Diabetologia 4, 161–163 (1968)

PRELIMINARY COMMUNICATIONS

Fluorescence Angiography of the Iris in Recent and Long-term Diabetes

V. A. JENSEN and K. LUNDBÆK

Department of Ophthalmology and the Second Clinic of Internal Medicine, Kommunehospitalet, Aarhus University School of Medicine, Aarhus, Denmark

Received: October 9, 1967

Summary. Fluorescence angiographic studies have been carried out on a series of non-diabetics, young recent diabetics and long-term diabetic patients with retinopathy. — The time of appearance was 9—21 sec, the arterial phase lasted 3—5 sec, not significantly different in the three groups of patients. — In the non-diabetics and the young patients with recent juvenile diabetes, tiny fluorescent dots along the pupillary seam were observed for a short interval of time. — In long-term diabetic patients a characteristic pattern was observed, consisting of the development of coarse, irregular dots along the pupillary border, showing confluence and culminating in a glow which lasted for the entire period of observation (50 sec). This pattern is interpreted as the expression of an abnormal capillary permeability of the vascular arcades of the annulus minor. — The abnormal pattern of confluence and glow was observed in long-term diabetic patients before the development of visible rubeosis iridis. — The rubeosis vessels filled after the appearance of the confluent dots and emptied into the veins.

Angiographie par fluorescence de l'iris chez des diabétiques récents et des diabétiques anciens

Résumé. On a effectué des études angiographiques par fluorescence sur un groupe de non-diabétiques, de jeunes diabétiques récents et de diabétiques anciens avec rétinopathie. — Le temps d'apparition était de 9—21 sec, la phase artérielle durait 3—5 sec, et n'étaient pas significativement différents chez les trois groupes de patients. — Chez les non-diabétiques et chez les patients jeunes ayant un diabète juvénile récent, on a observé de minuscules points fluorescents au bord de la pupille, pendant un court intervalle. — Chez les diabétiques anciens on a observé une image caractéristique, consistant en un développement de gros points irréguliers au bord de la pupille, qui confluaient et culminaient en une luminosité qui durait pendant toute la période d'observation (50 sec). Cette image est interprétée comme l'expression d'une perméabilité capillaire anormale des arcades vasculaires de l'annulus minor. — L'image anormale de confluence et de luminosité est observée chez les diabétiques anciens, avant le développement du rubeosis iridis visible. — Les vaisseaux du rubeosis se remplissent après l'apparition des points confluents et se vident dans les veines.

Fluoreszenz-Angiographie der Iris bei Diabetikern mit kurzer oder längerer Krankheitsdauer

Zusammenfassung. Fluoreszenz-angiographische Untersuchungen wurden bei Nichtdiabetikern, Jugendlichen mit relativ kurzer Krankheitsdauer und Langzeitdiabetikern mit Retinopathie durchgeführt. — Der Farbstoff erschien nach 9—21 sec, die arterielle Phase dauerte 3—5 sec ohne signifikante Unterschiede zwischen den 3 Patientengruppen. Bei den Nichtdiabetikern und den jungen Patienten mit kurzfristig aufgetretenem Diabetes wurden für einen kurzen Zeitraum winzige fluoreszierende Punkte am Rande des Pupillarsaums beobachtet. — Bei den Langzeitdiabetikern ergab sich ein charakteristisches Bild, bei dem sich relativ große, unregelmäßig begrenzte Punkte am Rande der Pupille bildeten, die konfluierten, um für die gesamte Beobachtungsperiode (50 sec) weiter zu leuchten. Wir vermuten, daß es sich dabei um die Auswirkung der gesteigerten Kapillarpermeabilität der Gefäßschlingen des Annulus minor handelt. — Dieses abnorme Bild mit Konfluenz und Leuchten wurde bei Langzeitdiabetikern schon vor der Entwicklung einer sichtbaren Rubeosis iridis beobachtet. Die Rubeosisgefäße füllen sich nach dem Auftreten der konfluierenden Punkte und entleeren sich in die Venen.

Key-words: Fluorescence, angiography, diabetes mellitus, angiopathia diabetica, rubeosis iridis diabetica.

The study of diabetic retinopathy with the fluorescence technique has considerably increased our knowledge and understanding of this abnormality. Retinopathy is, however, only one of the ocular manifestations of diabetic angiopathy. The final deterioration, when the patient loses his eyesight, is often caused by a combination of retinopathy and iridopathy (OHRT, 1967).

The following is a short preliminary report of fluorescence angiographic studies of the iris in recent and long-term diabetic patients, with and without rubeosis iridis diabetica, as well as in a group of non-diabetic subjects.

Method

A slight modification of NOVOTNY and ALVIS' fluorescence technique for studying the retinal vasculature (1961) was used. In this technique a few ml of a solution of fluorescein is rapidly injected either intravenously, or intraarterially in the carotid artery. Photographs of the retina are taken with a fundus camera during the rapid first passage of fluorescein through the retinal vessels. An electron-flash through a blue filter is used as the source of activating light, and exposures are made through a green filter. The fluorescein-containing blood makes the vessels appear white on the copy of the black and white film.

In our studies of the iris we have used a Zeiss Fluorescence Angiographic apparatus with built-in automatic time recording (LITTMANN, 1965), permitting a series of exposures at intervals of 0.6—2 sec. A lens with a focal length of 0.2 m was placed in front of the objective of the fundus camera.

To obtain good exposures with the Zeiss apparatus,

it proved necessary to work with the maximal strength of the electron-flash generator (720 Watt-sec). Under these conditions, however, the time intervals have to be kept at 1.5 sec or more, because shorter intervals caused a dropping out of flashes. The passage of the primary wave of fluorescein, lasting 15—20 sec, is therefore depicted in only 10 or 12 exposures. In long-term diabetic patients it turned out to be of interest to follow the events for another 20 to 30 sec.

Five ml of a 10% fluorescein solution was injected in an arm vein, directly or through a catheter, in the course of 1—3 sec.

Film: Ilford HP 4 (24 × 36 mm ASA 400 DIN 27). Developer: Perutz fine-grain. The 34 consecutive exposures were studied on enlarged prints, 84 × 94 mm.

Patients

Non-diabetics: 16 patients with various mild medical disorders, aged 17—78 years. These patients had no symptoms of diabetes mellitus, no glycosuria, and their eyegrounds were normal.

Diabetics: 34 patients. 7 were young patients with recent juvenile diabetes (age 19—37 years, average duration of diabetes 2 years). 27 were long-term diabetics with various degrees of diabetic retinopathy, (age 26—76, average duration of diabetes: 24 years). Fifteen of these patients had typical rubeosis iridis diabetica ("primary rubeosis iridis", OHRT, 1967), i.e. tiny capillary bushes near the pupillary seam or a fine network of vessels on the annulus minor on slit-lamp examination. Cases with coarse vessels travelling over the iris surface ("secondary rubeosis iridis", OHRT, 1967) were not included.

Results

Non-diabetics: Appearance time, i.e. the time interval from the start of the injection to the first appearance of fluorescence in the iris vessels, was 9—15 sec.

Fluorescence appeared first in the peripheral zone of the annulus major; but on the next exposure, 1.5 sec later, it had already spread to the collarette or sometimes even all the way to the pupillary seam. In some cases fluorescence appeared a little earlier in one area of the iris surface than in another. In patients with very light and sparse stroma, the vessels of the annulus minor sometimes showed-up as closely packed arcades, the bends pointing towards the pupillary seam. Three to five seconds after the first appearance of fluorescence a pattern of tiny luminous dots, spread evenly along the pupillary seam, was observed in many of the patients. The dots disappeared again in the course of about 10 sec. Many of them were found to be localized at the tip of a small artery at the place where it reached the pupillary seam.

The venous system could sometimes be differentiated as a fluorescence beginning in the annulus minor 3—6 sec after the first appearance in the arteries.

The vascular fluorescence pattern faded gradually in the course of 7—8 sec, but did not disappear entirely. As a result of this residual fluorescence, the structure of the iris was better defined at the end of the period of examination than at the beginning.

In brown-eyed persons the iris vessels were either very faintly seen or not evident, due to the heavy pigmentation.

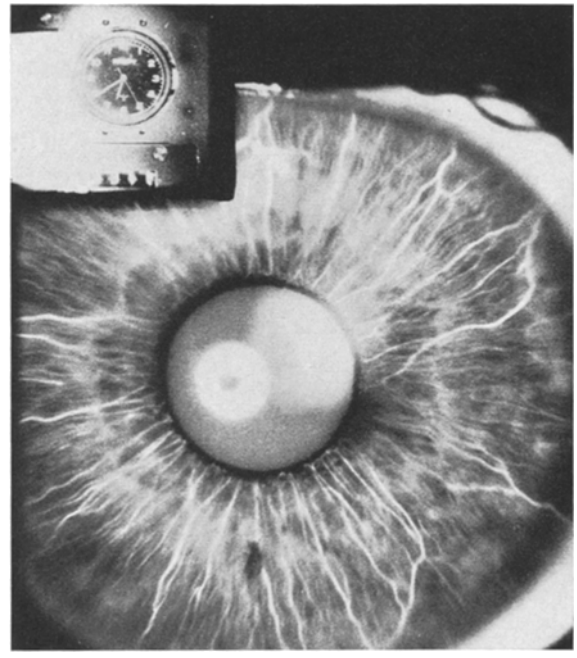

Fig. 1. Iris of a 44-year-old non-diabetic woman. 10 sec after injection of fluorescein. Note a few tiny dots at the pupillary seam

Diabetics: The time course of the flow did not seem to be different from that of non-diabetics. Appearance time was 9—21 sec, the time interval from arterial to venous filling was 3—5 sec.

In young patients with *recent juvenile diabetes*, the entire series of events was similar to that observed in non-diabetic patients.

In the *long-term diabetics* a characteristic pattern was observed, which did not occur in recent diabetics or non-diabetics. 2—6 sec after the first fluorescence in the iris was observed, a series of small dots of varying size appeared along the pupillary seam. They increased rapidly in number and size and began to show confluence. A few second later they changed: growing larger, showing blurred outlines, and finally appearing as an irregular, more or less continuous, glowing ring around the pupilla. In some of the patients the glow was so strong that it could be observed directly during the examination.

Confluence appeared a few seconds after the first dots were seen, the glow followed 2—10 sec later. It faded gradually, but was still present at the end of the examination, i.e. after about 50 sec.

This pattern was observed, more or less distinctly, in all the long-term diabetic patients of the present series, both those with and those without rubeosis iridis. In patients with rubeosis iridis it appeared first and was most pronounced in regions where abnormal vessels had been observed on slit-lamp examination, but it spread out quickly to the whole circumference

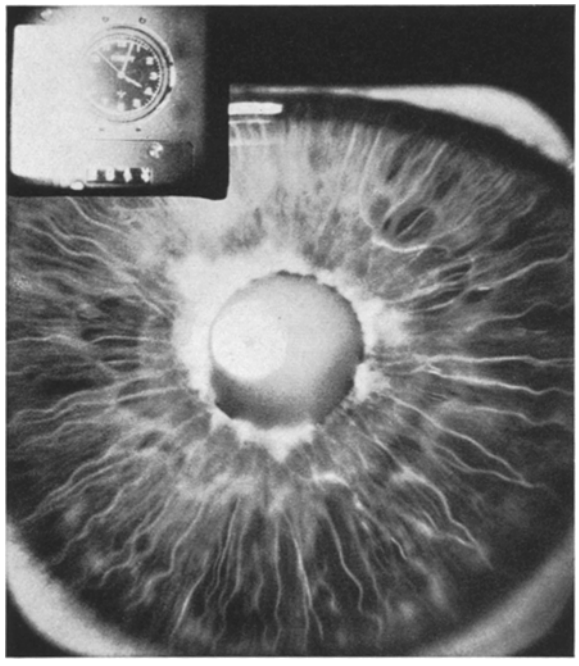

Fig. 2. Iris of a 65-year-old woman with a known duration of diabetes of 19 years, proliferative retinopathy and mild rubeosis iridis diabetica. Confluence and glow are seen

of the iris. No clearcut difference was observed between the patterns observed in the two eyes of patients with unilateral rubeosis iridis.

The smallest bushes of abnormal capillaries along the pupillary seam, observed biomicroscopically in the very earliest phases of rubeosis iridis, have not been visualized in the present study. However, in more pronounced cases, where a network of vessels was present on the annulus minor, these vessels have been observed to fluoresce and to fill slowly after the appearance of the irregular, blurred dots.

In a few cases we have seen the fluorescein-containing blood flowing from a tiny twig of the abnormal capillary network directly into an iris vein.

Discussion

The small dots that appear for a moment along the pupillary border in many non-diabetics and in patients with recent juvenile diabetes represent the bending points of small vessels, and can be easily distinguished from the coarser ones of long-term diabetics, which show confluence and glow lasting for 50 sec or more.

The pattern of confluence and glow must be caused by a leakage of the fluorescein through the capillary wall at the turning point of the arcades. The glow itself may be due to penetration of the fluorescein into the fluid of the anterior chamber, around the pupillary border. AMSLER et al. (1947) who studied the blood-aqueous humour barrier by measuring the fluorescence of the anterior chamber at intervals for 30 min, found it increased in "40 per cent of the diabetics studied".

It is interesting that the phenomenon of confluence and glow is also observed in patients without even the slightest degree of rubeosis iridis on slit-lamp examination. This pattern reveals a weakness of the vascular wall, preceding the appearance of visible rubeosis iridis. The exudation of plasma at this localization may perhaps act as an irritant, leading to the formation of new abnormal capillaries or to the opening up of preëxisting "latent" networks.

Further studies of the fluorescence pattern of the iris in diabetic patients are in progress.

References

AMSLER, M., F. VERRAY and A. HUBER: Zur Physiopathologie einer Gewebsflüssigkeit. Schweiz. Med. Wschr. **77**. 1321–1326 (1947).

LITTMANN, G.: Fundus-Photographie mit schneller Bildfolge. Ber. dtsch. ophthal. Ges. **67**, 393–394, (1965).

NOVOTNY, H.R., and D.L. ALVIS: A method of photographing fluorescence in circulating blood in the human retina. Circulation **24**, 82–86 (1961).

OHRT, V.: Diabetic Iridopathy. Aarhus: Universitetsforlaget 1967.

K. LUNDBÆK
Kommunehospitalet
Aarhus, Denmark