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RETINAL VEIN OCCLUSION*†

A COMPARATIVE STUDY OF FACTORS AFFECTING THE PROGNOSIS, INCLUDING A THERAPEUTIC TRIAL OF ATROMID S IN THIS CONDITION

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THE group of conditions loosely termed retinal venous occlusions present many interesting problems with regard to pathogenesis, natural history, and treatment. The present investigation was undertaken with the objectives of collecting a series of these patients and studying the natural history and possible effects of treatment with the drug Atromid S.

Method of Study

Patients presenting with venous thrombosis of the retina were referred to a clinic specially instituted for the study of these conditions. Those attending the clinic initially were given a full ophthalmic examination, which included ophthalmoscopy, applanation tonometry, and ophthalmodynamometry. The following biochemical investigations were routinely carried out: blood sugar, blood urea, erythrocyte sedimentation rate, blood film and haemoglobin, Wassermann reaction, electrophoresis for serum protein, cholesterol, calculated triglycerides, and total fatty acids. A fundus photograph was taken to show the initial appearance and changes in fundus picture as they occurred.

In all, fifty patients were seen at least once, and 43 were followed up for at least 6 months and 41 for a year.

Patients who showed clinically central or branch vein occlusion were given a prescription for capsules which contained Atromid S or a placebo. The dosage used was 2 capsules four times a day for one week, then 2 three times a day for one week, then 2 four times a day for one year. A private record of which patients were taking the drug and which the placebo was kept by the hospital pharmacist. The code was broken at the end of the trial. The results of the serum lipid studies were kept separately and not revealed to the authors until the completion of the trial. This was because a knowledge of changing lipid values might have offered evidence whether the drug was being taken or not. In addition, 41 of these patients were given a physical examination by one of us (W. D. S.) and this included a complete cardio-vascular overhaul, the resting blood pressure, chest *x* ray, and electrocardiogram.

In assessing the results two criteria were used: the recorded change in the visual acuity and the change in the fundus picture. The patients were classed in four groups as regards visual acuity and fundus:

Visual Acuity	*Fundus*
A. Good improvement (more than 2 lines on Snellen chart)	A. Good improvement
B. Slight improvement (less than 2 lines)	B. Slight improvement
C. Unchanged	C. Unchanged
D. Worse	D. Worse

The fundus changes were discussed independently by two of us (D. B. C. and J. M. E.). There was usually agreement, but in a few cases an initial difference of opinion was settled by discussion. The data obtained were all recorded on punch cards and ultimately the code was also recorded on the cards.

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Clinical Findings

Age.—Range 39 to 81 years, the majority of patients being in the 7th and 8th decades.

Age (yrs)	30–39	40–49	50–59	60–69	70–79	80+
No. of Cases	1	1	8	13	16	2

Blood Pressure.—The distribution of resting diastolic pressures (mm. Hg) was as follows:

Diastolic Pressure	Less than 80	80–	90–	100–	110–	120–	130+
No. of Cases	2	7	13	10	6	1	2

Ischaemic Heart Disease.—A total of seven patients showed evidence of coronary artery disease: history of angina (3), previous myocardial infarction (2), abnormal ischaemic ECG without clinical evidence of myocardial disease (2).

Valvular Heart Disease.—Two cases were recorded: aortic incompetence (1); mitral incompetence (1).

Cerebrovascular Disease.—Five cases were recorded: cerebral thrombosis (3); vertebral basilar insufficiency (1); carotid artery stenosis (1).

Peripheral Vascular Disease.—One patient had a clear history of intermittent claudication with abnormal peripheral pulses and in one the pulses were clearly abnormal.

Miscellaneous.—There was one case of diabetes and one of bronchial neoplasm.

Chest X-ray Findings.—These were reported as follows:
normal (13); transverse diameter of heart increased (16: 6–left ventricular hypertrophy, 2–right ventricular hypertrophy); unfolding of aorta (14); miscellaneous abnormalities (10), *e.g.* basal fibrosis, calcified tuberculosis, kyphoscoliosis.

Electrocardiogram Findings: Normal (24); ventricular extrasystoles (4); left ventricular hypertrophy (3), left ventricular hypertrophy and strain (7); ischaemic changes (3); miscellaneous abnormalities (3) *e.g.* wandering pacemaker, atrial extrasystoles, right bundle branch block.

Effect of Treatment with Atromid S

We adopted the criterion of Cullen, Ireland, and Oliver (1964) that treatment with Atromid should cause a fall in lipid values of 15 per cent. Of 23 patients who were on Atromid S, the cholesterol or calculated triglyceride fell by 15 per cent. from previous values in fifteen. By contrast, of twenty patients who were on the placebo, only two showed a 15 per cent. reduction in lipid values. There can, therefore, be no doubt of the efficiency of Atromid in lowering the cholesterol and triglyceride values. No serious general or ocular side-effects were noted. Many patients reported an increased sense of wellbeing on the drug. There were, however, a few complaints of nausea and one patient

had to be withdrawn on account of uncontrollable nausea. The effects on the visual acuity and the fundus picture are tabulated below.

Group		A	B	C	D	Total
Visual Acuity	Atromid S	6	7	6	4	23
	Placebo	5	4	8	3	20
Fundus	Atromid S	8	10	4	1	23
	Placebo	7	9	2	2	20

Atromid does not, therefore, appear to influence the prognosis. One patient developed a recurrence of thrombosis in the other eye while on treatment with the drug. There were two cases of thrombotic glaucoma both of which had the placebo.

Applanation Pressure Readings

There were sixteen patients with complete or incomplete central vein occlusion. Of these, five had applanation readings above 21 mm. Hg, and two of them developed thrombotic glaucoma. By contrast, of 27 patients with tributary vein occlusion, only two had an applanation pressure above 21 mm. Hg.

Ophthalmodynamometry

Systolic ophthalmodynamometry readings were taken in all 43 patients. We found that in six patients there was a fall in at least 15 per cent. in the dynamometry reading in the affected eye. Vernon Smith (Paton, Rubinstein, and Smith, 1964) found that the systolic dynamometry reading was reduced in 30 per cent. of his patients.

Serum Proteins

A total of nine patients out of the 43 had abnormal serum proteins, the values being those seen in less than 5 per cent. of the population. In all, seventeen separate abnormal components were found. The α_2 globulin was raised in seven cases, β globulins in five, and γ globulins in five. There were no abnormalities in albumin or in α_1 globulin. Three patients were highly abnormal, in that they each had raised α_2, β, and γ globulins.

Effect of Age on Visual Prognosis

Group		A	B	C	D	Total
Visual Acuity	Below 66	5	6	7	4	22
	Above 66	6	5	7	3	21
Fundus	Below 66	9	7	5	1	22
	Above 66	6	12	1	2	21

Sex related to Visual Prognosis

Group		A	B	C	D	Total
Visual Acuity	Male	5	3	5	4	17
	Female	6	8	9	3	26
Fundus	Male	6	7	2	2	17
	Female	9	12	4	1	26

Presence or Absence of Associated Cardiovascular Disease related to Visual Prognosis

Group		A	B	C	D	Total
Visual Acuity	No CVD	4	7	4	3	18
	CVD	7	4	10	4	25
Fundus	No CVD	9	7	0	2	18
	CVD	6	12	4	3	25

Thus patients who are free from cardiovascular disease appear to fare little better than those with cardiovascular disease.

Site of Occlusions related to Visual Prognosis

Group		A	B	C	D	Total
Visual Acuity	Lower Hemisphere	1	2	5	1	9
	Upper Hemisphere	5	8	5	0	18
Fundus	Lower Hemisphere	1	6	1	1	9
	Upper Hemisphere	9	8	1	0	18

These data show eyes with occlusions in the lower half do much worse than those with occlusions in the upper half.

Discussion

Natural History.—In studying the natural history of central vein occlusion, one has to bear in mind the probable pathogenesis of the condition. Recent work has shown that these conditions are not simply venous occlusions but are probably due to the combined effect of arterial insufficiency and venous occlusion. Hayreh (1965) showed that, to produce central vein occlusion experimentally, it is necessary to occlude both the central artery and the vein. In a symposium held in 1964, Rubinstein demonstrated the passage of fluorescein through the supposedly occluded segment of the vein, Vernon Smith showed that low ophthalmodynamometric readings often occur in the affected eye, and Paton showed that these patients often have arterial insufficiency elsewhere in the body.

We frequently noted narrowing and sheathing of arterial segments, which often became evident later when the haemorrhages were absorbed. Some of our patients showed ophthalmodynamometric evidence of arterial insufficiency and arterial insufficiency was commonly found elsewhere.

There have been few studies of the natural history of the disease. Lister and Zwink (1953) studied 25 cases and demonstrated that there was an extraordinary variety of end-results. They also stated that initial visual acuity is a guide to final visual acuity. We found this to be true for some cases only.

The natural history appears different according to the type of occlusion. In 16 cases of central occlusion the visual acuity and fundus picture were classed as follows:

Group	A	B	C	D	Total
Visual Acuity	5	1	4	6	16
Fundus	6	4	3	3	16

There is a frequent association of this condition with chronic simple glaucoma, and five of our sixteen cases had applanation readings above the normal.

Prognosis.—Most occlusions in the lower hemisphere occurred at the disc, and were infero-temporal in distribution. Without exception these all did very badly. Clinically, the initial visual acuity was poor, but even if a good initial acuity was found, this frequently fell. While most cases of superior temporal occlusion cleared in 7 to 8 months, the infero-temporal occlusions had not cleared even after the full year of the trial (Figure).

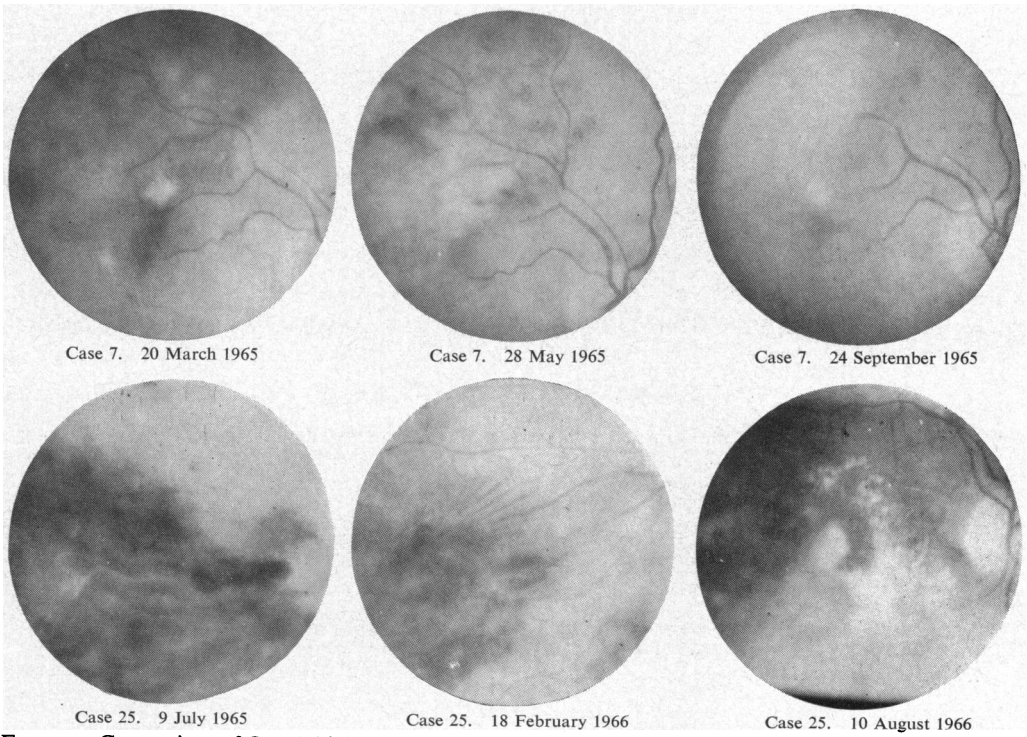

FIGURE.—Comparison of Case 7 (right superior temporal vein occlusion) and Case 25 (right inferior temporal vein occlusion), showing worse prognosis of the latter.

The fall in visual acuity appeared to be due to macular oedema, which often went on to cystic degenerative changes with a circinate ring of exudates around the macula. In general, poor final visual acuity was frequently associated with a cystic change at the macula; such cystic changes occurred in five of our 43 cases.

Treatment.—At the start of the trial the question had to be faced whether it was justifiable to deny any treatment to the 50 per cent. of patients who would receive only the placebo. We are not, however, aware of any treatment of proven value in this condition. Lister (1964) said he was not convinced that anticoagulants were of any use, although Vannas and Orma (1957) claimed that they had a favourable effect.

The pharmacological and clinical indications for Atromid therapy were discussed by Oliver (1964). The drug lowers the serum cholesterol and is said to affect platelet stickiness and to have a fibrinolytic action (Carson, McDonald, Pickard, Pilkington, Davies, and Love, 1963). The exact part played by thrombus formation in these conditions is not fully understood, but it is reasonable to suppose that a drug with the reputed actions of Atromid S might benefit these patients. Unfortunately, as our results show, the use of Atromid S does not materially affect the outcome, although it is valuable in cases of diabetic retinopathy (Cullen and others, 1964). The finding that it reduces the lipid exudates in the diabetic retina is interesting because these exudates are also found in branch vein occlusions. We have often noted such exudates in the later stages of retinal vein occlusion of the disease, but Atromid therapy did not appear to prevent their formation.

The finding of abnormal serum proteins deserves further study. Macroglobulinaemia is known to be associated with central retinal vein occlusion, but was found in none of our patients. Nevertheless, serum protein abnormality may be involved in the pathogenesis of the condition.

Summary

(1) Treatment with Atromid S does not appear to affect the outcome of retinal vascular occlusions.

(2) Age and sex do not appear to affect the prognosis in vascular occlusion.

(3) Patients who are free from cardiovascular disease elsewhere in the body do not appear to do better than those who have associated cardiovascular disease.

(4) Occlusions in the lower hemisphere have a poorer prognosis than those in the upper hemisphere.

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