DIABETES IN ASIANS AND AFRICANS IN AND AROUND DURBAN

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SIZE OF THE SERIES, RACIAL GROUPS INVOLVED, AND HOW THE CLINIC IS RUN

1. Growth and Constitution of the Clinic

The population of Durban is 650,000, divided roughly equally into 3 ethnic groups — Asians, Africans and Europeans. The King Edward VIII Hospital in Durban (1,760 beds) is solely a hospital for non-White people. Apart from Africans and Asians actually resident in Durban and its environs, the hospital drains numbers of patients from other communities, particularly from the coastal regions of Natal, but not from very far inland, where patients generally go to the Edendale Hospital in Pietermaritzburg, 50 miles from Durban. It is impossible to say accurately what proportion of Durban non-Whites attend the King Edward VIII Hospital, because of the large number of smaller hospitals and clinics in and around Durban, and because of the large numbers of Natal Indian people who are able to afford private medical attention. However, it is highly probable that the hospital serves a larger African than Asian population. The total outpatient attendances at the Hospital number 600,000 annually, and about 60,000 people are admitted every year. A Diabetic Clinic was started in the Medical Outpatients Department of the Hospital in August 1958, and by August 1963 5,018 new diabetic patients had been registered. The growth of the Clinic by 6-monthly periods and by racial group is shown in Table I:

TABLE I. GROWTH OF THE CLINIC

Time in months	*6*	*12*	*18*	*24*	*30*	*36*	*42*	*48*	*54*
Africans (Zulus)	88	182	245	323	408	518	633	754	860
Asians (Natal Indians)	337	696	1,054	1,501	1,923	2,326	2,746	3,160	3,549
Totals	425	878	1,299	1,824	2,331	2,844	3,379	3,914	4,409

The number of new registrations has risen constantly. In the first 4 years the respective total annual registrations were 878, 946, 1,020, and 1,070. Unfortunately (because of staff shortage), we have just moved part of the Clinic into the middle of an Indian area of the town, which will be very convenient to Natal Indians, and we fear and anticipate massive registration of new diabetics.

2. African Diabetics

The African diabetics in Durban are chiefly Zulus. In an earlier study[1] 98% were found to be of the Nguni race (95% Zulus, and 3% Bacas and Pondos), and 2% were Sothos (all Basutos).

3. Natal Indian Diabetics

We take particular pains to refer to our Asians in Durban as Natal Indians since we deal predominantly with a community whose members have a lower economic status than, for instance, the Indians in the Transvaal who are on the whole better off and who form more of a genetic isolate. The poor Natal Indians outnumber the rich Natal Indians greatly; a recent study suggests that 70% of the Natal Indians live below the poverty datum line.[2,3] This is interesting in view of the fact that R60,000,000 of property in Durban and its vicinity is owned by Indian people.[2]

For the practical purposes of assessing diabetics, the Natal Indians are conveniently divided into Hindu and Muslim groups, because of the fairly uniform dietary habits in these 2 groups and the high rate of consanguineous marriages in the Muslims. Thus we recognize in our aetiological studies: (1) Muslims, talking *Gujarati* and *Urdu,* (2) Hindus, talking *Tamil, Telegu, Hindustani* and *Gujarati.*

Energetic proselytization, especially to Islam, has resulted in circumstances which affect diabetic emergence; and thus people of similar language, ethnic and geographical origins, have now been split apart—chiefly by matrimonial and dietary habits.

As regards areas of origin, the Natal Indians come chiefly from 3 regions: *i.* The South and South-East of India—the Dravidian (Tamil-Telegu) peoples. *ii.* The United Provinces (Uttar Pradesh), Bihar and Orissa—Hindustani stock. *iii.* The Bombay Area—the Gujarati peoples, both Hindu and Muslim. (*i*) and (*ii*) were 'indentured' labourers whose fares to South Africa were paid by this Government, and (*iii*) were 'passenger' Indians, who came about 40 years later at their own expense to be traders and professional men.

The Dravidian (Tamil-Telegu) peoples talk 5 main languages in India, and for practical purposes are represented by 2 of these in Natal—Tamil and Telegu. The Tamilian people are the numerically largest of the language groups in Natal. Both these languages are similar, with the exception of the fact that Telegu contains far more Sanskrit words: both tongues share a remarkable complexity of grammar and pronunciation, and Europeans are earnestly advised not to attempt learning them. These people have been the quickest of the lower social groups to learn English; some believe that this is because the children find their own tongues so difficult to learn that they have fallen back on the easier English. The Dravidians come from areas of great poverty, and it is probably because few villages were able to afford their own priests, that extensive proselytization took place in India, chiefly by Christian missionaries of the Catholic, Wesleyan and Baptist faiths. Unlike Islamic conversion of Natal Indians, Christianization took place chiefly in India itself.

Indians from the North of India (Uttar Pradesh, Orissa, Bihar) were all originally of the Hindu faith talking Hindustani; they came to Natal by way of Calcutta and are sometimes referred to as 'Calcutta' Indians—most inaccurately—since Calcutta is a Bengali area. All these people were indentured labourers; vigorous Islamic proselytization took place among them when they reached Natal, and this has resulted in our Urdu-speaking Muslim people. Urdu and Hindustani are virtually identical tongues, with the exception of words of Mogul influence in the Urdu; these are the easiest languages for a European to learn. The Hindustani-speaking Hindus[3] are the second largest language group in Natal. The

converted Urdu-speaking Muslims represent the Muslim working class in Natal. Interestingly enough, diabetes would appear to be inordinately common in these people.

Indians from the Bombay area comprise the Gujarati-speakers, Muslim and Hindu, and they were almost all 'passenger' Indians, sufficiently well-off to pay their own fares. The Muslims are the numerically commoner of the Gujarati speakers, and they comprise some of the wealthier citizens of the Republic. They eat very well, and consanguineous marriages are the rule—so it is said—to keep the wealth in the family. The Hindu Gujaratis (so-called Bunyas, or shrewd businessmen) are the smallest significant language group in Natal; they are invariably well-bred and well-educated, and include some of the greatest scholars in Natal—the Mahatma Gandhi having been such a person. They are very strict vegetarians who do not even eat eggs or milk, and they eat almost invariably at home. Their diet includes large amounts of purified carbohydrates, and a diabetic diet is very hard to institute without making it very dull. Most of them can afford private medical services, and they are seldom seen at our Clinic.

4. How the Clinic is Run

Running a diabetic clinic for poor and illiterate people presents 2 great problems: (*i*) Most of our patients are unable to diet properly, either because of inflexible habits, or because they are too poor to pay for non-carbohydrate foods; and (*ii*) we get a very high default rate, especially if an attempt is made to control patients upon diet alone. Those who can pay are charged 40c per visit, and they do not relish getting saccharine and further advice to lose weight for this. Drug treatment is greatly facilitated by the fact that less than 3% of our patients are truly dependent upon exogenous insulin; thus the problem of ketosis is not nearly as great as that found overseas in temperate climates. As a basis for treatment, the following sheet is handed out to all patients:

THE KING EDWARD VIII HOSPITAL DIABETIC CLINIC
DIET SHEET

Diabetics must not eat the following foods at all:

Sugar
Sweets
Bread (brown or white) except for small amounts
Potatoes
Cakes, beer, jam or tinned fruits
Putu, samp, mealie rice
Lemonade, Fanta, sweet syrups, or sweetened fruit juices

Diabetics can eat the following:

Three small slices of brown bread daily
All green vegetables or herbs
Small amounts of rice (white or brown)
Fresh fruit (only one banana daily)
Lettuce and salads
Meat, cheese, tripes, chicken, eggs
Boiled fish
Small amounts of broad beans

Brown bread is not better than white for dieting
Brown rice is not better than white for dieting
Use saccharine instead of sugar — we will give it to you
Boil or grill your foods
Eat 3 equal-sized meals daily
Drink 2 glasses of water before each meal
Use vinegar instead of salad dressing
If you are hungry, take tea or coffee with saccharine or eat green leaf vegetables

2 important rules are:

Diet carefully — keep your weight down.
Attend the clinic regularly for supervision of your treatment.

Please bring your syringe and empty bottles with you, if taking insulin.

To persons conversant with the handling of such patients this document must seem rather naive, but it does fulfil the purpose of guiding those who are able and willing to diet. This diet sheet was formerly used in a Zulu version, but we did not persist in its use, for those that can read Zulu can generally read English. Those interested in the Zulu version are referred to the ample section on the Diabetic Clinic in Campbell and Lugg's *Handbook to Aid in the Treatment of Zulu Patients*.[5] We advise illiterate patients to show the diet sheet to their employers or educated members of their families, who can translate it for their use. In the majority of cases, the only effective dietary adjustment achieved has been the substitution of saccharine for sugar. When patients can and do diet, then results are generally good: conscientious diabetics in our clinic are invariably hungry.

Our high default rate is chiefly due to initial improvement on drug treatment, which is often sustained for some months without further drug therapy even though patients may have put on weight. Patients default at once if they are not given hypoglycaemic or anorectic drugs. In one clinical trial we achieved, with a great deal of trouble, a significant follow-up in 93% of over 200 patients—something not achieved since.[4] In regard to the taking of histories, we make every endeavour to speak to patients in their own language. All workers in the clinic are heartily sceptical of 'information' gleaned through interpreters; one cannot help recalling the old Italian proverb *traduttore traditore*—a translator is a traitor. All workers speak Zulu, one speaks Telegu, one basic Hindustani and Urdu, and we speak to Tamilian and Gujarati patients, who do not speak English, in a common tongue, Zulu. Information gathered through interpreters by doctors too lazy to establish direct doctor-patient language relationship is not admitted in our unit.

The King Edward VIII Hospital does not serve Coloured people (i.e. people of Black-White mixed stock); these attend the Addington Hospital for Europeans in Durban.

LOCAL DIABETIC PREVALENCE STUDIES

To carry out diabetic prevalence surveys in this Province presents a number of difficulties, the greatest of which is that it is hard to get access to populations that are not constantly changing. Further, attempts to do surveys among rural African populations which are virtually static generally results in the disappearance of many people into the hills! Such a reason has been put forward to explain the discrepancies between census figures and the actual numbers of people in a given area; in certain instances, census figures were found to be less than 2/3 of actual figures.[6] Thus our studies here have had to be confined to what static Asian communities we have available, and these have included a sub-economic housing scheme at Springfield in Durban,[7] and the large static multiracial community of the Tongaat Sugar Company on the Natal North Coast.

1. Results of Sample Testing of a Lower Class Natal Indian Population at Springfield[7]

The first diabetes survey reported from Natal was that of Wood,[7] who was working on tuberculosis in Durban. She sampled a group of over 5,000 working-class Natal Indians in a sub-economic housing scheme at Springfield in Durban, testing 250 people. These people were screened by means of urine tests, those with positive results being subsequently subjected to fasting blood sugars to 'establish' the diagnosis. In the light of our subsequent observations (see below) we believe now that fasting blood sugars in the Natal Indians are not only useless, but misleading.

Wood concluded that the probable prevalence of diabetes in adults of over 20 years was 5·5%, and over 30 years, 8·8%. Half these cases were undiscovered before the survey. These figures are similar to those of Batchelor and Campbell (see below), in a very low-class Natal Indian community, in whom postprandial urines were tested.

2. The Tongaat Village Dwellers Survey

Of the glycosuria surveys planned upon the Natal Indian population of Tongaat by Batchelor and Campbell, the first was upon the inhabitants of the village itself, that is to say, upon people who were *not* actual employees of the Company, who owned their own houses, and who came from a middle-class population. In this survey the urines of 1,619 people of all ages was tested, between 1 and 2 hours after the main meal of the day in the evening, by means of the glucose-oxidase

strip. The large numbers of people between the ages of 10 and 19 are explained by the fact that many school children were included in the survey; these disproportionately many young people were 'ironed out' by the use of Oettlé's Standard Theoretical Population (see below). Note that in this survey there were no Gujarati-speakers, testifying that these people did not come from the highest social stratum.

As might have been expected, the highest incidences in the various age groups was in the over-50 year age groups (Table II). As these numbers are large we can apply them to Oettlé's Standard Theoretical population (Table IV[5]), which shows in this study there is a prevalence of postprandial glycosuria of 7·2% (7,207 per 100,000) in the population over the age of 10 years.

3. The Tongaat Mill Barracks Survey

The second survey planned by Batchelor and Campbell included the employees of the Tongaat Sugar Company, who lived in houses provided by the Company and who are people of probably the very lowest social stratum in the Natal Indian people. The urines of 3,354 such people were tested by means of the glucose oxidase strip, 1 – 2 hours after the evening meal. The results are summarized in Table III.

Thus when these results are applied to Oettlé's standard population, the apparent prevalence of postprandial glycosuria in the village dwellers over the age of 10 (7·2%) is twice as high as that in the Mill Barrack dwellers (3·3%). The apparently equally low incidence in all language groups in the Mill Barracks survey is interesting and would appear to bear out the fact that irrespective of the rate of intermarriage in the various groups, the glycosuria prevalence will be low in all if social status is equally low in all of them.

4. Postprandial Urines in Pondo (African) Labourers from the Transkei

We are at present screening all Pondo labourers applying for work in the cane fields of the Tongaat Sugar Company by means of testing postprandial urines with the glucose oxidase strip. So far, 1,812 such people, all males of the younger age groups, have been tested with the glucose oxidase strip, and in 3 a trace of glucose has been detected. These patients have not yet been followed up further. They are all of very poor peasant stock. As they return annually to renew their employment, it will be of value to test them annually to see what effect the very high sugar intake to which they are exposed in Natal, will have upon them.

5. Routine Screening of Natal Indian Insurance Proposers, believed Suitable for Life Cover

194 Natal Indian Insurance proposers, who were thought fit for life cover on the grounds of conventional insurance clinical examination, testing of random urines for sugar, and, in some cases, ECGs, were submitted to routine blood-sugar screening. They were submitted either to the 100 G. 2-hour

TABLE II. SURVEY OF 1,619 TONGAAT VILLAGE DWELLERS SHOWING TOTALS BY SEX AND LANGUAGE GROUP, AND THE NUMBERS IN EACH INSTANCE WITH POSTPRANDIAL GLYCOSURIA IN BRACKETS

Age group	*Languages*								*Group percentage positive*
	Tamil		*Telegu*		*Hindustani*		*Urdu*		
	Males	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*	
10–19	315 (1)	159 (1)	127 (0)	67 (0)	171 (0)	103 (2)	76 (1)	56 (2)	0·7
20–29	35 (1)	51 (0)	10 (0)	20 (1)	19 (0)	28 (0)	13 (2)	23 (1)	2·5
30–39	25 (1)	36 (6)	18 (1)	20 (0)	15 (1)	20 (4)	12 (2)	17 (0)	9·2
40–49	21 (6)	18 (3)	13 (3)	10 (2)	15 (3)	10 (2)	5 (0)	6 (0)	19·3
50–59	10 (3)	11 (3)	6 (4)	3 (1)	5 (2)	6 (0)	2 (2)	2 (0)	33·3
60–69	4 (0)	4 (0)	2 (1)	2 (0)	6 (1)	2 (0)	3 (2)	2 (1)	20·0
70 plus	4 (2)	3 (0)	3 (1)	2 (0)	— —	— —	1 (0)	2 (1)	26·6
Totals	414 (14)	282 (13)	179 (10)	124 (4)	231 (7)	169 (8)	112 (9)	108 (5)	
Language group totals	696		303		400		220		1,619
Positives	27 (3·9%)		14 (4·6%)		15 (3·8)%		14 (6·4%)		(70)

TABLE III. TONGAAT MILL BARRACKS SURVEY—SHOWING TOTALS BY SEX AND LANGUAGE GROUP, AND THE NUMBERS IN EACH INSTANCE WITH POSTPRANDIAL GLYCOSURIA

Age group	*Languages*								*Group percentage positive*
	Tamil		*Telegu*		*Hindustani*		*Urdu*		
	Males	*Females*	*Males*	*Females*	*Males*	*Females*	*Males*	*Females*	
10–19	455 (1)	418 (3)	150 (—)	138 (2)	90 (1)	81 (—)	18 (—)	21 (—)	0·5
20–29	215 (3)	302 (6)	62 (1)	98 (1)	32 (—)	43 (1)	7 (—)	25 (—)	1·5
30–39	149 (3)	208 (11)	41 (4)	39 (3)	18 (1)	37 (3)	8 (—)	5 (—)	4·9
40–49	108 (6)	122 (7)	39 (1)	53 (4)	29 (—)	28 (2)	5 (1)	4 (—)	5·4
50–59	108 (15)	90 (8)	37 (2)	18 (2)	13 (1)	15 (2)	4 (—)	7 (1)	14·8
60–69	50 (8)	23 (3)	11 (2)	8 (—)	4 (—)	4 (—)	1 (—)	1 (1)	13·7
70 plus	26 (1)	16 (4)	6 (—)	5 (1)	2 (—)	5 (2)	2 (—)	1 (—)	12·7
Totals	1,111 (37)	1,142 (42)	206 (10)	359 (13)	205 (3)	213 (10)	55 (1)	63 (2)	
Language group totals	2,253	79	565	23	418	13	118	3	3,354
Positives	79 (3·5%)		23 (4·1%)		13 (3·1%)		3 (2·5%)		(118)

TABLE IV. RESULTS OF SURVEYS IN TABLES II AND III, APPLIED TO OETTLÉ'S STANDARD POPULATION

Age group	*Number of people in standard population*	*Mill Barracks Survey (Table III)*		*Village dweller Survey (Table II)*	
		Percentage	*Estimated number*	*Percentage*	*Estimated number*
0–	20,000	—	—	—	—
10–	20,000	0·5	100	0·7	140
20–	20,000	1·5	300	2·5	500
30–	20,000	4·9	980	9·2	1,840
40–	10,000	5·4	540	19·0	1,930
50–	5,000	14·8	740	33·3	1,665
60–	3,000	13·7	411	20·0	600
70–	2,000	12·7	254	26·6	532
Totals	100,000		3,325		7,207

glucose screening test, or to the standard 50 G. test, with fasting blood sugar, and half-hourly levels until 2½ hours. The results are summarized in the following Table:

TABLE V. RESULTS OF SCREENING TESTS PERFORMED IN 194 NATAL INDIAN PROPOSERS BELIEVED SUITABLE FOR LIFE COVER

Test performed	*Number found to be diabetic*	*Equivocal results*	*Normal*	*Totals*
50 G. tests ..	23	3	14	40
100 G. tests ..	39	13	102	154
	62	16	116	194

Of the 16 equivocal tests, 10 were labelled as 'lag' curves. In view of the commonness of heavy glycosuria between normal blood-glucose readings, fasting and at 2 hours, these tests were repeated with figures at either ½, 1, or 1½ hours, and some very high one-hour levels were found. If these exceeded 195 mg. per 100 ml. we have advised that the patient be regarded as being diabetic; indeed there is now very good evidence anyway that the 'lag' curve is indeed a latent diabetic phenomenon.[9] Thus, if we include those with high 1-hour levels, (10 patients) the number of positives now number 72 out of a total of 194, i.e. 37%. Once again, it must be borne in mind that these people were a selected group in that others with uninsurable conditions such as hypertension and diabetes had been excluded by conventional insurance examinations. By and large their ages were less than those of the ward and outpatient group mentioned below. The difference between these blood-screening tests and the apparent prevalence of postprandial glycosuria in the Tongaat Village study (people from insurable social groups), is most striking and emphasizes the uselessness of even postprandial glycosuria as a basis for studying blood-glucose tolerance.

6. Screening of 'Non-diabetic' Control Ward Patients and Outpatients

McKechnie[88] carried out this study completely independently of the insurance survey mentioned above, using a different laboratory and a different method of blood-glucose estimation. 112 Hospital Natal Indian ward patients and outpatients, not known or suspected of being diabetic, were screened by means of the 100 G. glucose-screening test. Of these no less than 67 were found to be diabetic by present standards. He emphasizes that since these comprise a group of hospital patients they must be regarded in a sense as a selected group, even though there was no suspicion that they might have been diabetic. This shows that no less than 60% of these patients were diabetic. These patients were older than the insurance group quoted above and were thus closer to the theoretical age at which maximum diabetic incidence would be expected. The higher incidence here can be explained by the fact that uninsurable patients had not been screened out by means of a clinical examination. Interestingly enough, one of his undisclosed diabetics had a blood-sugar level of 480 mg. per 100 ml. at 2 hours with the 100 G. test without any glycosuria!

7. Screening of Apparently Non-diabetic Tuberculosis Patients

Vidor[76] screened 30 apparently non-diabetic female Natal Indian patients in the wards of the King George V Tuberculosis Hospital in Durban by means of the 100 G. 2-hour test. Of these (bearing in mind the diabetogenic action of INAH) no less than 8 were found to have unequivocal evidence of diabetes, one patient actually having a 2-hour level of 380 mg. per 100 ml. This patient had been suffering from severe miliary tuberculosis, with bone and joint involvement, and had proved to be very resistant to treatment. The clue to her stormy illness undoubtedly lay in undiscovered diabetes. This observation must be of the greatest importance to those treating Asian diabetics in this country.

8. Genetic Considerations of the Above Results of Screening Tests[73]

Full evaluation of the factors concerned in the genetic predisposition for diabetes mellitus in the Natal Indians is not yet complete, but preliminary figures are startling and merit comment. It is generally accepted today that the predisposition towards diabetes depends upon a single autosomal recessive genetic mechanism with incomplete penetrance. Greater penetrance obtains with increasing population age, and it becomes more apparent when more definitive diagnostic methods are employed. Thus diabetes is more likely to be detected in elderly patients where blood-glucose studies are used in preference to urine studies. Based on these precepts, one of the King Edward studies (see above, Section 6), showed that in a group of unselected ward patients and outpatients, 60% of Natal Indians had abnormal responses to a glucose load when judged by blood-sugar levels. This figure will be used for illustrative purposes here:

(i) If a recessive defect is implicated, then, according to the Hardy-Weinberg equation, the gene frequency in the population is 75%, the heterozygous carrier rate 37·5%, and the homozygous normal accounts for only 2·5%! Such figures are quite extraordinary and are not observed even in balanced polymorphism where heterozygous advantage operates.

(ii) In general, recessive disorders are not characterized by incomplete penetrance. Both the family trees of the Natal Indian diabetics and this problem of penetrance can be reconciled in the basis of intermediate dominance. Again, according to the Hardy-Weinberg law, and assuming here 100% penetrance, the gene frequency would be 36%, DD diabetics 14%, Dd diabetics 46% (making the observed total of 60%), and the dd normals 40%. It is the Dd heterozygotes who will show variable penetrance, and a demonstration of difference in severity of diabetes in this group would be a further valuable confirmation.

(iii) The Natal Indians constitute a social genetic isolate, or more correctly, a group of isolates, in which the consanguinity rate is raised. The religious restriction upon random matings does to an extent mitigate the use of the Hardy-Weinberg equation in (i) and (ii) above. It is also possible that the original immigrants from India comprised a high percentage of diabetes-prone individuals and that genetic drift has occurred. On the other hand, only a limited period of 'reproductive time' has been spent in Natal.

(iv) The social and economic environment of the Natal Indian differs on the whole markedly from that of his cousin in India. It is highly probable that overt diabetes there is very much less common than it is in the Natal Indian. Using the 'thrifty genotype' hypothesis,[10] it may be postulated that the predisposition for diabetes is actually very high in India (undetected by diagnostic means currently available), where it has been of survival value in a land of very variable food intake. Immigrants to Natal have been exposed to one of the 'boons' of Western type of civilization — i.e. a constantly adequate or over-adequate intake of sugar or other purified carbohydrates, which has uncovered latent diabetes. In terms of evolution, the Natal Indian represents a genotypic anachronism.

(v) We must not exclude the possibility that hereditable genes may exist that may act at the genetic level of the endocrine (especially pituitary-adrenal) pathways, as has been suggested by the somatotype of many Natal Indian diabetics.[11]

Whatever view is held or later substantiated, it is apparent now that the environmental component assumes gargantuan proportions, and that it is unlikely that measures aimed at genetic drift or at the consanguinity rate or at the genotype will in any way be practicable or beneficial at this stage. Modification of the exogenous environment, on the other hand, is not only likely to be of benefit, but is feasible and becomes imminently imperative.

AETIOLOGY OF DIABETES IN THE ZULU AND THE NATAL INDIAN

1. Dietary

i. The Zulu diabetic. If diabetes is indeed an illness of well-being, then it is natural to look towards those Zulu families who have enjoyed a fortunate economic position for many years. The classical example is that of the Zulu Royal Family. The emergence of diabetes in this family almost certainly coincided with the passing of the superbly fit front-line Kings, Chaka and Dingaan, and with the accession of their slothful and stay-at-home brother, Mpande. Mpande's chief interests were his large harem and his eating, and he became so fat that he actually couldn't walk and had to be dragged about on ox-skins. He died from what was classically referred to as the 'King's illness' or 'Mpande's illness' (*Umxkhobokho*), which is described as being an illness 'which afflicts those that are fat, and yet it wastes their bodies and muscles from the inside.'[1] Since then diabetes, as it probably was, has assumed epidemic proportions in both direct and cadet lines, aided incidentally by intermarriage with other notable families with diabetes. Recent research has shown that diabetes occurs also in the Basuto Royal Family.

In our first 150 Zulu diabetics the surname 'Dhlamini' occurred so frequently without apparent family relationship, as to stimulate enquiry as to whether this appearance was significant. The percentage of Dhlamini's attending our diabetic clinic was exactly 10 times that found in 200 consecutive Zulu outpatients at the MOPD of the hospital. The name, interestingly enough, is made up of 2 words, *'idla'* (eat) and *'emini'* (in the middle of the day), and it denotes a family of people who eat heavily in the middle of the day, that is to say, as well as at night—the normal time of the heavy meal! Studies of dietary aetiology are greatly facilitated by the virtual absence of diabetes in rural areas[32] and the very great differences in diet of the peasant and town-dwellers, especially in regard to sugar intake. Thus we studied and compared the food intake of Zulu peasants in Nongoma in rural Zululand[71] with that of Zulus in an urban location (Lamontville) in Durban.[70] These diets are summarized as follows:

TABLE VI. COMPARISON OF DIETS OF URBAN ZULUS AND PEASANTS IN ZULULAND RURAL AREA

Foodstuffs	*Settled Urban Zulu*[70] *(1957)*		*Rural Zulu Peasant*[71] *(1953)*	
	Calories	*Percentage of total calories*	*Calories*	*Percentage of total calories*
Cereals (maize products, bread) ..	1,476	55	1,376	47
Sugar	419	16	30	1
Milk (milk products)	112	4	224	8
Animal tissues ..	191	7 } 15	40	2
Fats and oils ..	124	8 }		
All vegetables and fruit	268	10	1,200	42
	2,590		2,870	

a. The average daily caloric intake was higher in the peasant (non-diabetic group).

b. The diet of the urbanized (tend-towards-diabetes) group contains very much more sugar than the peasant diet. Most of the cereals eaten in the towns is in the form of white bread.

c. If milk products, animal tissue and oils and fats are totalled in the 2 diets, it will be seen that the totals of these products comprise 10% of the peasant and 19% of the urban diet: this difference is less striking than in respect of sugar intake.

Caloric intake would appear to play a smaller part in this study in the emergence of diabetes than does, for instance, the intake of sugar.

In the last few years sugar intake has risen drastically in Natal because of very efficient advertising and because sugar has obviously reached as high an addictive status in our non-White people as in the Whites. The latest figures[72] show that the average (per person) annual intake of sugar in town Zulus is 89 lb., and in the rural areas the figure has risen enormously to 39 lb. *per annum*. Further, we are becoming aware of the huge intake of workers on the Sugar Belt: all cane workers get a weekly ration of 1½ lb. and it is estimated that they can augment this by chewing sugar cane to the extent of ½ – 1 lb. *daily*! Further, most of these people eat their weekly ration, raw, within an hour of getting it: it will indeed be interesting to follow up our glucose-screening survey on such labourers coming from the Transkei.

In 1959, when taking careful dietary histories from fat, middle-aged Zulu diabetics, I found a remarkably constant period in years of exposure to town life and food before the rural Zulu, who had moved into permanent residence in town, developed diabetes. The peak 'incubation period' in 80 such diabetics lay between 18 and 22 years; I thus put forward the 'rule of 20 years'.[13] Since then Cohen[14] and his co-workers have studied the emergence of diabetes in Yemeni Jews who moved from Yemen to Israel. He noted that diabetic emergence was highest 25 years after such a move. His careful dietary studies show that fat and protein intakes were the same in both countries and that the only difference lay in sugar consumption. In Yemen sugar consumption was 4 kg. per person *per annum*, whereas in Israel it is 36 kg. per person *per annum*.[37] Diabetes is unknown in Yemen and common in Israel. Recently I had a letter from Dr. Albertssen of Iceland, who has studied diabetes there for many years. With the lowering of proportions of fat and protein in the diet and the increase of purified carbohydrates, diabetes is becoming very common, and the peak emergence after this dietary change is 'between 15 and 20 years'.[15]

ii. The Natal Indian. It is interesting to speculate why moving an Indian from his mother country to Natal will increase his chances of developing diabetes about 10-fold. Ajgaonkar, of Bombay,[16] believes that this is because the Natal Indians eat too much and work far less than their cousins in India. One thing is evident: the overall *per capita* consumption of sugar in India is 5·4 kg.[17] Even in Natal Indian working-class people preliminary studies show a probable intake of sugar in all forms of 35 kg.[33] *per annum*, and it would appear highly probable that that of the higher class Indians is in the region of 50 kg.—an intake approaching that of people in Britain. Certainly obesity in our Natal Indian women is common. It is interesting to note that in India 70% of diabetics are males, whereas in Natal 64% are females. This may be a measure of the emancipation experienced by Indian women in Natal. It is probable that parity rates are no higher than those found in India. It is almost certain that heightened food intake (and especially sugar intake) accounts for this high prevalence of diabetes in Indian immigrants in Natal.

Previously I proposed,[18] when studying the simultaneous emergence of diabetes in connubial diabetics, that the mustard oil (n-allyl-isothiocyanate) might be a diabetogenic substance because of a thiol-immobilizing action. On the grounds of this observation Butterfield, of Guy's Hospital, fed this substance to rats and found that it increased food intake by one-third as compared with controls.[19] Perhaps some such non-specific effect on appetite may have contributed to diabetic emergence; certainly there is a remarkable similarity between *per capita* consumption of mustard oil[95] in the Natal Indian people and numbers of people who became diabetic over the same years —both curves rising to a peak at 1958 – 1959 and falling after this, though many factors may account for this.

There must be little doubt that this remarkable rate of diabetes represents an abuse of a 'thrifty genotype' mechanism in the grossly higher consumption of sugar in Natal. For some time it has been a matter for thought why, under the more favourable conditions that obtain in Natal, the *working-class* Muslims would appear to have a higher prevalence of diabetes and, in 2 out of 3 family history surveys, have had a higher incidence of diabetic family histories of diabetes than the wealthier Gujarati Muslims. An explanation emerges if one bases one's thoughts on the thrifty genotype. The Gujarati people came out here as people of affluence, who had enjoyed favourable economic circumstances for many years, while the Urdu-speaking Muslims were people of Hindu origin from areas of great privation and poverty in North India, where food uncertainty over countless generations had caused development of the 'thrifty genotype'. In Natal these people were converted to Islam, and the census shows[20] that they have made more rapid economic advancement as a group than other people of Hindu stock. Thus their systems conditioned to food deprivation over generations have not been able to withstand the high sugar intake in Natal. Perhaps the lower incidence of diabetes in urban Zulus, exposed to much similar intake of sugar, is due to the fact that until the disastrous cattle rinderpest in 1895 (only 2 generations ago) they were meat eaters and were never short of regular protein.

The commonness with which we find low fasting blood sugar levels in undisclosed or recently diagnosed diabetics, is another point in favour, in the Natal Indian, of the agile

insulin production of the 'thrifty genotype'. This certainly favours the presence of plenty of circulating insulin in the fasting state. It has recently been shown that glucose is the most powerful stimulus to the release of insulin from the pancreas;[24] further, other workers[68,69] have demonstrated with fluorescin-tagged insulin that insulin causes an antigen-antibody response with the degenerative material in diabetic micro-aneurysms and in the glomeruli of the Kimmeltsiel Wilson kidney. Thus it is not hard to visualize how the high sugar intake of the Natal Indian can have contributed to the genesis and development of vascular disease, which has been shown to exceed greatly that in the Zulu. Furthermore, the labile insulin system of the 'thrifty genotype' can account for low fasting blood-sugar levels, high one-hour figures in the 100 G. test, and the fact that these figures can be followed by normal figures at 2 hours in Natal Indian diabetics. Finally, the very low incidence of insulin-dependent diabetics in our clinic would testify to the generally satisfactory production of insulin from the islet cells, even in very young diabetics (see below) in whom ketosis is very rare indeed.

2. Family Studies

i. Natal Indian diabetics. (*a*) Family history surveys. Our difficulties before the various Tongaat surveys noted above of getting suitable Indian populations on which to work, made us fall back upon studies of family history incidences in the various language groups. Firstly, it is important to realize that to a Natal Indian the word 'family' means his wife and living children; therefore, in asking him whether there is diabetes in his family it is important to *mention,* brothers, sisters, mother, father, grandparents, uncles, aunts, cousins' children and grandchildren. This is time-consuming, but unless it is done, very low figures are obtained. We have checked all patients repeatedly, each check bringing further information; some have been checked 10 times. In 1959, Cosnett[21] reported that 28% had a family history of diabetes (207 patients). In 1961[22] a family history incidence of 47·8% was noted in 493, and in 1962 we found a family history incidence of 45·6% in 1,293 patients.

In our family history survey, we recognize 3 degrees of family relationship:

(1) Consanguineous: { 1st degree. Father, mother, sister, brother, children. 2nd degree. Grandparents, uncles and aunts, cousins, grandchildren.

(2) Environmental: 3rd degree. Connubial diabetes, i.e. in the spouse.

Our results in the present survey of 2,000 frequently-checked consecutive Natal Indian diabetics, who were aware of having diabetic relations and in whom information was considered reliable, is summarized in the following Table:

The Table shows how the Hindus predominate; however, it is interesting to see that the proportions in our clinic attenders is the same as in the general population, something that would not be expected in what is virtually a charity clinic. Muslims had an apparently higher incidence of family histories, and this may be the result of intermarriage. As regards connubial diabetes, a total of 115 patients (5·75%) gave a history of having had diabetic spouses.

(*b*) Connubial diabetes, that is to say the occurrence of diabetes in both the husband and the wife, has been observed very commonly in our clinic.[28] We have information about 232 such pairs, *plus* a further 18 in whom information is valueless. Further, we have actually collected 7 connubial Zulu diabetic pairs. This study is at present under analysis, but one important point emerges, and that is that regardless of the differences in ages between the spouses, there is a remarkable tendency for spouses to become aware of being diabetics, either simultaneously or within a short period of one another.[24] One other interesting finding is that not only do connubial diabetics develop diabetes at the same time, but they have tended to develop the disorder at the same time as other connubial diabetic pairs. This speaks very strongly for some environmental factor, especially in that we have had a child of an elderly connubial diabetic pair developing diabetes simultaneously with her husband and at almost the same time as her parents. We have had 3 remarkable multiple connubial relationships, where 2 diabetic men have had 2 diabetic wives each, and one women had 2 diabetic husbands. This would tend to contradict what was said above, but in each case, the particular spouse has developed diabetes simultaneously with the second spouse. Our average parity of connubial diabetic pairs is 7, and if the disease is inherited as a recessive disorder, then these children must be one of the finest studying grounds of the latent diabetic state in the world! I cannot now believe that my earlier contention, that a *specific* article of foodstuff may be responsible for simultaneous emergence in connubial diabeticism, is now tenable, having reviewed the diets of a large number of these people.

(*c*) Family genetic isolates. There is a remarkable tendency among our Muslim Indians to consanguineous marriages, which up till recently have been practised on a large scale in order, some say, to keep the wealth in the family. These date from the era of 'arranged' matches. Two brothers will often marry 2 sisters to whom they are

TABLE VII. LANGUAGE GROUP REGISTRATIONS AND FAMILY HISTORY INCIDENCE IN 2,000 CONSECUTIVE NATAL INDIAN DIABETICS

Religion	*Muslim*		*Hindu*				*Totals*
Language	*Urdu*	*Gujarati*	*Gujarati*	*Tamil*	*Hindustani*	*Telegu*	
Total patients in the language group, with percentage of total	231 (11·65%)	135 (6·75%)	3 (0·15%)	798 (39·90%)	656 (32·80%)	177 (8·85%)	2,000
Number in which family history was found and percentage of language group	124 (53·70%)	75 (55·50%)	3 —	324 (40·6%)	290 (44·2%)	77 (43·50%)	893 (44·65%)
Made up of: First degree	114	68	3	308	276	71	
Second degree	10	7	—	16	14	6	
No family history of diabetes	107	60	—	474	366	100	1,107 (55·35%)
3rd degree family history (environmental), and percentage of total language group	25 (10·80%)	8 (5·9%)	—	32 (4·00%)	44 (6·70%)	6 (3·40%)	115 (5·75%)

Note: In this Table the 3rd degree, or environmental relationship, is quoted separately, and numbers are not included as such in the general Table.

related, and matches between the children of these people are the rule. Even if young Muslims were sent back to India to get wives, they invariably stayed with blood relations in the Bombay Province area, among whom they generally found a spouse. Our genetic and prevalence studies mentioned above suggest that consanguineous marriages as a factor in the emergence of diabetes in the Natal Indian need no longer concern us, since the genetic component in diabetic emergence would appear to have been swamped in importance by environmental factors.

ii. Zulu diabetics. The fact that we have been able to collect 7 connubial diabetic pairs from close on 1,000 Zulu diabetics is interesting, in the light of the finding that only 5% of these people give a family history of the disease. Incidentally, Zulus give a remarkably good family history. This would suggest that genetic factors, again, are completely subservient to environmental factors in diabetic emergence. The remarkable incidence of diabetes in the Zulu Royal Family has been noted above, as well as the apparent inordinate occurrence in Zulus with the surname 'Dhlamini'.

3. Endocrine and Metabolic Aetiology

i. The adrenal cortex. Natal Indian diabetics, especially the females, are fat, have buffalo-hump obesity and frequent white cutaneous striae; hypertension in postmenopausal females is almost invariable; they are very hairy indeed—significantly more diabetic women having moustaches and side-burns than non-diabetic women;[21] and they are short in stature, rarely dependent upon insulin and yet develop severe and rapidly progressive vascular disease. The absence of ketosis and low rate of insulin-dependence in them would suggest satisfactory insulin production by the islet cells, or low levels of insulin antagonists. Their short stature and, again, absence of ketosis are strongly suggestive of absence of growth hormone effect.[21] Probable adrenal overaction is indicated in the androgen field in extreme hirsutism and high libido, and in the glucocorticoid field by the body obesity, cutaneous striae, frequent hypertension, and rapid progression of vascular disease.

On clinical grounds we suggested that the glycosuric syndrome in the Natal Indian is one characterized by normal or near-normal amounts of circulating insulin, by minimal growth-hormone effect, and by adrenal cortical overactivity—a concept that fits in well with the work of Gillman *et al.*[25] on baboons that had had their adrenals, pancreases and pituitaries removed.

The significance of blood and urinary hormone studies in such diabetics is difficult to define, especially in the light of McLean Baird's recent observations[26] showing significantly higher 17-ketogenic steroid levels in the urines of women suffering from simple obesity than compared with a control group, and a fall to normal levels with effective dietary restrictions. With such unusual vascular and other features in the Natal Indian diabetics one cannot help believing that tissue response to *normal* levels of circulating adrenal hormones may be abnormal.

Recently, we observed in a single, recently diagnosed middle-aged Natal Indian diabetic male, rapid improvement in blood and sugar levels with the use of metapirone (SU-4885) which specifically blocks the formation of hydrocortisone from Compound S. Triparanol (Mer 29) is an adrenal suppressant if used in large (1 G. daily) doses, and in a series of 12 patients in whom it was so used for a short trial, there was slight improvement in the diabetic state, with falls in blood-cholesterol and uric-acid levels.[28] Subjective improvement was marked here, though no control series was done.

A middle-aged Natal Indian male who was subject to moderately severe diabetes responded well to chlorpropamide, but developed an explosive light-sensitivity dermatitis, proceeding to exfoliation. This required large doses of suppressant steroids, and for nearly 2 years he has been on 6 x 4 mg. tablets of medrol (6-methyl-delta-1-hydrocortisone) daily with complete remission of his diabetes, in spite of weight gain. It would appear that we have depressed the production of naturally occurring adrenal diabetogenic steroids in his case, which we have replaced with a non-diabetogenic substance. This case has given cause for considerable speculation! One wonders if there might not be a place for the use of the suppressant steroids in large doses in the treatment of severe retinal or renal vascular disease, by the production of a 'chemical adrenalectomy'.

It is highly probable that the adrenal gland is an important factor in the initiation and progression of vascular disease and in the severity of diabetes in all races. I would venture to suggest that its importance in the Natal Indian diabetic (and in other diabetic races with low insulin-dependence rates) may be very marked indeed.

ii. Uric-acid studies.[21] The Natal Indian suffers from a common and often very severe gout syndrome, and in view of suggestions that an intermediate product of uric-acid metabolism may be diabetogenic, McKechnie,[21] in our clinic, attempted to confirm a diabetogenic action in Natal Indians. Of 26 hyperuricaemic patients 9 had raised fasting blood-sugar levels. Of 16 clinically gouty patients, 10 had abnormal glucose-tolerance tests. In a series of 174 Natal Indian diabetics (102 females and 72 males), 10·8% of the males and 2·9% of the females had serum uric-acid levels over 6·0 mg. per 100 ml. Mean serum uric-acid levels for the sexes in this series showed higher levels in the males (4·24 as to 3·62 mg.) and higher levels for the females (3·56 as to 3·24 mg.) as compared with the findings of Beckett and Lewis[29] in their large series of 812 diabetics.

iii. Pancreatic disease. Recently we completed an extensive postero-anterior X-ray survey of the abdomens of 1,254 new diabetics registering at our Clinic. Of these, 961 were Natal Indians and 293 Zulus. Only 3 of them (2 Indians and 1 Zulu) had the classical picture of pancreatic calcification as seen in the Northern Hemisphere. In no case did the X-ray picture resemble the rather coarse type of calcification described from Uganda by Shaper.[30] In 9 other patients there was calcification which might have been confused with pancreatic disease, but subsequent examinations ruled this out. All patients with calcification had had abdominal symptoms suggesting pancreatic disease, and one was subjected to a total pancreatectomy.

In an earlier plasma-iron survey by Hathorn[31] we found 3 patients with levels suggesting haemochromatosis. One was a woman with a kaffir-beer intake of 2 gallons daily! Treatment is a problem; to bleed a Zulu is to weaken him, and both males absconded from the clinic after single venesections.

SPECIAL CLINICAL AND PATHOLOGICAL FEATURES

1. Clinical

i. Diabetic variants and nomenclature. The more one sees of tropical or sub-tropical diabetics, the farther one leans away from the concept of diabetic types or variants. The terms 'Type I' and 'Type II' are meaningless in any diabetic context and are being dropped by informed workers. Simultaneous and independent papers from

Jamaica[32] and our clinic[33] exploded the myth of the 'J' type of diabetic, and indeed one worker in Britain showed that over 3% of all patients attending diabetic clinics in Britain came into the 'J' category.[34] Shaper's 'K' type is palpably redundant.[35] The American term 'ketoacidosis-resistant' can be dismissed as a ghastly example of a portmanteau word made up by doctors using inadmissible medical jargon.

Against the kaleidoscopic background of odd diabetics seen in warm climates, Dunlop's verbal teachings and classification in Edinburgh are by far the most rational. Numbers of patients vary their therapeutic status so frequently as to lend themselves to a descriptive diabetic terminology. Further, when one has to deal with the teaching of students whose home language is not English, a descriptive terminology is essential.

For practical purposes, patients are either 'insulin-dependent' or 'insulin-independent'. To signify age connotations, if this is considered necessary, we say that they are either 'young' (up to 35 years at onset), 'middle-aged' (35 – 60 years at onset), or 'elderly' (over 60 years at onset). Thus patients are 'insulin-independent young diabetics'[36]—a group to whom we drew attention because of their ability to go through pregnancy without insulin; or they are 'insulin-dependent elderly', or 'insulin-independent middle-aged diabetics'. Nothing could be simpler, and we have done away completely with code names and other meaningless tags. In other contexts, patients can be called 'acromegalic insulin-dependent', or 'pancreatic insulin-dependent diabetics'. Thus not only students, but other people like surgeons, can understand what we are talking about. One cannot help feeling, and I have said it in many papers, that the adoption of such descriptive and simple terminology would contribute much to doing away with the great confusion of thought that exists in the field of tropical diabetes today.

ii. The course of pregnancy. In 1961 I put forward the concept of the 'insulin-independent young' diabetic[36] on the grounds of certain Zulu and Natal Indians, who were diabetic when they fell pregnant, and who went through pregnancy without needing insulin—without becoming ketotic when pregnant, even though not on insulin.

We combined lately with the Cape Town workers[37] to describe the outcome of 40 patients treated throughout pregnancy with the sulphonylurea drugs, and to compare them with 50 control patients. The disproportionately high incidence of perinatal mortality seen in patients treated with the sulphonylurea drugs, as compared with control patients on diet alone or diet and insulin, was almost totally due to the use of chlorpropamide—especially in doses of 500 mg. daily, and in elderly patients. There was no difference in perinatal mortality in the tolbutamide-treated and control series. Chlorpropamide is contraindicated in the treatment of insulin-dependent young diabetics during pregnancy. In view of the modern tendency to treat pregnant, latent diabetics with a sulphonylurea, this observation is of importance.

iii. Surgery in Natal Indian diabetics. We have always marvelled at the remarkably low mortality rate in our diabetic patients, especially in view of the fact that the hospital is so busy as to preclude close liaison between diabetic clinic and surgical staff. Naidoo, working in the clinic, has just studied surgical records in diabetic patients. He believes, on the basis of studying 96 Natal Indian surgical diabetics, that the middle-aged patient can undergo major surgical procedures without any pre-operative diabetic control. He believes that better postoperative diabetic control will contribute to better wound healing and less sepsis. Mortality is seldom due to the diabetes in these cases, with the exception of the fact that renal failure was the cause of death in one-third of the 9 who died; they may have been partly diabetic.

iv. Clinical studies of vascular disease in the Zulus and Natal Indians. Our findings in Zulus and Natal Indian diabetics in regard to vascular disease are:

(*a*) Regardless of standards of diabetic 'control' (staggered blood-sugar levels on treatment), vascular disease is very much more common in Natal Indian diabetics of the same duration of clinical diabetes,[37] as shown in Table VIII.

TABLE VIII. INCIDENCE OF DIABETIC VASCULAR DISEASE IN 133 ZULUS[1] AND 207 NATAL INDIANS[21]

Group	*Zulus*	*Natal Indians*
Patients who had had 'diabetes' for over 5 years (%)	19·5	15·9
Coronary disease (%)	Nil	1·5*
Diabetic retinopathy (%)	9·0	26·6
Diabetic nephropathy (diabetic retinopathy, albuminuria, hypertension) (%)	1·0	15·5
Cerebral vascular disease (%)	2·0	6·0
Peripheral vascular disease	0·5	9·2

*We believe this to be unduly low.

Certainly there would be good grounds for believing, from this study, that the tendency towards developing diabetic vascular disease can be linked to an ethnic background: previously, we thought that this might be a genetic factor, but (see below) we now believe that *exogenous* factors may also play a part in the genesis of specific diabetic angiopathy.

(*b*) The presence or speed of development of diabetic angiopathy in the Natal Indian bears no relationship to how long the patient has been aware of having had clinical diabetes.[33]

(*c*) That specific diabetic angiopathy (retinopathy, or in a few cases, nephropathy) may not uncommonly precede the clinical diabetic state in the Natal Indian. Patients present at the eye clinic with dimness of vision owing to retinopathy, associated with an albuminuria and absence of glycosuria. This is now being seen in the Zulus.

(*d*) In the Natal Indian specific diabetic angiopathy can be seen proceeding speedily to a fatal outcome, without the patient ever having had ketones in his urine. Thus ketosis is by no means a necessary prerequisite of severe and lethal diabetic vascular disease.

(*e*) Diabetic retinopathy is more common and advanced in Natal Indians who have been treated with insulin,[38] especially if this insulin has been unnecessary. Furthermore the progression of diabetic retinopathy or nephropathy may be particularly rapid, at the same time as the patient responds satisfactorily to sulphonylureas *or diguanides*!

(*f*) Diabetes can present as non-specific vascular disease in the Natal Indian. We showed before[33] that the unfortunately common myocardial infarction in the young Natal Indian male is seldom seen in patients who, if not diabetic, have not a strong family history of diabetes—for instance having both parents diabetic. Thus Vallance Owen and Ashton's recent observations[39] are most interesting in the light of my observation of 2 years ago, made upon purely clinical grounds in Natal Indians. They have shown that in an unselected series of cases of myocardial infarction, there is a much higher proportion of cases with increased antagonism to insulin associated with their plasma albumin—a similar state that obtains in 'essential' diabetics, prediabetics, or the consanguineous relations of diabetics. They believe that it is reasonable to say that many cases of myocardial infarction are constituted as essential diabetics, although they rarely show carbohydrate intolerance. McKechnie and Davidson[40] recently studied 95 Natal Indian patients who had had a myocardial infarction. In an earlier screening survey 50 were found to have unequivocal abnormal glucose-tolerance tests (53%). In view of later observations on diagnosis of diabetes in Natal Indians, they retested a number of patients, and with more critical evaluation of some of the borderline cases, arrived at a final figure of 63 of the 95 having positive glucose-tolerance tests—giving a final figure of 66% being diabetic. In the majority of these cases the condition was not known to patient or doctor. These figures are eloquent evidence to the thesis that diabetes can present as non-specific vascular disease.

(*g*) The predominantly higher incidence of vascular disease in Natal Indian diabetics is clearly reflected in marked differences in certain blood constituents in Zulu and Natal Indian diabetics and control groups (see below).[37]

(*h*) It has been suggested that the Natal Indian may be suffering from a form of 'steroid diabetes'. The speed of development of vascular disease is very reminiscent of the progression of diabetic retinopathy in diabetic cats induced by Lukens and his co-workers[41] with varying doses of corticotrophin.

(*i*) Where in the past, in Zulu diabetics, specific vascular disease came on generally after some years of clinical diabetes, a very recent survey in our clinic has shown that, not only are Zulu diabetics now presenting with established retinopathy when they first present for treatment, but we have recently seen 2 cases of established nephropathy (diabetic retinopathy, hypertension, and heavy albuminuria) in Zulu diabetics presenting for the first time with symptoms of diabetes. Indeed one patient presented with uraemia and a uraemic pericarditis and with thirst and polyuria at the same time. This is a very different pattern from what obtained even 5 years ago.

For some years, therefore, on the basis of our studies in African and Asian diabetics, we have been very sceptical, like other workers, of the thesis that vascular disease is a 'complication' of diabetes—it is plainly an integral part of the disease. Further, it has been easy for us to show that the presence of progression of diabetic angiopathy bears no relationship to the duration of the syndrome of clinical 'diabetes'. In addition, it is abundantly evident that ketosis or 'poor control' is not necessarily a prerequisite or concomitant feature of severe, common and advancing diabetic vascular disease.

2. Postmortem and Histological Studies

i. Postmortem studies. Unfortunately, we are gravely restricted in obtaining postmortems in the Natal Indian people because of religious convictions, and we regard this as being a severe hiatus in our diabetic studies. We have had postmortem studies in a few African diabetics, but the numbers have been too small for significant comment. In the few cases that we have seen, undiagnosed nephropathy of the Kimmelstiel Wilson variety was a good deal commoner than we found clinically.

ii. Endometrial histology in postmenopausal Natal Indian diabetics. Quinlan,[42] who has been working in our clinic for the past year, had been investigating oestrogenization in postmenopausal diabetics with particular attention to a comparison between endometrial histology in diabetics and non-diabetics, and the correlation of these appearances with the vaginal histological picture.

He finds that there is indeed the picture of hyperoestrogenism in 130 such postmenopausal Natal Indian diabetics as compared with controls. The cornification index of the vaginal histology correlates well with the endometrial picture. In view of the obvious difficulty in assuring that the control group are in fact non-diabetic, all patients in his series have been proven diabetic or non-diabetic by means of the 100 G. glucose-screening test.

3. Laboratory Studies

i. Diagnosis of diabetes. The remarkable differences in percentages of positive results to postprandial urine tests and positive postprandial glucose levels in the blood accentuate the fact that screening tests that are not primarily based upon postprandial blood-sugar levels are valueless and even misleading. It will achieve little in screening a group of Natal Indian people to perform glucose-tolerance tests on only those that have a postprandial glycosuria. In the survey of non-diabetic tuberculosis patients noted above, the highest 2-hour level in the 100 G. test without glycosuria was 380 mg. per 100 ml. In McKechnie's study[38] his highest level in the 2-hour test without glycosuria was 480 mg. per 100 ml. It is obvious under these circumstances that if postprandial glycosuria is relied upon to choose patients on whom later to perform glucose-tolerance tests, then large numbers of diabetics will be missed. It is also wise to remember that fasting blood-sugar levels in recently diagnosed or undisclosed diabetics are generally normal and frequently strikingly low.

It is particularly important to realize, when using the simplified 100 G. 2-hour glucose-screening test, that Natal Indians can respond with very high levels at 1 hour, showing a significant glycosuria, and yet at 2 hours have normal levels (less than 140 mg. per 100 ml.). Though we have not surveyed enough full (½, 1, 1½ and 2 hour) 100 G. glucose-tolerance tests on these people, we now advise insurance offices to augment the earlier test with 2-hour levels only by taking extra blood at least at one hour. If this is over 190 mg. per 100 ml. the patient can be regarded as being a diabetic, even if the 2-hour figure is less than 140 mg. per 100 ml. We are not content to regard such a response as benign, especially since these people invariably have a family history of diabetes. Once again, we refer to the most modern view[9] that the 'lag' curve is a latent diabetic phenomenon.

The more we see of the results of screening tests in the Natal Indians, the more, in the light of modern views, do we subscribe to the observation that if a Natal Indian has sugar in his urine he is almost certainly a diabetic (or latent diabetic). It would appear, further, that many Natal Indian diabetics do not develop glycosuria till a much later stage of the diabetic syndrome as compared with other races, because of an already high, or rising, renal threshold to sugar.

In regard to the diagnosis of diabetes in African people, the course of the disorder can be regarded as being rather more like that seen in Europeans, with patients presenting with normal renal thresholds, and with the classical symptoms of polyuria and thirst. However, we have recently been rather surprised, in screening a small series of African women, to find cases of undisclosed diabetics by virtue of a high renal threshold. Thus it would appear highly likely that the diabetic syndrome in previously poor and underfed people, in whom standards of living rise rapidly, has changing methods of presentation and diagnosis, the longer they are exposed to these higher standards.

ii. Studies of blood components in Natal Indian and Zulu diabetics and controls.[37] In view of the remarkable apparent discrepancy between the incidence of vascular disease in Natal Indian and Zulu diabetics, a study of certain blood components in the 2 groups (total 178 diabetics) and controls was carried out. These included estimations of plasma fibrinolytic activity, plasma fibrin, serum mucoproteins, serum total lipids, and serum-cholesterol levels. The results are summarized below (the original paper should be referred to for actual detailed results and statistical evaluation):

There were no significant sex differences in mean plasma-fibrin levels between males and females in each of the control and diabetic groups. Mean plasma-fibrin levels of Indian male diabetics and Zulu male and female diabetics were higher than respective controls. None of the differences in serum-mucoprotein levels in the different groups reached the 5% level of significance. The highest serum total lipid levels were among the female Natal Indian diabetics, and these were higher than the mean level of all the other groups. The mean serum total lipid level of the male Natal Indian diabetics was greater than that of control Indians. In serum-cholesterol levels the only significant difference was between Indian and Zulu diabetic males. There was no difference in euglobulin-lysis time (ELT) between Zulu male and female diabetics, in contrast to the Natal Indian diabetics in whom the females had longer ELTs than the males. ELTs

were also longer in Indian male diabetics than in either male or female Zulu diabetics, and ELTs were longer in Natal Indian diabetics of both sexes than in Zulu male and female diabetics. In the male and female Natal Indian diabetics a long ELT tended to be associated with a high serum total lipid level. In the same male and female diabetics high serum total lipid levels were associated with high cholesterol levels, an association that was not found in Zulu diabetics or in either of the control groups.

Thus it would appear highly likely, on the basis of this study of blood components in 2 diabetic groups of differing ethnic origin in whom standards of diabetic control was equally 'bad' if judged by random blood sugars, that control had nothing to do with the incidence of vascular disease, and it appeared highly likely that the development of vascular disease might be a diabetic phenomenon peculiar to certain races. As far as I know no such other comparison of ethnically pure diabetic populations exists.

TREATMENT

Our findings as regards treatment are summarized below. Fortunately, less than 4% of our total patients are truly dependent upon insulin, and we have thus used oral therapy on a very large scale. The numbers quoted are the latest figures available of patients who have been at least 3 months on the particular drug.

1. Criteria of Control

We have set out the following criteria of control, having regard to the time available for handling our patients, the shortage of staff, and the circumstances which obtain in a clinic handling large numbers of uneducated patients.[44]

i. Excellent: Completely asymptomatic. Urine always free of sugar on treatment.

ii. Good. Completely asymptomatic. Occasional (even heavy) glycosuria.

iii. Fair. Not completely asymptomatic, but greatly improved. Postprandial glycosuria probably invariable. Weight still higher than when treatment was begun.

iv. Poor. Symptoms not relieved at all, heavy glycosuria constant, further weight loss.

In assessing response to treatment, we have noted in both African and Indian diabetics that there is frequently delayed response to therapy. In India, for instance, some workers will persist with treatment even for 3 months without apparent improvement before they say that the patient has failed primarily to respond to treatment. It is our practice to augment therapy much earlier in order to relieve symptoms—the paramount aim in treating uneducated diabetics.

2. Diet

Dietary control, except in intelligent or fully-employed patients, is difficult. In the majority of Natal Indian females (our commonest patients) we have been able to achieve little more than to have substituted saccharine for sugar, since few can afford non-carbohydrate foods. In patients who are able or willing to accept dietary measures, results are very good. Treatment by diet alone is the chief cause of default from the clinic, since most of our patients expect drug treatment.

3. Insulin

As stated above, less than 4% of our total series of patients are truly dependent upon insulin. In such patients, lente insulin is the preparation of choice, because of its convenience. Fortunately, insulin dosage need not be very precise, and good control from a practical point of view can be obtained with standard doses in multiples of 20 units (20, 40, 60, 80 and rarely 100 units). An invariable finding in these non-White diabetics on insulin that we may see for the first time is: the larger the dose of insulin, the less likely the patient is to need it. Patients truly dependent upon insulin seldom need more than 40 - 60 units and frequently very much less. In the last 300 new Natal Indian patients registered, only 3 needed insulin, and in the last 300 Zulus only 4.

4. The Sulphonylurea Drugs

i. Metahexamide. This drug proved satisfactory and effective in 86 Natal Indian patients in a 5-month trial. Unfortunately, we encountered certain severe side-effects, which necessitated our stopping its use.[45]

ii. Tolbutamide. This drug has been used more widely than any other. Its use in 1,575 patients (325 Zulus and 1,250 Natal Indians) has been surveyed and a primary resistance found in 144 (over 8%)—a figure somewhat better than those reported in the Northern Hemisphere.[46] In Zulus primary resistance was found in 12%, and excluding those who had been on insulin, 8%. In Natal Indians primary resistance was found in 8%, and excluding those who had been on insulin, 6·5%. Thus this drug has had a good record, and has been remarkably free of side-effects.

iii. Chlorpropamide. In a world-wide survey of oral treatment in tropical countries,[47] it was found that workers using this drug can be divided into 2 groups: firstly, those with very large experience,[44,48] including ourselves, who are extremely cautious about the use of the drug, and secondly, those with little experience, who believe that it is still the drug of choice in tropical diabetics.[49] It has a half-life of 35 hours and thus cumulative effects can occur. Now that the effective and non-toxic agent acetohexamide is available with a half-life of 24 hours, we feel that the value of chlorpropamide has been diminished. We regard chlorpropamide as having been valuable as a strong hypoglycaemic agent during the search for a substance that combines its effectiveness with the absence of side-effects of tolbutamide. Acetohexamide would appear to fit the bill. In very overcrowded clinics the intervals between visits must be made as long as possible to try to reduce the numbers attending. Thus standards of supervision must fall. Though severe reactions with chlorpropamide have not been common, they have been so strikingly dangerous in certain instances as to make us uncomfortable with its use in a large clinic such as ours.[75] In the last 1,200 new diabetics registered we have only put 42 on chlorpropamide and we are beginning to regard as its only indication the patient who is resistant to or nauseated by acetohexamide. Chlorpropamide is not indicated in women of childbearing age because of the high perinatal mortality rate reported.[27] All workers in our clinic feel that chlorpropamide has outlived its usefulness. Cosnett,[50] of Pietermaritzburg, has never been really happy about this drug, and with his earlier fears we now concur.

iv. Acetohexamide. We have analysed the use of this drug in 60 patients who had been treated for over 18 months (47 Natal Indians and 13 Zulus). The drug is as

strong a hypoglycaemic agent as chlorpropamide and, as stated above, has a much shorter half-life (24 hours)—something that would tend to militate against cumulative effects. We have found it remarkably effective and remarkably free of side-effects.[51] Two patients became nauseated with the drug and had to be taken off it. We have not had any skin or liver damage as described in our experience with chlorpropamide.[75] In the 60 cases reviewed, only 4 appeared to have primary resistance.

v. Ba - 28,616 (N'-p-toluenesulphonyl-N"-beta-nitrophenylethylurea). This drug was assessed in careful ward studies on 5 non-White patients and was found to be devoid of hypoglycaemic action. All subsequently responded well to other sulphonylureas.

5. The Diguanides

i. Metformin (dimethyl diguanide). 108 patients were treated, of whom 78 (51 Natal Indian and 27 Zulus) were included in this survey. In 51 Natal Indians, mostly on combined therapy with other oral agents in a trial lasting up to 1 year, only 12 can be said to have had a very good response to the addition of metformin. In 18 moderate improvement was noted and in 21 the metformin had no effect whatsoever. In 27 Zulus 6 did really well with added metformin, 10 moderately well, and 11 showed no benefit. Side-effects were not encountered. Metformin alone or in combination with other drugs was disappointing.[52]

ii. Phenformin. We reported earlier on a small trial of this drug[53] in 18 patients, but since then have used it on a wide scale. In the earlier survey we found that there was a definite place for the use of this drug in combination with insulin or sulphonylurea in our non-White diabetics. It could not be substituted for insulin in patients who became ketotic when insulin was withdrawn. Side-effects were negligible.

6. Anorectic Agents

i. Ba - 18, 189. (1-(B-hydroxy-ethyl)-2-diphenyl-methyl-piperidine hydrochloride). In view of the effects of carbohydrate intake upon islet cell function and because of the sudden deterioration in vascular disease that we have noted with the use of the hypoglycaemic agents, we are beginning to feel that anorectic agents might play a larger part in the treatment of our type of diabetic who is unable to diet. It is difficult to control a trial of this nature especially if patients are being treated with one of the sulphonylureas at the same time, because most of our patients on these drugs tend to gain weight and this has to be taken into account when assessing the effect of an anorectic. We used the drug in 156 patients.[54] Of these only 98 attended regularly enough to be included in the final survey. 62 control patients were chosen at random, being new patients and people who had been attending. These control patients on sulphonylureas gained an average of 6·2 lb. during the trial period of 10 weeks. In the 98 patients on trial, where results were corrected, there was a statistically significant weight loss of 6·0% of body weight over the mean time of 10 weeks of the trial. We are now embarking on trials of other anorectic agents—most of which are unfortunately expensive drugs.

7. Salicylates

McKechnie[55] embarked upon a short trial of salicylates. This trial was complicated by the large number of pills that the patients had to carry away. Control improved significantly in few cases, and the trial was discontinued, especially in view of the commonness of peptic ulcers among Natal Indian people.

In conclusion, even though we know that patients take their saccharine and anorectic drugs regularly, we must ask ourselves critically when dealing with working-class and often illiterate diabetics, whether they do take their hypoglycaemic drugs or not? We have ample 'grape-vine' evidence that a flourishing drug black market in Durban is supported by our Hospital, of which the oral antidiabetic agents play a paramount role. Indeed, this market was thrown into confusion when we started our acetohexamide trial, because the tablet is yellow and shaped like a vaginal pessary. They were apparently refused quotation on the market until our using them for some months stamped them with respectability, and their status is now equal to the other sulphonylureas. Some patients are being suspected of withholding treatment and taking extra carbohydrate before a clinic visit so as to be maintained on the largest possible dosage. Under the advice and guidance of Dr. L. P. Naidoo (Research Fellow in our clinic), who is probably slightly harder of heart than earlier workers, we have systematically halved the dose of sulphonylurea of every attender in the last 4 months who was not on combined therapy, and it will be interesting to see the effect of this, both on our patients and on the black market!

FUTURE WORK AMONG NON-WHITE DIABETICS IN NATAL

1. Public Health Aspects and the Prevention of Diabetes

The public health accent in the world today in diabetes is chiefly upon detection drives. I believe that we have done enough work in our diabetes study group in Durban to establish that diabetes is assuming epidemic proportions in the Natal Indians. Furthermore, the syndrome is an ominous one in many ways, being characterized by the absence of classical symptoms because of a high renal threshold and early onset of lethal vascular disease. Thus it is not surprising that patients can present with established vascular disease and albuminuria when they first seek treatment for diabetes. In other words, they lack the 'alarm' symptoms that bring the patient earlier to his doctor in other races. On the grounds of the surveys noted above, we believe that further work upon diabetes detection is of academic interest only. Earlier detection may bring earlier treatment, but we have found that this may actually be harmful. Where in postprandial glucose studies in the urine only 188 out of 4,973 Natal Indians were positive to 'tes-tape' (glucose oxidase strip), 2 blood-sugar surveys shown above have shown that in certain sections of the Natal Indian people over one-third of the adults have blood-sugar levels compatible with diabetes. Regardless of further detection drives, we believe that urgent steps on a large scale are indicated to halt the spread of this disease. It is almost certain that genetic factors have been completely outweighed by environmental factors as regards the emergence of diabetes in the Natal Indians.

The first practical measure that can be taken is to advise the relatives of known diabetics to try to restrict their carbohydrate intakes. This is something that the patient can understand. If we succeed in this, it will certainly facilitate our endeavours to spread propaganda throughout the Natal Indian people as a whole, especially the upper and middle social groups. It would appear likely that the Natal Indians have reached the remarkable genetic state where it is not nearly so important to try to restrict consanguineous marriages, even in diabetic families. Cer-

tainly, at present, the Muslims, with their intermarriage customs, have only slightly higher rates of family histories of diabetes. In one survey noted above (the Tongaat Mill Barracks survey) it was shown that if economic circumstances are equally low, there is no significant difference in diabetic prevalence between those that intermarry and those that do not. Plainly, energies directed towards further detection drives would be far better employed in spreading information about the desirability of diet adjustment.

To give advice of this nature, we must consider what environmental factors may lie behind this large-scale emergence of diabetes. Overfeeding is almost certainly the paramount factor, and it is tempting to couple this with the 'thrifty genotype' hypothesis—the theory that suggests that diabetes is an atavistic adaptation for maintaining blood-sugar levels in time of starvation and food uncertainty.[10] Thus diabetics are fat because they are diabetic, and not diabetic because they are fat. They tend to produce overmuch insulin, which in turn stimulates the appetite so that they can make the most of food that is available in better times. We must not lose sight of the fact that parity may play a part in the emergence of diabetes in *both* parents. Wexler of Cincinnati[56] has shown, for instance, that arterial vascular disease increases *pari passu* in both parents in the experimental rat, according to the number of litters borne. The Natal Indian diabetic has 7 children on the average that reach maturity. Comparable figures from the Addington Hospital for Europeans in Durban shows that the average diabetic's family consists of between 2 and 3 children.[57] Earlier we embarked upon an extensive parity study in Natal Indian women. When we saw the results of screening surveys mentioned above, we realized that the most time-consuming part of this study would be to establish that our control series were in fact non-diabetics. Shortage of staff and facilities have made this impossible, and this study has been shelved. However, we believe that it is still desirable that Natal Indian diabetics should restrict their families. Having married young, they frequently have 5 children before the age of 23, with low foetal wastage. Many are anxious for sterilization, but this is not feasible. One wonders if the answer might not lie in the teams sent out in India to sterilize males—some of these actually sterilize 1,400 men in a day.

Ajgaonkar of Bombay[16] believes that the Natal Indians eat too much and work too little. Certainly the total *per capita* food intake (and especially *per capita* sugar intake) is vastly greater in Natal than in India. Unfortunately, sugar is very cheap in Natal and is available in large quantities to even the poorest. As noted above, 2 years ago I suggested that n-allyl-isothiocyanate (mustard oil) might have been an 'oral diabetogen' by means of thiol-blocking action.[18] Butterfield[19] found that it increased food intake in the rat by 30% as compared with controls. Thus it might have a non-specific action. It is almost as if the mustard oil has reproduced the labile insulin supply in the 'thrifty genotype'.[10]

In many instances diabetes is an illness of well-being. In an unpublished survey of the world-wide incidence of diabetes and the *per capita* sugar consumption in various countries from our clinic, certain interesting facts emerge: In those countries in the tropics (with very few exceptions), where annual *per capita* intake of sugar in all forms is less than 30 kg., diabetes is 'uncommon'.[58] Where the intake is over 30 kg. diabetes is 'common'. This survey was done by listing all tropical countries where diabetes was described as 'common',[58] and averaging out *per capita* sugar intake. This was 40·6 kg. (figures from the International Sugar Year Book[17]). In countries where diabetes is 'uncommon' the average intake is 14·3 kg. These figures may be paralleled by many other environmental factors. However, there are many instances where (1) either the sugar intake has increased greatly in the last 2 decades (Red Indians,[59] Maoris,[60] Icelanders,[61] Eskimos,[62,63,67]) or (2) people have migrated from low to high sugar consumption areas (Yemeni Jews,[14] Kurds,[64] rural Zulus,[1] Natal Indians), where incidences of diabetes have been found not only to equal those of Westernized countries, but also, in certain racial groups, to exceed them. It is palpably unwise to strain the 'thrifty genotype' mechanism by overloading it with sugar!

The moral would appear to be to try to limit the intake of sugar in all its forms if we want to cut down the emergence of diabetes in Natal Indians or in other people in whom diabetes is becoming very common. Pure sugar would be the easiest to campaign against, since it is so readily replaceable by sweetening agents such as saccharine, or the 'sweeter' sodium cyclamate. The sales of mustard oil are falling off,[65] but again, this represents a move towards 'Westernized' diets with liberal intake of sugar. The problem of the diabetic explosion in the Natal Indian people has assumed such proportions that it should be tackled at a State level.

As regards the Zulu people, it would be quite impossible to restrict the high intake of purified carbohydrate foods in the towns. Though traditional meat eaters until the disastrous cattle rinderpest 70 years ago, urbanization and the efficient advertising of the sugar distributors have made them into sugar addicts.

In the context of rising consumption of sugar, one cannot help recalling a comment made in the discussion at the 1963 Nutrition Congress in Durban:

'. . . indeed, faced as we are with the overproduction and maldistribution of sugar supplies in the world today, I would go so far as to say that those of us living in the so-called socially-advanced countries are in very real danger of being turned, rather like Lot's wife, into pillars of sugar!'[44]

2. Future Plans

Our most fruitful field in academic research will be the study of the children of our numerous connubial diabetic pairs. Certainly, they must present the finest ground for the study of latent diabetes in the world, for if the geneticists are right, all of them must be diabetics one day if they live long enough and if their environment is right. Studies on these people would include serial routine and augmented glucose-tolerance tests, serial studies of plasma-insulin levels, serial electron microscopy of basement membranes, and further work upon lipid constituents of the blood. For these studies outside help will be necessary. We are pleased that we have now a consultant ophthalmologist in our clinic. The brittle vascular tree of the Natal Indian diabetics make them an ideal group to study the effects of treatment (whether bad or good) on the retinal and renal vessels. After all, the object of treating diabetics is to try to halt the progression of vascular disease which exists in some form in every one of them regardless of duration of clinical 'diabetes'. Unfortunately our paramount aim in our patients is to relieve symptoms. If we do not do this, the patient will pass from

supervision. If, however, we find that treatment significantly aggravates vascular disease in these people, then it will be difficult to correlate our objectives.

However interesting these academic studies may sound, they are now, in my opinion, completely secondary to an energetic campaign to try to adjust the dietary habits of the whole Natal Indian people, and we intend to embark on the organization of such a programme as soon as possible.

SUMMARY AND CONCLUSIONS

1. There is an inordinately high prevalence of diabetes mellitus among the Natal Indian people—probably the highest in the world in any racial group of significant size. Diabetes is infinitely more common in Indians in Natal than in India.

2. Diabetes would appear to be far more common among urban-dwelling than in rural-dwelling Zulus.

3. The main difference in the diets between the Natal Indian and his cousin in India, and between the urban and the rural Zulu, is in respect of sugar intake, which we hold to be the most important aetiological factor in the emergence of diabetes in the Natal Indian and the urban Zulu.

4. In these and other populations where diabetes has been a concomitant or result of speedy increase of social and economic standards, the disorder, even in thin, young people, has been almost exclusively an insulin-independent form of diabetes. This is accentuated by the fact that diabetic girls can go through pregnancy without insulin, and Natal Indians survive even major surgery when diabetic without insulin. Thus we have made extensive use of the oral antidiabetic agents.

5. There is a remarkable difference in the incidence of vascular disease in diabetics of similar 'duration' of diabetes in the Zulu and Natal Indians, the Indians having a very much higher incidence of lethal diabetic vascular disease. This observation supports the contention that the presence of diabetic vascular disease may be an ethnic phenomenon.

6. If 'control' of diabetes can be defined as maintaining blood-sugar levels between certain extremes, then it is obviously unlikely, on the basis of this study upon 2 pure ethnic groups, that such 'control' bears any relationship whatsoever to the emergence or progression of vascular disease in diabetics. More retinopathy has actually been seen in patients who had been treated with insulin, especially when its use was unnecessary.

7. The presence or progression of diabetic vascular disease is frequently believed to be a function of the duration of the disease. On the basis of this study this is patently not so. Vascular disease is an integral part of the disease, in other words, 'complications' do not exist in the diabetic vascular context. Indeed, we begin to believe that *exogenous* factors apart from therapeutic antidiabetic substances may be capable of modifying the course of diabetic vascular disease. Thus diabetes may present at an unusually early age in Natal Indians as non-specific vascular disease, e.g. as a myocardial infarction.

8. Genetic studies upon our prevalence surveys in the Natal Indians would suggest that the genetic component of diabetes is now completely subservient to environmental factors. Indeed, in attempting to halt the spread of this disease, there is fairly good reason for not needing to advise against consanguineous marriages.

9. We believe that urgent propaganda measures are indicated on a wide scale to halt the epidemic of diabetes in the Natal Indian people; especially should we warn against the intake of sugar, since there is now good evidence for giving this warning.

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