

VISUAL PROGNOSIS OF PROLIFERATING DIABETIC RETINOPATHY*

BY

WILLIAM PARKES BEETHAM

From the Harvard Medical School, the Massachusetts Eye and Ear Infirmary, and the New England Deaconess Hospital, Boston, Massachusetts

SINCE we are not yet able to prevent retinal changes in diabetic patients we must be content to accept, lessen, or slow the progress of these degenerative retinal vascular changes. The latest method of lessening them is the "Houssay phenomenon", which is said to have a favourable effect in diabetic retinopathy through destruction of the pituitary gland.

The percentage of diabetic patients with retinopathy is not accurately known, but in a survey undertaken in 1933 of 2,000 consecutive diabetic patients seen at the Joslin Clinic for advice, education, and control, 18 per cent. had retinopathy, irrespective of age, sex, and duration or severity of diabetes. When this survey was made, the severe proliferating type of retinopathy was found in 8 per cent. of those affected, and no one doubts the marked increase in frequency of proliferating retinopathy during the past few decades. Statistics from my office practice give no proper estimate, as I see so many severely-ill diabetics with poor control, who come to Boston in desperation, so that as many as 30 per cent. of those seen by me have the proliferating type of retinopathy. Those with the non-proliferating type, as described by Jaeger (1855), often have severe retinal changes and visual loss but, in contrast to the proliferating type, they rarely proceed to total blindness.

During the past 20 years, I have seen 1,149 diabetics with proliferating retinopathy as private patients, chiefly at the Joslin Clinic. I propose in this paper to describe and record for future statistical comparison the objective and subjective deterioration of vision in this large series.

I have empirically assumed four degrees of severity of proliferating diabetic retinopathy (P.D.R.): early, moderate, marked, and extreme. The opinion of the observer will have to suffice as to the degree of severity that exists, as there can be no standard description of these degrees for general use. The presence of a nest of new capillaries either on the optic disc or elsewhere in the fundus has been designated by me as "early", and a disorganized fundus with extensive new vessel and fibrous tissue formation as "extreme", "moderate" and "marked" being intermediate stages.

To show the time interval of objective deterioration as seen with the ophthalmoscope, about one-third of 351 patients followed by me from time

* Paper read at a joint meeting of the Irish Ophthalmological Society and the British Diabetic Association held in Dublin, April 25 to 27, 1963.

to time (they are included in Groups C and D below) are represented in Table I. Some eyes deteriorated at an average rate of 1.1 years per degree, and others at a rate of 1.9 years per degree (mean 1.6 years). We can therefore suggest that an average deterioration from slight-to-extreme takes place in approximately 5 years. The degree of ophthalmological change (objective findings) need not necessarily agree with the changes in visual status (subjective findings or visual acuity).

TABLE I
RATES OF CHANGE IN DEGREE OF PROLIFERATING DIABETIC RETINOPATHY

Change in Degree of Proliferating Diabetic Retinopathy	Time Interval (yrs)			Total No. of Eyes	Average Rate of Change (yrs)
	1	2	2+		
a. Slight to Moderate	32	24	19	75	1.9
b. Moderate to Marked	18	12	4	34	1.6
c. Marked to Extreme	25	12	14	51	1.9
d. Slight to Marked	3	11	15	39	2.6 (1.3 per degree)
e. Slight to Extreme	10	13	9 13 12 (3) (4) (4+)	57	3.3 (1.1 per degree)

I have also designated four stages of visual status:

- (1) Good vision.—6/6 to 6/12
- (2) Economic blindness.—6/15 to 6/30
- (3) Legal blindness.—6/60 or less
- (4) Total blindness.—Perception of light, shadow vision, nil.

The figures quoted by various authors of the numbers of persons who are "blind" from diabetes presumably include those who are *legally* blind, and many of these are not, in fact, *totally* blind but can care for themselves without becoming a social liability.

Table II (opposite) shows how my 1,149 cases have been arranged in four groups for study, and subdivided into "growth-onset" and "mature" diabetics*.

Group D is the most remarkable group, as none had proliferating retinopathy, and most had no retinopathy at all, when first seen by me, but they all developed it some months or years later.

Group C, with P.D.R. present at the initial examination, includes many patients who maintained good vision for a long time (until last seen).

Group B contains those seen on one occasion only; they all had P.D.R. and can be combined with the first observation of those in Group C to form a larger group of 977 patients.

* "Growth-onset" diabetics are those who develop the disease during the first 20 years of life and are considered non-insulin producers. "Mature" diabetics are those who develop diabetes after age 20 and do produce a certain amount of insulin.

TABLE II

EVALUATION OF 1,149 PRIVATE PATIENTS WHO DEVELOPED PROLIFERATING DIABETIC RETINOPATHY (P.D.R.).

Group	Observations	No. of Cases		
A	Insufficient data to evaluate	63		
B	Observed on one occasion only, P.D.R. present	Grow-onset diabetics Mature diabetics	290 445	735
C	Observed from time to time, P.D.R. present at first examination	Growth-onset diabetics Mature diabetics	131 111	242*
D	Observed from time to time, P.D.R. not present at first examination, but appeared during observation period	Growth-onset diabetics Mature diabetics	65 44	109*
Total		1,149		

* Groups C and D together comprise the 351 patients who were seen more than once.

Table III shows the degree of vision present in these 977 patients when I first examined them: 47 per cent. had good vision and 53 per cent. were economically blind, the latter including 34 per cent. legally and 7 per cent. totally blind. It will be seen that the number with good vision in the "growth-onset" category is almost twice that in the "mature category", while the legally blind are only half as numerous. The growth-onset diabetics are thus much better off, visually speaking, than the mature diabetics.

TABLE III

VISUAL STATUS AT FIRST OBSERVATION IN 977 PATIENTS IN GROUPS B AND C

Group B (observed one occasion only. P.D.R. present) 735 }
 Group C (observed from time to time. P.D.R. present at first observation) 242 } 977

Visual Status	Type of Diabetic					
	Growth-Onset		Mature		Combined	
	No.	Per cent.	No.	Per cent.	No.	Per cent.
(1) Good Vision (6/6, 6/10, 6/12)	269	64	193	35	462	47
* (2) Economic Blindness (6/15, 6/20, 6/30)	152	36	363	65	515	53
* (3) Legal Blindness (6/60, 3/60, 1/60)	94	22	239	43	333	34
* (4) Total Blindness (Perception of light, Shadow vision, Nil)	21	5	45	8	66	7
Total	421	—	556	—	977	

* (2) includes the more severely affected who are also shown separately under (3) and (4).

Table IV shows that very few in the growth-onset category had had diabetes mellitus for as little as 10 years, but even so there were eleven patients in this class, and half of them deteriorated rapidly to legal blindness. It is surprising to find so many, 162 (28 per cent.), of the mature category with diabetes of less than 10 years' duration, and 79 of these were legally blind. This Table also shows that P.D.R. develops sooner after the onset of diabetes in the mature than in the growth-onset diabetics.

TABLE IV
VISUAL STATUS IN RELATION TO DURATION OF DIABETES IN 977 PATIENTS IN GROUPS B AND C

Group B (observed one occasion only. P.D.R. present) 735 } 977
Group C (first observation. P.D.R. then present) 242 }

Type of Diabetic	Visual Status	Total Cases			Duration of Diabetes (yrs)			
		Patients		No. of Eyes	10 or Less	11-20	21-30	31-40
		No.	Per cent.		Patients (Eyes)	Patients (Eyes)	Patients (Eyes)	Patients (Eyes)
Growth-Onset	(1) Good Vision	269	64	(410)	5 (10)	154 (231)	96 (147)	14 (22)
	*(2) Economic Blindness	152	36	(432)	6 (12)	93 (261)	48 (142)	5 (7)
	(3) Legal Blindness	94	22	(318)	5 (11)	57 (189)	30 (106)	2 (12)
	(4) Total Blindness	21	5	(120)	1 (3)	16 (76)	4 (34)	0 (7)
	Total (1) + (2)	421	—	(842)	11 (22)	247 (492)	144 (289)	19 (29)
Mature	(1) Good Vision	193	35	(260)	41 (48)	97 (140)	46 (59)	9 (13)
	*(2) Economic Blindness	363	65	(852)	121 (271)	164 (384)	65 (161)	13 (36)
	(3) Legal Blindness	239	43	(661)	79 (207)	107 (305)	45 (122)	8 (27)
	(4) Total Blindness	45	8	(221)	14 (74)	19 (93)	10 (40)	2 (14)
	Total (1) + (2)	556	—	(1,112)	162 (319)	261 (524)	111 (220)	22 (49)

* (2) includes (3) and (4).

Table V (opposite) shows that, of the 111 mature diabetics in Group C (those with P.D.R. present at the initial examination) who were all followed for fairly long periods of time, only 56 (50 per cent.) had good vision when first seen, and 23 (40 per cent.) of these maintained good vision during the period of observation, while 24 (40 per cent.) became legally blind. Of the 131 growth-onset diabetics, 100 (almost 80 per cent.) had good vision when first seen, 59 (60 per cent.) maintained good vision, and 26 (25 per cent.) became legally blind. Table V also indicates the number of years during which these patients were under observation.

The most remarkable group is that of the 109 patients in Group D who were observed before the onset of P.D.R. and were followed for various lengths of time thereafter. Table VI (opposite) and Table VII (overleaf) give particulars of these 109 patients. There were 65 in the growth-onset category (with average age at onset of P.D.R. 29.6 years, and interval between onset of diabetes and of P.D.R. 20.5 years) and there were 44 in the

TABLE V
DEGREE AND RATE OF VISUAL LOSS IN 242 PATIENTS IN GROUP C
(Observed from time to time. P.D.R. present at first observation)

Type of Diabetic	Visual Status		No. of Patients	Duration of Observation Period (yrs)													
	First Seen	Last Seen		1	2	3	4	5	6	7	8	9	10	11	12	13	
Growth-Onset	a. Good	Good Vision	59	12	11	11	8	5	3	4	1	—	1	1	1	1	
	*b. Good	Economic Blindness	41	6	8	11	3	4	3	1	2	1	—	2	—	—	
	c. Good	Legal Blindness	26	1	7	10	1	1	2	1	1	1	—	1	—	—	
	d. Good	Total Blindness	12	—	2	6	—	1	2	1	—	—	—	—	—	—	
	Total Good Vision when first seen (a + b)		100														
	Total Less than Good Vision when first seen		31														
Total Patients			131														
Mature	a. Good	Good Vision	23	3	8	3	5	2	1	—	1	—	—				
	*b. Good	Economic Blindness	33	—	14	4	6	3	1	2	1	—	2				
	c. Good	Legal Blindness	24	—	9	4	5	2	1	2	1	—	—				
	d. Good	Total Blindness	6	—	1	3	1	—	1	—	—	—	—				
	Total Good Vision when first seen (a + b)		56														
Total Less than Good Vision when first seen		55															
Total Patients			111														

* b includes c and d.

mature category (average age at onset of P.D.R. 53.4 years, and interval between onset of diabetes and of P.D.R. 16.4 years). The growth-onset category included 60 per cent. with good vision and P.D.R. for an average of 5.1 years, and the mature category included 34 per cent. with good vision and P.D.R. for an average of 3.4 years.

The progression of P.D.R. from onset to legal blindness took about the same time for the two categories, 3.3 and 3.1 years respectively, but the percentage was much smaller in the growth-onset category (22 per cent.) than in the mature category (34 per cent.).

TABLE VI
MEAN AGES AT ONSET OF DIABETES AND OF P.D.R. OF 109 PATIENTS IN GROUP D
(Observed from time to time. No P.D.R. at first observation)

Type of Diabetic	Age of Patients (yrs)						Interval between Onset of Diabetes and of P.D.R.	Duration of Observation Period (yrs)				
	First Seen		Last Seen		Onset of P.D.R.			Total		With P.D.R.		
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Growth-Onset	24.9	8-46	34.5	21-22	29.6	19-47	20.5	12-31	9.4	2-20	5	1-13
Mature	48.9	35-64	56	34-72	53.4	33-66	16.4	2-30	6.8	1-14	4	1-11

TABLE VII
DEGREE AND RATE OF VISUAL LOSS IN 109 PATIENTS IN GROUP D
(Observed from time to time. No P.D.R. at first observation).

Type of Diabetic	Visual Change	Duration of P.D.R. (yrs)													Mean Duration (yrs)	Total			
																Patients		Eyes	
		1	2	3	4	5	6+	7	8	9	10	11	12	13		No.	Per cent.	No.	Per cent.
Growth-Onset	a. Good Vision Maintained	9	3	1	5	6	3	2	1	6	—	1	1	1	5.1	39	60	63	49
	*b. To Economic Blindness	10	3	4	3	3	3								2.9	26	40	67	51
	c. To Legal Blindness	3	4	1	3	3	1								3.3	15	22	51	39
	d. To Total Blindness	—	—	1	1	—	—	2							5.2	4	6	22	17
	Total (a + b)															65	—	130	—
Mature	a. Good Vision Maintained	4	1	5	1	1	1	1	1						3.5	15	34	19	22
	*b. To Economic Blindness	11	5	8	1	1	3								3.9	29	66	69	78
	c. To Legal Blindness	5	2	2	3	—	3								3.1	15	34	34	39
	d. To Total Blindness	—	1	—	2	1									2.6	4	10	14	16
	Total (a + b)															44		88	

* b includes c and d.

Spontaneous Arrest

A few patients who develop proliferating retinopathy belong to a very special group. They usually go through the turmoils of visual variation, caused by retinal changes and vitreous haemorrhages, and then, for some unknown reason, some months or years later, the haemorrhages cease, the retinal-vascular picture becomes quiescent, the proliferating tissue thins and becomes reticulated, the retinal veins lose their distended appearance and become almost normal in size, the retinal arteries become small and attenuated, and many obliterated vessel branches may be seen as white lines; the fundus picture thus becomes less angry and haemorrhagic and may remain so for many years. This, of course, is the process sought by hypophysectomy,* if possible before the eyes become economically or legally blind. Vable VIII (opposite) gives the particulars of eight such patients who have shown a quiescent fundus picture for more than 4 years; 27 others show a similar ophthalmoscopic picture, but have been observed for shorter periods (6 for 3 years, 3 for 2 years, and 18 for 1 year). This makes a total of 35 (10 per cent.) of the 351 patients in Groups C and D (those whom I have been able to observe from time to time).

* The Houssay phenomenon mentioned above.

TABLE VIII

PARTICULARS OF EIGHT PATIENTS OF GROUP D WHO SHOWED SPONTANEOUS ARREST OF P.D.R. LASTING 4 YEARS OR MORE

Case No.	Period of Arrest (yrs)	Period of Observation (yrs)	Interval between Onset of Diabetes and of P.D.R. (yrs)	Duration of Diabetes at Onset of Arrest (yrs)	Duration of Diabetes at Last Observation (yrs)	Visual Acuity at Last Observation
1	9	12	15+	18	27	6/30
2	8	10	28+	30	38	6/15
3	7	17	22	31	38	6/7
4	6	19	26	32	38	6/10
5	6	11	29	34	40	6/12
6	5	10	18+	23	28	6/7
7	5	12	15+	22	27	6/30
8	4	8	14	18	22	3/60

Of the eight patients with more than 4 years of arrest, every one has carried on a useful occupation; even the one patient with a visual acuity of only 3/60 travels alone wherever he wishes to go, and acts as a guide for fishing parties in the lakes of New England in the summer time. The average duration of diabetes mellitus for these 8 patients is 35 years; the average period of observation by me is 13 years; and they have had P.D.R., including the stage of arrest, for an average of 10 years. The case histories of three of these eight patients are given in detail below.

Reports of Cases 8, 7, and 6 in Table VIII

Case 8 (4 years arrested P.D.R.), a 19-year-old male, was first seen by me in September, 1956, with a duration of diabetes of 14 years, and an insulin requirement of 78 units. He had many microaneurysms and round haemorrhages, and some striate haemorrhages in each retina. The retinal veins were markedly distended. There were two small areas of new vessel formation in the right fundus. The visual acuity was recorded as 6/6 in each eye. During the ensuing year the retinal pathology increased, and several areas of new vessel formation were noted in the right eye, and one small area in the left. The visual acuity was still recorded as 6/6 in each eye.

In October, 1958, the retinal pathology had increased. Many areas of oedema and striate haemorrhages were noted, but the visual acuity was still good, 6/7 in each eye.

During the next 7 months the retinopathy increased markedly, with new vessel and new tissue formation in each fundus in increased amounts. Visual acuity had fallen to 6/15 in the right eye and 6/12 in the left, and marked deterioration occurred during the following 3 months. Extensive proliferating retinopathy was then present in each eye, and the visual acuity had fallen to 6/30 in the right eye and 6/60 in the left.

At the next examination (March, 1961) haemorrhagic glaucoma and rubeosis iridis was present in the right eye with vision recorded as nil. In the left eye there was extensive fibrous tissue and new vessel formation involving the entire fundus. The retinal veins were less distended than at previous examinations. No retinal haemorrhages or microaneurysms could be seen. Visual acuity had fallen to 3/60.

One year later the ocular picture was unchanged, except that a good many obliterated retinal vessels were noted. The retinal arteries were very small and irregular in calibre and the retinal veins were irregular in calibre but not distended. The visual acuity was

2/60. At the last visit (March, 1963) no change could be seen in the appearance of the left eye, and the visual acuity was still 3/60. The right eye had bullous keratopathy and high intra-ocular pressure, but there was no congestion and no pain.

Case 7 (5 years arrested P.D.R.), a 29-year-old male, was first seen by me in December, 1950, with a duration of diabetes of 15 years, and an insulin requirement of 60 units. Severe haemorrhagic retinopathy was present in each eye with many haemorrhages of various sizes and shapes. There were many areas of oedema and soft exudates. The retinal veins were very distended and quite irregular in calibre. Several areas of new vessel formation were present in each fundus. The visual acuity was 6/30 in the right eye, and 6/7 in the left.

One month later a massive vitreous haemorrhage occurred in the right eye, and a preretinal haemorrhage was seen in the left. The visual acuity had fallen to perception of light in the right eye, but was still 6/7 in the left.

No change occurred in the right eye during the next 10 months. The haemorrhage and oedema were somewhat less in the left eye, but at least five areas of proliferating retinopathy were noted. One year later (October, 1952), the ophthalmoscopic reflex was still absent in the right eye, and vision was nil.

In July, 1953, the vitreous in the right eye had cleared somewhat and one could see extensive proliferating retinopathy. Much new tissue formation surrounded the left optic disc with festoons extending into various quadrants. A modest number of deep haemorrhages was present. The visual acuity remained 6/6.

In May, 1954, haemorrhagic glaucoma and rubeosis iridis were present in the right eye, but there was no pain or discomfort. A good many haemorrhages could still be seen in the left fundus, with many areas of new vessel and new tissue formation. Marked beading of the retinal veins was noted. The visual acuity was reduced to 6/10.

One year later the ocular picture was similar, but the visual acuity had decreased to 6/15.

In May, 1956, there was extensive proliferating retinopathy involving the entire left fundus. Only a few small haemorrhages could be seen and the retinal veins were less distended. The visual acuity was 6/30. One year later the ocular picture had not changed.

In May, 1958, no haemorrhages and only a few microaneurysms could be seen. Many obliterated vessels were present. The visual acuity was 6/20.

In June, 1959, no haemorrhages or microaneurysms could be seen, and the visual acuity remained at 6/20.

In May, 1960, the right eye had bullous keratopathy and markedly increased intra-ocular pressure, but no discomfort.

One year later a prosthesis was being worn over a phthisical right eye. The proliferating tissue in the left fundus had thinned considerably. Many obliterated vessels could be seen. A thin posterior cortical lens opacity was present. The visual acuity was 6/30.

The last examination was in May, 1963, when there had been no change in the ocular picture during the preceding 2 years. The visual acuity remained at 6/30.

Case 6 (5 years arrested P.D.R.), a 23-year-old female, was first seen by me in September, 1953, with a duration of diabetes of 18 years, an insulin requirement of 52 units, and a pregnancy of 3 month's duration. A marked degree of proliferating retinopathy was present in the right eye and a moderate degree in the left. Many new vessels and areas of new tissue were present on each optic disc and surrounding retina; there were other isolated areas of new vessel formation, a few dots of waxy exudate, a few areas of retinal oedema, and many round and some striate haemorrhages. The retinal veins were markedly dilated and irregular in calibre. The visual acuity was 6/10 in the right eye and 6/7 in the left. A successful pregnancy ended 6 months later.

In May, 1955, patient was again 4 months pregnant. There was marked proliferating retinopathy in the right eye and much less in the left, with sheathing and distension of some of the retinal veins, and a few round haemorrhages and microaneurysms. The visual acuity was 6/10 in the right eye and 6/6 in the left. This pregnancy ended unsuccessfully. In December, 1955, the patient was again 4 months pregnant, and this pregnancy also ended unsuccessfully.

In March, 1956, there was a small preretinal haemorrhage in the right eye and also some round and striate haemorrhages. In the left eye the new vessel formation had become less visible and the new tissue had thinned considerably.

In June, 1958, the new tissue had thinned in each retina and few new vessels were visible. A few microaneurysms were present in each fundus. The visual acuity was 6/7 in each eye.

In August, 1960, the patient was 7 months pregnant, and the pregnancy ended successfully a few weeks later. A few microaneurysms were present in the right eye but none in the left.

In November, 1961, the proliferating tissue in each eye was thin, reticulated, and veil-like, and no haemorrhages or microaneurysms were present. The visual acuity was 6/7 in each eye.

The same ocular picture was present in August, 1962.

In early 1963 it was learnt that the patient had good vision in each eye and no ocular symptoms.

Summary

(1) Approximately 50 per cent. of the patients with proliferating diabetic retinopathy (P.D.R.) seen by me had fairly good vision.

(2) Approximately 30 per cent. were legally blind, some becoming so with considerable rapidity.

(3) No more than 7 per cent. were totally blind.

(4) The prospects were much worse, visually speaking, in the "mature" diabetics than in the "growth-onset" diabetics.

(5) The average rate of objective deterioration was about 1.5 years per degree of change; some progressed quite slowly, and a few rather rapidly.

(6) 35 patients (10 per cent. of the 351 followed by me at intervals) experienced spontaneous arrest of the P.D.R.

These statistics indicate to me that the visual outlook of these patients may not be as gloomy as previously supposed.