Section of Ophthalmology

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Retinal and Choroidal Blood Flow Problems

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Experimental Venous Occlusion

Retinal branch vein occlusion in the human produces a variable clinical picture, with hæmorrhages and cotton-wool spots in the acute stage. Most patients have hypertension and arteriosclerosis. In the affected quadrant it is not uncommon to see gross arterial changes, but the part played by arterial disease in the pathogenesis of branch vein occlusion has not been established.

The majority of patients with retinal branch vein occlusion have good central vision. Those who have persistent poor vision do so because of macular œdema. A further group of patients lose vision due to recurrent vitreous hæmorrhages from new vessels that develop either at the optic disc or from retinal vessels in the area of the occlusion.

Our objectives in undertaking the study of experimental venous occlusion in rhesus monkeys were to establish the role of retinal arterial disease in the pathogenesis of the clinical picture and also to see if persistent macular œdema or new vessel formation could be induced.

The argon laser was chosen to produce the occlusion because a high energy burn accurately placed can be applied directly to the vein, so minimizing the chance of damaging the adjacent retinal artery. The laser at the time of occlusion produced blanching of the blood column and some surrounding coagulation at the level of the pigment epithelium. Within hours of the occlusion retinal hæmorrhages developed (Fig 1). Many of the hæmorrhages were superficial, small and flame-shaped but occasionally a larger hæmorrhage occurred just temporal to the macula.

The fluorescein picture produced following occlusion of the vein was somewhat variable. In some monkeys in the early stages the picture was predominantly one of vascular leakage, while in other monkeys the picture was one of vessel closure.

Following occlusion, the flow of fluorescein within the major veins had reversed (Fig 2), and preferential channels opened up conveying the fluorescein from the affected quadrant to the adjacent quadrants with intact venous drainage.

These preferential channels were most numerous and obvious between the superior and the inferior temporal quadrants and were best seen in the macular area and temporal to macula in

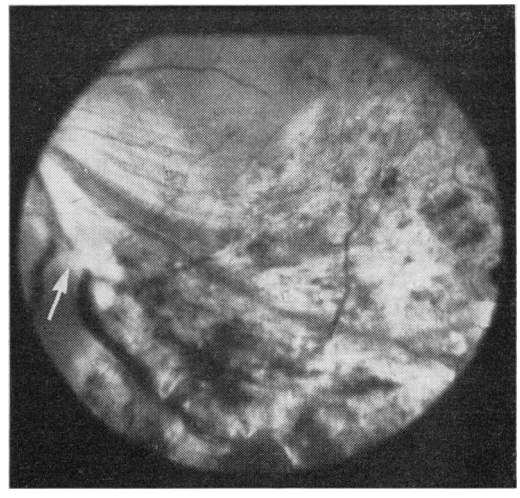

Fig 1 *From a colour photograph taken 24 hours after occlusion. Site of occlusion arrowed*

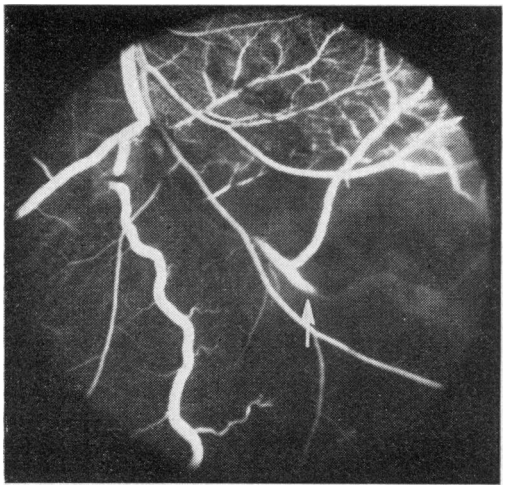

Fig 2 *Fluorescein photography showing reversal of flow in major vein (arrowed)*

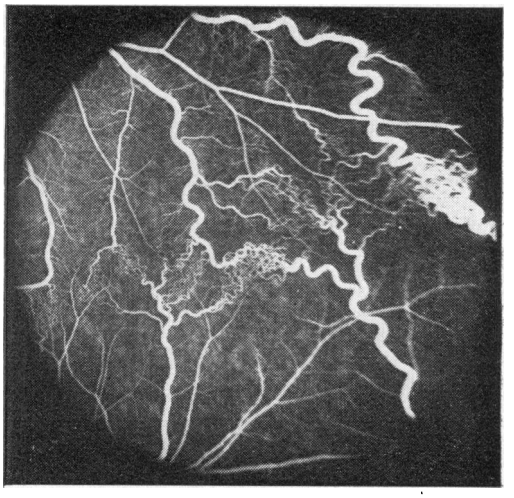

Fig 3 *Fluorescein photograph temporal to macula in horizontal meridian showing dilated preferential channels*

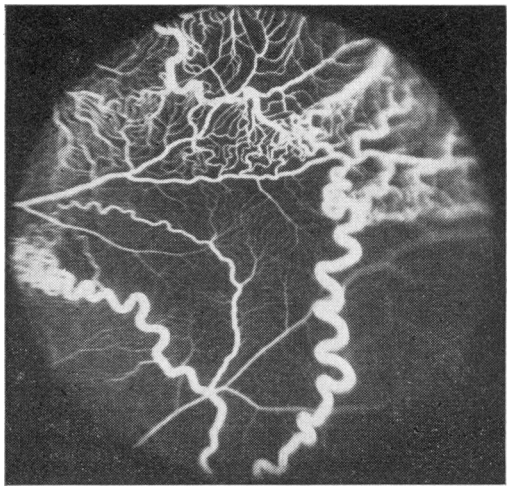

Fig 4 *Fluorescein photograph showing dilatation of capillaries temporal to macula in the horizontal meridian*

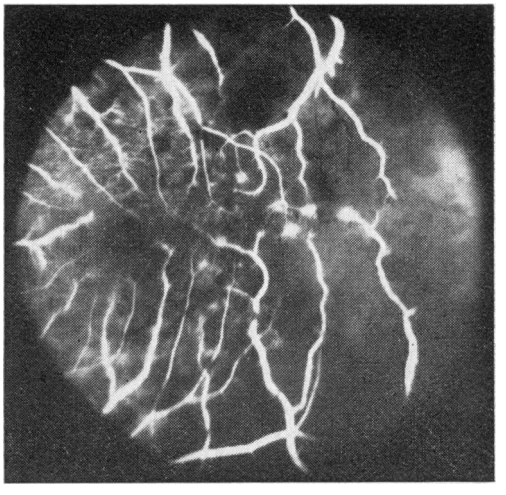

Fig 5 *Fluorescein photograph showing nonperfused areas temporal to macula*

the horizontal meridian (Fig 3). During the following weeks the preferential channels became more obvious in the region temporal to the macula. The larger veins became tortuous and there was remodelling of the smaller capillary channels. The surrounding areas showed perfusion by capillaries that were dilated, did not leak fluorescein and were possibly reduced in number (Fig 4).

The artery supplying the affected quadrant appeared normal for several weeks after occlusion. Within two months of the occlusion the retinal artery was sheathed, narrowed and irregular in appearance.

The human branch vein occlusion appearance with hæmorrhages and vascular closure could therefore be reproduced in monkeys by occluding a single retinal vein without apparent damage to the artery. Vascular leakage and retinal œdema occurred during the initial stages but rapidly resolved. Secondary arterial changes with narrowing and sheathing occurred, but no new vessels have been seen after intervals of up to four months following occlusion.

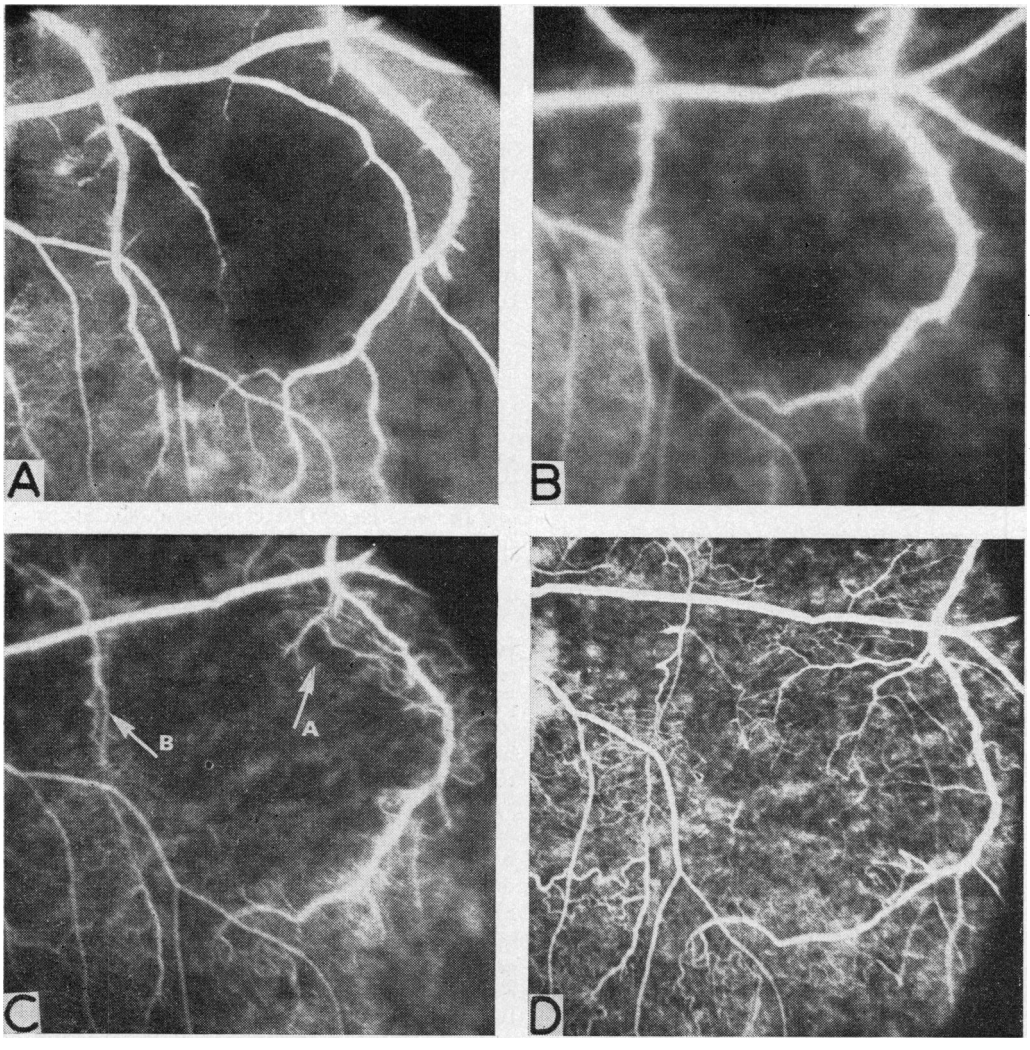

Fig 6 *Fluorescein photographs of superior temporal area.* A, *one week after occlusion.* B, *two weeks later, with further arteriolar and venular occlusion.* C, *three months after occlusion, with revascularization on nonperfused area* (A) *and reduplication of a vein* (B). D, *five months after occlusion, with almost complete revascularization but no fluorescein leakage*

No persistent macular œdema was produced in the above model, and it was therefore decided to embarrass further the circulation by occluding both the upper and lower temporal veins at an interval of one week.

A week after occlusion of the second vein, fluorescein angiography showed extensive vessel closure in an area temporal to the macula with some capillary leakage but no marked macular œdema (Fig 5).

The degree of capillary closure is comparable to that seen in diabetic retinopathy. We considered, therefore, the possibility that this was a favourable milieu for the development of new vessels.

The superior temporal quadrant one week after the second occlusion showed areas of vessel closure (Fig 6A) and over the next two weeks further arteriolar and venular occlusion occurred (Fig 6B). During the next two months vessels had developed extending into the ischæmic area and there was reduplication of an existing vein (Fig 6C). Five months after the second occlusion the whole ischæmic area was almost completely revascularized (Fig 6D), but there was no leakage of fluorescein from these vessels. Similar growth of vessels occurred into other ischæmic areas.

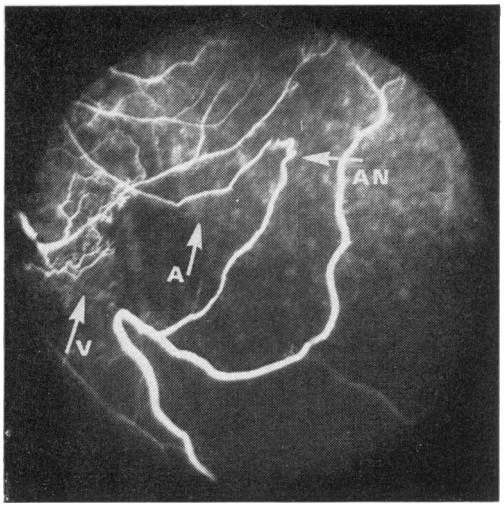

Fig 7 *Fluorescein photograph five months after occlusion showing secondary arterial occlusion* (A), *venous occlusion* (V) *and arteriovenous anastomosis* (AN)

Within a few weeks of the second venous occlusion secondary arterial changes of sheathing and narrowing were seen. After five months fluorescein angiography revealed secondary venous and arterial occlusion and an arteriovenous anastomosis had developed adjacent to the macula (Fig 7).

Comment

The experimental models of retinal vein occlusion which we have explored separate definitively the arterial and venous components. The arterial supply to the damaged retinal sectors was meticulously spared. The resultant lesion could therefore be attributed to venous obstruction alone. Clear-cut capillary occlusion, as well as secondary arteriolar and venular obstruction resulted. Additionally, revascularization of infarcted retina with similarities to human retinal neovascularization ensued. The experimental procedure described did not, however, lead to the two salient sequelæ of human vein occlusion, namely: neovascularization out of the plane of the retina with fluorescein leakage and persistent œdema of the macula. The possibility that antecedent arterial disease is required for the development of these phenomena cannot be excluded.

Summary

Using the monkey as an experimental model with a single venous occlusion but with no arterial damage, the features of human branch vein occlusion can be reproduced.

With double venous occlusion, widespread areas of vessel closure occur and these areas are gradually revascularized. The new vessels are seemingly dissimilar to those originally present but do not leak fluorescein on angiography. Secondary arterial and venous changes develop shortly after occlusion.

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The Iris in Central Retinal Vein Thrombosis

Iris neovascularization in eyes with central retinal vein thrombosis was first reported in detail by Coats in 1906, but its pathogenesis has remained an enigma. Since then, iris new vessels have been observed in a wide variety of conditions including carotid-cavernous fistula, carotid stenosis, central retinal artery thrombosis, Coats' and Eales' diseases, diabetic and sickle cell retinopathies, retinal detachment, and tumours of the retina, choroid, and iris (Schulze 1967). Iris neovascularization has also been produced experimentally by occluding the long posterior or anterior ciliary arteries (Schulze 1967, Anderson & Morin 1971). Anterior segment fluorescein angiography has recently been performed in many conditions including studies of central retinal vein thrombosis (CRVT) (Raitta 1968, Vannas & Raitta 1972) and retinal artery thrombosis (Karjalainin 1971).

The observations presented in this study are derived from a personal study of 78 cases referred from the Casualty Departments of Moorfields Eye Hospital and King's College Hospital during the last three years (J M C). Also some data derived from several cases of Dr E Kohner examined by one of the authors (J M C) is included.

Rubeosis is defined here as the progressive development of new vessels on the iris observed clinically. Three topics will be briefly discussed in this paper: the vascular changes in the iris following CRVT (demonstrated by fluorescein angiography); the natural history of these changes; and the ocular and systemic abnormalities associated with rubeosis.