support their concern.

It should again be emphasized that the criteria by which corneal vascularization was diagnosed in this study were those as discussed in Duke-Elder[18] and recommended by McMonnies et al[16]: the presence of blood vessels *outside the zone of normal limbal translucency* in clear corneal tissue. During biomicroscopy, this was best scrutinized by using high slit-lamp magnifications (25.6–40.0×), high intensity red-free illumination and a combination of direct and indirect retro-illumination techniques.

Prevalence

We found that 33.9% of soft contact lens wearers had corneal vascularization compared to 2.0% of the control group. Moreover, 10/18 cases of vascularization in the control group were due to distinctly identifiable pathological causes: keratitis and ocular injuries. Hence only 8/900 cases (0.9%) of the entire control group were actually diagnosed as having corneal vascularization of unknown causes. By comparison, none of the soft contact lens wearers had known pre-existing identifiable pathological conditions which could have been expected to produce corneal vascularization. If one deducts the 0.9% of cases of corneal vascularization of unknown origin which were found in the control group from the 33.9% found in the soft contact lens group, the prevalence of soft contact lens related vascularization would then be 33.0%. The reason why corneal vascularization does not develop in all soft contact wearers is a question which remains to be answered. The answer may lie not only in how soft lenses alter normal corneal physiology but also how individual differences in patient corneal oxygen requirements influence the maintenance of corneal health.

Virtually all soft contact lens wearers with corneal vascularization were unaware of its presence. There were no subjective symptoms reported, except in severe instances in which the vessels had advanced 4.5 mm from the limbus. The ocular symptoms then reported were: burning and itching, redness and blurred vision, as a result of the advanced stages of corneal edema, epithelial disturbance and limbal vascular injection, all of which were observed in these cases.

Magnitude

Corneal vascular responses of low magnitude occurred in far greater numbers in soft contact lens wearers than in non-contact lens wearers (Figs. 12 and 13). Note that the majority of soft contact lens related corneal vascular responses are within 0.5 mm of the limbus, followed by rapidly decreasing amounts in subsequent ranges, whereas in the control group there is an almost constant vascularization frequency as a function of vessel penetration distance from the limbus. In the control group, we know that 10/18 or 55.6% of the cases of corneal vascularization had causes of an acute nature: keratitis and ocular injuries, rather than slowly progressive conditions. Also, in every one of these cases the magnitude of the vascular response was 2.0 mm or greater. This is in direct contrast to the soft lens group which had the majority of cases of corneal vascularization magnitudes within 0.5 mm of the limbus, followed a smooth and rapid decrease in the number of cases as corneal vessel penetration distance increased from the limbus. This dissimilarity in the distributions of vascularization magnitudes attests to the slowly progressive, chronic nature of soft contact lens induced corneal vascularization.

When one considers that the oxygen transmissibility of soft contact lenses may be somewhat less than optimal to sustain normal corneal health, it is conceivable that certain patients' corneas are in a chronically oxygen-deficient state; enough so that low-grade edema may be present virtually all of the time. This chronic low-grade edema might not be sufficient to cause subjective symptoms in the early stages, so that over a period of time corneal vascularization could develop without the patient's awareness. This interpretation would correspond to the findings of this study: most soft lens patients with corneal vascularization were totally unaware of its presence.

In both the study and control groups, the maximum vessel penetration distance did not exceed 4.5 mm into the cornea. In the soft contact lens group, 96.8% of

TABLE 14
Prevalence of Vascularization For Each Daily Wearing Time Period (Study Group N=827)

D.W.T. (Hr)	Males	Females	Totals
0-4	0/10 (0.0%)	3/12 (25.0%)	3/22 (13.6%)
4-8	4/34 (11.8%)	14/77 (19.5%)	19/111 (17.1%)
8-12	23/75 (30.7%)	57/200 (28.5%)	80/275 (29.1%)
12-16	53/111 (47.7%)	95/235 (40.4%)	148/346 (42.8%)
16-20	11/20 (55.0%)	4/10 (40.0%)	15/30 (50.0%)
20-24	6/12 (50.0%)	9/31 (29.0%)	15/43 (34.9%)
	97/262 (37.0%)	182/565 (32.2%)	280/827 (33.9%)

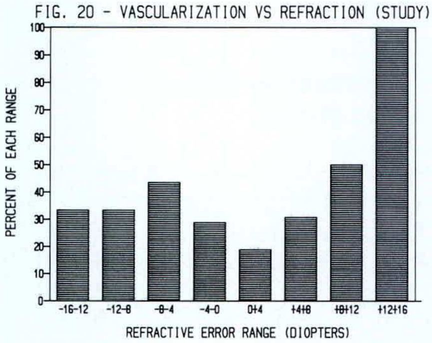

Figure 20
Prevalence of corneal vascularization in the soft contact lens (study) group by refractive error.

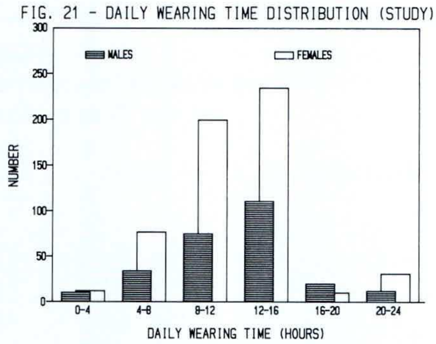

Figure 21
Number of patients in the soft contact lens (study) group by daily wearing time.

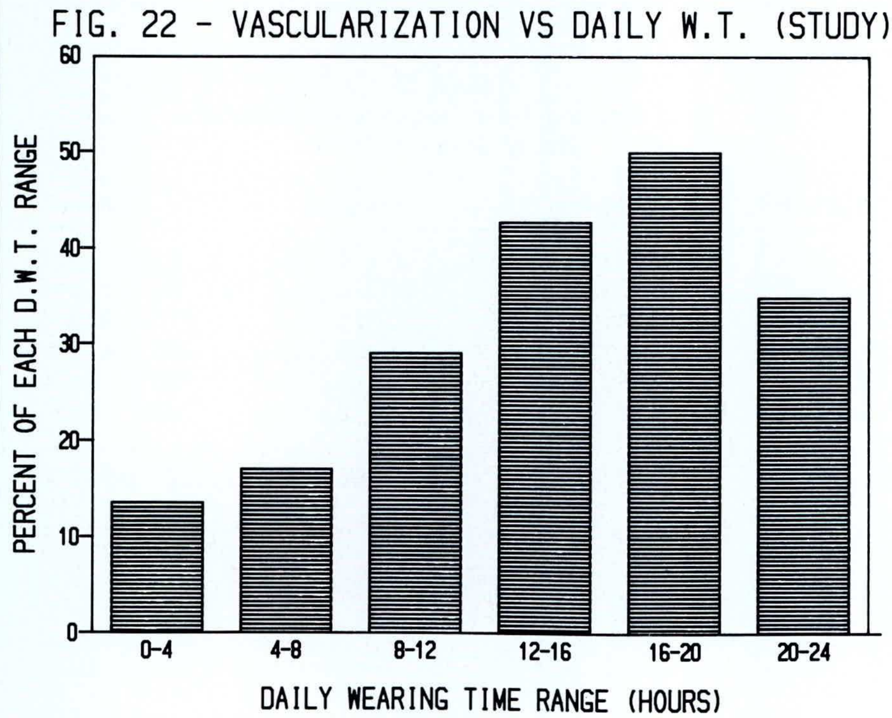

Figure 22
Prevalence of corneal vascularization in the soft contact lens (study) group by daily wearing time.

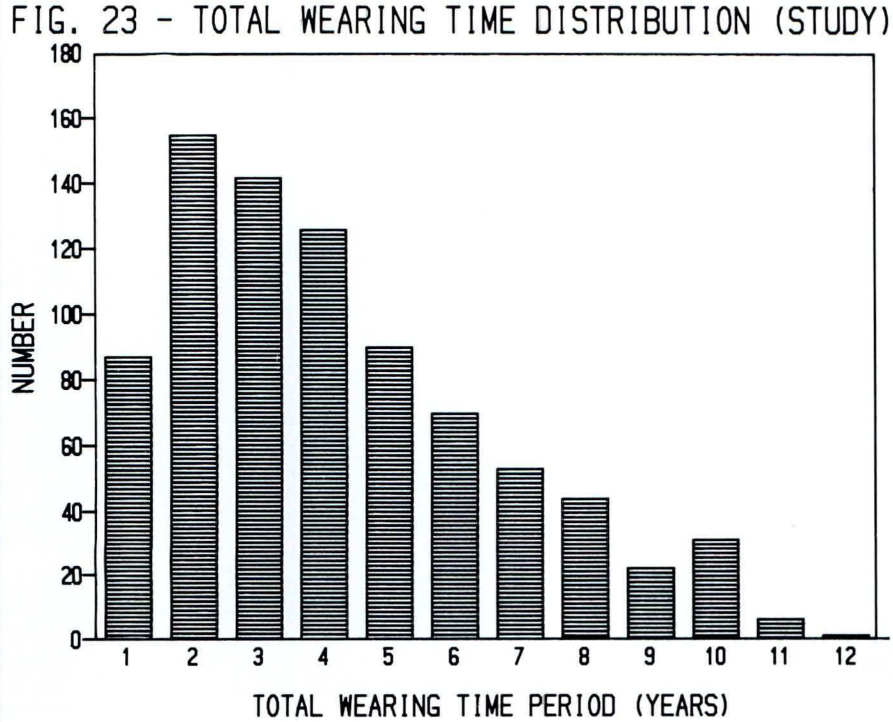

Figure 23
Number of patients in the soft contact lens (study) group by total wearing time.

TABLE 15
Total Wearing Time Frequency Distribution
(Study Group N=827)

T.W.T. (Yr)	Males	Females	Totals
1	33 (4.0%)	54 (6.5%)	87 (10.5%)
2	56 (6.8%)	99 (12.0%)	155 (18.7%)
3	53 (6.4%)	89 (10.8%)	142 (17.2%)
4	34 (4.1%)	92 (11.1%)	126 (15.2%)
5	34 (4.1%)	56 (6.8%)	90 (10.9%)
6	17 (2.1%)	53 (6.4%)	70 (8.5%)
7	17 (2.1%)	36 (4.4%)	53 (6.4%)
8	8 (1.0%)	36 (4.4%)	44 (5.3%)
9	3 (0.4%)	19 (2.3%)	22 (2.7%)
10	6 (0.7%)	25 (3.0%)	31 (3.7%)
11	1 (0.1%)	5 (0.6%)	6 (0.7%)
12	0 (0.0%)	1 (0.1%)	1 (0.1%)
	262 (31.7%)	565 (68.3%)	827 (100.0%)

the vascular responses were within 1.5 mm of the limbus. There was one case of a soft contact lens wearer displaying a severe vascular response in which vessels penetrated 4.5 mm into the cornea, although this represented only 0.4% of the study group. The fact that 96.8% of the vascular responses in the study group were limited to the peripheral 1.5 mm of the cornea, thus avoiding the central optic zone, explains why visual symptoms were reported only in the most advanced cases. By comparison, only 44.4% of vascular responses were 1.5 mm or less into the cornea in the control group, indicating the more serious nature of the conditions which caused the corneal vascularization in these cases.

Corneal edema and the formation and accumulation of vaso-stimulating substances such as lactic acid have been found to play an active role in corneal vascularization[14]. In soft contact lens wearers, it would appear that the effect of corneal edema and vaso-stimulating substances is most often limited to a peripheral annual zone extending inward about 1.5 to 2.0 mm from the limbus. In theory, this observation would concur with the fact that 93.6% of patients in the study group were myopes whose soft lenses would therefore be thicker peripherally than centrally, with correspondingly lower oxygen transmissibilities in the periphery. This could conceivably result in an annular area of localized edema and/or vaso-stimulating substance accumulation in the corneal periphery which could ultimately stimulate, while at the same time limit, corneal vascularization to this specific area.

Type

Another indicator of the fundamental difference in etiology of corneal vascularization in the study group from that of the control group is seen in Fig. 14. A much larger number of cases of superficial stromal corneal vascularization are observed in the study group compared to the control group. This could be explained by the fact that the conjunctival limbal circulation would be expected to be primarily involved in the vascular process in a group of soft contact lens wearers since soft lenses impinge physically upon the limbal vessels and corneal adnexa. However, as Tomlinson and Haas[15] reported, it is not the physical action of the contact lenses upon the limbal area which is the cause of vascular injection and corneal vascularization, but rather corneal hypoxia which interferes with aerobic metabolism in this area. This would result in the development of corneal edema as well as the buildup of the byproducts of anaerobic metabolism such as lactic acid (a known vaso-stimulating substance), which are both required in the pathogenesis of corneal vascularization[14].

Age and Sex

The age and sex of patients were not found to be significant factors in the prevalence of corneal vascularization. This would indicate that there is no specific physical or physiological differences between sexes or between age groups which would predispose one particular group to corneal vascularization.

Refractive Error

Patients whose refractive errors were in the ranges from -8.00 to -4.00 D, 0.00 to +4.00 D and +4.00 to +8.00 D had corneal vascularization frequencies which were not significantly different from one another but *were* significantly higher than patients in the −4.00 to 0.00 D range. This could be explained if the oxygen transmissibility of soft lenses in the −4.00 to 0.00 D range was greater than that of lenses outside this range. We do not have specific data to confirm this, however it would seem to be a reasonable assumption since the average thickness of soft lenses in the −4.00 to 0.00 D range would be less than lenses outside this range. Oxygen transmissibility (Dk/L) is dependent upon Dk (oxygen permeability of the lens material) as well as L (average thickness of the lens material), so the greater the average thickness of a lens of a given water content, the less oxygen which is going to be available to the eye. Eyes wearing soft lenses of increasingly greater average thickness would therefore be expected to develop increasingly greater levels of corneal vascularization more often, as was in fact found.

Daily Wearing Time

Theory would predict that the longer the daily period of sustained corneal hypoxia due to soft contact lens wear, the greater the level of corneal edema and related corneal physiological changes; hence the greater the number of corneal vascular

TABLE 16
Prevalence of Vascularization For Each Total Wearing Time Period (Study Group N=827)

T.W.T. (Yr)	Males	Females	Totals
1	5/33 (15.2%)	11/54 (20.4%)	16/87 (18.4%)
2	14/56 (25.0%)	21/99 (21.2%)	35/155 (22.6%)
3	22/53 (41.4%)	29/89 (32.6%)	51/142 (35.9%)
4	14/34 (41.2%)	31/92 (33.7%)	45/126 (35.7%)
5	12/34 (35.3%)	16/56 (28.6%)	28/90 (31.1%)
6	9/17 (52.9%)	21/53 (39.6%)	30/70 (42.9%)
7	10/17 (58.8%)	16/36 (44.4%)	26/53 (49.1%)
8	7/8 (87.5%)	16/36 (44.4%)	23/44 (52.3%)
9	2/3 (66.7%)	6/19 (31.6%)	8/22 (36.4%)
10	2/6 (33.3%)	12/25 (48.0%)	14/31 (45.2%)
11	0/1 (0.0%)	3/5 (60.0%)	3/6 (50.0%)
12	0/0 (0.0%)	1/1 (100.0%)	1/1 (100.0%)
	97/262 (37.0%)	183/565 (32.4%)	280/827 (33.9%)

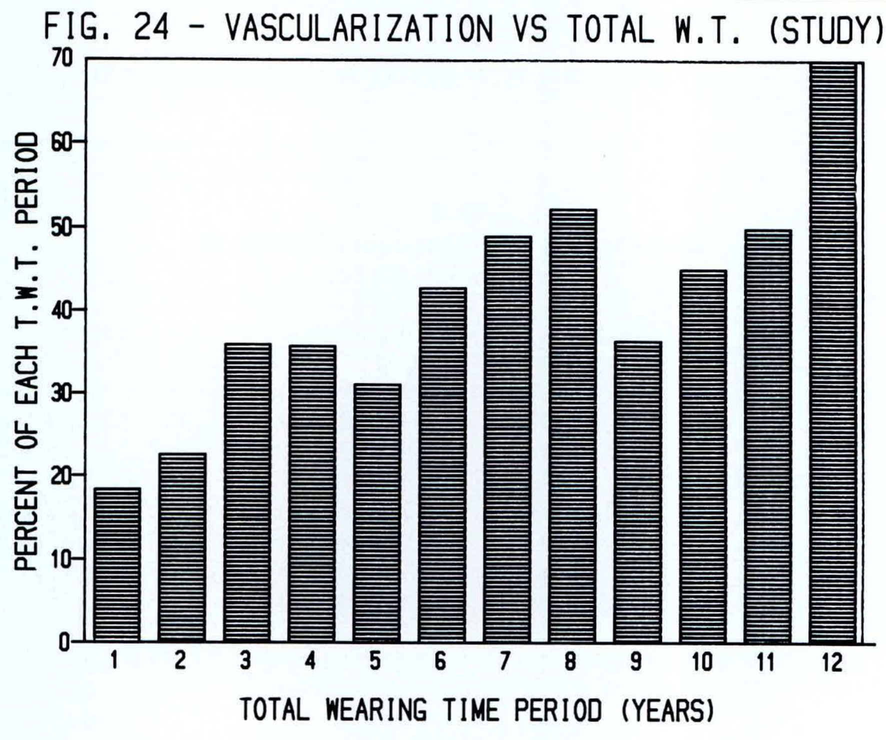

Figure 24
Prevalence of corneal vascularization in the soft contact lens (study) group by total wearing time.

responses. Increasing vascularization frequency as a function of daily wearing time is exactly what was found in this study, with one exception (Fig. 22). Note that as the daily contact lens wearing times increase, the frequency of corneal vascularization also increases until the 20–24 hour daily wearing time is reached, at which point a slight drop in vascularization frequency is noted. The drop in vascularization frequency at the 20–24 hour level could be explained by the fact that all of the patients of this wearing time group were extended-wear patients who were wearing soft lenses with greater oxygen transmissibility than the daily-wear lenses which the remainder of the study group were wearing.

Statistically, the frequency of corneal vascularization found in the extended-wear group was no different than that found in patients who wore daily-wear lenses 12 hours per day or less. Interestingly, both of these groups had significantly lower frequencies of corneal vascularization than patients wearing daily-wear lenses 12–20 hours per day. This does not imply that extended-wear lenses are not associated with significant levels of corneal vascularization: the frequency was 34.9% in the extended-wear group. Nor is the implication that daily-wear lenses worn less than 12 hours per day are without problems: the average vascularization frequency for the three daily-wearing time groups under 12 hours was 19.9%. It does imply, however, that patients who are wearing daily-wear lenses 12–20 hours per day are likely experiencing greater levels of corneal hypoxia and edema than those who are wearing daily-wear lenses less than 12 hours per day or patients who are wearing extended-wear lenses on an extended-wear basis.

Total Wearing Time

The prevalence of corneal vascularization found in patients during the first and second years of soft contact lens wear was not significantly different ($p<0.01$), but both were significantly lower than that found in patients after three years of soft lens wear ($p<0.01$). After three years, no statistically significant changes in the prevalence of corneal vascularization were found ($p<0.01$). Thus corneal vascularization may take as long as three years to develop in soft contact lens wearers, indicating once again the slowly progressive nature of the condition.

Summary

1. Corneal vascularization was found in 33.9% of patients who had worn soft contact lenses for at least one year.
2. 96.8% of the vascular responses did not penetrate more than 1.5 mm into the cornea from the limbus.
3. Symptoms were almost never reported by patients who had soft contact lens related corneal vascularization.
4. Age and sex were not related to the prevalence of corneal vascularization in soft contact lens wearers.
5. Corneal vascularization was found in signficantly greater numbers in soft contact lens patients whose refractive errors were outside the range −4.00 to 0.00 D.
6. Patients who wore daily-wear soft lenses 12–20 hours per day had a significantly higher prevalence of corneal vascularization than patients who wore daily-wear lenses less than 12 hours per day, or patients who wore extended-wear soft lenses on an extended-wear basis.
7. Corneal vascularization increased over the first three years of soft contact lens wear after which time the prevalence remained constant.

Conclusions

Corneal vascularization is a relatively frequent occurrence in soft contact lens wearers. Although the condition itself does not cause serious visual problems, the fact that it occurs at all indicates a physiological intolerance to contact lenses which must be addressed. The fact that corneal vascularization is asymptomatic in the early stages confirms the need for monitoring the corneal health of soft contact lens wearers on a periodic and continuing basis.

Acknowledgements

This study was supported in part by the Canadian Optometric Education Trust Fund. The authors gratefully acknowledge the invaluable assistance of David R. Jantzi who wrote the computer analysis programs, and Dr. Brenda Horner who organized and performed the slide analysis.

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