RETINOPATHY IN WOMEN OVER 45 YEARS OF AGE ATTENDING A DIABETES CLINIC

INCLUDING ITS RELATIONSHIP TO THERAPY WITH SULPHONYLUREAS*

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This simple clinical study was started in order to find out whether the degree of parity in women bore any relation to the occurrence or severity of diabetic retinopathy, as part of an investigation into the diabetogenic effect of pregnancy.[1,2] A further analysis of our results seemed worth reporting, especially with relation to race and to the use of sulphonylureas in therapy. We are not aware of any study so far undertaken to ascertain whether the sulphonylureas tend to hasten or to delay the development of retinopathy.

Subjects and Methods

Women over 45 years of age attending the Diabetes Clinic were randomly referred to one of us (C.G.), who worked in a darkened room in the clinic. Retinopathy was graded as follows:

Nil	
+	aneurysms only
++	aneurysms plus haemorrhages and/or exudates
+++	more advanced involvement plus venous engorgement
++++	retinitis proliferans.

(No account was taken of blood pressure; although many of the subjects were hypertensive, all cases of retinopathy included here showed features considered to be specific for diabetes, e.g. capillary aneurysms.)

A proforma was filled in for each patient. Proformas included spaces for name, age, race, family history, parity (i.e. number of pregnancies lasting longer than 7 months), control ('good, medium or poor'), duration of diabetes, body build, whether insulin used and for how long, whether tablets used for more than one year, retinopathy (0 to 4+) and other ocular features. 'Control' of the diabetes was crudely estimated from the results of blood and urine tests as entered in the clinic records — 'good' if glycosuria was usually absent and blood-sugar readings normal or near-normal, 'poor' if glycosuria was constant and blood sugar usually over 200 mg. per 100 ml. 'Tablets' indicated a sulphonylurea, taken for at least one year, usually much longer—in some cases for over 5 years. The actual sulphonylurea was not specified, and latterly a diguanide had been used in combination in a few cases. Where patients had received both tablets and insulin an entry was made against that drug which had been used for the longer time.

The great majority of the subjects had diabetes of 'maturity-onset' type; very few had ever shown ketosis, but this was not specially recorded.

Results

The total number of women examined was 272, of whom 112 or 41% had retinopathy. In 19 or 7% the retinopathy was of severe grade, 3 or 4+.

Race. Retinopathy was found in 44% of 122 Coloured† diabetics and 39% of 150 White patients (Table I). This difference is not significant.

TABLE I. RETINOPATHY AND RACE

	No retinopathy	*Retinopathy present*	*Total*
Coloured	68	54 (44%)	122
White	92	58 (39%)	150
Total all races	150	112 (41%)	272

Parity. Table II indicates that we found no significant difference between the prevalence of retinopathy in different parity groups, although there was 4% more retinopathy in the over-6 para group than in the nulliparae. There was no evident difference in the severity of the retinopathy in different parity groups (not shown in table).

TABLE II. RETINOPATHY AND PARITY

Parity	*No retinopathy*	*Retinopathy present*	*Total*
0	21 (62%)	13 (38%)	34
1–5	84 (60%)	57 (40%)	141
6+	56 (58+)	41 (42%)	97

No statistical difference between incidence of retinopathy in different parity groups.

Control. Patients whose diabetes was noted as well controlled had a prevalence of retinopathy of 38% as against 50% in poorly-controlled subjects, and 41% in the intermediate group (Table III). These differences border on statistical significance. Severity of retinopathy did not appear to be related to control, for the 3 and 4+ grade were evenly divided among the different control groups.

TABLE III. RETINOPATHY AND CONTROL OF DIABETES

	Poor control	*Medium control*	*Good control*
No retinopathy	27	56	66
Retinopathy present ..	27 (50%)	39 (41%)	41 (38%)

Difference between incidence of retinopathy in 'poor' and 'good' control cases is not significant at 5% level.

Age. Age bore no relation to retinopathy in this series (not shown in tables). The mean age of the whole series was 62 years. The mean ages of the 3 treatment groups were identical.

Duration. As indicated in the last column in Table IV, retinopathy became more frequent with increasing duration of diabetes, although 24% of women whose diabetes was of less than 5 years' duration were affected. Twelve of the 19 subjects with grades 3 and 4 retinopathy had been diabetic for more than 10 years. On the other hand no retinopathy was found in 7 patients out of 19 whose diabetes was of greater duration than 20 years.

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† Coloured signifies people originating from 4 principal stocks: Hottentot, Bushman, European and, more recently, Bantu.

TABLE IV. RETINOPATHY IN RELATION TO DURATION OF DIABETES AND TYPE OF THERAPY

Duration in years:	*Insulin*		*Tablets*		*Diet only*		*Total all therapies*	
	No retinopathy	*Retinopathy present*	*No retinopathy*	*Retinopathy present*	*No retinopathy*	*Retinopathy present*	*No retinopathy*	*Retinopathy present*
0–4	7	8	38	15	36	3	81	26 (24%)
5–9	16	12	20	16	9	1	45	29 (39%)
10+	14	42 (75%)*b*	12	8 (40%)*b*	6	2	32	52 (62%)
Total	37	62 (62%)*a*	70	39 (36%)*a*	51	6 (10%)	158	107

'Insulin' indicates insulin taken for the greater part of the total duration.
'Tablets' indicates tablets taken for at least one year.
If both were applicable, that taken for the longer time is included.

Difference between percentages *a*, *a* is highly significant (p. < ·001)
Difference between percentages *b*, *b* is significant (p. < ·01)

Type of therapy (Table IV). Among patients who had taken insulin for the greater part of their diabetic lives retinopathy was present in 62%. This was significantly higher than the 36% with retinopathy found among subjects who had been on sulphonylureas for more than a year. Among those diabetics using dietary measures only, 10% had retinopathy.

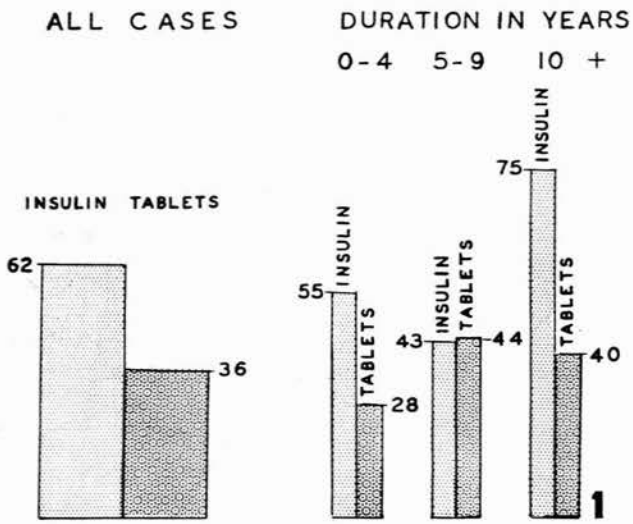

Fig. 1. Comparing percentage incidence of retinopathy in diabetics treated with insulin and those treated with sulphonylureas (1) in all cases and (2) according to duration of diabetes (see text).

The results have been subdivided according to duration of diabetes in Table IV and Fig. 1. Among patients whose diabetes was of under 5 years' and of over 10 years' duration, more retinopathy was found in those treated with insulin than in those who took tablets. In the 5 - 9 year group, the prevalence among insulin-treated and tablet-treated subjects was virtually identical.

The mean ages of the 3 therapy groups were identical (62 years); in the long-duration group those patients treated with insulin appeared on the whole more poorly controlled, with 35% classed as 'poor control' as against 20% in those not insulin-treated.

Discussion

The 41% prevalence of retinopathy seems to be roughly that expected from other reports,[2-5] or rather higher,[6,7] but the selection of cases was nowhere identical to our own. Certainly the present maturity-onset group of patients seem just as vulnerable as growth-onset diabetics.[8,9]

Race. We had previously found that retinopathy was distinctly commoner among Coloured women than among White women.[10] In the present series, however, the difference is slight and appears unimportant. The incidence of retinopathy in both the White and Coloured groups is known to be higher than that found in pure Bantu or other tropical races, with the exception of the Natal Indian.[11]

Parity. As discussed elsewhere,[1,2] parity appears to play little or no part in the occurrence or severity of retinopathy.

Control. Our evidence that good control of the diabetes lessens the liability to retinopathy is inconclusive, though our previous report appeared more definite.[10]

Duration. We found, as is generally agreed,[4,6-8] that the occurrence of retinopathy rose with the duration of diabetes. Also the majority of the cases of severe retinopathy (3 and 4 +) occurred in the long-term diabetic group.

Type of therapy (Table IV). When we observed that retinopathy was more frequent in insulin-treated than in sulphonylurea-treated or diet-only patients, we first thought that this could be largely explained if the insulin-treated group included, on the whole, diabetics of longer duration. However, Table IV and Fig. 1 illustrate that this is not the whole explanation, since in long-duration cases retinopathy was significantly more frequent in the insulin-treated group. Among those patients who had diabetes of intermediate duration (5 - 9 years) the occurrence of retinopathy in insulin and tablet-treated groups was identical. In the short-duration cases it is possible that insulin was more likely to have been used in those patients in whom retinopathy was already present, and the frequency of retinopathy in insulin-treated patients in this group may be so explained. In the long-duration cases it could be argued that it was the severer diabetics that had received insulin, and they would be more liable to retinopathy on account of the severity of their metabolic disturbance. Matthews[6] reported very similar findings and reached the same conclusion. This suggestion is further supported by the finding that the insulin-treated group on the whole appeared to be more poorly controlled than the others. (This explanation in reverse could also be invoked to explain the lower percentage of retinopathy in 'diet-only' patients, who may be considered to have the mildest type of diabetes.) An alternative explanation is that the use of insulin actually in-

creased the liability to retinopathy. We do not wish to resurrect these old nagging doubts concerning insulin, although they have never been finally laid.

It would at least seem reasonable to conclude that the sulphonylureas do not appear to enhance the diabetic's susceptibility to retinopathy.

SUMMARY

From examination of the fundi of 272 women over 45 years of age attending our Diabetic Clinic we found retinopathy in 41%, and on analysis:

1. No significant differences appeared between the White and Coloured groups, nor between different parity groups.

2. Poor control of the diabetes may have played some part, but this could not be shown statistically.

3. The frequency of retinopathy increased with duration of diabetes.

4. Retinopathy was commoner in insulin-treated diabetics than in tablet-treated, and commoner in tablet-treated than in diet-only patients. This could not be entirely explained by differing duration of diabetes in the 3 treatment groups, but it may also reflect differing severity of the diabetic state in the 3 groups.

These findings do not answer the question of the relationship of the sulphonylureas to diabetic vascular disease, but at least they suggest that these drugs are not grossly deleterious.

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