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COMMUNICATIONS

DENIG'S OPERATION FOR TRACHOMATOUS PANNUS*

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DENIG (1911), operated first in 1910, following the work of Ichikawa, who proved the continuity of trachoma from fornix through the conjunctiva bulbi and so to the cornea. He transplanted first the conjunctiva of the healthy eye, but soon changed to the mucosa of the lip. In the first few years he performed 42 operations with 8 recurrences and failure of the mucosa to heal up on the eye in 5 cases. Ogata in 1930 saw good results from the operation in 95 cases. L. Pines in 1931 reported his results in 406 cases, with no improvement in 42 and recurrences in 16. Since then a considerable literature has arisen about this operation, partly for it, partly against it. The first controversy was about the nature of pannus

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itself. There are three theories. The oldest, and, in my opinion hardly tenable, would ascribe the appearance of the pannus to the mechanical action of the infected upper lid, that is to say, the lid rubs the trachoma infection into the cornea. The aetiology of pannus—by continuity or by contact—is still debated. Parsons (1942) is against the continuity and so is Fuchs (1933). Wolff (1944) and Duke-Elder (1938) hold that there is a simultaneous infection of the cornea and conjunctival fornices. Prokrowsky and Taborisky (1914) (Ophthalmological Congress, Moscow, 1913), were partisans of continuity. But between 1911 and 1913 Ichikawa in Japan, Prokowsky and Taborisky in Russia proved the existence of trachomatous follicles in the conjunctiva bulbi and in the cornea itself by microscopical examination. The formation of follicles in the cornea itself was confirmed by many writers. Pasheff (*Klin. Monatsbl. f. Augenheilk.*, p. 361, 1938), R. Huber, *Ibid.*, Vol. LXXI (original article).

How deep do the vessels of the corneal pannus lie? Arkin (*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVII, p. 428, 1926), thinks that there are two forms of pannus—one secondary to the infection of the conjunctiva, and the other a primary infection of the cornea. The blood vessels lie below the membrane of Bowman. All those points must be kept in mind when describing the technique of the operation. The conjunctiva bulbi, under local anaesthesia, is cut starting from the limbus or retreating 0.5 mm. from it towards the periphery making a wound half as wide and as long as the base of the pannus—say from 9 o'clock to 3 o'clock. It is important to cut right through down to the episclera removing all tissues and laying the episclera bare. While an assistant is stopping the considerable haemorrhage by applying swabs with saline and pressing on the wound the surgeon proceeds to cut out and prepare a graft from the mucosa of the lip. Under local anaesthesia a special lip forceps is applied and the graft is cut out slightly longer and wider than the wound of the conjunctiva. The graft is put into warm saline and the wound of the lip is closed by one uninterrupted suture. The surgeon then washes his hands again and while the patient gargles his mouth, the graft is put with the mucosa downwards on a plate of glass or on the hands of the surgeon and the whole of the fat is removed from it so that only the mucosa and submucosa are left.

In my opinion it is not advisable to try and make the graft too thin, but care must be taken not to cut into the graft. Then the graft is put on the wound, mucosa upwards the submucosa downwards on the sclera and is fixed with fine silk to the three sides of the wound, the corneal part remaining free.

It is sometimes advisable, if the wound is too long, to cut the

graft in two portions, cutting at 12 o'clock and readjusting and joining by stitching the two portions. If the cornea is badly ulcerated, the upper part of it may be scraped or cauterised and the graft allowed to cover it. Otherwise the lower part of the graft, if overhanging the cornea, may be trimmed. Sulphonamide powder and sterile vaseline may be put into the operated eye. Binocular dressing for 2-3 days. If the operation is successful, the graft—deadly pale during the operation—will be pink and slightly oedematous when the eye is first dressed. Binocular again. Stitches may be removed after 5 days. The improvement of the eye is usually striking. If the operation is not successful, the whole of the graft or its middle part remains pale, freely movable and is better removed after 5 days. But the eye is still considerably improved. Let us now discuss the different stages of the operation.

Denig used the mucosa of the lip because he believed in this way to present to the trachoma invading the cornea an impenetrable wall of tissue, that cannot be invaded by trachoma as the mucosa of the lip does not possess lymphatic tissue. But the issue is not as simple as that. Why then in unsuccessful cases (one of mine too), is the improvement obtained and maintained for a number of years? Obviously because the trachomatous tissue was cut deeply right to the episclera and so the invasion was interrupted. The trachoma was not very active and the consequent scar of the wound of the conjunctiva remained free from the trachoma. The performed deep peritomy together with the nearly quiescent stage of the trachoma of the conjunctiva (but not of the cornea—obviously a separate stage of the trachoma) would be the explanation, but not the peritomy by itself (only too often failing in cases of active trachoma and pannus). Let me be clear—Denig's operation is suitable only for the third or the fourth stage of trachoma by MacCallan's scheme but no biopsy or clinical examination will be able to gauge the intensity of the still remaining infection.

The surgeon's impression and experience remain decisive. This is why I cannot agree with the opinion of Karlowsky (*Kritische Bemerkung uber Den. Op.*, *Klin. Monatsbl. f. Augenheilk.*, 1936), or Hallas (*Ibid.*, Vol. LXXXII, p. 401, 1929), that all the benefit of Denig's operation is due to a deep peritomy. Szokolik definitely rejects Denig's operation in favour of a deep peritomy, as proposed by Whitehead in Leeds in October 13, 1922 (*Ibid.*, Vol. LXXVIII, p. 693, 1927). It is safer, therefore, in my opinion, to perform Denig's operation and not the deep peritomy alone. The second point to consider is the interruption not of the course of the infection, but of the toxins only (Kershmamm, *Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVIII, p. 694, 1927). This opinion I think is highly improbable as nobody has yet isolated the toxins of trachoma.

Besides the interruption of the continuity of the trachomatous process, the graft being richly vascularised, improves the nutrition of the cornea. This is quite correct. After 5-10 days the cornea is clear, brilliant and transparent.

Many writers are of the same opinion (Kershman and L. Pines, *Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVII, p. 400, 1926, and Vol. LXXVIII, p. 693, 1927). Kolen (original article, *Ibid.*, Vol. LXXXVII, p. 790, 1931).

But is mucosa of the lip really an impenetrable wall against the invading trachoma? Opinions are sharply divided. Derkach (*Klin. Monatsbl. f. Augenheilk.*, p.409, 1930) saw after Denig's operation that the graft of the mucosa was involved in the trachomatous process as early as 2-3 weeks after operation. In a few weeks time he saw the graft disappear completely in the pannus tissue. He prefers therefore a graft from skin. Ogada (*Ibid.*, Vol. LXXXVII, p.142, 1931) leaves this question of immunity of the graft from trachoma still undecided.

Czukurach (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 262, 1931) made a biopsy of the graft in four cases and saw heavy changes in the epithelium, but the follicles were not typical for trachoma. Ballas (*Ibid.*) found in his histological examination a process very near to trachoma. The same is the opinion of Loewenstein (original article, *Ibid.* p. 390). Seefelder (*Ibid.*, Vol. LXXXI, 1928, original article) saw by microscopical examination trachoma invading the graft of the mucosa. He saw not only follicles, but even the Provazek's bodies in the graft. Similar is the opinion of Tovbin (*Ibid.*, Vol. XCI, 1933). The evidence therefore is very solid and considerable. But a whole phalanx of surgeons are all of a favourable opinion *re* the fate of the graft—it is not invaded by trachoma and forms a protective wall against it.

Such are Denig himself, Kershman, L. Pines (185 operations, *Klin. Monatsbl. f. Augenheilk.* Vol. LXXVIII, p. 694, 1927). Arkin (*Ibid.* p. 428), Endelman (*Ibid.* Vol. LXXV, p. 809, 1925), Budel, who still saw good results two years after Denig's operation, (*Ibid.* Vol. LXXIX, p. 688, 1927), Thies (*Ibid.* Vol. LXXXI, p. 393, 1928), Malkin (*Ibid.* Vol. LXXX, p. 561), Zakas, Blascovitz, Dekers (*Ibid.* Vol. LXXXII, p. 401), Kolen (extensive list of literature). (*Ibid.* Vol. LXXXVII, p. 790), B. Pines (*Ibid.* Vol. LXXXIX, p. 419) *et cetera*. What may be the cause of such a difference? In my opinion, it all depends upon the stage of the inflammation at the time of the operation. Denig's operation is not a panacea for all forms of trachoma of the cornea, but only for an isolated and stubborn pannus when the rest of the process is already quiescent. If it is not, conservative or surgical treatment of the whole affected conjunctiva is necessary before the pannus itself is tackled.

Filatoff and his school look upon the transplantation of the mucosa as a form of irritation or tissue therapy.

They speak favourably of the results of Denig's operations, but for the last few years Filatoff and his school use certain modifications. Besides cutting out a piece of conjunctiva and placing there a free graft of mucosa of the lip, they simply make a hole in the conjunctiva, then undermine it and in so formed corridor they plant a piece of mucosa or a piece of sclera or a piece of cartilage—the results being uniformly very good.

The graft is usually taken from a cadaver and preserved for 4-5 days in the dark at a temperature of 4°.

What is the fate of the graft of the mucosa? Does it remain unaltered, is it replaced by ordinary fibrous tissue or by conjunctiva? This very interesting and rather important question has hardly ever been considered. The surgeons simply were profuse in their laudatory remarks about the suitability of mucosa grafts in the plastic surgery of the eye, but the ultimate fate is usually not discussed.

Thies (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXII, p. 780, 1924) speaks about the reparation of the injured eye and freely uses the mucosa grafts for it, but in his opinion, sooner or later they disappear in the conjunctival tissue. Kershman and L. Pines (*Ibid.* Vol. LXXVII, 1926) simply state that the grafts grew much whiter in colour 12 months after the operation. Budle (*Ibid.* Vol. LXXIX, p. 88, 1927) saw good results in pannus cases operated on by the method of Denig, but he never attempted a microscopical examination of the graft. Gernett (*Ibid.* original article, Vol. LXXXII, p. 230) saw mucosa of the graft still present on the margin of the lid 20 years after the operation, but he did not examine it microscopically. Denig himself (*Ibid.* Vol. LXXXIII, p. 716, 1929) advocates free grafts of mucosa in many torpid inflammations and especially for all injuries of the eye by acid and recommends, if necessary for cosmetic reason, the later removal of the grafts.

Derkach (*Klin. Monatsbl. f. Augenheilk.* p. 409, 1930) saw a graft after Denig's operation disappearing completely in the pannus tissue after a few weeks. Czurrach (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 262, 1931) made a biopsy in four cases in Denig's operation and saw heavy changes in the epithelium. Ballas (*Klin. Monatsbl. f. Augenheilk.*) saw a process very near to trachoma (microscopical examination). Loewenstein (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 390, 1931) thinks that the graft is often invaded by trachoma and becomes assimilated in the surrounding tissues especially in margin plastics of the lid. Ichikawa and Noichefsky, as quoted by Kolen (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVII, p. 790, 1931) think, that the graft of the mucosa cannot be involved in trachoma and no follicles can be formed there,

as no adenoid tissue is present. Kreiker (*Klin. Monatsbl. f. Augenheilk.* Vol. LXXXVIII, p. 695, 1932) thinks that the grafts disappear after many years, as a result of a chronic inflammatory process and are probably replaced by conjunctiva, but they always disappear.

In the experience of Filatoff and his school the homoplastic grafts of tissues in Denig's operation disappear very quickly, but the conjunctiva less quickly, the mucosa of the lip still less so and the latest of all would be the skin. With the autoplasic tissues, the remnants of the grafts could be seen even 2-3 years after the operation, but in two cases the graft of the mucosa was invaded by a recurrent pannus 2 years 4 months after the operation. The graft was removed and replaced by one of the preserved cadaver conjunctiva. But Scarsky saw the disappearance of the graft of the cadaver mucosa even 30-40 days after the operation.

The above mentioned references are really isolated extracts from rather considerable literature and give a general idea of the prevailing opinion.

Let us now discuss my own cases—not many, but giving a good illustration of the pro's and contra's of Denig's operation.

The first case is that of a woman now 60 years of age, a native from Dwinsk near Vitebsk, in Russia, who arrived here nearly forty years ago with healthy eyes. She caught trachoma here and, in her opinion, it started with a dirty ball hitting her eye, when children were playing in the street near her home. When first seen at the London Jewish Hosp., in 1930-31, she was a case of trachoma cicatricum, third to fourth stage of MacCallan's classification, with partial distichiasis of both lids, especially the lower of the right eye, and pannus, especially of the right eye. A graft of the mucosa of the lip was done on the right lower lid for distichiasis and from 10 to 2 o'clock on the right eyeball for pannus. Both operations were successful, especially that of Denig. Mucosa still can be recognised now, after nearly 9 years.

The second one is that of a man of similar condition, but no distichiasis, only troublesome and recurring pannus. On the right eye Denig's operation was performed 12 years ago from 10 to 12 o'clock. Both ends of the graft took, but the middle part, from 11 to 3 o'clock did not take and started sloughing on the 4th day and on the 6th day I cut it off, leaving the two successful ends intact. The eye remains quiet. The graft at 4 o'clock was removed by me and sent to Mr. E. Wolff for microscopical examination. It still retained all the characteristics of mucosa of the lip 12 years after the operation. On the left eye Denig's operation was performed successfully three years ago and the graft took. The eye remains quiet.

The third case is of exceptional interest. It is a man of over 70 years of age, a native of Kieff, Russia; he was healthy there. In 1925 he emigrated to Berlin and soon afterwards started to suffer from chronic inflammation of both eyes. He arrived here in 1936. In 1943 he presented himself at an ophthalmic hospital in London with an epithelioma of the left upper lid. The epithelioma was removed and he was sent for X-ray therapy. The eyeball became rapidly worse. It was a pannus crassus of the cornea, with a thickened and scarified tarsal plate, with a severe inflammation of the whole of the conjunctiva bulbi forming a wall of angry tissue round the cornea, when first seen by me in October 1946. Vis. = counting fingers at 2-4 feet. No conservative treatment being of any use, I decided to perform Denig's operation from 11 to 2 o'clock. The graft took. The vision in 2-3 weeks time improved to 4/60. But then the pannus started to come back, from under the graft new vessels appeared growing into the cornea. Cauterisation did not stop them. Pannus started to grow from all the circumference of the cornea, which became completely vascularised. The Roentgenologist, to whom he was sent for regular inspection, hearing my opinion, that it was probably trachoma gave him 2 seances of irradiation. The eye became immediately much more inflamed, the cornea more vascularised and a symblepharon began to form in the internal angle between both lids and the eyeball. It was evident to me then, that it was a mixed process of trachoma, aggravated by X-ray irradiation. The eye is sensitive to X-ray and the inflammation is due chiefly to that. The graft is as vascular and angry, as the rest of the conjunctiva bulbi now a year after the operation. The fate of the eye as far as the sight is concerned, is very dark indeed. In the future lurks the danger of xerosis.

The fourth case is that of a woman of 65 years of age, with trachoma chronicum cicatricum and distichiasis who presented herself in the London Jewish Hospital 19 years ago with a tremendous serpiginous ulcer of the right eye and chronic dacryocystitis. The lacrymal sac was removed, and the eye, but not the eye-sight, was saved by a large graft of the mucosa of the lip, from 10 o'clock to 4 o'clock, right across the cornea and sufficiently wide to cover the ulcer. The ulcer healed up with a huge leucoma and after 7 days the middle part of the graft was removed, leaving the well ingrown ends of the bridge intact. The 4 o'clock end was removed and sent to Mr. E. Wolff for microscopical examination. It is still mucosa of the lip 19 years after the grafting.

If the characteristic part of trachoma is the scarring and shrinkage of the conjunctiva, then it is advisable to use the graft of the mucosa as frequently as possible in any plastic operation on a trachomatous eye, as it is excellently tolerated by the eye and increases the shrunk conjunctival surface.

I was defeated only in one series of cases. In 1917, when in charge of an eye department on the front of the Russian Army, I had many cases of trachoma where the chief feature was the mucous degeneration of the upper fornix, the cornea and tarsal plate being only slightly affected. I excised the fornix only and grafted on the wound a strip of the mucosa of the lip. It took on, but in 50% of my patients it produced a leucoma of the upper part of the cornea. I stopped the grafting and simply excised the fornix and never had any leucomata afterwards.

Summary

1. Denig's operation is highly advisable in cases of isolated pannus and quiescent trachoma of the lids and bulbi. Any active trachomatous focus must be destroyed first.
2. Mucosa of the lip, if grafted on the eye in these conditions remains unchanged for many years.
3. More frequent use of mucosa grafts is advocated for any plastic operation of the trachomatous eye.

Case Reports

Mr. A. S., aged 54 years. Both eyes trachoma chronicum cicatricum. Right eye, Denig's operation 12 years ago (1935).

The middle part of the graft did not take. The end of the graft at 3 o'clock was removed and sent for investigation.

Special thanks are due to Mr. Eugene Wolff, F.R.C.S., and to Mr. W. H. Gordon, Assistant Pathologist to Royal Westminster Ophthalmic Hospital, who kindly examined the specimen and reported.

FIG. 1.

FIG. 2.

The following is their report:—

The epithelium throughout the section is stratified, squamous, without cornification. It is not of uniform thickness, being much thicker over about half the section at one end than over the remainder, and the thicker half shows slight oedema of the prickle-cell layers (acanthosis). The papillae are stunted for the most part, though in the area of thin epithelium there are one or two considerable downgrowths of epithelium, which, however, remains quite regular in arrangement. The immediate subepithelial connective tissue is fairly close-fibred and in only one place (in the thick epithelium area) is there slight round-celled infiltration. The deeper connective tissue is looser and vascular.

The characters of the whole graft, therefore, are those of mucous membrane, slightly modified by stunting of the papillae; and in part, by acanthosis.

Female, aged 60 years. Both eyes trachoma chronic cicatricum. Right eye, serpiginous ulcer 19 years ago. Healed by graft of the mucosa of the lip.

Report of examination of biopsy specimen.

The specimen consists of connective tissue and its covering of stratified squamous epithelium.

The epithelium, 8 or 9 cells thick shows:—

- (i) Basal cells, which are cubical or low columnar, whose oval nuclei stain moderately with haematoxylin, and contain a few deeply-staining chromatin particles.
- (ii) Intermediate polyhedral cells between which are cell-bridges.
- (iii) Surface cells which are flattened but not keratinised.
- (iv) Adventitious cells—an occasional polymorphonuclear leucocyte.

The outline of the deep surface of the epithelium is somewhat undulating, presumably representing the succession of imperfectly formed papillae and inter-papillary downgrowths.

In addition there are seen in the sections two epithelial downgrowths, a small solid one extending horizontally just below the epithelium, whereas the other, which has a hollow cavity, extends vertically to the surface for a distance equal to three or four times the thickness of the usual epithelial layer.

The subepithelial tissue consists of loose connective tissue, appearing somewhat oedematous in places, and well supplied with blood and lymphatic capillaries. Just below the epithelium it is infiltrated with lymphocytes and plasma cells in considerable numbers, together with some endothelioid cells. Situated also in this tissue are a few tubulo-racemose glands, whose acini are lined by columnar cells with nuclei near the cell-base, whilst an outer cell-layer is formed of darker small cubical cells. These glands resemble buccal glands.

Opinion. In the specimen the structure of the original mucous membrane graft is maintained both in its epithelial and subepithelial parts.

My most sincere thanks are due to Mr. E. Wolff and Mr. W. H. Gordon for their invaluable co-operation in preparing, examining and reporting on two pathological specimens of mine.

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