certain families. This type of mechanism probably accounts for a large part, but not all, of the increased risk of having a second mongol child which young mothers of mongols appear to run. Carter & Evans (1961) put this increased risk to mothers who have their first mongol child before the age of 25 years as 30- to 60-fold.

Chromosomal mosaicism suggests another cause of familial mongolism. The possibility exists that some 'normal' people, perhaps with abortive signs of mongolism, have a proportion of trisomic cells. Should the gonads be involved in this mosaicism, or be entirely of the trisomic type it may be expected that the extra chromosome would be passed to a proportion of the gametes. This is then potentially a second cause of familial mongolism.

A further probable cause of a high incidence of mongolism in certain families is a predisposition, which may be inherited, to misdivision of the type leading to trisomy. This may occur either during gametogenesis or during embryogenesis.

Clinical Features and Cytology

Although it may be suggested that the chromosome abnormalities found in mongolism are the result of mongolism, not the cause, the pedigree described above and similar pedigrees (Penrose *et al.* 1960, Hamerton *et al.* 1961) show that this is not so. The abnormal chromosome, which may differ in detail in different families, is already present, in balanced form, in a physically normal parent.

Perhaps even more convincing evidence of the genetic origin of mongolism comes from the results of pregnancies in mongol females. Of the eight recorded offspring (Penrose 1961) four are certainly mongols. In the only example of an affected mother and child examined for karyotype both were of the standard trisomic condition.

Although the pathogenesis of mongolism is still obscure, there can be no reasonable doubt that the extra genetic material is responsible for the numerous developmental anomalies characteristic of mongolism.

Medical Applications

Cases of mongolism difficult to diagnose do occur, especially in the newborn. It is a simple and speedy matter to examine the karyotype. The identification of an extra chromosome in the 21–22 group is good confirmatory evidence of mongolism.

Young mothers of mongols have a greatly increased risk of bearing a second mongol child. This increased risk is sometimes the result of a chromosome abnormality in balanced form. It is now possible to identify these parents.

Acknowledgment: I wish to thank Mrs Audrey Bishop for her assistance in preparing the figures.

REFERENCES
Carter C O & Evans K A (1961) *Lancet* ii, 785
Carter C O *et al.* (1960) *Lancet* ii, 678
Clarke C M, Edwards J A & Smallpeice V (1961) *Lancet* i, 1028
Fraccaro M, Ikkes D & Lindsten J (1960) *Lancet* i, 724
Hamerton J L *et al.* (1961) *Lancet* ii, 788
Lejeune J, Gautier M & Turpin R
(1959) *C.R. Acad. Sci., Paris* **248**, 602
Penrose L S
(1934) *Proc. roy. Soc.* Ser. B, **115**, 431
(1961) *Brit. med. Bull.* **17**, 184
Penrose L S, Ellis J R & Delhanty J D A
(1960) *Lancet* ii, 409
Polani P E *et al.* (1960) *Lancet* i, 721

Professor Paul E Polani presented a paper entitled **Sex Chromosome Abnormalities**

REFERENCES
Polani P E (1961) *Brit. med. Bull.* **17**, 200
Polani P E (1962) In: Chomosomes in Medicine. Ed. J L Hamerton. London; p 73

Meeting February 27 1962

Short Papers

Progression and Regression of Diabetic Retinopathy

by F I Caird DM MRCP & C J Garrett MB DTM&H
(Radcliffe Infirmary, Oxford)

The literature contains many brief references to the variable rate of progression and not infrequent regression of diabetic retinopathy (Friedenwald 1950, Lawrence 1951, Becker 1952, and others). There is little quantitative evidence apart from the very few controlled trials of treatment (Bedrossian *et al.* 1953, Keen & Smith 1959). The present study was designed to provide an estimate of the rate of change of the ophthalmoscopic appearances of diabetic retinopathy.

Since 1949 ophthalmologists have regularly examined the fundi, through dilated pupils, of most patients attending the Oxford Diabetic Clinic. These examinations are largely random (i.e. only rarely carried out as the result of specific ocular symptoms), and the interval between them is usually two to six years. Of the 1,750 patients at present attending the clinic, 168 fulfilled three criteria: (1) There were one or more observations after the one at which diabetic retinopathy was

Table 1
Rates of change of ophthalmoscopic appearances of diabetic retinopathy

	Year	Annual rate % 1	2	3	4	5	Cumulative five-year rate (%)
Regression of microaneurysms	All cases	16·1	12·4	6·5	4·7	2·7	36·3
	Men under 40 at diagnosis of D.M.	19·3	22·2	7·9	7·5	6·1	49·8
	Others	15·8	7·3	5·2	1·8	1·1	28·1
	Good control	29·0	17·3	8·7	2·0	1·5	48·3
	Poor control	5·1	7·1	2·8	6·6	4·8	24·6
		Mean annual rate % ± S.E.		*Significance of difference*			*Cumulative five-year rate (%)*
Progression of microaneurysms	All cases	13·0±2·2		—			50·2
	Men under 40 at diagnosis of D.M.	7·2±2·6		P<0·05			34·6
	Others	17·2±3·4		P<0·05			60·9
	Good control	11·1±2·7		N.S.			44·5
	Poor control	15·5±3·7		N.S.			56·6
Regression of hæmorrhages and/or exudates	All cases	6·2±0·85		—			27·4
	Men under 40 at diagnosis of D.M.	10·0±2·7		N.S.			41·0
	Others	5·4±0·88		N.S.			24·2
	Good control	6·2±1·2		N.S.			27·4
	Poor control	6·1±1·2		N.S.			27·0

D.M = diabetes mellitus. N.S. = not significant

recorded. (2) The retinopathy could be classified into one of two types: either microaneurysms alone, or hæmorrhages and/or exudates with or without microaneurysms. (3) There was no other ocular condition which might obscure the ophthalmoscopic picture (e.g. gross cataract, senile macular degeneration, or hypertensive retinopathy).

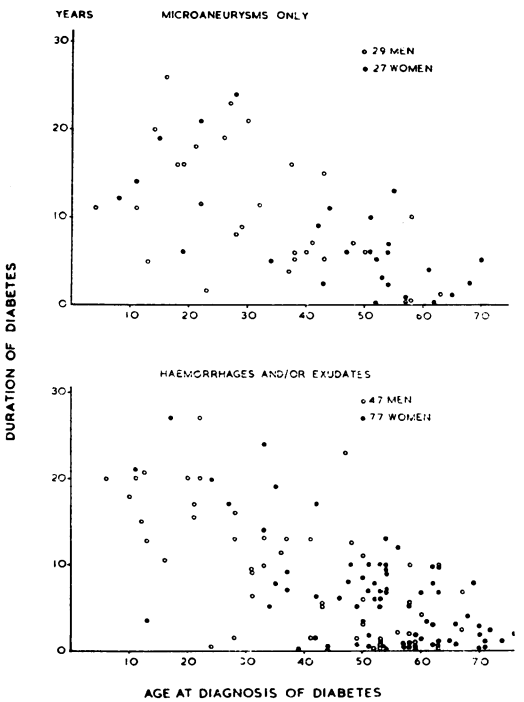

Fig 1 *Relation between age at diagnosis of diabetes, sex, and duration of diabetes at the time of first observation of retinopathy in 56 patients with microaneurysms alone (upper) and 124 with hæmorrhages and/or exudates (lower)*

There were 56 patients with 82 eyes with microaneurysms alone, and 124 patients with 211 eyes with hæmorrhages and/or exudates. Twelve patients were in both groups, with one eye in each. Fig 1 shows the relation between sex, age at diagnosis of diabetes, and duration of diabetes at the time of first observation of retinopathy. In both groups men predominate among the patients whose diabetes was diagnosed before the age of 40, and the duration of diabetes falls with increasing age at diagnosis of diabetes. Thus these three variables, sex, age at diagnosis, and duration of diabetes, are closely linked.

In the eyes with microaneurysms alone, two events were considered: (1) Progression (i.e. the development of hæmorrhages and/or exudates) and (2) regression (i.e. the disappearance of all visible microaneurysms, leaving a normal fundus). In the eyes with hæmorrhages and/or exudates only regression was considered (i.e. the disappearance of all hæmorrhages and exudates, leaving either microaneurysms alone or a normal fundus), since the data were not adequate to study the development of retinitis proliferans. A maximum likelihood method (Harris *et al.* 1950) was used to determine annual rates of occurrence of the three events. The rates for progression of microaneurysms and for regression of hæmorrhages and/or exudates were each uniform over a five-year period. Mean annual rates with standard errors were therefore calculated for these events by the University's computer. The annual rates of re-

gression of microaneurysms fell steadily with time, doubtless because of the operation of an opposite process of reappearance which has been described by Keen & Smith (1959) and observed in a few patients in this study. Standard errors could not be determined for these regression rates.

Table 1 shows the rates found. After five years 50% of eyes with microaneurysms alone show progression and 36% regression. Regression occurs in 27% of those with hæmorrhages and/or exudates in a similar period. Men under 40 at the time of diagnosis of diabetes show a lower rate of progression of microaneurysms and higher rates of regression of microaneurysms and hæmorrhages and/or exudates, but only in the first instance is the difference from the rate found in other patients statistically significant.

Control of diabetes has been simply measured by the proportion of routine urine tests at the clinic which show 2% glycosuria. Those with a proportion under 10% are arbitrarily defined as having good control, those with over 10% poor control. The regression rate of microaneurysms is higher in those with good control than in those with poor control, but the significance of this difference cannot be assessed. There is no significant difference between the rates of progression of microaneurysms or of regression of hæmorrhages and/or exudates found in those with good and those with poor control.

Conclusions: (1) Diabetic retinopathy of slight or moderate degree can regress. (2) Rates of progression and regression can be measured with fair accuracy. (3) The prognosis is better in younger men (this is contrary to the usual view). (4) There is some evidence that control of diabetes may affect prognosis.

REFERENCES
Becker B (1952) *Ann. intern. Med.* **37**, 273
Bedrossian R H, Pocock D S, Harvey W F & Sindoni A S (1953) *Arch. Ophthal., Chicago* **50**, 277
Friedenwald J S (1950) *Amer. J. Ophthal.* **33**, 1187
Harris T E, Meier P & Tukey J W (1950) *Hum. Biol.* **22**, 248
Keen H & Smith R (1959) *Lancet* **i**, 849
Lawrence R D (1951) *Proc. R. Soc. Med.* **44**, 742

Sjögren's Syndrome

by A M Heaton MB DO
(*Institute of Ophthalmology, London*)

Sjögren's syndrome is a type of chronic conjunctivitis, sometimes called keratoconjunctivitis sicca, which is associated with various systemic disturbances. Its generalized nature was first pointed out by Gougerot (1926) and Sjögren (1933), although various aspects had been recorded previously; for example, Hutchinson (1888) described a case of dry mouth and erythematous lupus.

It has been estimated that about 2·3% of the entire population suffer from rheumatoid arthritis or degenerative arthritis. Since about 12% of those with rheumatoid arthritis have Sjögren's syndrome it is far from being the rare disease it is often thought to be, apparently for two reasons. One is that it falls between the specialties of ophthalmology, general medicine and rheumatology. The other reason is that it is liable to be missed unless specifically sought.

The patient is usually a woman between 40 and 60 years of age. Only about 10% of cases occur in men. The chief ocular complaints are of burning and smarting, a feeling that there is something in the eyes, photophobia, and occasionally dryness or itching. The condition is nearly always bilateral.

The eyes may look a little suffused, with a lot of sticky mucus in the conjunctival sacs and diminished tear flow as measured by Schirmer's test. Confirmation of the diagnosis is obtained by the characteristic staining of the bulbar conjunctiva and cornea with rose-bengal dye.

There are many components of the syndrome. Usually the patient has a dry mouth and upper respiratory tract as well as dry eyes and sometimes a dry vagina. Rheumatoid arthritis is found commonly, as is arthralgia. Raynaud's phenomenon occurs in about one-third of cases. Less commonly there is periodic enlargement of one or more of the salivary and lacrimal glands – Mikulicz's disease – which has the same histological appearance. Felty's syndrome – leucopenia, splenomegaly and rheumatoid arthritis – may also be associated with Sjögren's syndrome. Other conditions such as pleurisy and pneumonitis, pericarditis, lesions of the central nervous system, vasculitis and sarcoidosis may occur.

Is there a hypothesis which will unite these seemingly diverse conditions which are described under the label Sjögren's syndrome? A destructive auto-immune process attacking diverse but immunologically related tissues would help to account for many features of the syndrome (Heaton 1959).

Hashimoto (1912) remarked on the close resemblance between the histology of the thyroid in Hashimoto's disease and the lacrimal gland in Sjögren's syndrome. Since a destructive auto-immune process is thought to play an important part in Hashimoto's disease, Jones (1958) looked for and found a precipitating auto-antibody in Sjögren's syndrome. Anderson *et al.* (1961) found that two precipitating antigen-antibody systems were involved but that the antigens were not specific, being present in a wide range of cellular tissues. So far organ-specific antibodies to Sjögren's syndrome have not been demonstrated as they have in Hashimoto's disease.