Peripheral retinal vasculature in normal Jamaican children

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Abstract
A prospective study of the peripheral retinal vasculature in a Jamaican cohort of subjects with sickle cell disease has been in progress over a period of 12 years using fluorescein angiography. Various vascular patterns were identified but their significance was unclear since no comparable records were available in subjects of a similar age with normal (AA) haemoglobin genotype. Fluorescein retinal angiography and angiography have been performed in 76 haemoglobin AA controls participating in the cohort study. The peripheral retinal capillary bed could be seen and photographed in a limited portion of the temporal peripheral fundus in a majority of this group, and there was considerable variation in the vascular pattern which could be characterised. These observations allow deviations from normal to be identified in the retinal vasculature in subjects with sickle cell disease.

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Materials and methods
A cord blood screening programme for sickle cell disease was initiated at the main government maternity hospital in Kingston in mid 1973 with the intention of detecting all cases with different genotypes of sickle cell disease in 100 000 consecutive normal deliveries. This programme detected 315 infants with homozygous sickle cell (SS) disease of whom the first 125 were each matched with two controls of the same sex, born closest in time to the index case, but with a normal haemoglobin (AA) genotype. Of the 250 controls admitted to the study, 180 were aged over 16 years, alive, non-defaulter, and living in Jamaica at the study date (April 1991 to February 1993). Of these, 76 participated in a special ophthalmic assessment at the Sickie Cell Clinic, University of the West Indies, Kingston, Jamaica.

The 76 subjects (152 eyes) comprising 40 males and 36 females were aged 16–19.5 years and all were systemically well at the time of the examination. None had been born prematurely or had a refractive error of greater than 2 dioptres.

Each subject had corrected Snellen visual acuity measured, retinal examination through dilated pupils, and fluorescein angiography and angiography following intravenous injection of 3–4 ml of 20% sodium fluorescein. The temporal retinal vasculature was photographed with a Zeiss fundus camera (Zeiss, Oberkochen, Germany) using Ilford FP4 black and white film. Positive and negative transparencies were examined under magnification.

Ethical approval for this study was obtained from the ethics committee of the Faculty of Medical Sciences; University of the West Indies, Kingston, Jamaica, and signed informed consent was obtained from each subject.

Results
The ora serrata could be seen in a small number of the subjects without indentation. The anterior limit of the retinal vascular bed was visible by fluorescopy in 109 of the 152 eyes. Less than 60° was seen in eight eyes, 60°–120° in 29 eyes, 120°–180° in 38 eyes, 180°–270° in 34 eyes, and in no eye was more than 270° seen. The circumferential extent of the detectable border was symmetrical between the two eyes in all but three subjects in whom it differed by 60°.

The marginal vasculature was sufficiently posterior to be photographed in 99 eyes which allowed the border to be characterised. The circumferential border of perfusion was formed by arteriovenous loops of varying calibre and length, presenting a pattern of vascular arcades (Fig 1). The border was typically convex anteriorly, but was occasionally less regular, with areas of wedge-shaped or U-shaped posterior extension (Fig 2). In all eye the retinal vasculature extended anterior to the equator.

Towards the periphery the density of the capillary bed became progressively less, the capillaries being longer and fewer in number (Figs 2–4). In a small number the thinning of the capillary bed was irregular giving rise to lacunae of non-perfused retina internal to the margin of the vascular bed (Figs 2, 4). The capillaries, venules, and arterioles were sometimes tortuous, and hairpin loops were seen in four eyes (Fig 5). There was no evidence of asymmetry between the eyes in density of the peripheral capillary bed.
Discussion

Our knowledge of the development and morphology of the peripheral retinal vasculature is derived from histological studies of animal1-3 and human4-12 eyes. The present study seeks to characterise the angiographic appearance of the peripheral retina in normal Jamaican adolescents. Despite the technical difficulties inherent in photographing the periphery of the retina, it is possible to define normal patterns of peripheral vasculature, and to formulate criteria by which deviation from normal can be established.

The ease with which the anterior retina could be assessed depended to some extent upon patient cooperation, pupil size, and anatomical variability. However, it is most likely that the differences in findings between subjects reflect anatomical variability since all subjects cooperated well, and all pupils were well dilated. The peripheral vasculature is visible by fluoroscopy and can be photographed in a majority of subjects, although this is usually limited to a proportion of the temporal periphery. Certain general statements can be made concerning the size and density of capillaries as the periphery is approached, but considerable variation in the angioarchitecture exists between subjects.

The variation in the appearance of the peripheral retinal capillary bed between subjects is likely to reflect the process of retinal vascularisation during development. Normal retinal vascular development begins in the fourth month of uterine life when a circumferential ring of undifferentiated avascular mesenchyme grows centrifugally from around the hyaloid vascular system at the optic disc, quickly spreading within the inner retinal layers.13 This is followed closely by the development of vascular perfusion. Although cellular differentiation and vascular development are more advanced and more extensive on the temporal side of the fundus in the early stages, the anterior limit of the retinal vascularisation reaches the ora serrata first on the nasal side.14 By the seventh to eighth month of intrauterine life, the retina is fully vascularised nasally and inferiorly whereas temporally retinal blood vessels have only reached the equator.15 In full term neonates the extent of the retinal vasculature is variable especially temporally and superiorly where the peripheral avascular zone

Figure 1  Right eye of 19 year old male. Vascular border consists of arteriovenous loops with adjacent low density capillary bed in temporal periphery.

Figure 2  Left eye of 16 year old male. Larger calibre vessel forms part of the border of perfusion. The capillary density becomes progressively less as the border is approached, with lacunae of non-perfused retina within the border.

Figure 3  Left eye of 17 year old male. The border is formed of small vessels with progressive decrease of the capillaries density as the border is approached.

Figure 4  Right eye of 17 year old female. There is a large capillary-free zone posterior to an arteriovenous loop.
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Figure 5  Left eye of 16 year old female. Angiogram showing a region of vascular tortuosity and hairpin loops (arrow).

may be up to 1.5 mm in width. This is believed to widen with postnatal growth of the globe, and has been measured at 3-5 mm in one adult. The findings in the present study are consistent with the data from histological observations and the concepts concerning the development of the retinal vascular bed. That the margin of perfusion is seen almost exclusively temporally would be expected.

The margin of perfusion is formed by arteriovenous loops, which reflects the pattern seen by histology, and in a fluorescein angiographic study by Asdourian and Goldberg. The appearance of fine hairpin loops protruding into areas of avascular retina posterior to the margin of perfusion was unexpected. Such hairpin loops have been well described in the eyes of diabetic and hypertensive adults, and are thought to represent revascularisation of retina rendered avascular by focal capillary loss. Similar loops have been identified histologically during development at the advancing edge of the embryonic retinal vascular bed but are believed to disappear during the third to the fifth months after birth as a consequence of vascular remodelling. Our data imply that they may survive into adult life, and that alone they do not imply disease. It appears likely that areas of non-perfused retina appear, large marginal vessels form, and tortuous vessels develop during the time of remodelling. The wide variation in the appearances found in normal subjects in this study suggests that this process may vary greatly from one subject to another.

These observations allow criteria to be established whereby abnormalities of the peripheral vasculature can be identified in sickle cell disease.

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5 Michelson IG. The mode of development of the vascular system of the retina with some observations on its significance for certain retinal diseases. Trans Ophthalmol Soc UK 1948; 68: 137-80.
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