AGE, CATARACT AND HYPERGLYCAEMIA*

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Since 1962, I have asked for a modified glucose-tolerance test to be done on all private patients who have had any sign of cataract. The results of 200 consecutive White private patients are recorded in Tables I, II and III. All patients have denied knowledge of glycosuria or diabetes. Known diabetics are not included in the survey.

The stage of cataract has varied from the earliest signs of suture infiltration, fluid vacuoles, dot and cuneiform opacities and enough nuclear sclerosis with amber colouration to reduce the visual acuity or to alter the refraction significantly. At the other end of the scale, are the mature cataracts and in some cases one or both lenses had been removed. Being private patients, the majority were in the higher income group.

The blood sugars were determined by the Folin and Wu method in 71 and by King's method in 129 patients. The blood was collected by the finger prick technique (capillary blood). Fasting blood sugars are about 5 mg./100 ml. higher in the finger prick than those for venous blood. After ingestion of 100 G of glucose, the difference may increase to as much as 30 mg./100 ml. Values by the Folin and Wu method are about 20 mg./100 ml. higher than those by King's method (true glucose).

I have avoided the word *diabetes* as I have found it difficult to define in terms of the exact borderline levels of blood sugar and glucose tolerance. The results are reported as numbers of patients with blood sugar in mg./100 ml. above or below the increasing figures for specimens taken after fasting overnight and 1 and 2 hours after taking 100 G of glucose by mouth after the fasting blood sugar has been collected. I also avoid the term diabetes in talking to patients both because of the varied pictures the term evokes in their minds and the occasional irritation caused to their general practitioner by the suggestion of diabetes when he has found the patient's urine to be sugar-free. While it is the level of the blood sugar that is the subject for discussion, it is appreciated that this is only one aspect of biochemical and organic change. It is but one manifestation of variations in insulin supply, availability, or effectivity; metabolic efficiency of the body generally and of the liver particularly; and is influenced by various endocrine, vascular and circulatory factors. The result of blood-sugar tests on the same patient may vary greatly on different days and may be upset by emotional stress and intercurrent illness, particularly infections. The selection of fasting blood sugar, and the 1- and 2-hour specimens was made to indicate the lowest level of the blood sugar, how high it might go after the 100 G load and how well the rise is controlled after 2 hours. For reasons to be discussed, I wished to have an indication of how much the blood-sugar levels might fluctuate under the extreme conditions of the test.

With cataract the common factor in these tables, a relationship between increase in age and increasing percentage of raised blood-sugar levels is clear, particularly in the lower grades of hyperglycaemia. An abnormal glucose tolerance should be suspected in patients with cataract who are less than 60 years old, but might normally be expected in those over 70.

In 9 cases the 1-hour blood sugar varied between 180 mg./100 ml. (Folin and Wu) and 160 mg./100 ml. up to 296 mg./100 ml. (King) while the fasting blood sugars were below 120 mg./100 ml. (Folin and Wu) or 100 mg./100 ml. (King) and the 2-hour blood sugars were below 140 mg./100 ml. (Folin and Wu) and 120 mg./100 ml. (King). These would have passed as normal on the fasting and 2-hour blood sugars alone.

In 3 cases the fasting blood sugar was above normal while the 1- and 2-hour specimens were within normal limits (Table IV).

A raised renal threshold was indicated in about 8% of the 200 patients who had blood sugars of 183 - 262 mg./100 ml. at some stage of the test without any reducing substance being detected in the urine. In only 1 patient, a man of 53 whose fasting blood sugar was 290 mg./100 ml., was there any sugar in the first urine taken simultaneouly with the fasting blood sugar. A low renal threshold was suggested in about 17% of cases where the blood sugar was not recorded as being over 180 mg./100 ml. However, peaks above the normal threshold between the recorded hourly blood-sugar levels cannot be excluded. These results suggest that the urine tests should be treated with reserve. However, where a glucose-tolerance test has indicated a suitable relationship between glycosuria and hyperglycaemia, a urine chart may be of great value in estimating the effectivity of control.

The tables indicate an increasing proportion of abnormal levels when comparing fasting, 1-hour and 2-hour blood sugars so that fasting blood sugars do not indicate an abnormal glucose tolerance except in about a quarter of the cases suggested by the 2-hour blood sugar. The normal range of fasting blood sugar is 80 - 120 mg./100 ml. by the Folin and Wu method and 50 - 100 mg./100 ml. by King's method. I have regarded the upper levels of normal for the 1-hour blood sugar as 180 mg./100 ml. (Folin and Wu) and 160 mg./100 ml. (King) and for the 2-hour specimen as 140 mg./100 ml. and 120 mg./100 ml. for Folin and Wu and King's methods respectively. A diagnosis of diabetes might be made at these levels or at higher levels as desired, but my own concern has been with actual levels of the blood sugar as possibly affecting cataract surgery or cataract development while leaving the consideration of systemic disease to the patient's physician.

DISCUSSION

The investigations have been motivated with two aims in view. Firstly with the hope that control of any hyperglycaemia might retard, arrest or reverse the advance of the cataract. Secondly to determine the state of the blood sugar with regard to possible cataract surgery.

The latter will be discussed first. In 1962, I removed the lens of a private patient 46 years of age. The urine had

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been sugar-free, the fasting blood sugar had been 95 mg./100 ml. by the Folin and Wu method (normal range being 80 - 100 mg./100 ml.) 3 months before the operation. A week after the operation he had uveitis with hypopyon which did not improve on antibiotic treatment. On the 10th day rubeosis iridis was seen and the Benedict's test for urinary sugar was green. The fasting blood sugar 20 minutes after 10 units of soluble insulin had been given in error was 147 mg./100 ml. (venous blood—Folin and Wu) on the eleventh day. The hypopyon cleared and the iris vessels decreased dramatically 24 hours after sub-conjunctival Depo-Medrol 0·5 ml. (40 units/ml.), as might happen in a non-infective uveitis such as the diabetic type. It transpired that the patient had suffered the loss of 2 close relatives in the past month and his father had died in the same ward on the same day some years previously. His emotional stress was severe and I blamed this for the change in his blood-sugar control. In the weeks following, similar postoperative complications were observed in Asiatic and Bantu patients in King Edward VIII Hospital, where urines had been sugar-free, but the blood sugars that were determined because of postoperative complications of the diabetic type, were found to be well above normal. I concluded that normal fasting blood sugar results and negative urine tests for sugar were not reliable in excluding the possibility of diabetic postoperative upsets. I have since found significantly raised blood sugars, especially in the 1- and 2-hour specimens in patients whose lens extractions done months or years before had been attended by prolonged and severe uveitis, hyphaemia, scarring and glaucoma and whose urines had been sugar-free at the time of the operation.

It is likely that these postoperative complications are related to vascular changes such as thickening of capillary basement membranes, occlusion of the lumen of smaller blood-vessels and unhealthy neovascularization with atrophy and fibrosis of delicate anterior chamber tissues such as ciliary epithelium iris and trabeculae rather than simply to lack of insulin. It seems unlikely that structural changes in the vessels and connective tissue would benefit materially from the control of hyperglycaemia by insulin for a day or two before surgery. At the suggestion of Dr. John McKechnie, patients with abnormal glucose tolerance were treated by low-carbohydrate diet, and if necessary, oral antidiabetic tablets for some weeks before surgery. It was hoped that prolonged control of the carbohydrate metabolism before surgery would reduce the postoperative complications. In our limited experience there was an appreciable reduction in postoperative complications, attributable to diabetes.

The modified glucose-tolerance test on first diagnosis of the cataract usually gave warning of possible diabetic complications in good time for any benefit that prolonged reduction of intermittent hyperglycaemia might provide.

The other reason for requesting this modified glucose-tolerance test on all cataract patients was the hope that by finding and controlling intermittent hyperglycaemia, the development of the lens opacities might be retarded so that surgery might be either delayed or avoided. This investigation in a way is a revolt against the need to give a hopeless prognosis with the unpleasant diagnosis of cataract. I wished to explore any avenue which might mitigate against inevitable reduction of vision, and surgery, not without hazard, in the patient's declining years.

The only factor of practical importance that can be controlled and might retard the advance of the cataract is hyperglycaemia. Other factors such as parathyroidism, uveitis, intraocular haemorrhage, congenital influence, radiation and trauma are not discussed here.

It is well authenticated that lens opacities are common in the young insulin-insufficient diabetic and may clear with efficient control of the hyperglycaemia. Senile cataract is said to be commoner and to occur earlier in the diabetic. Experimental work so extensively reviewed by Van Heyningen and Pirie[1] had shown a clear causal relationship between hyperglycaemia and cataract. They have shown that in rats, a blood-glucose level of 225 mg./100 ml. or more induces cataract. The onset of the cataract is earlier the younger the animals and the higher the blood-glucose level is raised above 225 mg./100 ml. Cataract was prevented by reducing the blood sugar either by a protein and fat diet or by insulin. The biochemical reactions contributing to cataract formation and particularly the role of sorbitol have been discussed comprehensively by Van Selm[2] in his address on 'Incipient cataract and the glucose-tolerance curve'. I shall restrict my discussion to the physical changes in osmotic pressure rather than to chemical factors.

The clinician so often finds an elderly subject with the frailties of his years in whose ageing eyes are senile lenses whose metabolism is wearily and with decreasing efficiency attempting to maintain the clarity which is essential to good vision. Where there are opacities in the lens, there are areas of debilitated or dead lens fibres. Where there are vacuoles in the lens substance or under the lens capsule, the evidence is of failure of the lens epithelium, capsule and lens fibres, to maintain that state of relative dehydration which is essential for the clarity of the lens (and incidentally of the cornea). In experimental cataracts, reduction in soluble lens protein (α crystalin) and gluthathione indicating loss of metabolites and reduction of metabolically active tissue, regularly precede the appearance of the opacity. While senile cataract is not completely comparable with experimental cataract, the point that a cataractous lens is a sick and devitalized organ has substance.

The glucose concentration in the aqueous is proportional to the plasma and that of the lens varies as these vary (Table V). A rise of 120 mg./100 ml. in the plasma leads to a rise of about 100 mg./100 ml. in the aqueous. The resulting change in the osmotic pressure is 95 mm.Hg.[4] Compared with the +5,000 mm.Hg osmotic pressure of plasma this is small proportionately, but as a pressure difference compared with the intraocular pressure of up to 20 mm.Hg and the capillary pressure of 15 - 45 mm.Hg it is considerable. Such a rise in glucose concentration occurring over an hour as in the 100 G glucose-tolerance test, or after a carbohydrate breakfast on a fasting stomach, must alter the osmotic pressure balance between blood/aqueous and aqueous/lens capsule and lens tissue spaces/lens fibre barriers. Resulting water and glucose exchanges and adjustments in the constituents of the dialysate are made to maintain equilibrium. In my opinion the

ability of the ageing lens and ciliary body to make these adjustments should be questioned and the desirability of relieving them of this metabolic burden seems apparent. While a healthy lens can maintain its clarity in the presence of very high and widely-fluctuating glucose levels, the ability of an already cataractous lens to do so is questionable. The 1-hour blood sugar was included to give an indication of the type of fluctuation which might be expected in a high-carbohydrate diet. A diet low in carbohydrates must reduce the general level of the blood glucose and more especially should reduce the fluctuations in its levels before and after meals. It is my practice to request the general practitioner to advise the patient on such a diet, assuming of course that he knows of no systemic contraindication. It is left to his discretion to decide whether oral antidiabetics are required. Where the glucose tolerance is normal, the patient is advised to reduce carbohydrates in the absence of any other measure which might be helpful. Visual acuity has improved in some cases with low blood-sugar levels, but in some cases with sugar in the urine there might have been peaks in the blood sugar not shown by the hourly blood-sugar estimations. Sometimes reduced glucose tolerance has been shown by tests done at a later stage.

An authority on diabetes, when he visited us in Durban, told of the high incidence of cataract among the Turks who are great eaters (Turkish delight) and the rarity of cataract in Germany during the severe dietary restrictions during the war. He suggested that a factor causing cataracts was plain overeating, which is another argument for a reduced carbohydrate diet.

Whether impaired blood supply to the ciliary body, the toxic effect of sorbitol, plain overeating or all or any of these is the mechanism for producing or aggravating cataract, reduction in the metabolic work demanded of the ailing cataractous lens from violent osmotic pressure changes seems reasonable. Whether this helps to prevent cataract must largely be a matter of conjecture until time and numbers supply adequate statistical tests. In my opinion, obviously, the concept is worth practising. The rationale is implicit in the review of Van Heyningen and Pirie[1] and is stated by Caird, Hutchinson and Pirie[6] as: 'That control of the blood-sugar level should have particular relevance for maintenance of clarity of the lens is reasonable for a consideration of its peculiar metabolism. There exists at least the theoretical possibility of prevention, or delay in maturation of cataract in some patients, by early control and diagnosis of the diabetes'.

In the last 2 years most private cataract operations I have undertaken have been on patients who presented with advanced opacities. Lens opacities have advanced to require surgery in only 3 patients this year. One had a normal result in the modified glucose-tolerance test as described and one had a 2-hour level of 153 mg./100 ml. (Folin and Wu). The last patient's visual acuity had decreased from 6/12 partly to 6/24 partly in 4 years, but this was, at least in part, due to some macular degeneration. Her blood sugars were 110, 208, 187 mg./100 ml. for fasting and 1- and 2-hour specimens at the age of 85 years.

Since adopting this practice of routine blood-sugar tests and reduced carbohydrate diets as described, my private cataract surgery has decreased significantly. Observation of many patients whose visual acuity has improved 1, 2 or even 3 lines on the Snellen chart and whose improvement is still maintained after as long as 3 years with continued control of hyperglycaemia, encourages the hope that this paucity of private cataract surgery is at least partly due to validity of this theory in practice, even if the rationale is not completely understood.

I have found great encouragement from the paper 'Incipient cataract and the glucose-tolerance curve' by Dr. van Selm of Cape Town particularly as neither he nor I knew that the other held similar views before presentation of the papers. When 3 cases whose fasting blood sugars alone were above normal and 9 cases whose 1-hour specimens alone showed values above normal are added to the 115 whose 2-hour blood sugars were above the 140 mg./100 ml. (Folin and Wu) or 120 mg./100 ml. (King), the total of those showing minimal abnormality is increased to 127 out of 200 or 63·5%. This figure is very close to Van Selm's 122 out of 183 or 66·7% with an abnormal 50 G conventional glucose-tolerance curve.

SUMMARY

The results of the modified glucose-tolerance test of fasting blood sugar followed by 100 G of glucose then further blood sugars after 1 and 2 hours collected by fingerprick, and associated urine tests for glucose and acetone on private patients are reported. The inadequacy of urine and fasting blood sugar tests in excluding hyperglycaemia is indicated. Control of intermittent hyperglycaemia as a beneficial influence for cataract patients is suggested and discussed.

TABLE I. FASTING BLOOD SUGARS IN 'NON-DIABETIC' CASES OF CATARACT. BLOOD SUGARS DETERMINED BY THE METHODS OF A. (FOLIN AND WU) AND B. (KING) IN MG./100 ML.

Age	*A(1) Under 120*	*A(2) 121 or more*	*B(1) Under 100*	*(B2) 101 or more*	*A(1)+B(1)*	*A(2)+B(2)*	*% A(2)+B(2)*
39–49	6	0	9	1	15	1	6·2
50–59	12	2	17	3	29	5	14·8
60–69	20	4	37	4	57	8	12·3
70–79	17	5	38	7	55	12	17·9
80–	5	0	7	6	12	6	33·3
Total	60	11	108	21	168	32	16·0
	Under 140	*141 or more*	*Under 120*	*121 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	19	1	32	2	5·9
60–69	22	2	40	1	62	3	4·6
70–79	21	1	45	0	66	1	1·5
80–	5	0	11	2	16	2	11·1
Total	67	4	124	5	191	9	4·5
	Under 160	*161 or more*	*Under 140*	*141 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	19	1	32	2	5·9
60–69	23	1	40	1	63	2	3·1
70–79	21	1	45	0	66	1	1·5
80–	5	0	11	2	16	2	11·1
Total	68	3	124	5	192	8	4·0
	Under 180	*181 or more*	*Under 160*	*161 or more*			
39–49	6	0	10	0	16	0	0
50–59	13	1	20	0	33	1	2·9
60–69	24	0	40	1	64	1	1·5
70–79	22	0	45	0	67	0	0
80–	5	0	13	0	18	0	0
Total	70	1	128	1	198	2	1·0

TABLE II. BLOOD SUGARS OF CATARACT PATIENTS 1 HOUR AFTER 100 G GLUCOSE BY MOUTH DETERMINED BY METHOD OF A. (FOLIN AND WU) AND B. (KING) IN MG./100 ML.

Age	A(1) Up to 180	A(2) 181 or more	B(1) Up to 160	B(2) 161 or more	A(1) + B(1)	A(2) + B(2)	% A(2) + B(2)
39–49	3	0	8	3	11	3	21·4
50–59	7	2	15	5	22	7	24·1
60–69	10	9	25	17	35	26	42·6
70–79	7	13	21	20	28	33	54·1
80–	2	3	5	8	7	11	61·1
Total	29	27	74	53	103	80	43·7
	Up to 200	*201 or more*	*Up to 180*	*181 or more*			
39–49	3	0	10	1	13	1	7·1
50–59	7	2	17	3	24	5	17·1
60–69	17	2	31	11	48	13	21·3
70–79	12	8	30	11	42	19	31·1
80–	3	2	6	7	9	9	50·0
Total	42	14	94	33	136	47	25·7
	Up to 220	*221 or more*	*Up to 200*	*201 or more*			
39–49	3	0	10	1	13	1	7·1
50–59	8	1	17	3	25	4	13·8
60–69	18	1	38	4	56	5	8·2
70–79	14	6	37	4	51	10	16·4
80–	5	0	7	6	12	6	33·3
Total	48	8	109	18	157	26	14·3
	Up to 240	*241 or more*	*Up to 220*	*221 or more*			
39–49	3	0	10	1	13	1	7·1
50–59	8	1	18	2	26	3	10·3
60–69	19	0	41	1	60	1	1·6
70–79	16	4	39	2	55	6	9·8
80–	5	0	11	2	16	2	11·1
Total	51	5	119	8	170	13	7·1
	Up to 260	*261 or more*	*Up to 240*	*241 or more*			
39–49	3	0	10	1	13	1	7·1
50–59	8	1(328)	18	2(296) (249)	26	3	10·3
60–69	19	0	42	0	61	0	0
70–79	17	3(329) (312) (270)	39	2(272) (266)	56	5	8·2
80–	5	0	12	1(300)	17	1	5·6
Total	52	4	121	6	173	10	5·5

TABLE III. BLOOD SUGARS OF CATARACT PATIENTS 2 HOURS AFTER 100 G GLUCOSE BY MOUTH DETERMINED BY METHODS OF A. (FOLIN AND WU) AND B. (KING)

Age	A(1) Up to 140	A(2) 141 or more	B(1) Up to 120	B(2) 121 or more	A(1) + B(1)	A(2) + B(2)	% A(2) + B(2)
39–49	5	1	6	4	11	5	31·2
50–59	7	7	12	8	19	15	44·1
60–69	10	14	19	22	29	36	55·4
70–79	5	17	16	29	21	46	68·7
80–	1	4	4	9	5	13	72·2
Total	28	43	57	72	85	115	57·5
	Up to 160	*161 or more*	*Up to 140*	*141 or more*			
39–49	5	1	8	2	13	3	18·7
50–59	12	2	17	3	29	5	14·8
60–69	18	6	26	15	44	21	32·3
70–79	8	14	26	19	34	33	49·3
80–	4	1	4	9	8	10	55·6
Total	47	24	81	48	128	72	36·0
	Up to 180	*181 or more*	*Up to 160*	*161 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	12	2	19	7	31	3	8·8
60–69	22	2	28	13	50	15	23·1
70–79	14	8	30	15	44	23	34·3
80–	5	0	7	6	12	6	33·3
Total	59	12	93	36	152	48	24·0
	Up to 200	*201 or more*	*Up to 180*	*181 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	19	1	32	2	5·9
60–69	22	2	33	8	55	10	15·4
70–79	16	6	38	7	54	13	19·4
80–	5	0	8	5	13	5	27·8
Total	62	9	107	25	169	31	16·5

(*Continued in next column*)

	Up to 220	*221 or more*	*Up to 200*	*201 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	20	0	33	1	2·9
60–69	22	2	37	4	59	6	9·2
70–79	17	5	42	3	59	8	11·9
80–	5	0	10	3	15	3	16·7
Total	63	8	118	11	181	19	9·5
	Up to 240	*241 or more*	*Up to 220*	*221 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	20	0	33	1	2·9
60–69	22	2	40	1	62	3	4·6
70–79	19	3	43	2	62	5	7·5
80–	5	0	11	2	16	2	11·1
Total	65	6	123	6	188	12	6·0
	Up to 260	*261 or more*	*Up to 240*	*241 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	20	0	33	1	2·9
60–69	22	2	40	1	62	3	4·6
70–79	19	3	45	0	64	3	4·5
80–	5	0	12	1	17	1	5·6
Total	65	6	126	3	191	9	4·5
	Up to 280	*281 or more*	*Up to 260*	*261 or more*			
39–49	6	0	9	1	15	1	6·2
50–59	13	1	20	0	33	1	2·9
60–69	22	2	41	0	63	2	3·1
70–79	20	2	45	0	65	2	3·0
80–	5	0	12	1	17	1	5·6
Total	66	5	127	2	193	7	3·5
	Up to 300	*301 or more*	*Up to 280*	*281 or more*			
39–49	6	0	10	0	16	0	0
50–59	13	1(400)	20	0	33	1	2·9
60–69	23	1(304)	41	0	64	1	1·5
70–79	20	2(310) (322)	45	0	65	2	3·0
80–	5	0	12	1(320)	17	1	5·6
Total	67	4	128	1	195	5	2·5

TABLE IV. RESULTS IN 9 CASES WHERE THE BLOOD SUGAR WAS ABOVE 180 MG./100 ML. (FOLIN AND WU) OR 160 MG./100 ML. (KING) 1 HOUR AFTER 100 G OF GLUCOSE AND WHERE THE FASTING BLOOD SUGAR AND THE BLOOD SUGAR 2 HOURS AFTER 100 G OF GLUCOSE WERE NORMAL

Age		*Fasting blood sugar*	1 *hour*	2 *hours mg./100 ml.*
63	F & W	103	212	109
65	F & W	105	200	126
68	F & W	89	226	99
54	King	70	296	67
60	King	70	173	80
64	King	76	185	113
69	King	86	170	70
72	King	98	161	90
73	King	65	171	110

TABLE V.[3] GLUCOSE CONTENT OF LENS AND AQUEOUS HUMOUR OF RABBITS WITH NORMAL, HIGH AND LOW BLOOD SUGARS (FROM WEEKERS, AVERAGE VALUES)

	Plasma (citrated)	*Aqueous humour*	*Lens*
Normal	124	102	67
Hyperglycaemic	236	186	77
Hypoglycaemic	69	59	41

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