# SPECIFIC INFLAMMATION OF THE CORNEA IN CHICKENPOX

BY

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INFLAMMATION of the iris leaves behind recognisable changes in the tissues. These results—the remains of posterior synechiae, and lucidity of the iris resulting from patchy atrophy of the pigment-epithelium—are not characteristic. But the resolving of an inflammation of the iris is in certain cases associated with very significant sequelae, especially in the case of so-called vitiligo iridis.

(1) Leopold Müller, fifty years ago, described circumscribed depigmented spots in the iris, which he believed to be produced by a foetal inflammation. The three cases described had all suffered from *smallpox*. Fuchs had already stressed in his well-known text-book the relation between smallpox and these spots in the iris. I have illustrations of three cases of vitiligo iridis—two in dark-pigmented irides and one in a blue iris—all subsequent to smallpox in childhood. Alajmo and Argüello have communicated parallel cases. The spots are greyish-white, sharply-defined, predominantly situated in the ciliary part of the iris, in groups, but distinct from each other—especially striking in dark irides, but more difficult to distinguish in grey or blue irides. (Figs. 1, 2).

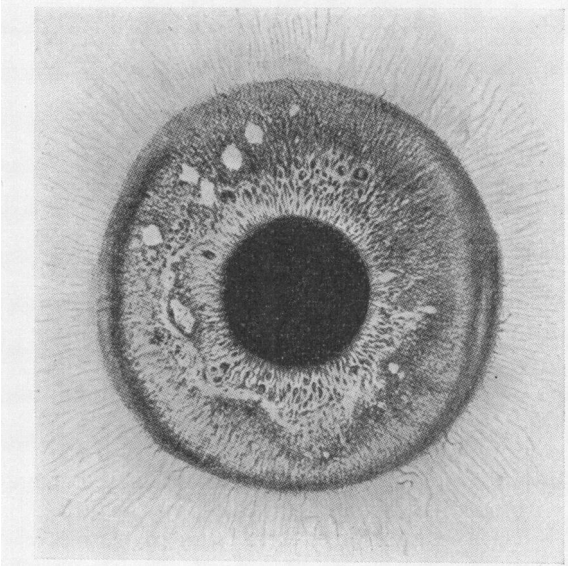

FIG. 1.

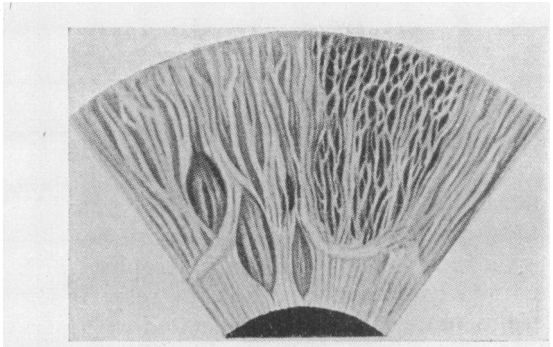

FIG. 2.

Vitiligo iridis *smallpox*, *dark* (Fig. 1) *blue* (Fig. 2) iris.

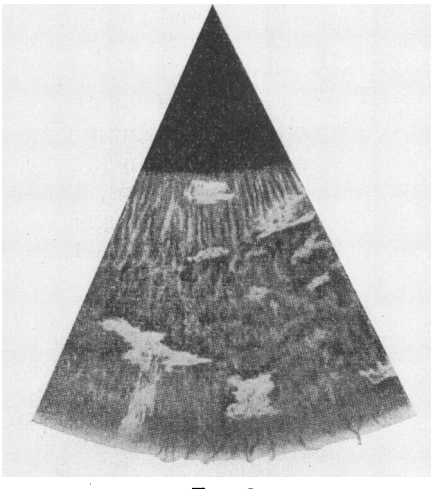

FIG. 3.

Vitiligo iridis (*herpes virus*) inoculation in the anterior chamber of a dark rabbit.

(2) When I injected the virus of *herpes febrilis* (from the vesicles on the lips) into the anterior chamber of dark-pigmented rabbits, a violent inflammation arose. Depigmented spots in the iris remained after healing—very striking, jagged, sharply-defined, and reaching deeply into the tissue. (Fig. 3).

(3) These depigmentations are known in the rare *herpes iridis* (Machek, Gilbert, Meller, Loewenstein). They occur usually in association with relapsing haemorrhages in the anterior chamber. The disease is very severe and suffers from many relapses.

Variola, vaccinia and herpes virus are near relatives. Biologically, the reactions in the rabbit's cornea and iris are very similar too.

(4) On the other hand many reports have been published regarding the very close relationship between the viruses of *herpes zoster* and *chickenpox*. Since Bokay observed long ago that patients in the same room with chickenpox-infected children often contract herpes zoster, the very near relationship—even the identity—of these viruses is very commonly assumed. I have known and observed very carefully the iris affection in smallpox (Figs. 1, 2), in herpes iridis (herpes zoster), in the inoculated herpes iridis in rabbits (febrilis) (Fig. 3), and in vaccinia. I knew the biological relationship of these viruses in chickenpox, so I expected a parallel affection in chickenpox.

After long searching, I found the first case by chance some years ago. A six year old girl had had absolutely normal eyes till the end of her second year. She developed chickenpox—a very severe form—with a vesicular exanthem of the whole body. All four lids especially were covered with large and small vesicles. The girl could not open her eyes for more than a week. No eye specialist had seen her. Some weeks afterwards the mother observed for the first time on the iris a white spot, which remained unchanged.

*Right eye.* Small paracentral macula corneae without vessels; walnut brown iris. A nasal area of about 20° is coloured clear grey; the sphincter part is completely depigmented; the ciliary part almost completely (Fig. 4). The margin of the depigmented zone is sharp, and within this zone the iris stroma is impoverished and not so dense as elsewhere. Above this zone there are two very small whitish spots in the dark iris. The deeper parts of the eye are normal.

*Left eye.* Quite normal.

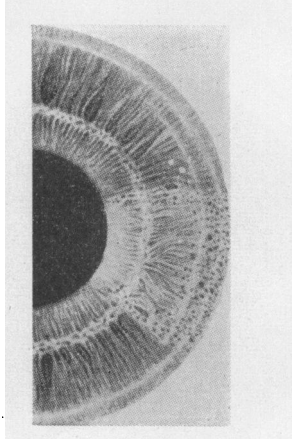

FIG. 4.

Vitiligo iridis (*chickenpox*).

I assumed that the chickenpox virus had infected the cornea and the iris, and caused a specific keratitis and iritis, healing without treatment. After the healing of the corneal affection, the opacity of the cornea and the vitiligo of the iris remained. It will be readily understood that I hoped to find the assumed specific corneal process, unknown before, as I was convinced of its existence.

Finally I was lucky enough to detect a fresh corneal infection in chickenpox, and to control its development with the slit-lamp.

2. VI. *Sp. John* (four years old) developed chickenpox — a specially serious case with many vesicles all over the skin. All four lids were covered with vesicles and scabs, and for some days would not open. The eyes had already been sore since two weeks before the infection. Ten days after the beginning of the skin trouble, the cornea began to be hazy and so the house doctor sent the little patient to the clinic.

26. VI. Well-nourished child with no trace of skin disease. W.R. negative.

*Right eye.* Ciliary injection, more above than below, but no photophobia—no loss of substance in the corneal tissue. The central part of the cornea (see slit-lamp picture, Figs. 5 and 6) is dim and opaque, the epithelium is coarsely irregular, but without vesicles. The opaque area is bordered by a ring of a polygonal shape infiltrated uniformly a clear grey. The surrounding ring runs without interruption round the central opacity and is prominent against the remaining corneal level. There is to be seen at one point only a separate small infiltration of higher density. Otherwise the infiltration ring is absolutely uniform. Seen with the narrow beam of the slit-lamp, the optical section shows a thickening at the linear marginal infiltration, and here the tissue is more opaque than in the parenchyma of the cornea. Many punctate and streaky

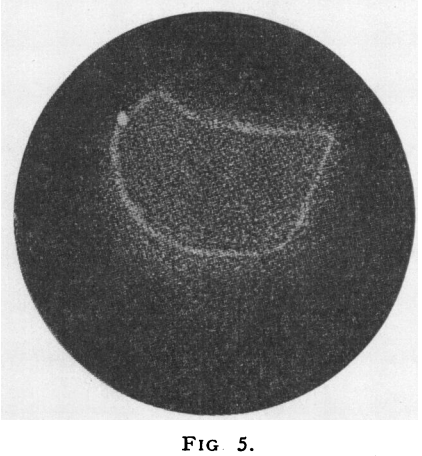

FIG. 5.

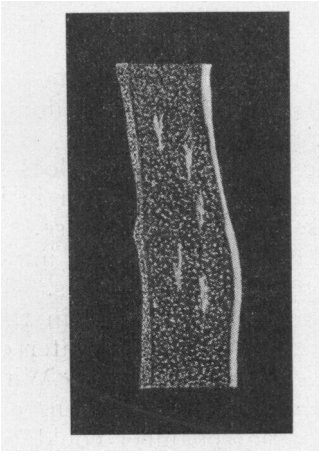

FIG. 6.

Chickenpox keratitis.

opacities are to be seen—more in the higher parts of the cornea than in the lower. Above they are more deep in the parenchyma; below more in the middle layers. The opacity fades off on all sides from the linear prominence. There is nothing at the posterior corneal surface and no corpuscular elements in the fluid of the anterior chamber. The iris is coloured slightly green, but there is no indefiniteness in its structure, and no enlargement of the vessels. The pupil is a little narrower than the left one. The sensibility of the cornea is equal in the two eyes. The fundus is normal.

29. VI. Parenchymatous opacity in the interior of the ring a little more dense. The inner limits of the ring are not too sharply-defined, the epithelium is irregular. There is a small vesicle in the epithelium not far from the outer and upper, and one in the inner and lower margin of the infiltration. The anterior lens capsule is covered with very tiny pigment spots.

30. VI. No photophobia; the eye very little irritated; the whole parenchymatous tissue within the linear margin equally opaque and thickened: no vascularisation.

1. VII. The cloudy infiltration is diminished; the tiny exudate in the anterior lens capsule very difficult to recognise.

3. VII. The opaque area is reduced in size.

6. VII. The area further reduced; the density of the parenchymatous cloudiness is diminished.

8. VII. Parenchyma clearer; but epithelium more irregular and (with the narrow beam of the slit-lamp) tiny white spots are detected. Exudate has disappeared from the anterior lens capsule.

10. VII. The parenchymatous opacity is very small; has cleared up; no sharp margin outlined. The epithelium is very irregular,

even in and down from the old margin. No irritation; eye quite white. On holiday.

2. VIII. Tiny macula, ill-defined at the centre of the cornea. Two points of irregularity of the epithelium; no irritation; no vascularisation.

The condition in the disease described does not correspond with any known change of the cornea. Neither in its aspect nor in its course can it be confused with anything else. The clinical picture reminds me of that which I obtained with intra-corneal inoculation of the rabbit with attenuated vaccinia virus. The affection of the deeper layers of the corneal parenchyma in the first weeks of the infection and the rising to the surface later on, is striking. The concomitant iritis is a very slight one. With the slit-lamp we recognise only the tiny exudate on the lens capsule; no opacities in the fluid of the anterior chamber could be detected; no new formation of vessels in the cornea. The most remarkable sign is the lack of photophobia even towards the end of the inflammation where the surface layers (epithelium) are more involved.

I think that in this observation we have found the long sought "missing link." On biological grounds, being aware of the appearance of a vitiligo iridis in chickenpox, we expected to find the process causing the acute disease—a process which had previously escaped observation. As the assumed virus of chickenpox is related to the virus of herpes, it was to be expected that the clinical picture of chickenpox keratitis would be very similar to that of a deep herpes. This assumption proved to be true.

Experimental work with herpes zoster has been published twice already. Kundratitz inoculated the *content of zoster vesicles* into the *skin* of suckling *infants* and got rising varicellar vesicles after 9 to 17 days. A secondary general exanthem with eruption of clear vesicles followed in some inoculated cases between 15 and 19 days. Lipschütz could demonstrate in the affected skin his nuclear "zoster corpuscula." There was no reaction similar to the herpes zoster from which the material was taken. All 17 cases showed a local or generalised chickenpox only. Kundratitz succeeded twice in a *second* transmission of the virus. Grüter provoked a *keratitis vesiculosa* in a glaucomatous blind eye by *experimental inoculation of chickenpox* virus. After healing, the cornea was immune against a new inoculation. According to Grüter the experimental varicellar keratitis had an incubation time of ten days, and left a real immunity of the affected cornea. Even the long time of incubation corresponds with the clinical experience in our case. It is not surprising that we did not confirm precisely the findings of Grüter with respect to the form of the keratitis. The stages of the artificial infection with the knife are and must be very different from the natural one—the kind of lesion, the quantity of the virus are not of course identical

in the two cases, even when the analogy of both corneal inflammations is absolutely evident. In my case no inoculations of the corneal infiltration were made into the rabbit's cornea.

As *differential diagnosis*, a commencing interstitial keratitis has to be taken into consideration. But the ring formation, the whole course and the negative W.R.'s testify against this diagnosis. Disciform keratitis—very nearly related—is a more uniformly opaque infiltration, the limits are a bit sharper, and it is not common in children.

It is astonishing how this corneal affection has not yet been described, as chickenpox is so very widespread. I do not believe that the corneal affection in chickenpox is a rare one. But the majority of chickenpox cases heal without medical assistance. All parents know that even the eye complications are not dangerous. That is the reason that the eye specialist does not see these cases.

How does the inflammation of the cornea arise? The patient's mother relates that before the skin disease appeared the eye was inflamed. It is possible that that means a locus minoris resistentiae and that the establishing of the virus in the cornea was thus made possible. That would correspond with the well-known settling of other forms of virus in injured tissues. But it is possible too that the irritated eye was rubbed and as the virus was to a great extent in the vesicles of the lids, it was spread into the conjunctival sac. Rubbing in the affected conjunctiva or cornea would facilitate the adhesion of the virus which had been introduced. Quite a long time of incubation is to be expected. The first signs of corneal haziness were observed about ten days to a fortnight after the appearance of the skin affection. That corresponds exactly with the results of the experiments. I do not believe that there will remain more than a thin, fine corneal macula. The capability of regeneration of the corneal tissue is incredible in such young patients.

(5) In the past, three cases of vitiligo iridis have been described in *scarlet fever* also (Carmi, Alajmo, Loewenstein). All three cases

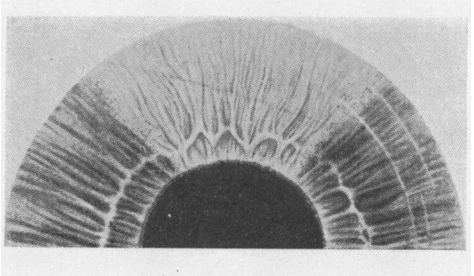

FIG. 7.

Vitiligo iridis (*scarlet fever*).

had a sharply limited pigment defect in the anterior layer of the iris—the anatomical structure of the iris tissue was not changed. The pigment defect occupied both the sphincter zone and the ciliary part of the iris; the pupillary margin in the case observed by me was intact. (Fig. 7.) In my case there were no scars in the cornea.

Such changes are unknown in streptococcal diseases—vitiligo iridis is reserved for *virus diseases only*. Our observations therefore support the opinion of many authors who believe that the appearance of *streptococci* in the blood stream in scarlet fever is only a *secondary* infection—streptococci and the virus are so-called synergetic symbionts (v. Prowazek). The primary virus is a filterable one of the group variola, vaccinia, chickenpox, herpes, probably measles too. The affection of the iris corresponds with the enanthems associated with the infectious exanthems.

## Summary

The previously unknown clinical picture of corneal infection with chickenpox virus is described, with slit-lamp pictures. An earlier observation of the author, who had found vitiligo iridis after chickenpox, is thus completed. The now recognised forms of vitiligo iridis in smallpox, chickenpox, herpes iridis (zoster), inoculation iritis in rabbits (herpes febrilis), and scarlet fever present a unity from which we can deduce a biological relationship between their germs.

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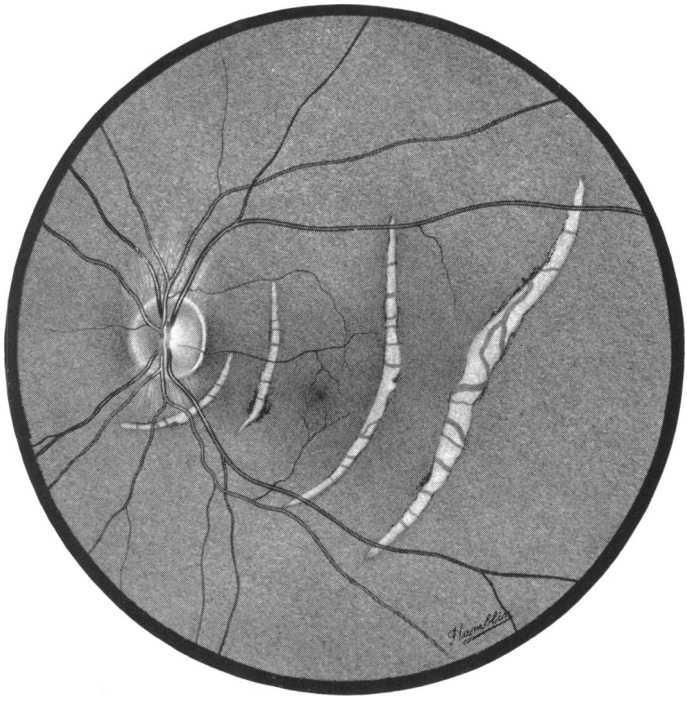

FIG. 1.

Four ruptures of the choroid.