

DIABETES PREVALENCE AND
RELATED FACTORS IN A NATAL
NORTH COAST TOWN

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A Thesis

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For My Mother and Father

" The work is not yours to
finish but neither are you
free to take no part in it "

Rabbi Tarphon.
Ethics of the Fathers
Chapter 2, Verse 21.

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-----TABLE OF CONTENTS-----

<u>Part 1. INTRODUCTION TO STUDY</u>	Page
1. <u>Background To Study</u>	1
(i) General Introduction	1
(ii) Diabetes And Indians In Natal	1
(iii) Reasons For Study	3
(iv) Brief Outline Of Study	5
2. <u>Tongaat</u>	7
(i) History of Tongaat	7
(ii) Tongaat Today	9
(iii) Representativeness of Tongaat	11
(iv) Demographic Aspects	19
 <u>Part 2. METHODOLOGY</u>	
3. <u>Detailed Program of Study</u>	26
(i) Prevalence Survey	26
(ii) Repeat G.T.T. And Other Investigations	27
4. <u>Sampling Technique And Screening Methods</u>	29
(i) Scope of Survey	29
(ii) Screening Criteria	23
(iii) First Survey	24
(iv) Second Survey	27
(v) Method Of First Survey	29
(vi) Method of Second Survey	42
(vii) Difficulties	43

	Page
5. <u>Biochemical Investigations And Diagnostic Criteria</u>	46
(1) Glucose	46
(ii) Insulin	52
(iii) Non-esterified Fatty Acids	53
6. <u>Clinical Investigations And Diagnostic Criteria</u>	55
(1) Body Weight	55
(ii) Ischaemic Heart Disease	55
(iii) Diabetic Retinopathy	56
(iv) Peripheral Vascular Disease	57
(v) Peripheral Neuritis	58
 <u>PART 3. RESULTS AND DISCUSSION</u>	
7. <u>Recovery of Positive Screens</u>	59
(1) First Survey	59
(ii) Second Survey	60
8. <u>Diabetes Prevalence</u>	63
(1) First Survey	63
(ii) Second Survey	64
(iii) Composite Survey	67
(iv) Comparative Diabetes Prevalence	68
(v) Prevalence By Differing Criteria	93
(vi) Prevalence By Age-dependent Criteria	96
(vii) Prevalence By Screen Criterion	99
9. <u>Glycosuria Prevalence</u>	101
(1) First Survey	101
(ii) Second Survey	101
(iii) Composite Survey	103

	Page
9. <u>Glycosuria Prevalence</u> (cont.)	
(iv) Glycosuria And Diabetes Prevalences Compared	105
(v) Comparative Glycosuria Prevalence	107
(vi) Application to Future Surveys	109
10. <u>Sex Influence On Diabetes and Glycosuria Prevalences</u>	112
(i) Diabetes Prevalence	113
(ii) Glycosuria Prevalence	116
11. <u>Glycosuria/Glycaemia Relationships</u>	123
(i) Glycosuria Aetiology	123
(ii) Diabetic Glycosuria By Age	128
(iii) Diabetic Glycosuria By Glycosuria Degree	129
(iv) Glycosuric Plasma Glucose Distribution by Glycosuria Degree	129
(v) Glycosuric Plasma Glucose Distribution by Age	132
(vi) Non-Diabetic Glycosuria Prevalence	134
12. <u>Influence of Age, Sex and Body Weight on Screen <u>PLASMA GLUCOSE PROFILES</u></u>	136
(i) Age and Sex	136
(ii) Genetic Applications	147
(iii) Body Weight	152
13. <u>Sensitivity and Specificity</u>	155
(i) Plasma Glucose Screening	156
(ii) Glycosuria Screening	160
(iii) Plasma Glucose vs. Glycosuria Screening	163

	<u>Page</u>
14. <u>Predictability and Reproducibility</u>	167
(1) Predictability	167
(ii) Reproducibility	174
(iii) Diurnal Variation	177
15. <u>Glucose, Insulin and Non-esterified Fatty Acid Relationships</u>	180
(1) Introduction	180
(ii) Statistical Considerations	181
(iii) Age Influence on Newly-Diagnosed Diabetics	184
(iv) Age Influence on Positive Screenings with Normal G.T.T.	191
(v) Influence of Obesity	194
16. <u>Clinical Aspects</u>	201
(1) Age/Sex Distribution of Diabetics	201
(ii) Known/Unknown Diabetes Ratio	202
(iii) Diabetic Disease	203

PART 4. SUMMARY

17. <u>Summary</u>	210
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STATISTICAL APPENDIX

BIBLIOGRAPHY

----- TABLES -----

	<u>Page</u>
1. Monthly p.c. Protein Consumption, Tongaat and Durban	17
2. Monthly p.c. Fat Consumption, Tongaat & Durban	17
3. Monthly p.c. Vegetable Consumption, Tongaat and Durban	18
4. Age/Sex Distribution of Both Survey Populations	19
5. Comparison of Age Structure of Natal, Durban - Pinetown, Inanda - Lower Tugela and Tongaat - Verulam Indian Populations by Decade of Age - All Ages	21
6. Comparison of Age Structure of the First and Second Survey Populations with that of the Populations of Natal, Durban-Pinetown, Inanda-Lower Tugela and Tongaat-Verulam	23
7. Residential Composition of Three Socio-Economic Groups.	33
8. Total Number of Available Houses, Houses Yielding "Screenees" and Total Population in Each Area	34
9. First Survey - "screenee" yield	37
10. Second Survey - Number of Houses in Each Zone	37
11. Second Survey - "Screenee" Yield	38
12. G.T.T. Diagnostic Criteria - Other Centres	49
13. First Survey : Recovery of Positive "Screenees "	59
14. Distribution of Screen Plasma Glucose Values in 21 Untested Positive "Screenees" - Hyperglycaemics	60
15. Second Survey : Recovery of Positive "Screenees "	61
16. Distribution of Screen Plasma Glucose Values in 13 Untested Positive "Screenees" - Hyperglycaemics	61
17. Diabetes Prevalence by Decade of Age (Both Sexes) 1st Survey	64

	<u>Page</u>
18. Diabetes Prevalence by Decade of Age (Both Sexes)- 2nd Survey	65
19. Total Diabetes Prevalence by Decade of Age (Both Sexes)	67
20. Diabetes Prevalence in Tongaat by Decade of Age - Birmingham Criteria	77
21. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Birmingham criteria	80
22. Diabetes Prevalence in Tongaat by Decade of Age - Bedford Criterion	81
23. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Bedford Criterion	82
24. Percentage Abnormality in Tongaat by Age Group (H.E.S. Grouping)	86
25. Percentage Abnormality - Tongaat (2 hour criterion) vs. H.E.S. (1 hour criterion)	87
26. Tongaat Diabetes Prevalence by Decade of Age - Sudbury Age Grouping	89
27. Direct Method of Calculation of Total Diabetes Prevalence for Standardised (Sudbury) Tongaat Population	89
28. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Bedford Criterion, Ages 20 Years and Above	90
29. Comparison of Age Structure of Tongaat and Mamelodi Surveys	91
30. Different Diagnostic Criteria Applied to Tongaat Data	94
31. Age-Dependent Tongaat 2-Hour Criteria	97
32. Hyperglycaemia Prevalence by Age-Dependent 2-Hour Criterion	97

	<u>PAGE</u>
33. Total Diabetes Prevalence by Decade of Age Diagnosed by Single 2-Hour Criterion	99
34. Glycosuria Prevalence by Decade of Age (Both Sexes) 1st Survey	101
35. Glycosuria Prevalence by Decade of Age (Both Sexes) 2nd Survey	102
36. Total Glycosuria Prevalence by Decade of Age (Both Sexes)	104
37. Prevalence of Glycosuria vs. Diabetes by Decade of Age - Total Survey	105
38. 80th Percentile of One Hour Blood Glucose (mg./100ml.) for Persons Challenged within 4 Hours of Eating by Age and Sex	113
39. Total Diabetes Prevalence by Age and Sex	114
40. Known Diabetes Prevalence by Age and Sex	115
41. Newly-Diagnosed Diabetes Prevalence by Age and Sex	116
42. Total Glycosuria Prevalence by Age and Sex	116
43. Glycosuria Prevalence by Screen Plasma Glucose Level Male vs. Female	119
44. Significance between Male-Female Total Glycosuria Prevalence by Plasma Glucose Grouping	121
45. Glycosuria Aetiology - 1st Survey	124
46. Glycosuria Aetiology - 2nd Survey	124
47. Glycosuria Aetiology - Composite Survey	124
48. Diabetic Glycosuria by Age	128
49. Glycosuria Degree & Diabetes Probability	129
50. Glycosuric Diabetes Prevalence by Glycosuria Degree Screen Criterion vs. G.T.T. Criteria	131
51. Mean Screen Plasma Glucose Value by Age and Sex	141
51A. Non-Diabetic Glycosuria by Age	134
52. Mean Screen Plasma Glucose Value for Non-Diabetics by Age and Sex	145

	<u>PAGE</u>
53. Diabetes Prevalence by Percent Deviation of Average Weight	152
54. Diabetes Prevalence in Non-Obese and Obese Screenees	153
55. Diabetes Probability by Screen Plasma Glucose	156
56. Accumulative Number Diabetic and Non-Diabetic by Plasma Glucose Screening Level	158
57. Sensitivity and Specificity by Plasma Glucose Level	157a
58. Diabetes Probability by Glycosuria Degree	161
59. Accumulative Number Diabetic and Non-Diabetic by Glycosuria Degree	161
60. Sensitivity and Specificity by Glycosuria Degree	162
61. Sensitivity of Plasma Glucose & Glycosuria Screening at Identical Levels of Specificity	163
62. Afternoon (screen) vs. Morning (G.T.T.) 2 Hour Plasma Glucose Value	178
63. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Response during G.T.T. In Newly-Diagnosed Non-Ketosis Prone Diabetics by Age	188
64. Glucose, Insulin and N.E.F.A. Response in Newly-Diagnosed Non-Ketosis Prone Untreated 10-29 Year Old Diabetics	190
65. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Response during G.T.T. in Positive Screenees with Normal Glucose Tolerance	193
66. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Differences in Positive Screenees with Normal Glucose Tolerance by Weight Category	197
67. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Differences in Newly-Diagnosed Diabetics by Weight Category	200
68. Cardiac Ischaemia in Discovered Diabetics by Age	206
69. Cardiac Ischaemia in Discovered Diabetics by Sex	207
70. Diabetes Prevalence in Total Discovered Ischaemics by Sex	208

----- FIGURES -----

	<u>PAGES</u>
1. Geographical Situation of Tongaat	9
2. Age Distribution of Natal, Durban-Pinetown, Inanda-Lower Tugela and Tongaat-Verulam Populations - All ages	22
3. Age Distribution of 1st & 2nd Survey Populations compared with Populations of Natal, Durban-Pinetown, Inanda-Lower Tugela & Tongaat-Verulam, 1st Decade of Age excluded	24
4. Diagram of Tongaat, Urban & Rural	30
5. Urban Tongaat	31
6. Diabetes Prevalence by Decade of Age, 1st Survey vs. 2nd Survey	66
7. Total Diabetes Prevalence by Decade of Age	68
8. Comparison of Current Age Structure of Tongaat and English/Welsh Populations	79
9. Age-Adjusted Tongaat Diabetes Prevalences compared with Current Estimates of Prevalence for General Population of England & Wales	83
10. Screen Plasma Glucose Frequency Distribution - Tongaat vs. Hamelodi	92
11. Total Tongaat Diabetes Prevalence - Application of other Diagnostic Criteria	95
12. Diabetes Prevalence by Decade of Age - Screen Criteria vs. G.T.T. Criteria	100
13. Glycosuria Prevalence by Decade of Age - 1st Survey vs. 2nd Survey	103
14. Total Glycosuria Prevalence by Decade of Age - Both Sexes	104
15. Total Glycosuria Prevalence compared with Diabetes Prevalence by Decade of Age	106
16. Diabetes Prevalence by Age and Sex	114
17. Glycosuria Prevalence by Age and Sex	117

	<u>PAGE</u>
18. Diabetes Prevalence vs. Glycosuria Prevalence in Each Sex by Age Group	118
19. Glycosuria Prevalence by Screen Plasma Glucose Load - Male vs. Female	120
20. Diabetic Glycosuria - Tongaat compared with other Survey Data	126
21. Glycosuric Plasma Glucose Distribution by Degree of Glycosuria	130
22. Glycosuric Plasma Glucose Distribution by Age	133
23. Influence of Age on Screen Plasma Glucose Frequency Distribution - Males	137
24. Influence of Age on Screen Plasma Glucose Frequency Distribution - Females	138
25. Mean Screen Plasma Glucose Value by Age Group : Male vs. Female	140
26. Frequency Distribution of Screen Plasma Glucose : Male vs. Female	142
27. Effect of Age on Screen Plasma Glucose Distribution in Non-Diabetics - Male & Female	144
28. Mean Plasma Glucose Value in Non-Diabetics by Age Group : Male vs. Female	146
29. Sensitivity of Plasma Glucose & Glycosuria Screening at Identical Levels of Specificity	164
30. Fasting Plasma Glucose vs. 1 Hour Plasma Glucose in Discovered Diabetics	168
31. Fasting Plasma Glucose vs. 2 Hour Plasma Glucose in Discovered Diabetics	169
32. Two Hour Plasma Glucose vs. One Hour Plasma Glucose in Discovered Diabetics	170
33. Fasting Plasma Glucose vs. 1 Hour Plasma Glucose in Non-Diabetics	172
34. Fasting Plasma Glucose vs. 2 Hour Plasma Glucose in Non-Diabetics	173

35. Two-Hour Screen Plasma Glucose vs. Two-Hour G.T.T. Glucose in Positive Screenings	175
36. Frequency Distribution of N.E.F.A. in Positive Screenings during G.T.T.	183
37. Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Newly-Diagnosed Untreated Non-Ketosis Prone Diabetics	187
38. Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Positive Screenings with Normal Glucose Tolerance	192
39. Effect of Body Weight on Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Positive Screenings with Normal Glucose Tolerance	196
40. Effect of Body Weight on Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Newly-Diagnosed Diabetics	199
41. Total Number and Sex Distribution of Diabetics by Decade of Age	201
42. Known/Unknown Diabetes Ratio by Age Group	202

PART ONE

INTRODUCTION TO STUDY

BACKGROUND TO STUDY

(1) General Introduction

This study in essence, constitutes an exercise in epidemiology. Diabetes mellitus, in common with other chronic disease states, is of more than academic interest to the epidemiologist. The true prevalence of the disease in any given community is likewise of vital interest to the far-sighted public health administrator. It must influence the planning of public health programs, such as diabetes detection drives, and touch upon such diverse sections of the economy as life insurance and the food industry.

All knowledge of diabetes prevalence stems from an accurately planned and executed population survey. Today, the literature is replete with countless diabetes survey reports, all contributing towards the knowledge of current diabetes prevalence. Obviously the spectrum of individual survey value is extensive, ranging from studies from which only the most limited conclusions can be drawn, to data of real and lasting benefit.

(11) Diabetes and Indians in Natal

With a report by Cosnett in 1957², attention was drawn to various aspects of diabetes in Indians in Natal, South Africa. This worker collated the clinical records of 10,000 Indian in-patients at a Durban hospital and stated that by comparison with hospital admissions in England and

Wales, diabetes was more common in Indians. In 1959, Cosnett³ reviewed the clinical aspects of Indian diabetics.

In 1960, Wood⁴ carried out a glycosuria survey encompassing a 10% sample of a sub-economic housing scheme in Springfield, Durban. Her conclusions were that the prevalence of diabetes for Indians above the ages of 20 years and 30 years, was 5.5% and 8.8% respectively.

Campbell emphasized Cosnett's findings and in a series of publications, ⁵⁻¹² drew attention to many facets of the disease in Indians in Natal. Some of the points made were, firstly that there existed an inordinately high prevalence of diabetes in Indians in Natal, secondly that the vascular component of the disease was especially pernicious and malignant, thirdly that glycosuria per se was indicative of diabetes thus rendering blood tests unnecessary, and fourthly that true insulin-dependence was extremely rare.

Other workers studied patterns of serum lipid and fibrinolytic activity in Indian and African diabetics,¹³ relationships between hyperuricaemia and abnormal carbohydrate metabolism,¹⁴ and the incidence of diabetes in a small group of Indians with coronary artery disease.

Small surveys of special limited groups of Indians have been made in the Transvaal, mostly by Walker and Seftel and their colleagues^{15,17} which have indicated the presence of

a high frequency of diabetes in these groups.

The author has not seen fit to include at this stage the many milestone studies relating to diabetes prevalence in other parts of the world and concerning various other peoples. These important works will be discussed in context where valuable comparisons and conclusions can be drawn.

(iii) Reasons For Study

Most of the cited publications emphasized a high prevalence of diabetes in the Indian and certain relationships between glycosuria and diabetes. Yet the only cited prevalence rate was the estimate by Wood. Her survey was confined to adults (20 years and older) and the sample totalled 223 subjects, of whom 12 were designated as being diabetic.

With an Indian population in Natal which in 1960 numbered close to 395,000 persons,¹⁸ and moreover with a population which in general has developed from two roots, Dravidian and Aryan, each with its own cultural and anthropological characteristics,¹⁹ it is speculative to extrapolate a finding from a highly restricted number of subjects (233) to the Indian population of Natal. Furthermore the Indians in Natal can be said to belong to 5 groups on the basis of Indian language spoken, namely the Tamil, Telegu,

Hindi, Gujjerati, and Urdu speakers, and also into 3 groups on the basis of religion, namely Hindu, Muslim and Christian adherents. This fragmentation has not been made with an academic purpose. Any study of a disease such as diabetes where diet plays such an important role in management, and probably plays an important part in aetiology, all factors tending to differentiate a people into distinct socio-economic groups must be taken into careful consideration.

Thus Wood's findings can only apply to the sub-economic housing scheme where the survey was carried out. The findings cannot be extrapolated to provide a prevalence rate for the total Indian population of Natal. For any survey amongst Indians to carry any validity for such extrapolation, careful assessment of the representativeness of the survey population is required.

The only other prevalence survey which was reported, was a glycosuria survey by Batchelor and Campbell.¹¹ Here some attempt at language grouping was made, but the age structure of the survey population does not resemble that of the general Indian population. Blood glucose studies were not undertaken and thus diabetes prevalence could only be estimated albeit with caution.

In view then of the oft-repeated statement that diabetes was highly prevalent in Indians in Natal, substantiated by

very limited studies, the necessity for an objective diabetes prevalence survey was obvious. Such a survey would provide valuable information regarding glycosuria/glycaemia relationships, the influence of sex and obesity, and constitute a careful inquiry into some of the current concepts concerning diabetes in Indians in Natal.

(iv) Brief Outline of Study

Aspects of diabetes in Indians in Natal have been studied and the plan of investigation can be outlined as follows:

- (a) Tongaat, a Natal northcoast town was selected to be the centre of a diabetes prevalence survey.
- (b) A sample population of 2,427 Indians living in and around Tongaat, was subjected to an oral glucose challenge. All suspect diabetics (positive screenings) had a 50 G oral glucose tolerance test (G.T.T.) with coincident immuno-reactive insulin (I.R.I.) and non-esterified fatty acid (N.E.F.A.) determination, in the fasting state and at one and two hours after glucose ingestion.
- (c) All positive screenings underwent clinical examination to determine the incidence and degree of "diabetic disease" in the newly-diagnosed diabetics.

- (d) A socio-economic survey and a dietetic survey were carried out under the author's surveillance by two workers, in the Tongaat area. The object of these investigations was to assess the representativeness of Indians in Tongaat in comparison with Indians in Durban and Natal.

CHAPTER 2

TONGAAT

It would not be inappropriate to devote a few pages to the history of Tongaat and its present status. Its selection and the representativeness of its Indian population are crucial to some of the conclusions of this study.

(1) History of Tongaat

As with many similar Natal towns, Tongaat's origins, development and existence are inextricably bound up with the advent of the sugar cane farmers. The name is derived from the Tongaat river which runs to the Indian ocean some 20 miles north-east of Durban. For centuries the land alongside the river was known as the Tongaat.

In 1848, a Cape Town merchant Edward Lorenzo Chiappini, was allocated a farm in the Tongaat. Soon he realised that the presence of an experienced sugar cane farmer was essential and as a result, a certain James Renault Saunders of Mauritius became manager of the Tongaat Estate in October 1854.

In 1859, the Legislative Council of the Colony of Natal gave powers to the Government of Natal to introduce labourers from India to work in the sugar cane fields.

The first indentured Indian immigrant-labourers arrived in Natal in November 1860.

These immigrants went to work in various sugar cane estates in Natal, and Saunders employed 52 men. These Indians constituted the kernel for the growth of the present-day Indian population of Tongaat.

In 1930, Tongaat consisted of a little village which housed Indians and Africans, largely all employees of the Tongaat Sugar Company (T.S.C.) which had succeeded the Tongaat Estate at the turn of the century. Indian traders and shopkeepers had by this time established themselves.

Malaria, which was endemic, swept the north coast in 1930, and ravaged unchecked amongst the villages. On the advice of A.E. Charter, Provincial Secretary of Natal, an ordinance was passed which provided for the establishment of new local authorities, called health committees. The first such health committee was established at Tongaat, and the Provincial Executive invited the T.S.C. to join hands with the Province to combat the epidemic. That point marked the beginning of the liaison between the T.S.C. and the local authority to improve the welfare at the village.

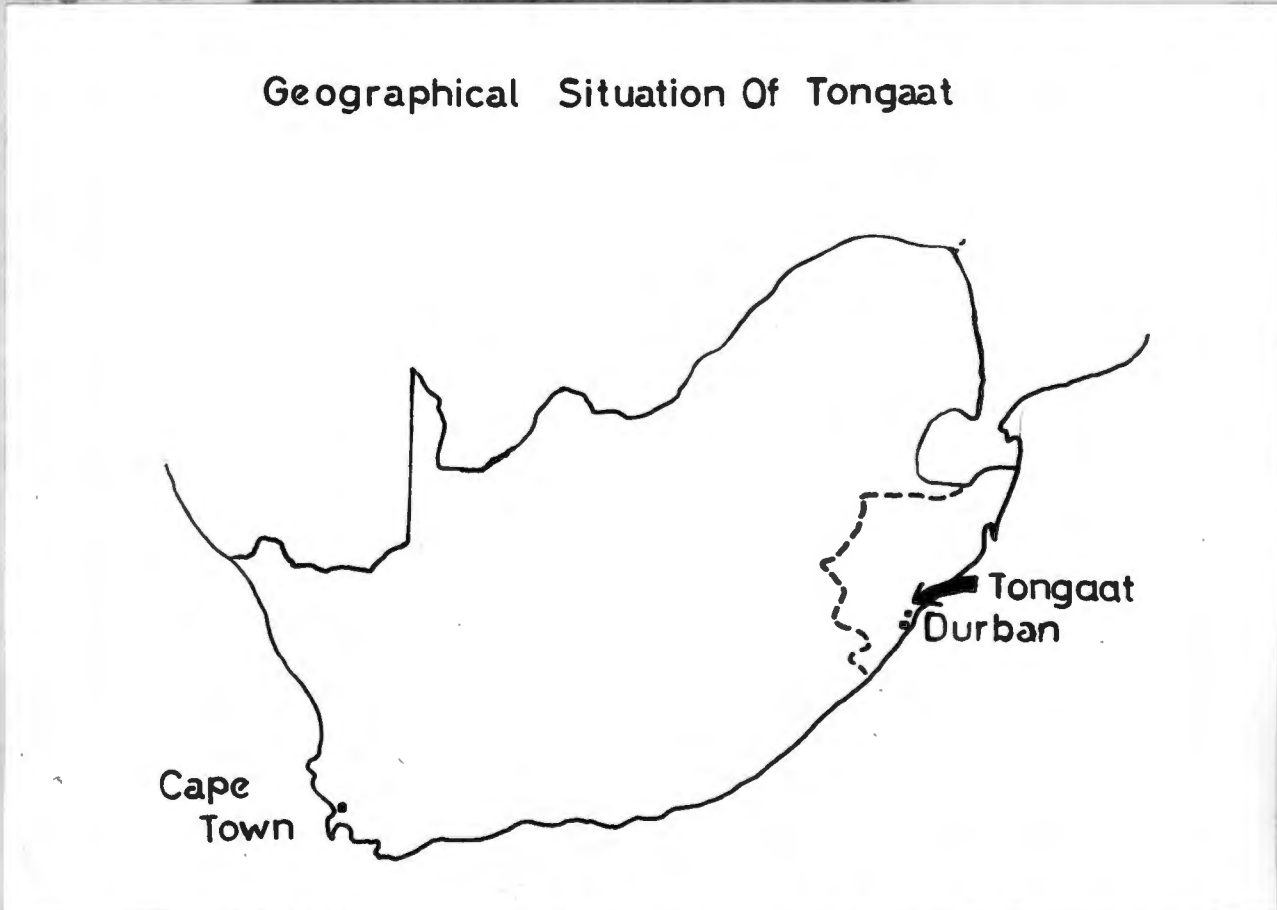
In 1939, the building of a Model Native Village (as it was then called) was commenced by the T.S.C. This sparked off further progress in the housing of Indian

employees. Side by side with the economic expansion of the T.S.C. and the resultant growth of Tongaat, has been the progress of Indian businessmen, shopkeepers, traders and professionals to settle in the town and establish themselves.

(ii) Tongaat Today

Tongaat today stands a thriving town situated about 4 miles inland from the seashore and approximately 20 miles northeast of Durban

Figure 1. Geographical Situation of Tongaat



The total population in 1960 stood at 9051 persons, of which 5,996 were Indians, 2465 were Africans, 573 were whites, and 17 were Coloureds.²⁰ The mean annual rate of

growth of the Indian population has been 2.4% since 1936.²¹ The estimated Indian population of Tongaat in 1965 was thus 6,700 persons.

After Durban, Tongaat is the town with the 3rd largest Indian population, being exceeded only by Pietermaritzburg and Pinetown.

The layout of Tongaat is similar to that of most other Natal towns. The main street forms the growth~~/~~point of all businesses, shops, and other commercial and professional offices. The residential areas fringe this street and spread out a little way on either side, embracing an intersecting system of roads and paths.

Housing in Tongaat consists of privately owned dwellings which flank the main street, as well as numbers of private residential areas where houses are let to families by the Town Board. There are large aggregations of houses ~~and~~ let built and maintained by the T.S.C. for its employees.

A High School and 8 Junior schools cater for the Indian youth; there are 2 Junior schools for Africans and 1 Junior school for the Whites.

The health requirements of Tongaat rest largely upon the Health Clinic which has a full-time medical officer. T.S.C. employees plus dependants make use of their own hospital and out-patient department. There are also several doctors in private practice.

Surrounding the town, in a rural setting are a number

of hamlets (so-called) which house T.S.C. employees with their families. These hamlets are set in the midst of the sugar cane fields and all lie within a ten-mile perimeter of the town. The number of houses in each hamlet varies from 25 to 50. The inhabitants of these hamlets constitute the rural Indian population of the Tongaat area.

(iii) Representative^{ness} of Tongaat

From the brief outline of Tongaat's history and its present day description, it is apparent that Indian arrival and growth in the town has paralleled that of Indians in Natal. Indeed it seemed that the Indian community of Tongaat represented a microcosm of Indian society in Natal. All strata of Indian society, all language, religious, and other socio-economic groupings seemed to be present in Tongaat. Furthermore the choice of the town together with its rural Indians would be included in the survey; 19% of all Indians in Natal live in rural areas¹⁸

During the prevalence survey, two workers, the late Miss Y. Dinath B.A. (Hons.) Witwatersrand and Mrs. E. Newby-Fraser B.A. Soc. Sc. Natal, carried out detailed socio-economic and dietetic surveys of the entire Tongaat area, urban and rural. Both surveys encompassed the local¹⁵ in which the prevalence survey was carried out. A 20% sample of all the houses in the area was drawn, yielding a total of 200 households. A random technique was employed

in that 1 house in every 5 was selected, usually by street number where that was possible. Each house - family was visited by each worker. Miss Dinath carried out the socio-economic survey and Mrs. Newby-Fraser, the dietetic study. Both workers concluded independently, that the Indian population of Tongaat and its environs was representative of Indian society in Natal with particular reference to Durban, which embraces 60% of the total Indian population of Natal. ²⁰

The author is indebted to each worker for permission to quote verbatim a summary of each report.

Socio-Economic Report

In the compilation of her data, Miss Dinath compared the findings in Tongaat with those in Durban, principally because information concerning Indians in Natal as a group, is confined to items such as age and sex structure, and language spoken. Socio-economic aspects more germane to the assessment of the representativeness of the Indians in Tongaat were to be found concerning only Indians in Durban. Miss Dinath's summary is quoted in full to enable the reader to obtain a birds'eye view of Indians in and around Tongaat as compared with Indians in Durban. "In comparing the various socio-economic parameters of the Tongaat and Durban Indian populations, similarities in many factors are found. In summary, the following similarities and dissimilarities were found in the

following structures.

(a) Age Structure:

Both populations display a similar "triangular" structure identical to the Indian population in Natal. Half the population is aged less than 16 years, and a very small proportion falls into the 65 years and older group.

(b) Religious Affiliations:

In both ages, Hindus comprise 70-85%, Muslims 12-15%, and Christians 5-7% of the population.

(c) Family Structure:

The average family density appears to be slightly lower in Tongaat than in Durban, the respective means being 7.5 and 9.0 persons. There are also less joint families in Tongaat than in Durban.

(d) Education:

Comparisons between educational status of Durban and Tongaat Indians are difficult to make because of the differences in the compilation and presentation of our data and that of the census statistics. There appears to be a slightly high percentage of children attending school in Tongaat than in Durban.

(e) Occupation:

For both populations, the percentages of gainfully employed persons (25 - 26%) are practically identical. The percentages of gainfully employed men and women are also virtually identical, approximately 23% and 2.5%

respectively. However as one would expect, there are regional variations in the occupational structures of the two populations. There are higher percentages of farmers and professionals in the Tongaat population as opposed to a higher percentage of artisans in the Durban population. There is a lower proportion of unemployed in Tongaat as compared with Durban.

(f) Employment:

The median Employed/Dependency ratio of 1:3-4 corresponds to the finding of Woods and Kuper *et al*, who found that on the average, a Durban worker had to support himself and 3 - 4 other persons.

(g) Income:

The percentages for four broad categories of income in both populations correspond very closely with slightly higher percentages for the Tongaat population in the two extreme categories. When income and religious groups were correlated, it was found that approximately 70% of Hindu and Christian households, and 51% of Muslim households fall into the "less than R100 per month" category; 16.7% of Muslims fall into the "R200 or more" category with the corresponding figures for Hindus and Christians at 6.6% and 0% respectively. While the Muslim community has the highest income categories, it also has high dependency rates and consequently low ^{per} capita incomes.

Analysing the religious groups according to per capita

incomes, the Hindu group fares the best with its per capita incomes distributed over a wider income range. This corresponds to the findings of Kuper et al, in their analysis of dependency rates for the Durban Indian population.

It can be seen therefore that the Tongaat Indian population closely resembles the Durban Indian population in respect of basic structural factors or parameters. Taking into account the fact that no two societies can be truly comparable since each will have its own cultural "ethos", a resultant of many factors, some of which will be unique to a particular society the similarities outlined above provide sufficient justification for assuming that the Tongaat Indian population is a fair reflection of the Indian population in Durban. "

Dietetic Report.

In contrast to the ready availability of much socio-economic data, there was very little recent information concerning the diet of the Indian in Durban or Natal. Consequently Mrs. Newby-Fraser sampled a representative sector of Durban Indian society. This sector covered the entire socio-economic spectrum, including Tin Town and the Springfield sub-economic housing scheme, and the suburbs of Riverside, Springfield and Asherville.

A summary of the report follows:

(a) Cereal Consumption:

Monthly per capita (p.c.) consumption of basic cereal

foods is closely similar in Tongaat and Durban. The monthly p.c. consumption (lbs.) of 4 widely consumed cereals in Tongaat as compared with Durban is given as follows (the Durban consumption is given in parenthesis):

		plus
Rice	- 5.6 (4.4)	"
Mealie Rice	- 5.3 (5.7)	"
Flour	- 3.3 (2.9)	"
Bread	- 16.8 (15.5)	"

(b) Sugar Consumption:

Sugar consumption in Tongaat was slightly higher than in Durban. Monthly p.c. consumption (lbs.) of sugar^{plus} (direct and indirect) in Tongaat was 6.1 as compared with 5.5 in Durban.

(c) Legumes:

Legumes consist of two main varieties, dried beans and dhol (dried split peas). Dhol is eaten at least once a week in most homes as a frequent accompaniment to curry. Monthly p.c. consumption (lbs) of beans and dhol in Tongaat with the Durban value in parentheses is 0.9 (0.7) and 1.6 (1.3) respectively.

(d) Protein Value:

The average intake of animal protein is low. The overall meat intake is due to the combined influences of poverty, religious teaching and customs.

Hinduism teaches that excessive meat eating retards spiritual development and often affluent Hindu families maintain one or two fleshless days a week. The Hindu is

also forbidden beef and while the Muslim and Christian have no such tabu, little beef is consumed as it is regarded as an inferior meat. In Tongaat and Durban, an identical 2% of the population consists of vegetarians. The following table indicates the close similarity between Tongaat and Durban with respect to protein intake.

Table 1. Monthly p.c. Protein Consumption, Tongaat and Durban

	Monthly p.c. Consumption				
	Milk Pints	Meat lbs.	Fresh Fish lbs.	Tinned Fish lbs.	Eggs No.
Tongaat	10.3	3.9	1.3	1.0	9.9
Durban	8.3	3.8	1.3	0.8	9.1

(e) Fats and Oils

Apart from the fat content of meat and fish, the main sources of fats and oils are in butter, butter-ghee and cooking oils. Ghee is an oil made from clarified butter, but due to its prohibitive price, the majority of the Indians use a locally made substitute, vegetable-ghee. The following table provides the Tongaat - Durban comparison for fats and oils.

Table 2. Monthly p.c. Fat Consumption, Tongaat & Durban

	Monthly p.c. Consumption		
	Butter Butter-ghee (lbs.)	Veg. Ghee (lbs.)	Oils (Btls)
Tongaat	0.9	0.6	1.2
Durban	0.8	0.6	1.6

(f) Vegetables

The three vegetables which are bought regularly by all Indian families are onions, tomatoes and potatoes. They are indispensable in the preparation of different curries. The following table provides Tongaat - Durban comparisons.

Table 3. Monthly p.c. Vegetable Consumption, Tongaat and Durban

	Monthly p.c. Consumption		
	Tomatoes (lbs.)	Onions (lbs.)	Potatoes (lbs.)
Tongaot	2.6	1.7	4.1
Durban	3.0	2.2	3.4

Other vegetables include carrots, beans and peas, but these are bought infrequently and are subject to price and seasonal fluctuations.

This outline concerning p.c. consumption of the important foodstuffs contains sufficient similarities and trends to indicate that the dietetic habits of the Tongaat population is similar to that of Durban



The value of these socio-economic and dietetic observations cannot be overstressed. They serve to indicate that the Tongaat Indian population is reasonably representative of the Durban Indian population. As the Durban Indian population constitutes such a major proportion

of the total Natal Indian population, it is likely that Tongaat's representativeness can be validly extended to the total population.

All too often diabetes surveys of similar communities or areas fail to take such essential observations into consideration and conclusions drawn from the findings are extended to whole peoples or nations. ^{22,23} Such extrapolations are invalid.

(iv) Demographic Aspects:

Though the age structure of the Tongaat population has been briefly mentioned in the socio-economic summary, demographic aspects of this study need detailed analysis to ensure that the sample population is closely identical to the general population with respect to age structure.

The following table indicates the age and sex distributions of both survey populations.

Table 4. Age/Sex Distribution of Both Survey Populations.

1st Survey			Age Group (Years)	2nd Survey		
Male	Female	Total		Male	Female	Total
375	339	714	10 - 19	65	87	152
207	330	537	20 - 29	33	71	104
97	191	288	30 - 39	29	42	71
78	140	218	40 - 49	18	29	47
69	77	146	50 - 59	13	11	24
49	33	82	60 - 69	6	6	12
16	8	24	70+	6	2	8
891	1118	2009	All Ages	170	248	418

It is seen that in both survey populations the sexes are distributed with approximate equality in most decades.

While the survey excluded those persons aged 0 - 9 years, it is important to compare existing age structure data from the Tongaat area which includes this age group, with identival data extending in coverage to include the total Indian population of Natal. Only then can the survey age structure (10 years and above) be used to make similar comparisons.

It is fortunate that comparisons can be made with the total Indian populations of :

- (a) the Tongaat - Verulam region²¹
- (b) The Inanda - Lower Tugela region,²⁴ in which Tongaat is the largest town.
- (c) the Durban - Pinetown area²⁴ which contains the largest number of Indians in Natal.
- (d) Natal (as the province)¹⁸

The value here is that the local area population (Tongaat - Verulam) can be compared with the economic region population (Inanda - Lower Tugela), in turn with the Durban - Pinetown, and total provincial populations. The following table provides the structure of the Indian population by decade of age in each of these 4 areas.

Table 5. Comparison of Age Structure of Natal, Durban-Pinetown, Inanda-Lower Tugela and Tongaat-Verulam Indian Populations By Decade of Age - All Ages

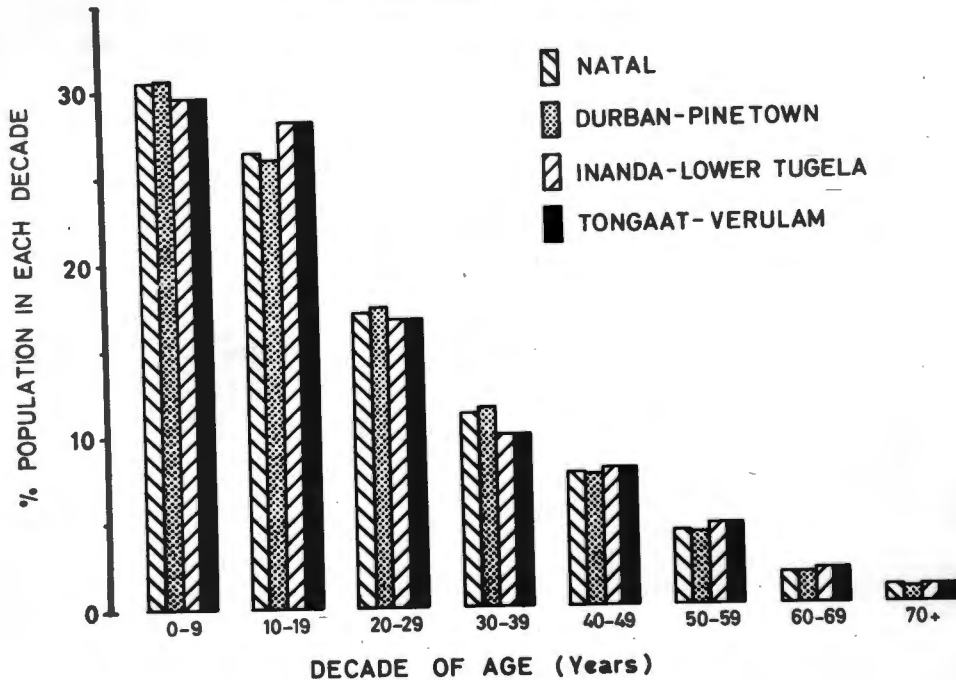
Age Group (Yrs)	Natal		Durban Pinetown		Inanda Lower Tugela		Tongaat Verulam	
	No.	%	No.	%	No.	%	No.	%
0-9	120,447	30.5	72,571	30.6	20,499	29.6	6,846	29.6
10-19	104,304	26.4	61,735	26.0	19,419	28.1	6,486	28.1
20-29	67,625	17.1	41,206	17.4	11,515	16.7	3,486	16.7
30-39	44,248	11.2	27,401	11.5	6,915	10.0	2,311	10.0
40-49	30,221	7.7	18,129	7.6	5,467	7.9	1,827	7.9
50-59	16,935	4.3	9,005	4.2	3,271	4.7	1,093	4.7
60-69	7,195	1.8	4,219	1.8	1,381	2.0	460	2.0
70 +	3,869	1.0	2,100	0.9	690	1.0	230	1.0
All Ages	394,854	100.0	237,246	100.0	69,157	100.0	23,099	100.0

It is readily apparent that the Tongaat-Verulam population is closely comparable to that of its surrounding populations in respect of age structure. This is best illustrated by means of the following figure.

Figure 2. Age Distribution of Natal, Durban-Pinetown, Inanda-Lower Tugela and Tongaat-Verulam Populations - All Ages

AGE DISTRIBUTION OF NATAL, DURBAN-PINETOWN, INANDA -
LOWER TUGELA, & TONGAAT-VERULAM POPULATIONS

ALL DECADES INCLUDED



Now that the local area population has been demonstrated to be very representative for all age groups, the actual survey populations can be compared in similar fashion. As the survey excluded the age group 0-9 years, this group must be excluded from populations considered for comparison. Percentage population in each decade must thus be calculated from the lesser total and must change accordingly. The following table indicates the age structure of both survey populations and compares it with that of the other population groups.

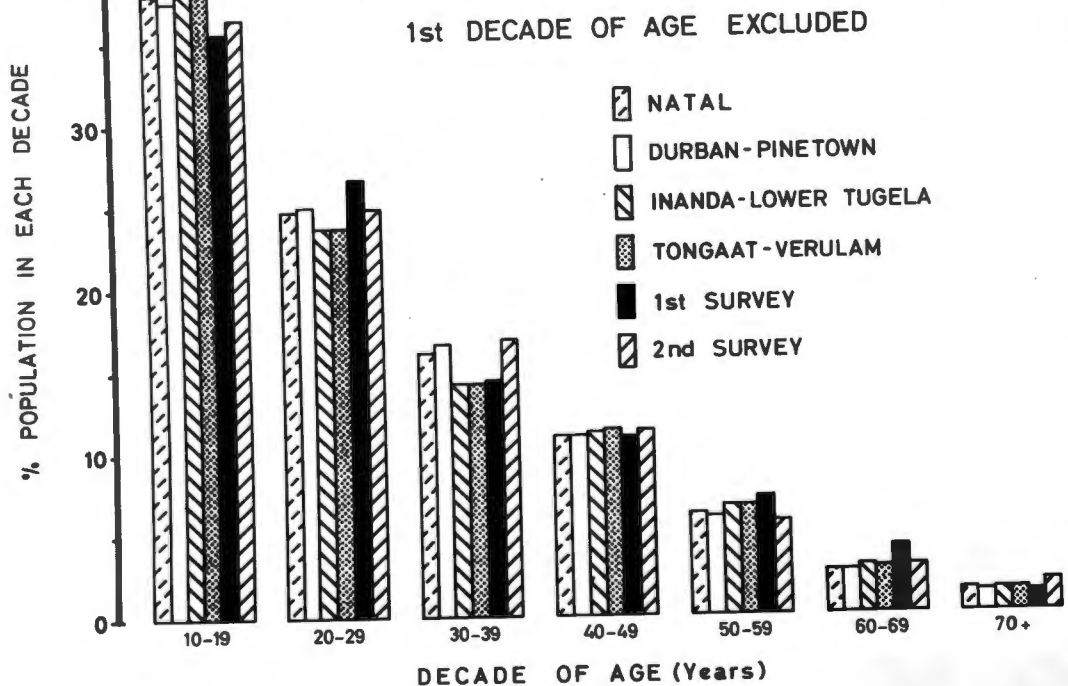
Table 6. Comparison of Age Structure of the First and Second Survey Populations with that of the Populations of Natal, Durban-Pinetown, Inanda-Lower Tugela and Tongaat - Verulam

Age Group (Years)	Natal		Durban-Pinetown		Inanda - Lower Tugela		Tongaat-Verulam		1st Survey		2nd Survey	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
10-19	104,304	38.0	61,735	37.5	19,419	39.9	6,486	39.9	714	35.5	152	36.4
20-29	67,625	24.7	41,206	25.0	11,515	23.7	3,846	23.7	537	26.7	104	24.9
30-39	44,258	16.1	27,401	16.6	6,915	14.2	2,311	14.2	288	14.4	71	16.9
40-49	30,221	11.0	18,129	11.0	5,467	11.2	1,827	11.3	218	10.9	47	11.3
50-59	16,935	6.2	9,885	6.0	3,271	6.7	1,093	6.7	146	7.2	24	5.7
60-69	7,195	2.6	4,219	2.6	1,381	2.9	460	2.8	82	4.1	12	2.9
70 plus	3,869	1.4	2,100	1.3	690	1.4	230	1.4	24	1.2	8	1.9
ALL AGES	274,407	100.0	164,675	100.0	48,658	100.0	16,253	100.0	2,009	100.0	418	100.0

It is obvious that the age structure of both survey populations mirrors that of the local area population, the economic region population, the metropolitan and provincial populations. The following figure illustrates this comparison

Figure 3. Age Distribution of 1st & 2nd Survey Populations Compared with Populations of Natal, Durban-Pinetown, Inanda-Lower Tugela & Tongaat-Verulam - 1st decade of age excluded.

AGE DISTRIBUTION OF 1st & 2nd SURVEY POPULATIONS COMPARED WITH POPULATIONS OF NATAL, DURBAN-PINETOWN, INANDA-LOWER TUGELA, & TONGAAT-VERULAM.



As diabetes is more common in the elderly, these comparisons are vital if a valid prevalence rate for the survey population is to be expressed. That both survey populations are closely similar to populations drawn from various populous areas in Natal, some extrapolation of survey conclusions may be permitted to Indians in Natal as a whole. The author would nonetheless stress that any such extrapolation must needs be interpreted with caution.

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PART TWO

METHODOLOGY

----- CHAPTER 3 -----

DETAILED PROGRAM OF STUDY

As outlined previously the study took the form of a diabetes prevalence survey followed by retesting (G.T.T.) of all positive screenings.

(1) Prevalence Survey:

A total of 2427 Indians aged 10 years and above, of both sexes, were given an oral 50 G glucose challenge. Venous blood and urine were collected two hours later. Prior fasting was not insisted upon. At the time of close ingestion each screening's height and weight were measured.

These 2427 persons were screened in 2 subsurveys (hereafter called 1st Survey and 2nd Survey) which covered the entire Tongaat area, urban and rural with the exception of a small urban housing estate of thirty houses (Gandhi Nagar).

The precise sampling technique and survey methodology is detailed in the following chapter.

All blood samples were transported to Durban where plasma glucose concentration of each sample was determined by a standardised technique. All urine samples were tested immediately for the presence of glucose.

All glycosurias and all screenings whose plasma glucose equalled or exceeded 120 mg./100 ml. were designated positive screenings. Initially 110 mg./100 ml. constituted the screen

criterion but was discarded in favour of 120 mg./100 ml. when on retesting it became obvious that less than 5% of all screenings with values between 110 mg./100 ml. and 119 mg./100 ml. proved to be diabetic.

(11) Repeat G.T.T. And Other Investigations

All positive screenings underwent standard 50 G G.T.T. with venous sampling at 30 minute intervals for the majority of subjects, and at hourly intervals for a minority. Serum and plasma were separated in the fasting state, and at 1 and 2 hours post-glucose, deepfrozen, and dispatched to Cape Town for I.R.I. and N.E.F.A. determinations. All subjects were rested for a minimum period of 30 minutes prior to G.T.T. Smoking was not permitted.

Shortly after arrival at the clinic where G.T.T. was carried out, homatropine 2%, was dropped onto the bulbar conjunctiva of all subjects, having first assessed the intra-ocular tension clinically and after careful questioning had failed to reveal possible symptoms of glaucoma.

In the intervals between venesection all subjects underwent clinical examination as follows:

1. history of angina pectoris, myocardial infarction, intermittent claudication.
2. resting electrocardiography

3. measurement of blood pressure
4. presence and degree of albuminuria (not pursued further)
5. presence of ankle, knee reflexes
6. presence of peripheral vibration sense and pin-prick sensation
7. presence of pedal pulses (dorsalis pedis, posterior tibial)

Diabetes was diagnosed only by G.T.T. and all discovered diabetics were notified by the author and given a referral letter, detailing the G.T.T. results. Each diabetic was advised to attend either the Diabetes Clinic of the King Edward VIII Hospital, Durban, or the Tongaat Health Clinic, or Central Hospital, or a practitioner of their choice.

----- CHAPTER 4 -----

SAMPLING TECHNIQUE AND SCREENING METHODS

(1) Scope of Survey

The total survey comprised of 2 separate surveys.

The 1st survey was confined to the inhabitants of T.S.C. houses, urban and rural, as well as the occupants of 2 Tongaat Town Board housing estates. In this survey, every house was visited to obtain screenings. There was no sampling.

The 2nd survey covered the remaining houses of the town. This encompassed all families unassociated with the T.S.C. Sampling by a set pattern of 1 : 3 houses being visited, was adopted.

Figure 4 illustrates the relationship of the rural hamlets to the town.

Figure 4. Diagram of Tongaat, Urban and Rural

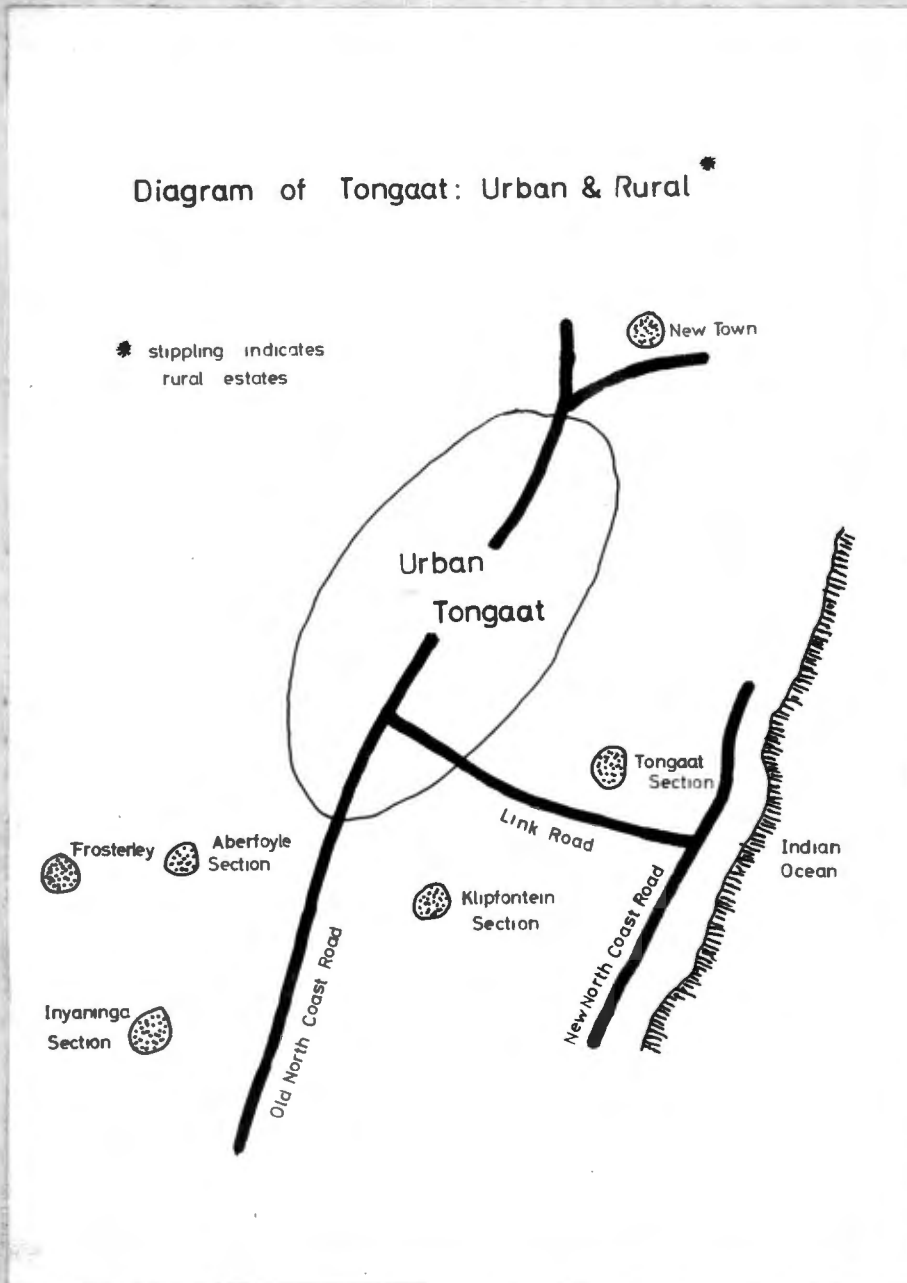
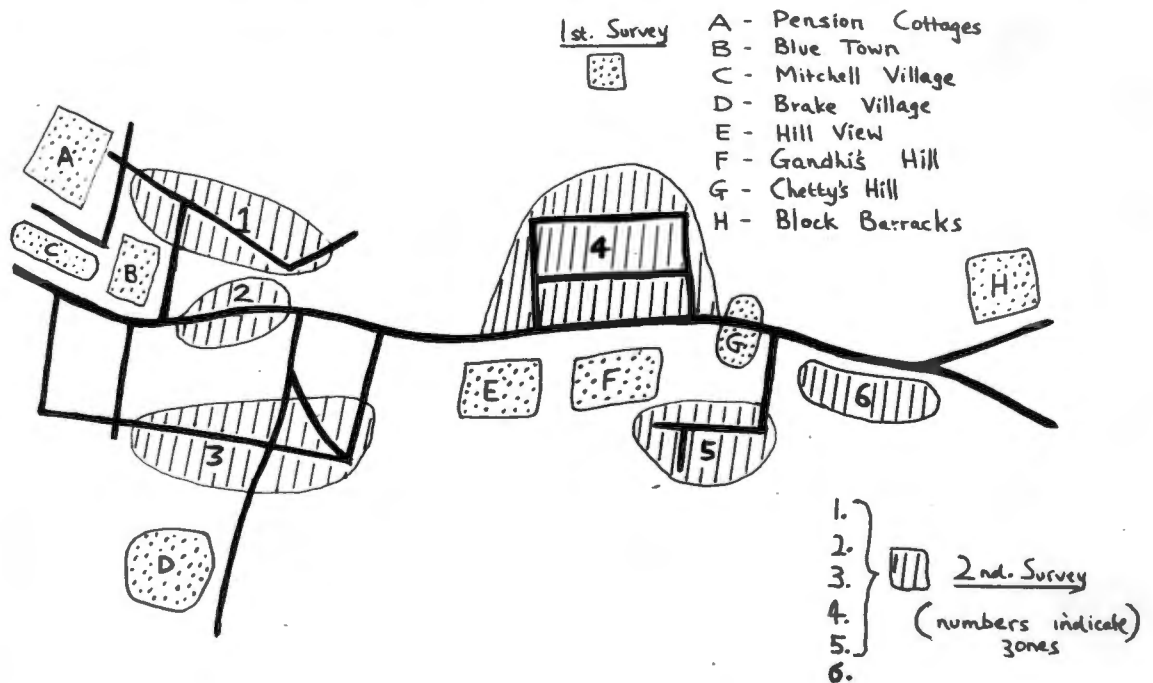


Figure 5 indicates the location of various T.S.C. and Tongaat Town Board Housing Estates in the urban area.

Figure 5. Urban Tongaat

Geographical Distribution Of Houses (Both Surveys)



Reference to these two figures indicates the total housing of the Tongaat area and the areas covered by the 1st and 2nd surveys respectively.

The 1st survey can be described as covering the poorer to middle-income Indians. The occupations of these persons varied from fieldworkers, gardeners, machinists and mechanics to clerks, secretaries, hospital personnel and similar responsible categories. The second survey covered the middle to upper-income groups, the shopkeepers, merchants, teachers, clerks and professional men. As a generalisation the 1st survey covered the less affluent while the 2nd included the more affluent.

Miss Dinath has divided the 1st survey population into 2 groups - rural and urban. She has shown that considering such aspects of p.c. income, items of expenditure, level of education etc., the urban and rural (1st survey) and urban (2nd survey) populations can be grouped as follows :

- 1st Survey - (1. Rural dwellers - Sections
(T.S.C.)
(2. Urban dwellers - Barracks
(T.S.C. & Private)
- 2nd Survey - (3. Urban dwellers - Village
(Private)

Degree of affluence, p.c. income, level of education and other socio-economic parameters, are graduated from the

Sections, through the Barracks, to the Village (these terms being those of Miss Dinath).

The following table indicates the residential composition of each group. Reference to figures 4 and 5 will provide the reader with the approximate geographical situation of each residential area. The number of households interviewed in each area by Miss Dinath, and Mrs. Newby-Fraser is indicated in parentheses.

Table 7. Residential Composition of Three Socio-Economic

<u>GROUPS</u> (no. of households)				
<u>Village</u>		<u>Barracks</u>		<u>Sections</u>
Tongaat Village (3+)		Gandhi's Hill)		Klipfontein)
Fairbreeze (5)		Chetty's Hill)	(37)	Inyaninga)
Hoodsburg (8)		Hill View	(11)	New Town (9)
Gandhi Nagar (7)		Pension Cottages(9)		Block Barracks (13)
Mitchell Village(9)		Brake Village (15)		Tongaat S. (10)
Blue Town (13)				Aberfoyle)
				Frosterley) (10)

(ii) Screening Criteria :

In both surveys, screening criteria were identical and were as follows :

1. All persons aged 10 years and above
2. Both sexes
3. Inclusion of all known diabetics

(111) First Survey

The scope of this survey has been described.

Date of commencement : 2.6.65

Date of completion : 22.9.65

Total number screened : 2009

This survey encompassed the inhabitants of 14 separate housing estates of which all but 2 were T.S.C. establishments. These 2 were Blue Town and Mitchell Village. Figure 4 illustrates the relative positions of the rural estates, while figure 5 indicates the locality of the urban estates.

The total number of houses in these 14 estates was 720 of which 556 yielded screenings. The total population living in these houses was 4112 persons. Table 8 provides a detailed analysis of the population supported in each area.

Table 8. Total Number of Available Houses, Houses yielding Screenings and Total Population in Each Area.

<u>Residential Area</u>	<u>No. Houses yielding Screenings</u>	<u>Total No. Houses</u>	<u>Total Population</u>
Brake Village	52	79	581
Tongast Section	43	50	247
Hill View	28	42	222
Gandhi's Hill(93) Chetty's Hill(64)	157	199	961
Pension Cottages	24	44	148
Blue Town	14	18	102 *
Aberfoyle	27	33	215

<u>Residential Area</u>	<u>No. Houses yielding Screenees</u>	<u>Total No. Houses</u>	<u>Total Population</u>
Mitchell Village	36	42	239 *
Newtown	42	63	330
Inyaninga	25	32	204
Block Barracks	59	67	493
Klipfontein	32	34	256
Frosterley	17	17	114
All Areas	556	720	4112

The population figures in respect of T.S.C. housing estates were supplied by the Company.²⁵ The populations denoted by the asterisk are estimates as no data was available. The total number of houses in each of the two areas was multiplied by 5.7 (being the occupancy rate of the houses in the other 12 areas).

Thus 556 of 720 houses yielded screenees. It is stressed that this figure of 720 houses represents the total number in January 1966, when the above population figures were provided by the T.S.C. The actual survey commenced 7 months earlier and ended in September 1965. The total number of houses (and persons) was considerably less at the time of the survey. The yield of 556 houses represents a recovery of 77.2%

The total population living in these 720 houses numbered 4112 persons. The percentage of the Indian population of the Tongaat-Verulam region (Verulam is a town 7 miles south of Tongaat) which falls into the age group 0-9 years is 30%.²¹ As this group was not included in the survey, the total available population was :

$$\frac{70}{100} \times \frac{4112}{1} = 2878 \text{ persons}$$

As the survey yielded 2009 screenees, the absolute recovery was 70%. As only 77% of the total number of houses yielded screenees, it is probable that a similar percentage of persons were not living in the survey area at the time of the survey. The calculated number of persons available would thus be :

$$\frac{77}{100} \times \frac{2878}{1} = 2216 \text{ persons}$$

During the survey a record was kept of the total number of persons qualifying for the survey, i.e. satisfying the screenee criteria, in the houses, at their places of employment, or at school. This represents a census taken by the author as the survey proceeded. The total number of persons enumerated was 2182 which compares favourably with the calculated number (2216). The following table indicates the survey recovery whatever total available persons, is used

Table 9. First Survey - Screenee Yield.

	<u>Gross No.</u>	<u>Calculated No.</u>	<u>Enumerated No.</u>
Total	2878	2216	2182
Total Screened	2009	2009	2009
Recovery (%)	69.8	90.7	92.1

It is probable that the true recovery lies between 70% and 90%.

(iv) Second Survey :

The scope of this survey has been described

Date of commencement : 11.3.66

Date of completion : 14.4.66

Total Persons Screened : 418

This survey encompassed the inhabitants of the town who were not included in the 1st survey. A survey of the total number of houses in the town in the residential areas excluded by the 1st survey, was undertaken by the author. The number of houses totalled 301 which included 34 flats contained in 6 blocks. The houses followed a natural grouping of 6 zones. The distribution of these zones can be seen in figure 5. The zones are numbered 1-6. Table 10 indicates the total number of houses in each zone.

Table 10. Number of Houses in Each Zone

Zone	1	2	3	4	5	6	Total
No. of Houses	27	138	28	68	25	15	301

It was decided to sample 1 : 3 houses and screen the entire family living in each house thus selected. Thus approximately 100 houses would be visited and thus 100 families screened. The average number of persons per family was estimated to be 7, and the total sample population was expected to be 700 persons. As 30% of the population falls into the first decade of age,²¹ this group must be excluded to provide the total screenable population.

$$\text{Thus } \frac{70}{100} \times \frac{700}{1} = 490 \text{ persons}$$

Working from one end of the town to the other, zone by zone and street by street, a total of 92 houses were visited and these 92 families invited to participate in the survey. Five families refused any participation. The total number of persons contained in these 92 families was 522 persons aged 10 years and above. The following table indicates the survey recovery which was 80%

Table 11. Second Survey - Screenee Yield

	<u>House</u>	<u>Persons</u>
No. Visited	92	522
Total Screened	87	418
Recovery (%)	95	80

The actual number of houses included in the survey (92) compares favourably with the estimate of 100. The actual number of persons available (522) compares likewise with the estimate of 490.

(v) Method of 1st Survey :

It was essential to obtain cooperation with local industry and community leaders. Accordingly an introductory tour was undertaken and valuable rapport established with the T.S.C., high school principal, local doctors, and religious leaders. An introductory letter was circulated amongst the population to be screened, explaining the aims of the survey and inviting the participation of all. Permission was obtained to screen children at the high school, i.e. those children who resided in areas selected for the survey (many children attending the school live outside Tongaat and had to be excluded from the survey).

The most prominent house in a residential area or estate to be screened, or alternatively the house of the local "sirdar" (community leader) was selected as the "local testing centre". All the houses surrounding this centre were visited in turn each afternoon and the name, age and sex of each person living therein, and able to attend for the test the following morning, was recorded. In this way all those persons who in fact were not working in the morning or were not at school, were invited to present themselves for the test which would be carried out at the local testing centre. A record was kept of all persons able to attend. This record could be compared with records of those persons who actually did attend.

The subjects were asked to meet at the local testing centre at 8.00 a.m. the following morning. Prior 12 hour fasting, while stressed, was not insisted upon. That morning a roll-call was taken to ensure that all who were able to attend, were in fact present. The administration of glucose was then carried out as follows:

each subject stepped onto a scale and stood alongside a measuring rod while weight and height were noted; a solution of 50 G glucose in 210 ccs. cold water without flavour additives was swallowed within one minute; a clean urine container was given and the subject instructed :

- (a) to fast and rest until the completion of the test
- (b) to avoid smoking until the completion of the test
- (c) to discard urine after an interval of one hour
- (d) to return in 1½ hour's time with a urine sample passed just prior to departure.

Venesection was carried out exactly 2 hours after glucose ingestion and blood transferred immediately to glass tubes containing sodium fluoride (Na F). Urine was tested for the presence of glucose with the glucose-oxidase paper strip (Testape). Each subject was informed that if the "blood sugar" was raised, a second test would be necessary and if this test was indicative of diabetes, steps would be taken to initiate treatment.

Each afternoon was thus spent in preparing the ground for the following morning's tests.

It is stressed that everyone in a housing estate or suburb able to attend the test was recorded, and energetic attempts were made to test everyone so listed. It is obvious that in such residential areas, the majority of screenees would of necessity be housewives, the elderly or unemployed, men free in the morning as a result of night shift work, and children who were not at school. The men and women at work in the morning and school children were tested at their places of employ and at the high school.

These places of employment of the T.S.C. (urban and Rural) and the high school were visited. Here it was explained that only those persons living in those housing estates/suburbs where screening had taken place or alternatively where future screening was to be carried out, were eligible for the test. This was necessary as a small number of adults at work and children at school, resided outside Tongaat, and thus had to be excluded from the survey.

Thus the author was assured that only those persons whose families had been screened at home, would be tested. The family unit was thus gradually built-up.

All screenees requiring G.T.T. were notified personally. These tests were carried out at the Tongaat Health Clinic.

All diabetics were informed of their disease and given a letter of referral for treatment.

(vi) Method of 2nd Survey

The method of this survey was essentially similar to that of the first. It differed only in one respect. It was carried out in the mid-afternoon - early evening. This was necessary as the working members of the family were in private employment and could only be screened during working hours with the greatest difficulty. Thus the entire family had to be screened in the early evening when the workers were at home. Each mid-afternoon, houses in the selected area (zones 1-6) were visited in strict 1 : 3 order, and entire families invited to present themselves for blood tests the following early evening at 6.00 p.m. Complete records were kept of each family visited, aged 10 years and above. In each area, a prominent house was selected and the local screenees requested to be present at that house at the appointed time.

This survey did not require any testing at the high school, or places of employment. The family unit was thus tested at one full swoop, in contrast to the delayed accumulative method of the first survey. All positive screenees were retested at the Tongaat Health Clinic.

(vii) Difficulties Encountered

The entire survey (1st and 2nd) was remarkably free from any real difficulties. Those that arose were minor and easily circumvented or overcome. These difficulties could be grouped into three categories.

(a) General Population Suspicion

The Indian population of Tongat in common with many similar populations, has scant knowledge and experience of the broader field of preventative medicine. Epidemiological studies and the aims of medical research are largely unknown. The belief that one consults a physician only when one has disease symptoms or signs is widespread. Thus any field study such as the present, which entailed the momentary pain of a venesection, was certain to meet some initial resistance in suspicious or frightened persons. This was indeed encountered and probably accounted for a certain number of screening absentees. The personal approach which was employed continuously, together with the help of local canvassers often overcame such resistance.

(b) Resistance Inadvertently Engendered By Local Medical Practitioners

This was an unexpected problem and resulted from the screening who shunned the test because :

1. misguided loyalty to his personal physician
2. the belief that he could not be diabetic as a result of a negative glycosuria check by a physician
3. the belief that having been found to be anaemic by a physician, his anaemia would be exacerbated or recovery delayed, by parting with the required amount of blood.

(c) Religious Customs and Festivals

This aspect was encountered occasionally. Among the Tamil-speaking Hindus, a young girl having just experienced the menarche, is required to shelter indoors for 9 days during which time she has no communication with males at all. For such a girl to present herself for a blood test would be a serious contravention of tradition and accepted morals.

The end of December 1965 ushered in the commencement of the month of Ramadan when all devout Moslems fast from well before sunrise to sunset each day. Appointments to retest positive screenees of the first survey who were bound up by this observance, had thus to be delayed.

Among all religious groups, there was a general aversion on the part of young mothers having recently given birth, to undergo venesection.

It is emphasized that notwithstanding these stumbling blocks, population response was excellent and enthusiastic,

and resistance was rarely encountered that could not be overcome by personal approach, explanation and reassurance.

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CHAPTER 5

BIOCHEMICAL INVESTIGATIONS AND DIAGNOSTIC

CRITERIA

(1) Glucose Determination

(1) Choice of plasma

All glucose determinations were carried out on venous plasma. The advantage of plasma over whole blood is that differences in haematocrit are avoided. It has been demonstrated that variation in haematocrit, e.g. in anaemic and polycythaemic states, can cause significant variations of whole blood glucose, while plasma glucose concentration in both states is identical. ^{26,27,28}

The degree of anaemia in Indians in Natal is unknown but in any population group, where the frequency of child-bearing is high with poverty in close attendance, anaemia may well be of sufficient prevalence and degree to affect whole blood glucose determination.

The use of venous plasma obviated any such effect.

(2) Anticoagulation and Preservation of Blood

The anticoagulant/preservative used was Na F in a concentration of 10 milligrams (mg.) per millilitre (ml.) whole blood. All blood samples were refrigerated prior to separation of the plasma. Glucose concentration in the plasma was determined within 24-36 hours after venesection.

Kantor and Wilkerson²⁹ have demonstrated that Na F possesses good preservative qualities and that its anti-glycolytic effect is enhanced by lowering of temperature.

(3) Prior Carbohydrate Intake

The diet of the average Indian is largely composed of many varieties of curry which is accompanied by large quantities of rice, white bread, or home-made bread (hand-roti). This consumption ensures that falsely raised glucose values cannot occur due to excessively low or deprived carbohydrate (CHO) intake. Wilkerson et al³⁰ in a study of the effects on the whole blood glucose level of changing the CHO intake from 400 G to 50 G daily, concluded that there was no need for a high CHO diet prior to G.T.T. in a person who presents no history or physical evidence of restricted food intake.

(4) Glucose Load

The survey glucose challenge as well~~s~~ as the G.T.T., employed a 50 G dose of dextrose monohydrate in approximately 210 ml. cold water without flavour additives.

It is realised that the choice of this load is arbitrary. As yet no uniformity in glucose load has been adopted in prevalence work. Glucose load varies from the straightforward 50 G or 100 G, to dosage calculated from body weight either as 1.75 G/kilo ideal body weight or 1.0 G/kilo actual body weight. Proposals that glucose load be determined by

surface area have also been made,³¹

The 50 G load generally causes less nausea than larger amounts,^{32,33} and consequently is more likely to be absorbed normally.³⁴

(5) Method of Glucose Determination

Glucose concentration of the venous plasma was determined on a continuous sampling automated apparatus.* This apparatus employs a modification of the Hoffman method³⁵ of glucose determination for macro quantities.

(6) Diagnostic Criteria

(a) Diabetes Diagnosis

From a consideration of some of the prominent contemporary surveys as well as criteria from established diabetes clinics the following basic criteria were adopted and necessary adjustments made to allow for methodological differences :

1 hour true venous whole blood glucose equalling or exceeding 150 mg./100 ml.

2 hour true venous whole blood glucose equalling or exceeding 110 mg./100 ml.

This choice was an arbitrary one. The following table indicates some of the criteria used to guide the author in his choice.

* Auto-Analyser Technicon Instruments Corporation, Chauncey, New York. U.S.A.

Table 12. G.T.T. Diagnostic Criteria - Other Centres

Centre	Blood	Method	Load(G)	Hourly Criteria mg./100 ml.
Arbroath ³⁶	Venous	Enzymatic	50	0 90 1 2 150 105
Mayo Clinic ³⁷	Venous	Auto-Analyser	1G/Kilo	- 150 110
New York ³⁸	Venous	Auto-Analyser	100	- 150 110
Joslin Clinic ³⁹	Venous	Somogyi-Nelson	100	110 150 120
Fajans & Conn ⁴⁰	Venous	Somogyi-Nelson	1.75G/Kilo	- 160 120

It is seen that the basic criteria adopted for this study are well in keeping with the criteria displayed above. Furthermore the fasting value has been omitted as a diagnostic criterion in three of the above sets of criteria.

In a survey such as the present study as in any similar field study, the subject is under surveillance only from the time he arrives for G.T.T. It is always possible that breakfast or a light snack may have been ingested prior to G.T.T. This information may or may not be divulged by the subject. During the study all subjects were asked leading questions before G.T.T. to ensure that they were in fact, in a fasting state. The author however feels that, in an attempt to please him, some subjects may have consciously broken the prior 12 hour fast, and didn't divulge this information.

While individual fasting values have not been used diagnostically, in the statistical correlates mean fasting

values and other grouped analyses have been used as it is felt that the effect of a few spurious fasting values (negligible as they may well be) would be minimal when included with the vast majority of true fasting values.

O'Sullivan and Kantor,⁴¹ and McDonald⁴² showed the precise relationship between plasma and whole blood glucose. These two reports differed only in degree of relationship.

With the basic criteria adopted namely one hour and two hour values of 150 and 110 mg./100 ml. respectively, the following "escalations" must be made :

<u>Whole Blood</u>		<u>Plasma</u>
<u>1 hour</u> : 150 mg./100 ml.	=	(171 mg./100 ml. (O'Sullivan) or (180 mg./100 ml. (Mc.Donald)
<u>2 hour</u> : 110 mg./100 ml.	=	(125 mg./100 ml. (O'Sullivan) (135 mg./100 ml. (McDonald)

The author has taken the mean for each criterion, namely :

1 hour plasma glucose - 175 mg./100 ml.

2 hour plasma glucose - 130 mg./100 ml.

Glucose determination in this study was carried out by a modification of the Hoffmann method of potassium ferricyanide reduction. This, while providing a very close true glucose content, is not identical with an enzymatic method. Sunderman⁴³ has compared the Hoffmann modification method, with the glucose oxidase method, using the Auto-Analyser (Technicon)

and has found that the latter method averages 7% less than the former. He used venous plasma solely, thus obviating any differences in medium. Values of 150 and 110 mg./100 ml. (enzymatic method) would thus convert to 160 and 117 mg./100 ml. respectively.

To convert the basic criteria of 150 and 110 mg./100 ml. whole venous blood (enzymatic) to those using venous plasma (Heffmann modification), these differences of 10 and 7 mg/100 ml. respectively, must be added onto the calculated values of 175 and 130 mg./100 ml.

The final criteria are thus:

1 hour value > 185 mg./100 ml.

2 hour value > 140 mg./100 ml.

For a diagnosis of diabetes, both criteria must be satisfied; if only one criterion is satisfied the subject is said to be abnormal but not diabetic. It is interesting to note that both Dillon²⁶ and Tustison et al,²⁷ using identical apparatus and methodology of the present study, have suggested venous plasma criteria at one and two hours after glucose ingestion of 185 and 140 mg./100 ml. respectively. Furthermore Seadat in 1967,⁴⁴ with likewise identical methodology, used criteria of 190 and 145 mg./100 ml. respectively.

(b) Glycosuria Diagnosis

All urine samples were tested for the presence and degree of glycosuria, with a glucose oxidase-peroxidase strip. *

* Tes-Tape. Lilly Laboratories, Isando, Transvaal, South Africa

Glycosuria was graded from + to + + + + according to colour change from the original yellow to varying shades of green.

(ii) Insulin Determination

(1) Preparation of Serum

During G.T.T., venous blood in the fasting state and at 1 and 2 hours, was allowed to clot at room temperature. After 2 hours, serum, separated with a centrifuge at 3000 r.p.m. for 30 minutes.

(2) Storage and Transfer to Cape Town

The serum was deepfrozen at -20° C. and despatched to the Cape Town laboratory by air. To ensure that the serum in testtubes arrived at the laboratory in a deep-frozen state, the testtubes were placed in a pre-frozen brine mixture of 10% calcium chloride contained within large vacuum buckets. The average time interval between removing the testtubes from the Tongaat deepfreeze and their arrival in the Cape Town laboratory was 7-8 hours. In every case, serum arrived in a satisfactory condition.

(3) Method of Determination

Serum insulin was determined by a radio-immunoassay method described by Hales and Randle,⁴⁵ incorporating some of Morgan and Lazerow's procedures.^{46,47} The method is described in detail in a data sheet by the Radiochemical Centre, Amersham.⁴⁸

(4) Diagnostic Criteria

It is not proposed to detail specific criteria of abnormality of insulin response during G.T.T. In the course of this thesis where insulin response is discussed, trends will be indicated and some conclusions drawn. It is the author's contention that while insulin is the primary blood glucose lowering factor, diagnostic criteria applicable to the hormone cannot be employed.

Serum insulin concentration is expressed in micro-units per ml. (μ U/ml.)

(iii) Non-Esterified Fatty Acid Determination :

(1) Preparation of Plasma

During G.T.T. venous blood in the fasting state and at 1 and 2 hours, was collected in heparinised tubes at room temperature. Plasma was separated within 20 minutes with a centrifuge spinning at 3000 r.p.m. for 5 minutes.

(2) Storage and Transfer to Cape Town

Plasma was deepfrozen and transferred to the Cape Town laboratory in a manner identical to that of the serum specimens described previously.

(3) Method of Determination

Plasma N.E.F.A. was determined by Trout, Estes Jr., and Friedberg's⁴⁹ modification of the original method of Dole;⁵⁰ certain refinements to the technique were introduced

in the laboratory according to suggestions made by Geday, Aarhus, Denmark.

(4) Diagnostic Criteria

As with serum insulin, it is the author's contention that Plasma N.E.F.A. behaviour during G.T.T. cannot be rigidly defined into normal and abnormal response. Trends of N.E.F.A. response will be indicated and some conclusions drawn.

Plasma N.E.F.A. concentration is expressed in micro Equiv. per mL. (μ Equiv./mL.)

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CHAPTER 6

CLINICAL INVESTIGATIONS AND CRITERIA

(i) Body Weight

Weights (Kg.) and heights (cm.) of all subjects were measured using a standard centimetre measuring rod and a spring scale. All subjects removed heavy articles of outer clothing prior to measurement. Average weight of each subject was calculated from a consideration of the subject's sex, age and height. The tables used in this calculation are those of Documents Geigy, 6th Ed.,⁵¹ where all weights are inclusive of indoor clothing.

Actual weight was compared with average weight. Normal weight was defined when the actual weight did not exceed or fall short of 15% of the average weight. When the actual weight exceeded or fell short of these limits, overweight or underweight was denoted.

(ii) Ischaemic Heart Disease

All positive screens were questioned as to a history of angina pectoris and/or myocardial infarction. Answers were interpreted according to the recommendations of Rose.⁵² In addition all positive screens underwent resting 12 lead E.C.G. with a direct writing instrument at a paper speed of 25 mm./second. The majority of E.C.G.'s were recorded before glucose ingestion, the remainder being

recorded between 1 and 2 hours post glucose. Ostrander and Weinstein⁵³ have shown that glucose ingestion can produce some minor S-T segment deviations, T wave amplitude changes and variations in heart rate. They do not however relate the time interval following glucose ingestion with these changes.

In that no E.C.G.'s were recorded in the immediate post glucose period, it is hoped that these minimal changes would in fact be negligible, and that spurious patterns of myocardial ischaemia avoided.

All E.C.G.'s were interpreted by full-time cardiologists of the Cardiac Clinic, Grootse Schuur Hospital, Cape Town. The G.T.T. results were unknown to the E.C.G. interpreter. A diagnosis of ischaemic heart disease was made if there was unequivocal history of angina pectoris and/or myocardial infarction, or S-T segment depression indicative of sub-endocardial ischaemia, or evidence of past myocardial infarction.

(iii) Diabetic Retinopathy

All positive screens underwent direct fundoscopy with an ophthalmoscope.* This examination was carried out in a darkened room after mydriasis, by an independent observer who was unaware of the 2 hour plasma glucose value of each subject.

* Welch-Allyn. Type 115. Welch-Allyn Inc. Skaneateles Falls, New York, U.S.A.

Criteria of Abnormality

The presence of capillary microaneurysms was a minimum prerequisite for the diagnosis of diabetic retinopathy. In this study, a purely descriptive terminology has been used similar to that of Scott,⁵⁴ Johnsson,⁵⁵ and Janoff.⁵⁶

Retinopathy is described in 4 grades :

Grade 1. Microaneurysms.

Grade 2. Microaneurysms with a few small haemorrhages and discrete flecks of exudate.

Grade 3. Microaneurysms with larger haemorrhages and large confluent exudates.

Grade 4. Retinitis proliferans, vitreous haemorrhage, retinal detachment and gross degeneration.

(iv) Peripheral Vascular Disease :

All positive screenees were questioned as to a history of intermittent claudication and interpretation was based on Ross's⁵² recommendations. Physical examination to reveal the presence or absence of the pedal pulses (dorsalis pedis and posterior tibial) was carried out. P.V.D. was diagnosed on the following grounds :

1. Unequivocal history of intermittent claudication and/or,
2. Absent pedal pulses (unilateral or bilateral) or,
3. Obvious ischaemic signs such as gangrene or amputation resultant therefrom.

(v) Peripheral Neuritis :

The presence or absence of ankle jerks in all positive screenings was determined using a standard tendon hammer. Vibration sense was assessed over both ankle malleoli with a tuning fork. Peripheral neuritis was diagnosed by the bilateral absence of ankle jerks or the bilateral absence of vibration sense. It is realized that many cases of peripheral neuritis may have been missed as subjective symptoms such as pain and parasthesiae were not sought.

PART THREE

RESULTS AND DISCUSSION

----- CHAPTER 7 -----

RECOVERY OF POSITIVE SCREENINGS

As stated previously (chapter 3), a positive screening was one who manifested glycosuria irrespective of plasma glucose value, and/or one whose screen glucose value equalled or exceeded 120 mg./100 ml. Initially a value of 110 mg./100 ml. was chosen, but after 205 consecutive G.T.T.'s of which 71 were on screenings with values between 110 and 119 mg./100 ml.,* as of the 71 screenings, only 3 (4.2%) were diabetic by definition.

(1) First Survey :

The following table indicates recovery in this survey.

Table 13. 1st Survey : Recovery of Positive Screenings

	Hyperglycaemics	Glycosurics
	plasma glucose 120 mg./100 ml.	irrespective of glycaemia
Total No.	240	95
No. Retested	219	83
Recovery (%)	91	87

It is seen that the recovery for each group was virtually 90%. Thou many glycosurics fell into the hyperglycaemic category and thus are included in both recoveries, they are kept in a single group of 95 subjects as it makes for more understandable analysis later.

* The Value was raised to 120 mg./100 ml.

Positive screen failures

1. Hyperglycaemia

of the 21 subjects not retested, 13 could not be traced, 4 could not get permission from their employers to take the necessary time off work, 3 refused pointblank, and 1 had died (multiple injuries). The following table indicates the screen plasma glucose values for these 21 subjects.

Table 14. Distribution of Screen Plasma Glucose Values in 21 Untested Positive Screens-Hyperglycaemia

Plasma Glucose mg/100 ml.	120 129	130 139	140 149	150 159	160 169	170 179	180 plus
No.	11	5	1	0	0	0	4

Of these 21, the 4 with gross hyperglycaemia were most probably diabetic and have been designated as such while the remaining seventeen have been declared non-diabetic.

2. Glycosuria

There were 12 glycosurics who were not retested. Four were clearly diabetic, with screen values of 180 mg./100 ml. plus. The remaining 8 have been designated non-diabetic as the screen value in each case was less than 110 mg./100 ml.

(11) Second Survey :

The following table indicates recovery.

Table 15. 2nd Survey : Recovery of Positive Screens

Total No.	Hyperglycaemics plasma glucose > 120 mg/100 ml.	Glycosurics irrespective of glycaemia
		65
No. Retested	52	27
Recovery (%)	80	79

Recovery for both groups is virtually 80%. The same remarks apropos glycosurics being hyperglycaemics, apply in this survey as in the first.

Positive Screens Failures

1. Hyperglycaemics

It was not possible to obtain reasons for the non-attendance of the 13 absentees. Probably fear of losing employment was a principal factor. The following table indicates the screen plasma glucose values for these 13 subjects

Table 16. Distribution of Screen Plasma Glucose Values in 13 Untested Positive Screens - Hyperglycaemics

Plasma Glucose mg./100 ml.	120	130	140	150	160	170	180 plus
	129	139	149	159	169	179	
No.	7	1	1	0	0	0	4

The 4 screens with gross hyperglycaemia were most probably diabetic and have been designated as such, while the remaining 9 have been declared non-diabetic.

2. Glycosurics

There were 7 such untested glycosurics. Three were clearly diabetic, with heavy glycosuria and screening values in excess of 180 mg./100 ml. The remaining 4 are presumed non-diabetic as the screen value in each case was less than 125 mg./100 ml.

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----- CHAPTER 8 -----

DIABETES PREVALENCE

While each survey was a distinct entity, the methodology was identical and differed only in sampling procedure. It is intended to present all results with concomitant discussion from the composite data, both survey populations having been pooled using the standard formula for weighted means/proportions. Results from each survey, compared and contrasted, will be discussed where relevant.

(1) 1st Survey :

Of the 2009 screenings, 111 were found to be diabetic by definition, representing a prevalence of 5.5%. This figure includes all diabetics, known and newly-discovered. Of these 111, all but 4 were diagnosed by repeat G.T.T. These 4 were not retested and diabetes was diagnosed as the screen value in each case exceeded 180 mg./100 ml.

It is seen from table 17 that prevalence rises with increasing age, being less than 1% in the 2nd and 3rd decades, to almost 30% in the elderly.

**Table 17. Diabetes Prevalence by Decade of Age (Both Sexes)
1st Survey**

Age Group (Yrs.)	Total No.	No. Diabetic	% Diabetic
10 - 19	714	5	0.7
20 - 29	537	2	0.4
30 - 39	288	17	5.9
40 - 49	218	29	13.3
50 - 59	146	30	20.6
60 - 69	82	21	25.6
70 plus	24	7	29.2
All Ages	2009	111	5.5

There is a sharp increase from the 30's to the 50's thereafter the rise is much more gradual.

(11) 2nd Survey :

This included 418 screenings of whom 34 were found to be diabetic (known and newly-discovered). The prevalence was thus 8.1%. Thirty diabetics were diagnosed after repeat G.T.T., the remaining 4 being designated diabetic as their screen values exceeded 180 mg./100 ml. in every case. Reference to table 18 indicates the general trend of increasing prevalence with age.

**Table 18. Diabetes Prevalence by Decade of Age (Both Sexes)
2nd Survey**

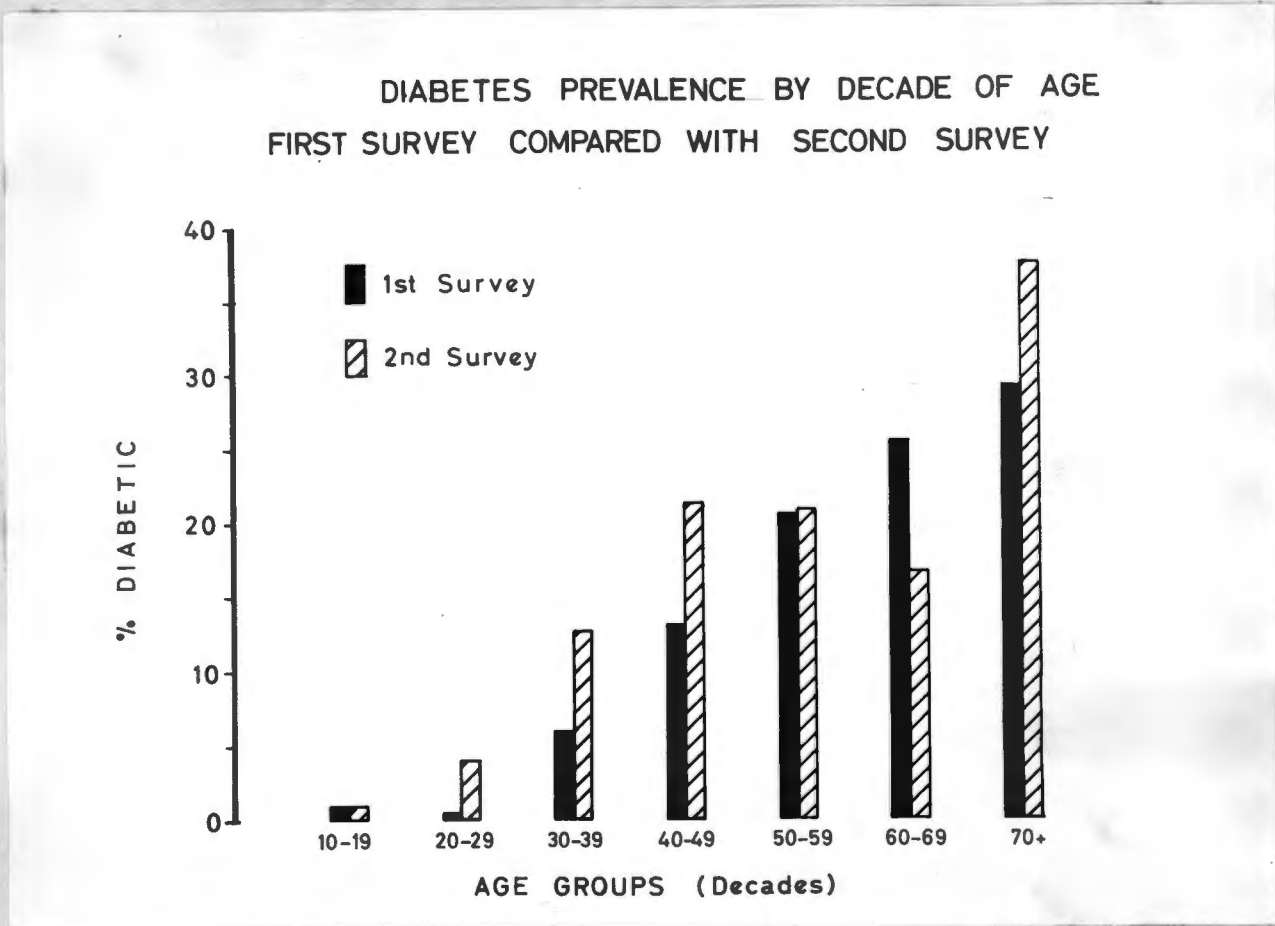
Age Group (Yrs.)	Total No.	No. Diabetic	% Diabetic
10 - 19	152	1	0.7
20 - 29	104	4	3.9
30 - 39	71	9	12.7
40 - 49	47	10	21.3
50 - 59	24	5	20.8
60 - 69	12	2	16.7
70 plus	8	3	37.5
All Ages	418	34	8.1

Here the rapid increase in prevalence with age is advanced a decade earlier and reached a virtual plateau in the 40's and 50's.

Diabetes prevalence in both surveys is will illustrated in the following histogram.

Overleaf

Figure 6. Diabetes Prevalence by Decade of Age,
1st Survey vs. 2nd Survey



It is realised that the smaller numbers of the 2nd survey, in particular the elderly age groups, may be responsible for the differences in the slope of the trend; for example the addition of one diabetic to the 60 - 69 year old group would raise that group's prevalence from 16.7% to 25.0%. It is probable that the larger numbers of the 1st survey are responsible for the gradual steady increase of prevalence with age.

Significance of observed differences between the two surveys, decade by decade, was assessed by the Chi-Squared test.* The only significant differences were seen in the 3rd and 4th decades; age group 20 - 29 years, $\chi^2 = 11.338$ $p < .001$ and age group 30 - 39 years, $\chi^2 = 3.890$ $p < .05$. For all other decades, no significant differences were observed, $p > .05$. The difference between the two overall prevalences of 5.5% (1st survey) and 8.1% (2nd survey) is significant, $\chi^2 = 4.192$ $p < .05$.

(111) Composite Survey :

Diabetes prevalence by age for the entire (composite) survey can be calculated by application of the standard formula for weighted means and proportions.

The total survey population is thus 2427 and the total number diabetic is 145, representing a prevalence of 6.0%.

Table 19 indicates the rising prevalence with age

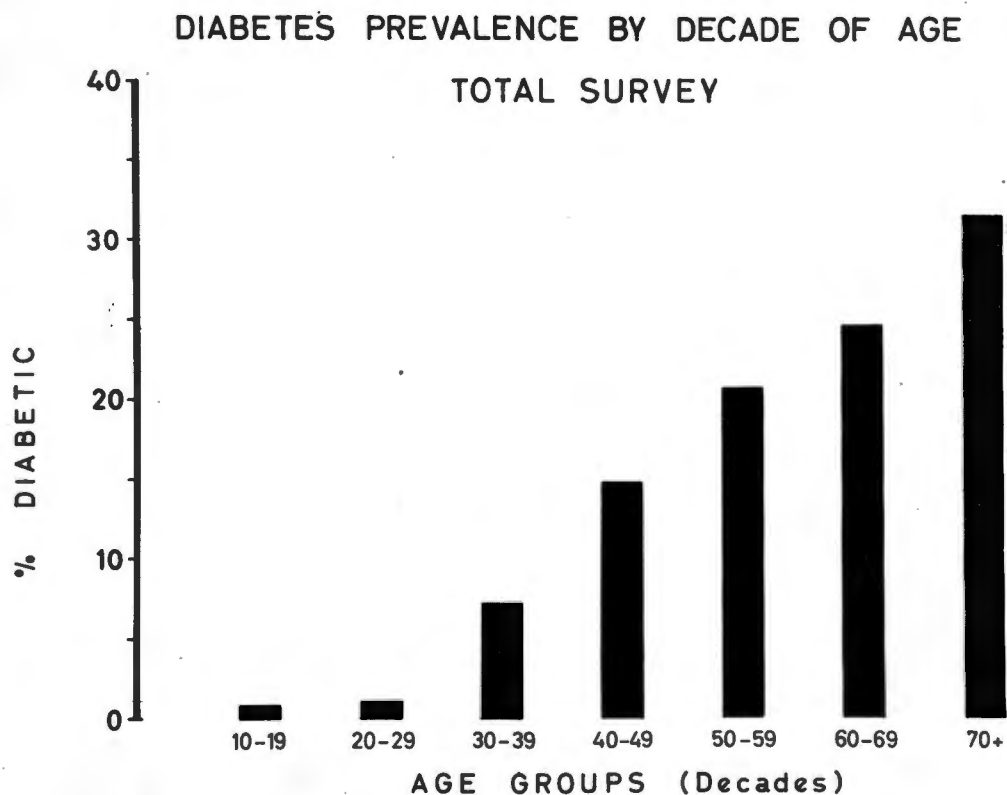
Table 19. Total Diabetes Prevalence by Decade of Age (Both Sexes)

Age Group (Yrs.)	Total	No. Diabetic	% Diabetic
10 - 19	866	6	0.7
20 - 29	641	6	0.9
30 - 39	359	26	7.2
40 - 49	265	39	14.7
50 - 59	170	35	20.6
60 - 69	94	23	24.5
70 plus	32	10	31.3
All Ages	2427	145	6.0

* See statistical appendix

This increase with age is best illustrated in the following histogram.

Figure 7. Total Diabetes Prevalence by Decade of Age



(iv) Comparative Diabetes Prevalence :

1. Introduction

In making valid comparisons with other data, careful attention must be paid to methodological differences if incorrect interpretations are not to be drawn. The plasma glucose/whole blood glucose difference has already been discussed (chapter 5). Capillary - venous blood glucose

differences, while negligible in the fasting state (2 - 3 mg./100 ml.), average a little over 20 mg./100 ml. at peak value after glucose ingestion; indeed the difference can be as marked as 80 mg./100 ml. The method of glucose determination is all-important, ranging from determination of total reducing substances e.g. the Hagedorn-Jensen or Folin-Wu procedures, through methods designed to eliminate most of the non-glucose reducing substances, e.g. the Somogyi-Nelson procedure or the K.Cn. Hoffmann modification, to the present-day enzymatic (glucose-oxidase) procedures which indicate true glucose content.

Demographic and socio-economic aspects are as important. The age and sex structure of the sample population and the general population should be closely identical before any extrapolation may be attempted. Reports on prevalence range from clinical impressions such as those of Albertsson who commented on some statistics concerning diabetes in Ireland, to Politzer et al's comments on diabetes incidence in a rural African area. Such observations are limited as methodology is imprecise and demographic considerations omitted. Then again, while actual numbers may be impressive, e.g. Patel et al's survey of 18,200 Indians, closer appraisal indicates the limitations of the data. These 18,200 subjects were visitors to a Bombay exhibition and thus their diabetes prevalence is that of exhibition-attenders and no more; it cannot be extended to include the general population of Bombay.

Similarly hospital or clinic attenders have been studied and results extrapolated to cover whole cities or nations. Rudnick and Anderson⁶⁵ studied 3851 outpatients in Hiroshima, Japan. In this study, the age distribution of the survey population was compared with that of the general population of Hiroshima. The gross differences in the majority of the age groups serves to indicate that the prevalence rate is applicable only to the closed clinic population and cannot be extended to the population of Hiroshima.

In 1947, Wilkerson and Krall⁶⁶ published their study of diabetes prevalence in a New England town. This study represented the first attempt at "total community investigation" in that attempts were made to screen all the inhabitants of the town. Subsequently, with greater sophistication similar surveys have been carried out. In 19⁶⁷, Jerde carried out the Bergen survey in which 5930 persons out of an available total of 11,193 (recovery, 53%) were screened. Though the diagnostic criteria are considered by many to be rather stringent, this survey represents an objectively planned diabetes prevalence investigation with strong epidemiological, demographic and socio-economic aspects.

The U.K. saw its first total community survey⁶⁸ in 1957 in the village of Ibstock. Here glycosuria was the sole screen criterion ; recovery was good, (81%). The Birmingham

survey⁶⁹ in 1962 covered 18,532 out of a possible 19,412 persons, with a glycosuria screen. These 19,000 persons were held to be representative of the general population of Birmingham and indeed of England and Wales. This was followed in 1964 by Butterfield's presentation⁷⁰ of the results of the Bedford diabetes survey - here out of a total population aged 21 years and above, numbering 38,400 persons, 27,701 were in fact screened by a glycosuria check. The same year saw Mitchell and Strauss³⁶ carry out a glycosuria screen on the total population aged 5 years and above of Arbroath, Scotland. Of the 17,000 persons available, 11,341 were in fact screened.

In all these 4 contemporary U.K. surveys recovery was good, ranging from 66% (Bedford) to 95% (Birmingham).

. In the U.S.A., Michigan and Massachusetts have experienced total community prevalence surveys. In 1965, all inhabitants aged 16 years and above in Tecumseh, Mich. were studied,⁷¹ the recovery being 76% (2983 screened of an available 3984). In 1966, the population aged 15 years and above of Sudbury, Mass., took part in a total community survey⁷² - here 4626 persons of an available 5976 were screened, a recovery of 77%.

Diagnostic Considerations

It is axiomatic that in prevalence work, the numbers of a particular disease state discovered, depend upon the stringency of the diagnostic criteria, in particular with diabetes where diagnosis rests purely upon biochemical criteria.

The laxer the criteria the greater the diabetes prevalence and vice versa. A recent (1965) diabetes survey in Malta ²² illustrates the point - here a survey population of 5757 out of a possible 6597 was studied by an initial post-prandial glycosuria screen. All Glycosurics were subjected to G.I.T. The report concludes with an overall prevalence of 20% for the population (all ages), which would assuredly place the Maltese as amongst the most diabetes-prone people yet known. The diagnostic criteria are very low and could possibly apply if venous blood had been used, in particular the criterion of 150 mg./100 ml. which applied equally to the $\frac{1}{2}$, 1 and/or $1\frac{1}{2}$ hour values is probably at least 20 mg./100 ml. too low. Results must thus be interpreted in this light and while prevalence rates are obviously valid for the stated criteria, they cannot be used for comparative purposes.

An example at the other end of the spectrum is that of the Sudbury study. ⁷² Here the prevalence rate for the tested population was 1.9%. The diagnostic criteria are those recommended by the U.S.P.H.S. ⁷³ These criteria are more stringent than most including those of Fajans and Conn, ⁴⁰ the American Diabetes Association and the British Diabetes Association. ⁷⁵ If the criteria of Fajans and Conn and those of the B.D.A. are independently applied to a random sample of the Sudbury population, prevalence rates of 5.6% and 6.8% are obtained. Mention will be made subsequently of other

factors possibly responsible for the low finding in Sudbury.

Screening Considerations

The adequacy or rather the "potency" of a particular screening test must be assessed in evaluation. Potency denotes the ability of a screening test to indicate the possibility of glucose intolerance and thus prevalence rates must depend basically on the potency of the screen. The greater the potency, the greater the number of positive screenings and thus the greater the number of discovered diabetics.

As the most practical and widely accepted diagnostic test for diabetes diagnosis is the G.T.T., it follows that a glucose challenge followed by blood glucose determination as the screen manoeuvre, must be the most potent screen method short of such refinements such as steroid priming. This is well illustrated by the Sudbury findings,⁷² where post-glucose versus post-prandial blood glucose values resulted in a mean difference of 58 mg./100 ml. In broad support, O'Sullivan⁷² has stated, "Now all the studies that have been done on post prandial blood sugars, including Oxford, have given the rates about 2%. What we are beginning to witness is that when we do studies involving blood sugars following a glucose challenge, we are getting a much higher prevalence rate."

Methods in order of decreasing potency are post prandial blood glucose, post glucose glycosuria, post prandial glycosuria and random glycaemia/glycosuria checks.

This realisation must result in diabetes prevalence surveys being designed employing a basic glucose determination. Indeed as Jackson⁷⁶ has put it, "surveys based on glycosuria as a screening procedure are virtually useless as prevalence studies."

The author feels that this preamble has been essential before any comparisons are made between diabetes prevalence as revealed in Tongaat and that from other parts of the world. That the present survey employed a basic glucose challenge followed by blood glucose determination (and glycosuria) as the screen procedure, limits its comparison to other published works which have either employed a similar procedure in toto, or in part. The Tongaat results cannot be compared with surveys which have employed a glycosuria screen alone and caution must be observed with some of the few studies which have employed initial post prandial blood glucose screening.^{77,78,79}

Estimated Tongaat Prevalence - All Ages

The overall Tongaat prevalence for the sample population (10 years and above) was 6%. Though children comprising the 1st decade were not surveyed, the author feels that they can be assumed to include no diabetics. Certainly there were no known diabetics in this group. Table 19 indicates the rapid and precipitous drop in prevalence from the 4th decade (7.2%) to the 2nd (0.7%). Further extension of this drop to the 1st decade would hypothetically reveal minimal diabetes prevalence,

if at all. While ^{80,81} has commented that the incidence in the childhood population of U.S.A. (under 15 years) is 0.04%. This incidence would drop lower if the age group 10-14 years was excluded.

The total survey population was 2427 persons. As 30% of the Indian population falls into the 1st decade, ¹⁸ the calculated total survey population (all ages) would be :

$$\frac{100}{70} \times \frac{2427}{1} = 3467 \text{ persons}$$

On the premise that this extra 1040 persons would have harboured no diabetics, the total diabetes prevalence for all ages would be :

145 diabetics out of 3467 subjects
or
4.2%

(11) Comparative Diabetes Prevalence :

At the time of writing valid comparisons can be made with the following studies only :

Birmingham (U.K.)	- 1962	69,82
Bedford (U.K.)	- 1964	70
Arbroath (U.K.)	- 1964	36
Health Examination Survey (U.S.A.)	- 1964	83
Sudbury (U.S.A.)	- 1966	72
Mamelodi (S.A.)	- 1967	84

1. Birmingham/Bedford

In these 2 English surveys, post-prandial glycosuria screening was employed with G.T.T. being carried out on all glycosurics. Methodology and diagnostic criteria were very similar in both surveys. G.T.T. (Birmingham) was following a 50 G glucose load, and both 1 and 2 hour capillary whole blood values of 180 mg./100 ml. and 120 mg./100 ml. had to be satisfied for diabetes diagnosis. The method of glucose determination was identical to that employed in Tongaat. The criteria and those suggested by Fitzgerald and Keen⁷⁵ on behalf of the B.D.A., and correspond to venous whole blood glucose values of 160 mg./100 ml. and 110 mg./100 ml. respectively. In terms of venous plasma, these criteria correspond to values of 185 mg./100 ml. and 130 mg./100 ml. respectively.^{26,27}

The Bedford survey employed a 2 hour capillary blood glucose value of 120 mg./100 ml. to establish diabetes diagnosis. This value corresponds to a venous whole blood glucose value of 110 mg./100 ml. which in turn is equivalent to 130 mg./100 ml. venous plasma.

The Tongaat criteria are thus almost identical to those of Birmingham as is the single Bedford criterion.

Both these surveys confirmed current estimates of diabetes prevalence as being between 1% and 2%; i.e. when

glycosuria is used as the screen criterion. Both surveys however went a step further in that age/sex matched aglycosuric controls underwent G.T.T. In Birmingham, of the 345 controls, 27 satisfied the criteria and were designated diabetic, a prevalence of 7.8%, while Bedford followed suit when 90 diabetics were discovered out of the 570 controls, a prevalence of 15.8%.

These results led to revised diabetes prevalence rates by the respective authors. The Birmingham group put the diabetes prevalence for the total general population of England and Wales at 6.2%, whilst Butterfield in Bedford raised this estimate to 12 - 14 %.

Before any comparison between Tongaat and Birmingham be made, it is necessary to apply the equivalent Birmingham criteria (185 and 130 mg./100 ml.) to the Tongaat data. This has the effect of raising the prevalence in 3 decades and the overall prevalence minimally. The following table indicates the "revised" prevalences.

Table 20. Diabetes Prevalence in Tongaat by Decade of Age - Birmingham criteria

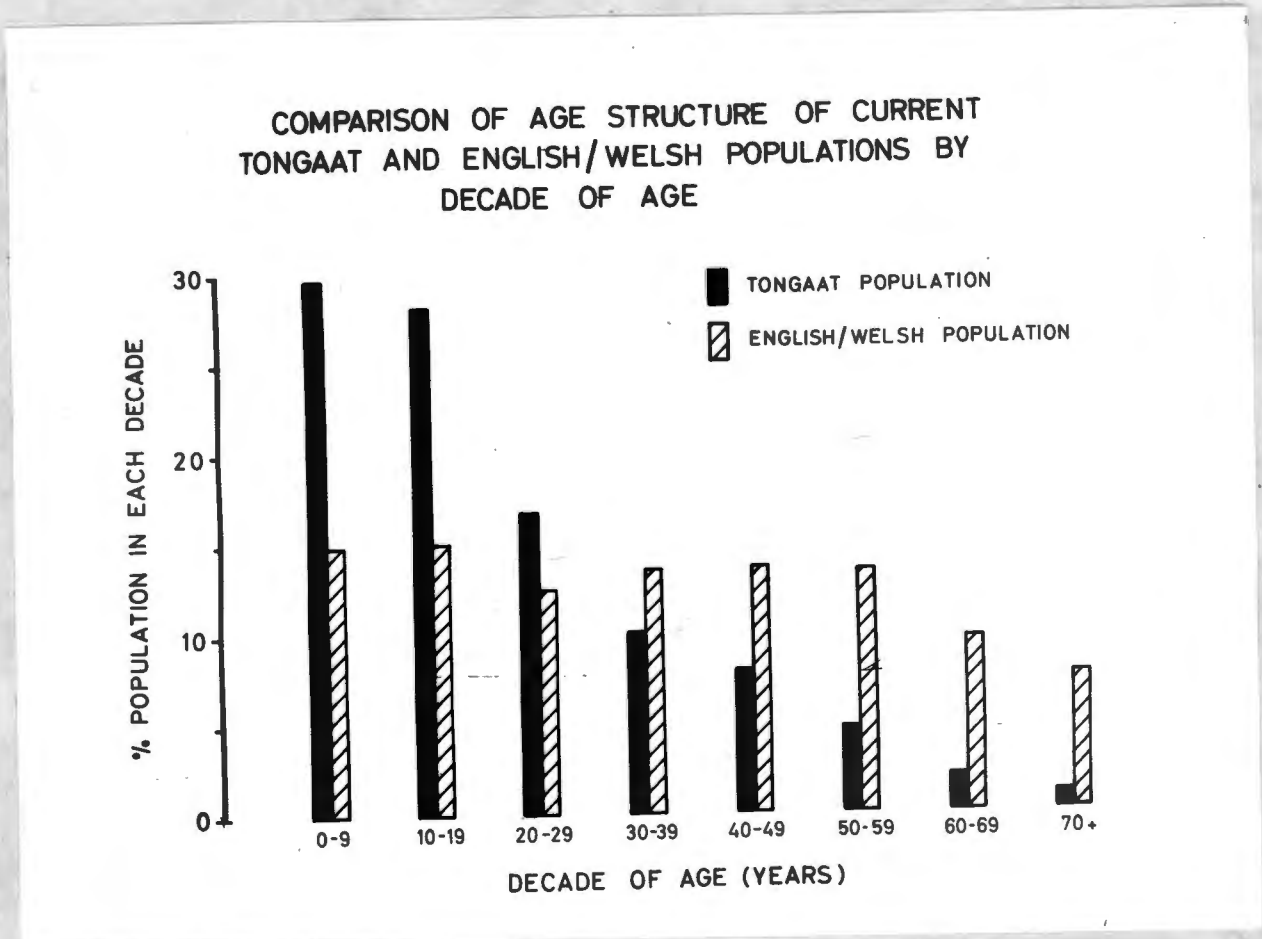
Age Group (Yrs)	Total No.	No. Diabetic	% Diabetic
10 - 19	866	6	0.7
20 - 29	641	6	0.9
30 - 39	359	26	7.2
40 - 49	265	41	15.5 *
50 - 59	170	35	20.6
60 - 69	94	24	25.5 *
70 plus	32	11	34.4 *
All Ages	2427	149	6.1 *

Prevalences which have been altered by the new criteria are denoted by the asterisk.

The next step is one of age-adjustment as the age structure of the Tongaat population is markedly dissimilar to that of the general population of England and Wales. In Tongaat, as in Natal, the Indian population is particularly juvenile in age structure with at least 50% of the populace below the age of 20 years while the middle-aged and elderly comprise a small section. The population of England and Wales displays a more equal age distribution, ⁸⁵ with a virtual plateau spreading itself through all decades of age with a slight drop in the elderly. The following figure quantitates these differences.

Overleaf

Figure 8. Comparison of Current Age Structure of Tongaat and English/Welsh Populations



As diabetes increases with advancing age, prevalence rates in both populations cannot be compared without age adjustment to equalise these differences.

The direct method of standardisation as suggested by Bradford Hill⁸⁶ has been used. The prevalence rates in the Tongaat population are applied to the general population of England and Wales, by identical decade. The total calculated

number of diabetics in that population, and thus diabetes prevalence in the Tongaat population estimated, if it had an identical age structure to that of the English/Welsh population. This method is illustrated below :

Table 21. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Birmingham Criteria

Age Group (Years)	Total No. Eng./Welsh Pop.	Diab. Prev. Tongaat	Calc. No. Diabetic
0 - 9	6,859,307	0.0	0
10 - 19	6,925,824	0.7	48,480
20 - 29	5,724,450	0.9	51,520
30 - 39	6,226,199	7.2	448,286
40 - 49	6,265,339	15.5	971,128
50 - 59	6,148,854	20.6	1,266,663
60 - 69	4,436,856	25.5	1,131,398
70 plus	3,517,719	34.4	1,210,095
All Ages	46,104,548		5,127,570

Diabetes prevalence would be 11.1% Previously it was stated that prevalence for the age group 0 - 9 years (Tongaat) was assumed to be nil; if however White's ^{80,81} rate of 0.04% for this group was applied, the calculated total number diabetic would increase by 2743 persons which does not alter the prevalence rate.

The Bedford workers employed a single 2 hour glucose value as their diagnostic criterion. The equivalent Tongaat value

being 130 mg./100 ml., all those screenings meeting this criterion (irrespective of classification by subsequent G.I.T.) have been designated diabetic and prevalence has been calculated by decade of age. This is indicated in the following table.

Table 22. Diabetes Prevalence in Tongaat by Decade of Age - Bedford Criterion

Age Group (Years)	Total No.	No. Diabetic	% Diabetic
10 - 19	866	21	2.4
20 - 29	641	15	2.3
30 - 39	359	33	9.2
40 - 49	265	49	18.5
50 - 59	170	41	24.1
60 - 69	94	26	27.7
70 plus	32	12	37.5
All Ages	2427	197	8.1

The prevalence for Tongaat can now be calculated in like manner. Table 23 indicates the method.

Overleaf

Table 23. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Bedford Criterion

Age Group (Years)	Total No. Eng./Welsh Pop.	Diab. Prev. Tongaas	Calc. No. Diabetic
0 - 9	6,859,307	0.0	0
10 - 19	6,925,824	2.4	166,220
20 - 29	5,724,450	2.3	131,662
30 - 39	6,226,199	9.2	572,810
40 - 49	6,265,339	18.5	1,159,088
50 - 59	6,148,854	24.1	1,481,874
60 - 69	4,436,856	27.7	1,229,009
70 plus	3,517,719	37.5	1,319,144
All Ages	46,104,548		6,059,808

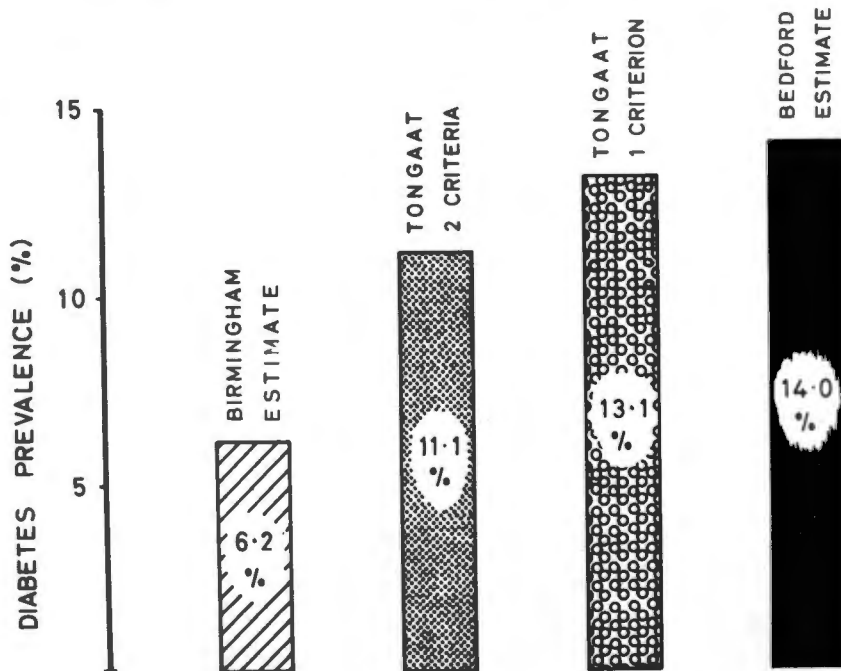
Diabetes prevalence would be 13.1% The remarks concerning diabetes prevalence in the 1st decade are equally applicable ; an assumption of total absence of diabetes or White's ^{80,81} rate of 0.04% does not alter the total prevalence rate.

Only now can valid comparisons be made. The following figure quantitates these comparisons and illustrates that the age-adjusted Tongaat prevalences fall between the Birmingham estimate of 6% and that of Bedford, 14%.

Overleaf

Fig. 9. Age-Adjusted Tongaat Diabetes Prevalences Compared with Current Estimations of Prevalence for General Population of England and Wales

AGE-ADJUSTED TONGAAT DIABETES PREVALENCES COMPARED WITH CURRENT ESTIMATIONS OF PREVALENCE FOR GENERAL POPULATION OF ENGLAND & WALES



On the strength of these calculations and extrapolations, the author feels that the Tongaat prevalence is probably closely similar to that of the general population of England and Wales. That the Tongaat prevalence is approximately five times greater than that previously found or even anticipated in Western communities is not denied, but the Birmingham and

Bedford estimates indicate an equally high prevalence rate ranging from three to seven times that previously described. Thus, by comparison, the Tongaat rate is not excessive and does not warrant description as being representative of one of the most diabetes-prone people in the world.

2. Arbroath

Further support for the growing realisation that prevalence rates for the West must be revised and increased four to eight fold, comes from data from the Arbroath survey. Here, as in Birmingham and Bedford, an initial glycosuria check screened out suspect diabetics from supposedly normal screenees and post-prandial followed by standard G.T.T. studies were carried out on glycosurics. For every glycosuric, an age/sex matched control underwent identical studies. Methodology was identical to that of Tongaat and diagnostic criteria were practically identical; Tongaat's basic criteria being 1 and 2 hour levels of 150 and 110 mg./100 ml. respectively (whole venous blood-enzymatic method), while Arbroath's levels were 150 and 105 mg./100 ml. respectively (whole venous blood - enzymatic method) - in addition a fasting level of 90 mg./100 ml. was introduced.

, In the control aglycosuric group (277), 32 were diabetic which represents 13%. While no prevalence rate for the Arbroath population was expressed, this finding emphasises the

greatly increased prevalence rate when G.I.T. is carried out regardless of urine testing and heavily underlines the findings and estimates of the Birmingham and Bedford studies.

3. Health Examination Survey

From 1960 to 1962, The Health Examination Survey (H.E.S.) of the U.S. Department of Health, Education and Welfare, undertook an investigation of the prevalence of certain chronic diseases in the U.S.A. A nation-wide probability sample of 7710 persons aged 18 - 79 years was drawn of which 6672 cooperated, a recovery of 87%. Glucose tolerance was evaluated by means of a 50 G oral glucose challenge with venous blood collected after 1 hour and a urine sample collected after a further 30 minutes. Whole blood glucose concentration was determined by the Somogyi-Nelson method; glycosuria was assessed with the glucose-oxidase paper strip (Tes-Tape).

As the time interval following glucose ingestion differs in that Tongast employed a 2 hour interval, direct comparisons cannot be made. Glucose determination in both surveys provides virtually identical values. ⁸⁷ The Tongast criteria (185 and 140 mg./100 ml. at 1 and 2 hours respectively) are the equivalent of Fajans & Conn's criteria of 160 and 120 mg./100 ml. (whole blood - Somogyi-Nelson method), the differences being due to the higher glucose value

for plasma as compared with whole blood. ^{26,28}

It is proposed that a comparison be made by comparing percentage abnormality in Tongaat as defined by the 2 hour plasma glucose value equalling or exceeding 140 mg./100 ml., with percentage abnormality in the H.E.S. as defined by the one hour whole blood glucose value equalling or exceeding 160 mg./100 ml. In effect the comparison is between the 2 hour F & C criterion (Tongaat) and the 1 hour F & C criterion (H.E.S.), both criteria being indicative of glucose intolerance.

In the following table, the Tongaat sample population has been broken into age groups identical to those of the H.E.S. and percentage abnormality by age group is indicated.

Table 24. Percentage Abnormality in Tongaat by Age Group (H.E.S. Grouping).

Age Group (Years)	Total No.	No. \geq 140 mg./100 ml.	% \geq 140 mg./100 ml.
18 - 24	592	6	1.0
25 - 34	463	12	2.6
35 - 44	296	22	7.4
45 - 54	234	46	19.7
55 - 64	133	26	19.6
65 plus	67	18	26.9
All Ages	1785	130	7.3

In the following table, these findings are compared with H.E.S. data at screening levels of 160 mg./100 ml. as well as at 170 mg./100 ml. (U.S.P.H.S. criterion).

**Table 25. Percentage Abnormality - Tongaat (2 hour criteria)
vs. H.E.S. (1 hour criterion)**

Age Group (Years)	H.E.S. (%) \geq 160 mg./100 ml.	Tongaat (%) \geq 140 mg./100 ml.	H.E.S. (%) \geq 170 mg./100ml.
18 - 24	3.4	1.0	2.1
25 - 34	6.2	2.6	4.2
35 - 44	11.0	7.4	8.0
45 - 54	16.5	19.7	12.0
55 - 64	26.4	19.6	20.9
65 plus	36.0; 41.5	26.9	27.2; 34.6

Points requiring emphasis are :

1. The age group, 65 years and older represents two groups, firstly 65 - 74 years and secondly 75 - 79 years ; hence the two percentages quoted for this age group in the H.E.S. The Tongaat data included all ages at 65 years and above.
2. The H.E.S. excluded known diabetics, definitely proven and questionable.

It is seen that the percentage abnormality in Tongaat by identical age groups is less than that recorded in the H.E.S. with the sole exception of the 45 - 54 year old group.

Furthermore exclusion of known diabetics and persons aged 80 years and above must tend to minimise the H.E.S. findings in all age groups, and more than emphasises the apparently lesser degree of glucose intolerance in Tongaat.

4. Sudbury

In 1964, a population study of the town of Sudbury, Mass., U.S.A. was undertaken.⁷² Venous blood samples were taken 1 to 2 hours post-prandially and all persons whose values (Auto-Analyser, macro-Hoffmann method) equalled or exceeded the population's 92nd percentile had a repeat post-prandial sample taken. Of these only those whose glucose values equalled or exceeded the 98th percentile had 100 G. oral G.T.T. Diabetes was diagnosed according to current U.S.P.H.S. criteria.⁷³

The survey included all residents aged 15 years and above. Of 5976 defined residents, 4626 cooperated, a recovery of 77%.

Diabetes prevalence was put at 1.9%. made up of 1.1% known diabetics and 0.8% new diabetics. These results thus rank as low-prevalence findings. A random 5% sample of the entire population (232 persons) was also drawn and G.T.T. irrespective of post-prandial test result was offered to these 232 persons, of whom 176 underwent G.T.T. - recovery was 76%.

Application of U.S.P.H.S. criteria,⁷³ those of Fajans and Conn,⁴⁰ and those of the B.D.A.⁷⁵ to this 5% sample resulted in respective prevalence rates of 1.2%, 5.6% & 6.8%.

For comparative purposes, the Tongaat prevalence has been analysed by age groups, identical to the Sudbury grouping. Diagnostic criteria are those of Fajans and Conn⁴⁰ (corresponding to 185 and 140 mg./100 ml. Tongaat). The following table indicates the rising prevalence with age.

Table 26. Tongaat Diabetes Prevalence by Decade of Age - Sudbury Age Grouping

Age Group (Years)	Total No.	No. Diabetic	% Diabetic
	1004	5	0.5
15 - 24	463	15	3.2
25 - 34	296	28	9.5
35 - 44	234	50	21.4
45 - 54	133	25	18.8
55 - 64	67	19	28.4
65 plus	2197	142	6.5

In the following table the estimated diabetes prevalence in a Tongaat population of identical age distribution to that of Sudbury⁸⁸ has been calculated using these prevalence rates.

Table 27. Direct Method of Calculation of Total Diabetes Prevalence for Standardised (Sudbury) Tongaat Population

Age Group (Years)	Total No. (Sudbury)	Diab. Prev. (%) Tongaats	Calc. No. Diabetic
15 - 24	762	0.5	4
25 - 34	1239	3.2	40
35 - 44	1452	9.5	138
45 - 54	625	21.4	134
55 - 64	308	18.8	58
65 plus	240	28.4	68
All Ages	4626		442

Total prevalence is 9.5%. Thus after age-adjustment and employing identical criteria it appears that Tongaat has a higher prevalence than that of Sudbury (5.6%). The Sudbury 5% sample however numbered only 176 persons and its finding must be interpreted in the light of its paucity of numbers.

Further comparison of an indirect nature may be made. The Sudbury workers age-adjusted their population to that of the Bedford survey population and applied Bedford's equivalent 2 hour criterion to their data. This resulted in a prevalence of 21.8% for Sudbury as compared with 15.8% for Bedford. Age-adjustment of the Tongaat population to that of Bedford and application of the same criterion results in a prevalence of 17.8% for Tongaat. The following table illustrates this calculation.

Table 28. Direct Method of Calculation of Total Diabetes Prevalence for Standardised Tongaat Population - Bedford criterion, Ages 20 years and above

Age Group (Years)	Total No. (Bedford)	Diab. Prev. (%) Tongaas	Calc. No. Diabetic
20 - 29	3905	2.3	90
30 - 39	5546	9.2	570
40 - 49	5792	18.5	1072
50 - 59	4677	24.1	1127
60 - 69	3334	27.7	924
70 plus	2099	37.5	787
All Ages	25,353		4510

It appears thus that while Tongaat diabetes prevalence is higher than that in Sudbury, the reverse obtains following "mutual" age-adjustment to a third survey (Bedford) and applying the equivalent 2 hour criterion. These findings must needs complicate any conclusions as to relative prevalence. The author can offer no suitable explanation for this apparent paradox. One possibility is that a far greater number of Sudbury screenees rated as diabetic by the equivalent Bedford criterion, normalised upon application of the criteria of Fajans and Conn.

5. Mamelodi

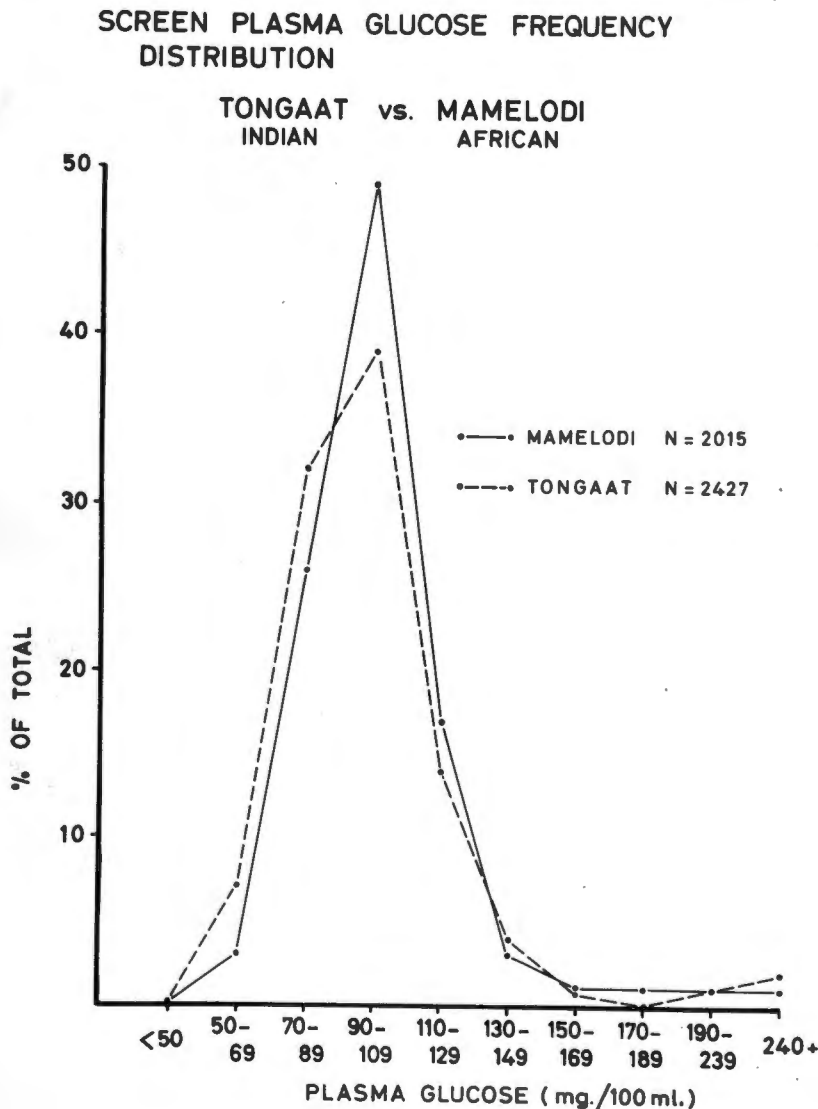
In 1966, Ribeiro ⁸⁴ carried out a diabetes prevalence survey on a sample population in Mamelodi (population 40,000), a northern Transvaal town close to Pretoria. The author is greatly indebted to Dr. Ribeiro for permission to examine the Mamelodi data and publish some of the findings.

The survey numbered 2015 subjects with methodology being in every way identical to the Tongaat study. The age structure of both surveys is closely identical. Table 29 indicates this similarity.

Survey	Age Group (Years)						
	10-19	20-29	30-39	40-49	50-59	60-69	70plus
Tongaat(%)	35.7	26.4	14.8	10.9	7.0	3.9	1.3
Mamelodi(%)	39.8	19.7	14.7	13.2	6.8	3.8	2.9

After the initial screen, no repeat G.T.T.'s were carried out on the Mamelodi sample. Accordingly the frequency distribution of plasma glucose values in each survey as a whole, has been compared. The following figure illustrates this comparison.

Figure 10. Screen Plasma Glucose Frequency Distribution -
Tongaat vs. Mamelodi



It is clear that these two distribution curves are closely similar. Both have the identical mode (90-109 mg./100ml.) which includes 39% of the Tongaat sample as opposed to 49% of Mamelodi. At other corresponding points on each distribution curve, the two surveys match each other closely.

Analysis of the Tongaat data has indicated that a screen plasma glucose value of 140 mg./100 ml. provides an accurate "cut-off" point for an estimation of total diabetes prevalence (refer chapter).

Taking the same cut-off point for Mamelodi, 84 screenings would be termed diabetic, prevalence thus being 4.2%. Tongaat screened out 136 persons at that point, a prevalence of 5.6%. This difference just attains statistical significance, $X^2 = 4.817, .025 < p < .05$.

The data presented indicate that the two survey populations have a similar pattern of glycaemia response to an oral glucose challenge. The slightly higher prevalence of hyperglycaemia (140 mg./100 ml. and above) in Tongaat, while of statistical significance must await confirmation by repeat G.T.T. on all Mamelodi positive screenings.

(v) Tongaot Prevalence by Differing Criteria :

It is obvious that artificial differences in diabetes prevalence may be created if varying criteria are applied to the same data. Thus O'Sullivan and Williams, reported prevalences ranging from 1.2% to 15.8% when varying criteria

were applied to the Sudbury data.

This effect has been explored by application of 4 widely accepted sets of criteria to the Tongaat data and comparing the resultant prevalence rates with the Tongaat finding.

These 4 sets of criteria are those of :

1. Fajans & Conn - 1 and 2 hour ⁴⁰
2. B.D.A. - 1 and 2 hour ⁷⁵
3. B.D.A. - 2 hour ⁷⁰
4. A.D.A. - 1 and 2 hour ⁷⁴

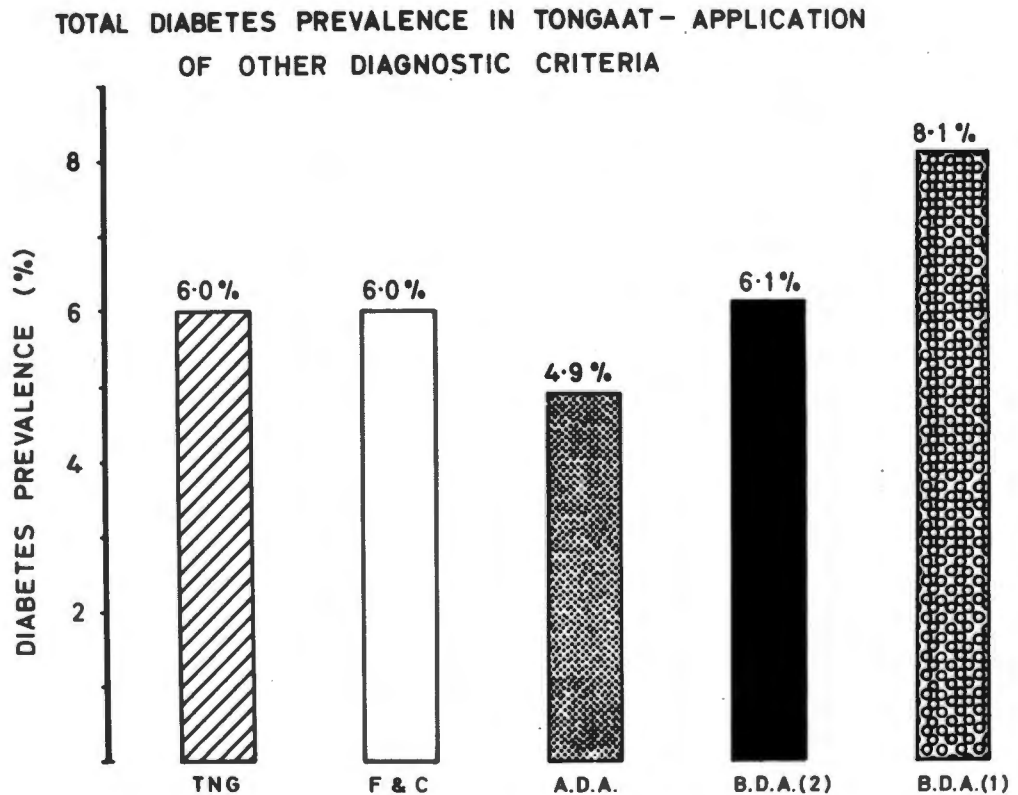
The following table indicates pertinent features of these criteria. A possible discrepancy arises in applying A.D.A. criteria as the 2 hour criterion (120 mg./100 ml.) "translates" into a venous plasma value of 145 mg./100 ml. according to Paupe⁸⁹, whereas Tustison et al²⁷ prefer a value of 140 mg./100 ml.

Table 30. Different Diagnostic Criteria Applied to Tongaat Data

Source & Author	Glucose Lead (G)	Blood Sample	Method	Actual Criteria	Equiv. Values Tongaat
Tongaat Goldberg	50	Venous Plasma	A-A	1 hr.-185 2 hr.-140	185 140
Fajans & Conn	100	Venous Wh.Blood	S-N	1 hr.-160 2 hr.-120	185 140
A.D.A. Wilkerson	100	Venous Wh.Blood	S-N	1 hr.-170 2 hr.-120	205 145
B.D.A. Fitzgerald & Keen	50	Venous Wh.Blood	A-A	1 hr.-160 2 hr.-110	185 130
B.D.A. Fitzgerald & Keen	50	Venous Wh.Blood	A-A	2 hr.-110	130

Application of these criteria results in prevalence rates varying from 4.9% to 8.1%. These differences are quantitated in the following figure.

Figure 11. Total Diabetes Prevalence in Tongaat - Application of other Diagnostic Criteria



It is seen that the Tongaat prevalence while identical to that produced by application of Fajans and Conn's criteria, differs only fractionally from that produced by the B.D.A. criteria. The A.D.A. criteria, being the most stringent, results in the lowest rate with the single B.D.A. criterion producing the highest rate.

There certainly is not the marked variation in prevalence as described in Sudbury.⁷² However it has not been possible to apply U.S.P.H.S. criteria which require a fasting and a 3 hour value in addition to 1 and 2 hour values. If this had been possible, it is highly likely that a prevalence rate yet lower than 4.9% would have resulted.

By and large, the close similarity and agreement between the prevalence rates, provides further justification of the Tongaat criteria.

(vi) Tongaat Prevalence by Age-Dependent Criteria

The prevalence rate of 6.0% for the Tongaat sample has resulted from the uniform application of the chosen criteria irrespective of age. As glucose tolerance deteriorates with age (chapter 8), it could be reasoned that age-dependent criteria should be adopted.

For this study, a single 2 hour age-dependent criterion has been calculated by 2 methods. In the first, the criterion is represented by the mean plasma glucose value (\bar{x}) plus 2 standard deviations (S.D.) for each age group;

in the 2nd, the criterion is represented by the 97th percentile for each age group. The following table defines these criteria.

Table 31. Age-Dependent Tongaat 2 - Hour Criteria

Age Group (Years)	Mean 2 hr. Plasma Glucose	S.D. (mg./100 ml.)	Diagnostic Crit. (mg./100ml.)	
			\bar{X} plus S.D.	97th P'tile
10 - 19	92.8	17.0	127	125
20 - 29	91.9	34.4	161	128
30 - 39	98.8	32.9	165	168
40 - 49	112.0	57.2	226	256
50 plus	126.0	73.8	274	345

These criteria are remarkably similar for the 2nd, 4th and 5th decades. It is also obvious that the criteria for the 2 oldest age groups are in the grossly hyperglycaemic range.

Table 32 indicates the number of screenses designated as diabetic or better termed hyperglycaemic by application of criteria for each method.

Table 32. Hyperglycaemia Prevalence by Age-Dependent 2 - Hour Criterion

Age Group (Years)	Total No.	No. Hyperglycaemic	
		\bar{X} plus S.D.	97th P'tile
10 - 19	866	25	35
20 - 29	641	4	20
30 - 39	359	12	12
40 - 49	265	16	9
50 plus	296	17	12
All Ages	2427	74	88

Total hyperglycaemia prevalence is seen to differ slightly, namely 3.1% as opposed to 3.6%. This difference is not significant. Each rate is considerably lower than that obtained by application of the 2 hour screen criterion of 140 mg./100 ml. to the total sample which results in 136 hyperglycaemias (5.6%).

The crucial question raised by this study and all others is whether the subject designated as being diabetic by application of chosen criteria indicative of hyperglycaemia, does in fact have an increased tendency to diabetic disease. There have been several studies indicating a relationship between vascular disease and hyperglycaemia. Keen et al⁹⁰ found clinical vascular disease to be more prevalent in subjects with borderline glucose intolerance than in those with ^{normal} glucose tolerance. Similarly Ostrander and colleagues⁹¹ demonstrated that hyperglycaemia was an independent risk factor at least as important as hypertension or hypercholesterolaemia in the development of cardiovascular disease.

What really is essential is to follow-up a total community such as Tongaat, or Sudbury, or Tecumseh,⁷¹ and investigate glucose tolerance related to several clinical aspects at regular intervals over a sizeable period of time. The development of diabetic disease in diabetes diagnosed by any of the current diagnostic criteria, could then be assessed.

Needless to say, such a prospective study would raise serious moral and ethical problems as it would be very difficult to withhold treatment from the grossly hyperglycaemic asymptomatic subject who is clinically normal.

(vii) Tongast Prevalence by Screen Criterion

As the 2 hour criterion (G.T.T.) was 140 mg./100 ml., diabetes prevalence has been explored by application of this criterion to the screen population and then comparing the results with definitive diabetes prevalence as indicated by repeat G.T.T. The following table is indicative.

Table 33. Total Diabetes Prevalence by Decade of Age - Application of Single 2 - Hour Criterion

Age Group (Years)	Total No.	No. Diabetic	% Diabetic
10 - 19	866	7 (6)	0.8 (0.7)
20 - 29	641	10 (6)	1.6 (0.9)
30 - 39	359	16 (26)	4.5 (7.2)
40 - 49	265	35 (39)	13.2 (14.7)
50 - 59	170	35 (35)	20.6 (20.6)
60 - 69	94	21 (23)	22.3 (24.5)
70 plus	32	12 (10)	37.5 (31.3)
All Ages	2427	136(145)	5.6 (6.0)

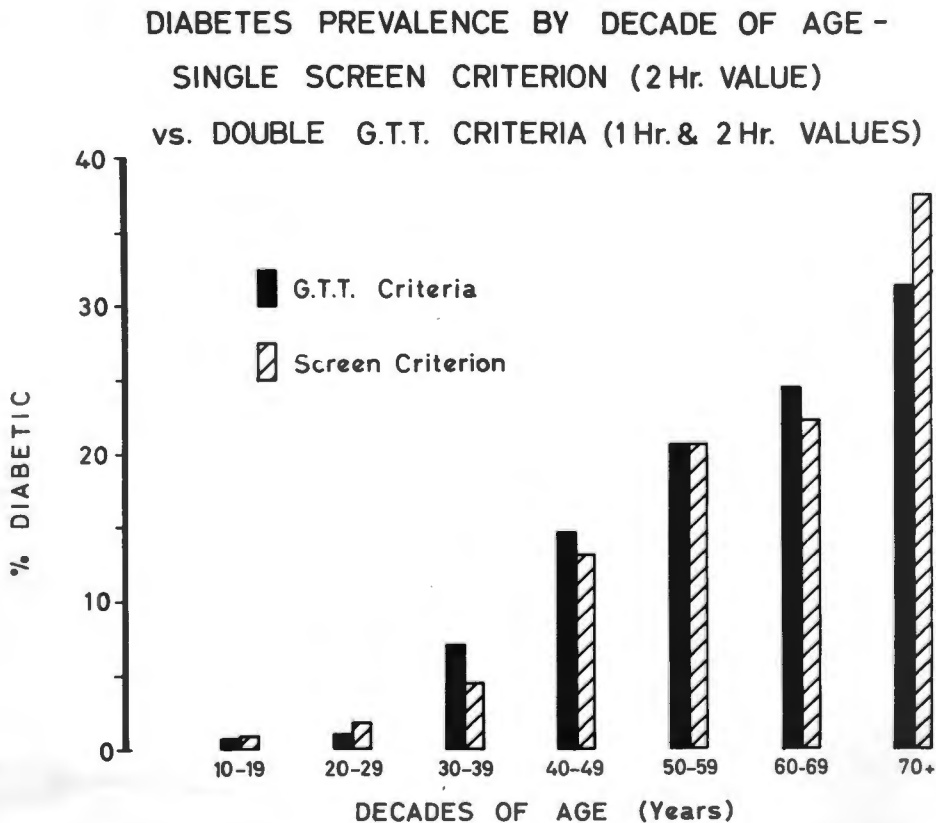
The figures in parentheses indicate the true numbers of diabetics together with the true percentages.

A very close similarity is apparent. Obviously the vast

majority of those who would have been diagnosed diabetic by the single criterion, have repeated their diabetic response during G.T.T. There were also a small number who proved to be non-diabetic at G.T.T. although they satisfied the screen criterion, and conversely some whose screen values were less than 140 mg./100 ml., who proved to be diabetic. These "losses and gains" by and large were self-cancelling.

Individual variation will be discussed in a later chapter. This similarity is best illustrated in the following figure.

Figure 12. Diabetes Prevalence by Decade of Age - Screen Criterion vs. G.T.T. Criteria



----- CHAPTER 9 -----

GLYCOSURIA PREVALENCE

(1) 1st Survey

Of the 2009 subjects, there were 95 glycosurics, representing a prevalence of 4.7%. The following table indicates the steady rise with increasing age.

Table 34. Glycosuria Prevalence by Decade of Age (Both Sexes)
1st Survey

Age Group (Years)	Total No.	No. Glycosuric	% Glycosuric
10 - 19	714	4	0.6
20 - 29	537	8	1.5
30 - 39	288	12	4.2
40 - 49	218	28	12.8
50 - 59	146	20	13.7
60 - 69	82	15	18.3
70 plus	24	8	33.3
All Ages	2009	95	4.7

A sharp rise is seen in the 40's whereafter the increase is more gradual with a spurt in the oldest group.

(11) 2nd Survey

Of the 418 subjects, 34 were glycosuric, a prevalence of 8.1%. Table 35 indicates a similar increasing prevalence with age, and as with diabetes prevalence, the increase is advanced a decade earlier in this survey as compared with the 1st.

Table 35. Glycosuria Prevalence by Decade of Age (Both Sexes)
2nd Survey

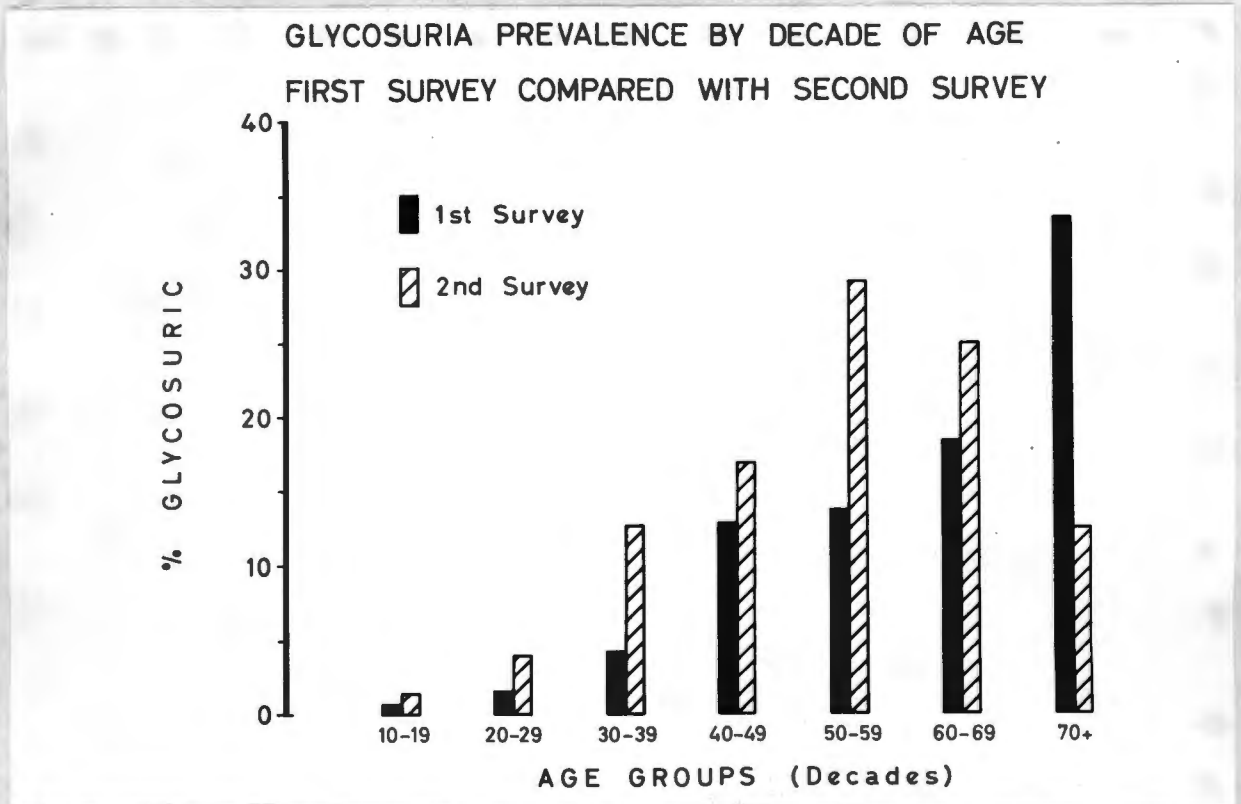
Age Group (Years)	Total No.	No. Glycosurics	% Glycosurics
10 - 19	152	2	1.3
20 - 29	104	4	3.9
30 - 39	71	9	12.7
40 - 49	47	8	17.0
50 - 59	24	7	29.2
60 - 69	12	3	25.0
70 plus	8	1	12.5
All Ages	418	34	8.1

The drop in prevalence in the oldest age group must be interpreted in view of the small numbers involved. An additional 2 glycosurics in this group would raise the prevalence rate by 25% to 37.5%.

The differences between the 2 surveys are illustrated in the following histogram

Overleaf

**Figure 13. Glycosuria Prevalence by Decade of Age -
1st Survey vs. 2nd Survey**



Significance of differences between the 2 surveys was assessed by means of the Chi-Squared Test. The only significant difference was that for the 4th decade, $p < .01$. The differences for the other decades were not significant. The total prevalence rates of 4.7% and 8.1% were significantly different, $p < .01$.

(iii) Composite Survey :

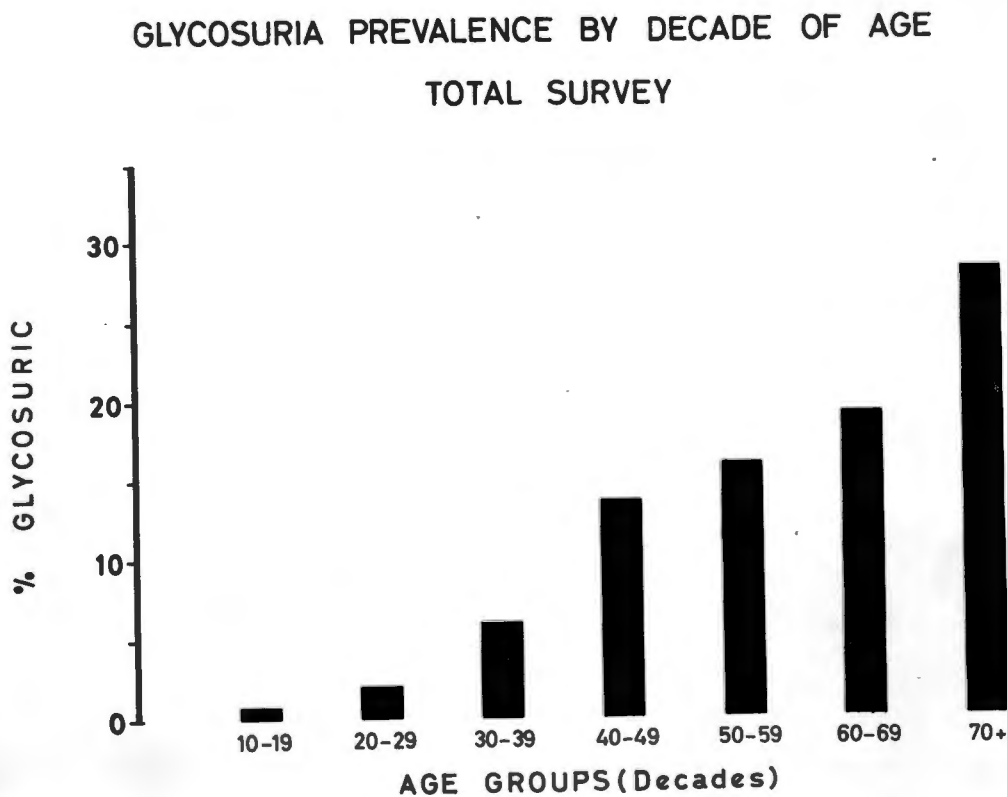
To be more meaningful the results of both surveys have been combined by the standard formula for weighted means and proportions. The following table indicates the composite data.

Table 36. Total Glycosuria Prevalence by Decade of Age (Both Sexes)

Age Group (Years)	Total No.	No. Glycosuric	% Glycosuric
10 - 19	866	6	0.7
20 - 29	641	12	1.9
30 - 39	359	21	5.9
40 - 49	265	36	13.6
50 - 59	170	27	15.9
60 - 69	94	18	19.1
70 plus	32	9	28.1
All Ages	2427	129	5.3

This steady rise with age is illustrated in figure 14.

Figure 14. Total Glycosuria Prevalence by Decade of Age



(iv) Glycosuria Prevalence Compared with Diabetes Prevalence :

The total prevalence rates for glycosuria (5.3%) and diabetes (6.0%) are similar. This similarity is maintained for each survey separately. Thus in the 1st survey overall glycosuria and diabetes prevalences were 4.7% and 5.5% respectively, while in the 2nd survey the respective prevalences were 8.1% and 8.1%. The following table indicates the respective prevalences, decade by decade.

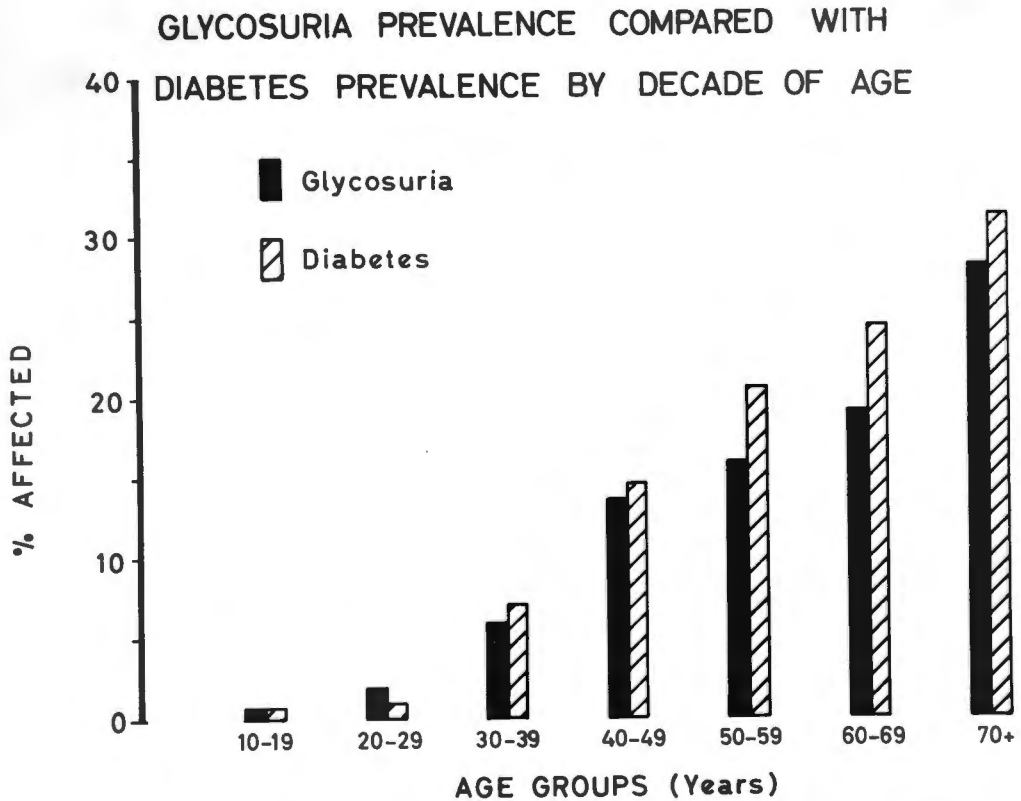
Table 37. Prevalence of Glycosuria vs. Diabetes by Decade of Age - Total Survey

Age Group (Years)	Glycosuria Prev. (%)	Diabetes Prev. (%)
10 - 19	0.7	0.7
20 - 29	1.9	0.9
30 - 39	5.9	7.2
40 - 49	13.6	14.7
50 - 59	15.9	20.6
60 - 69	19.1	24.5
70 plus	28.1	31.3
All Ages	5.3	6.0

From the 4th decade and above, diabetes is slightly more prevalent though this difference is not marked.

Diagrammatically this close similarity is best illustrated as follows :

Figure 15. Total Glycosuria Prevalence compared with Diabetes Prevalence by Decade of Age



Significance of difference by decade between glycosuria and diabetes prevalence was assessed by means of the Wilcoxon Signed - Rank Test,⁹³ which demonstrated that none of these differences were significant.

This obvious similarity is a surprising finding as it would be expected that diabetes prevalence would be in excess of glycosuria prevalence. The similarity does not however

indicate that glycosuria = diabetes. Of the diabetics there were many who exhibited no glycosuria and likewise there were many glycosurics who proved to be normal by subsequent G.T.T. Thus while the glycosuria rate may indicate the approximate diabetes rate for a sizeable group, the same does not apply to the individual.

(v) Comparative Glycosuria Prevalence :

As with diabetes prevalence, the total (5.3%) glycosuria rate can be discussed as an absolute or relative finding. Many of the methodological differences which excluded comparison with other diabetes surveys, fall away as most diabetes surveys today employ one of the various glucose oxidase paper strips; glycosuria is either present or absent, thus it is a qualitative estimation. Demographic differences are likewise important and adjustments must be made where necessary.

The other important factor is the screening procedure. Here differences in potency will produce similar differences in prevalence. As with diabetes detection, the most potent stimulus in raising the blood glucose to levels which may exceed the renal threshold is a glucose challenge. Post-prandial glycosuria rates can not be compared with post glucose rates. Random glycosuria rates are even less indicative of true glycosuria prevalence.

Direct evidence of the considerable increase in glycosuria rate following glucose challenge is afforded by the Birmingham^{69.82} and Bedford⁷⁰ surveys. In Birmingham, the post-prandial

glycosuria rate was 3.3%; when however the aglycosuric control group (345) was subjected to a 50 G oral glucose load, 51 developed glycosuria after 1 hour, i.e. 15%. The Birmingham study does not indicate whether glycosuria did not develop in any of the remaining 294 persons (who were aglycosuric at 1 hour), in the 2nd hour. The Bedford experience is similar. Here 4% of the survey population developed post-prandial glycosuria, yet the aglycosuric control group (570) developed a prevalence of 30% following the 50 G glucose load, the Birmingham rate being thus doubled.

The Sudbury survey⁷² affords evidence of the increase in blood glucose level post glucose as opposed to post-prandial. Here post glucose levels averaged 58 mg./100 ml. higher than post-prandial levels for a roughly comparable time interval in the same group of subjects. The Sudbury workers did not comment on glycosuria but this finding must provide indirect evidence of an increased glycosuria rate (post glucose) with renal blood flow and tubular reabsorption being constant.

Only in the light of these findings then, can the Tongaat rate be assessed. It is incorrect and misleading to compare the Tongaat prevalence (5.3%) with current estimates in total communities elsewhere, which have been veriously put at 4%,⁹⁴ where at best post-prandial urine testing has been carried out.

While the Birmingham and Bedford studies have produced revised diabetes prevalence rates, the same has not been applied to glycosuria, and as Sudbury confined itself solely to diabetes prevalence, the Tongaat glycosuria rates can only be expressed as absolute values. However in view of experience elsewhere indicating a greatly increased glycosuria prevalence following glucose loading, it is felt that the Tongaat prevalence is one of modest proportion and considering the potency of the challenge, cannot be described as exceptional.

(vi) Application to Future Diabetes Surveys :

Diabetes surveys in general comprise 2 distinct groups. The one group includes those surveys and campaigns designed to discover the hidden diabetic. These surveys embrace the diabetes-prone, e.g., the elderly, those with strong family histories, women with recurrent miscarriages, stillbirths and large babies, and so forth. In such surveys, individual diabetes diagnosis is essential necessitating G.T.T.

The other group comprises those studies designed to indicate the true prevalence of the disease in a given community. It is with reference to this group that the following comments are directed.

With methodology increasing in sophistication, the time taken, the overall cost and the number of personnel involved, becomes all-important.

The present study has indicated that the total numbers of glycosurics and ^{hyperglycaemics} ~~hyperglycosurics~~ (i.e. 2 hour plasma glucose level equalling or exceeding 140 mg./100 ml.) by decade of age are very similar, and that a cut-off point of 140 mg./100 ml. provides an accurate indication of diabetes prevalence. Thus if prevalence was a survey's sole objective, a glucose challenge followed by a 2 hour glycosuria screen would be the cheapest method of estimating diabetes prevalence with a high degree of accuracy. No single glycosurie however, could be labelled diabetic save those with heavy glycosuria and thus individual diagnosis would be impossible.

In a later chapter, where sensitivity and specificity is discussed, the precise relationship of glycaemia and glycosuria to diabetes will be indicated.

It certainly is not the author's aim to recommend that glycosuria screening be adopted universally, but in those countries where no information concerning diabetes prevalence is available, a 2 hour post-glucose glycosuria screen could well provide an approximate estimate. All the work can be undertaken by unskilled personnel, no laboratory training is required and cost would be minimal.

It must be stressed that these suggestions are based solely on the Tongast findings. It would be essential to carry out identical surveys on many other and diverse population groups to establish whether these recommendations

can validly be applied elsewhere. The Birmingham^{69,82} and
Bedford⁷⁰ data, indicate that the post-glucose glycosuria rate
is approximately double the diabetes rate.

The need for further study is thus emphasised.

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SEX INFLUENCE ON DIABETES AND GLYCOSURIA PREVALENCE

It has been generally taught that little or no sex difference obtains in diabetes of juvenile onset as opposed to the female predominance amongst the middle-aged and elderly; these teachings have largely been applied to Western countries. Tulloch,⁹⁵ in reviewing aspects of diabetes in the tropics has drawn attention to an apparent general male predominance, in diabetes incidence in Uganda, India, and Ceylon. He does emphasise that this finding may have resulted from a reluctance on the part of the female in these countries to attend hospital and/or to provide urine for analysis.

More recently Malins et al⁹⁶ indicated a change in the sex incidence of diabetes. They commented on census mortality statistics from England and Wales, and showed a change in the male/female diabetes mortality ratio, tending to sex parity.

Evidence from recent American surveys lends support to this finding. Thus H.E.S.⁸³ registered total known diabetes prevalence for the male as being 1.3%, and 2.1% for the female. The Tecumseh study⁷¹ indicated a similar finding for known diabetes prevalence,⁹¹ namely 1.5% for males and 2.2% for females. This study also indicated that mean blood glucose values by decade of age for the 20th, 50th and 80th percentiles for the total survey population, differ but minimally between the sexes.

Mean values at the 80th percentile by decade of age are indicated in Table 38.

Table 38. 80th Percentile of 1 Hour Blood Glucose (mg./100 ml.) for Persons Challenged within 4 Hours of Eating by Age and Sex

Age (Yrs)	16-19	20-29	30-39	40-49	50-59	60-69	70-79
Blood M	122	137	158	176	185	198	226
Glucose F	137	145	161	174	200	196	224

Here it is seen that the female displays a slightly higher mean blood ^{glucose} value for the three younger age groups, but that from the 5th decade (with 1 exception) this sex difference is reversed. Further it is obvious that these sex differences are minimal and as such are probably not significant.

The Sudbury study⁷² carries the trend yet further. Prevalence of confirmed stated diabetes in males aged 15 years and older was 1.8% whilst female prevalence was 0.6%. Concerning newly diagnosed diabetes, here there was virtual sex parity, male and female prevalences being 0.6% and 0.7% respectively.

Analysis of the Tongast data follows.

(1) Diabetes Prevalence :

1. Total Prevalence

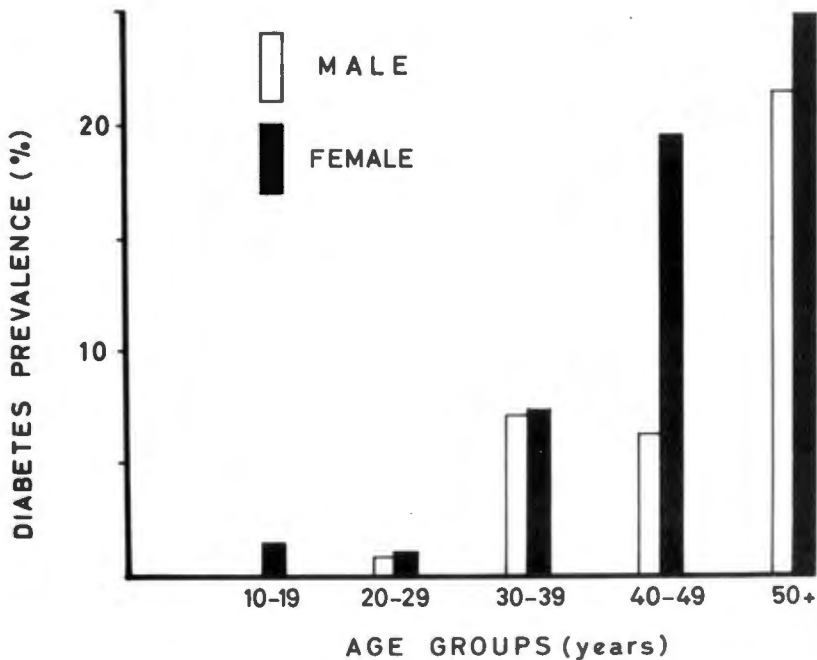
Total (known and newly diagnosed) diabetes prevalence for each of 5 age groups by sex, is indicated in table 39 and the differences quantitated in figure 16.

Table 39. Diabetes Prevalence by Age and Sex

Age Group (Years)	Male			Significance χ^2	Female		
	Tot. No.	No. Diab.	% Diab.		% Diab.	No. Diab.	Tot. No.
10 - 19	440	0	0.0	-	1.4	6	426
20 - 29	240	2	0.8	N.S.	1.0	4	401
30 - 39	126	9	7.1	N.S.	7.3	17	233
40 - 49	96	6	6.3	$p < .01$	19.5	33	169
50 plus	159	34	21.4	N.S.	24.8	34	137
All Ages	1061	51	4.8	$p < .01$	6.9	94	1366

Figure 16. Diabetes Prevalence by Age and Sex

DIABETES PREVALENCE BY AGE GROUP
MALE vs. FEMALE



It is apparent that diabetes prevalence is higher in the female for every age group although statistical significance is attained only in the 5th decade, through an inordinately high female prevalence which must account largely for the overall significantly higher female prevalence. The findings do indicate that while the female does possess the higher prevalence, the margin of difference is not excessive, the male : female ratio being 1 : 1.4. The findings thus tend to support the thesis of a change or a tendency towards a change in the sex differences of diabetes prevalence.

2. Known Diabetes

This includes only those known diabetics whose diagnoses were confirmed by plasma glucose values. Table 40 indicates prevalence by sex.

Age Group (Years)	Male			Significance	Female		
	Tot. No.	No. Diab.	% Diab.		% Diab.	No. Diab.	Tot. No.
10 - 19	440	0	0.0	-	0.0	0	426
20 - 29	220	2	0.8	-	0.0	0	401
30 - 39	126	3	2.4	N.S.	0.9	2	233
40 - 49	96	1	1.0	p < .05	7.1	12	169
50 plus	159	13	8.2	N.S.	7.3	10	137
All Ages	1061	19	1.8	N.S.	1.8	24	1366

Here overall prevalence is identical while by respective age group the male has the higher prevalence with the exception of the 5th decade where the female prevalence is higher and significantly so.

3. Newly-Diagnosed Diabetes

Here as indicated in the following table, it is evident that the female possesses the higher prevalence for all age groups, although statistical significance is not reached.

Table 41. Newly-Diagnosed Diabetes Prevalence by Age & Sex

Age Group (Years)	Male			Significance χ^2	Female		
	Tot. No.	No. Diab.	% Diab.		% Diab.	No. Diab.	Tot. No.
10 - 19	440	0	0.0	-	1.4	6	426
20 - 29	240	0	0.0	-	1.0	4	401
30 - 39	126	6	4.8	N.S.	6.4	15	233
40 - 49	96	5	5.2	N.S.	12.4	21	169
50 plus	159	21	13.2	N.S.	17.5	24	137
All Ages	1061	32	3.0	N.S.	5.1	70	1366

(11) Glycosuria Prevalence

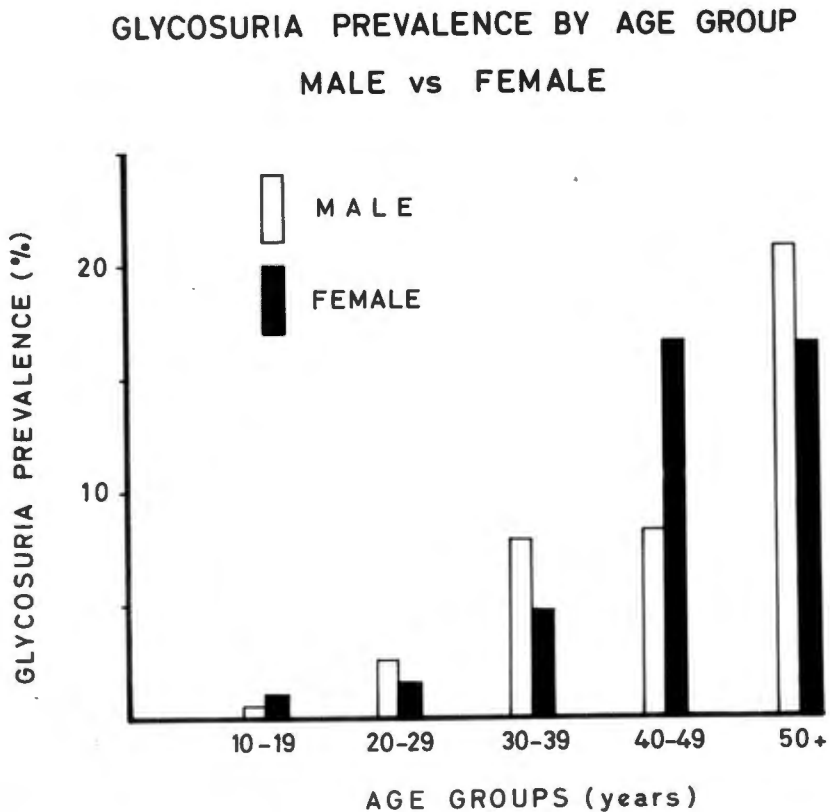
Glycosuria prevalence by age for each sex is indicated in the following table.

Table 42. Total Glycosuria Prevalence by Age and Sex

Age Group (Years)	Male			Significance χ^2	Female		
	Total No.	No. Glyc.	% Glyc.		% Glyc.	No. Glyc.	Total No.
10 - 19	440	2	0.5	N.S.	0.9	4	426
20 - 29	240	6	2.5	N.S.	1.5	6	401
30 - 39	126	10	7.9	N.S.	4.7	11	233
40 - 49	96	8	8.3	N.	16.6	28	169
50 plus	159	32	20.1	N.S.	16.1	22	137
All Ages	1061	58	5.5	N.S.	5.2	71	1366

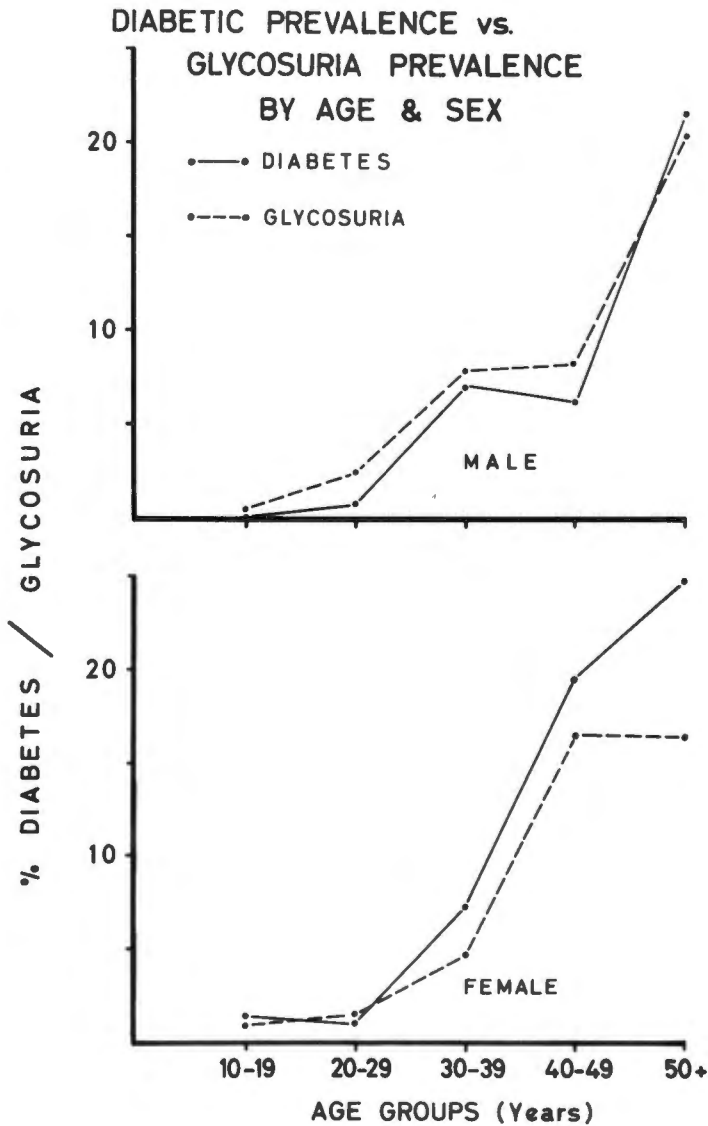
It is seen that male prevalence is higher in all age groups with the exception of the 2nd and 5th decades of age. In view of the exceptionally high female diabetes prevalence in the 5th decade, it is not remarkable that glycosuria prevalence in that decade is almost equally high. None of the sex differences including the overall difference, attain statistical significance. Figure 17 Quantitates these differences.

Figure 17. Total Glycosuria Prevalence by Age and Sex



As diabetes prevalence is higher in the female, while the male possesses the higher glycosuria prevalence, these two prevalences have been compared by age group in each sex. These comparisons are depicted in the following figure.

Figure 18. Diabetes Prevalence vs. Glycosuria Prevalence
In Each Sex By Age Group



As glycosuria is partly related to blood glucose (the other 2 variables being renal blood flow and renal threshold for glucose), it is necessary to examine glycosuria prevalence by sex in relation to plasma glucose concentration. It is realized that while the plasma glucose accurately reflects glycaemia at precisely 2 hours after glucose ingestion, no such accuracy can be obtained (in this study) for glycosuria. At its best the glycosuria would reflect urine excreted between 1 and 2 hours after glucose ingestion.

Table 43 indicates the relationship between plasma glucose and glycosuria for each sex.

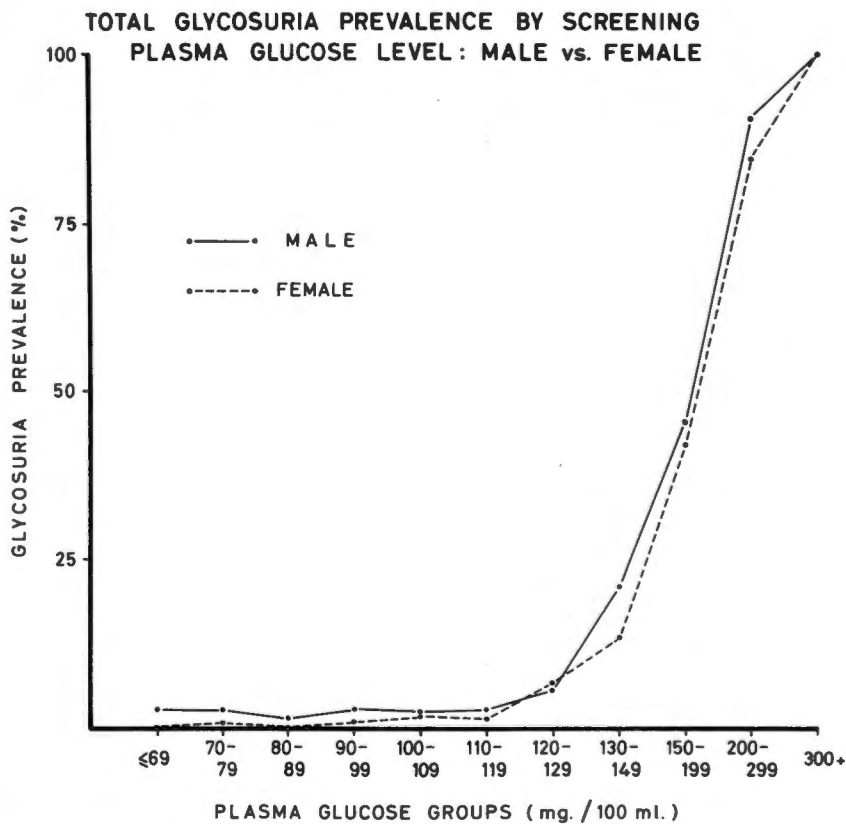
Table 43. Glycosuria Prevalence By Screen Plasma Glucose Level

<u>Plasma Glucose</u> <u>mg./100 ml.</u>	<u>Male</u>			<u>Female</u>		
	<u>Total</u> <u>No.</u>	<u>No.</u> <u>Glyc.</u>	<u>%</u> <u>Glyc.</u>	<u>%</u> <u>Glyc.</u>	<u>No.</u> <u>Glyc.</u>	<u>Total</u> <u>No.</u>
≤ 69	139	4	2.9	0.0	0	40
70 - 79	185	5	2.7	0.7	1	146
80 - 89	216	3	1.4	0.0	0	232
90 - 99	225	6	2.7	1.0	3	303
100 - 109	127	3	2.4	1.8	5	285
110 - 119	72	2	2.8	1.3	2	151
120 - 129	35	2	5.7	6.8	5	74
130 - 149	28	6	21.4	13.6	9	66
150 - 199	11	5	45.5	42.4	14	33
200 - 299	12	11	91.7	84.6	22	26
300 plus	11	11	100.0	100.0	10	10
All Ranges	1061	58	5.5	5.2	71	1366

To provide greater numbers for more meaningful comparisons, the 10 mg. grouping is abandoned at 130 mg./100 ml. for a 20 mg. group, and then a 50 mg. group at 150 mg./100 ml.

Figure 19 depicts this analysis graphically.

Figure 19. Glycosuria Prevalence By Screen Plasma Glucose Level - Male vs. Female



For all plasma glucose levels with only one exception (120 - 129 mg./100 ml.) the male has the higher prevalence. It is seen that prevalence for both sexes is uniformly low and reasonably parallel up to 120 mg./100 ml. when prevalence begins its precipitous rise. This is not altogether unexpected as sensitivity/specificity analyses (chapter 13) have shown that diabetes probability becomes meaningful at a level of 120 mg./100 ml. and increases rapidly with increasing plasma glucose value.

To assess the significance of the male - female difference at virtually all plasma glucose levels, the data has been arranged into 2 groups. The 1st group comprises all screenings with values less than 120 mg./100 ml. and the 2nd comprising those screenings with values equalling or exceeding 120 mg./100 ml. The 1st group has an extremely low diabetes probability as compared with the high probability of the 2nd. The following table indicates this comparison.

Table 44. Significance Between Male - Female Total Glycosuria Prevalence By Plasma Glucose Grouping

Plasma Glucose mg./100 ml.	Male			Significance χ^2	Female		
	Total No.	No. Glyc.	% Glyc.		% Glyc.	No. Glyc.	Total No.
≤ 119	964	23	2.4	p < .02	0.9	11	1157
≥ 120	97	35	36.1	N.S.	28.7	60	209

A significant difference is obtained in the low diabetes probability group. It is likely that though the male has the higher prevalence rate throughout, the presence of diabetes tends to nullify or render less this difference thus contributing towards the difference in the high diabetes probability group, ^{not attaining significance -} of the 35 males and 60 females, no less than 33 males and 50 females respectively, were in fact diabetic.

These findings indicate that the male has a higher glycosuria prevalence than the female, a finding that is maintained at identical plasma glucose levels. This is in keeping with findings of the H.E.S.,⁸³ where Gordon, noting the higher glycosuria prevalence for males (17.9% - males, 10.8% - females), has stated, "this sex differential, as might be expected, holds for all levels of blood glucose concentration."

----- CHAPTER 11 -----
GLYCOSURIA / GLYCAEMIA RELATIONSHIPS

(1) Glycosuria Aetiology :

In both surveys, all glycosurics irrespective of plasma glucose level were subjected to G.T.T. Glycosuria aetiology can be divided into 5 groups.

1. Diabetic : where the 1 and 2 hour plasma glucose values satisfy the diagnostic criteria.
2. Abnormal : where either the 1 or 2 hour plasma glucose value satisfies the diagnostic criterion.
3. Low Renal Threshold : where no plasma glucose value is ≥ 180 mg./100 ml. at any time interval or ≥ 140 mg/100 ml. at 2 hours.
4. Lag Curve : where the $\frac{1}{2}$ hour value is ≥ 180 mg./100 ml., other values being normal.
5. Unclassified : where glycosuria was not repeated and all plasma glucose values were normal.

First Survey :

Here 83 glycosurics of a total of 95 underwent G.T.T. - a recovery of 87%. The following table illustrates aetiology in these 83 glycosurics.

Table 45. Glycosuria Aetiology - 1st Survey

	61 Diabetic	-	73%
	1 Abnormal	-	1%
83 Glycosurics	7 L.R.T.	-	9%
	3 Lag Curve	-	4%
	11 Unclassified	-	13%

Second Survey :

Recovery was 77%. as of the 34 glycosurics, 27 underwent G.T.T. Here, though the numbers are smaller, the aetiology trend in the above table, repeats itself.

Table 46. Glycosuria Aetiology - 2nd Survey

	21 Diabetic	-	78%
	2 Abnormal	-	7%
27 Glycosurics	0 L.R.T.	-	0%
	0 Lag Curve	-	0%
	4 Unclassified	-	15%

The most important finding is the close similarity between the 1st and 2nd surveys with respect to diabetic glycosuria, namely 73% and 78% respectively. Both survey results have been combined to provide for more meaningful conclusions. Table 47 indicates this result.

Table 47. Glycosuria Aetiology - Composite Survey

	82 Diabetic	-	74%
	3 Abnormal	-	3%
110 Glycosurics	7 L.R.T.	-	6%
	3 Lag Curve	-	3%
	15 Unclassified	-	14%

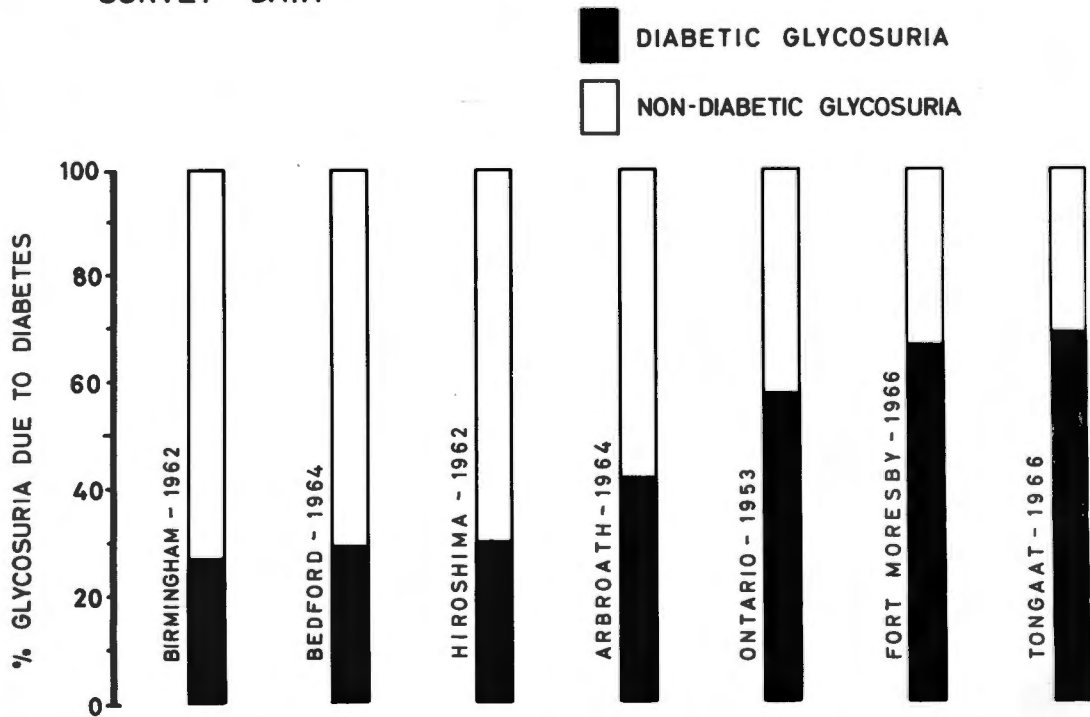
Recovery here is 85%, 110 cases out of a possible 129. Diabetes accounted for approximately 75%. This drops slightly when the 19 glycosurics who did not undergo G.T.T., are considered. Of these 19, 7 are clearly diabetic with 2 hour plasma glucose values in excess of 190 mg./100 ml., while the remainder are probably not diabetic, their values all being less than 125 mg./100 ml. Thus including these 19 glycosurics, the degree of diabetic glycosuria is 69% (89 diabetics out of 129 glycosurics).

Comparison With Other Surveys

The few studies suitable for comparison indicate a wide range of diabetic glycosuria as is illustrated in the following figure, where data from Birmingham,^{68,82} Bedford,⁷⁰ Hiroshima,⁶⁵ Arbroath,³⁶ Ontario,⁷⁸ and Fort Moresby²³ have been compared with Tongaat.

Figure 20. Diabetic Glycosuria - Tongaat compared with other Survey Data

DIABETIC GLYCOSURIA: TONGAAT FINDING COMPARED WITH OTHER SURVEY DATA



This in the 2 large English surveys, slightly less than 30% of all glycosurics were diabetic; this figure climbing steadily to 67% registered in a very recent study in Fort Moresby, New Guinea. This finding is virtually identical with the Tongaat result.

It appears that the Tongaat Indians have a high degree of diabetic glycosuria, but it must be remembered that the glycosuria-producing challenge in Tongaat was a 50 G glucose load, as opposed to a conventional meal in all other studies. The Birmingham and Bedford studies indicate changes when a glucose challenge is substituted for a conventional meal. In the Birmingham aglycosuric control group of 345 subjects, 51 developed glycosuria with 27 being classified as diabetic. The report does not indicate whether these 27 diabetics all developed glycosuria, although it is highly probable. Diabetic glycosuria would thus climb from 27% (post-prandial) to 53% (post-glucose). The Bedford workers indicate a similar escalation. Here 171 of the 570 aglycosuric controls developed post-glucose glycosuria, while 90 were classified as being diabetic. This report too does not clarify whether all diabetics were in fact glycosurics. If this was the case (and it is highly probable) then diabetic glycosuria escalated from a similar 29% to 53%.

These 2 calculations are however based on the premise that the diabetics were in fact glycosurics and thus cannot

be used in direct substantiation of a possible increase in diabetic glycosuria following a glucose load. Rather they may indicate a trend which may account for the large difference between the Tongaat and Birmingham/Bedford results.

(11) Diabetic Glycosuria By Age

Closer inspection reveals that diabetic glycosuria increases with age. Glycosuria in the adolescent and young adult, is highly likely to be non-diabetic, whereas in the elderly close to 90% of all glycosurics are diabetic. This finding is illustrated in the following table. The 2nd and 3rd decades have been combined in one group, as have all ages sixty and above. This has been necessary to provide sufficient numbers for meaningful analysis.

Table 48. Diabetic Glycosuria By Age

Age Group (Years)	No. Glycosurie	No. Diabetic	% Diabetic
10 - 29	18	4	22
30 - 39	21	14	67
40 - 49	36	28	78
50 - 59	27	20	74
60 plus	27	23	85
All Ages	129	89	69

It would seem that age is the determining factor in the probability of glycosuria being of diabetic origin or not.

(111) Diabetic Glycosuria By Degree Of Glycosuria

Before age is incriminated as the only factor influencing diabetes probability in glycosurics, it is necessary to examine any possible effect that degree of glycosuria can exert. The following table indicates that increasing glycosuria degree is associated with an increased diabetes probability.

Table 49. Glycosuria Degree and Diabetes Probability

Glycosuria Degree	No, Glycosuric	No, Diabetic	% Diabetic
+	39	13	33
++	21	13	62
+++	39	35	90
++++	30	28	93

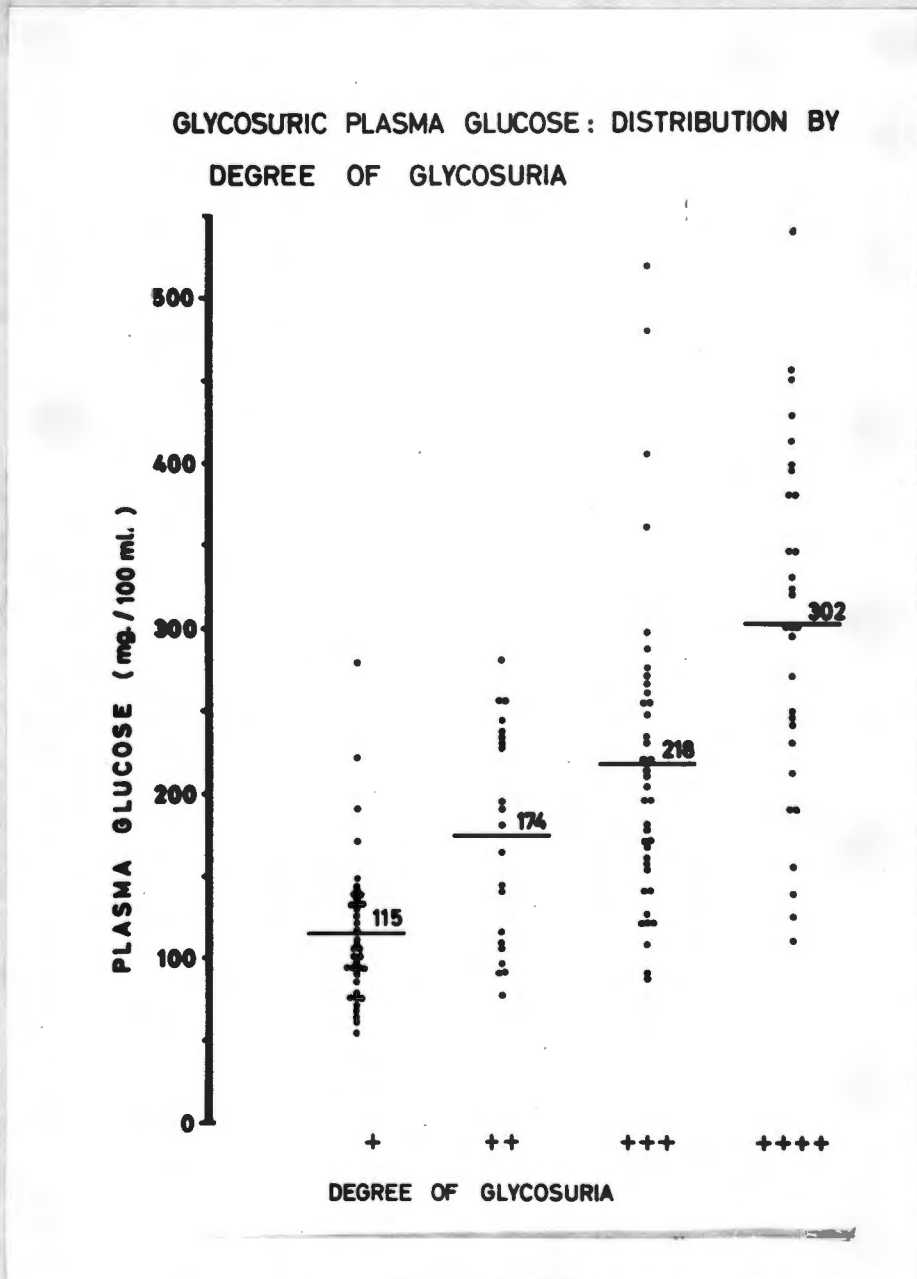
Thus in broad outline, + glycosuria indicates diabetes in $\frac{1}{3}$ of cases, ++ in two thirds, while +++ and ++++ glycosuria both have a diabetes probability bordering on three thirds. In 1953, Kenny and Chute reported a similar finding where diabetic glycosuria rose from 19% in those with minimal glycosuria to 80% in those with heavy glycosuria.

(iv) Glycosuria Plasma Glucose Distribution By Glycosuria Degree

The effect of age must be reconsidered. If glycosuria in the 10 - 29 year old group is predominately +, and heavy glycosuria dominates in the succeeding age groups, then the increase in diabetic glycosuria with age is coincidental and a false correlate. The distribution of plasma glucose values by degree of glycosuria must be examined. Glycosuria is only a

sign. It is not in itself a disease state but tends to reflect the blood glucose concentration. The following figure illustrates this distribution, for all 129 glycosurics.

Figure 21. Glycosuric Plasma Glucose Distribution by Degree of Glycosuria



The horizontal lines indicate the mean value for each degree of glycosuria.

These findings would thus explain the increasing diabetes probability with increasing degree of glycosuria.

In an earlier chapter, diabetes diagnosis by the screen criterion of 140 mg./100 ml. was demonstrated to compare favourably with diagnosis by G.T.T. In similar fashion, diabetes diagnosis amongst the glycosurics (by degree of glycosuria) has been compared employing the identical screen criterion as opposed to the G.T.T. criteria. The following table indicates the close similarity in prevalence between the 2 methods.

Table 50. Glycosuric Diabetes Prevalence By Glycosuria Degree
Screen Criterion vs. G.T.T. Criteria

Glycosuria Degree	No. Glycosuric	Diabetes Diagnosis		% Diabetes	
		Screen	G.T.T.	Screen	G.T.T.
+	39	7	13	18	33
++	21	14	13	67	62
+++	39	32	35	82	90
++++	30	27	28	84	93
All Degrees	129	80	89	62	69

The glycosurics designated as diabetic by each method display a close similarity, being slightly less with the screen criterion. This is not unexpected as diagnosis by G.T.T. irrespective of glycosuria, has been demonstrated to pick out

more diabetics than sole application of the screen criterion (chapter 8), although the differences as such were not significant. Assessment of the differences indicated in the above table indicates that significance was not attained for each of the 4 glycosuria degrees, or for the glycosurics as a single group.

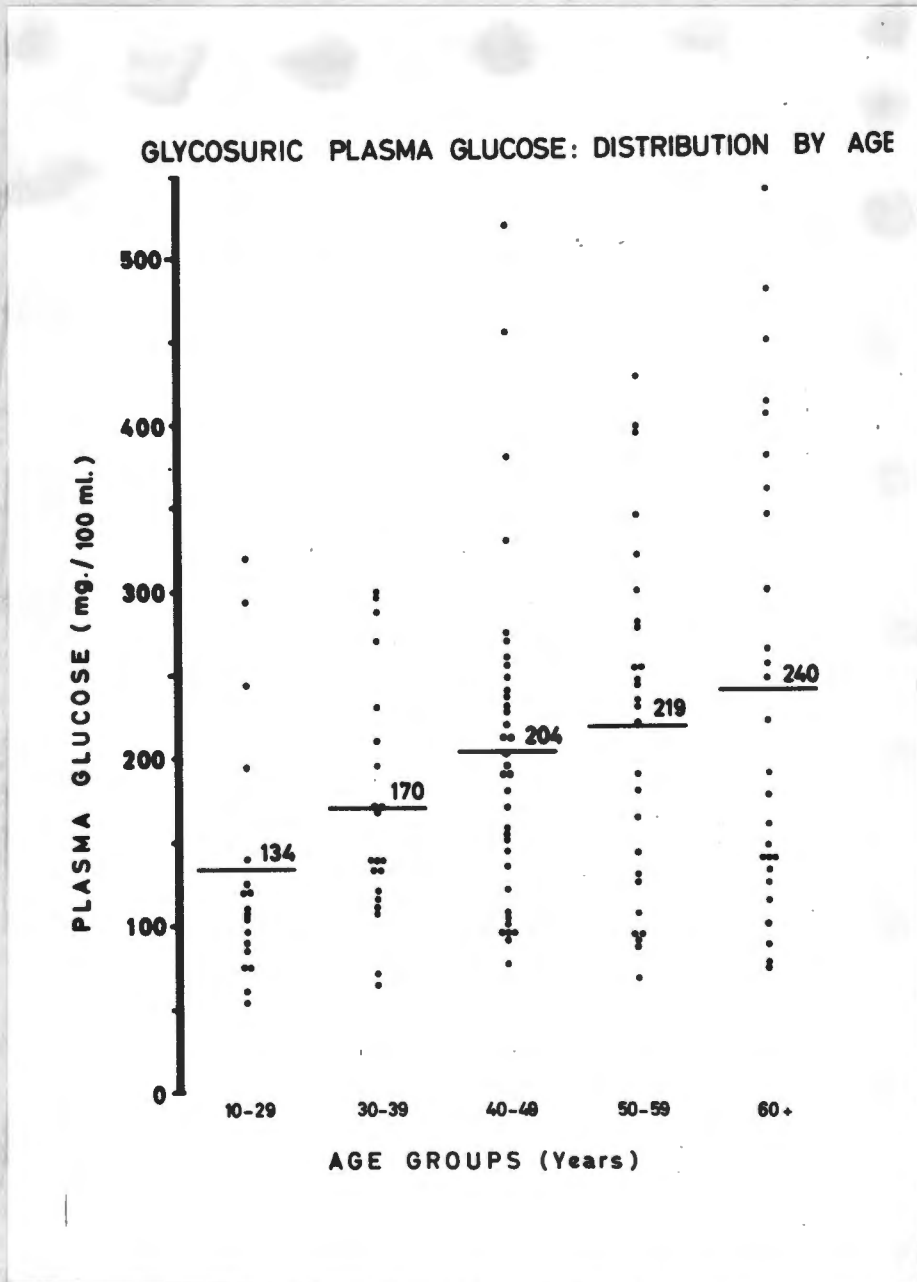
Points which emerge are :

1. Minimal glycosuria is associated with plasma glucose values which are mainly in the normal range, and that an increase in glycosuria degree is accompanied by a "migration" of the majority of the plasma glucose values into the diabetic range. This progression into the diabetic range is matched by a rise in mean plasma glucose value from 115 mg./100 ml. at + glycosuria to 302 mg./100 ml. at ++++glycosuria.
2. The number of glycosurics in each of the 4 glycosuria degrees who are in fact diabetic (G.T.T.), does not differ significantly from those designated as being diabetic by application of a screen criterion.

(v) Glycosuric Plasma Glucose Distribution By Age

The influence of age on the probability of glycosuria being diabetic can now be reassessed. The following diagram illustrates plasma glucose values of all glycosurics in each of 5 age groups.

Figure 22. Glycosuric Plasma Glucose : Distribution By Age



The increasing hyperglycaemia with age is obvious and must thus account for the concomitant increase in "diabetic glycosuria". As it has been demonstrated that glycosuria degree is largely

dependent upon plasma glucose value, it follows that the youngest glycosuric group (10 - 29 yrs.) would contain the greatest number of minimal (+,++) glycosurics, while heavy glycosuria (+++,++++) would predominate in the older groups.

Thus the low "diabetic glycosuria" rate in the younger group is due to their plasma glucose values being largely in the normal range, and the high "diabetic Glycosuria" rate in the elderly is due to a migration of their plasma glucose values to the diabetic range.

Plasma glucose level determines glycosuria degree irrespective of age, and as plasma glucose level determines diabetes, glycosuria degree can indicate diabetes probability.

(vi) Non-Diabetic Glycosuria Prevalence

Non-diabetic glycosuria prevalence for the survey population as a group and by age group, is indicated in the following table.

Table 51A Non-Diabetic Glycosuria By Age

Age Group (Years)	Total No.	No. Non-Diab. Glycosurics	% Non-Diab. Glycosurics
10 - 29	1507	14	0.9
30 - 39	359	7	1.9
40 - 49	265	8	3.1
50 - 59	170	7	4.1
60 plus	126	4	3.2
All Ages	2427	40	1.6

There is in fact an increasing non-diabetic glycosuria prevalence rate with age. The increase is admittedly slight with a slight fall in the oldest age group. The overall prevalence is 1.6%

----- 0 -----

----- CHAPTER 12 -----

INFLUENCE OF AGE, SEX, AND BODY WEIGHT ON SCREEN

PLASMA GLUCOSE PROFILES

(1) Age and Sex

Earlier it has been demonstrated that diabetes prevalence rises sharply with increasing age. As it has been demonstrated elsewhere that the distribution of blood sugar in any population is distinctly unimodal ^{96,97}, it is of importance to assess the influence of age on frequency distribution.

In each sex, the total survey population has been arranged into 5 age groups, 10 - 19, 20 - 29, 30 - 39, 40 - 49 and 50 years and above. Plasma glucose frequency curves of each sex by these respective age groups are depicted in the following figures.

Figure 23. Influence of Age on Screen Plasma Glucose Frequency Distribution - Males

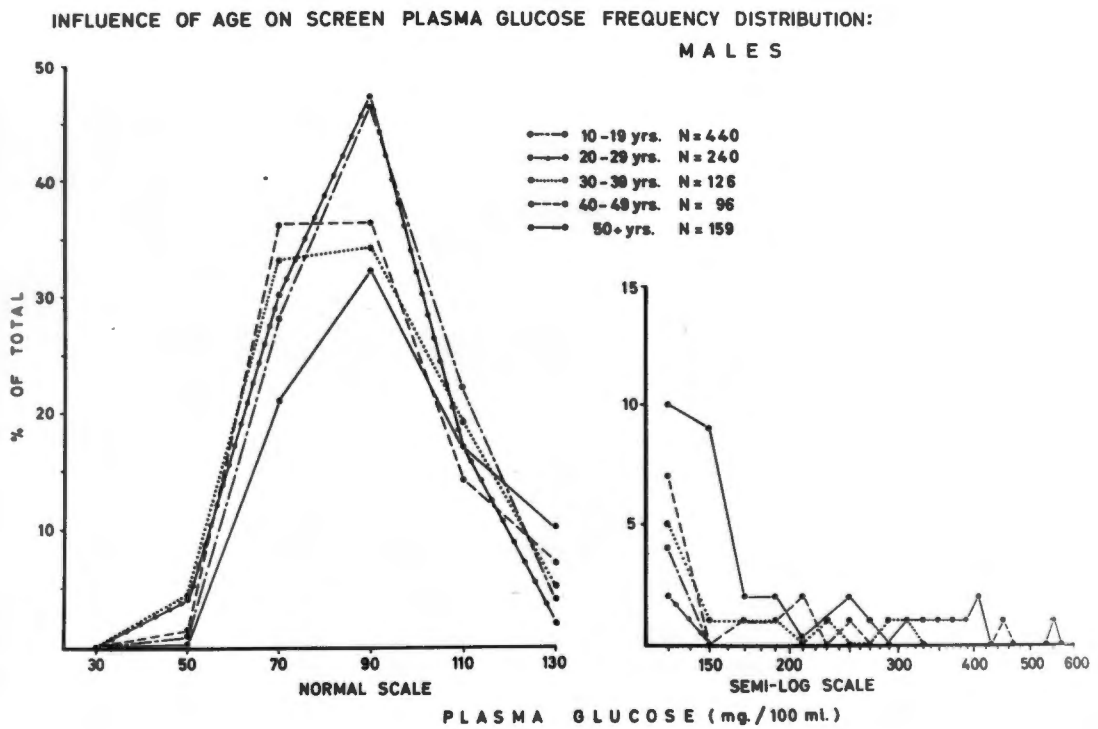
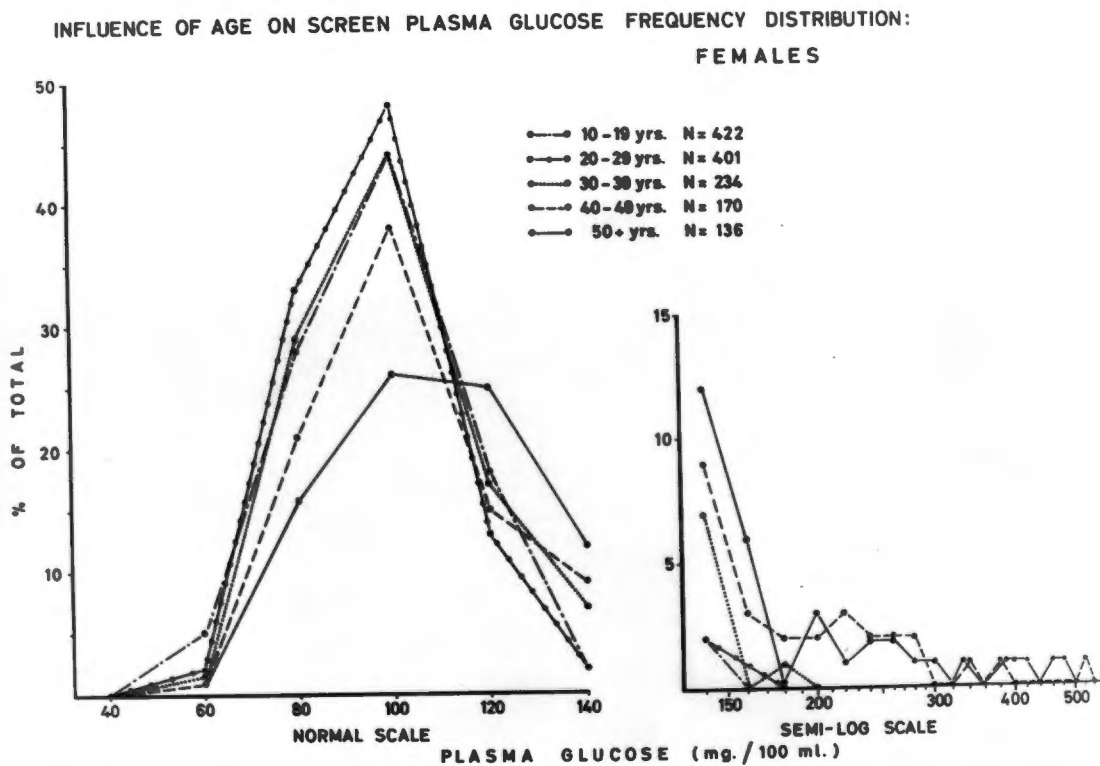


Figure 24. Influence of Age on Screen Plasma Glucose Frequency Distribution - Females



For each sex the frequency distribution curves have been interrupted at the 130 mg./100 ml. (males) and 140 mg./100 ml. (females). Up to this level of glycaemia, i.e. including the normal or euglycaemic range, the scale is normal. The curves thereafter, extending into the hyperglycaemic range, are expressed on a logarithmic scale, in addition the ordinate has been expanded. The object of this method of presentation is to indicate clearly the influence of age in the hyperglycaemic range which otherwise would be lost on a normal scale.

Each sex exhibits similar findings. It is seen that while the mode for each age group is approximately identical, the percentage of screenees constituting the mode decreases with increasing age as increasingly more screenees exhibit upper limit normal, to grossly hyperglycaemic responses.

Thus in the female, 44% of screenees in the 2nd decade constitute the mode (plasma glucose 90 - 109 mg./100 ml.) as compared with 48%, 44%, 38% and 26% of the 3rd, 4th, 5th decades and the oldest group. As the plasma glucose level climbs so the percentage of screenees drops out but far more so in the younger age groups. Thus a level between 130 and 149 mg./100 ml. includes only 2% of 2nd decade screenees as compared with the oldest group's 12%. The 3rd, 4th and 5th decades include 2%, 7% and 9% screenees respectively at that level. These curves continuing into the grossly hyperglycaemic range are confined solely to the 2 oldest groups, the 2nd, 3rd

and 4th decade screenings not extending beyond levels of 130 - 149, 150 - 169 and 170 - 189 mg./100 ml. respectively.

These findings are repeated to a similar extent in the male.

Age thus has the effect of "pushing" the distribution of plasma glucose increasingly into the hyperglycaemic ranges. This effect can be quantitated in terms of mean plasma glucose rise with age. This is illustrated in the following figure and the values are provided in the accompanying table.

Figure 25. Mean Screen Plasma Glucose Value By Age Group : Male vs. Female

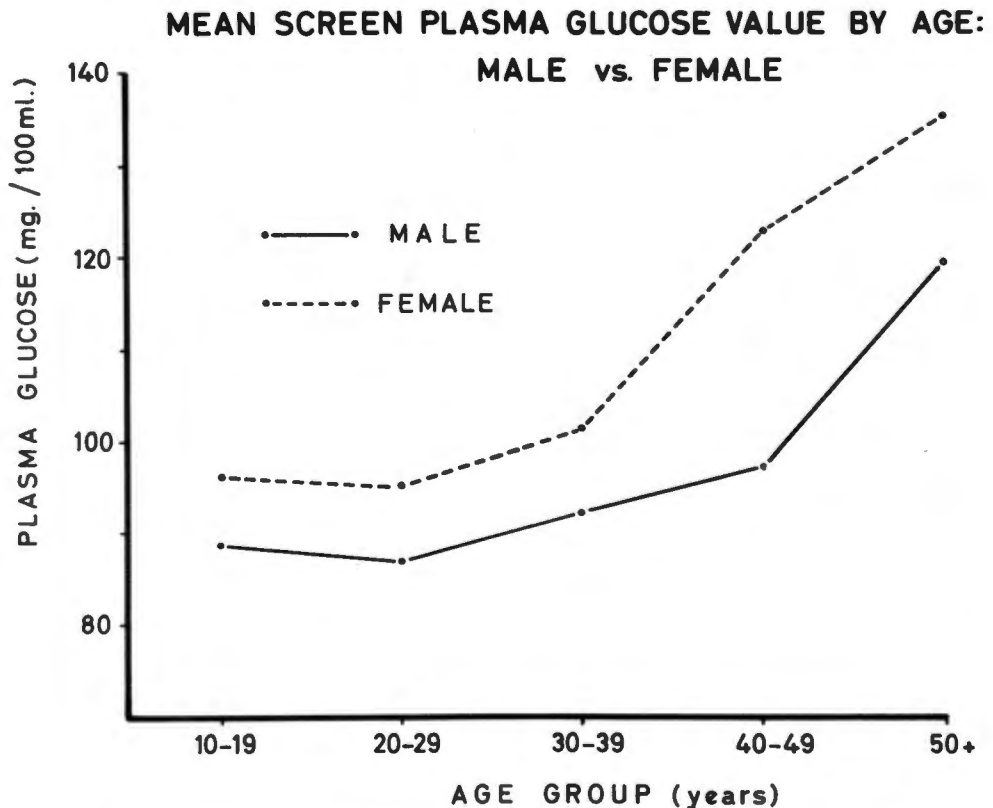


Table 51. Mean Screen Plasma Glucose Value by Age and Sex

Sex	Mean Plasma Glucose in each Age Group (mg./100 ml.) (Years)				
	10 - 19	20 - 29	30 - 39	40 - 49	50 plus
M	88.9	87.0	92.3	97.1	119.5
F	96.2	95.1	101.4	122.9	135.2

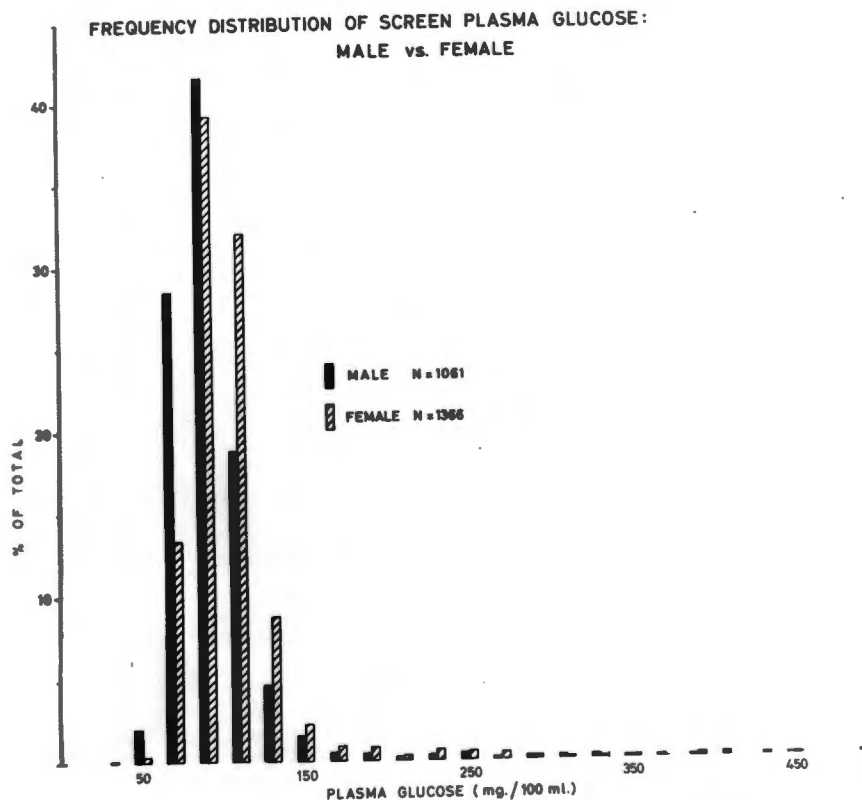
Apart from confirming the evidence afforded by the frequency distribution curves in that the mean plasma glucose value rises with age, it is seen that the mean value of the 2nd decade is slightly higher than that of the 3rd. This finding is corroborated by close inspection of the frequency distribution curves of those 2 decades in each sex, where it is seen that while both curves are closely similar, that of the 3rd decade does in fact tend slightly more towards the lesser plasma glucose values. A large proportion of screenings constituting the 10 - 19 year old group were children aged 10 - 13 years.

In such subjects, it is possible that the 50 G glucose load may have constituted too severe a challenge with abnormally raised plasma glucose levels resulting. This could in part explain the slightly higher mean value of the 2nd decade. ⁹⁸ Pickers et al have published figures for normal blood glucose response during G.T.T. for children which are certainly higher ⁹⁹ than those seen in healthy young adults. Similarly Danowsky

quotes mean figures for oral G.T.T. on 30 children which are likewise high, the 2 hour mean value of 111 mg./100 ml. in particular.

The higher mean plasma glucose value for the female is also indicated in the previous figure and table, the sex difference being maintained for all age groups. This is in keeping with the higher diabetes prevalence in the female. This sex difference is further illustrated in the following figure.

Figure 26. Frequency Distribution of Screen Plasma Glucose : Male vs. Female



In this histogram, it is obvious that the male possesses the lower the/frequency distribution values. Thus up to and including the mode (80 - 89 mg./100 ml.), the male possesses the greater percentage of subjects, e.g. at levels of 40 - 59 and 60 - 79 mg./100 ml., the male percentages are 2.0% and 28.5% respectively in contrast to those of the female of 0.2% and 13.3%.

At virtually all levels of plasma glucose following the mode, the female exhibits the greater percentage of subjects. Thus for levels at 100 - 119, 120 - 139, 140 - 159, 160 - 179, the female percentages are 32.0, 8.7, 2.2 and 0.9 respectively, in comparison with those of the male of 18.8, 4.6, 1.5 and 0.5. At levels of increasing hyperglycaemia, this sex difference though minimal, is generally maintained.

Influence of Age on Plasma Glucose Distribution in Non-Diabetics

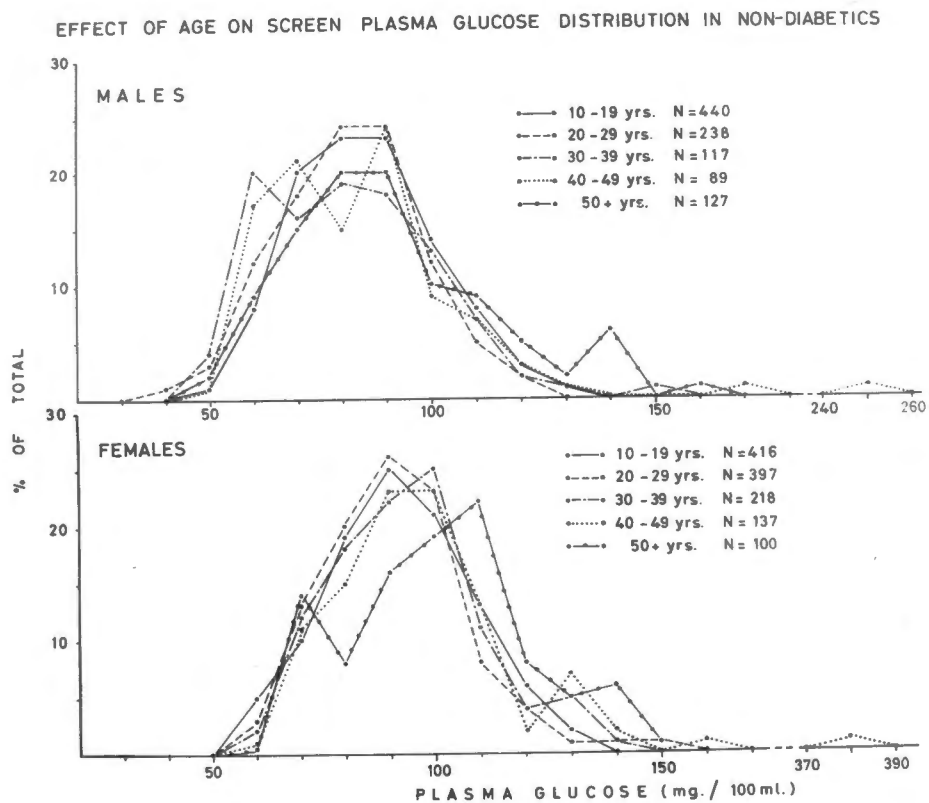
It has been demonstrated that there is a gradual deterioration in glucose tolerance with increasing age, this being evidenced by the increase in diabetes prevalence, the shift of frequency distribution curves to the right and the rise in mean plasma glucose value.

It is of considerable importance to assess whether increasing age exerts a similar effect on subjects designated as being non-diabetic. The plasma glucose frequency distribution curve being unimodal in shape, mitigates against any accurate demarcation of the diabetic from the non-diabetic

population. Nonetheless by application of the diagnostic criteria it is hoped that the diabetic population (145) contains as few false diabetics, as spurious non-diabetics contained in the non-diabetic population (2287).

Plasma glucose frequency distribution curves for each of 5 age groups in each sex are depicted in figure 27.

Figure 27. Effect of Age on Screen Plasma Glucose Distribution in Non-Diabetics - Male and Female



For each sex, the distribution curves vary but slightly with increasing age. In the female, the shift to the hyperglycaemic range is more pronounced than in the male, where such a shift is confined to the oldest age group. The shift for each sex is of doubtful significance.

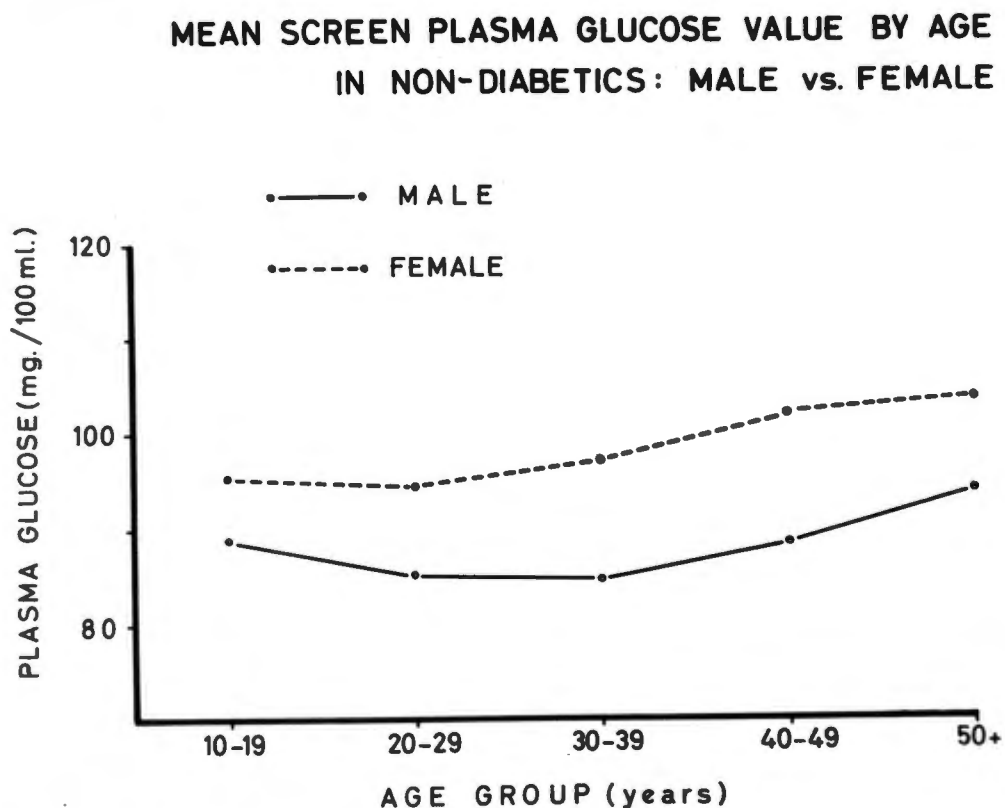
The mean plasma glucose value by age group in each sex is indicated in the following table.

Table 52. Mean Screen Plasma Glucose Value for Non-Diabetics by Age and Sex

Sex	Mean Plasma Glucose in each Age Group (mg./100 ml.)				
	10 - 19	20 - 29	30 - 39	40 - 49	50 plus
M	88.9	85.2	84.9	88.5	94.0
F	95.4	94.6	97.1	102.1	103.8

This is illustrated in the following figure.

Figure 28. Mean Plasma Glucose Value in Non-Diabetics
by Age Group : Male vs. Female



The mean plasma glucose thus does exhibit a rise with age in non-diabetics. In the male, this is only manifest in the oldest age group, while in the female it commences two decades earlier. In both sexes, the rise is less than 10 mg./100 ml.

As with the total population (diabetics and non-diabetics), the female exhibits the higher mean value for each age group.

When the sexes (non-diabetics) are combined the mean values for each of the 5 age groups, 10 - 19, 20 - 29, 30 - 39, 40 - 49 and 50 plus years, are 92.0, 91.0, 92.8, 96.8 and 98.3 mg./100 ml. In fact the rise from the nadir at 91.0 mg./100 ml. is but 7.3 mg./100 ml.

It is obvious that by the exclusion of all diabetics, the great majority of screenings constituting the hyperglycaemic "tail" of the frequency distribution curve, has been excluded. Thus any rise in mean glucose value with age in non-diabetics cannot be expected to be excessive. Viewed in this light, the rise with age, though of minimal proportions, does become meaningful.

(11) Genetic Applications :

This section comprising Pages 148 to 151 and references 100 to 110 inclusive has been deleted.

(111) Body Weight :

Height and weight measurements on the first 431 screenees were inadvertently not taken. Of the remaining 1996 screenees, 1980 were measured; the remaining 16 constituted the infirm, bedridden etc. The following analyses thus relate to these 1980 screenees. Body weight per se has not been considered, but rather the degree of obesity or leanness which is expressed quantitatively by the percentage deviation from average weight for each screenee's age, sex and height.⁵¹ The influence of these variables is thus eliminated.

The correlation coefficient (r) for percentage deviation from average weight and plasma glucose value follows: for the male $r = 0.020$, $n = 993$; for the female $r = 0.048$, $n = 987$; for the sexes combined $r = 0.025$, $n = 1980$ - significance being unattained.

When diabetes prevalence however is related to percentage deviation, then a relationship appears. The following table is indicative.

Table 53. Diabetes Prevalence by Percent Deviation of Average Weight

% Deviation Ave. Weight	Total No.	No. Diabetic	% Diabetic
25 - 44	3	0	-
45 - 64	33	1	3.0
65 - 84	757	14	1.9
85 - 104	807	47	5.8
105 - 124	267	26	9.7
125 - 144	85	15	17.7
145 plus	28	5	17.9

Diabetes prevalence rises steadily with a rapid climb into the obese groups. Obesity has previously been defined as indicative of the actual weight exceeding the average weight by 15%. When actual weight equals average weight, then δ deviation = 100, thus obesity is 115% + . If the screened population is divided into a non-obese and an obese group, and diabetes prevalence in each group compared as in the following table, then the difference is found to be highly significant ($p < .001$).

Table 4. Diabetes Prevalence in Non-Obese and Obese Screenings

Screening Group	Total No.	No. Diab.	% Diab.
Non-Obese < 115%	1766	77	4.4
Obese \geq 115%	214	31	14.5

Diabetes thus has a very definite relationship to body weight, whereas plasma glucose and body weight does not display a significant correlation.

This finding receives support from O'Sullivan and Mahan¹⁰⁶ who showed that the relationship between post-prandial blood sugar and body weight in the Oxford survey was not significant by multiple regression analysis which included age, height, and sex as other variables. These workers did however demonstrate that diabetes was significantly more prevalent (19.7%) in overweight subjects (20% plus ideal weight) than in

underweight subjects (5.9%).

The Sudbury workers⁸⁸ indicated that the small rise in post-prandial blood sugar level with increasing body weight was not significant when adjusted for the accompanying increase in age. They do however indicate a significant correlation ($r = 0.35$, $p < .01$) between body weight and blood sugar in the small (176 persons) sample who had a glucose challenge. This finding is in contrast to that of Tengast.

----- CHAPTER 13 -----

SENSITIVITY AND SPECIFICITY

In any survey such as the present study, it is of considerable importance to be able to predict with reasonable certainty the ability of a screening test at a particular criterion to include all true diabetics, while simultaneously excluding all true non-diabetics. This is referred to as the sensitivity and specificity. Sensitivity is defined as the percentage of true diabetics rated as positive by a given test; specificity on the other hand, is the percentage of true non-diabetics rated as negative by a given test.¹¹¹ The calculation is illustrated below :

$$\text{Sensitivity (at a given criterion)} = \frac{\text{No. True Diabetics (at same criterion)}}{\text{Total No. True Diabetics}}$$
$$\text{Specificity (at a given criterion)} = \frac{\text{No. True Non-Diabetics (at same criterion)}}{\text{Total No. True Non-Diabetics}}$$

Plasma glucose value as well as glycosuria presence determined retesting by G.T.T. in this survey. This affords the opportunity of calculating sensitivity and specificity by differing plasma glucose criteria and also by differing degree of glycosuria. The efficiency of plasma glucose screening as opposed to glycosuria can thus be assessed.

This calculation of sensitivity and specificity is based on the premise that the screen criteria were sufficiently low and complete as to include all diabetics in the population.

Though this is really a Utopian ideal, it is felt to be not unreasonable as the screen itself was a modified G.T.T. and with the cut off point at 110 mg./100 ml. initially, followed by 120 mg./100 ml., it is highly unlikely that more than a few diabetics were in fact excluded.

(1) Plasma Glucose Screening :

The following table indicates diabetes probability in each of 8 plasma glucose screening categories irrespective of glycosuria

Table 55. Diabetes Probability by Screen Plasma Glucose

Screen Level (mg./100 ml.)	Total No.	No. Diabetic	% Diabetic
180 plus	73	71	97.3
170 - 179	6	5	83.3
160 - 169	12	9	75.0
150 - 159	12	8	66.7
140 - 149	33	10	30.3
130 - 139	52	11	21.2
120 - 129	91	23	25.6
110 - 119	71	3	4.2

Diabetes probability increases rapidly from 4.2% (110 - 119 mg./100 ml.) to 97.3% in the grossly hyperglycaemic (180 mg./100 ml. plus) group. It is of interest that even at this level, one can expect a small number of subjects to be non-diabetic on retesting.

Proceeding from table 55, the accumulative number diabetic and non-diabetic out of the total number diabetic and non-diabetic, can be calculated. The survey encompassed 2427 persons and as the total number diabetic was 145, it follows that the total number non-diabetic was 2282. At 180 mg./100 ml. plus, there were 71 diabetics, at 170 - 179 mg./100 ml. there were 5 and so on. Thus the accumulative number diabetic at 180 mg./100 ml. plus remains 71, at 170 mg./100 ml. plus, it is 85 etc. This means that if only those persons who had screen values of 160 mg./100 ml. plus were retested, then a total of 85 diabetics would have been discovered. As the total number diabetic is 145, the sensitivity of plasma glucose screening at 160 mg./100 ml. is $\frac{85}{145}$ as a percentage, or 58.6%

In identical fashion, the accumulative number non-diabetic out of the total number non-diabetic can be calculated. At 180 mg./100 ml. plus, there were 2 non-diabetics, at 170 - 179 mg./100 ml. there was 1, at 160 - 169 mg./100 ml. there were 3, and so on. Thus the total number non-diabetic at 180 mg./100 ml. plus remains 2, at 170 mg./100 ml. plus, it is 3, at 160 mg./100 ml. it is 6 etc. Thus by testing all subjects whose screened at 180 mg./100 ml. plus, only 2 non-diabetics would have been included. As the total number of non-diabetics is 2282, the number of non-diabetics which would have been excluded from retesting at that screen level, is 2282 minus 2, namely 2280 which is the accumulative number non-

Table 57. Sensitivity & Specificity by Plasma Glucose level

Plasma Glucose (mg./100 ml.)	Sensitivity (%)	Specificity (%)
180 plus	50.0	99.9
170 "	52.4	99.8
160 "	58.6	99.7
150 "	64.1	99.6
140 "	71.0	98.6
130 "	78.6	96.8
120 "	94.5	93.8
110 "	96.6	90.8

diabetic at that level. The specificity of plasma glucose screening at that level is thus 2280/2282 expressed as a percentage, i.e. 99.2%

The following table indicates the accumulative number diabetic and non-diabetic at identical screen levels.

Table 56. Accumulative Number Diabetic and Non-Diabetic
By Plasma Glucose Screening Level

Screen Level (mg./100 ml.)	Accum. No. Diabetic	Accum. No. Non-Diabetic
180 plus	71	2280
170 "	76	2279
160 "	85	2276
150 "	93	2272
140 "	103	2249
130 "	114	2208
120 "	137	2140
110 "	140	2072

Sensitivity and specificity at these screen levels is provided in Table 57 (previous page). The table indicates that sensitivity increases as specificity decreases. Consequently a high screening level while including very few false positives (non-diabetics), will include a limited number of true positives (diabetics). Lowering the screening level will result in a greater percentage of diabetics being included, i.e. a greater sensitivity. It will also result in the inclusion of a greater number of false positives, i.e. a lesser specificity. For

example, by retesting all screenees with levels of 130 mg./100 ml. plus, 78.6% of all diabetics would have been identified (sensitivity), while 96.8% of non-diabetics would have been excluded (specificity).

Table 57 indicates that the best screening criterion would be at 110 mg./100 ml. or 120 mg./100 ml. At either of these 2 criteria, sensitivity and specificity are both at least 90%. Of the two, it would appear that the 120 mg./100 ml. level is the most practical; the minimal decrease in sensitivity (from this level to 110 mg./100 ml.) of 2.1% is more than compensated by an increase in specificity of 3.0%. Practically it means that only 3 diabetics would have been missed whereas 68 non-diabetics would have been spared repeat G.T.T. This thus supports the ultimate adoption of 120 mg./100 ml. as the screen criterion.

It is of considerable importance in future surveys to choose a screen criterion which combines maximum sensitivity with maximum specificity. Only then, can unnecessary repeat tests be rendered minimal. Obviously any screen level must be a compromise between the ideal and the practical; by setting the screen level low enough, one could ensure 100% sensitivity ~~specificity~~ at the sacrifice though, of specificity. Conversely a level high enough to produce 100% specificity, would result in a very low sensitivity.

In this survey, the screen level of 120 mg./100 ml. is remarkably "high yielding". At this level, 95% of all diabetics have been included with 94% of all non-diabetics excluded.

Wilkerson et al¹¹² found that the most practical screen criterion 2 hours after a meal was 120 mg./100 ml, sensitivity being 82.8% and specificity 91.8%. A report by Ramein and Wilkerson⁷³ in identical circumstances found the most practical criterion to be 110 mg./100 ml. with a sensitivity and specificity of 85.7% and 84.1% respectively.

The present study indicates that glucose challenge as opposed to test meal, provides the more efficient stimulus when sensitivity is balanced against specificity. At its optimum screening level, the test meal will include only 83 - 86% of diabetics while excluding 92 - 84% of non-diabetics. These figures are inferior to those when a glucose load constitutes the challenge.

(11) Glycosuria Screening :

All glycosurics irrespective of screen plasma glucose level, were subjected to repeat G.T.T. Sensitivity and specificity by degree of glycosuria can be determined. The method of calculation is identical to that described before.

The following table indicates diabetes probability by glycosuria degree.

Table 58. Diabetes Probability by Glycosuria Degree

Glycosuria Degree	Total No.	No. Diabetic	% Diabetic
++++	30	28	93
+++	39	35	90
++	21	13	62
+	39	13	33

The accumulative number diabetic and non-diabetic out of the total number diabetic and non-diabetic can now be calculated. Thus + + + + glycosuria identified 28 diabetics, + + + and heavier glycosuria identified 63, + + and heavier identified 76, and + and heavier (i.e. all degrees of glycosuria) identified 89 diabetics.

The total number of diabetics in the survey was 145, consisting of these 89, and a further 56 who did not manifest glycosuria during the screen. The sensitivity of + + + + glycosuria as a screen criterion is thus $28/145$ expressed as a percentage, or 19.3%, of + + glycosuria is 52.4%, $\frac{76}{145} \times \frac{100}{1}$

The following table illustrates the accumulative numbers diabetic and non-diabetic by degree of glycosuria.

Table 59. Accumulative Number Diabetic and Non-Diabetic by Glycosuria Degree

Glycosuria Degree	Accum. No. Diabetic	Accum. No. Non-Diabetic
++++ plus	28	2280
+++ "	63	2276
++ "	76	2268
+ "	89	2242

The accumulative number non-diabetic of the total number non-diabetic can be calculated. At + + + +, + + +, + + and + glycosuria there were 2,4,8 and 26 non-diabetics respectively (refer table 58). The total number of non-diabetics at + + + + glycosuria remains 2, at + + + glycosuria it is 6 (2 plus 4), at + + it is 14, and at + glycosuria and greater which includes all glycosurics, it is 40. Thus in repeating the G.T.T. in all glycosurics, there would have been 40 false positives. The total number of non-diabetics being 2282, the accumulative number at + glycosuria would be 2282 minus 40, namely 2242. At + + glycosuria, only 14 false positives would be included. The accumulative number at this screen level would be 2282 minus 14, namely 2268.

At this level, specificity is thus 99.4% ($2268/2282 \times 100/1$); specificity at + glycosuria and greater is 98.3%, 2242 out of 2282 as a percentage.

Sensitivity and specificity by glycosuria degree is indicated below.

Table 60. Sensitivity and Specificity by Glycosuria Degree

Glycosuria Degree	Sensitivity (%)	Specificity (%)
+ + + + plus	19.3	99.9
+ + + "	43.4	99.7
+ + "	52.4	99.4
+ "	61.4	98.3

At its best, glycosuria has poor sensitivity. If all glycosurics were retested, only 61% of all diabetics would in fact have been identified. With respect to specificity though, glycosuria screening demonstrates a high degree of effectiveness. At any degree of glycosuria, the chances of including true non-diabetics out of the total non-diabetic population are exceedingly slim. If all glycosurics were retested, fully 98% of all true non-diabetics would be excluded. Reinin and Wilkerson⁷³ have reported similar rates.

(iii) Plasma Glucose vs., Glycosuria Screening :

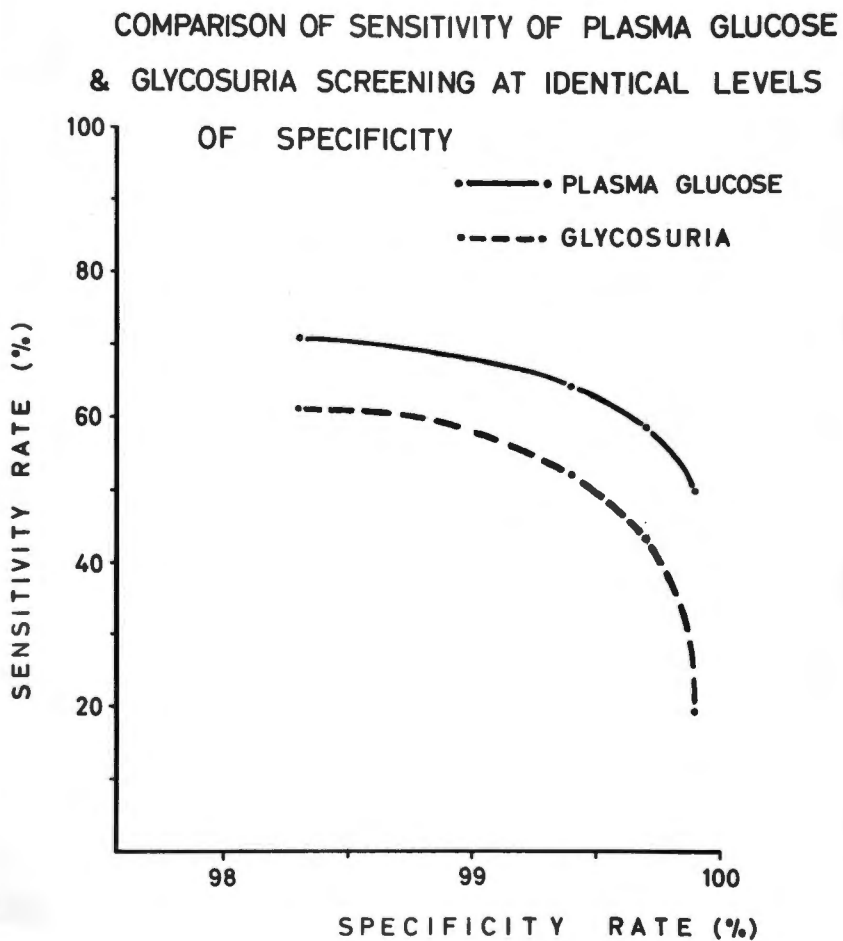
It is possible to compare sensitivity for each screen criterion independently, at 4 levels of specificity. The following table is indicative.

Table 61. Sensitivity of Plasma Glucose and Glycosuria Screening at Identical Levels of Specificity

<u>Sensitivity (%)</u>		<u>Specificity (%)</u>
<u>Plasma Glucose</u>	<u>Glycosuria</u>	
50.0	19.3	99.9
58.6	43.4	99.7
64.1	52.4	approx. 99.4
71.0	61.4	" 98.3

For each level of specificity at which comparison can be made, plasma glucose screening proves its superiority. This is illustrated in the following figure.

Figure 29. Sensitivity of Plasma Glucose and Glycosuria Screening at Identical Levels of Specificity



Some apparent contradictions may have arisen out of discussion of this concept, and the author feels that it will be of value to define these, in order to add greater clarity to the concept of sensitivity and specificity.

1. In chapter 8, it was noted that decade by decade, the total number of subjects screening at or greater than 140 mg./100 ml. (136) was very similar to the total number of proven diabetics (145). The difference was not significant. The reader may well inquire as to the apparent difference in sensitivity at this screen level (71%) as compared with the close similarity mentioned above.

These two analyses/comparisons cannot be compared. Sensitivity refers specifically to the percentage of true diabetics rated as positive by a given test. Thus while it would be reasonably accurate to count all those screening at 140 mg./100 ml. and above, and express this number as being indicative of general diabetes prevalence, in actual fact only 71% of true diabetics would be included, the remaining 29% being non-diabetic.

2. Concerning glycosuria, a similar apparent contradiction may arise. It has been shown in chapter 9, that total glycosuria prevalence was closely similar to total diabetes prevalence, any differences being not significant. That being so, it may be asked why glycosuria sensitivity (all degrees) is not close to 100%. whereas it is in fact only 61%. At the risk of repetition, it must be reiterated that sensitivity is

a specific indication of the percentage of true diabetics rated as positive by a given test. And thus while the total number of glycosurics is similar to the total number of proven diabetics, it is not correct to assume that every glycosuric is a diabetic.

To give a hypothetical example, if a 1000 persons were screened in an identical manner to that of the present study, it would be reasonably correct to estimate with a high degree of accuracy, the diabetes prevalence by numbering all subjects screening at or greater than 140 mg./100 ml. and express this number as being the total number diabetic. It would likewise be reasonably correct to number all glycosurics, and express this number as being the total number diabetic.

However, no individual in either group designated as being diabetic, could with accuracy be in fact diabetic. Of the subjects screening at or greater than 140 mg./100 ml., in fact only 71% of the total number of diabetics, would be identified, while the glycosuric group would include only 61%

----- CHAPTER 14 -----

PREDICTABILITY AND REPRODUCIBILITY OF GLYCAEMIA RESPONSE
TO ORAL GLUCOSE

The material for this investigation is provided by those positive screenees who underwent G.T.T.

(1) Predictability

Severity of diabetes is often assessed by the fasting blood glucose value. Diabetics are often practically split up into 2 groups, those with fasting euglycaemia and those with fasting hyperglycaemia. The rationale is that the metabolic disorder of diabetes is considered to be of a lesser degree in the former group than in the latter.

The validity of this rationale can be partly investigated by exploring the relationship between the fasting plasma glucose and the 1 and 2 hour levels during G.T.T. In an attempt to demonstrate such a relationship, correlations between the fasting plasma glucose (independent variable) and the 1 and 2 hour levels (dependent variables) have been explored. These correlations are expressed separately for each of 2 groups, namely the diabetics and the non-diabetics.

1. Diabetics

Figures 30 and 31 illustrate the correlation between the fasting plasma glucose and the 1 and 2 hour responses respectively.

Figure 30. Fasting Plasma Glucose vs. 1 Hour Plasma Glucose
in Discovered Diabetics

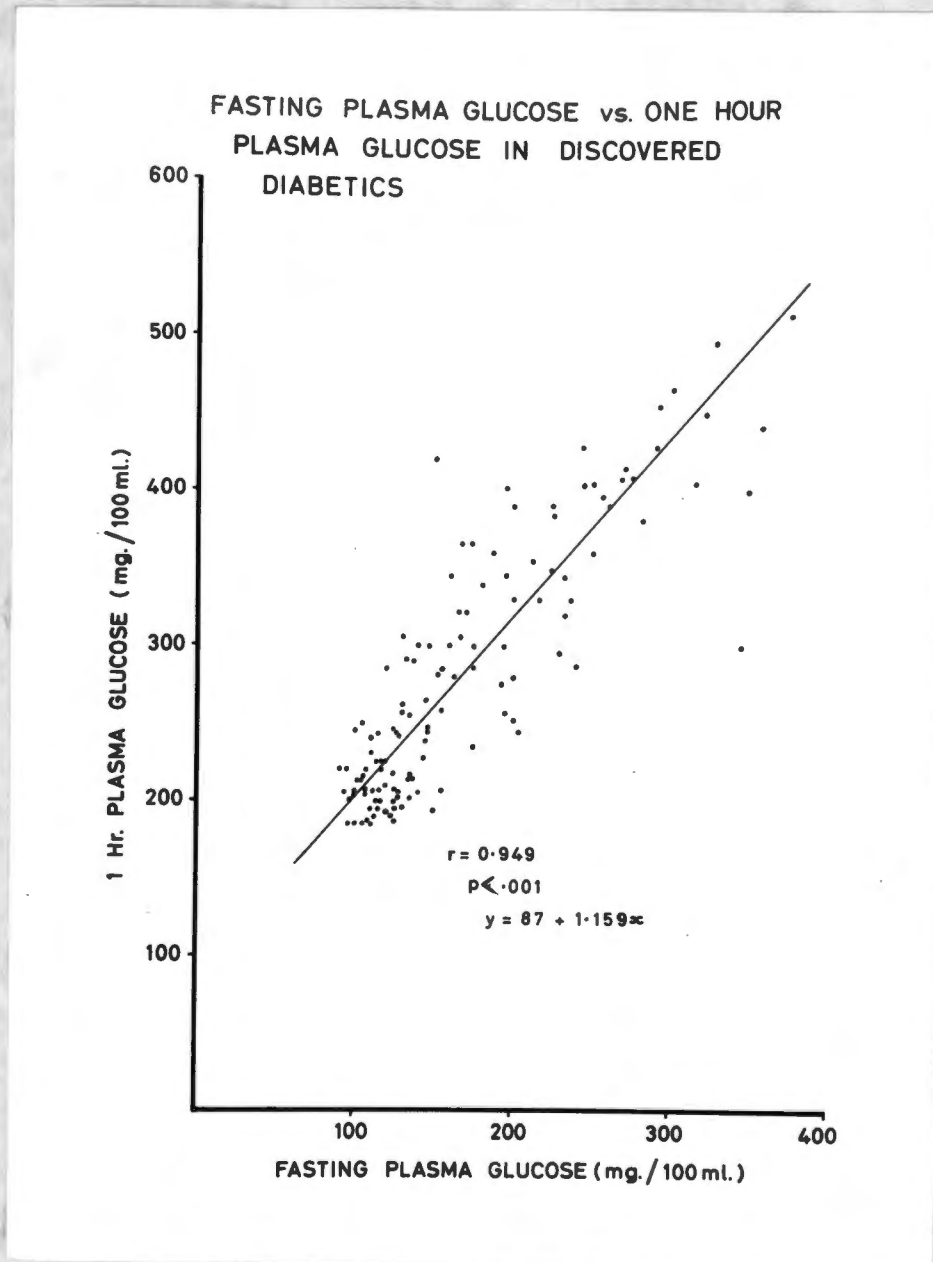
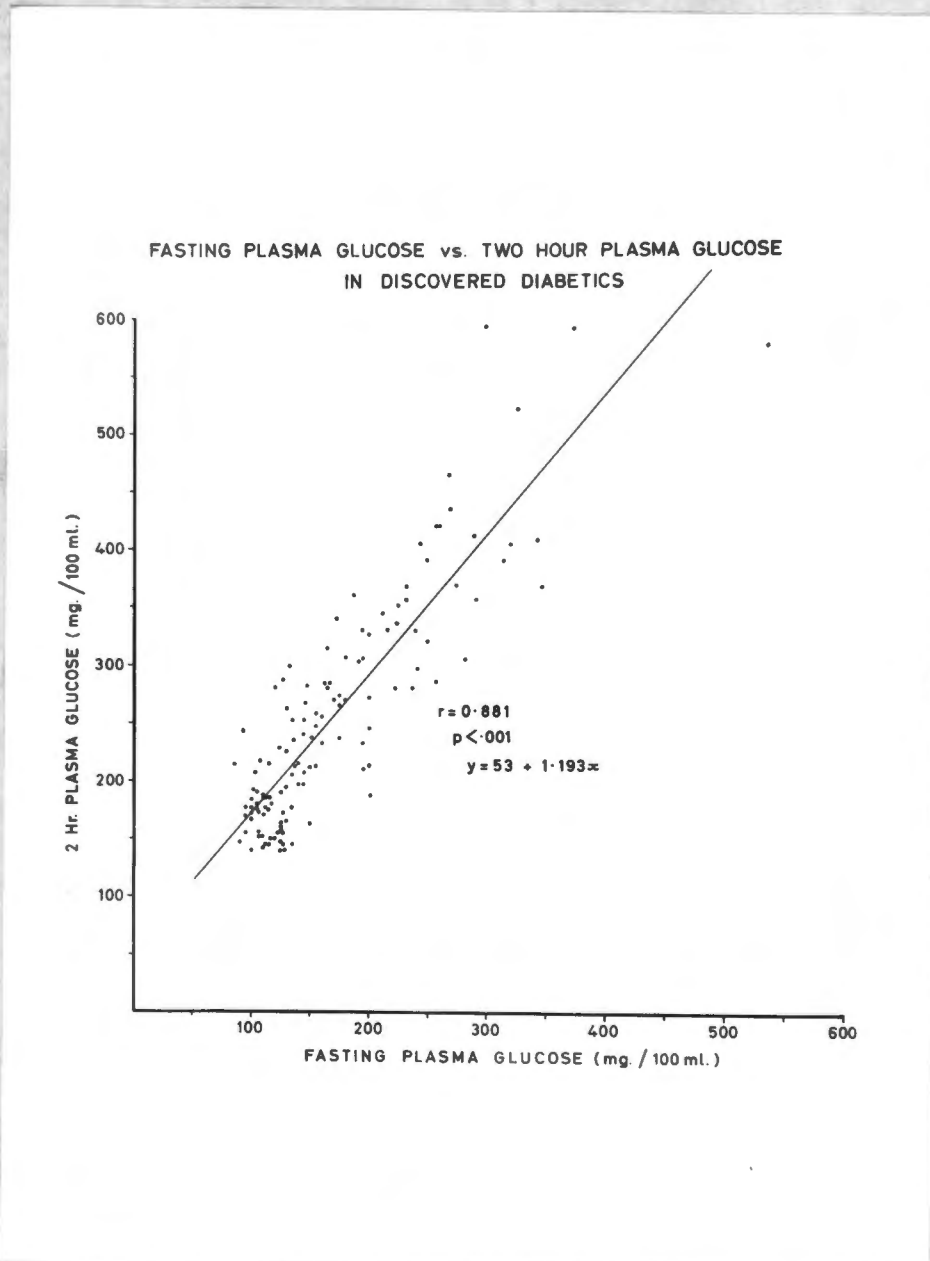
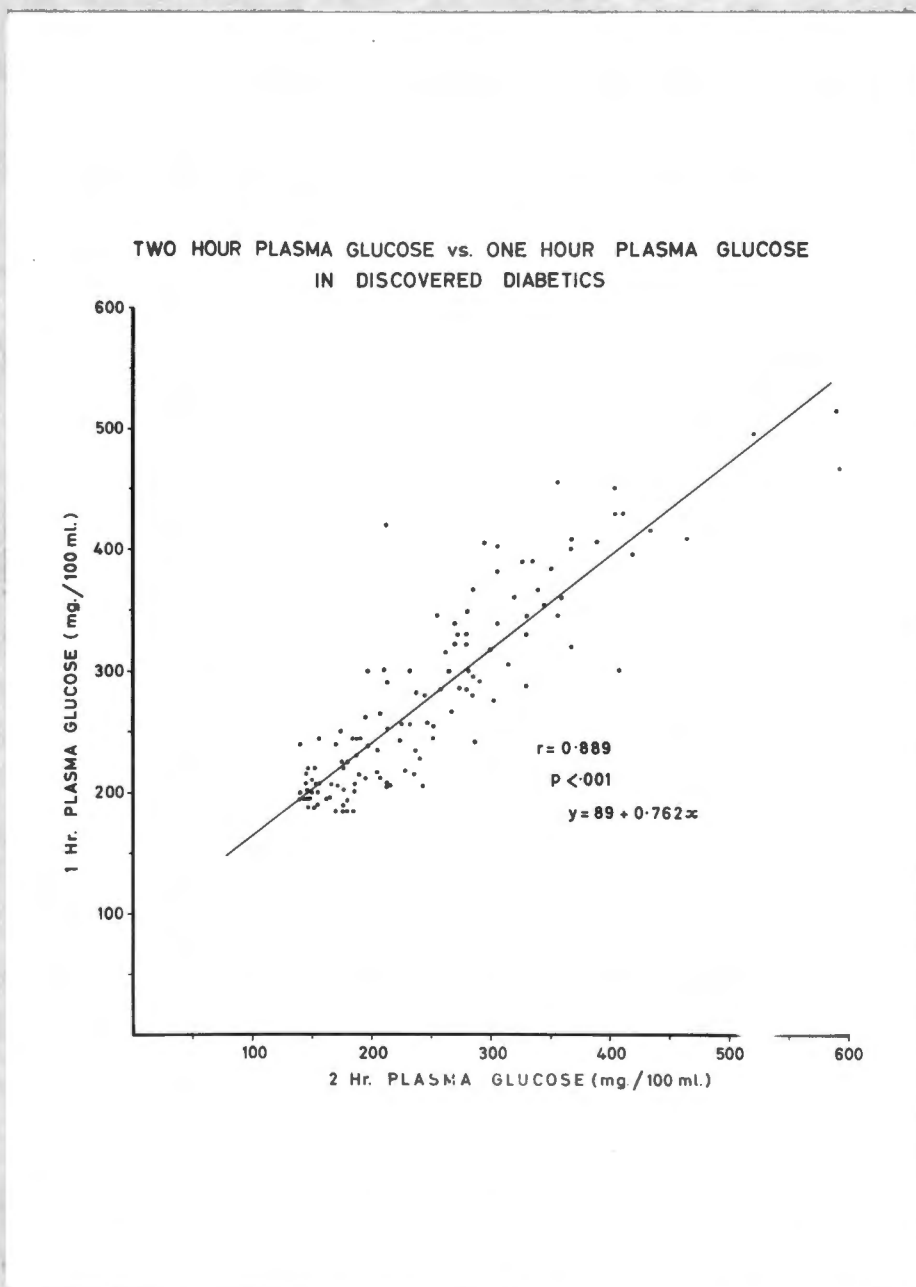


Figure 31. Fasting Plasma Glucose vs. 2 Hour Plasma Glucose
in Discovered Diabetics



In both relationships, there is a highly significant degree of correlation. The following figure indicates the relationship between the 2 and 1 hour plasma glucose values.

Figure 32. Two Hour Plasma Glucose vs. One Hour Plasma Glucose in Discovered Diabetics



It is clear that the fasting plasma glucose value has a high predictive value. The relationship between it and the 1 and/or 2 hour plasma glucose value is constant and linear. The diabetic with an euglycaemic fasting value does not exhibit as gross a response to oral glucose as his constantly hyperglycaemic fellow-sufferer. Hence the division mentioned earlier is justified. It is also of interest that the 2 hour value is equally predictive with respect to the 1 hour value.

2. Non Diabetics

Figures 33 and 34 illustrate the correlation between the fasting plasma glucose and the 1 and 2 hour responses respectively.

Figure 33. Fasting Plasma Glucose vs. 1 Hour Plasma Glucose in Non-Diabetics

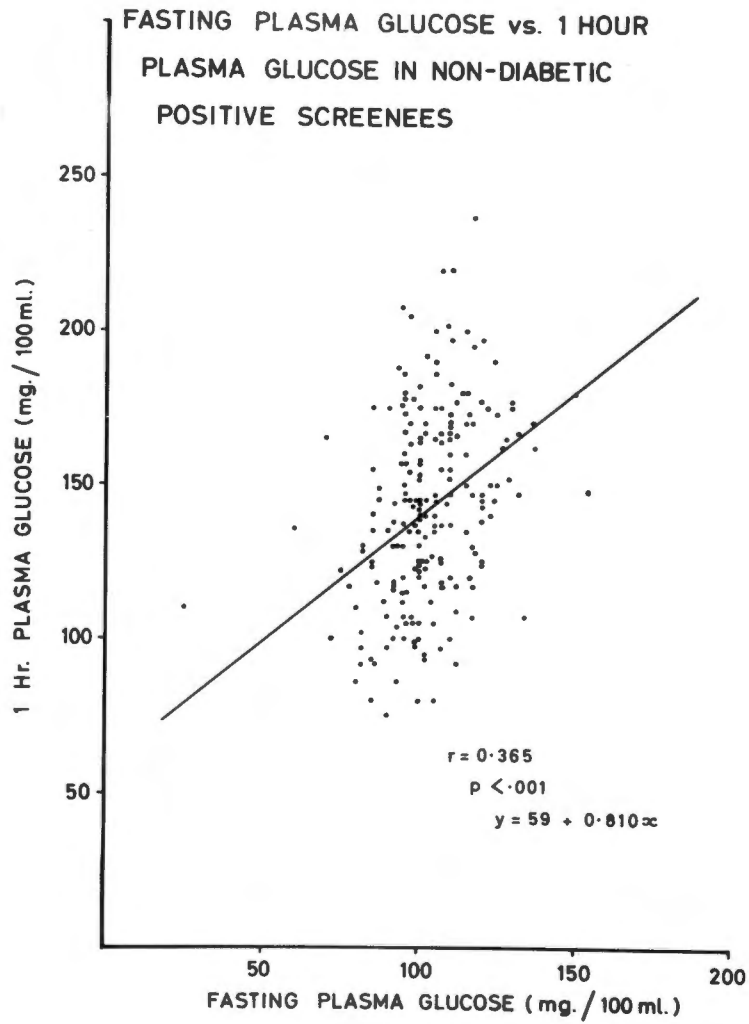
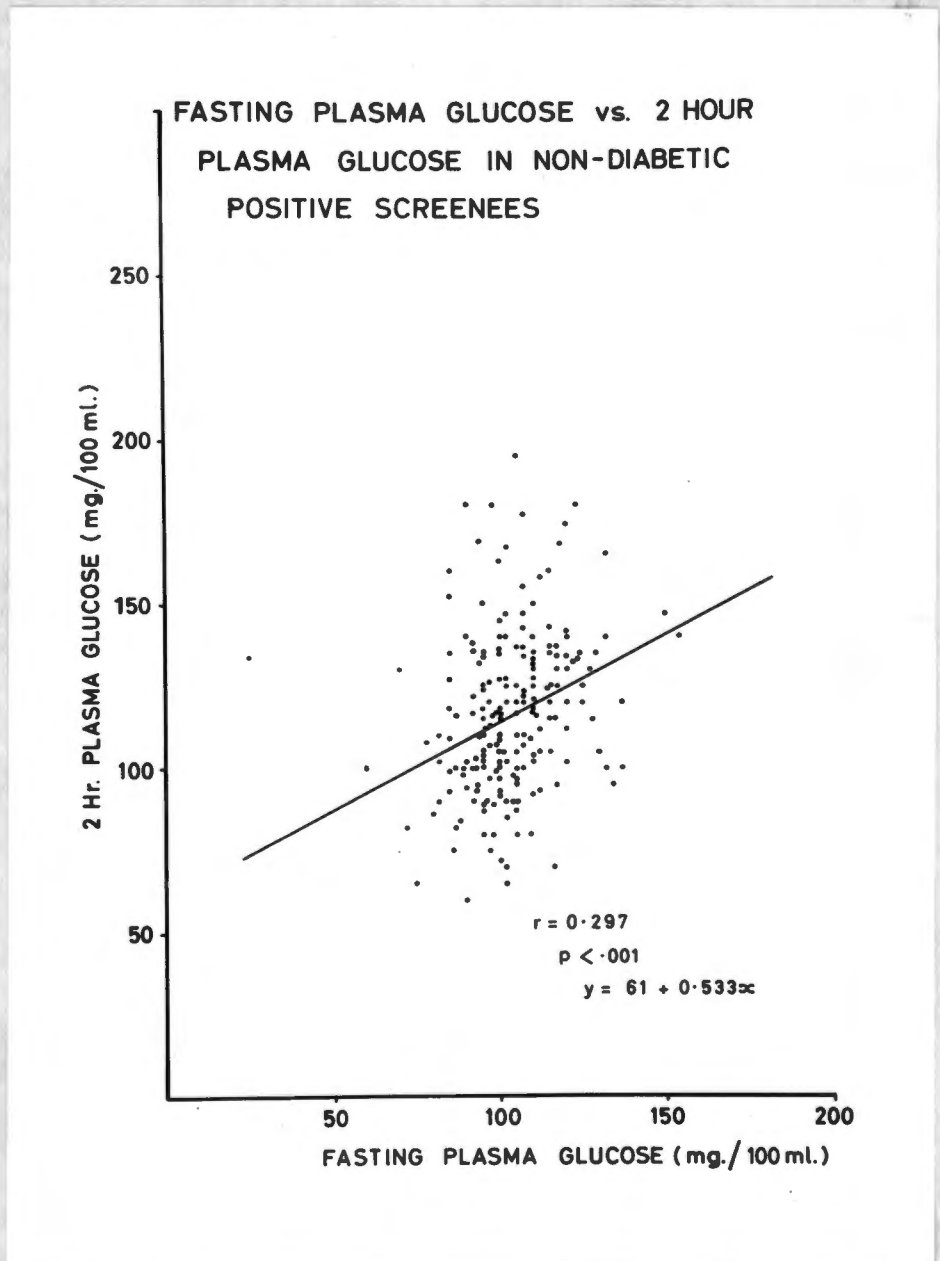


Figure 34. Fasting Plasma Glucose vs. 2 Hour Plasma Glucose in Non-Diabetics



At both time intervals, the fasting plasma glucose value (as with the diabetics) exhibits a significant correlation and this is of predictive worth.

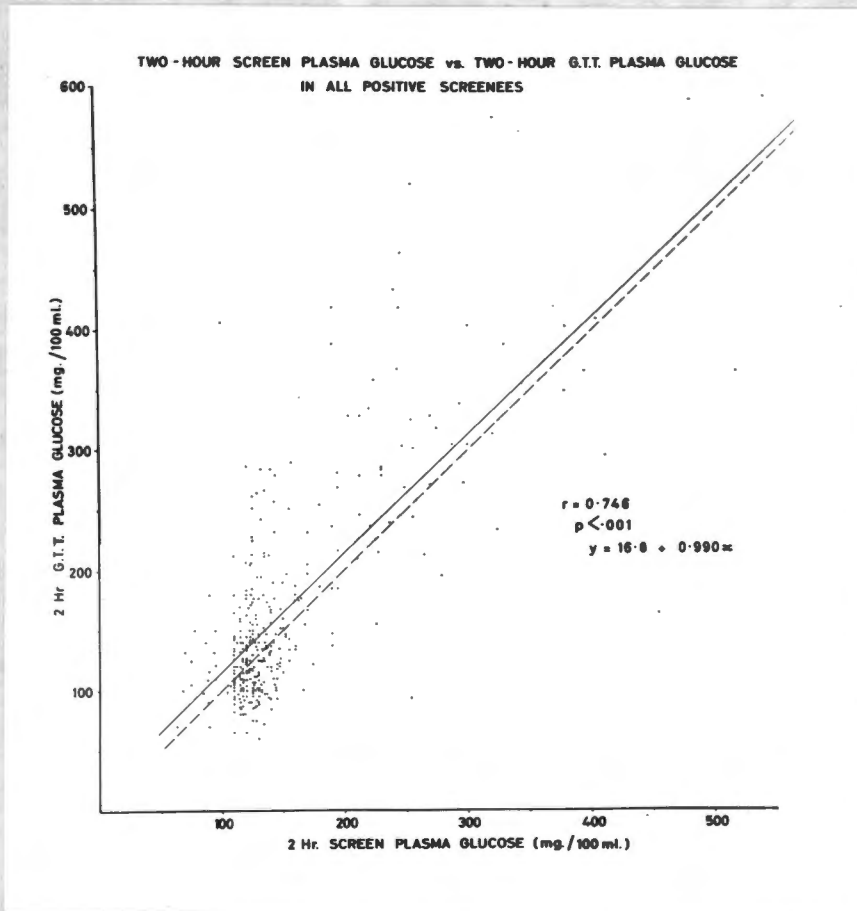
(11) Reproducibility :

It is well recognised that there is considerable variation in the reproducibility of the individual G.T.T.^{113,114} McDonald et al¹¹⁵ studied G.T.T. reproducibility in detail in 443 non-diabetic institutionalised volunteers. Each subject underwent identical 100 G G.T.T. at 2-monthly intervals over 1 year. For each subject, the mean blood glucose value and standard deviation in the fasting state, and at 1, 2 and 3 hour time intervals during G.T.T. was provided. This detailed study indicates that there is a wide range in reproducibility. The median standard deviations (mg./100 ml.) at these 4 time intervals were 2.8, 17.2, 12.2 and 10.9 respectively.

Present Study

The relationship between the 2 hour screen plasma glucose and the 2 hour G.T.T. plasma glucose in each positive screening has been explored. No distinction has been made between screenings of the 1st and 2nd surveys, or between those rated as diabetic or non-diabetic. The following figure illustrates this relationship.

Figure 356. Two-Hour Screen Plasma Glucose vs. Two-Hour G.I.T. Plasma Glucose in Positive Screenees



The correlation is highly significant ($r = 0.746, P < .001$). Furthermore the line of regression (continuous line) closely parallels the hypothetical line (interrupted line) of perfect correlation. The figure does indicate that a considerable number of screenees had wide individual variations. The mean G.T.T. plasma glucose value was 166.4 mg./100 ml. while that for the screen was 151.1 mg./100 ml.

An explanation for the higher mean G.T.T. value may lie in a methodological difference between screen and G.T.T. Prior to G.T.T. the standard 12 hour fast was rigidly adhered to, while prior fasting in the screen, though emphasised, was not insisted upon. Though it is highly probable that the majority of screenees of the 2nd survey had fasted a minimum of 5 hours prior to glucose challenge, no such claim can be made for the 1st survey screenees who provided the majority (308) of the total number of positive screenees (363).

Bang¹¹⁶ was the first to observe that if carbohydrate is given orally in 2 doses, the blood glucose rises less after the 2nd than after the 1st. This phenomenon has been confirmed by Staub¹¹⁷ and also Troughton¹¹⁸ and more recently by Somersalo¹¹⁹.

In Tongaat, the screen plasma glucose challenge may have constituted in effect such a 2nd carbohydrate load in a sufficient number of screenees to produce a lower mean plasma glucose value in comparison to the mean 2 hour glucose value when such screenees underwent G.T.T.

The hypothesis receives support from the Tacumseh survey where Haynor and colleagues⁷¹ investigated the effect of recent food intake on the 1 hour blood glucose level. They concluded that the apparent effect of having eating in the immediate 4 hours prior to glucose challenge, was to depress the 1 hour level by approximately 25 mg./100 ml.

(iii) Diurnal Variation

Bowen and Reeves¹²⁰ recently, have described a variable response during G.T.T. in the same individual when the test is carried out in the afternoon as opposed to the morning, the 2 tests being separated by a number of days. Blood glucose values during G.T.T. at 1 and 2 hour intervals, were significantly higher in the afternoon, the mean increment being 77 and 40 mg./100 ml. respectively.

Present Study

The 2nd survey (in contrast to the 1st) was carried out in the late afternoon, all positive screenees having repeat G.T.T. at a later date in the morning. While conditions in this survey differed from those of the G.T.T. in that prior fasting though continuously stressed, was not insisted upon, it is highly probable that the majority of screenees had fasted a minimum of 5 hours if not the full 12. As methodology in the screen and G.T.T. was essentially identical, it is felt that comparison of the screen and G.T.T. 2 hour plasma glucose values

in each positive screening would provide material to investigate such an apparent variability. As Bowen & Reeves confined their studies to healthy non-diabetic volunteers, only those screenings (27) demonstrated to be non-diabetic have been considered.

The following table provides pertinent information concerning these 27 subjects.

Table 62. Afternoon (Screen) vs. Morning (G.T.T.) 2 Hour Plasma Glucose Value

<u>Age of Subject</u> <u>(Years)</u>	<u>Sex</u>	<u>Afternoon</u> <u>(mg./100 ml.)</u>	<u>Morning</u> <u>(mg./100 ml.)</u>	<u>Diff.</u> <u>(mg./100 ml.)</u>
15	M	120	95	plus 25
23	F	155	134	" 21
41	F	147	123	" 24
19	F	120	134	-14
30	F	144	100	plus 44
27	F	155	143	" 12
59	F	145	110	" 35
19	F	134	107	" 27
17	F	125	174	-49
16	M	125	75	plus 50
13	F	127	86	" 41
20	F	120	138	-18
47	F	120	116	plus 4
47	M	174	122	" 52

Age of Subject (Years)	Sex	Afternoon (mg./100 ml.)	Morning (mg./100 ml.)	Diff. (mg./100 ml.)
12	M	128	92	plus 36
24	F	140	84	" 56
68	M	145	93	" 52
38	M	150	115	" 35
42	F	160	134	" 26
35	F	136	135	" 1
65	M	75	105	-30
39	F	107	104	plus 3
37	F	115	150	-35
15	F	85	98	-13
52	M	90	180	-90
52	M	95	121	-26
30	F	122	169	-47

Each subject's afternoon and morning values were treated as paired comparisons. The "t" test for paired comparisons was then applied.

Variation ranged from + 56 to -90 mg./100 ml. with a mean of + 8.2 mg./100 ml. This finding is not significant ($p > 0.05$). Moreover it is well within individual day to day variability.¹¹⁵ It is also in accord with the Tecumseh study⁷¹, where no significant diurnal variation was found.

----- CHAPTER 15 -----

GLUCOSE, INSULIN AND NON-ESTERIFIED FATTY ACID RELATIONSHIPS

(1) Introduction :

Though insulin was first isolated in 1921,¹ accurate measurement of circulating insulin in man by the immunoassay technique pioneered by Berson and Yalow¹²¹ was only described in 1960¹²². Since that time, these workers have refined their techniques and others have developed their own refinements.^{45, 46}

These studies have indicated a trend of insulin response to oral glucose. Range of response is high and standard deviations, where given, allow for considerable overlap. Basically, in the healthy young adult, the fasting insulin value rises 5 to 10 fold after glucose ingestion within 60 minutes and then commences its drop to its basal level^{122,123} which is reached after 2 hours. In the early or mild maturity-onset diabetic, the insulin rise is sluggish and prolonged, reaching higher levels than that seen in young healthy adults and the fall is likewise sluggish and prolonged.¹²²

N.E.F.A. behaviour following oral glucose was first reported in 1956 by Dole,⁵⁰ and Gordon and Cherkas.¹²⁴ These workers noticed that orally administered glucose produced a rapid and consistent drop in plasma N.E.F.A. to a nadir between 1 and 3 hours post-glucose. N.E.F.A. then began to climb and in many cases had reached levels that were higher than

those in the fasting state. In 1957, Bierman et al¹²⁵ reported that the fasting N.E.F.A. value in diabetics was elevated and that its drop and subsequent rise following glucose, was sluggish and prolonged.

The fall of N.E.F.A. following oral glucose is brought about by the metabolism of glucose to α glycerophosphate which is an acceptor of fatty acids, leading to the synthesis of adipose tissue triglyceride. This esterification of fatty acids together with the direct effect of glucose in inhibiting the release of stored N.E.F.A. results in the N.E.F.A. level drop.¹³² The effect of insulin on glucose metabolism and N.E.F.A. release can closely be duplicated by raising the glucose concentration to high levels.¹³³ It is generally thought that insulin alone, in the absence of glucose does not suppress N.E.F.A. release.¹³⁴ It is reasonable to attribute the primary effect of insulin on fat metabolism to its stimulation of glucose utilisation by adipose tissue.

This resume serves to introduce this chapter in which glucose, insulin and N.E.F.A. response during G.T.T. in positive screenings, will be discussed.

(11) Statistical Considerations :

It is necessary to devote a little space to a consideration of the statistical methods used to evaluate the data.

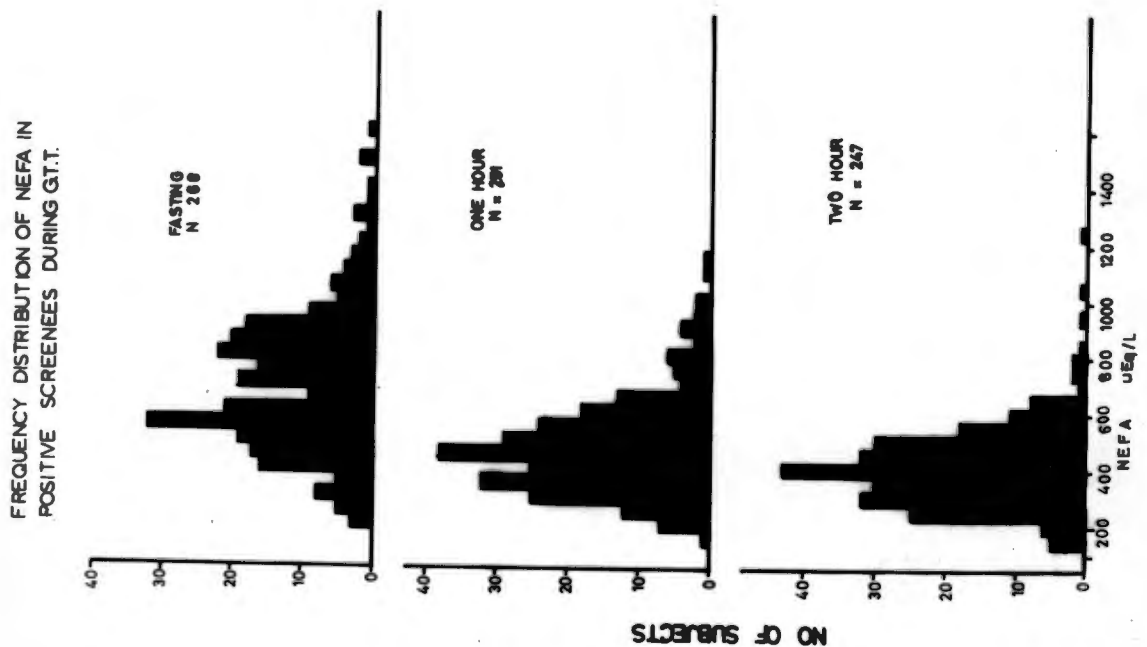
In assessing the significance of any difference between 2 sets of results, a comparison is often made between the mean

values by means of the "t" test. The validity of this test which relies on the standard deviation, is subject to the distribution of the substance under measurement (e.g. glucose) being approximate or closely identical to that of the normal or Gaussian distribution. The closer this approximation, the greater the validity. Where the substance has no particular form of distribution and/or where it does not conform broadly to the normal distribution, the "t" test cannot be used as incorrect conclusions may be drawn.

In this section, comparisons will be made between various groups for each of 3 substances, namely glucose, insulin and N.E.F.A. Glucose and N.E.F.A. have frequency distributions which can be described as approximately normal. Figure 10 illustrated the screen plasma glucose frequency distribution - 2427 observations. There is a slight "tail" to the right but this is negligible and accounts for a very small number of observations.

The distribution of N.E.F.A. in positive screenees who underwent G.T.T. is illustrated in figure 36 for each of 3 time intervals.

Figure 36. Frequency Distribution of N.E.F.A. in Positive Screenings during G.T.T.



These distributions approximate that of the normal. The curves are not as smooth as that seen with glucose, but the number of observations is far less. As with glucose, there is a tail towards the right.

It is felt that presentation of these data provide sufficient evidence of an approximately normal distribution for glucose and N.E.F.A., and allows for valid use of the "t" test.

Insulin values however do not conform in any way to the normal distribution. Evaluation between means by means of the "t" test is thus invalid. Welborn et al¹²³ have attempted to circumvent this stumbling block by converting all insulin values into Log 10 values which are then used to calculate means and standard deviations. The author feels that a non-parametric test, i.e. one which assumes no particular distribution, and which utilises the original values, is preferable. Such a test is the Mann-Whitney U Test¹²⁶ which has been employed exclusively for insulin evaluation.

(iii) Influence of Age on Recently-Diagnosed Untreated Non-Ketosis Prone Diabetics

Apart from congenital diabetes which typically is of a temporary nature,¹²⁷ spontaneous diabetes in man usually expresses itself in 2 distinct forms, namely the juvenile-type and the maturity-onset type. Juvenile diabetes is characterised by severe glucose intolerance, a marked tendency to keto-acidosis and insulin therapy is obligatory. This form is commonly seen in children, adolescents and young adults but it can afflict the elderly as well. In maturity-onset diabetes blood glucose levels may be excessively raised but there is little tendency to keto-acidosis and control usually consists of diet and/or oral agents. Insulin is seldom used.

While the onset of juvenile diabetes can frequently be accurately defined due to the acute onset of symptoms, maturity-onset diabetes because of its insidious onset and

frequent chance discovery, possesses no such advantage. The actual onset of the disease, as indicated by departure from glucose tolerance to intolerance, usually remains unknown.

Diabetes of the maturity-onset type can occur in children and young adults. Fajans and Conn¹²⁸ have described 10 children with this variety of diabetes in whom treatment consisted of diet and/or tolbutamide. Considerably earlier, Hugh-Jones¹²⁹ described several Jamaican diabetics with severe hyperglycaemia controlled by insulin alone, but who did not develop ketosis following insulin withdrawal. In 1960, Campbell⁶ reported similar insulin-ⁱⁿdependent young Indian diabetics, stressing that these subjects were generally overweight in contrast to the Jamaicans. In 1967, Johansen and Lundbaek¹³⁰ reported 3 cases of maturity-onset type diabetes in young adults aged 15, 19 and 20 years. In these subjects insulin behaviour during G.T.T. was certainly not typical of maturity-onset diabetes and these workers posed the question whether the findings could represent an early phase of classical juvenile diabetes or develop ultimately into diabetes of the maturity-onset type. Hales¹³¹ has attempted to answer the question in part. He has described a 12 year old boy in whom G.T.T. performed 4 years before the onset of diabetic ketosis revealed a minor abnormality of glucose tolerance, as evidenced by raised fasting N.E.F.A. and glycerol values, a sluggish insulin response and an abnormal predFisone-augmented G.T.T.

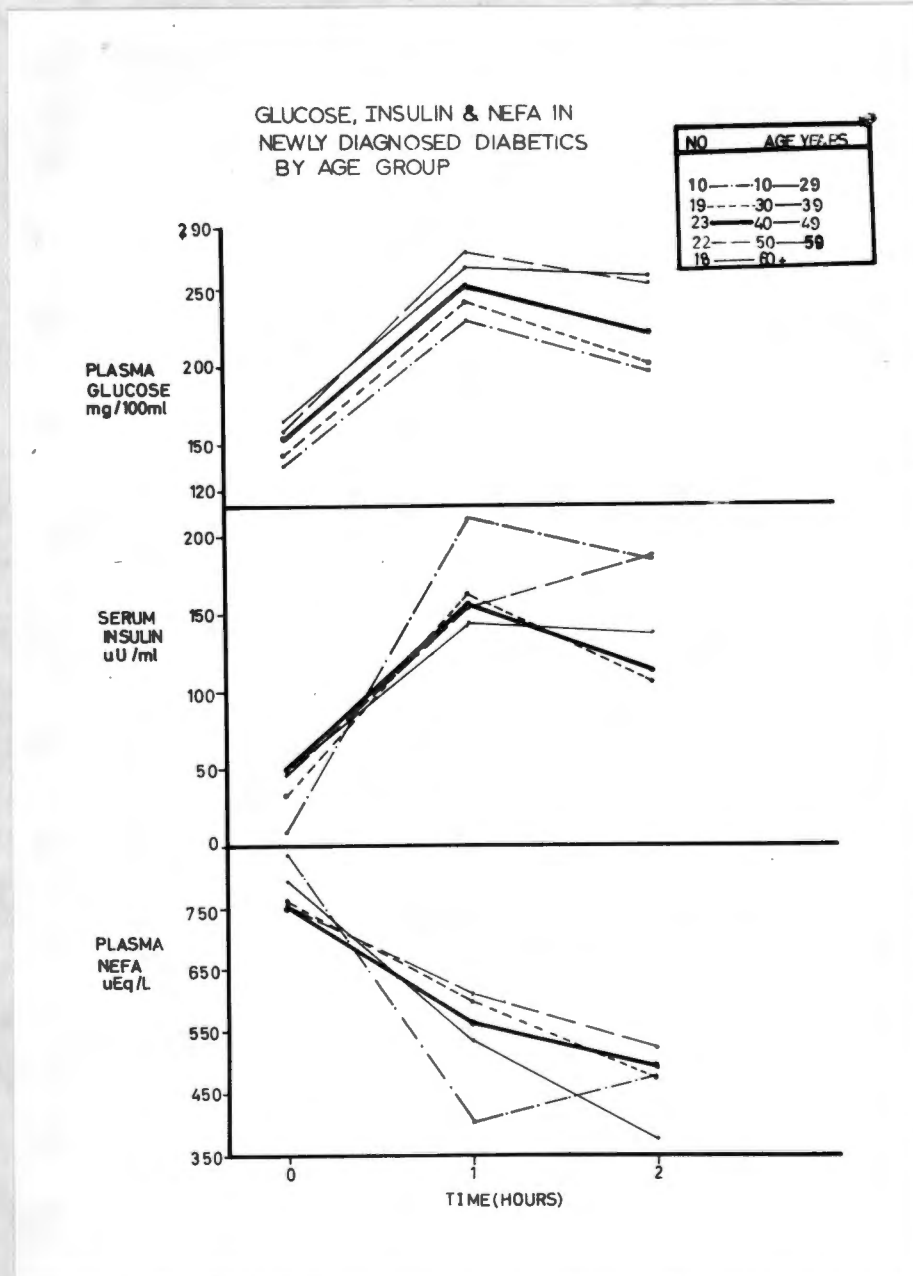
This finding is used to indicate that juvenile type diabetes may not have the acute onset so commonly believed, but that minor degrees of carbohydrate intolerance may precede it by a sizeable period of time.

Tongaat Data :

Of the 145 diabetics, 6 were aged 10 - 19 years, and 6 were aged 20 - 29 years. Two diabetics in the 3rd decade were "known", and as therapy may have altered their biochemical responses, they have been excluded from all analyses. To provide greater validity, these 10 diabetics have been considered as a single group containing thus 6 juvenile and 4 young adult diabetics.

A comparison of mean glucose, insulin and N.E.P.A. responses between this group and other diabetics, may provide valuable information as to the probable nature of their disease. Five groupings have been utilised, the 10 - 29 year group mentioned before, and the 30 - 39, 40 - 49 50 - 59 and 60 years and older. The following figure illustrates the inter-age comparisons.

Figure 37. Mean Plasma Glucose, Serum, Insulin and Plasma N.E.F.A. Response during G.T.T. in Newly-Diagnosed Untreated Non Ketosis-Prone Diabetics



Statistical evaluation of the differences between mean values is provided in the following table. The "t" test has been used to evaluate glucose and N.E.F.A. differences, while the Mann-Whitney U Test deals with the insulin difference.

Table 63. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Response during G.T.T. in Newly-Diagnosed Non-Ketosis-Prone Diabetics by Age

Age Group (Years)	Glucose			Insulin			N.E.F.A.		
	0	1	2	0	1	2	0	1	2
<u>10-29/30-39</u>	NS	NS	NS	NS	NS	NS	NS	p < .01	NS
/40-49	NS	NS	NS	p < .01	NS	NS	NS	p < .05	NS
/50-59	NS	NS	NS	p < .01	NS	NS	NS	p < .05	NS
/60 plus	NS	NS	NS	p < .01	NS	NS	NS	NS	NS
<u>30-39/40-49</u>	NS	NS	NS	NS	NS	NS	NS	NS	NS
/50-59	NS	NS	p < .05	NS	NS	NS	NS	NS	NS
/60 plus	NS	NS	NS	NS	NS	NS	NS	NS	NS
<u>40-49/50-59</u>	NS	NS	NS	NS	NS	NS	NS	NS	NS
/60 plus	NS	NS	NS	NS	NS	NS	NS	NS	p < .05
<u>50-59/60 plus</u>	NS	NS	NS	NS	NS	NS	NS	NS	p < .05

There is a steady deterioration of mean plasma glucose tolerance with age although the differences are not significant, with the sole exception of the 2hour 30-39/50-59 difference. Insulin response with the exception of the 10-29 year old group, behaves similarly, with some divergence at 2 hours. In the fasting state, there is some statistically significant difference between the 10-29 year old group and most of the other age groups. N.E.F.A. suppression is seen in all age

groups, the 10 - 29 year old group exhibiting the highest fasting level, and the greatest degree of suppression. Statistically significant differences are recorded at the 1 and 2 hour time intervals between the 10 - 29 year old group and the 50 - 59 year old group.

The topically important age group is the youngest, as these subjects constitute in the main, juvenile diabetics. They do not behave like juvenile diabetics though. In the fasting state, their mean insulin value is significantly lower than that for 3 of the 4 older age groups, their insulin response to glucose is maximal with no significant differences at 1 and 2 hours. N.E.F.A. response is likewise similar with this group exhibiting the highest mean fasting value and the greatest suppression.

These young diabetics behaved like maturity-onset diabetics. They certainly did not develop any obvious ketosis, and months after the survey, the author was unaware of any illhealth amongst them which could be attributed to diabetes. The author postulates that diabetics as with those of Fajans and Conn, and Johansen and Lundbaek, will continue to behave like maturity-onset diabetics. Continued follow-up of these subjects is essential to establish with any certainty their ultimate status. The following table indicates relevant information concerning these 10 subjects.

Table 64. Glucose, Insulin and N.E.F.A. Response in Newly-Diagnosed Non Ketosis-Prone Untreated 10-29 Year Old Diabetics

Age	Sex	% Dev.	Survey Glucose	Glucose mg./100 ml.			Insulin μ U/ml.			N.E.F.A. μ E ₂ /L				
				0	1	2	0	1	2	0	1	2		
16	F	89	150	125	180	160	18	350	-	-	-	-	-	-
14	F	102	143	112	190	177	5	211	300	-	-	-	-	-
15	F	143	125	110	185	185	2	37	250	897	258	489	-	-
14	F	91	150	109	187	152	4	29	362	441	472	472	-	-
15	F	76	120	115	195	145	5	300	318	918	272	406	-	-
11	F	95	244	258	396	420	36	22	0	-	577	-	-	-
25	F	104	152	90	220	147	4	6	13	1323	458	542	-	-
24	F	100	195	180	339	270	10	250	54	-	-	-	-	-
25	F	128	128	150	195	163	-	-	-	-	-	-	-	-
27	F	106	123	112	207	145	4	500	-	630	-	487	-	-

All 10 diabetics are female. In one subject, the 1 hour criterion has not been met but in view of the survey result, diabetes has been diagnosed. In 7 of the remaining diabetics, while both criteria have been satisfied, the margin of "satisfaction" for at least one criterion has been minimal. It is possible that repeat G.T.T. could well convert these subjects into borderline or normal categories.

No such possibility exists for the 2 remaining diabetics; one being an 11 year old girl with gross hyperglycaemia and a

a flat insulin response; the other being a 24 year old woman with equalby gross hyperglycaemia but where a tremendous insulin "kick" at 1 hour is followed by a rapid return to near normality at 2 hours. Unfortunately insufficient blood was withdrawn for N.E.F.A. investigation, however the solitary 1 hour level of 577 Eq./L in the young girl is elevated.

These 2 subjects were informed of their diagnoses. The younger was hospitalised and was discharged on tolbutamide therapy. It is not known whether the other individual sought medical advice. The remaining subjects were not informed of their diagnoses, but their medical attendants were notified and provided with the individual results.

(iv) Influence of Age on Positive Screenings with Normal Glucose Tolerance :

The subjects in this section comprise those positive screenings whose subsequent G.T.T. was completely normal. These subjects cannot be considered as normal controls as they were in fact positive screenings.

The following figure illustrates glucose, insulin and N.E.F.A. response during G.T.T. by age group. The accompanying table indicates statistical evaluation.

Figure 38. Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Positive Screenses with Normal Glucose Tolerance

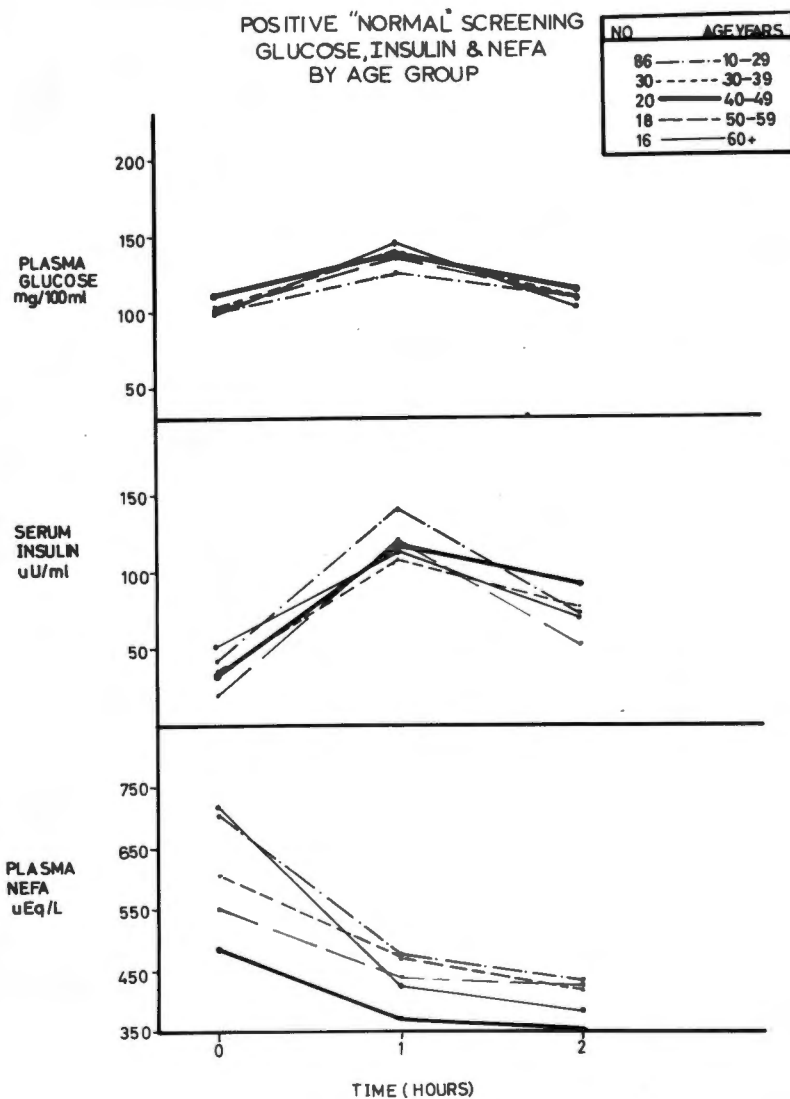


Table 65. Statistical Evaluation of Glucose, Insulin & N.E.F.A. Response during G.T.T. in Positive Screenings with Normal Glucose Tolerance

Age Group (Years)	Glucose			Insulin			N.E.F.A.		
	0	1	2	0	1	2	0	1	2
10-29/30-39	NS	p < .01	NS	NS	NS	NS	NS	NS	NS
40-49	p < .001	NS	NS	NS	NS	NS	p < .001	p < .01	p < .05
50-59	NS	NS	NS	NS	NS	NS	p < .05	NS	NS
60 plus	NS	p < .01	NS	NS	NS	NS	NS	NS	NS
30-39/40-49	p < .05	NS	NS	NS	NS	NS	p < .05	p < .05	NS
50-59	NS	NS	NS	NS	NS	NS	NS	NS	NS
60 plus	NS	NS	NS	NS	NS	NS	p < .05	NS	NS
40-49/50-59	p < .05	NS	p < .05	NS	NS	NS	NS	NS	NS
60 plus	NS	NS	p < .05	NS	NS	NS	p < .001	NS	NS
50-59/ 60 plus	NS	NS	NS	NS	NS	NS	p < .05	NS	NS

It is obvious that mean glucose and insulin responses are each similar in each age group. Some glucose differences do attain significance, but none of the insulin differences attain such significance. N.E.F.A. response exhibits a wide divergence. Fasting means vary greatly and the differences ^{are} significant for the majority. The youngest and oldest age groups have similar means, both of which are abnormally high. Suppression following glucose is constant with a levelling off at 2 hours.

Do these results tend to indicate that ageing does not influence insulin response? An answer must needs await age/sex matched control studies.

(v) Influence of Obesity :

Excessive insulin response to intravenous glucose in obese subjects with normal glucose tolerance was reported by Karam,¹³⁵ in 1963. In this study, the glucose response of the obese group was virtually identical to that of the normal weight group, and led to the postulate that the obese subjects required increased insulin secretion and release to maintain normoglycaemia. In 1965, the same workers¹³⁶ demonstrated that a group of non-obese maturity-onset diabetics had a significantly lower insulin response (oral glucose load) as compared with an obese group. These workers further postulated that obesity was the factor governing excessive insulin response in the maturity-onset diabetic. Buchanan and McKiddie¹³⁷ reported a similar finding in 1967.

Influence of obesity on N.E.F.A. response to oral glucose has been studied by Hanley et al¹³⁸, in 1967. They treated the N.E.F.A. response (at varying time intervals) as a single unit - the mean plasma N.E.F.A. level and in a multiple linear regression analysis quantitated the effects of variables such as glycaemia, weight and height. The analysis showed that adiposity has only minor effects on the form and magnitude of the N.E.F.A. response, and influences chiefly the location of the response through its effect on the fasting N.E.F.A. level.

Tongaat Data

The diabetics, and the positive screenees with normal G.T.T. constitute the 2 groups. In each group, comparisons are made between overweight, normal weight and underweight subjects.

Positive screenees with Normal G.T.T. :

The following figure illustrates mean glucose, insulin and N.E.F.A. values during G.T.T. by these groupings. The accompanying table provides statistical evaluation of the differences between means in each group.

Figure 39. Effect of Body Weight on Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Positive Screenees with Normal Glucose Tolerance

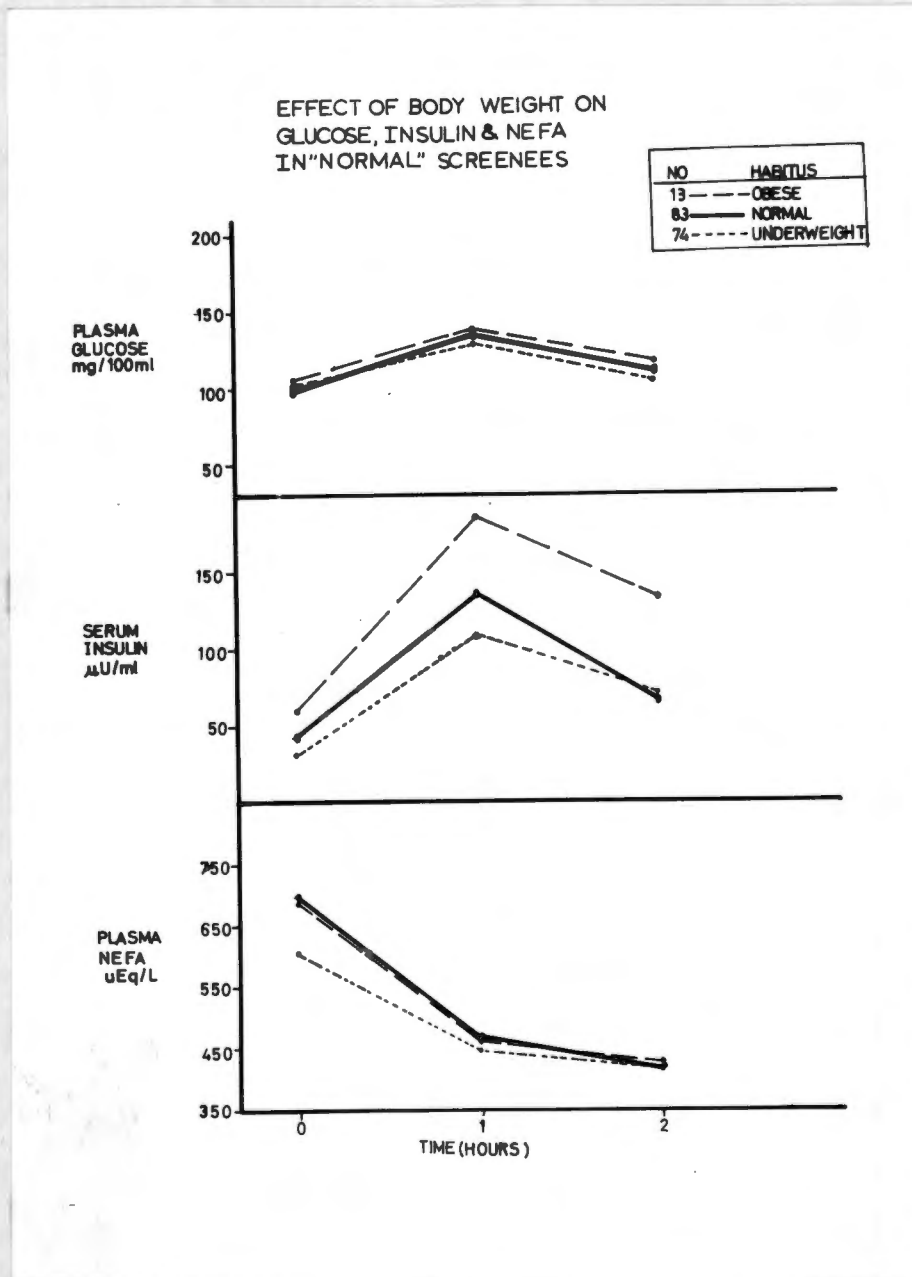


Table 66. Statistical Evaluation of Glucose, Insulin & N.E.F.A. Differences in Positive Screenings with Normal Glucose Tolerances by Weight Category

Weight Group	Glucose			Insulin			N.E.F.A.		
	0	1	2	0	1	2	0	1	2
Overweight/ Normals	p<.05	N.S.	N.S.	N.S.	N.S.	p<.01	N.S.	N.S.	N.S.
/Under W.	N.S.	N.S.	p<.01	N.S.	N.S.	p<.01	N.S.	N.S.	N.S.
Normals/ Under W.	N.S.	N.S.	p<.05	N.S.	N.S.	N.S.	p<.05	N.S.	N.S.

The data indicates that the obese group possesses a higher mean glucose and insulin response, and a raised fasting N.E.F.A. value. Highly significant differences for 2 hour mean insulin values are attained between the overweight and normal weight and underweight groups respectively. Furthermore the differences at the 1 hour interval, while not attaining significance, are very close to such attainment. Mean insulin response in the normal weight group is higher than that in the underweight group, but not significantly so.

Mean glucose response is closely identical in each group, with the obese response overlapping the normal weight, which in turn overlaps the underweight group. Fasting N.E.F.A. values for the obese and normal weight groups are very similar and are considerably greater than that of the underweight group. All groups demonstrate suppression following glucose with flattening out at 2 hours.

These results indicate that in this group, obesity does tend to produce elevated insulin levels, thus confirming the

findings of Karam et al¹³⁵. But furthermore, the underweight group has exhibited the lowest mean glucose, insulin and N.E.F.A. responses which however are only significantly different in 2 instances. Nevertheless the trend is obvious.

Do these findings imply that in obese subjects, excessive insulin production results from excessive insulin antagonism, or rather that insulin itself is partly deficient in its actions, thus likewise resulting in elevated levels, to maintain suglycaemia? Does this elevated insulin response indicate a greater probability to diabetes? Long-term follow-up of these subjects with regularly repeated G.T.T. may provide some of the answers.

Newly-Diagnosed Diabetes

The following figure illustrates mean glucose, insulin and N.E.F.A. values during G.T.T. The accompanying table provides statistical evaluation of the differences between the group.

Figure 40. Effect of Body Weight on Mean Plasma Glucose, Serum Insulin and Plasma N.E.F.A. Response during G.T.T. in Newly-Diagnosed Diabetics

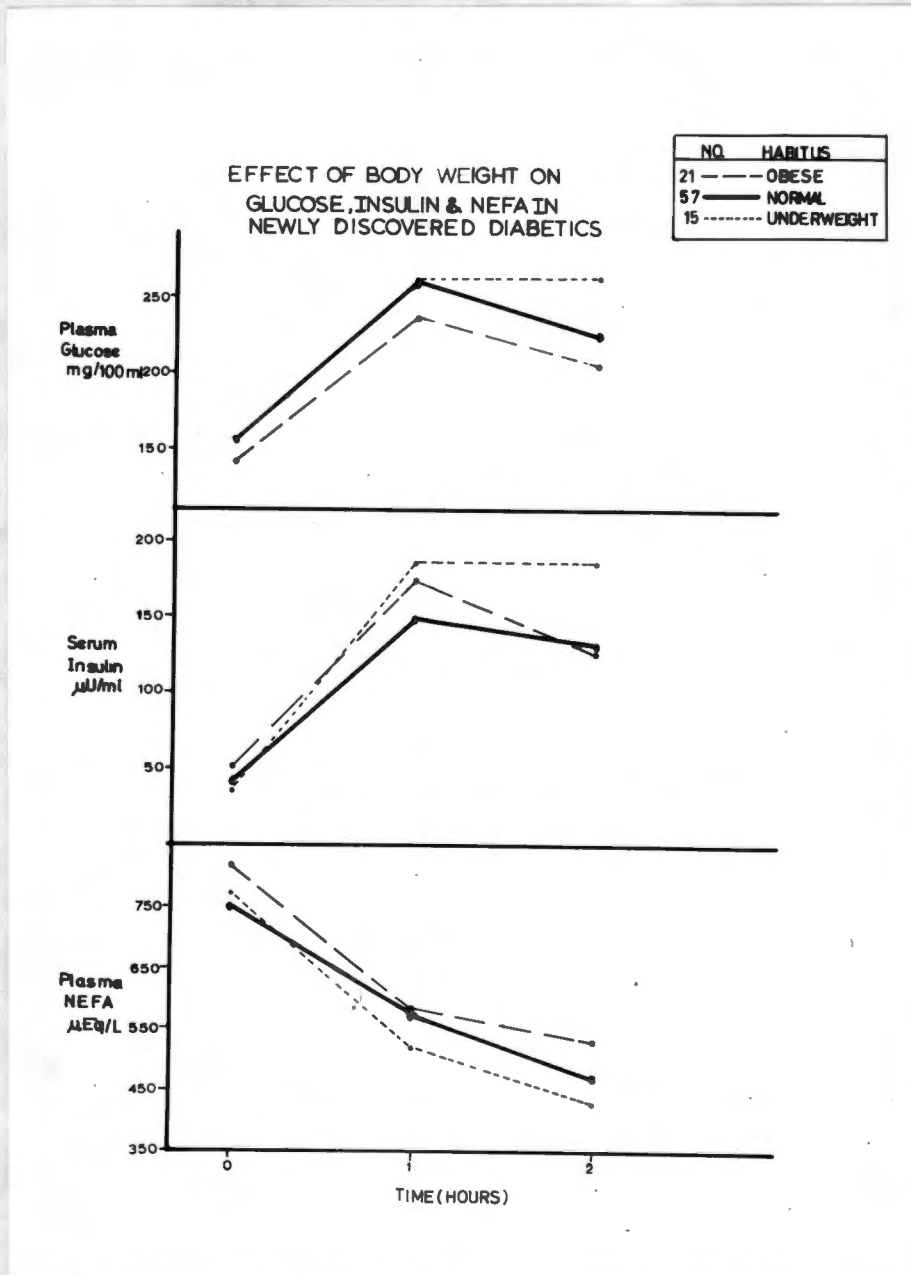


Table 67. Statistical Evaluation of Glucose, Insulin and N.E.F.A. Differences in Newly-Diagnosed Diabetics by Weight Category

	Glucose			Insulin			N.E.F.A.		
	0	1	2	0	1	2	0	1	2
Obese/ Normal	NS	NS	NS	NS	NS	NS	NS	NS	NS
/Under	NS	NS	NS	NS	NS	NS	NS	NS	p<.05
Normal/ Under	NS	NS	NS	NS	NS	NS	NS	NS	NS

These findings indicate that the underweight group has the higher mean glucose and insulin response. Fasting N.E.F.A. mean values are all elevated with the obese group, possessing the highest value. Apart from a solitary significant difference in N.E.F.A. comparisons, none of the differences are significant.

The results do not indicate that the normal or underweight diabetic has a lower insulin response. It may well be that maturity-onset diabetes (where hyperinsulinism is the rule) may obscure any independent effect that obesity or its converse may exert.

----- CHAPTER 16 -----

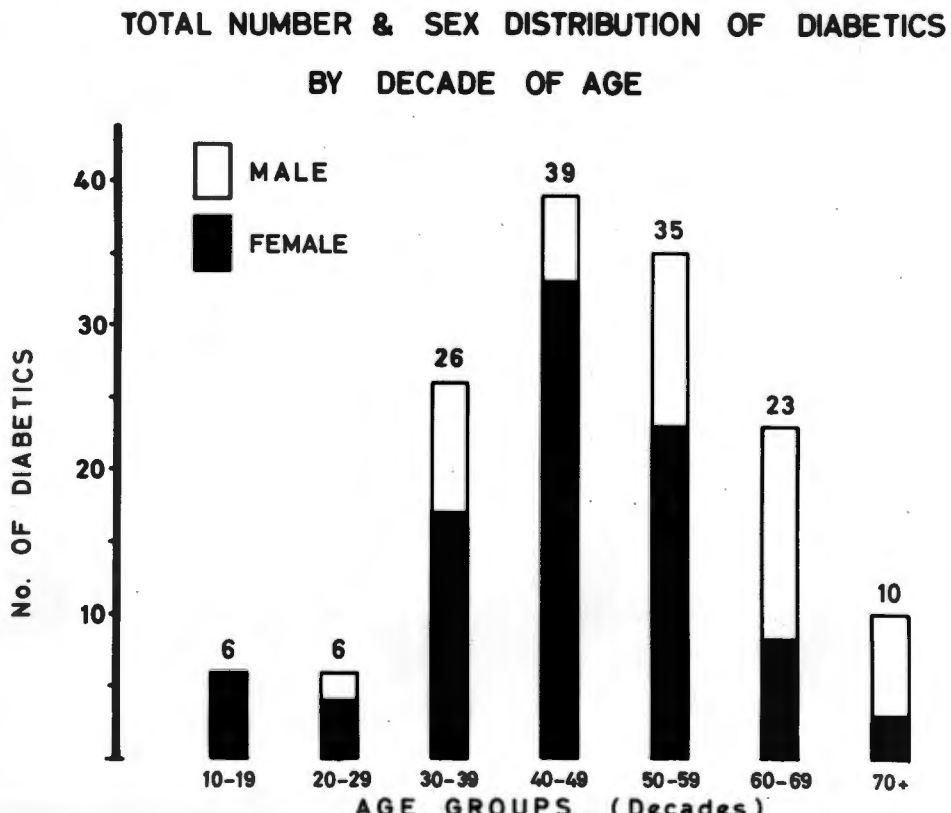
CLINICAL ASPECTS

(1) Age/Sex Profile of Diabetics

The total number of discovered diabetics was 145. Figure 41 indicates their distribution by decade of age. It is readily apparent that the majority of diabetics fall into the age group of 40 - 59 years. In this age group are aggregated 74 diabetics, or a little over 50% of the total number.

Of interest, are the changes in sex preponderance with increasing age. In the younger age groups, females far outnumber males, but with increasing age, this female preponderance decreases. In the 7th and 8th decades the male predominates.

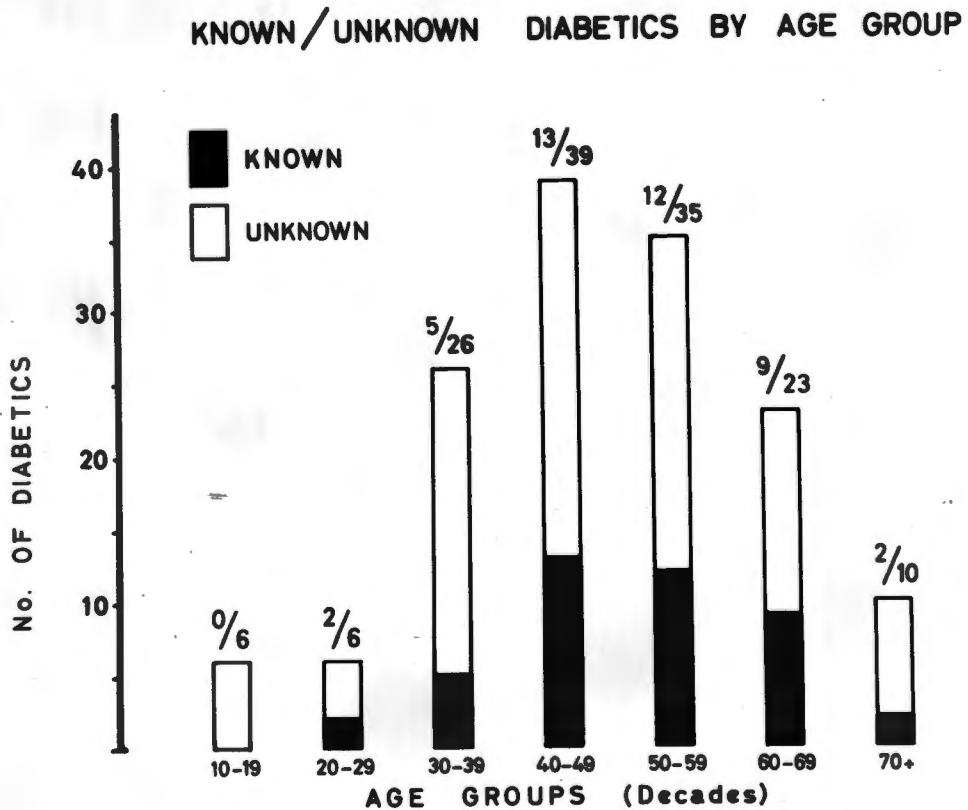
Figure 41. Total Number and Sex Distribution of Diabetics by Decade of Age



(11) Known/Unknown Diabetes Ratio :

As 43 of the 145 diabetics were aware of their disease, the known/unknown ratio is approximately 1 : 2.4. Figure 42 illustrates the ratio by decade of age. It is seen that the highest proportion of known diabetics are found in the middle-aged groups.

Figure 42. Known/Unknown Diabetes Ratio by Age Group



This finding differs from that elsewhere,^{66,69} where the ratio is approximately 1 : 1. But there glycosuria has constituted the screen procedure,^{and} as the aglycosuric population harbours many "hidden" diabetics, these ratios need revision.

(iii) Diabetic Disease

Diabetic disease is defined as those disease states or signs of disease states, which are frequently found in association with diabetes. Investigations concerning the following disease states will be discussed :

- Diabetic Retinopathy
- Ischaemic Heart Disease
- Peripheral Vascular Disease
- Peripheral Neuritis

Of these 4 disease states, it is only retinopathy that can be diagnosed with reasonable certainty, as being specifically diabetic in origin, in that capillary microaneurysms are an essential prerequisite for diagnosis. There are however other causes of such microaneurysms but these are rarely encountered.^{139, 140, 141}

Difficulties arise when the other 3 entities are assessed. The finding of any of these disease states in a diabetic, cannot justify the assumption that diabetes is the sole aetiological agent. It rather indicates an association bearing in mind though, other important factors such as nutrition, age, sex and race.

Each of these 4 disease states will be discussed separately. Apropos retinopathy, "known" and "unknown" diabetics will be treated as separate groups as known duration of the disease plays an important role in the development of retinopathy. For the other disease states, no such separation has been carried out, and all diabetics will be treated as a single group.

1. Diabetic Retinopathy

Known Diabetics

Examination was possible in all 43 diabetics, and revealed that retinopathy was present in only 3. Two were females, aged 42 and 49 years, and one was a male, aged 52 years. In none, was the retinopathy of a severe degree, being grade 2, grade 1 and grade 2 respectively.

The prevalence of retinopathy in this group is 7%. As an expression of retinopathy prevalence in a group of known diabetics, this is a surprisingly low finding. An unknown factor is duration at the disease. If diabetes in all, or the majority of this group, was of very recent onset, i.e. known duration of less than 1 year, then this finding would be compatible with experiences elsewhere.^{142,143} It is unlikely though, that the disease in this group, was uniformly of such short duration.

Unknown Diabetics

Of the 102 diabetics, satisfactory examination was carried out in 86. Retinopathy was not observed in any of these diabetics. This finding contrasts with Seftels report¹⁴⁴

of 6 cases of retinopathy in 20 similarly discovered, Indian diabetics in the Transvaal.

These 86 diabetics fall into the category of chemical diabetics, i.e. persons with a diagnostic G.T.T. but without obvious symptoms or signs associated with diabetes. The natural history of diabetes, commencing at conception, and passing through prediabetes to chemical diabetes and finally symptomatic diabetes, may provide an explanation for the absence of retinopathy in this group.

As the known duration of diabetes increases, the prevalence of retinopathy rises sharply^{142, 145} with at least 50% of diabetics manifesting retinopathy at a known duration of 10 years and above.^{146, 147} With the exception of those diabetics discovered during detection drives, it is probable that the majority of diabetics at initial diagnosis, are symptomatic. At such diagnosis, the prevalence of retinopathy is negligible.^{145, 148} During the phase at chemical diabetes, it could well follow, that a less significant prevalence be expected.

Diabetic Retinopathy Preceding Glucose Intolerance

A previous publication⁸ has drawn attention to a not uncommon finding of diabetic retinopathy preceding glucose intolerance in Indians in Natal. It is of interest to report that of 215 positive screenings with subsequent normal G.T.T., no case of retinopathy was observed.

2. Ischaemic Heart Disease

Two approaches to the data have been made. Firstly a consideration of the prevalence of ischaemia in the diabetics, and secondly, the prevalence of diabetes in all subjects with ischaemia.

(a) Cardiac Ischaemia in Diabetics

Satisfactory examination was carried out on 111 diabetics. Table 68 indicates the age and sex distributions of these diabetics together with the numbers manifesting ischaemia in each group.

Table 68. Cardiac Ischaemia in Discovered Diabetics by Age

Total No.	<u>Males</u>		<u>Females</u>	
	No. Isch.	Age Group (Years)	Total No.	No. Isch.
6	0	10 - 39	24	1
5	1	40 - 49	24	5
9	1	50 - 59	19	3
14	5	60 plus	10	5
34	7	All Ages	77	14

It is seen that there is little sex difference in ischaemia prevalence in identical age groups. The prevalence for each sex, all ages included, is very similar (Table 69); 21% of males being ischaemic as compared to a prevalence of 18% in females. This difference is not significant. If only those diabetics falling in the higher risk age groups namely 40 years and older, are considered, each sex has an identical prevalence of 25%.

Table 69. Cardiac Ischaemia in Discovered Diabetics by Sex

Sex	Tot. Diab.	Tot. Isch.	% Isch.
M	34	7	21
F	77	14	18
Both	111	21	19

Of the total group of 111 diabetics, 21 manifested ischaemia. The overall prevalence is thus 19%. This compares favourably with experiences in the Cape,¹⁴⁶ where 20% of a group of White and Coloured diabetics, had evidence of coronary artery disease.

(b) Diabetes in All Subjects with Ischaemia

Numerous studies^{149,150,151} have demonstrated a high prevalence of diabetes in patients with myocardial infarction, ranging from 41% to 76%. Other reports^{152,153} have indicated a similar finding in patients with angina pectoris.

It is of interest to report the prevalence of diabetes in those positive screenings who manifested ischaemia. Of these 37 ischaemic subjects, 21 were diabetic (Table 70). Prevalence of diabetes in this group is thus 57%. This is slightly higher than the finding¹⁵ of 47% in a group of hospitalised Indians with severe coronary artery disease.

Table 70. Diabetes Prevalence in Total Discovered Diabetics
By Sex

Sex (M/F)	Total Isch.	Total Diab.	% Diabetic
M	13	7	54
F	24	14	58
Both	37	21	57

3. Peripheral Vascular Disease

Satisfactory assessment was possible in 131 diabetics. P.V.D. was present in 8, the prevalence being thus 6.1%. This is similar to Cosnett's³ series (9.2%), but considerably less than that reported in a series of American Diabetics¹⁴³ (15%).

4. Peripheral Neuritis

Examination was possible in 131 diabetics. Peripheral neuritis was present in 32, the prevalence is thus 24.5%. This is similar to Cosnett's³ finding of 17%, while Wada and colleagues¹⁵⁴ recorded a prevalence of 22% in a group of Japanese diabetics.

Conclusion :

The object of this presentation has been to cast some fresh light on some of the pertinent clinical features concerning diabetes in Indians in a Natal town. Retinopathy prevalence in the small group of "known" diabetics is unaccountably low. The absence of retinopathy in the "unknown" diabetics is a surprising finding, but a possible explanation has been offered. The findings in the other disease states, do not

appear excessive or dissimilar to those reported elsewhere.

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PART 4

SUMMARY

----- CHAPTER 17 -----

SUMMARY

1. A diabetes prevalence survey has been carried out on the Indian inhabitants of Tongaat, a Natal northcoast town. The survey population numbered 2427 persons.
2. The Indians in and about Tongaat are highly representative of Indians in Durban, and Natal as a whole.
3. Screening recovery was good, being at least 70% and 80% for the 1st and 2nd surveys respectively.
4. Total diabetes prevalence (persons aged 10 years and older) is 6%. This prevalence rate has been compared with estimates from other recent surveys, with due concern for methodological differences.
5. Total diabetes prevalence by application of other commonly-used diagnostic criteria has resulted in rates which do not differ widely.
6. Diabetes prevalence by decade of age and for the total survey population is considerably less when age-dependent criteria are applied.
7. Total glycosuria prevalence (persons aged 10 years and older) is 5.3%. This does not differ significantly from total diabetes prevalence.
8. A sex difference for total diabetes and glycosuria prevalence is present. The female predominates in the former, in contrast to the male predominance in the latter.

Known diabetes prevalence displays no sex difference.

9. Diabetes accounts for approximately 75% of all glycosuria.

10. With increasing glycosuria degree, there is an obvious increase in diabetes probability.

11. Glycosuria degree has a constant relationship to plasma glucose level - the higher the plasma glucose, the heavier the glycosuria.

12. Plasma glucose frequency distribution is unimodal with slight skewing to the right. This distribution is age-determined - the older the age group, the more hyperglycaemic the distribution curve. This is indicated by a substantial rise in mean plasma glucose value with increasing age.

13. Plasma glucose frequency distribution in the non-diabetic population varies minimally with increasing age - this is mirrored by a negligible rise in mean plasma glucose value with age.

14. The sex difference seen with diabetes prevalence, holds for frequency distribution, with the female displaying the more "hyperglycaemic" curve, and also the higher mean plasma glucose value by decade of age.

15. Diabetes is definitely more common in the overweight than the normal or underweight groups. There is no significant correlation between plasma glucose and degree of obesity.

16. Plasma glucose screening possesses a far greater sensitivity than glycosuria screening. The optimum screening level is 120 mg./100 ml. with sensitivity and specificity being approximately equal at 94%.
17. The fasting plasma glucose level has a constant and highly significant relationship to the 1 and 2 hour levels in both diabetics and non-diabetics. There is a high degree of reproducibility between the screen 2 hour level and the G.T.T. 2 hour level, in the same subjects.
18. In diabetics, there is a steady deterioration in glucose tolerance with increasing age. Insulin response to glucose is similar for all age groups. N.E.F.A. suppression is seen in all age groups, the youngest group having the highest mean fasting N.E.F.A. value.
19. A small group of juvenile diabetics with maturity-type insulin response, and with no tendency to keto-acidosis, is described.
20. Mean glucose and insulin responses in positive screenees with normal G.T.T., are very similar despite wide age differences.
21. Obesity tends to produce elevated insulin levels in non-diabetic positive screenees, particularly at the 2 hour time interval. This effect is not apparent in the diabetic group.

22. The majority of diabetics are middle-aged with a female predominance falling away with increasing age.
23. Retinopathy in the small group of known diabetics is minimal. The absence of retinopathy in the newly-diagnosed diabetics is noted. Concerning ischaemic heart disease, peripheral vascular disease and peripheral neuritis, the findings do not appear excessive or dissimilar to those reported elsewhere.

STATISTICAL APPENDIX

1. Calculation of the Mean (\bar{x})

$$\bar{x} = \frac{\sum x}{n}$$

n = number of observations

X = sum of observations

2. Calculation of the Standard Deviation (S.D.)

$$S.D. = \sqrt{\frac{\sum x^2 - \frac{(\sum x)^2}{n}}{n-1}}$$

Ref: Bradford Hill, A. Principles of Medical Statistics
London. The Lancet Limited. P.100. 1966

3. Comparison Between Two Means With The "t" Test

$$t = \frac{\bar{x}_1 - \bar{x}_2}{\sqrt{\frac{s^2}{n_1} + \frac{s^2}{n_2}}}$$

s^2 = estimate of the standard deviation of the universe

$$= \frac{\text{Sum } (x_1 - \bar{x}_1)^2 + \text{Sum } (x_2 - \bar{x}_2)^2}{n_1 + n_2 - 2}$$

look up "t" table for $(n_1 + n_2 - 2)$

Ref: Bradford Hill, A. Principles of Medical Statistics.
London. The Lancet Limited. P.147. 1966

4. Comparison Between Two Sets of Observations Carried Out on Same Sample

$$t = \frac{\bar{d}}{\sqrt{\frac{S_d^2}{n}}}$$

$$\bar{d} = \frac{\sum d_i}{n}$$

where $\sum d_i$ = arithmetic sum of the differences between the individual observations

$$S_d^2 = \frac{\sum d_i^2 - (n)\bar{d}^2}{n-1}$$

look up "t" table for (n-1)

Ref: Keeping E.S. Introduction To Statistical Inference
Van Nostrand Co. Inc. Princeton. P.185. 1962

5. Assessment of Significance Between Descriptive Categories (e.g. diabetics and non-diabetics) - Where Quantitative Expressed - χ^2 test)

$$\chi^2 = \frac{(ad - bc)^2 (a + b + c + d)}{(a+b)(c+d)(a+c)(b+d)}$$

~~Refer to the table for illustration of specimen values of~~

If the numbers involved are small, the value of χ^2 will be more accurately given by the following formula (Yates correction) :

$$\chi^2 = \frac{\{ad - bc - \frac{1}{2}(a+b+c+d)\}^2 (a+b+c+d)}{(a+b)(c+d)(a+c)(b+d)}$$

look up χ^2 table for (n-1) d.f.

Ref: Bradford Hill, A. Principles of Medical Statistics
The Lancet Limited. London. P.172. 1966

6. Calculation of the Correlation Coefficient (r)

(a) Line of Regression

$$b = \frac{\sum xy - n\bar{x}\bar{y}}{\sum x^2 - n\bar{x}^2}$$

$$a = \bar{y} - b\bar{x}$$

Equation to line - $Y = a + bX$

X = variable 1

Y = variable 2

(b) Correlation Coefficient (r)

$$r = \frac{\sum xy - n\bar{x}\bar{y}}{\sqrt{(\sum x^2 - n\bar{x}^2)(\sum y^2 - n\bar{y}^2)}}$$

(c) Significance of r

$$t = \frac{r}{\sqrt{\frac{1-r^2}{n-2}}}$$

look up "t" table for (n-2)

Ref: Alder, H.L., Roessler, E.B. Introduction to Probability and Statistics. W.H. Freeman & Co. San Francisco & London. P.146. 1960

7. Comparison Between Two Means Where Underlying Populations Do Not Follow A Normal or any Particular Distribution

$$Z (\text{Variate}) = \frac{[N_1(N+1) - 2R_1] - 1}{\sqrt{\frac{N_1 N_2 (N+1)}{3}}}$$

N_1 = No. in sample A

N_2 = No. in sample B

N = $N_1 + N_2$

R_1 = Sum of ranking values of observations of sample A

Ref: Siegel, S. Non-Parametric Statistics For the Behavioural Sciences. McGraw-Hill Book Co. Inc. New York. P.116. 1956

Where N_1 and N_2 each are greater than 25, the N (0 - 1) table is used. Where N_1 and N_2 each are less than 25, the table provided in the original paper (below) is used

Mann, H.B., Whitney, D.R. On A Test of Whether One of Two Random Variables Is Stochastically Larger Than The Other. Ann. Math. Statist. 18, 50. 1947.

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