MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

October 26, 1967

DIABETIC RETINOPATHY AND THE ROLE OF PITUITARY ABLATION

Case Presentation: [redacted]

This 28 year old [redacted] man was admitted to [redacted] for the eleventh time on [redacted] 1967 in a comatose state. The patient was a known insulin dependent diabetic who had had a pituitary stalk section for advancing diabetic retinopathy two and a half years previously. He had been in his usual state of health the night prior to admission when prepared for sleep by his wife. The following morning when she attempted to awaken him at 8:00 AM she was unable to do so. The patient was taken to a private hospital by ambulance where he was found to have a blood sugar of 16 mgs%. Blood pressure was 50 systolic with no diastolic obtainable. One hundred cc of 50% glucose was given intravenously and a continuous infusion of glucose was begun. He was then transferred to Parkland Hospital. On arrival blood pressure was unobtainable. The pupils were dilated and unreactive, and myoclonic movements of the upper extremities were noted. Blood sugar on arrival was 1500 mgs%. Aramine was started and 250 mgs of hydrocortisone was added to the IV drip. Fifty units of regular insulin was given.

On physical examination the patient was completely unresponsive and breathing shallowly. B.P. with Aramine was 100/60. Pulse was 84, respirations 18, and temperature 100°. Fundoscopic examination was difficult, but the optic discs were sharp. Numerous hard exudates were visible. The neck was supple and the thyroid not felt. The lungs showed decreased breath sounds with rales and rhonchi in the right base posteriorly. The heart was normal except for a grade ii systolic ejection murmur at the base. Abdominal exam showed a supra-pubic cystostomy tube in place. The liver and spleen were not felt. The patient was paralyzed and areflexic below the level of T_4. Spontaneous jerking movements were noted in the arms.

In addition to the blood sugar of 1500 mgs%, initial laboratory workup revealed:

Hb	- 8.7 grams%
Hct	- 27%
WBC	- 4,500 with left shift
Urinalysis	- 4+ sugar, negative acetone, no cells
BUN	- 27 mgs%
CO_2	- 25 meq/liter
Sodium	- 127 meq/liter
Potassium	- 4.1 meq/liter

Chest x-ray confirmed the presence of pneumonia in the right lower lobe.

Past history was of considerable interest. The patient was first diagnosed as having diabetes at age 5 when he was brought to [redacted] in diabetic ketoacidosis.

Three of five siblings in the family were known to have diabetes. He did relatively well following this episode and was not admitted again to [redacted] until 1964. For some months prior to this time the patient had noted decreasing visual acuity and on examination was found to have advanced diabetic retinopathy with hemorrhages and microaneurysms in the left eye and retinitis proliferans on the right. He was admitted electively for pituitary stalk section in an attempt to arrest the progressive retinopathy. Surgery was performed through a trans-frontal incision and was tolerated well by the patient. Shortly before discharge, however, it was noted that the metal plate inserted over the sella to prevent re-growth of the stalk had slipped. Additional surgery to replace the plate was refused by the patient. Three weeks following discharge, while bowing his head to say grace at a meal, the patient developed a sharp pain in the neck and became paralyzed. X-rays showed that the plate had slipped into the cervical cord with transection. Cervical laminectomy was performed but to no availl. The patient has been paraplegic since 1964.

Since that time he has had 8 admissions for recurrent pyelonephritis and one episode of ketoacidosis. Replacement therapy has consisted of 0.2 mg l-thyroxine and 20 mg of hydrocortisone daily. His diabetes following surgery was fairly well controlled on 15-20 units of NPH insulin daily whereas previously 50-60 units had been required. On several occasions blood sugar determinations in the clinic were below 100 mgs%, and on at least two occasions symptomatic hypoglycemia had occurred. The patient had been cheerful and in good spirits the day prior to admission and had been given his usual 15 units of insulin by his wife. He did not miss a meal during the day.

Following the stalk section the patient subjectively felt that vision had improved. Objectively some clearing of the hemorrhages and microaneurysms occurred in the left eye with little change in the proliferative lesions on the right. His vision immediately prior to his last admission showed the capacity to detect light and shadows, but finger counting was not possible.

The patient received permanent damage from the hypoglycemic episode. Whereas previously intellectual function was good, he was unable to perform simple addition or subtraction. In addition, where he was previously cheerful he was now short tempered and childlike. He was discharged to a nursing home three weeks after admission.

Table 1.

The Effect of Hypophysectomy on Diabetic Retinopathy

This represents a compilation of all the cases reported in the literature to date. Cases are tabulated arbitrarily as improved, unchanged, or worsened. In view of the expected progression of the disease most authors consider either of the first two categories as a beneficial response.

Author	Number	Operative mortality	Effect on retinopathy		
			Improved	Unchanged	Worsened
Luft	20	5	2	6	12
Kinsell	9	0	9	-	-
Recant	1	1	-	-	-
Andersson	2	0	2	-	-
Hernberg	10	1	6	3	1
Ainslie	7	1	4	1	2
Lundbaek	14	0	5	4	5
Gordon	22	6	16	-	6
Bryan	7	2	2	1	4
Sjögren	26	2	1	19	6
Lawrence	83	0	18	29	32
Flohr	1	0	-	-	1
Chow	4	0	1	2	1
Field	75	3	45	-	18
Rand	4	1	2	1	1
Lourie	1	0	1	-	-
Ray	42	4	23	-	7
Pearson	25	1	17	-	-
Cullen	7	0	2	2	3
Cullen	10	1	7	1	1
Harrold	15	1	8	3	3
Joplin	38	3	9	8	1
Scott	18	1	3	8	4
Fager	52	1	24	5	18
Tassman	15	0	5	2	8
Totals:	508	34	212	95	136

Total evaluated 443

Stabilized or improved 307 (69%)

Table 2.

Experiences With Pituitary Ablation For Diabetic Retinopathy

The following are tabulated from Field and represent the most recent figures from 10 centers.

Author	Type of ablation	Number	% Improved
Field	Stalk section	108	65
Joplin	Yttrium 90	63	50
Bradley	Stalk section-hypox	50	50
Ray	Hypox	51	55
	Yttrium 90	21	48
Pearson	Yttrium 90	46	48
Gastineau	Stalk section	30	73
Rand	Cryo-hypox	12	67
Linfoot	Proton beam	135	55
Kjellberg	Proton beam	93	70
Zervas	Radio frequency hypox	8	75

Table 3.

The Effect of Pituitary Ablation on Diabetic Retinopathy-Controlled Series

The data from the controlled series of patients reported by Joplin, et al, are listed below. Treatment by Yttrium 90.

	Number	Number of patients changed for better (b) or worse (w)									
		Hemorrhage		Exudate		Venous		New vessels		Proliferans	
		b	w	b	w	b	w	b	w	b	w
Control	22	1 (22)	3	2 (20)	4	0 (15)	1	0 (15)	1	0 (13)	3
Treated	19	9 (18)	0	1 (12)	1	3 (16)	1	5 (16)	1	0 (17)	4

Table 4.

Visual Acuity in Diabetic Retinopathy

The visual acuity of the patients listed in Table 3 are tabulated below.

Visual acuity	Control		Treated	
	Initial	Latest	Initial	Latest
6/5 - 6/6	6	6	2	6
6/9 - 6/12	9	8	7	7
6/18 - 6/24	3	2	5	2
6/36 - 6/60	3	4	4	2
> 6/60	1	2	1	2

Table 5.

Hypophysectomy For Diabetic Retinopathy-Controlled Series

The data from the controlled series of Lundbaek, et al, are presented below. These data differ from those previously reported in that figures are given for diabetic eyes, rather than diabetic patients.

Condition	Changes in Hemorrhages, Microaneurysms, and Exudates	
	Control	Hypophysectomy
Progression	2	0
Regression	8	12
Unchanged	11	5
Very mild changes	2	3
Retina not seen	7	8
	30	28

Table 6.

The Effect of Hypophysectomy on New Vessel Formation

Condition	Control	Hypophysectomy
No change	4	11
Progression	5	2
Severe progression	18	10

Table 7.

The Effect of Hypophysectomy on Visual Acuity

The change in visual acuity in the Lundbaek series is listed below.

Condition	Control	Hypophysectomy
Improved	1	6
Unchanged	5	6
Worsened	15	10

Table 8.

Condition of Patients at Time of Evaluation

The following represent activity of the control and operated patients at latest evaluation 1-5 years after inclusion in the series. Full time means that the patient was carrying out gainful employment in his pre-treatment occupation.

Condition	Control	Hypophysectomy
Full time	10	9
Part time	2	3
Disabled	3	2
Dead	0	1

Table 9.

Prognosis for Vision in Diabetic Retinopathy

The following data are taken from Caird and Garrett. Controls were diabetics with no detectable retinopathy. Categories of vision based on visual acuity; Good, 6/6 to 6/18; impaired, 6/24 to 6/60; and "blind", > 6/60. *

Category	Group	Number	Percent deterioration of vision	
			per year	per 5 years
Good to Impaired	Control	290	2.4 ± 0.4	11.3 ± 1.8
	Retinopathy	189	7.5 ± 1.0	33.6 ± 3.0
Good to "blind"	Control	290	0.31± 0.1	1.6 ± 0.7
	Retinopathy	185	3.0 ± 0.6	14.5 ± 2.6
Impaired to "blind"	Control	19	1.3 ± 1.3	6.3 ± 6.1
	Retinopathy	39	13.1 ± 3.1	50.3 ± 8.8

* Glaucoma, cataract, macular degeneration, etc, excluded. Change due only to retinopathy.

REFERENCES

A. Diabetic retinopathy: nature, development, prognosis

1. Ashton, N. "Diabetic Retinopathy. A New Approach". Lancet 2:625, 1959.
2. Ashton, N. "Studies of the Retinal Capillaries in Relation to Diabetic and Other Retinopathies". Brit. J. Ophthal. 47:521, 1963.
3. Beetham, W. P. "Visual Prognosis of Proliferating Diabetic Retinopathy". Brit. J. Ophthal. 47:611, 1963.
4. Berkow, J. W., Shugarman, R. G., Maumence, A. E., and Patz, A. "A Retrospective Study of Blind Diabetic Patients". J.A.M.A. 193:867, 1965.
5. Bloodworth, J.M.B. "Diabetic Retinopathy". Diabetes 11:1, 1962.
6. Brown, I. K., and Jones, A. T. "Retinopathy and Diabetic Control". Brit. J. Ophthal. 48:148, 1964.
7. Caird, F. I., and Garrett, C. J. "Prognosis For Vision in Diabetic Retinopathy". Diabetes 12:389, 1963.
8. Chester, E. M., and Banker, B. Q. "The Role of Lipid Thrombi in the Pathogenesis of Diabetic Retinopathy". Arch. Int. Med. 120:397, 1967.
9. Coleman, S. L., Becker, B., Canaan, S., and Rosenbaum, L. "Fluorescent Insulin Staining of the Diabetic Eye". Diabetes 11:375, 1962.
10. Cogan, D. G., and Kuwabara, T. "Capillary Shunts in the Pathogenesis of Diabetic Retinopathy". Diabetes 12:293, 1963.
11. Cogan, D. G. "Diabetic Retinopathy". New Eng. J. Med. 270:787, 1964.
12. Davis, M. D. "Vitreous Contraction in Proliferative Diabetic Retinopathy". Arch. Ophthal. 74:741, 1965.
13. Dobree, J. H. "Proliferative Diabetic Retinopathy. Evolution of the Retinal Lesion". Brit. J. Ophthal. 48:637, 1964.
14. Dollery, C. T., and Oakley, N. W. "Reversal of Retinal Vascular Chance in Diabetes". Diabetes 14:121, 1965.
15. Gay, A. J., and Rosenbaum, A. L. "Retinal Artery Pressure in Assymetric Diabetic Retinopathy". Arch. Ophthal. 75:758, 1966.
16. Hausler, H. R., and Sibay, T. M. "Observations on the Microaneurysms of Diabetic Retinopathy". Diabetes 10:452, 1961.
17. Hill, D. W. "The Diabetic Eye". Postgrad. Med. J. 40:696, 1964.
18. Jain, I. S., Luthra, C. L., and Das, T. "Diabetic Retinopathy and Its Relation to Errors of Refraction". Arch. Ophthal. 77:1, 1967.
19. Kohner, E. M., Dollery, C. T., Patterson, J. W., and Oakley, N. W. "Arterial Fluorescein Studies in Diabetic Retinopathy". Diabetes 16:1, 1967.
20. Larsen, H-W. "Atlas of Diabetic Retinopathy. A Photographic Study". Acta Ophthal. Supp. 55:1, 1959.
21. Levene, R., Hortan, G., and Gorn, R. "Flat Mount Studies of Human Retinal Vessels". Amer. J. Ophthal. 61:283, 1966.
22. Oliveira, F. de "Pericytes in Diabetic Retinopathy". Brit. J. Ophthal. 50:134, 1966.
23. Root, H. F., Mirsky, S., and Ditzel, J. "Proliferative Retinopathy in Diabetes Mellitus. Review of 847 Cases". J.A.M.A. 169:903, 1959.
24. Safir, A., Poulsen, E. P., Klayman, J. and Gerstenfeld, J. "Ocular Abnormalities in Juvenile Diabetes". Arch. Ophthal. 76:557, 1966.

25. Scott, D. J., Dollery, C. T., Hill, D. W., Hodge, J. V., and Fraser, R. "Fluorescein Studies of Diabetic Retinopathy". Brit. M. J. 1:811, 1964.
26. Tolentino, F. I., Lee, P-F., and Schepens, C. L. "Biomicroscopic Study of Vitreous Cavity in Diabetic Retinopathy". Arch. Ophthal. 75:238, 1966.
27. Toussaint, D., and Dustin, P. "Electron Microscopy of Normal and Diabetic Retinal Capillaries". Arch. Ophthal. 70:96, 1963.
28. Wolter, J. R. "Diabetic Retinopathy". Amer. J. Ophthal. 51:1123, 1961.
29. Wolter, J. R. "The Nature of Capillary Microaneurysms in Diabetic Retinopathy". Diabetes 11:126, 1962.

B. The Role of Hypophysectomy in Diabetic Retinopathy

30. Ainslie, D., Logue V., and Nabarra, J.D.N. "Surgical Hypophysectomy For Diabetic Retinopathy". Diabetes 11:463, 1962.
31. Andersson, E., and Kjerulf, K. "Hypofysectomy ved suaer diabetes med udtaltretinopathie". Ugesk. f. Laeger 120:700, 1958.
32. Bradley, R. F., Rees, S. B., and Fager, C. A. "Pituitary Ablation in the Treatment of Diabetic Retinopathy". Med. Clin. N. Amer. 49:1105, 1965.
33. Bryan, J. B. "Hypophysectomy in Patients with Diabetic Oculovascular and Renal Sequelae:. Diabetes 11:472, 1962.
34. Contreras, J. S., Field, R. A., Hall, W. A., and Sweet, W. H. "Ophthalmological Observations in Hypophyseal Stalk Section". Arch. Ophthal. 67:428, 1962.
35. Cullen, J. F., Harris, P., Munro, J. F., and Duncan, L.J.P. "Pituitary Stalk Section For Advancing Diabetic Retinopathy". Brit. J. Ophthal. 49:393, 1965.
36. Cullen, J. F., Harris, P., Turner, J. W., Donaldson, H. A., Munro, J. F., and Duncan, L.J.P. "Pituitary Ablation by Yttrium 90". Brit. J. Ophthal. 49:405, 1965.
37. Fager, C. A., Rees, S. B., and Bradley, R. F. "Surgical Ablation of the Pituitary in the Treatment of Diabetic Retinopathy". J. Neurosurg. 29:727, 1966.
38. Field, R. A., Schepens, C. L., Sweet, W. H., and Appels, A. "The Effect of Hypophyseal Stalk Section on Advancing Diabetic Retinopathy". Diabetes 11:465, 1962.
39. Field, R. A. "Hypophysectomy in Diabetic Retinopathy". Diabetes Mellitus: Diagnosis and Treatment Vol. II. G. J. Hamwi and T. S. Danowski, Editors. Amer. Diab. Assn. New York, 1967.
40. Flohr, L. J., and H. W. Maxwell. "Pituitary Stalk Section in Treating Advanced Diabetic Retinopathy". Tex. State J. Med. 59:1091, 1963.
41. Gordon, E. S., and Javid, M. "Metabolic Studies in Hypophysectomy For Diabetic Vascular Disease". Diabetes 11:470, 1960.
42. Harrold, B. P., Gough, K. R., Tulloh, C. G., Cates, J. E., and James, J. A. "Use of Trans-sphenoidal Hypophysectomy in Diabetic Retinopathy: Preliminary Assessment". Brit. M. J. 2:727, 1965.
43. Hernberg, C. A., Björkesten, G. Af, and Vannas, S. "Hypophysectomy in the Treatment of Retinopathy and Nephropathy in Severe Juvenile Diabetes". Acta Endocrinol. 31:241, 1959.
44. Javid, M., Gordon, E. S., and Erickson, T. C. "Hypophysectomy in Severe Diabetes". J. Neurosurg. 15:504, 1958.
45. Joplin, G. F., Fraser, R., Hill, D. W., Oakley, N. W., Scott, D. J., and Doyle, F. H. "Pituitary Ablation For Diabetic Retinopathy". Quart. J. Med. 34:443, 1965.
46. Joplin, G. F., Oakley, N. W., Hill, D. W., Kohner, E. M., and Fraser, T. R. "Diabetic Retinopathy. II. Comparison of Disease Remission Induced by Various Degrees of Pituitary Ablation by Y^{90} ". Diabetologia 3:406, 1967.

47. Kinsell, L. W. "Hypophysectomy in Unstable Diabetes with Progressive Retinal and Renal Vascular Disease". Bull. N. Y. Acad. Med. 33:171, 1957.
48. Kinsell, L. W. "Hypophysectomy in Patients with Diabetic Vascular Disease". Diabetes 11:473, 1962.
49. Lawrence, J. H., Tobias, C. A., Linfoot, J. A., Born, J. L., Gottschalk, A., and Kling, R. P. "Heavy Particles, the Bragg Curve and Suppression of Pituitary Function in Diabetic Retinopathy". Diabetes 12:490, 1963.
50. Lawrence, J. H., Tobias, C. A., Born, J. L., Gottschalk, A., Linfoot, J. A., and Kling, R. P. "Alpha Particle and Proton Beams in Therapy". J.A.M.A. 186:236, 1963.
51. Lee, P-F., and Field, R. A. "Hypophyseal Stalk Section and Intraocular Pressure". Amer. J. Ophthal. 62:11, 1966.
52. Luft, R., Olivecrona, H., Ikkos, D., Kornerup, T., and Ljunggren, H. "Hypophysectomy in Man. Further Experiences in Severe Diabetes Mellitus". Brit. M.J. 2:752, 1955.
53. Luft, R. "The Use of Hypophysectomy in Juvenile Diabetes Mellitus with Vascular Complications". Diabetes 11:461, 1962.
54. Lundbaek, K., Malmros, R., Andersen, H. C., Ohrt, V., and Jensen, V. A. "Hypophysectomy For Diabetic Angiopathy". Diabetes 11:474, 1962.
55. Lundbaek, K., Malmros, R., Andersen, H. C., Rasmussen, J. H., Bruntse, E., Madsen, P. H., and Jensen, V. A. "Hypophysectomy For Diabetic Angiopathy. A Controlled Clinical Trial". Excerpta Medica, in press.
56. Pearson, O. H., Greenberg, E., Pazianos, A., Dominguez, J. H., and Ray, B. S. "Hypophysectomy in Diabetic Patients with Progressive Retinopathy". Diabetes 11:469, 1962.
57. Pearson, O. H., Ray, B. S., McLean, J. M., Peretz, W. L., Greenberg, E., and Pazianos, A. "Hypophysectomy for the Treatment of Diabetic Retinopathy". J.A.M.A. 188:116, 1964.
58. Poulsen, J. E. "Diabetes and Anterior Pituitary Insufficiency". Diabetes 15:73, 1966.
59. Ray, B. S. Cited by Bradley, et al (32).
60. Recant, L., and Hartroft, W. S. "Surgical Hypophysectomy For Diabetic Retinopathy". Amer. J. Med. 22:949, 1957.
61. Scott, J. K. "Trans-sphenoidal Hypophysectomy For Diabetic Retinopathy". Arch. Otolaryngol 84:77, 1966.
62. Sjögren, B. "Effect of Hypophysectomy on Diabetic Retinopathy". Diabetes 11:479, 1962.
63. Sprague, R. G. "Comments on Reports of the Effect of Hypophysectomy, of Hypophyseal Stalk Section, and of Adrenalectomy on Diabetic Retinopathy". Diabetes 11:491, 1962.
64. Tassman, W. "Treatment of Diabetic Retinopathy and Oculopathy". Mod. Treat. 4:62, 1967.