THYROID THERAPY IN DIABETIC RETINOPATHY

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In a previous publication a classification of diabetic retinopathy was presented. Stage 1 consisted of microorganisms, tortuosity of the finer venules and changes in the larger veins such as phlebosclerosis, coils or knots along their course, and distension.

Stage 2 was a cyclical stage characterized by the appearance and disappearance of dot and blot haemorrhages and exudates. This stage could be subdivided into 3 types: haemorrhagic, exudative and mixed. Occasionally the retinopathy remained stationary or even regressed over a period of time.

Stage 3 manifested itself by the occurrence of neovascularization which in turn led to vitreous haemorrhage, retinitis proliferans and detachment of the retina.

The spontaneous cyclical changes noted in stage 2 have resulted in difficulty in assessing the effect of medical therapy in diabetic retinopathy. This was noted in the course of trials using low-fat diet and nor-androstenalone phenyl propionate. It was decided, therefore, that in any future trials the minimum period of observation should be 2 years and that improvement in the retinopathy should be maintained for at least that period of time. As a result of chance observation of improvement in retinopathy in a patient receiving thyroid gland therapy it was decided to embark on a trial of this form of treatment.

MATERIAL AND METHOD

Nineteen maturity-onset diabetic patients attending the Diabetic Clinic of Johannesburg Hospital were subjected to thyroid gland treatment with Proloid (Warner), a thyroglobulin preparation. Sixteen presented with stage 2 mixed type retinopathy, one with stage 1, one with stage 2 exudative and one with stage 3. The dosage of Proloid varied from gr. ½ to gr. 1 thrice daily, continued for at least 2 years in those who responded to treatment. Treatment of diabetes continued as before, no attempt being made to improve diabetic control.

Fundal photographs were taken before commencement and at varying periods during the course of therapy. Improvement was gauged by an over-all decrease in the number of haemorrhages and exudates maintained for a period of at least 2 years.

RESULTS

Twelve patients showed definite improvement, while 7 cases were considered to be failures. Of the latter, 4 were outright failures, one was still showing cyclical changes after 5 years of therapy, one remained static after 3½ years of therapy, and one patient showed improvement for a period of 2 years but then disappeared for a year, during which time therapy was discontinued entirely. On her return to the clinic the retinopathy had deteriorated markedly.

The 4 outright failures were constituted as follows: One patient exhibited a Kimmelstiel-Wilson syndrome with worsening of the retinopathy during the 2-year period of observation. A second complained of pain in the eyes and refused treatment after 3 months. The remaining 2 progressed from stage 1 to stage 2 and from stage 2 to stage 3 over periods of 20 and 6 months, respectively.

A detailed analysis of the cases is given in Table I and a summarized version in Table II. Figs. 1 - 10 demonstrate some of the changes noted.

DISCUSSION

Twelve of 19 cases of diabetic retinopathy have shown improvement while on thyroid gland therapy for periods exceeding 2 years. Both haemorrhages and exudates decreased in size and number, the improvement being maintained for the whole period of treatment. One case has even shown total disappearance of the lesions while on treatment for over 6 years.

Beetham has reported 10% spontaneous arrest of diabetic retinopathy, and Patz found it to be 25%, but in the present series 63% of the cases have shown improvement. It is therefore suggested that therapy played a part in the improvement found in the present series.

Marked improvement in exudates has been noted by several authors when patients have been treated on a low-fat diet, not in serum lipids, particularly cholesterol and triglycerides, during the period of treatment.

In 5 of 8 of our improved cases serum cholesterol studies showed no such reduction; in fact the figures rose (260 - 306; 210 - 247; 252 - 276; 250 - 326; 234 - 276 mg./100 ml.). Reduction was noted in the other 3 (240 - 200; 306 - 282; 311 - 216 mg./100 ml.). The improvement in retinopathy could not be related to cholesterol levels. Nor was any correlation found with serum triglycerides which also revealed a rise in 4 of 5 improved cases (135 - 206; 249 - 625; 192 - 440; 82 - 148 mg./100 ml.), with a fall from 116 to 91 mg./100 ml. in the fifth. Similarly, no correlation could be found between improvement noted

Figs. 1 - 3. Case 8 (left eye): disappearance of exudates—stage 2 exudative retinopathy. Fig. 1: Before treatment. Fig. 2: After 3 months' treatment. Fig. 3: After 4 years' treatment.
Figs. 4 - 6. Case 1 (right eye): disappearance of exudates—stage 2 mixed retinopathy. Fig. 4: Before treatment. Fig. 5: After 5 months' treatment. Fig. 6: After 2 years' treatment.
Figs. 7 - 8. Case 3 (left eye): disappearance of haemorrhages and exudates—stage 2 mixed retinopathy. Fig. 7: Before treatment. Fig. 8: After 2½ years' treatment.
Figs. 9 - 10. Case 2 (left eye): disappearance of haemorrhages and exudates—stage 2 mixed retinopathy. Fig. 9: Before treatment. Fig. 10: After 10 months' treatment.
Fig. 11. Marked retinopathy without glaucoma in the right eye.
Fig. 12. Same patient as Fig. 11, showing no retinopathy but marked glaucoma cupping in the left eye.

*Date received: 17 December 1968.
and control and treatment of diabetes which remained the same as before therapy was commenced. Control was good in 3, fair in 5 and poor in 4 cases, and treatment varied, one patient being on diet only, 4 on insulin and 7 on oral antidiabetic drugs. This lack of correlation with the type of treatment is of particular importance in that hypothyroidism has been related to sulphonylurea therapy.

All cases treated were in stage 2 retinopathy, with the exception of one case in stage 1 and one in which one eye was in stage 3. This last patient failed to improve, and it was thought wiser to confine the investigation mainly to stage 2 cases.

In one case the patient complained of eye pain while on therapy. There was no change in the condition of the eyes but treatment was withdrawn and the pain disappeared. Apart from this no side-effects were noted; nor did any precordial discomfort or cardiac symptoms present in spite of the often associated arteriosclerosis and hypertension.

Mooney\(^1\) has stated that the association of diabetic retinopathy with glaucoma is rare, and he has mentioned a case with retinopathy in the eye with normal pressure and no retinopathy in the glaucomatous eye. He suggests the possibility that increased intra-ocular pressure, by compressing the capillaries and venules, retards the development of retinopathy. Figs. 11 and 12 demonstrate a similar case found at our clinic. Conversely it is well known that hypotony is usual in diabetic coma, and this condition has lately been recorded in diabetic retinopathy.\(^1\)

It has been our experience that fluctuations in intra-ocular pressure, far greater than normal, are a feature of diabetic retinopathy. Furthermore, while venous pulsation is found in 70 - 80% of normal eyes,\(^1\) its occurrence is far less frequent in diabetic retinopathy. In addition the more extensive retinopathy has been noted in the eye with lesser or absent pulsation. While these observations are preliminary and will require further study, the theory is suggested that diabetic retinopathy is related to marked fluctuations in intra-ocular pressure over a prolonged period of time, thus accounting for the usual time-lag between the commencement of the diabetic state and the appearance of retinopathy. Whether thyroid gland extract stabilizes intra-ocular pressure to the extent that the fluctuations are lessened and hypotony is prevented is a problem which presents itself for future study.

**SUMMARY**

A classification of diabetic retinopathy is presented. Difficulties are described in the assessment of therapy owing to natural cyclical variations of retinopathy.
A series of 19 cases of retinopathy in a maturity-onset diabetic group of patients were treated with thyroid gland extract for periods ranging up to 6 years. Twelve cases showed a decrease in both size and numbers of haemorrhages and exudates, the improvement being maintained for at least 2 years. This compares well with figures of 10% and 25% reported for spontaneous arrest of diabetic retinopathy. Diabetic control, type of diabetic therapy and alterations in serum cholesterol or triglycerides were not involved in the improvement.

A tentative theory for the action of thyroid gland extract is presented.

We wish to thank our colleagues Drs S. Lopis, I. Cohen, I. Yudaken and B. Gollach for their ready cooperation; Drs T. Pienaar and G. G. du Plessis and Mr G. Ho for fundal photography; and Sister D. Maxwell for her invaluable assistance. The publication of the fundal photographic reproductions was sponsored by Warner Pharmaceuticals.

REFERENCES
   Chicago: Year Book Medical Publishers.

PASSING EVENTS : IN DIE VERBYGAAN

South African Institute for Medical Research, Johannesburg. Staff Scientific Meetings. The next meeting will be held on Monday 14 April at 5.10 p.m. in the Auditorium, North Block, SAIMR. Mr G. A. Gilman, of the Research Unit of the National Cancer Association of South Africa at the Institute, will speak on 'Food storage and harvesting methods as used by the Bantu in South Africa'. All interested persons will be welcome.

University of Cape Town and Association of Surgeons of South Africa (M.A.S.A.), Joint Lectures. The next meeting will be held on Wednesday 9 April at 5.30 p.m. in the E-floor Lecture Theatre, Groote Schuur Hospital, Observatory, Cape. Prof. J. E. Kerch will speak on 'Hazards of misinterpreting chemical pathology results'.

Universiteit van Pretoria, Chirurgiese Afdeling, en Pretoria Tak van Vereniging van Chirurgen van Suid-Afrika (M.V.S.A.), Gekombineerde Lesings. Die volgende vergadering vind plaas op Maandag 14 April om 5.00 nm. in die Onderste Lesingsaal, Kliniese Gebou, H. F. Verwoerd-hospitaal, Pretoria. Prof. C. H. Derksen sal as spreker optree oor 'Nuwere konsepte oor behandeling van spatate'.

Southern Africa Cardiac Society, Johannesburg Branch. The next meeting will be held on Thursday 24 April at 8.15 p.m. in the Pneumoniosis Lecture Theatre, Joubert Street, Johannesburg. This will be a medical evening, and Dr P. Schamroth will speak on 'The Wolff-Parkinson-White syndrome and related disorders'. Members are asked to note the change in date.

Southern Transvaal Branch (M.A.S.A.), Medical Graduates Association of the University of the Witwatersrand and the Witwatersrand Faculty of the College of General Practitioners: Combined Clinical Meeting. The next meeting in the series designed to afford the medical profession an opportunity of meeting the new professors will be held on Tuesday 15 April at 8.15 p.m. in the Harveian Lecture Theatre, Medical School, Johannesburg. Prof. T. H. Bothwell, Head of the Department of Medicine, will speak on 'A topic of current interest'.

Dr Dick Kukard, obstetrician and gynaecologist, part-time consultant at Groote Schuur Hospital, is now practising with Dr Sydney B. Cooper at 519 Medipark, Foreshore, Cape Town. Telephone: rooms 3-4294 and 3-6203, residence 65-2762.

Dr. Dick Kukard, ginekoloog en verloskundige, deeltyds konsulent by Groote Schuur-hospitaal, praktiseer nou saam met Dr. Sydney B. Cooper te Medipark 519, Strandgebied, Kaapstad. Telefoonnummers: spreekkamer 3-4294 en 3-6203; woning 65-2762.

D. P. de Villiers Clinical Club. The next meeting of this club will be held on Tuesday 8 April at 8.15 p.m. in the Non-White Teaching Unit, Conradian Hospital, Pinelands, Cape. Dr M. B. Bennett will speak on 'Radiotherapy today'. All interested persons will be welcome.

University of Cape Town Medical History Club. The next meeting of the club will be held on Monday 14 April at 8.15 p.m. in the Doctors' Room, Medical Library, Anzio Road, Observatory, Cape. Dr W. Schneewine, Director of the South African Cultural History Museum, will deliver an illustrated lecture entitled 'Weapons and war wounds in ancient times'. All interested persons will be welcome.

Dr J. A. H. Campbell, histopathologist, is now practising at 711 Medipark, Foreshore, Cape Town. Telephone number remains the same.

Dr. J. A. H. Campbell, histopatoloog, praktiseer nou te Medipark 711, Strandgebied, Kaapstad. Die telefoonnummer by onveranderd.

Glaxo Award in Endocrinology and Metabolism. To stimulate interest in the field of endocrinology, metabolism and diabetes in South Africa, Glaxo-Allemenburs (SA) (Pty) Ltd have agreed to make available to the Society for Endocrinology, Metabolism and Diabetes a sum of R250 for an annual prize. Any research in this field, published or unpublished, and completed in the year preceding the closing date for the annual award, may be eligible for the prize. The award will be limited to South African clinicians or research workers, under the age of 35 years.

The winning paper will form part of the scientific programme of the Annual Congress of the Society for Endocrinology, Metabolism and Diabetes.

Applications must be submitted not later than 31 May 1969 to Dr B. L. Pimstone, Honorary Secretary, Glaxo Award in Endocrinology and Metabolism, Department of Medicine, Medical School, Observatory, Cape.

Educational Council for Foreign Medical Graduates—Examinations. Graduates of medical schools outside the USA, Canada and Puerto Rico who wish to study or practise medicine or to receive internship or residency training at hospitals in the USA are required to pass the ECFMG examinations, held biannually all over the world.

Further information and application forms to sit for the examination are available from the Educational Council for Foreign Medical Graduates, 3930 Chestnut Street, Philadelphia, Pennsylvania 19104, USA. 10 June 1969 is the closing date for completed applications for the next examination, to be held on 10 September in both Cape Town and Johannesburg.