CAUSES OF DEATH AND SURVIVAL AMONG DIABETICS

by

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PART I

CAUSES OF DEATH AND SURVIVAL AMONG DIABETICS

INTRODUCTION

Patterns of morbidity and mortality have always varied from time to time and these variations have been most marked since the beginning of the last century. In the past, when bacteriology was yet in its infancy, and chemotherapy had not even been thought of, infectious diseases accounted for the greater part of morbidity and mortality throughout the world. Periodical epidemics and pandemics of the major infectious diseases such as plague, small-pox and cholera were a common occurrence, and these contributed in no small measure towards maintaining the average life-expectancy at a comparatively low level. However, with improvement in the knowledge of the aetiology of most diseases, and the advent of chemotherapy and antibiotics, the risk of people succumbing to such diseases has been greatly reduced. The average life expectancy has increased considerably in almost all parts of the world, and, as one would normally expect, the more chronic diseases such as diabetes mellitus, arteriosclerotic and degenerative heart disease and also malignant diseases have begun to occupy important roles in the overall mortality picture at the present day.

Notwithstanding the great volume of research into the aetiology and pathogenesis of arteriosclerotic heart disease and diabetes mellitus, there are certain aspects of these diseases which have not yet been fully investigated. Survivorship among diabetics, and the exact causation of their deaths are two such problems. Although diabetes mellitus has always been considered as an important cause of morbidity and mortality throughout the world and referred to

as such even in the oldest medical texts, [1][2] statistical data relating to survival and underlying causes of death are few and are available only for a few countries of the world.

We have, therefore, been interested to find out what happened to people once the diagnosis of diabetes mellitus was made, as to how long they lived and what effect the diabetic state had on their working capacity and general health and well-being.

In order to do this, an enquiry was designed, with a view to obtaining further information regarding survivorship and underlying causes of death of patients who suffer from diabetes mellitus. The study is based primarily on the follow-up of two cohorts of individuals who had attended the diabetic clinic at the Royal Infirmary, Edinburgh, for diagnosis and treatment of glycosuria during the years 1939/1940 and 1949/1950. Only those patients residing in the South-Eastern Region of Scotland (with the exclusion of Fife), and those who were actually confirmed as suffering from diabetes were considered in the study.

The total number of patients in both groups was 959. Of these, we were able to trace the death certificates of 632 patients who had died subsequently at some time or another. Of the remainder, we saw and interviewed 249 patients. We were also in contact with a further 35 patients and were able to confirm that they were alive, although we were unable to interview them personally for reasons given later.

The remaining 43 patients we were unable either to interview

or contact by letter.

This thesis will discuss in detail the general question of survivorship of patients once the diagnosis of diabetes mellitus has been made, the cause of death in patients suffering from diabetes mellitus, and the particular results obtained in the enquiry that we have conducted.

A BRIEF REVIEW OF THE INTERNATIONAL CLASSIFICATION OF CAUSES OF DEATH AND ITS INFLUENCE ON DEATH CERTIFICATION OF PATIENTS DYING WITH DIABETES MELLITUS

"Diabetes mellitus has always been considered an important cause of morbidity and mortality, not only in itself but more particularly on account of the way in which it aggravates the course of a number of other disorders."(3) The importance in which it was held can be seen by the fact that it was already included in the Bertillon Nomenclature, which was adopted as the International List as far back as 1893. Subsequently, as medical knowledge advanced, several conditions originally associated with diabetes mellitus were dropped at various periods, thereby obtaining a more exact definition of the disease and ensuring a greater degree of accuracy in the relevant statistical data. Diabetes insipidus was the first to be omitted from the original rubric (in 1909), diabetic pigmentary cirrhosis or "bronzed diabetes" was dropped in 1938, and "renal glycosuria" or "renal diabetes" in 1948.

For obvious reasons, these changes did not produce any significant effect on the statistical series. However, there were present, and are still found, a number of variable factors which profoundly influence the enumeration of statistical data for diabetes in particular. Among these factors are :-

inexact diagnosis of causes of death; imperfect death registration systems which are still to be found in the less developed countries; and variations in the criteria adopted for the determination of the cause of death when multiple causes were mentioned in the death certificate.

In order to overcome this difficulty, a number of countries established certain rules for the selection of the cause of death to which the death is to be assigned when multiple causes were mentioned in the death certificate. These rules, however, were not uniform throughout the countries of the world, so that there were bound to be considerable divergences in the statistical series for deaths from diabetes mellitus, not only from one country to another, but also in the same country over different periods. The only era to which this perhaps does not apply is that of the last few years, since the application of the Sixth Revision of the International List in 1948. The rules adopted in this Revision specified that where the medical certification was properly completed, the underlying cause of death indicated by the physician was to be used for purposes of tabulation.

The consequences of the adoption of new rules for the determination of the underlying cause of death is well illustrated by a study of the changes that took place in certain countries like the United States of America and in Denmark following the introduction of these rules.

In the United States of America, the figures for deaths attributed to diabetes mellitus dropped from 38,638 in 1948 to 25,089 in 1949, in which year the Sixth Revision of the International List was applied. This led to an apparent decline in the mortality rate from diabetes mellitus, from 26.4 to 16.9 deaths per 100,000 population. Joslin[4] believes that this change in the practice of classification introduced by the Sixth Revision has had the effect of reducing the

diabetic death rate almost by one-half (vide Table 1) at least in the United States.

Table 1

Number of deaths from all causes - Deaths and death rates from Diabetes and ratio of deaths from all causes: Registration areas, 1900, 1920, 1930, 1940, 1945, 1950, 1955 and 1956.

Year	Total Deaths	Diabetic Deaths			Ratio of Diabetic deaths to total deaths - %	
		Number	Rate/100,000			
			Old Revision	Sixth Revision	Old Revision	Sixth Revision
1956*	1565000	26340		15.8		1.68
1955	1528717	25488		15.5		1.67
1950*	1452454	24419		16.2		1.68
1950	1450270	25010	29.7	16.6	3.09	1.72
1945	1401719	35160	26.6	15.1	2.51	1.42
1940	1417269	35015	26.6	15.1	2.47	1.41
1930	1343356	22528	19.0		1.67	
1920	1142558	14062	16.0		1.23	
1910	805412	8040	14.9		1.00	
1900	539939	3996	9.7		0.55	

* Data based on a 10% mortality sample.

Source: National Office of Vital Statistics of the U.S. Public Health Service (adapted from "Treatment of Diabetes Mellitus" by Joslin, E.P., Root, H.P., White, P. and Marble, A. 10th Ed.)

The same thing happened in Denmark too, in 1951, on the introduction of the new system of classification. The figures for mortality from diabetes mellitus fell from 966 deaths (a rate of 22.6 per 100,000 inhabitants) in 1950, to 294 deaths (6.8 per 100,000 inhabitants) in the following year. Prior to 1951, the deaths of all diabetic patients, with the exception of only those dying from tuberculosis, cancer or violent deaths would have been attributed to diabetes mellitus. The present position is that only deaths from diabetic coma and deaths of persons on whose death certificate diabetes is the only disease mentioned, or else occurs in the first place, are included in diabetic mortality statistics.

Table 2, which is an extract of an analysis made by K. Dreyer and A. Hey (1954)[5] illustrates very clearly the interruption in the continuity of the mortality statistics of diabetes mellitus in 1951.

Table 2 /-

Table 2

Distribution in Denmark according to the two methods of Classification of Underlying Causes of Death in connection with which Diabetes Mellitus is mentioned.*

Death attributed to	Danish rules for selection of underlying cause - %	New rules for selection of underlying cause - %
Diabetes as underlying cause	54	7
Other underlying causes	46	93
Including		
Diseases of circulatory system	22	55
Malignant neoplasm	10	10
Diseases of genito urinary system	3	10
Tuberculosis (all forms)	2	2
Diseases of respiratory system	1	5
Other causes	8	11

* With respect to 1953, medical certificates of death from January 1949 to 30th June 1957, percentage of certificates mentioning diabetes mellitus.

In England and Wales the changes took place at a considerably earlier period. The new rules for the statistical classification of causes of death were applied in 1940 and these were very similar to the international criteria which were to be adopted later in the Sixth Revision of the International List.

OTHER FACTORS WHICH MAY INFLUENCE THE MORTALITY DATA OF DIABETES MELLITUS

Besides the changes brought about by the periodical revision of the International List of Classification of Causes of Death, there are certain other variable factors which may significantly influence the enumeration of statistical data about diabetes mellitus. They are :- Incompleteness of diagnosis of new cases and inexact diagnosis of causes of death; imperfect death registration systems and variations in the criteria adopted for the determination of the underlying cause of death when multiple causes were mentioned in the death certificate. The implications of this last factor has been dealt with briefly in the preceding section.

(a) Incompleteness of diagnosis of new cases:

Diabetes mellitus is essentially a chronic disease. A large proportion of cases belong to the mild obese type, which occurs during middle life and generally sets in insidiously. Quite a large proportion of individuals suffering from diabetes mellitus do not present the classical symptoms and signs of polyuria, polydipsia and weight loss. These symptoms are present only among a moderate percentage of all diabetics; e.g. Andrews[6] in his study of a group of diabetics in West Cornwall in 1957 found that only 41.4 percent of the 573 clinic patients whom he investigated had the classical symptoms of thirst, polyuria and weight loss at the onset of the illness. 21 patients (3.7 percent) were diagnosed at routine medical

examination, and 56 patients (9.8 percent) were diagnosed while they were being investigated for other incidental illness. Some of these latter cases were picked up by observant general practitioners looking after minor illnesses such as influenza, at the patient's home.

Some authors[7] believe that for every patient diagnosed as having diabetes mellitus there is another patient suffering from the disease in the same community.

The extent to which cases of diabetes mellitus remain undiagnosed has been investigated by Munro, Eaton and Glen.[8] They are of the opinion that those cases that are undiagnosed tend to be mild and without definite symptoms. They also showed that the lack of symptoms affected the two sexes to a different degree. For example, genital pruritus was the chief complaint in 26 percent of their female cases, whereas it accounted for only 0.8 percent among the male patients. They believe that a large number of their female patients would never have come for a diagnosis were it not for the pruritus.

The extent to which diabetes remained undiagnosed was believed to vary at different ages in the Scottish population. The authors were able to make a direct approach to the problem of the true number of diabetics in the population by using the data accumulated at the examination of army recruits. Among a group of 413,110 consecutive male and female Scottish recruits between the ages of 17 - 45 years for males, and 17 - 35 years for females, they found an incidence rate of diabetes mellitus of 1.74 per 1000 males and 0.37 per 1000 females. Although numerically the young adult

diabetics form an important group, the authors state that they are unable to present data for the middle-aged group in the population who are subject to a greater incidence of the disease. The disparity between the actual number of persons with diabetes mellitus and the number of persons with recognised disease may thus be quite considerable.

(b) Inexact diagnosis of causes of death:

The failure to include the term 'Diabetes Mellitus' as the immediate or as an underlying cause of death in a person dying, either with or from diabetes, may be due to several factors.

First, as mentioned earlier, the condition could have been so mild and symptomless that it was never diagnosed during the life-time of the patient; secondly, the patient, although he may have been undergoing treatment for diabetes mellitus for a considerable time, may have ultimately died of some sudden severe illness such as a cerebral catastrophe or acute left ventricular failure, or even of cancer, in which case the greater importance of the immediate preceding cause of death tends to a certain extent to reduce the significance of the contributory part played by diabetes mellitus, so that it tends to be pushed into the background. Thirdly, the immediate cause of death may have no relationship whatsoever to diabetes mellitus, so that it never finds a place in the death certificate.

Joslin[9] believes that only two-thirds of all patients dying with diabetes have the term 'diabetes mellitus' entered in the

death certificate either as the primary or contributory cause of death. Other studies on mortality data too have helped to confirm this view. It has been shown by some workers[10][11] that as many as 30.6 percent among males and 16.6 percent among female diabetics failed to have the disease mentioned in the death certificate. It was further shown that the rate of omission of diabetes from the records was greater whenever coronary artery disease, cancer or accidents were mentioned in the certificate than it was for all males, whereas other heart conditions, cancers and accidents accounted for a higher rate of omission from the records of females. For both sexes, deaths at home and in nursing homes had a less complete diagnosis than those in hospitals, but the rate in hospitals was almost twice as great for males as for females, e.g. 23.5 percent of the hospitalised males observed by the authors did not have diabetes mentioned on the death records as contrasted with 12 percent of the females. In both sexes the percentage of medical-examiner cases (sudden deaths) without diabetes mentioned on the death certificate was high, viz. 77.6 percent for males and 72.2 percent for females.

Our own data which relate to the analysis of the death records of 632 diabetic patients will be presented in Part III of the thesis.

In general, most authors on this subject agree with Moriyama[12] of the Bureau of the Census of the United States of America that the mortality statistics give us the number of persons dying "with diabetes", but not necessarily "of diabetes" or its

complications, and that only some 60 percent of known diabetics are finally coded to diabetes.(13)

(c) Imperfect death registration:

The considerations enumerated above are true only for the economically advanced European and American countries which have efficient death registration systems. The data obtained from the economically under-developed countries are yet of a comparatively low standard of accuracy as to be available for the purpose of drawing comparisons between different countries,(14) because of the overwhelming lack of medical and other technical personnel which is common to most of these countries.

CHANGING PATTERN OF CAUSES OF DEATH AND FACTORS RESPONSIBLE FOR THIS CHANGE

Since the discovery of insulin in 1922 by Banting and Best, and the more recent advances made in the field of antiglycosuric agents, the prognosis and treatment of diabetes mellitus have undergone a considerable change for the better during the last four or five decades. The clinical picture and the course of the disease too, has undergone a dramatic change within the last few years. In the study carried out by Fitz and Murphy[15] of the Peter Bent Brigham hospital, on a group of diabetic patients who had died in that institution between the time it opened in 1913 and the commencement of the insulin era in 1923, it was observed that the four most common causes of death among diabetics were:-

(a) coma with or without a terminal infection

(b) sepsis

(c) cardio-vascular-renal disease, and

(d) pulmonary tuberculosis.

They also observed that coma and pulmonary tuberculosis tended to occur more frequently in the younger patients, whereas cardio-vascular-renal disease, including gangrene, tended to occur in the older age groups. Sepsis occurred with equal frequency among both groups.

The degree to which changes have occurred in the causation of death brought about by the introduction of insulin treatment is made clear from the study of John B. Flynn,[16] which involved a group of 917 diabetic patients who were admitted for the first time to the same hospital, between 1923 and 1933, out of whom 86 died in the

hospital. Of this group of 80 patients who died, the true cause of death was ascertained at necropsy in 43. Among these there were only two cases of uncomplicated coma; 12 cases had obvious sepsis or terminating acute infection. There were 3 cases of active pulmonary tuberculosis; 21 cases of cardio-vascular disease, including gangrene and chronic nephritis, and 5 cases had unusual complications such as acute nephritis (1 case) and carcinoma (4 cases). Table 3 illustrates the striking changes that have taken place in the causation of death among diabetic patients in the pre- and post-insulin eras.

Table 3

The Cause of Death in Diabetes Mellitus as proved by Necropsy

Cause of Death	1913 - 1922	1923 - 1933
	% of deaths	% of deaths
Coma	11	5
Sepsis	38	28
Cardio-vascular disease	24	49
Pulmonary Tuberculosis	19	7
Unusual complications	8	11

The difference observed between the two groups is quite striking, particularly with regard to deaths due to coma, pulmonary tuberculosis and cardio-vascular disease. Deaths from coma, sepsis and pulmonary tuberculosis showed a marked decrease whereas those

due to cardio-vascular disease and its sequelae have shown a considerable increase. Coma, sepsis and tuberculosis, which together accounted for about 70 percent of all diabetic deaths in the pre-insulin era, accounted for less than 40 percent of the deaths in patients who had the benefit of insulin treatment. On the other hand, cardio-vascular disease and its complications had increased to such an extent that they accounted for almost 50 percent of all diabetic deaths in the post-insulin era, whereas they accounted for only 24 percent in the period before 1922.

The authors are of the opinion that with the judicious use of insulin, "one might rightfully expect uncomplicated coma to disappear from hospital records as a cause of death in diabetes, save in those rare cases where the patient enters the hospital in a moribund state." The patients in both groups belonged to the pre-antibiotic era, yet there was a considerable reduction in the deaths attributed to sepsis in the latter group. The authors believe that the factor responsible for this increased resistance offered to infection and sepsis by the latter group of patients was probably due to their better nutritional status consequent to their taking a more substantial diet, whereas in the pre-insulin era the only method available for the control of glycosuria was to keep the patient on a sub-maintenance diet which ultimately tended to undermine his nutrition and thereby reduce his powers of resistance.

The remarkable impact that insulin had on the prognosis and treatment of diabetes mellitus is commented on by I.A. Mirsky,[17] who states that "it is a startling blow to our complacency to realise

that the discovery of insulin and its application to the treatment of diabetes has made it possible for us to keep the diabetic alive so long that he eventually dies with retinopathy, hypertension, glomerulosclerosis, neuritis and other vascular disturbances."

Further improvement in the ultimate prognosis of the diabetic patient was achieved with the introduction of chemotherapy and the use of antibiotics commencing with those of the sulphonamide group in 1935 and to a considerably greater extent after the introduction of penicillin in 1945.

The changes brought about are best illustrated by the study of Blumberg and Zisserman[18] which was made on all adult diabetic deaths at the Jewish hospital during the period 1930 - 1938,[19] consisting of a group of 155 patients and a second group of 247 patients covering the period 1939 through June 1950. Autopsies had been performed on 37.4 percent of the patients in the first group and on 34.8 percent of those in the second. The authors followed the standard methods of nomenclature and classification in their analysis of the data, except for the fact that they gave preference to the diagnosis of diabetes mellitus wherever it occurred. The detailed analysis of the two series illustrating the important differences between the causes of death among the two groups is given in Table 4.

Table 4

Causes of Death.

	1930 - 1938						1939 - 1950					
	Male	%	Female	%	M + F	%	Male	%	Female	%	M + F	%
Acute Coronary Thrombosis	3	5.8	5	4.8	8	5.1	15	18.8	35	20.9	50	20.3
Acute cerebral 'accident'	3	5.8	13	12.6	16	10.3	9	11.3	24	14.3	33	13.4
Hypertension and 'sclerotic' heart disease	9	17.3	17	16.5	26	16.8	19	23.7	22	13.2	41	16.6
All pneumonias	9	17.3	15	14.6	24	15.5	7	8.7	12	7.2	19	7.7
Other infections	10	19.2	15	14.6	25	16.1	4	5.0	16	9.6	20	8.1
Malignancy	3	5.8	4	3.9	7	4.5	4	5.0	14	8.4	18	7.3
Gangrene of legs	12	23.1	23	22.3	35	22.6	12	15.0	16	9.6	28	11.3
Diabetic coma	1	1.9	5	4.8	6	3.9	0	-	5	3.0	5	2.0
Blood dyscrasias	0	-	2	2.0	2	1.3	1	1.2	3	1.8	4	1.6
Others	2	3.8	4	3.9	6	3.9	9	11.3	20	12.0	29	11.7
TOTAL	52	100.0	103	100.0	155	100.0	80	100.0	167	100.0	247	100.0

The most significant changes in the causes of death between the two groups were noted among the deaths attributed to acute coronary thrombosis, all pneumonias and other infections. Relatively insignificant changes were observed in deaths resulting from malignancy and coma. The most marked increase was among the group of deaths attributed to acute coronary thrombosis where the increase was almost 400 percent. On the other hand, the incidence of deaths due to pneumonia or other infections had decreased by 50 percent in the second series. A similar decrease was observed in the frequency of deaths caused by gangrene of the legs and also of deaths due to diabetic coma.

The further changes that have occurred in the overall picture of the mortality pattern among diabetic patients is well illustrated by the study of Charles R. Shuman and Fred B. Rogers[20] who have cited the complications reported on a group of diabetic patients for the years 1950 to 1955. The recorded data are given in Table 5.

Table 5

Complications reported in diabetic deaths 1950 - 55.

Cause of Death	1950	1951	1952	1953	1954	1955
Acidosis	12	8	10	17	5	10
Gangrene	7	5	3	18	8	0
Infection	5	6	3	13	3	16
Heart disease	22	41	33	137	111	139
Tuberculosis	1	0	4	6	0	1
Malignancy	9	8	10	31	11	17
Cerebro-vascular "accident"	26	38	39	54	31	45
Renal	12	10	10	19	14	22
Pneumonia	13	2	8	20	10	12
Others	10	25	26	23	24	21
TOTAL	116	139	146	338	217	281

Analysis of the data showed that the diseases of the cardio-vascular-renal systems accounted for the majority of deaths reported in this group of diabetic patients. In Joslin's series, almost three-fourths of the deaths were due to this cause. Heart disease

alone was responsible for nearly half of this total and almost two out of every three cases attributed to heart disease were actually dying of coronary artery disease. Next in order of frequency were the vascular lesions of the central nervous system, cancer and nephritis. Among the last category, the majority of deaths were attributed to diabetic nephropathy which is a specific complication of diabetes mellitus of long duration. Cancer caused about 10 percent of all deaths and infections had reached a new low level of only one-twentieth of all deaths. Diabetic coma and gangrene were responsible for relatively few deaths.

The general concensus of opinion is that the insulin treatment has been so effective in preventing the the untimely deaths from coma and associated complications that a large number of diabetic patients survive long enough to reach the age groups where vascular diseases usually manifest in otherwise normal individuals. The specific part played by insulin in prolonging the expectation of life of the diabetic patient will be dealt with in greater detail in a later section.

This, however, is not the whole answer to the problem. Vascular disease may occur as a result of diabetes mellitus, as shown by the fact that juvenile diabetics develop arteriosclerotic changes comparatively early in life.[21][22][23][24] The experience of Joslin[25][26] has been altogether similar to the views expressed above. Table 6 gives the causes of death of 18,055 diabetic patients, classified according to the different eras in which they occurred, and gives an excellent summary of the events that have occurred through the different epochs in the history of the

management and prognosis of diabetic patients.

Table 6

The Cause of Death of 18,055 diabetics
(Percent of all cases)

Cause of death	Naunya era	Allen era	Banting era	Hagedora era		Charles H. Best era	
Coma present	63.8	41.5	8.3	2.8	1.7	1.3	1.1
Cardio-renal-vascular	17.5	24.6	54.4	65.8	71.3	76.3	77.7
Infections (total)	7.4	12.7	13.6	10.4	5.9	5.4	3.9
Pneumonia and other respiratory	4.3	7.7	6.8	5.5	3.6	3.2	1.3
Others	3.1	5.0	6.8	4.9	2.3	2.2	2.6
Cancer	1.5	3.8	8.7	9.0	9.7	10.3	11.3
Tuberculosis	4.9	4.9	4.1	2.2	1.7	0.7	0.2

Source: Treatment of Diabetes Mellitus. Elliot P. Joslin et al: 10th Edition, 1959.

The table illustrates clearly the characteristic reduction in deaths due to diabetic coma. It will be observed that at first almost two-thirds of the patients died of it, whereas between 1944 and 1949 only 1.7 percent of the deaths were attributed to coma. Infection too, has been responsible for a considerably fewer number of deaths in the recent past; the maximum percent of deaths from infection occurred in the period 1922 - 1936, during which it accounted for almost 13.6 percent of all deaths. This has come down

to 3.9 percent in 1956 and 1957. Deaths from pneumonia and other respiratory infections which were a frequent occurrence in the past have been observed to be less important as a cause of death in the later decades. As mentioned earlier, deaths from cardio-vascular-renal disease has increased to such an extent that they now account for almost 77.7 percent of all deaths among diabetics.

FACTORS RESPONSIBLE FOR THE CHANGES IN CAUSES OF DEATH AMONG DIABETICS

Among the important factors that have been responsible for bringing about these remarkable changes in the causation of death among diabetics, priority should invariably be given to such outstanding achievements as the introduction of insulin in 1922, and the use of chemotherapeutic agents and antibiotics a decade or so later. Perhaps of lesser importance are those factors related to changes in diets and eating habits of people, and changes in their modes of work and living consequent upon a gradual rising of living standards, which have been characteristic features during the last few decades.

I have already discussed very briefly the effects produced by the introduction of insulin and chemotherapeutic agents in a previous section. I shall now proceed to discuss in greater detail the actual effect produced by the introduction of insulin therapy, viz. the reduction of the mortality rates in a particular section of the diabetic population which resulted in a prolongation of the life of individuals belonging to this group, thereby exposing them to the various degenerative vascular changes which are common among normal individuals belonging to those age groups.

The Effect of Insulin on Death rates from Diabetes Mellitus.

The effect of insulin on the death rates from diabetes mellitus has been reviewed by Graham[27] in a critical analysis of the age specific death rates from diabetes mellitus during the period

1900 to 1940. Figure I shows the total deaths from diabetes mellitus per year from 1900 to 1940. The outstanding features of the curves for the males and females are that they both start from a very low level;

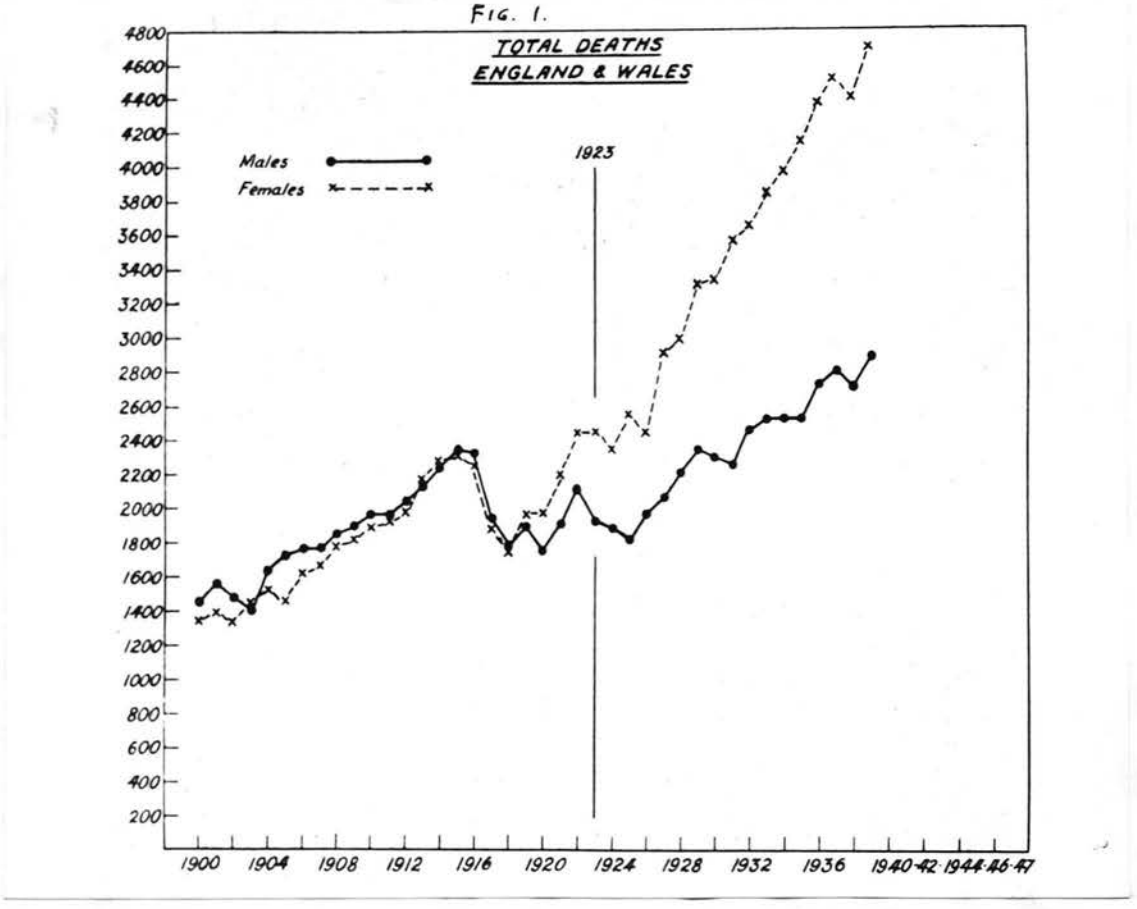


Fig. I. Total deaths from Diabetes Mellitus in England and Wales, 1900 to 1947.

Source: The Harben Lectures, 1949. J.R.I.P.H. & H. Vol. 13.

1455 deaths for males and 1312 deaths for females. The numbers continue to increase at a steady rate to reach a maximum total of

2310 deaths for males and 2228 deaths for females. Up to this period, the female rates are observed to be slightly less than those for males. The rates then show a decline in the next two years coincidental with the introduction of rationing. From 1919 onwards the female deaths exceed those for the males and the increase is maintained at a steady rate up to 1939.

Figure I does not in point of fact reveal the true nature of the situation. There can be no doubt whatsoever that insulin did have a strong influence on the ultimate outcome of diabetes. A study of Tables 7 and 8 will demonstrate the characteristic reduction that occurred in the total deaths from the disease during the war years and the subsequent fall that occurred following the introduction of insulin therapy, in all age groups up to 54 years. The deaths occurring in the age groups of 55 years and above do not show the beneficial effect of insulin, which is in fact what is to be expected. The deaths continued to increase and this increase was maintained right up to 1939.

Table 7. /-

Table 7

Mortality from Diabetes in 1920 to 1922
and subsequent years

Death Rates/Million Living

	Standardised Rates										
	All ages	0-55	55+	0-	15-	25-	35-	45-	55-	65-	75+
Males											
1920-22	93.7	47.9	477.5	14	22	60	69	133	309	661	772
1931	88.1	29.5	580.3	12	23	30	38	97	315	821	1161
1932	92.4	28.9	625.6	10	21	30	45	93	320	897	1310
1933	92.3	28.5	628.2	13	26	30	36	80	325	888	1326
Females											
1920-22	90.1	43.1	483.9	16	35	48	62	124	355	656	632
1931	110.9	33.4	762.0	11	26	31	45	121	473	1097	1218
1932	112.4	32.5	783.3	13	20	29	46	118	485	1143	1219
1933	114.3	33.5	793.0	12	25	30	48	118	470	1178	1275

Source: Registrar-General's Statistical Reviews, England and Wales. 1938-1939.(28)

Table 8 /-

Table 8

Mortality from Diabetes of Later years as a Percent of that in 1920 to 1922.

	Standardised Rates			0 -	15 -	25 -	35 -	45 -	55 -	65 -	75 +
	All Ages	0-55	55+								
Males:											
1923	96	79	110	79	79	80	87	74	104	113	114
1924	92	72	108	64	69	63	75	83	104	105	127
1925	87	67	104	79	52	72	62	70	93	106	120
1926	92	68	112	93	67	60	70	68	105	112	124
1927	94	67	116	79	74	68	58	63	107	116	133
1928	97	63	126	93	60	55	55	68	107	136	140
1929	101	73	125	86	60	60	90	79	106	130	150
1930	99	65	128	71	57	63	59	74	109	130	154
1931	94	67	122	86	52	50	55	73	102	124	150
1932	99	60	131	71	50	50	65	70	104	136	170
1933	99	59	132	93	62	50	52	60	105	134	172
Females:											
1923	104	95	112	69	86	92	95	115	110	112	116
1924	98	75	116	69	80	67	76	80	110	118	116
1925	104	80	122	69	86	67	85	90	111	131	128
1926	101	74	121	56	71	73	82	80	113	127	128
1927	112	76	139	69	71	67	73	91	131	135	173
1928	112	79	138	69	84	69	66	102	118	147	163
1929	123	81	155	69	63	65	84	106	135	157	195
1930	119	72	155	69	51	56	71	99	131	165	193
1931	123	77	157	69	74	65	73	98	133	167	193
1932	125	75	162	81	57	60	74	95	137	174	193
1933	127	78	164	75	71	63	77	95	132	180	202

Source: Registrar General's Statistical Reviews for England & Wales 1936.(29)

It will be evident from the above data that the net result of insulin therapy has been a considerable reduction in the total deaths occurring in the age groups below 55, and a transfer of these to age groups above 55 years. Thus the overall effect of insulin has been actually the prevention of untimely deaths from coma and associated complications, so that a large majority of patients suffering from diabetes mellitus are able to survive long enough to reach those age groups where vascular diseases usually become manifest in otherwise normal individuals.

The Effect of Changes in the Diet and Improved Standards of Living.

Before going into the implications of the effect of diet on the prognosis and its association with the onset of complications in patients already suffering from diabetes mellitus, a brief account will be given regarding the association observed between diet and the incidence of diabetes mellitus as judged from a study of mortality rates from the disease.

It would have been observed that, in general, the mortality rates from diabetes are higher in the highly industrialised countries in the western hemisphere than among the economically under-developed countries in the East. Diabetes mellitus is not the only such disease that has predominantly high mortality rates; similar data are also characteristic of pathological conditions such as cerebro-vascular disease, coronary atherosclerosis and other degenerative diseases. These may aptly be classified as the diseases of abundance and prosperity. The incidence of diabetes mellitus has been

found to be highest where the general economic standards and medical care services were of the highest standard. The observation made by Himsworth[30][31][32] that diabetes is most prevalent in those countries where high fat diets are consumed, is of considerable interest. It is a well known fact that foods with a high fat content are dearer than the easily available starchy foods which form the staple diet in most of the so-called under-developed countries, which in general are reputed to have a low incidence of diabetes mellitus. Tulloch[33] has mentioned that with a few exceptions such as the Masai and the Karamojong in East Africa, and most races in Hawaii, the pattern of the diet in tropical countries is the same, and that the bulk of the diet is provided by carbohydrates, and the protein which is generally second class, and fats, are consumed in minimal quantities. Mills[34] has observed that in countries like China and Japan the incidence of diabetes is comparatively low; and the disease itself is believed to be of a milder nature. It is believed to be infrequent and mild in India except among the richer classes. De Soyza[35] has observed that in Ceylon, although the incidence of diabetes mellitus is somewhat higher than in other countries in South East Asia, the disease itself is milder in character; acidosis and coma are comparatively rare; peripheral vascular disease, hypertensive heart disease and obesity are uncommon, and hypercholesterolemia is virtually absent. He attributes this to the high carbohydrate and low fat diet commonly consumed in Ceylon. A further analysis of the diabetics shows that diabetes is common among the upper class Sinhalese who consume a moderately high calorie diet, in which the percentage of fat is very much higher than

that in the other two groups. (Vide Table 9).

Table 9

The Dietetic Composition of the different Socio-Economic Groups among Sinhalese.

Economic Level	Total Calories	% CHO	% Protein	% Fat
I (Lower)	1987	71.4	10.9	17.7
II (Middle)	2521	70.1	11.9	18.1
III (Upper)	2878	60.1	11.8	28.1

The low incidence in Thailand[36] has been attributed to the national diet based on rice, which they share in common with other countries in this region. In this diet, fat accounts for only 10 percent and protein for 9 percent of the nutrients. However, observations made in Iceland by Albertson do not support this view. Here, the incidence in a carefully conducted study was less than 1 per 1000, and the annual diabetic death rate 1.9 - 4.0 per 1000. The average Icelandic diet contains about 44 percent of carbohydrate, 45 - 58 percent of proteins (almost entirely of high biological value proteins such as milk, meat and fish); the balance 10 - 12 percent is made up of fat. The feature in common between the two countries is the lack of obesity, which, in Albertson's opinion, is a more significant factor than the actual dietary composition.

These data have been studied in great detail by Himsworth.[37] By correlating the dietary habits throughout the world with the

available mortality tables, he demonstrated that there was a definite curve of relationship between the two; the groups utilising the greater carbohydrate and low fat diets, had the lowest incidence of diabetes mellitus, whereas the highest incidence rates were found amongst those who took a diet high in fat content.

Carbohydrates have been observed to have a considerable effect on the glucose tolerance tests by several observers. Pick[38] has reviewed the work of Greenwald, Gross and Samet,[39] who observed a distinct lowering of the glucose tolerance by experimentally feeding carbohydrate free diets; this effect appeared to be greater when the fat content of the diet was increased. These views are supported by the findings of Kempner[40][41] who found that patients suffering from diabetes mellitus tolerated a rice diet very well; in a significant number of patients, the blood sugar level and the insulin requirements were lowered and they were observed to develop complications such as hypercholesterolemia, renal and vascular diseases, less frequently than those on a normal diet. In fact, in the second series of patients studied by him, specific diabetic retinopathy and even retinitis proliferans were found to be improved in 25 percent of cases.

The theory has been put forward[42] that the underlying factors responsible for these complications are frequent hypoglycaemic attacks, physical and mental stresses and infections, which in turn stimulate the adrenal cortex. This view is further supported by the experimental work in which administration of ACTH in man gives rise to capillary microaneurysms of the retina, and cortisone injections

in alloxan-diabetic animals cause vascular changes similar to Kimmelstiel-Wilson syndrome. Hyperglycaemic attacks on the other hand, do not appear to have any deleterious effect. Other observers[43] have however, pointed out that insulin reactions per se do not appear to increase the liability to develop retinopathy and nephropathy.

Recent work[44] has shown that the substitution of a poly-unsaturated fat for saturated or mono-unsaturated fats resulted not only in a decrease in the plasma lipids, and in some cases, apparent improvement in existing retinopathy and/or nephropathy, but also in a significant reduction in the level of the blood sugar, although the diet remained unchanged. The difficulty lies however, in formulating a diet containing relatively large amounts of fat from vegetable sources with the exclusion of the more palatable sources of fats such as meat, eggs and dairy fats, which are composed mainly of saturated fatty acids. The differences in the total amount of fat and the relatively small amount of saturated fatty acids in the diet of the people living in most Asian countries may account to some extent for the low incidence of diabetes mellitus characteristic of these countries.

An overall reduction of the dietary intake occurred as a result of the rationing of food substances which was introduced in the two world wars. Gosta Rooth,[45] in a review of the mortality figures from diabetes mellitus in some European countries, illustrates the characteristic effect this has had on the mortality figures from diabetes mellitus, particularly among the combatant nations engaged

in the above wars.

Keys and co-workers[46][47][48] have focussed attention on the question of controlling serum cholesterol levels through selection of dietary fats. Extensive studies were carried out in many countries regarding the incidence of atherosclerosis, and it was noted that there was a high consumption of saturated fats among those nations which were economically better-off, and that there was a corresponding high incidence of atherosclerosis. Thus the prognosis is made still worse for the diabetic patient who consumes such a diet, because it has been shown that diabetics, in common with sufferers from myxoedema, nephrosis, hypertension and hyperthyroidism, usually show a disturbed lipoprotein metabolism with elevated levels of serum cholesterol.[49] It has been suggested[50] that a dietary regimen consisting of reduced saturated fats and increased unsaturated fats may, in the long run, help to check the ever increasing incidence of atherosclerosis.

A vast amount of clinical and experimental data have been accumulated to show the close relationship between atherosclerotic and other degenerative vascular diseases, and poor dietetic control of diabetic state.[51][52][53][54][55][56][57][58] Dunlp,[51] in an investigation carried out on 54 patients who were allowed a "free" diet over a period of nine years, found that the results were extremely bad, particularly as regards the incidence of pulmonary tuberculosis. In comparing the results in a well controlled, with a poorly controlled series, he found that cardio-vascular complications, nephropathy and neuropathy, were very much more common in the poorly controlled group. He suggests that the factor which was most important in the prevention

or postponement of degenerative lesions among diabetic patients was the careful control of their diabetic state by diet and insulin.

It has been observed that diabetes mellitus is commoner among the highly industrialised countries of the West than among those that are not so well developed. It is undoubtedly true that industrialisation does play an important role in raising the economy of a country and improving the living standard of its inhabitants. However, this prosperity can be achieved only at a considerable price, as there are a number of problems that follow closely in its wake.

Large scale mechanisation has produced a multiplicity of effects. First, it has helped to increase production and raise the general economy; secondly, it has considerably reduced the amount of energy expended by the labourer and at the same time has given him greater leisure. This means that he is able to buy more food than his counterpart living in the less well-developed countries, although his actual caloric requirements may be well below those of the latter. The net result is an increase in the frequency of obesity and a consequent increase in the incidence of diabetes mellitus. This has been commented on by most workers.(59)(60)(61)(62)(63)(64) For example, Harris(65) asserts that "the overall incidence of the disease at any particular time is related to the economic position, and more particularly to the dietetic habits of the population concerned; and that it is highest in populations economically more advanced and where there is on the average a greater food intake.

REVIEW OF THE LITERATURE - EXPERIENCES IN DIFFERENT COUNTRIES

The various changes that have occurred in the prognosis and the underlying causes of death among diabetics during the last few decades have been discussed earlier. With the widespread use of modern therapeutic aids, one would have expected to see some uniformity in the overall picture of mortality statistics throughout the world. This, unfortunately, is not the situation. Despite the fact that insulin and other powerful chemotherapeutic drugs have been available freely during the last two or three decades, the avidity with which different countries adopted these modern therapeutic aids has varied to a considerable degree.

The United States of America and Great Britain have always been well ahead of most other countries in the field of research on diabetes and in the adoption of the more modern therapeutic aids in its treatment. Therefore, in order to get a clear picture of the present situation with regard to mortality data, one would perforce have to look into the data available for these countries. The most recent data on this subject based on the experiences of the Joslin Clinic[66] are given in Table 10.

Table 10 / -

Table 10

The Cause of Death among 325 Diabetic Patients dying in 1950 - 1960. Experiences of Joslin Clinic.

Cause of Death	Number of Deaths		Percent of all causes	
	Male	Female	Male	Female
All causes	150	175	100	100
Diabetic coma (primary)	1	2	0.7	1.1
Cardio-vascular-renal	110	133	73.3	76.0
Arteriosclerotic	110	133	73.3	74.9
Cardiac	64	88	42.7	50.3
Coronary	45	60	30.0	34.3
Renal	25	15	16.7	8.6
Diabetic nephropathy	18	10	12.0	5.7
Cerebral	18	22	12.0	12.6
Gangrene	1	3	0.7	1.7
Other circulatory and rheumatic diseases	-	2	-	1.1
Infections - total	12	10	8.0	5.7
Pneumonia and respiratory	7	5	4.7	2.9
Gall Bladder	1	-	0.7	-
Kidneys (acute)	1	3	0.7	1.7
Other infections	3	2	2.0	1.1
Cancer	11	24	7.3	13.7
Accidents	3	1	2.0	0.6
Suicides	-	1	-	0.6
Insulin reactions	1	1	0.6	0.6
Other diseases	12	3	8.0	1.7
Average at death	61.5 yrs.	65.4 yrs.		
Average duration of Diabetes Mellitus	16.2 yrs.	16.0 yrs.		

This table illustrates the fact that the causes of death among diabetics is now beginning to approximate more closely to that or normal people, at least as far as the better developed countries

are concerned. As was to be expected, cardio-vascular-renal diseases account for almost 75 percent of all deaths for both sexes. Deaths from primary diabetic coma and gangrene have come to occupy quite an insignificant position in the list; infection too, does not account for any significant proportion of the deaths, whereas deaths due to cancer has apparently assumed an important place amongst the list. The other interesting feature noted here is that a higher percentage of female deaths is attributed to cardio-vascular diseases and cancer than that of males, whereas male diabetics are observed to suffer higher death rates from renal causes, infections and accidents. One possible explanation for this may be that male diabetics have an onset of the disease at a much younger age, and belong to the acute insulin-dependant type, whereas females generally tend to develop the disease later on, and generally belong to the mild, obese type.

Other studies have been made in the United States of America regarding the causes of death among diabetic patients as reported in death certificates, by the Metropolitan Life Insurance Company.(67) The data obtained from such an analysis have been compared by Marks, with the experience of the Joslin Clinic for diabetic individuals dying in 1954. (Vide Table 11).

Table 11./ -

Table 11.

Percent of Deaths ascribed to Specific Causes among Diabetic individuals, by sex; experience of Metropolitan Life Insurance Company Policy Holders and of Joslin Clinic compared.

Cause of Death	Metropolitan Life Ins.Co.*			Joslin Clinic †		
	Both Sexes	Males	Females	Both Sexes	Males	Females
All causes, excluding unknown	100.0	100.0	100.0	100.0	100.0	100.0
Diabetic coma (primary)	4.8	6.1	4.1	0.7	0.8	0.7
Arteriosclerotic	83.0	82.8	83.1	72.0	71.4	72.6
Cardiac	52.4	56.6	50.0	44.0	48.1	40.0
Coronary Angina	28.4	39.4	22.1	35.8	39.8	31.9
Renal	6.6	7.1	6.4	9.7	11.3	8.1
Diabetic nephropathy	2.6	5.1	1.2	5.6	4.5	6.7
Cerebral	14.8	7.1	19.2	14.6	9.8	19.3
Gangrene	5.9	7.1	5.2	2.6	1.5	3.7
Site unassigned	3.3	5.1	2.3	1.1	0.8	1.5
Cancer	5.9	5.1	6.4	11.6	9.8	13.3
Violence	0.7	-	1.2	4.9	6.0	3.7
Other diseases	5.5	6.1	5.2	10.8	12.0	9.6
Total number of deaths	285	104	181	268	133	135
Cause unknown	14	5	9	-		

* Deaths during the last two weeks of 1954.

† Deaths occurring during 1954, reported to December 21, 1954.

It will be observed that there is a considerable amount of understatement particularly with regard to deaths from violence and

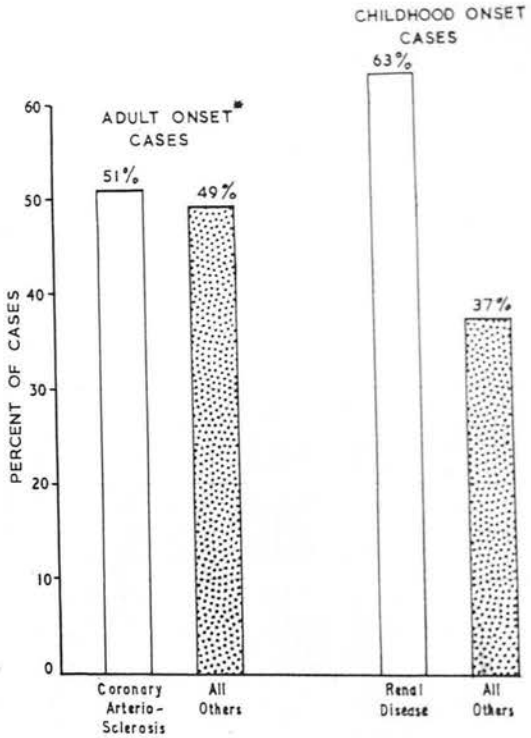
from malignant disease among the data from the Insurance Policy Holders. Diabetic coma and gangrene account for a very small proportion of deaths in either of the groups, whereas deaths from diabetic nephropathy were relatively fewer in the insured group than in the Joslin Clinic experience. Marks believes that this probably "reflects the difference in the reporting of the conditions, and perhaps also the higher proportion of cases of long duration in the Joslin Clinic experience."

Arteriosclerosis was the predominating cause of death among diabetic patients in both groups; and of these, heart disease accounted for nearly three-fifths of the total deaths for this condition. Cerebral accidents were next in frequency, accounting for about one-sixth of the arteriosclerotic deaths in the Metropolitan experience, and for one-fifth in that of the Joslin clinic's experience. Marks also quotes a similar analysis of death certificates for New York City in 1953 which showed "that 7.7 percent of the deaths ascribed to diabetes were reported as due to diabetic coma, and 13.2 percent to diabetic gangrene. On the basis of the estimated total number of deaths in which diabetes was mentioned in the death certificates, these proportions were approximately 3 percent and 5 percent respectively. All these figures quoted are well above those reported for the Joslin clinic."

FIG. 2

CAUSES OF DEATH AMONG DIABETIC PATIENTS ACCORDING TO AGE AT ONSET

SOURCE— WEST, K.M. ROOT H.F. "THE INCREASING INCIDENCE OF CORONARY ARTERIOSCLEROSIS IN DIABETES MELLITUS." -J. OKLAHOMA M.A.; 46:6, 1953.



* A consecutive autopsy series (1948–1951) of cases with onset after 21 yrs.

CAUSES OF DEATH AMONG DIABETICS IN RELATION TO AGE AT ONSET

The marked difference in the clinical course of diabetes, depending on the age of onset, has been commented on by most authors. West[68] believes that a great deal of harm is done by lumping the mortality figures of the older and younger groups together, which tends to present a mortality picture inappropriate for either group. This is evident from Figure 2, which shows the causes of death for a group of adult onset diabetics compared with that for a group who developed the disease in childhood.

The figure illustrates clearly the important part played by renal diseases in determining the terminal outcome of the young diabetic, whereas this position is taken over by coronary arteriosclerosis in the case of adult onset diabetics.[69] This fact is of primary importance in the epidemiology and prevention of diabetes mellitus and its complications. It becomes obvious that in order to help the young diabetic who acquires the disease early in life, we must concern ourselves primarily with the prevention or postponement of kidney lesions, while in the case of those having an onset in adult life, the major emphasis must be placed elsewhere. These views have since been confirmed by several other workers.[70][71]

Joslin[70] found an incidence of almost 51.0 percent of deaths from renal disease in a series of 135 deaths among diabetic children dying between 1937 and 1943. He also found that pulmonary tuberculosis and coma played a far more important part in mortality in this particular group than among all his other cases,

both young and old. These two complications accounted for 21.5 percent of the deaths. The prognosis regarding these two complications has improved considerably during the last few years. However, Joslin is convinced that "the future holds even greater promise for diabetic children because these conditions, as well as the number of deaths resulting from complications in the kidney can be reduced."

Root[72] has studied the causes of death in relation to duration, of 531 patients who had developed diabetes between infancy and thirty years of age. (Vide Table 12). It is seen that coma caused 56 percent of 166 deaths occurring during the first five years of diabetes mellitus, but thereafter declined as a cause of death. In the group of 142 deaths occurring after 15 years of diabetes, it was responsible for only 3 percent.

Table 12.

Cause of Death according to duration of Diabetes.
531 Diabetics with onset prior to
30 years of age.

Duration of Diabetes Mellitus at Death (yrs.)	No. of deaths	Coma %	Nephritis %	Heart %	Tuberculosis %	Pneumonia & Sepsis %	Miscellaneous %
0 - 4.9	166	56	4	5	8	12	13
5 - 14.9	223	28	13	8	12	15	22
15 - 20+	142	3	30	32	7	9	19
Total deaths	531	150	82	67	59	67	106

Another interesting feature is the striking increase in deaths from nephritis and arteriosclerotic heart disease from 5 to 32 percent of all deaths, which seems to occur after 15 years of diabetes mellitus.

The gradual change in the causes of death among diabetic individuals through the different epochs of therapeutic advance, is better illustrated in Table 13.

Table 13.

Causes of Death among Child Diabetics. Number and Percentage of Deaths from selected causes by eras of treatment. Experience of E.P. Joslin. 1898 to date.*

Cause of Death	Pre-Insulin Era		Insulin Era						Total duration	
	1898-6.8.1922		Banting Era 7.4.22-31.1.36		Hagedorn Era 1.1.37-31.12.43		Chas. H. Best Era 1.1.44 to date		1898 to date	
	Number	%	Number	%	Number	%	Number	%	Number	%
Diabetic coma (primary)	135	86.0	56	56.6	22	27.2	13	9.6	226	47.9
Cardio-Renal-Vascular (total)	1	0.6	5	5.1	14	17.3	76	56.3	96	20.3
Arteriosclerosis	-	-	2	2.0	14	17.3	76	56.3	92	19.5
Cardiac	-	-	-	-	3	3.7	21	15.6	24	5.1
Angina pectoris or coronary disease	-	-	-	-	2	2.5	14	10.4	16	3.4
Nephritis	-	-	2	2.0	10	12.3	50	37.0	62	13.1
Apoplexy	-	-	-	-	1	1.2	3	2.2	4	0.8
Gangrene	-	-	-	-	-	-	2	1.5	2	0.4
Other circulatory and rheumatic heart disease	1	0.6	3	3.0	-	-	-	-	4	0.8
Infections	10	6.4	23	23.2	20	24.7	10	7.4	63	13.3
Respiratory	7	4.5	10	10.1	5	6.2	5	3.7	27	5.7
Kidney	-	-	-	-	1	1.2	3	2.2	4	0.8
Others	3	1.9	13	13.1	14	17.3	2	1.5	32	6.8
Tuberculosis	-	-	8	8.1	8	9.9	16	11.9	32	6.8
Cancer	-	-	-	-	-	-	1	0.7	1	0.2
Accidents	1	0.6	2	2.0	5	6.2	6	4.4	14	3.0
Suicides	-	-	-	-	1	1.2	2	1.5	3	0.6
Other diseases and conditions	9	5.7	5	5.1	9	11.1	7	5.2	30	6.4
Unknown	1	0.6	-	-	2	2.5	4	3.0	7	1.5

* Deaths reported up to January 18th, 1950.

This Table illustrates clearly the changes that have occurred in the mortality picture of diabetic individuals who developed the disease in childhood. The incidence of deaths due to diabetic coma has dropped steadily from 86 percent in the pre-insulin era to 9.6 percent since 1944, while the frequency of cardio-renal vascular disease has risen from 0.6 percent to 56.3 percent during the same period. Of the cardio-vascular-renal group, the deaths from renal diseases have shown the maximum percent of increase during this period. In the period prior to 1937, only two cases on renal disease were recorded among deaths attributed to the cardio-vascular-renal group, whereas the figure rose to almost 37 percent by the year 1950. Similarly, angina pectoris or coronary disease did not appear as a cause of death until 1937, but since that timee has risen from 2.5 percent to 10.4 percent by 1950.

The Pattern of Causes of Deaths in Great Britain.

Large scale studies similar to those in the United States of America have not been conducted in Great Britain in the recent past. The data available at present deal with only small numbers spread over a few years so that accurate deductions can hardly be drawn from a study of such material. Andrews,(73) in his survey of diabetes carried out in West Cornwall, gives an analysis of the causes of death of 76 diabetics who had died in that area during a period of three years. (Vide Table 14).

Table 14.

Recorded Causes of Death in 76 Diabetic Cases

Cause of Death	No. of cases	%	Reg. General (Total Population)
Cerebrovascular accident	17	51.3	59
Coronary thrombosis	11		
Congestive failure	9		
Kidney disease	2		
Diabetic coma	7	9.2	
Respiratory infection	6	7.9	7
Cancer	6	7.9	17
Post operative deaths	4	5.3	
Senility	4	5.3	
Bleeding peptic ulcer	2	2.6	
Pulmonary T.B, suicide, appendix abscess, pulmonary embolism, acute pancreatitis, urinary infection, gangrene	8	10.5	

The figures in the third column are those derived from the returns of the Registrar-General for Cornwall for the year 1954. The data itself has not been analysed with regard to age at onset or duration of illness, so that it is difficult to draw any definite conclusions from the data presented. Further, the numbers dealt with are too small to be of any value in drawing any comparisons.

The only interesting feature observed is the low percentage of deaths from cardio-vascular-renal diseases, both when compared with that for the general population, and also for those of the Joslin Clinic. The deaths from diabetic coma on the other hand are considerably higher, although it would be difficult to comment on this as we are not aware of the age group of patients dying of this complication.

Denmark.

A follow-up study of a group of diabetic patients who could be regarded as a representative sample of the urban population of Denmark has been described by Lundback.(74) Among the group of patients followed up, which totalled 234, the number of patients dead were 59, and the authors were able to estimate the cause of death in 67 of the 69 dead patients. In 38 percent they found that the death was due to uncompensated heart disease; in 19 percent, to cerebral haemorrhage and in 14 percent, to chronic renal disease. A significant finding was the excessive incidence of pulmonary tuberculosis as a cause of death, which accounted for almost one-third of the deaths among patients who died before the age of sixty. None of the patients had died of diabetic coma.

In another study carried out in Denmark in 1953(75) on a group of 5608 deaths, consisting of 2380 males and 3228 females, information concerning the cause of death was available for 1539 cases (670 males and 869 females). The detailed analysis of the data is shown in Tables 15 and 16.

Table 15.

Distribution according to sex, age and cause of death of 1539 deaths among diabetic patients.

Cause of death	0 - 14yrs		15-44		45-64		65yrs + over		Unknown		Total			After correction		
	M	F	M	F	M	F	M	F	M	F	M	F	M+F	M	F	M+F
Diabetes	-	3	35	19	132	159	187	290	1	3	355	474	829	43	62	105
Renal disease	-	-	-	1	11	13	14	12	-	-	25	26	51	77	72	149
Cancer	-	-	2	1	18	27	42	58	-	1	62	87	149	62	87	149
Heart disease	-	1	3	-	38	45	68	80	-	-	109	126	235	235	321	556
Respiratory diseases	-	-	-	-	4	2	9	8	-	-	13	10	23	38	45	83
Arteriosclerosis	-	-	-	1	7	19	31	47	1	-	39	67	106	123	167	290
Tuberculosis	-	-	7	2	2	4	2	7	-	-	11	13	24	11	13	24
Other causes of death	-	-	6	-	23	29	27	37	-	-	56	66	122	81	102	183
TOTAL	-	4	53	24	235	298	380	539	2	4	670	869	1539	670	869	1539

Table 16.

Percentage distribution according to cause of death for each age group.

Cause of Death	0 - 14yrs		15-44		45-64		65yrs + over		Unknown		Total			After correction		
	M	F	M	F	M	F	M	F	M	F	M	F	M+F	M	F	M+F
Diabetes	-	75.0	66.0	79.2	56.2	53.4	49.2	53.8	50.0	75.0	53.0	54.5	53.9	6.4	7.1	6.8
Renal disease	-	-	-	4.2	4.7	4.4	3.7	2.2	-	-	3.7	3.0	3.3	11.5	8.3	9.7
Cancer	-	-	3.8	4.2	7.7	9.1	11.1	10.8	-	25.0	9.3	10.0	9.7	9.3	10.0	9.7
Heart disease	-	25.0	5.7	-	16.2	15.1	17.9	14.8	-	-	16.3	14.5	15.3	35.1	37.0	36.1
Respiratory disease	-	-	-	-	1.7	0.7	2.4	1.5	-	-	1.9	1.2	1.5	5.7	5.2	5.4
Arteriosclerosis	-	-	-	4.2	3.0	6.4	8.2	8.7	50.0	-	5.8	7.7	6.9	18.3	19.2	18.8
Tuberculosis	-	-	13.2	8.3	0.9	1.3	0.5	1.3	-	-	1.6	1.5	1.6	1.6	1.5	1.6
Other causes of death	-	-	11.3	-	9.8	9.7	7.1	6.9	-	-	8.4	7.6	7.9	12.1	11.7	11.9
TOTAL	-	100.0	100.0	100.1	100.2	100.1	100.1	100.0	100.0	100.0	100.0	100.0	100.1	100.0		

Sweden.

The causes of death among diabetics in Sweden has been studied by Hansson and Tillgren.(76) Their study was based on an analysis of data on 1872 diabetic patients from the Maria hospital and from the Söder hospital in Stockholm for the period of 1925 - 1944. Of this group, 248 had died and a detailed analysis of the causes of death amongst this group backed by post-mortem findings showed the percentage of cases attributed to the various causes were - diabetic coma 15.7 percent; cardio-vascular diseases 52.4 percent; infectious diseases 19.8 percent; malignant tumours 9.3 percent, and other causes 2.8 percent. (Vide Table 17).

Table 17. / -

Table 17.

Causes of Death in 248 patients.

Cause of Death		No. of cases	%
Diabetic coma		39	15.7
Cardio-vascular disease		130	52.4
cardio-arteriosclerosis	66		
Haemorrhage; embolism of brain	25		
Chronic myocarditis, cardiac disease	20		
Thrombosis, embolism	8		
Gangrene	3		
Nephrosclerosis, chronic nephritis	8		
Infectious diseases		49	19.8
Pulmonary tuberculosis	9		
Tuberculous meningitis	1		
Syphilis	2		
Pneumonia, acute bronchopneumonia	13		
Septicaemia, erysipelas, abscess	7		
Endocarditis	2		
Acute hepatitis, cirrhosis of liver	8		
Acute pancreatitis	2		
Acute peritonitis	3		
Cysto pyelitis	1		
Acute meningitis	1		
Malignant tumours		23	9.3
Cancer of oesophagus and stomach	4		
" " pancreas	6		
" " bile duct	2		
" " liver	1		
" " gall-bladder	1		
" " rectum	2		
" " prostate	1		
" " mammae	1		
" " uterus	1		
" " bronchi	2		
Melanosarcoma	1		
Hypernephroma	1		
Other causes		7	2.8
Thyrotoxicosis	1		
Anaemia (severe)	3		
Oesophageal varices	1		
Traumatic wound of oesophagus with perforation	1		
Senile marasmus	1		

The incidence of diabetic coma amongst women was found to be very much higher than that for men, viz. 94 as gainst 34 cases in men.

Pattern of Causes of Death in the Tropics.

The pattern of causes of death among diabetic patients is not the same throughout the tropics. An approximate idea of the prevailing situation may be assessed to some extent from a study of the material available for Jamaica. Tulloch[77] has described the cause of death of 98 diabetic patients who died at the University College Hospital of the West Indies, in Jamaica, between 1952 and 1961. (Vide Table 18).

Table 18. / -

Table 18.

Causes of Death of Diabetic Subjects, University College Hospital of the West Indies, Jamaica.

		Number of Cases
Diabetic Coma		16
Cerebro-vascular accidents		13
Infections		
Septicaemia	3	
Local infections	10	13
Gangrene		
Ischaemic	8	
Infective	2	10
Renal failure *		7
Myocardial infarction		5
Cancer		7
Cirrhosis of liver		6
Hypoglycaemic coma		6
Heart failure		5
Acute pancreatitis		2
? causes		2
Pulmonary tuberculosis		2
Other causes		3
Malignant hypertension		1

* One patient showed evidence of malignant nephrosclerosis at autopsy.

The most common causes of death among the group are diabetic coma, cerebro-vascular accidents, infections and gangrene. The characteristic difference noticed among this group is the proportionately larger percentage of deaths from coma, gangrene and infection, and infrequency of deaths from cardio-vascular-renal diseases in contradistinction to the situation prevalent in the United States of America and some of the Western European countries, where deaths from the latter group of causes account for almost 75 percent of all diabetic deaths.

The overall pattern of deaths among diabetics in other parts of the tropics is somewhat similar to that found in Jamaica, but accurate data are as yet not available for most tropical countries. A study of hospital mortality statistics show that diabetic coma still accounts for a considerable proportion of the deaths among diabetics in most tropical countries, with the notable exceptions of Fiji, Singapore, Hong-kong, Natal and Columbia, in which countries the picture is somewhat similar to what occurs in the economically better developed countries and show a high proportion of deaths occurring from cardio-vascular-renal causes, infections and a slightly smaller proportion from cancer.

EX BIBL. UNIV. EDINBURGENSIS

SELECTED CAUSES OF DEATH

(a) Cardio-Vascular-Renal Disease.

The prominent part played by cardiovascular-renal disease in deciding the ultimate prognosis in diabetes mellitus has been discussed earlier. According to the most recent figures available, they account for almost 75 percent of all deaths for each sex among diabetic patients. All workers are agreed on the increased frequency of atherosclerosis among diabetic subjects. The concensus of opinion of most workers is that diabetes hastens the development of arteriosclerosis and speeds its course.(78) The frequency with which it is associated with diabetes mellitus could be gauged by the statement made by Warren and Le Compte in the first edition of "Pathology of Diabetes Mellitus": "I have yet to see at autopsy a diabetic or to read the autopsy protocol of a diabetic, whose disease has lasted five years or more, free from arteriosclerosis, regardless of age."(79) They had to modify their statement subsequently because of the finding of a number of cases of patients with diabetes of more than 5 years standing without apparent evidence of arteriosclerosis.

The increased incidence of deaths from cardio-vascular causes is not limited to diabetes alone; the proportion of deaths attributed to this cause has been gradually increasing, hand in hand with the advancing average period of life-expectancy of the individual. However, the proportionate increase of deaths from this cause among diabetics is very much higher, as can be seen from the following data.

In 1956, the percentage of all deaths attributed to cardio-vascular diseases in the United States of America was 54 percent;(80)

whereas during the first nine months in the same year, the percentage of deaths from the same cause amongst 135 diabetic deaths was 83.7 percent.

Marks[81] stated in 1952 that diabetic persons were "notoriously" prone to have arteriosclerosis. While most patients with diabetes used to die from acidosis and coma before insulin was discovered, the available statistics showed that 82 percent of the deaths in diabetic patients were due to coronary, renal or other forms of arteriosclerosis.

In a study of 816 autopsies of diabetic patients carried out by Warren and Le Compte,[82] it was observed that 288 or 35 percent were due to arteriosclerosis and related conditions. Of this number, 124 cases were under 40 years of age, which further illustrates the importance of this condition as a cause of death, even at the younger age groups. Of 157 cases of diabetes of 15 years duration or over, 94 (60 percent) died from arteriosclerotic lesions. The figures given above were only a fraction of all cases showing arteriosclerotic changes in the body, as illustrated in Table 19. They refer only to cases where the cause of death could be attributed primarily to arteriosclerosis.

Table 19. /-

Table 19.

Incidence of Arteriosclerosis by decades.

Age at Death	Total cases	Total with Arterio-sclerosis	Deaths due to Arterio-sclerosis	Arterio-sclerosis absent
0 - 10 years	11	-	-	11
11 - 20 "	35	17	-	18
21 - 30 "	40	30	4	10
31 - 40 "	38	34	5	4
41 - 50 "	88	82	14	6
51 - 60 "	197	195	65	2
61 - 70 "	257	255	129	2
71 - 80 "	132	132	66	-
81 +	14	14	5	-
?	4	3		
TOTAL	816	762	288	54

Source: Pathology of Diabetes Mellitus. Warren & Le Compte, 3rd Edition, 1952.

The arteriosclerotic changes were most marked in the heart, accounting for almost 69.8 percent of the total deaths. This was followed by arteriosclerosis of the extremities associated with gangrene, which accounted for 27 deaths (9.4%). About the same incidence was observed for cerebro-vascular conditions, while vascular changes of the kidneys, which was not quite so uncommon, accounted for only 17 deaths (5.9 percent) of the total deaths

attributed to arteriosclerotic conditions.

The frequency with which atherosclerotic conditions are associated with diabetes has been commented on by several other workers. Von Constam et al,[83] quoted by Beaser[84] have stated that the incidence of atherosclerotic complications in diabetes is ten times that among the normal population. Only 20 percent were free from vascular complications after twenty years. They believed that this high incidence bore some relationship to inadequate control. The autopsy incidence of coronary occlusion has been found to be almost twice the normal rate among diabetics.[85]

The increasing incidence with which arteriosclerotic diseases are found even among young diabetics is commented on by Root.[86] Referring to the clinical and post mortem records at the New England Deaconess Hospital, he mentions that between 1938 and 1946, coronary atherosclerosis with partial or complete occlusion was present in seven out of twelve cases, among patients whose death occurred at ages between 25 and 32 years. Nephrosclerosis was present in six out of seven. He further observes that the characteristic feature observed in the post mortem study of these young diabetics, who had diabetes mellitus for over 10 years, was the fact that the arterial lesions observed were not of a single character. All three types of arterial degeneration, viz. intimal atheromatosis, Monkeberg's sclerosis, and arteriolar sclerosis, particularly of the vessels of the kidney, were evident. These lesions were essentially similar to those observed in diabetes of later life. The author concludes that the factor responsible for these lesions was most probably the long duration of diabetes mellitus. These views are supported by the studies of E. T. Bell(87)

who found an overall incidence of 27.2 percent of deaths from gangrene and coronary disease among a series of 606 autopsies of diabetic patients.

Matthews[88] (1954), in reviewing a series of 545 diabetic patients of all ages, found vascular degeneration in 53 percent, of whom 21 percent had retinopathy and 12 percent had albuminuria. The incidence of vascular disease was observed to increase with age, and, over the age of 50 years it was found to be higher in the diabetic than in the non-diabetic patients. The incidence was much higher in cases of severe diabetes requiring insulin and those of "poor" control, and also increased with the duration of the disease.

Various theories have been advanced as to the aetiology of atherosclerosis and to explain its increased incidence among diabetic patients. It has been pointed out earlier by Warren and Le Compte that fluctuations in the blood sugar concentration might aid in producing a swelling of the intimal ground substance through changes in osmotic pressure, which they believe is the starting point of this condition.

High levels of blood lipids, particularly cholesterol, have been suggested as an aetiological factor by many workers. However, "hyperlipaemia in the treated diabetic is neither so common nor so marked as has been previously supposed and it is doubtful that this is the sole cause of arteriosclerosis in this disease."[89] Although this may be true, most people believe that it is possible to minimise or postpone the onset of vascular disease by maintaining good control of glycosuria and hyperglycaemia.[90][91][92][93][94][95] These views are corroborated by various other workers. A.P. Skousby[96] in his

analysis of a series of 286 diabetic patients with an onset of the disease between 1924 and 1954, and who were treated either with the classical diet or with the "free" diet, found that sex and severity had no correlation with the incidence of late lesions; that the one important deciding factor in the development of complications was the degree of medical control maintained. This, however, is not the complete answer to the problem. In the series presented by Root, Pole and Freshner, as many as 24 percent of the patients who were on good control developed well marked retinopathy. Nor did "poor" control invariably give rise to vascular degeneration, as shown by the fact that 33 percent of the patients belonging to this category had no, or slight retinopathy.

The analysis made by Pathania and Sachar(106) on a group of 349 confirmed diabetics in Amristar, India, which showed a comparatively low incidence of cardiovascular complications in spite of the apparent lack of treatment, seems to confirm the view that poor control alone is not the only factor responsible for the complications.

This sort of disagreement in the findings has led to the idea that the development of vascular disease may indeed be a hereditary or constitutional matter, passed from one generation to another in much the same way that diabetes itself is genetically transmitted.

This problem of as to whether arteriosclerosis is a complication of diabetes or whether it is merely an integral manifestation of the basic disorder which causes diabetes, has been the subject of a great deal of discussion for some time past. Dry and Hines(97) have postulated an inherent weakness in the diabetic

constitution which affects both the insulin producing tissues and the vascular system with a common mechanism for the production of arteriosclerosis, retinopathy and neuropathy. Other workers too, have expressed the idea that this theory may be quite plausible,[98] although there is still a considerable amount of dissension among the workers as to its applicability.[99]

Other interesting theories have been advanced to explain the increasing incidence of complications among diabetics. One such theory is the idea put forward by Jan Muri[100] that "the development of vascular complications in diabetes resembles in many ways the increasing problem of coronary disease, which suggests the presence of harmful environmental influences." He suggests that frequent hypoglycaemic attacks, physical and mental stresses and infections stimulate the adrenal cortex and thus set off the events which lead to atherosclerotic changes. This theory is apparently supported by the fact that administration of ACTH in man gives rise to capillary microaneurysms in the retina and cortisone injections in alloxan-diabetic animals cause vascular changes similar to Kimmelstiel-Wilson syndrome. He believes that hyperglycaemia on the other hand, does not produce any harmful effects.

There is however, a strong body of opinion who are opposed to the views that have been expressed above.[101][102]. Mirsky[103] believed that so far as vascular disease is concerned it made little difference as to how the diabetic patient was treated. If he lived long enough, he was sure to develop one or the other forms of vascular disease. Dolger[104] too, has presented evidence to show that 100 percent of diabetic patients at some time in their lives will develop a

vascular disturbance even though it may be evanescent in some cases. The studies of Kramer and Perilstein[105] seem to agree with these views.

A great deal of research is still being carried out in an attempt to unravel the complex aetiology of atherosclerosis. Most of the research on atherosclerosis has, in recent years, been devoted entirely to the study of blood lipids and its possible role in the formation of atheromatous plaques on the arterial wall. In a brief review of the newer concepts of atherosclerosis, Le Compte[107] has drawn attention to two new lines of thought which are presently being investigated. The first of these, described by Duguid,[108] is the "thrombogenic theory" according to which mural thrombi may become incorporated into the lining of the artery in such a way that eventually a typical fibrous or fatty atheromatous plaque results. The second line of investigation is the one presented by Randerath and Diezel[109][110] - "These authors claim to have demonstrated fibrillar, highly polymerised mucopolysaccharides in greater abundance in the arterial walls of diabetics than in non-diabetics. The lesions have been so characteristic that they have dubbed them as "MPS plaques", and have postulated that "as a result of insulin deficiency protein-bound hexoses and hexamines of the blood accumulate in the intima of the artery."

(b) Diabetes and Pulmonary Tuberculosis.

The association between pulmonary tuberculosis and diabetes mellitus is not such a problem now as it was a few decades ago. Gould, W.R. and Lyall, A. (1947)[111] in reviewing tuberculosis as a complication

of diabetes, stated that at the end of the last century 50 percent of diabetics succumbed to pulmonary tuberculosis, and that despite the improvements brought about by the use of insulin and modern methods of therapy, the incidence of tuberculosis continued to remain high; in fact, in 1931 and 1934, it was three times as common in diabetics as in the general population. In recent years, the prognosis in those with the combined lesion has improved considerably due to the improved control of the diabetic state and the effective application of suitable chemotherapy. In the past, the disease was so common that every diabetic presenting himself for examination was invariably searched at the same time for evidence of pulmonary disease. The possibility of developing tuberculosis was increased by the lack of proper control of the diabetic state. It was particularly liable to follow diabetic coma. Joslin[112] has cited the evidence that between 1923 and 1929, pulmonary tuberculosis developed in 8 percent of 105 diabetic patients within three years of recovery from diabetic coma. It is the undernourished, in particular, who are liable to develop pulmonary tuberculosis; and diabetics in the pre-insulin era were naturally so, because they had to perforce remain on an inadequate diet in order to keep the diabetes under proper control. With the advent of insulin however, diabetics are now able to take a very much more nutritive diet which helps to maintain their nutritional state at a reasonably high level, and thus enables them to withstand infection.

(c) Diabetes Mellitus and Infection.

In a series of 818 fatal cases of diabetes studied by Warren and

Le Compte[113] at post mortem examinations, infection was found to be the cause of death in 213. These related only to deaths from acute infections and excluded conditions such as syphilis and tuberculosis. The improvement produced by the better control of the diabetic state and the wider use of chemotherapeutic agents and antibiotics is probably best shown by the fact that, up to 1938, (i.e. before the introduction of sulphonamides etc.), almost 38 percent of all diabetic deaths were attributed to infection, whereas since then, only about 6 percent of deaths have been due to this cause. Furthermore, it was observed that pneumonia was responsible for more deaths than any other localised infection. There were 38 deaths from bronchial pneumonia and 10 deaths from lobar penumonia.

The actual relationship between acute infections and diabetes mellitus has not yet been elucidated. However, all workers are agreed that diabetes is made more severe with the onset of infection. The effect is generally only temporary, except when the pancreas itself undergoes extensive damage, so that the patient's sugar tolerance, which would have undergone some alteration, quickly reverts to normal, once the acute phase of the infection is over.

A lowering of the tolerance for carbohydrate, either in the diabetic or non-diabetic could be due to one of four causes:[114] viz.

(1) lessened production of endogenous insulin;

(2) increased production of hormonal antagonists;

(3) destruction of insulin;

(4) interference with the storage and utilisation of glycogen.

Although none of the above hypotheses has been adequately proved, a great deal of work has been done to demonstrate the possibility of each of the above suppositions. Of particular interest is the statement made by Warren and Le Compte[113] that they have observed "toxic injury" to the islands of Langerhans in a number of instances both in diabetic and non-diabetic patients.

The type of infection which is most liable to effect the above changes varies; but pneumonia and pyogenic infections are believed to be more important in this respect than all other infections.

The factors possibly responsible for the increased susceptibility of the diabetic patient to infection have been considered by Marble, White and Fernald.[115] Among the more important factors are :-

(a) increased sugar content of the blood and tissues;

(b) decreased activity of blood elements associated with resistance to infection;

(c) inadequate functioning of fixed tissue cells;

(d) lowered capacity of tissues to react to antigenic stimuli;

(e) lowered state of general cellular nutrition.

(d) Gangrene.

This is considered to be one of the more serious complications of diabetes mellitus. In the series of 859 fatal cases studied by Warren and Le Compte, 144 cases were complicated by gangrene, and of these, 29 were accompanied by generalised sepsis, and 6 had developed gas gangrene. These data help to illustrate very clearly

the important role played by gangrene in laying open the whole body to septic invasion by virulent organisms.

Diabetic gangrene could be divided into two types,[116] viz.

(1) those cases in which infection is the primary factor;

(2) those in which occlusive vascular disease is the exciting cause.

The former is believed to be present mostly among the younger patients and is less common than senile diabetic gangrene. In these cases the arterial tree appears to be perfectly normal, and the gangrene is believed to be due to primary infection followed by secondary thrombosis of the digital vessels.

The second type generally occurs among elderly patients. The probable exciting factor in these cases is a gradual decrease in the vitality of the tissues and diminished resistance to infection secondary to degenerative changes occurring in the peripheral blood vessels. A significant feature observed in these cases is that the diabetes mellitus itself is usually mild or moderate in character.

The relative frequency with which atherosclerotic gangrene appears in diabetics in contrast to non-diabetics has been studied in considerable detail by E.T. Bell.[117] In an analysis of autopsy studies carried out on 50,184 non-diabetic and 1878 diabetic persons aged 40 years and above, during the forty-five year period from 1911 to 1955, he found 186 instances of atherosclerotic gangrene of one or both lower extremities in the non-diabetic, and 393 in the diabetic patients. This study demonstrated that atherosclerotic gangrene was fifty-three times more frequent in diabetic men and seventy-one times more frequent

in diabetic women over the age of sixty. Furthermore, two-thirds of the cases of gangrene in men less than 80 years of age and one-fourth of those in men more than 80 years were the result of diabetes, whereas 80 percent of cases of gangrene in women resulted from diabetes. He failed to observe any correlation between the development of gangrene and the severity of the diabetic state as indicated by the need for insulin. He also observed that while infection was an important factor in diabetic gangrene, it was not essentially so in the non-diabetic patient.

The average age at which gangrene developed was sixty-four years in Joslin's series of 750 cases of gangrene.(118) The youngest patient to develop gangrene was aged thirty-two years, and the oldest was eighty-nine years. The incidence of gangrene among the younger age groups was comparatively low. Only 12 patients were observed in the age group 20 - 29 years. The percentage distribution of cases according to the age at onset of gangrene is shown in Table 20.

Table 20. /-

Table 20.

Age at Onset of Gangrene in 1045 patients with Surgery.

Age at Onset	1898 - 1922		1923 - 1939		1.7.39 - 1.1.46		1.1.46-1.1.51		Total	
	No. of cases	Average age at onset	No. of cases	Average age at onset	No. of cases	Average age at onset	No. of cases	Average age at onset	No. of cases	Average age at onset
30-49 years	8	44	19	46	6	49	12	44	45	46
50-59 "	28	56	99	56	43	55	67	55	237	56
60-69 "	40	65	217	65	76	65	125	65	458	65
70-79 "	8	72	120	73	61	73	83	73	272	73
80 + "	0	0	6	84	19	83	8	82	33	83
TOTAL	84	61	461	64	205	64	295	64	1045	64

Source: Treatment of Diabetes Mellitus. E.P. Joslin et al. 10th Edition.

(e) Diabetic Coma.

Coma was at one time the commonest cause of death in diabetic patients, particularly among the younger age groups. It was an exceedingly rare event for a diabetic child to survive for more than two years, prior to the introduction of insulin therapy.(119) Sixty-three and eight-tenths percent of all patients dying from diabetes mellitus in the period up to 1914 died of diabetic coma. The figure gradually fell to 41.5 percent during the years 1914 to 1922, probably as a result of the improvements made in the management of the diabetic state by means of dietotherapy. Since the introduction of insulin, the situation has improved remarkably and has reached a new low level of only 1.5 percent among the patients under the care of

Joslin and his colleagues for the period between 1944 and 1957.

The factors that have probably contributed to the gradual decline of deaths from diabetic coma are the introduction of insulin therapy, the use of sulphonamides and other antibiotic drugs, and the wider use of special Diabetic Clinics, which, in particular, has helped in no small way in controlling both the diabetic patient and the disease. Perhaps of even greater importance in this respect is the contribution made by the general practitioner who is instrumental in making an early diagnosis of all cases of impending coma and carries out prompt and effective treatment.

The average age of the patients at the onset of coma varied between 27.9 and 31.1 years in Joslin's series of patients treated at the New England Deaconess Hospital from May 1923 to January 1st, 1957. Female diabetics were more prone to develop acidosis and coma as shown by the fact that among the 719 patients who did develop coma at one time or another, there were 472 females to 247 male diabetics. The sex incidence was however, more or less equal in the childhood group of diabetics studied by the author. The duration of diabetes prior to onset of coma was observed to vary from 3.2 years up to 9.3 years. (Vide Table 21).

Table 21. / -

Table 21.

Diabetic Acidosis and Coma.

Date	No. of cases	Age at Coma (yrs.)	Duration of Diabetes Mellitus (yrs.)	Fatal Cases	
				Number	%
1923 - 1931	179	30.9	3.2	27	15
1931 - 1940	284	29.1	4.6	28	10
1940 - 1946	188	27.9	6.3	6	3
1946 - 1951	153	31.1	9.3	5	3
1951 - 1957	165	29.0	8.5	8	4.8
1923 - 1957	969	29.2	6.6	74	7.6

Source: Adapted from "Treatment of Diabetes Mellitus." E.P. Joslin et al. 10th Edition.

(f) Diabetes Mellitus and Cancer.

It is generally believed that cancer is commoner among diabetic than among non-diabetic individuals. Jacobson,[120] who is a protagonist of this view, found at least one-third more cancer deaths than the expected number in his analysis of data consisting of death certificates and matched hospital case histories, for a selected sample of deaths among white persons in New York City.

Warren and Le Compte have reported an incidence of 10 percent of deaths from cancer in their series of 818 post mortems of diabetic patients. They however believe that this figure is unusually high because of the bias introduced by the fact that the New England

Deaconess Hospital (from where the cases were selected) is generally recognised as a centre for treatment of cancer as well as for diabetes.

Table 22, which has been adapted from a study of the causes of death of 18,055 diabetic patients, as reported by Joslin, illustrates clearly the progressive increase in the percentage of deaths from cancer among diabetics during the different eras of treatment.

Table 22.

Incidence of Cancer among Deceased Diabetics, 1898 - 1957. (Experience of Joslin Clinic).

Period	Deceased Diabetics	Cancer Deaths	Percent Cancer Deaths of all Deaths
1898 - 1914	326	5	1.5
1914 - 1922	836	32	3.8
1922 - 1936	4138	362	8.7
1937 - 1943	3623	326	9.0
1944 - 1949	4116	400	9.7
1950 - 1955	4376	452	10.3
1956 - 1957	640	72	11.3

The increase in the incidence of cancer among diabetic patients apparently commenced only after the introduction of insulin therapy in 1922. This could well be attributed to the increasing longevity of the diabetic, who now lives to reach the age zone in which cancer occurs most frequently in otherwise normal individuals.

POSSIBLE TRENDS IN THE FUTURE WITH REGARD TO CAUSES OF DEATH

From what has been mentioned earlier regarding the increased life span of the diabetic patient, one could now expect him to die of more or less the same causes as the non-diabetic individual. Deaths from acidosis and diabetic coma occur more and more infrequently with the advancement in knowledge regarding the metabolic abnormalities involved, and the possibility of treating all such cases without delay. Pease and Cooke[122] have stated that "the mortality from diabetic ketosis has fallen because diabetic pre-coma is treated more effectively", so that fewer cases progress to coma. They believe that the chief factors responsible for this remarkable improvement are :- The larger doses of soluble insulin given in the early stages of the illness; the more liberal use of intravenous fluids; a clearer understanding of the types of fluids which should be given; the realisation of the importance of gastric lavage, and the control of infection by the use of effective antibiotics.

In order to achieve any further improvement, they believe that greater stress should be placed on the possibility of educating the patient in the management of his diabetic state. This should, as it were, form the first line of defence against the onset of diabetic ketosis. Every diabetic patient should be aware of the premonitory signs and symptoms of ketosis and pre-coma, and should have a clear and precise idea as to what he should do in order to prevent them. In this connection the family doctor too plays an important part. It is he who is in close contact with the patient and therefore would be in a

position to know the likelihood of a particular patient developing ketosis. Early and effective treatment of all infections may help to reduce the incidence of coma.

A vast amount of research is being carried out in the field of antibiotics and other chemotherapeutic agents, and a large number of new discoveries are being made every day. It is possible that we may, in the course of time, be able to completely abolish deaths from infection among diabetic patients, with the help of such potent antibiotics.

As for pulmonary tuberculosis, the disease has been brought under control in most of the economically better-developed countries for a considerable number of years, although sporadic cases have occurred from time to time in most of these countries. Greater vigilance and effective chemotherapy will be required to stamp out the disease completely, as diabetics have shown a greater susceptibility to the tubercle baccillus.

The greatest problem that confronts the diabetic physician at present is the ever increasing number of patients who die of cardio-vascular-renal causes. Whatever measures that have yet been adopted in an attempt to reduce these have so far proved to be ineffective, because of inadequate knowledge regarding the aetiology and pathogenesis of the primary vascular disorder involved. However, a great deal of research is presently being carried out in this field, so that we may hope that with increasing knowledge of the pathogenesis of arteriosclerosis and the unravelling of the complex aetiology of diabetes, one may soon see a reduction in the extent of morbidity and mortality from these conditions among diabetic patients in the near future.

PART II

SURVIVAL AMONG DIABETICS

INTRODUCTION

The duration of life of the diabetic patient has been steadily increasing during the last half century. Prior to 1914, it was only 4.9 years, according to Joslin's experience. It was subsequently prolonged to 6.1 years, largely as a result of the improved methods of control of the disease by means of dieto therapy. No further improvement was observed until the advent of insulin in 1922; since then, the progress has been phenomenal. Quite a large proportion of diabetic patients are now able to achieve at least two thirds to three quarters of the average life expectancy.

The prognosis of diabetes depends on a variety of factors. First, it depends upon the general physical condition of the patient, apart from the existence of diabetes; secondly, upon his disposition, intelligence and upon his willingness to carry out treatment faithfully; thirdly, upon the nature of the disease itself as to whether it can be easily controlled; and finally, on the enthusiasm and zeal of the general practitioner upon whom the greater part of the responsibility is placed. The following are characteristics which indicate a favourable prognosis; the presence of obesity, a favourable heredity, and the history of mild and symptomless diabetes of several years duration. Early diagnosis and the institution of effective control without undue delay, help to a considerable extent, in prolonging the life of the diabetic.

The various factors which determine the survivorship of diabetic patients and the causes and effects of their increased life expectancy will be discussed in some detail in the following chapters.

FACTORS DETERMINING SURVIVAL AMONG DIABETICS

Some of the factors that influence the progress in diabetes mellitus have been enumerated. These, with certain other factors, which in general have some influence on the duration of life of the diabetic, will now be discussed in greater detail. Broadly speaking, the survival of the diabetic depends to a large extent on the type of diabetes, age at onset of illness, interval between onset and commencement of treatment, the degree of control of the diabetes, the extent to which the patient co-operates in the management of the illness, and finally, the presence or absence of any associated complications.

Type of Diabetes

It is generally accepted that the term 'Diabetes Mellitus' does not refer to a single disease entity, but covers a group of disorders differing in their aetiology and natural history. The one feature that is common to all these disorders is a persistant hyperglycaemia and an associated glycosuria.[123] In view of the lack of knowledge regarding the fundamental aetiology of diabetes, it has been a matter of considerable difficulty to formulate a comprehensive classification of the different types that are found among individual patients. Lawrence[124] has described two main types; viz. (i) An insulin-deficient type, and (ii) those who are not insulin deficient and whose condition is associated with a disturbance of fat storage. The first group comprises those patients, usually young and thin, who develop diabetes suddenly, and who, if they are deprived of insulin, quickly progress to ketosis and coma. They are sensitive to insulin and are entirely dependent on it for stabilisation.

The second type of diabetes has been divided again by Lawrence

into two subgroups, depending on the presence or absence of an excess of fat stores in the tissues of the body. The latter group, which is extremely rare, has been given the term - "Lipo-atrophic" and the former has been termed the "Lipoplethoric" type. He believes that the "Lipoplethoric" patient continues to increase his or her stores of fat, until a stage of saturation is reached, after which the deitary carbohydrate which normally would have entered the fat depots, tends to "spill over" into the blood stream. This group of patients are generally obese and relatively insensitive to insulin, and rarely if ever go into acidosis or coma. By simply reducing the weight of these individuals by restricting the intake of carbohydrates, one could not only rid them of their diabetic symptoms, but may even restore their glucose tolerance curves to normal.

Differentiation of diabetes into (1) Insulin-sensitive and (2) Insulin-resistant types, has been described in great detail by Himsworth.[125][126] He quotes the work done by Falta and his colleagues[127][128] who were the first to make this distinction into two groups. Himsworth states that on the whole, the insulin-sensitive diabetics tend to be younger and thin, and have normal blood pressure and normal arteries. He believes that the onset of diabetes mellitus among patients in this group is quite sudden and usually severe. On the other hand, the insulin-insensitive diabetics tend to be elderly and obese; the onset of the disease is often insidious and the disease is usually milder. These patients generally tend to have concomitant hypertension and arteriosclerosis and ketosis is extremely rare.

A similar classification of cases of diabetes into two groups on the basis of the insulin content of the pancreas has been suggested by Wrenshall and his co-workers.[129]

The division of cases into two groups, viz. Juvenile (insulin-sensitive), and maturity onset (insulin-insensitive) diabetes, is not complete, as various other types have been described in different parts of the world, particularly in the Tropics. Hugh-Jones(1955)[130] described the J - type in Jamaica, and a type known as "variant K" has been described by Shaper in Uganda.[131]

The distinguishing features of the J-type are, that the patients are usually young, and generally below forty years of age, thin, and require moderate amounts of insulin to keep them in good control, although they seldom or never go into ketosis and coma when insulin is withheld. The K-type generally occurs among Africans and Indians below the age of thirty-five years; the patients are usually thin and never develop ketosis and coma.

The different types of diabetes that have been described above, carry with them a somewhat different prognosis. It is generally agreed that the Juvenile type of diabetes mellitus is more severe in character and have a less favourable prognosis than the other types that have been described. Fatalities from the associated complications of ketosis and coma were a common occurrence in the past before the advent of insulin and the use of modern dietotherapy. On the other hand, the mild, insulin insensitive type, which occurs in the later decades of life, are subjected to the additional risks ushered in by atherosclerosis; indeed, their susceptibility to arteriosclerosis appears to be so great or ever greater

as that of patients with the more severe form of diabetes.

The concensus of opinion among most authors is that, as Goadsby[132] puts it, - " at whatever age it starts, diabetes found by chance on routine examination in the absence of the classical symptoms and of ketonuria, carries a better prognosis than if the patient starts with acute thirst, polyuria and loss of weight and strength."

Age at Onset

The current belief is that the survival rate is least affected the older the patient is, at the time he acquires diabetes. Variations may however occur. As we have described above, the type of diabetes mellitus is closely related to the age at onset of the disease. The younger the patient, the more likely he is to acquire the more severe type of disease with its characteristic features such as sensitivity to insulin; and liability to progress to acidosis and coma if insulin is withheld. The opposite holds true for the middle-aged or elderly diabetics. They generally acquire the milder type of the disease. Though there is no doubt that the concomitant presence of diabetes mellitus, accelerates the arteriosclerotic changes which are usually common at this age group, it does not however produce any significant effect on the overall survival rate of the middle-aged diabetic patient. The position seems to alter to some extent as the age of the individual advances. For example, the person who gets diabetes in extreme old-age, is more likely to suffer from the more severe type of the disease with its other concomitant features such as instability and increased liability to develop acidosis and coma. This

group too, is therefore bound to manifest a less favourable prognosis than the obese individual who develops diabetes in early middle life. These points are clearly illustrated in Table 23.

Table 23

Duration of Life Subsequent to onset of Diabetes among 18,055 deceased Diabetic Patients - (Experience of Joslin Clinic, 1897 - 1957).

Age groups at Onset.	1897 - 31. 5. 1914		1. 1. 30 - 31. 12. 1936		1. 1. 56 - 12. 11. 1957	
	Number of Cases.	Duration	No. of Cases	Duration	Number of Cases	Duration
All ages	326	4.9 †	2681	10.3 †	640	18.2 †
0 - 9 years	24	1.3	24	7.3	30	26.4
10 - 19 "	39	2.7	60	7.4	52	23.5
20 - 39 "	85	4.3	275	14.4	91	25.1
40 - 50 "	126	7.0	1444	11.6	304	18.7
60 and over	51	4.4	858	7.0	159	10.2
Unknown	1	-	20	-	4	-

† Based on cases with known duration.

Source: Adapted from "Treatment of Diabetes Mellitus". E.P. Joslin et al; 10th Edition. p.225.

Table 23 illustrates very clearly the sequence of changes that have taken place as regards prognosis of the diabetic patient during the last half century. It would be observed that prior to the application of insulin and other modern therapeutic aids in the management of diabetes, the prognosis of the condition was practically hopeless in both the young and old alike; the average duration of life of the young diabetic was then only 1.3 years from the onset of the disease, whereas the middle-aged individual with an onset between 40 and 59 years carried the best

prognosis, viz. 7 years. Considerable progress was made during the succeeding years as shown by the state of affairs in the middle 'thirties. By this time insulin was being used widely in all parts of the world and stricter control of diabetes was achieved by the combined use of insulin and dietotherapy. The age groups that appeared to have benefited most up to this time were those of the younger age-group; For example, those who had acquired diabetes between 0 - 19 years were now living on an average 7.3 years, viz. six times more than they used to in the pre-insulin era. Furthermore, the longest duration of diabetes was now being experienced by those individuals who had acquired the disease between 20 and 39 years, in contrast to what was observed in the pre-insulin era, when the longest duration of life was experienced by those who had acquired the disease between forty and fifty-nine years.

The position observed in the late 1950's when the beneficial effects of penicillin and other wide spectrum antibiotics had begun to be felt all over the world, was indeed remarkable. There was an all round improvement in the duration of the disease among diabetics of all age groups. The young diabetic now enjoyed an average duration of life of 26.4 years. This group indeed experienced the longest duration observed among all other diabetics. As a matter of fact, the life expectancy of the elderly diabetic was only a little less than the average life expectancy of a normal individual of his age.

There is, however, one very interesting feature, as shown in the data for 1956 - 1957. It shows quite a significant reduction in the duration of life for those individuals who had acquired the disease between

10 and 19 years. The implications involved are many and varied. Several hypotheses have been advanced to explain this situation, which indeed should not have arisen, in the usual course of events. Some of the views that have been so expressed will be discussed in the following section.

The increased life span of the juvenile diabetic has brought along with it the problem of progressive vascular disease, as a result of which, the presence of diabetic retinopathy and progressive blindness are not uncommon findings in a juvenile diabetic of twenty or twenty-five years' standing. These problems will be discussed in greater detail in a subsequent chapter.

Interval between the onset of Disease and Commencement of Treatment

The delay that commonly occurs between the first appearance of symptoms and the institution of proper treatment affects the prognosis in diabetes mellitus, just as it does in any other comparable disease. This is moreover, intimately tied up with what will shortly be described in a later section dealing with "Control of the Disease and Discipline". The extent to which diabetes mellitus remains undiagnosed in the community is quite considerable. Studies of Joslin[133] leads us to assume that at a rough estimate, there should be one diabetic person at large in the community for every person who has been diagnosed and is under supervision. These conclusions have been based on sound statistical data; e.g. the study of Wilkerson and Krall[134] showed that of the seventy cases of diabetes mellitus detected in their survey of 4,983 inhabitants of Oxford, Massachusetts, thirty people (43 percent) were previously undiagnosed. These findings have been corroborated by several other surveys carried out

subsequently in different parts of world.[135][136][137][138]

Most of these undiagnosed individuals were found to belong to the over 40 years age group; the majority of them were overweight, and hardly anyone required insulin for the management of the disease.

The apparent lack of symptoms and the mildness of disease, has led some workers[139] to advance the theory that diabetes is indeed inherent and begins at birth, and that before it is recognised clinically, it progresses through a stage, the magnitude of which is fully as great as that of the known diabetes which follows on recognition. In general, the more severe the disease, the earlier it will appear, and as a rule one could assume that the disease would have progressed through half its course, before it becomes clinically apparent.

So far as the long term complications of diabetes mellitus are concerned, most workers tend to believe that the duration of illness is the most important predisposing factor.[140][141][142][143] This is particularly true in the case of the juvenile diabetic. The probability of developing complications remains the same irrespective of whether the disease was clinically diagnosed or remained latent and symptomless.

Control of the Disease and Discipline

It has been mentioned earlier that arteriosclerosis and other cardio-vascular diseases account for over 70 per cent of all deaths among diabetics. Some authors[144][145] believe that although arteriosclerosis has no special characteristics in diabetic patients, it tends to occur with

greater frequency and severity, and generally at an earlier age among diabetics than among normal individuals. It has not been yet ascertained as to why these complications should occur prematurely among diabetics.[146][147] Some authors believe that there is often no relation between the duration and severity of diabetes, and the onset of complications, whereas others have produced evidence in favour of the hypothesis that complications do occur only in the absence of adequate control. Cited in favour of the former theory is the study of Beaser[148] who found that among one hundred and ninety diabetics, only sixty-five presented with the classical symptoms of diabetes, and that in as many as thirty-six, the so-called complications of diabetes, were in fact, the presenting complaints.

Dry and Hines[149] have postulated the theory that there is an inherent weakness in the diabetic constitution which affects both the pancreas and the vascular system; the primary defect is believed to be involvement of the nutrient vessels to these structures. They assert that this is the probable explanation of the fact that the diabetic individual may present, either with the classical signs and symptoms or only with those of its complications. Ellenberg[150] too, has failed to find any correlation between either the severity or the control of diabetes with the onset of the associated complications. These findings have been confirmed by the studies of Dolger[151] which demonstrated a lack of correlation between the methods of treatment and the onset of complications among his group of patients. Dolger holds the view that the duration of diabetes is perhaps the most important factor, which bears any relationship to the development of such complications. This hypothesis has received considerable support from many works, some of

whom have ventured so far as to state that - "it makes little difference how the diabetic is treated; if he lives long enough he will develop one or other form of vascular disease."[152]

Joslin and his colleagues[153] however have asserted that adequate control of the disease achieved by the combined efforts of the supervising medical practitioner, and the close co-operation of the patient, is absolutely essential in order to postpone the onset of complications. This view is supported by the studies of Wilson, Root and Marble[154] which showed that thirty seven patients out of a group of two hundred and forty seven young diabetes, who had maintained good control, failed to develop diabetic neuropathy after a considerably long period, whereas almost sixty two patients in the whole group developed such complications.

Dunlop[155] too obtained more or less the same results for his group of one hundred and sixty seven who had attended the Dietetic Department of the Royal Infirmary, Edinburgh, for periods varying from fifteen to thirty one years. Of this number, twenty-seven (16 percent) were found to be entirely free from complications. Such patients were four to five times commoner among the good control than among the "poor" control group. Cardio-vascular complications as evidenced by hypertension, coronary disease, defective pulsation in the dorsalis pedis and posterior tibial arteries, calcification of arteries or gangrene were present in sixty-three percent of cases, and neuropathy was present in nineteen percent. There was a striking correlation between the degree of control of diabetes and the presence of such complications in all these instances.

Mahallawy and Sabour[156] found the same relationship between the

onset of diabetic nephropathy and the degree of control of the diabetic state. The severity of the diabetic state did not appear to have any influence on the development of nephropathy, whereas the duration of diabetes did seem to have a definite relationship to the onset of this complication. A similar observation was made by Skouby[157] in 1956.

The reason for the failure to maintain satisfactory control of the diabetic state are multiple. Tunbridge[158] has suggested that this failure is due to three main groups of causes, viz. psychological, social and educational. He tends to believe that the psychological factor is of special importance in the case of the juvenile diabetic. The discovery of diabetes in the young patient is believed to produce in him a psychological trauma which is deeper and far more disturbing than the anxiety caused by other chronic diseases.[159] The physiological changes that occur secondary to emotional conflicts have been recorded by Heinkle and Wolf(1952).[160] They have shown that the fall in blood sugar and serum inorganic phosphate, and the rise in ketonaemia which occur as a result of stressful situations, is more marked in the diabetic individual than in the normal person.

They also observed characteristic changes in the glucose-tolerance curves corresponding to changes in the emotional state of the individual under examination. Situations leading to reactions of dejection, resentment and loneliness were associated with higher and prolonged glucose-tolerance curves, whereas situations fraught with anxiety and tension led to less-elevated curves; these were occasionally associated with a relative hypoglycaemia in the third to fourth hour. The tendency to overeating has been cited by many, as a characteristic response to stress.

These stresses are perhaps, in a way, reinforced by the insistence on the part of the physician regarding strict control of the patient's diet. The natural reaction of the child diabetic to these various situations is one of resentment and aggression. It is not therefore strange that he tends to deviate from the normal path set out before him. The result as expected, would be disastrous. This may perhaps be one explanation for the high mortality rate and the decreased life expectancy of the individual who acquires diabetes in the age group 10 - 19 years.

The need for greater recognition of the importance of psychological adjustment in the management of the young diabetic patient has been recently stressed by Jackson,[161] who states that steps should always be taken very early in the course of the disease, to educate both the patient and his family regarding the nature and the management of the disease; by so doing it would be possible to inculcate the correct mode of living in the diabetic subject before he had acquired any undesirable habits of living which would be prejudicial to maintaining good control.

Tunbridge seems to believe that one of the major reasons for the failure to follow a strict dietetic regime, is due to the lack of foresight shown by the responsible authorities in the past, when presenting diets without taking into consideration the social background of the individual patient. The average cost of the typical diabetic diet as assessed by Tunbridge[162] in 1948, was found to be approximately twenty-three shillings per week. This had of course varied from year to year, and by 1953, it had reached thirty-four shillings per week. The present high cost of the prescribed diabetic diet, may probably be one of the reasons why

many diabetics, particularly the elderly, are unable to stick to a strict dietetic regime. The apparent lack of knowledge regarding the nature of the disease and the correct method of treatment is perhaps the most important cause of failure to maintain satisfactory control of diabetes. The difficulties that one has to overcome in carrying out such an educational programme are multiple. In the first place, it should be clear from the very start that sufficient time is indeed essential to impart this knowledge to the people concerned. Tunbridge is of the opinion that even a man of high intelligence and good educational background requires a minimum of three months for proper educational and emotional adjustment. This would need to be considerably longer for the average diabetic patient.

Secondly, there is always the difficulty of getting a patient to change his or her habits; this is particularly so in the case of the elderly diabetics, who are generally loth to change their habits. Whereas it is a comparatively easy task to inculcate new ideas into a young individual, it would be considerably more difficult to achieve any success with an elderly lady set in her ways in dietetic as well as other matters, for a period of years.

Complications

Complications both special to diabetes mellitus, and those to which diabetics are more prone than non-diabetics, tend to worsen the prognosis. Those complications that are special to diabetes are acidosis and coma, diabetic nephropathy, neuropathy and retinopathy. Of these, acidosis and coma, which are by far the most severe and carry the greatest risk to the

patient, are now more or less under control. Prior to the introduction of insulin in 1922, almost ninety-five percent of the patients who presented with any degree of ketosis, died within a year of developing the disease. As far as severe peripheral neuropathy is concerned, the incidence is now considerably lower, and generally tends to arise in the older patient who has the milder form of the disease. Diabetic nephropathy (Kimmelstiel-Wilson Syndrome) is rare. Other minor ailments such as pruritus vulvae, which is especially common amongst obese patients, and various foot complications such as callosities, ulcers, gangrene, etc.,are fairly common, but in no way affect the long term prognosis of the condition.

Of the complications that are not special to diabetic patients, the most important are hypertension, coronary artery disease, cerebral and peripheral vascular disease. The diabetics appear to have a higher incidence of the above conditions than non-diabetic individuals of the corresponding age groups. With regard to hypertension, some authors (163) tend to believe that the prognosis need not necessarily be too gloomy and that it may exist without deleterious effect for years, even in patients who are found to have it in their early fifties. The author asserts that if such an obese, hypertensive glycosuric patient can be persuaded to lose weight by adhering to a strict diet, the blood-pressure would automatically revert to normal and that the glycosuria itself would disappear.

The prognosis in diabetic patients who present themselves with proteinuria is generally held to be very poor. In the normal course of events, diabetic nephrosis with its gross albuminuria and oedema, evenutally progresses to hypertensive renal disease. Remissions and exacerbations are

are believed to go on for about a year before their final demise. However, some authors[164] believe that this apparent severity of diabetic nephropathy has been over-stressed, because most of the work done in connection with survival among diabetics with proteinuria, have been based on post-mortem studies, which as a rule, tend to under-estimate the period of survival. The authors state that studies conducted on younger patients, on the other hand, have shown an improved prognosis with an average survival in fatal cases of up to eleven years from the onset of proteinuria.

REVIEW OF THE LITERATURE. EXPERIENCES IN OTHER COUNTRIES

Most of the work done up to now in connection with the survival of diabetics has been based purely on a study of mortality data. However, efforts have been made in recent times to make some form of allowance for the surviving diabetics at the time of making such estimations. It is therefore to be expected that there would be a considerable amount of under or over-estimation in all such calculations, based solely on mortality data.

An approximate idea of the situation prevailing in the middle and late 19th century, can be obtained from an appraisal of the works of Naunyn.(165) Naunyn has summarised the existing knowledge regarding diabetes mellitus in some considerable detail and with great clarity, although obviously, very little information was available regarding the pathologic physiology of the syndrome of diabetes mellitus in his time.

In general, he believed that the duration of the disease was determined chiefly by :-

(1) the type of diabetes mellitus

(2) the age at onset

(3) the social position of the diabetic individual.

He suggested that there were two main types of diabetes, viz:-

(i) "Organic" diabetes, which was presumably associated with or secondary to diseases of the liver, arteriosclerosis, etc.

(ii) "Pure" diabetes.

Apparently the patient suffering from "pure" diabetes had the worse prognosis, as shown in Table 24.

Table 24

Duration of Diabetes Mellitus according to Type of Disease (up to the time the patient left the author's observation).

Duration of Disease	of 66 cases of "Pure" Diabetes.	of 71 cases of "Organic" Diabetes.
Up to 1 Year	22	20
1 - 2 "	19	15
2 - 3 "	16	7
3 - 4 "	6	7
4 - 5 "	-	5
5 - 6 "	1	5
6 - 8 "	2	4
8 - 10 "	-	1
Over 10 "	-	7

Source: Der Diabetes Mellitus. B. Naunyn, wien 1906, Alfred Holder.

The author has however cited instances where diabetics survived for very much longer periods, ranging from twenty five to thirty one years, where the individuals concerned had died actually of gangrene setting in in old age. He also refers to the study of Griesinger-Pfeiffer who gave the duration of diabetes mellitus for one hundred and fifty three cases who had been followed up from the onset of disease up to death. These data are presented in Table 25.

Table 25/

Table 25

Duration of Diabetes Mellitus	Number of Cases	Duration of Diabetes Mellitus	Number of Cases
Up to ¼ Year	2	Up to 5 yrs.	4
" " ½ "	15	" " 6 "	3
" " 1 "	30	6 - 7 "	4
" " 2 "	47	7 - 8 "	1
" " 3 "	31	Up to 10 "	2
" " 4 "	12	" " 14 "	2
¼ year- 4 years	137	5 - 14 years	16

It will be observed that the average duration of life for this group of diabetics was little less than 2½ years. Naunyn's figures for his own one hundred and forty one cases observed from the time of diagnosis up to the time they left his supervision were not much better. These data are shown in Table 26.

Table 26/

Table 26

Duration of Illness	Number of Cases
Up to 1 year	42
1 - 2 years	35
2 - 3 "	23
3 - 4 "	14
4 - 5 "	5
5 - 6 "	7
6 - 8 "	6
8 - 10 "	1
10 - 12 "	6
Up to 16 "	1
Over 31 "	1
Total	141

Naunyn believed that the duration of the disease depended to a considerable extent on the age at which the patient acquired diabetes mellitus. When the disease occurred in children under the age of fourteen years, the duration was generally short, and the disease was more acute, and usually ran a rapid course. In a group of forty-six diabetic children under the age of fourteen years, almost two-thirds had a duration of less than six months, as could be seen in Table 27.

Table 27/

Table 27

Duration of Life of 46 Diabetic Children under the age of Fourteen Years.

Duration of Life	Number of Deaths
Up to ¼ year	16
" " ½ "	14
" " 1 "	5
" " 2 "	6
" " 3 "	4
" " 4 "	1

The rapidly fatal type of disease was believed to be rare in old age; the author had seen only four cases between the ages of fifty-seven and sixty who belonged to this category. He also believed that the social position of the individual diabetic patient determined to a considerable extent, the future prognosis of the disease. In his experience, the patients from the poorer social strata who availed themselves of the treatment meted out in clinics and public hospitals, survived a very much shorter period than those who were seen in private practice.

The subsequent improvement in the life expectancy of the diabetic patient, that has occurred through the last fifty years or so, is best illustrated by a perusal of the data accumulated by the Joslin Clinic.(166)

Table 28 shows the duration of life subsequent to onset of diabetes among 18,055 deceased diabetic patients who had been treated at the Joslin Clinic between 1897 and 1957.

Table 28

Duration of Life Subsequent to Onset of Diabetes, among 18,055 Deceased Diabetic Patients in each of the Important Eras of Treatment.

Age Group at Onset	Naunyn Era	Allen Era	Banting Era		Hagedorn Era		Charles H. Best Era	
	1897 - 5/	6/1/14 - 8/6/22.	8/7/22- 31/12/29	1/1/30- 31/12/36	1/1/37 - 31/12/43	1/1/44 - 31/12/49	1/1/50 - 31/12/55	1/1/56 - 12/11/57
	Duration	Duration	Duration	Duration	Duration	Duration	Duration	Duration
All ages	4.9†	6.1†	8.0†	10.3†	12.1†	13.7†	15.6†	18.2†
0 - 9 yrs.	1.3	2.9	2.8	7.3	10.3	18.5	20.6	26.4
10 - 19 yrs.	2.7	2.7	3.4	7.4	11.4	16.2	20.1	23.5
20 - 39 yrs.	4.3	4.9	8.9	14.4	16.9	18.8	21.8	25.1
40 - 59 yrs.	7.0	8.0	9.5	11.6	13.4	14.9	16.2	18.7
60 and over	4.4	6.4	5.5	7.0	8.6	9.2	10.0	10.2

† Based on cases in the known duration.

Source: Adapted from "Treatment of Diabetes Mellitus" E.P. Joslin,et al., 10th edition, 1959.

It will be seen that the prognosis of diabetes mellitus was extremely poor in the period prior to 1914, when there was no effective method of correcting the biochemical defect involved in the disease. In the succeeding decade however, the new idea of dietetic restriction as a means of controlling the glycosuria in diabetes began to establish itself, particularly in the United States. This measure resulted in a considerable improvement in the prognosis of the condition. The most remarkable improvement occurred only after the introduction of insulin. The very high mortality rates which were a common feature at the time among the younger age groups were reduced dramatically, enabling the diabetic patient to survive up to about two-thirds of the normal life expectancy for their age. The situation has undergone further improvement with the

passage of time; new long-acting insulins have been discovered and several oral antiglycosuric agents have come into regular use. Perhaps the most important factor from the diabetic patients' point of view was the advent of the Sulphonamides, Penicillin and the newer broad-spectrum antibiotics which have helped the diabetic patient to overcome severe infections which invariably ended up fatally in the pre-antibiotic era. Prior to the introduction of antibiotics, it was a rare event for a diabetic to recover from an attack of pneumonia; even the most minor infections had the tendency to upset the metabolic equilibrium of the diabetic patient and led to the production of acidosis and coma. These risks have now been considerably reduced by the combined use of insulin and the appropriate antibiotic substances.

Other authors[167][168] have recorded studies of groups of individuals surviving for even longer periods. In spite of the fact that the life expectancy of the diabetic patient has increased considerably in recent years, few diabetics if any, have survived their full life expectancy up to now. In the study reported by Millard and Root[169] only eight out of some one hundred and ten diabetic patients attained a normal life-expectancy; the average duration of life after the onset of diabetes, for this group of patients, was only 44 percent of the normal expectancy. On the other hand, Root and Barclay[167] have observed that among their group of patients, of a total of thirty male patients with fatal outcome, only five patients lived less than their life-expectancy; one attained full life-expectancy, and the remaining twenty-four exceeded life expectancy by periods varying from eleven to eighty percent above

normal expectancy. The position with regard to the female diabetics too, was satisfactory, as shown by the fact that out of fifteen female patients ending up fatally, there were only three patients who failed to attain their normal life-expectancy, and the remainder exceeded the normal expectancy, by periods varying from two to five percent over the normal.

A comparison of the expectations of life for diabetic patients at specific age groups, with those for the corresponding groups in the general population as to how the diabetic patients stands with regard to longevity, as compared with the normal individual. Such a table has been prepared by the Metropolital Life Insurance Company of the United States of America from an analysis of the data for the Joslin Clinic during the period 1947 - 1951.(170) (vide Table 29).

Table 29/

Table 29

Duration of Life and Mortality Rate at Selected ages among Diabetics and White Persons in the General Population. (Experience in 1947 - 57 for Diabetic Patients of Joslin's Clinic first Observed in 1930 - 51 and for the General Population of United States in 1949 - 51).

Attained Age	Expectation of Life (yrs)		Mortality Rate/1000	
	Diabetics *	General Population	Diabetics *	General Population
10	44.3	61.5	2.6	0.5
15	40.0	56.7	4.6	0.8
20	36.1	51.9	8.0	1.2
25	32.8	47.2	13.1	1.3
30	30.1	42.5	15.2	1.5
35	27.2	37.9	12.6	2.0
40	23.7	33.3	12.2	3.2
45	20.2	28.9	16.1	5.1
50	16.9	24.7	21.6	7.9
55	13.8	20.8	32.2	12.2
60	11.3	17.2	49.8	18.7
65	9.2	13.9	64.9	27.4
70	7.2	10.9	86.3	41.9

* Excludes deaths within one week of first observation or hospital discharge.

Note: Analysis of Joslin Clinic Experience by Metropolital Life Insurance Company.

It will be observed that on the whole, the longevity of diabetics continues to be well below that for non-diabetics, especially at the younger age groups. This of course only confirms our expectations, as it is not an easy matter to maintain perfect control over the disease, with the methods of treatment available at present; we should not, therefore, expect the diabetic patient to survive his full life expectancy, until such time as we can ensure absolute control over his diabetic state.

Numerous other studies concerning the duration of life of diabetics, have been carried out at various periods, in the United States of America. Of these, the investigation made by Blumberg and Zisserman is of particular interest, and this has compared the average duration of life for two groups of diabetic patients separated by an interval of approximately ten years. The relevant data are summarised in Table 30.

Table 30

Duration of Diabetes

DURATION (YEARS)	1930 - 1938				1939 - 1950			
	Males	Females	M+F	%	Males	Females	M+F	%
Not known on admission	12	22	34	21.9	15	13	28	11.3
Less than 1 Year	9	10	19	12.3	2	6	8	3.3
1 - 5 Years	13	21	34	21.9	16	33	49	19.8
6 - 10 "	7	24	31	20.0	14	46	60	24.3
11 - 15 "	5	7	12	7.8	9	17	26	10.5
Over 15 "	2	9	11	7.1	11	30	41	16.6
Inadequate History	4	10	14	9.0	13	22	35	14.2
TOTALS			155	100.0			247	100.0

The average duration of life of the diabetic was only 4.5 years for males and 6.7 years for the females in the first group; these increased to 7.3 years and 9.4 years for the males and females respectively in the 1939 to 1950 group.

Another analysis of some considerable interest, is the statistical study made by Henry J. John[172] on six thousand cases of diabetes mellitus. Table 31 gives the duration of diabetes according to the age at which diabetes mellitus developed for the fatal cases.

Table 31

Duration of Diabetes according to the Age Group when Diabetes Developed.

Diabetes Developed Decade	< 1 Yr.	1 - 5 yrs.	6-10 Yrs.	11-15 Yrs.	16-20 Yrs.	21-25 Yrs.	26-30 Yrs.	36-40 Yrs
0 - 9 Years	1	40	35	11	2	1	-	-
10 - 19 "	2	51	52	17	1	-	-	-
20 - 29 "	3	5	3	1	2	2	1	2
30 - 39 "	3	4	3	8	7	2	1	-
40 - 49 "	18	12	19	19	12	9	1	-
50 - 59 "	12	23	37	26	13	4	1	-
60 - 69 "	11	28	27	13	8	3	-	-
70 - 79 "	9	11	6	3	-	-	-	-
80 - 89 "	1	-	-	-	-	-	-	-

It will be evident from this table that the individuals who appear to have the most favourable prognosis are those who acquire the disease between the third and sixth decades.

Such detailed information regarding the life expectancy of diabetic patients as described above are not available for other countries.

In the survey carried out in Cornwall by C.T. Andrews[173] the causes of death and the age at death of a group of one hundred and twenty nine patients were recorded. These data are shown in Table 32.

Table 32

Age at Death of 129 Patients

	0-39	40-49	50-59	60-69	70-79	Over 80
Men	2	2	8	11	18	9
Women	2	1	16	32	26	2
Total	4	3	24	43	44	11

The average age at death of the fifty men was 68.9 years and that of the seventy-nine women was 66.1 years. For both sexes it was 67.1 years. No data was available as regards the duration of diabetic mellitus.

Eckerstrom[174] has studied the cause of death among diabetics more than sixty-five years of age, who had been hospitalised in the Geriatric Clinic of Gothenburg, Sweden from 1943 to 1953. He observed that the average duration of life for the patients was between seventy-five and eighty years (vide Table 33).

Table 33/

Table 33

Duration (Yrs.)	Female	Male
Less than 5 years	47	25
5 - 10 "	16	10
10 - 15 "	18	15
15 - 20 "	5	3
More than 20 "	1	1

This study does not by any means reveal the true position regarding the duration of life of diabetic patients in Sweden, as nearly eighty percent of the patients were more than seventy years of age at the time of diagnosis. In the remaining patients, diabetes was recognised between the ages of fifty and sixty years or even earlier.

The duration of life of the diabetics living in the Tropics is relatively short when compared with those living in other regions. However, adequate and reliable data are scarce, and are available for only a few places, e.g. among ninety-eight deaths recorded at the University College Hospital of the West Indies, in Jamaica, during the $8\frac{1}{2}$ year period from September 1952 to March 1961, the average duration of diabetes was found to be under ten years in sixty-nine cases, while the longest duration was forty-three years.(175) (Vide Table 34). Experiences in certain other parts of the tropics is believed to resemble those noted in Jamaica.

Table 34/

Table 34

Duration of Diabetes of Patients Dying in the University College Hospital of the West Indies, Jamaica.

Duration in Years	Male	Female	Total
Under 1	8	11	19
1 - 5	13	11	24
5 - 10	15	11	26
10 - 15	5	2	7
15 - 20	1	3	4
20 - 25	1	3	4
25 - 29	1	0	1
30 +	1	1	2
Unknown	5	6	11
Total	50	48	98

Source: Tulloch, J.A. Diabetes Mellitus in the Tropics - 1962.

CAUSES AND EFFECTS OF INCREASED SURVIVAL

A number of factors have contributed to this increase in the longevity of the diabetic patient. Among the most important ones are:

(1) Increase in knowledge regarding the pathogenosis of the disease and associated complications, and the ability to control them by means of suitable dietotherapy and other measures;

(2) Introduction of insulin and other anti-glycosuric agents;

(3) Widespread use of special diabetic clinics and other treatment centres;

(4) Earlier diagnosis and treatment of diabetes and its complications.

Prior to the discovery of insulin, the only methods of treatment available for the control of the disease were by means of dietotherapy and regulation of exercise. The credit of introducing an effective means of treatment in diabetes should go to Apollinaire Bouchardat (1806 - 1886).[176] Until he came on the scene diabetes had been considered a fatal and deadly disease. Bouchardat always believed that "barring serious complications, diabetics could live as long as most people".[177] It was Bouchardat who first observed that glycosuria had its origin in the sugar of the blood, which in turn came chiefly from the carbohydrate in the diet. He was the first to utilise exercise to control glycosuria. He even had some notion as to the important part played by the pancreas in the aetiology of diabetes, and insisted that all his patients carried out the strict regime of restricted diet and adequate exercise.

Among the other older physicians, Naunyn too, was a great advocate

of the increased exercise and restricted diet regime treatment of diabetes. Naunyn was the first to advocate reduction of weight and elimination of obesity, as a prophylactic measure against the development of diabetes.

The idea of restricting the diet, as a means of control of the metabolic disorder in diabetes mellitus, was developed further by Allen. The beneficial effects accrued from this form of treatment is best illustrated in Table 28.

There has always been a close correlation between the dietetic habits of people and the incidence of diabetes mellitus. It would be observed that in general, the mortality rates from diabetes are higher in the highly industrialised and prosperous countries in the Western Hamisphere, than among the economically under-developed countries in the East. The incidence of diabetes has been found to be highest where the general economic level and medical services were of the highest standard. The observation made by Himsworth[178] that diabetes is most prevalent in those countries where high fat diets are consumed, is of considerable interest. It is a well known fact that foods with a high fat content are dearer than the easily available starchy foods, which form the staple diet in most of the under-developed countries, which in general have a low incidence of diabetes mellitus.

Mills[179] has observed that in countries like China and Japan, the incidence of diabetes is comparatively low, and that the disease itself is of a milder nature. It is also believed to be infrequent and mild in India, except among the richer classes.[180] De Soyza[181] has observed that, in Ceylon, although the incidence of diabetes mellitus is

somewhat higher than in other countries in South-East Asia, the disease itself is milder in character; acidosis and coma are comparatively rare; peripheral vascular disease, hypertensive heart disease and obesity are uncommon, and hypercholesterolemia is virtually absent. He attributes this to the high carbohydrate and low fat diet commonly consumed in Ceylon (vide Table 35).

Table 35/

Table 35

Diets of the Sinhalese (Caloric Analysis).

	Age Group	No. of Subject	Mean Age	S.D.	Daily Calories		Carbohydrates		Fats		Percentage Calories	
					Mean	S.D.	Mean	S.D.	Mean	S.D.	CHO	Fats
Males												
Diabetics	15-45 Years	6	39 ± 3.2	8.4	3152 ± 434	870	2359 ± 215	527	509 ± 64	157	74.6	16.2
Non Diabetics		7	37 ± 2.4	6.1	2341 ± 341	1024	1712 ± 193	351	337 ± 33	87	73.1	14.4
Diabetics	46-75 Years	18	55 ± 1.0	4.5	3174 ± 116	492	2346 ± 118	500	426 ± 29.5	118	73.9	13.4
Non Diabetics		20	60 ± 1.8	8.2	2862 ± 117	587	2171 ± 111	496	372 ± 22.4	100	75.9	13.0
Females												
Diabetics	15-45 Years	14	35 ± 2.1	8	3678 ± 191	714	2925 ± 107	429	459 ± 22	82	79.5	12.5
Non Diabetics		16	26 ± 1	4	3726 ± 141	662	2049 ± 115	460	378 ± 19	74	75.2	13.9
Diabetics	46-75 Years	14	54 ± 2	7.7	3082 ± 112		2518 ± 132	494	488 ± 22	82	78.7	15.8
Non Diabetics		16	58 ± 1	4.3	2795 ± 82		2049 ± 114	456	432 ± 22	88	73.3	15.5
Total Diabetics					3272		2537		471		77.5	14.4
Non Diabetics					2681		1995		379		74.4	14.1

Source "An Investigation into the Aetiological Factors of Diabetes". V.P. de Soyza, 1946. Government Publications, Ceylon.

The low incidence of diabetes in Thailand[182] too, has been attributed to the national diet based on rice, which they share in common with the other countries in this region. In this diet, fat accounts for only ten percent and proteins for nine percent of the nutrients. However, observations made in Iceland by Albertsson do not appear to support this view. The incidence of diabetes mellitus in Iceland was less than 1 per thousand, and the annual diabetic death rate varied between 1.9 and 4.0 per 100,000. The average Icelandic diet contains about forty-four percent of carbohydrate, forty-five to fifty-eight percent of proteins (almost entirely of high biological value proteins such as milk, meat and fish); the balance, ten to twelve percent is made up of fat. The feature in common between Thailand and Iceland is the relative absence of obesity; this, according to Albertsson's opinion, is a more important factor in the aetiology of diabetes mellitus than the actual dietary composition.

This subject has been studied in considerable detail by Himsworth.[178] By correlating the dietary habits throughout the world with the available mortality tables, he demonstrated that there was a definite curve of relationship between the two; the group consuming the higher carbohydrate and low fat diets had the lowest incidence of diabetes mellitus while the incidence was greatest in those who consumed a relatively high fat, low carbohydrate diet.

Carbohydrates have been observed to have a considerable effect on the glucose tolerance curve by several workers. Pick[183] has reviewed the work of Greenwald, Gross and Samet[184] who observed a distinct lowering of the glucose tolerance by experimentally feeding carbohydrate free diets;

this effect appeared to be greater when the fat content of the diet was increased.

These views are supported by the findings of Kempner[185][186] who found that patients suffering from diabetes mellitus tolerated a rice diet very well; in a significant number of patients, the blood sugar level and the insulin requirements were lowered, and they were observed to develop complications such as hypercholesterolemia, renal and vascular diseases less frequently than those on a normal diet. In fact, in the second series of patients studied by him, specific diabetic retinopathy and even retinitis proliferous was found to be improved in twenty-five percent of the cases.

As mentioned earlier, some workers[187] are of the opinion that the underlying factors responsible for these complications are frequent hypoglycaemic attacks, physical and mental stresses and infections, which in turn stimulate the adrenal cortex. This hypothesis is further supported by the experimental work in which administration of A.C.T.H. in man, gives rise to capillary microaneurysms in the retina, and cortisone injections in alloxan diabetic animals, cause vascular changes similar to Kimmelstiel - Wilson Syndrome. Hyperglycaemic attacks on the other hand, do not appear to have any deleterious effect.

Other observers[188] have however shown that insulin reactions per se, do not appear to increase the liability to develop retinopathy and nephropathy.

The beneficial effect produced by the introduction of rationing

during the two world wars is well authenticated. Himsworth[189] considers that rationing of foods which was introduced in Great Britain in 1940 was the chief factor responsible for the reduction of diabetic death rates in this country. He believed that the most important single factor underlying this was the reduction in the ration of fat and a consequent reduction of the total caloric value of the diet. Other workers, however do not appear to agree with this view.

For example, Graham[190] believes that rationing probably had the effect of preventing the onset of the disease among the elderly, due to the low fat, low protein diet tending to keep these individuals within their normal weight limits. However, those who actually developed the disease were very unlikely to die within the first eight years due to better medical care and supervision, and the effective use of insulin and the newer antibiotics.

The Effect of Insulin on Survival among Diabetics

There is no doubt at all that insulin is the most important factor that contributed towards the prolongation of the life of the diabetic patient. The effect of insulin on the death rates from diabetes mellitus has been reviewed in considerable detail in Part I.

Widespread use of Special Diabetic Clinics

Increased interest has been shown in all countries towards providing greater facilities for the diagnosis and treatment of diabetes mellitus, special clinics and diagnostic centres have been introduced. This has been most pronounced in the United States of America. Not only has there

been a greater provision for treatment centres, there is also evidence to show that a considerable proportion of all diabetic patients avail themselves of the facilities that have been provided for them in such centres. In the survey carried out by Andrews[191] it was shown that 77.4 percent of all diabetic patients surveyed attended either a diabetic or a general medical clinic. The benefits obtained from such a procedure are enormous. Closer supervision of the diabetic patient leads to better control of the basic metabolic disorder involved, and earlier diagnosis of complications enables one to prevent their further deterioration, which may ultimately lead to permanent physical disability or even death.

Earlier diagnosis and Treatment of Diabetes Mellitus and its Complications

It has been mentioned earlier that the so-called complications of diabetes mellitus, particularly the cardio-vascular renal diseases, bear a close relationship to the duration of the disease. It therefore follows, that the earlier the condition is diagnosed and brought under control, the less chance there will be for the development of complications. This goal is being increasingly achieved in most of the economically advanced countries where considerable efforts have been made in the recent past in combating the harmful effects of the disease. The importance of early diagnosis of pre-coma and the timely administration of adequate doses of insulin before the dispatch of such cases to hospitals is widely known among the medical profession as well as the general public. The prominent part this has played in reducing the number of deaths from acidosis and coma has been repeatedly stressed by Joslin and other workers.[192]

Effects of Increase in Longevity

(a) Problems of Employment.

With the increase in survival rate of the diabetic, the problem of finding them suitable employment will sooner or later begin to manifest itself. Diabetic persons are entitled to register as disabled persons (193) although few people are believed to avail themselves of this priviledge. It is generally felt that most diabetic patients wish to keep to themselves all knowledge of the disease and resent being considered different from other people. The avenues of employment open to the diabetic are to some extent limited; for example, whereas the diabetic has comparable ease in finding temporary employment in Government service, he meets with considerable hardhsip when he attempts to find a place on the permanent staff of any Government Department. This situation has arisen for the simple reason that all Government posts are superannuated and the diabetic patient, with his "shorter-than-average" life span, is naturally rejected in such situations.

Work which involves great public responsibility, such as that of engine driver, driver of a public transport vehicle, or pilot of commercial planes, etc; are generally regarded as unsuitable for diabetic individuals, these have been allowed in a few instances under special circumstances. Also, certain types of employment, e.g. those involving extremes of physical exertion or long and variable hours of work, etc., create special problems for the diabetic because of the difficulty of maintaining satisfactory control of the disease throughout the week.

Several studies have been made regarding the suitability of diabetic patients for different types of work and to see whether the diabetic has increased susceptibility to illness which might result in temporary or permanent disability. In one study which was carried out in Holland[194] on a group of four hundred and sixty four male diabetic employees of three large companies, the following observations were made :-

(1) There was no significant difference in sick-absence between the diabetic employees and the control groups;

(2) There was a considerable number of the four hundred and sixty-four employees engaged in heavy work and also at other than normal day time working hours;

(3) In the investigation of working capacity, it was found that diabetics who perform non-heavy work during normal daytime working hours, in which risks resulting from a reduced level of consciousness are not encountered, constituted no specific occupational health problem.

In another survey carried out on four hundred and eight juvenile diabetics[195] aged between eighteen years and thirty-four years at the time of the survey, revealed the following very interesting features, viz:-

(1) Diabetes had not apparently prevented them from achieving an educational level which compared favourably with the general population;

(2) Vocational placements ranged over a wide area from unskilled to the skilled and the professional;

(3) It was easier for the adult-onset diabetic to find employment than the juvenile onset diabetic.

The suitability of the diabetics who are under normal control and who are free from complications, for ordinary employment, has been recognized by the Committee on Employment of the American Diabetes Association.[196] This view has been confirmed by several other workers.[197][198]

However, in spite of these favourable reports, there is still a reluctance on the part of a large number of employers to employ diabetics. This was well illustrated by the investigation carried out by the Committee on Employment of the American Diabetes Association[199] which showed that almost twenty five percent of the one hundred and twenty seven companies which participated in the enquiry, did not have diabetic patients in their employ.

As Joslin states[200] "it is apparent that the employment of diabetics in the future will largely depend upon the behaviour of the diabetics themselves".

With increasing knowledge regarding the improved outlook of the diabetic and better understanding about his near-normal working capacity, one could look hopefully towards the day when every well-controlled diabetic would be gainfully employed in some suitable occupation.

Likelihood of an Increase in Disabled Persons in the Community.

With the discovery of insulin and its application to the treatment of diabetes, it has made it possible for us to keep the diabetic alive through such serious complications as acidosis, coma and infectionswhich

were invariably fatal in the pre-insulin era, so that he now lives long enough to develop the long-term complications such as retinopathy and neuropathy. S ufficient evidence has been enumerated above to prove that these complications were dependant on two factors, viz :-

(1) The duration of the disease,

(2) the degree of control.

As stated earlier, some authors are convinced that almost 100 percent of diabetic patients, at sometime or another, do develop a vascular disturbance even though it may be evanescent in some cases. In the majority of cases however, they either leave a permanent physical disability or end fatally.

The most disabling and disturbing complications are those associated with neuropathy and retinopathy. Diabetes has always been one of the more frequent causes of blindness. It is believed to account for 5 percent of the total, who are registered as blind in England, and for 13 percent among people over fifty years of age.(201) It is believed that diabetic retinopathy affects females more often than males, and its highest incidence is in individuals over the age of fifty. Retinopathy usually occurs ten to twenty years after the onset of diabetes, and as many as seventy-five percent of all diabetics show evidence of retinal changes after twenty-five years, irrespective of the severity or the control of the disease.(202)

Furthermore, it was established in 1959 that there were approximately 500,000 diabetics in Great Britain,(203) and with the increasing longevity of the diabetic, a good proportion of them are bound to be elderly;

of these elderly diabetics, the majority are likely to be women; some of these will be in the "elderly and infirm" group, while the others would belong to the "chronic sick" category. The distinctionsbetween the two categories are clearly marked out on paper as far as administration is concerned. Difficulties have however occurred when these had to be actually carried out in practice. The Elderly and Infirm group are referred to in Part III of the National Assistance Act as :-

"Persons who by reason of age, infirmity or any other circumstances are in need of care and attention which is not otherwise available to them" The responsibility for the welfare of such persons rests with the Local Authority concerned.

The "Chronic sick" on the other hand are cared for under the "National Health Service Act", and are the primary responsibility of the Regional Boards. As Rogers has pointed out there is at present very little provision for the care and welfare of this ever increasing group of individuals in the community.

It is however encouraging to note that preliminary steps in this direction have been taken by the British Diabetic Association, who established their first Home for Elderly Diabetics in the United Kingdom at Fredrick Banting Home, Kingston Hill, Surrey, in 1953; and followed it up with a second home, the "Charles Best House", in Cheshire in 1956.

Conclusion:

The attention paid by the general public to diabetes mellitus falls into insignificance when one compares it with other comparable diseases such as tuberculosis, poliomyelitis and cancer. This in a way is to be expected as the latter group of diseases produce their effects in a more profound and dramatic manner, whereas diabetes mellitus is more insidious and produces its sinister effects over a prolonged period and in a less clear cut manner. A fact that is not universally known about diabetes is that it is rather more amenable to simple and definite methods of control than any of the other diseases already mentioned. It is however, encouraging to realize that there is at present an increasing recognition of the importance of this condition among emmbers of the medical profession, as well as among the general public all over the world.

A great deal of work has been done in an attempt to elucidate the aetiology and pathogenesis of diabetes mellitus, but our knowledge regarding these aspects is as yet anything but complete. The only facts accepted with any degree of conviction at the present day, are that, as far as all the presently known and reasonably well understood metabolic anomalies of diabetes mellitus are concerned, they are the direct or indirect consequence of a relative or absolute lack of insulin in the body. The fundamental change that is responsible for this deficiency of insulin is a matter that has not yet been unravelled.

The focus of attention has recently been directed towards the possible role of insulin antagonists in the aetiology of the disease.(204) Evidence in this connection was given by Drs. J. Vallance - Owen, and M.D. Lilley of Newcastle at a meeting of the Medical and Scientific Section

of the British Diabetic Association in London. Basing their research on the concept that plasma albumin of normal subjects is known to inhibit the action of insulin on the rat diaphragm, these workers demonstrated the albumin of pre-diabetes and obese diabetics contained an even greater concentration of the antagonistic substance in the serum. In contrast to this, they were unable to demonstrate the presence of this antagonist in the albumin of patients with diabetes due to haemochromatosis. Another very interesting and revolutionary idea expressed during the proceedings of this meeting was the suggestion that obesity, which is generally accepted as an important aetiological factor in the causation of diabetes, is in reality the result of the disease and not its cause as is generally accepted.(205) A similar view had been expressed earlier by O.P. Allen(206) who believed that diabetes mellitus was a state of depression of the organism to metabolise glucose, associated with a loss of weight which closely followed a period of overstimulation ranging from one to twenty-five years (with an average of twelve years), during which there were symptoms of hypoglycaemia and a gain in weight.

As stated earlier, diabetes is still acclaimed as a serious menace to health; and is believed to be the commonest cause of blindness in young people. Other progressive degenerative diseases arising from premature arteriosclerosis affecting the heart, kidneys, and the lower extremities, all contribute to the increasing disability due to the disease.

The need for concerted action against diabetes is being recognized in most countries, particularly in America. The U.S. public Health Service Diabetes Demonstration Unit has planned to provide a group of

professional people specially trained in the preventive aspects of the disease, as part of the Local Health Department.(207)

These groups were to be composed of a Public Health Physician, a Public Health Nurse, a health educator, a nutritionist, laboratory technicians, and clerical staff. Their function was to assist the Local Health Officer in inaugurating and developing a diabetes control programme, and to co-operate in the other voluntary agencies interested in diabetes. The basis of such a preventive programme developed in consultation with the local medical society, would be, education of the public with regard to prevention of the predisposing causes, recognition of the early symptoms, and the realization of the importance of seeking early diagnosis, and adequate treatment, in order to avoid complications and thereby prolong life and increase both mental and physical well-being.

It would be hardly necessary to comment any further on the efficacy or the advantages of such a preventive programme. It only remains to be stated that similar concerted and prolonged efforts are indeed necessary in all parts of the world if we ever hope to reduce the amount of suffering and disability caused by this disease.

PART III

THE RESULTS OF THE DIABETES MELLITUS FOLLOW-UP

INTRODUCTION

The inadvisability of using mortality data alone to establish valid conclusions regarding the causation of death and survival among diabetic patients has been described in some detail in Parts I and II. These objections could be overcome to a considerable extent by the successful follow-up of a group of confirmed diabetics over a long period, and analysing the data relating to them. Part III of this work concerns chiefly the analysis of the data accumulated for such a group of diabetic individuals who have been followed through a period ranging from 12 to 22 years.

The main objectives in carrying out this study were:-

(1) To assess as accurately as possible the duration of diabetes in individuals dying with the disease;

(2) To study the various factors which might influence the duration of diabetes mellitus and also to assess the extent to which they exert any such effect;

(3) To investigate the extent to which diabetes mellitus is mentioned in the death certificates of patients dying with the disease; and to determine the factors which were responsible or associated with such under-diagnoses;

(4) To assess the underlying causes of death in diabetic patients;

(5) The construction of a Life-Table for diabetics.

It should be mentioned that this study is based primarily on date accumulated for two groups of patients who had been first examined a decade or two previously, and therefore, in common with all

other retrospective studies, this analysis too, is open to such objections as have been discussed elsewhere.

Description of Material and Methods

The present study is based on the follow-up of two cohorts of patients - separated by an interval of 10 years, who had come for diagnosis and treatment of glycosuria to the Dietetic Department at the Royal Infirmary, Edinburgh. The Diabetic Clinic, which is run in association with the Dietetic Department was first established in 1924, and is one of the largest in the country. The extent to which it is utilised is clearly revealed by the survey which was carried out in 1959+ as a preliminary to our epidemiological research, in which a circular letter was sent to all general practitioners asking them how they dealt with their cases of diabetes mellitus. 82% of them said that they sent any case of whatever nature to the Dietetic Department of the Royal Infirmary, Edinburgh. The remainder sent some of their cases to the hospitals of the area, mainly to the Western General Hospital, Bruntsfield Hospital and the Sick Children's Hospital. Four out of 400 General Practitioners dealt with some cases of diabetes mellitus by themselves within their own practice. An equally small proportion sent some of their patients to private consulting practitioners. As far as one could judge at the time, a survey made using the cases attending the Royal Infirmary, Edinburgh, would be deficient in some of the young patients attending the sick-children's Hospital and also in representatives of the wealthier sections of the community attending private consultants.

+Personal communication by Dr. D. Cameron.

However, these deficiencies must have been considerably less in 1949/50 and still less in 1939/40 because at these times there was no Diabetic Clinic attached to the Sick Children's Hospital, and the other hospitals in Edinburgh seemed to attract very few patients. There is no way of judging what the size of the private consultants' practice was at the time. It seems therefore, that we are probably left with a small deficiency of the wealthier sections of the community in this study; but there is no reason to suppose that this would unduly vitiate the results obtained from it.

The cases considered for this study were obtained from the registers for first visits, maintained by the Dietetic Department, for the years 1939 - 1940 and 1949 - 1950. The case notes of the two groups of patients were studied carefully, and only those who were actually confirmed as diabetic after a consideration of the history of illness and a urine examination were included in the study. In a reasonable number of instances these preliminary investigations had

been followed up by a further blood examination whenever this had been indicated. Patients who were resident in the County of Fife were excluded from the Survey.

The material thus consists of these two groups of patients, a considerable proportion of whom are still attending the Diabetic Clinic for regular supervision. The major portion, however, has defaulted for one reason or another; of these , a few were known to have died and their dates of death were known. There were others whose addresses were known but who had not visited the clinic for some considerable period. The greatest difficulty was encountered with those who had defaulted for some years and whose present whereabouts were not known with any certainty. This problem was partly solved by having recourse to the Voter's Rolls. With a knowledge of the last date on which the patient was seen at the clinic, it was not very difficult to trace with some degree of accuracy the approximate year of death in those instances where the patient was dead. Where the patients had changed their addresses, the Voters' Rolls of the neighbouring Polling Districts were perused, and this proved to be a successful method of obtaining further information regarding the patients in a number of instances.

The next step in the study was directed towards an attempt at obtaining the death certificates of the patients who were dead. In doing this, it was considered that the best results would be achieved by assuming that the majority of those patients who had defaulted from the clinic for no valid reason for a period of six months or longer, and whose names were not included in the current Voters' Rolls, were dead. All such names were checked up at the General Register Office personally

by the writer, commencing from the year the patient was last seen in the clinic up to the time of his or her death.

Finally the weekly returns of deaths of the Medical Officer of Health, Edinburgh, were perused in an attempt to bring the records up to date, as the Index Registers of Death Certificates were only available up to 1959.

An attempt at tracing the patients who were presumed to be yet alive, and the completion of a questionnaire (see Appendix), formed the second part of the Survey. The patients whose addresses were known and who lived either in or in the outskirts of Edinburgh posed no great problem. The remainder were first written to at the address obtained from the Voters' Rolls, or else at the last known addresses which were available according to the clinic records, informing them of the nature of the Survey, and requesting their co-operation. On the receipt of a reply, another letter was despatched to each patient informing him of our desire to interview him regarding his illness. These patients were subsequently visited in the following week.

The results obtained in this Survey were quite encouraging, as shown in Table 36.

Table 36. / -

Table 36.

The present Status of the 959 Diabetic Patients included in the Diabetes Mellitus Follow-up.

Status	Males		Females		Total	
	1939/1940	1949/1950	1939/1940	1949/1950	No.	%
Dead	117	105	215	195	632	65.90
Alive and Visited	16	67	12	154	249	25.86
Alive - not visited	4	12	4	15	35	3.75
No trace	8	13	4	18	43	4.49
TOTAL	145	197	235	382	959	100.0

The total number of patients included in the follow-up was 959; of these, 380 patients (145 males and 235 females), belonged to the 1939/1940 group. Of these 380 patients, 332 (87.4 percent) were dead; 36 patients were alive and their addresses were known, but only 27 patients were interviewed, as the remaining 9 patients had left the district and were residing at a considerable distance away from Edinburgh. Only 12 patients (3.1 percent) were lost sight of completely in this group.

Of the 579 patients in the 1949/1950 group, 105 males and 195 females were dead (51.8 percent). Of the remainder, 221 patients (38.16 percent) were alive and visited; 27 were alive but were not visited as they lived too far away. No trace was found of the remaining 31 patients (5.3 percent).

When the two groups are considered together, 632 (65.9 percent) of the total of 959 patients were dead; 248 (25.86 percent) patients were visited and the questionnaire filled up; 36 (3.75 percent) patients were known to be alive but were not visited because of the excessive distance involved. Only 43 patients out of the whole group remained unaccounted for.

Before proceeding to the detailed analysis of the main data, a short account will be given of the 35 patients who were not visited and of the 43 patients of whom no trace was obtained.

Of the 35 patients who were alive but not visited, there were 6 patients who, on enquiry at the last known address, were found to be presently undergoing treatment in various hospitals and other institutions in Edinburgh.

In a second group of 5 patients, one was an elderly male diabetic who, on enquiry at the last known address, was reported to be in good health, but was presently residing with another relative away from the city. The second patient, a forty-two year old male diabetic from Clackmannanshire, was found to have changed his residence and was living in a different part of the town. A further attempt was made to trace him but no contact could be made due to the fact that he was employed at some distance away and was away from home for the greater part of the day. However, this patient too, was reported to be in good health. The three remaining patients were elderly female diabetics, one from Bathgate, and the other two from Kelso and Coldstream respectively. They were all reported to be in fairly good health but presently residing with relatives at some considerable distance away. Four other

elderly female diabetics were found to be away from home when they were visited after the usual preliminary letter. Four patients were presently living in Glasgow and were being cared for by the Victoria Infirmary, Glasgow, and were apparently maintaining reasonably good health, while a male diabetic from Lanarkshire, who had gone to reside in Ayrshire was reported to be presently retired from work due to ill-health and poor eyesight, although he was only 48 years old.

A middle-aged male diabetic from Berwickshire was found to be away on holiday, while two others, a young male and a female diabetic, had left Scotland altogether and were presently residing in England. Two patients were from Shetland and both were presumably enjoying normal health. Replies were also received from two patients who had at one time resided in Melrose and Pitlochry respectively, but who had since left these towns, to the effect that they were enjoying reasonably good health. The remaining group of eight patients which included seven males and one female, were not interviewed because of their refusal to co-operate in the survey.

Of the 42 patients who could not be traced, 9 were known to have left for England several years ago, while 5 others had migrated to Australia, New Zealand, Holland, India and Canada respectively. No information was available regarding the present whereabouts of the remaining 29 patients.

Sex Distribution.

Sex seems to play an increasingly important part in the

incidence and mortality in diabetes mellitus. At the present time, both the incidence and the mortality from diabetes mellitus appear to be higher among females than among males in practically all the countries of the world for which data are available, with the possible exception of Japan and Ceylon. (Vide Table 37). The possible explanations for these variations will be gone into later.

Table 37.

Diabetic Mortality in Various Countries: Male Death Rates expressed as a proportion of Female Death Rates.

Country	Year	Ratio (Male/Female)
England and Wales	1959	0.28
United States	1954	0.62
Sweden	1953	0.55
Norway	1953	0.68
Belgium	1953	0.44
Netherlands	1954	0.45
Denmark	1953	0.76
France	1954	0.51
Italy	1953	0.65
Spain	1953	0.58
Japan	1953	0.90
Ceylon	1954	1.95
Australia	1953	0.49
New Zealand	1953	0.53

Tables 38 and 39 show the mortality rates from diabetes mellitus by age and sex for the United States in 1957 and for England and Wales for 1959 respectively.

Table 38.

Death Rates per 100,000 from Diabetes Mellitus by age and sex - United States, 1957.

Age	Both Sexes	Male	Female
All ages. Crude	16.0	12.6	19.2
* Adjusted	13.5	11.3	15.4
Under 1 year	0.3	0.2	0.5
1 - 4 years	0.3	0.3	0.3
5 - 14 "	0.4	0.3	0.5
15 - 24 "	1.1	1.0	1.3
24 - 34 "	2.6	3.0	2.3
35 - 44 "	4.6	5.0	4.1
45 - 54 "	11.1	10.3	11.8
55 - 64 "	38.0	29.5	46.1
65 - 74 "	97.8	76.0	117.2
75 - 84 "	151.2	129.8	168.0
85 +	157.9	140.5	170.5

*Based on the age distribution of the total population of the United States, 1940.

Source: National Office of Vital Statistics (Vital Statistics of U.S. 1957, Vol. 1).

Table 39.

Death Rates/Million from Diabetes Mellitus by age and sex for England and Wales, 1959.

Age	Male	Female
All ages	25	89
Under 1 year (Per 1000 live births)*	0.00	0.01
1 - 4 years	1	2
5 - 14 "	1	4
15 - 24 "	4	3
25 - 44 "	13	5
45 - 54 "	28	24
55 - 64 "	74	122
65 - 74 "	253	371
75 +	564	686

* Rate calculated as number of deaths per 1000 live births.

Source: Registrar-General's Statistical Review. England and Wales, 1959.(207)

It will be observed that females have higher rates at all ages except in the 25 - 44 years age group, during which period the male rates are slightly in excess of the female rates. A somewhat similar trend is found in the rates for the two series in England and Wales. (1959).

This tendency has been noted already by different authors[208][209] who also observed that there was very little difference in the sex-incidence in the younger age groups, but that the preponderance of women began to be evident only after the age of 45. From that age onwards, they observed that women tend to outnumber men by at least three to two.

A similar effect is observed in morbidity surveys too,[210] when patients have been classified according to their ages at the time of the investigation. Table 40 gives the prevalence rate of known diabetics per thousand population, and the ratio of females to males for the United States as estimated in a sample survey.

Table 40.

Prevalence of known cases of Diabetes per 1000 population and ratio of Females to Males as reported in interviews: United States, July 1957 - June 1959.

Age Group	Prevalence/1000 Population		Ratio of Females to Males
	Female	Male	
All ages	10.0	8.2	1.25
0 - 24 years	-	-	-
25 - 44 "	3.9	4.9	0.79
45 - 54 "	13.7	11.2	1.22
55 - 64 "	31.5	25.2	1.25
65 - 74 "	50.3	34.4	1.46
75 +	38.8	31.5	1.23

Females are seen to outnumber males in every age group, and this is most marked between the ages of 65 and 74 years. The rate per thousand persons appears to drop for both sexes after 74 years; this change is more obvious in the females than in the case of the males. It is suggested that this particular feature may be due to the fact that patients in resident institutions such as old peoples' homes etc., have been missed out in this survey.

Analysis of the data accumulated for our present study too, shows a somewhat similar trend in the sex distribution among diabetic patients. Table 41 gives the sex distribution of the two groups of patients included in our present study as compared with those cited by C.T. Andrews, and Munro, Eaton and Glen for Cornwall and Glasgow respectively.

Table 41. /-

Table 41.

Sex Distribution of Diabetic Patients

	Males		Females	
	Number	Percent	Number	Percent
General Practitioner Survey*	234	39.5	359	60.5
Old clinic cases *	173	39.3	267	60.7
Truro clinic *	178	36.9	304	63.1
England, 1947 (Special ration certificates)		38.0		62.0
Victoria Infirmary, Glasgow†	402	30.7	907	69.3
Present survey				
1939 - 1940 group	145	38.15	235	61.85
1949 - 1950 group	197	34.0	382	66.0

* Cited by C.T. Andrews. Brit. M.J. 1, 427, 23 Feb. 1957.

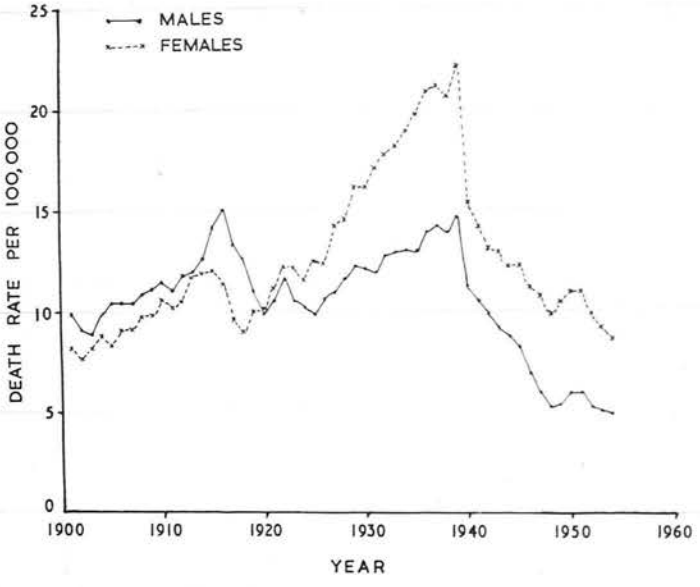
† Cited by Munro, H.N. Eaton, J.C. & Glen, A. Jour. Clin. Endocrinol. 9:1, 48 - 76, Jan. 1949.

It is evident from the above data that there is a considerable difference in the sex distribution of diabetic patients in England as compared with Scotland. There is apparently a greater predominence of female patients among diabetics in Scotland in general, as compared with those of England and Wales; also the change-over to a higher female incidence of diabetes mellitus is seen to occur somewhat later in the patients observed in our present study than that experienced in

FIG. 3.

THE TREND IN DEATH RATE FROM DIABETES MELLITUS ENGLAND AND WALES 1900–1954

SOURCE: W.H.O. EPIDEMIOLOGICAL AND VITAL STATISTICS REPORT VOL. 8 1955



most other countries, as will be described in a later section.

The progressive change that has taken place in the sex ratio in diabetic mortality figures has been noted in many countries of the world.(211) Using the population of England and Wales (1901) as the basis of standardisation, Stocks reported that the ratio of male to female deaths from diabetes had fallen from 2.05 in the 1861 to 1870 period, to 0.83 in the 1940 to 1941 period; similar changes have been observed in most other countries in Europe, America and Australia.(212)

A number of factors have been considered to be instrumental in bringing about this remarkable change. Factors that have been especially incriminated are :- the various hormonal changes that occur in females during pregnancy and menopause; the lessened degree of physical activity in the female, especially after the onset of menopause, with the resultant increase of obesity; the fact that improved economic status of the families, which has resulted from large scale industrialisation, has enabled them to purchase more expensive diets with a high fat content; and finally, the closer medical supervision that is maintained over females of these age groups. It is most likely that some or all of the above factors are responsible for the changes that have occurred.

A study of Figure 3, which illustrates the trend in the mortality rates from diabetes mellitus in England and Wales from 1901 to 1954, shows that the change-over from a higher male ratio to that of a higher female ratio took place in 1920; viz. the year following the termination of hostilities in the First World War. From then onwards, the excess of female over the male rates continued to increase

gradually, until the peak level was reached in 1939, in which year the Second World War commenced. A similar picture is noted in several other European countries that were involved either directly or indirectly in the hostilities that ensued at the time, notably in Norway and Sweden, where the change-over in the sex incidence took place in the years 1919 and 1920 respectively.

It is obvious that some unknown factor or a group of factors have been responsible for effecting these changes. It is just possible that the war produced this dramatic effect by altering the basic structure of the populations of the countries involved, due to a reduction in the male population in the age group 20 to 45 years. The effect of this sudden alteration in the population structure proved to be a continuous one as shown by the gradual increase in the excess of female rates over the male rates during the succeeding years; probably due to the reduction in the number in the male population groups reaching the susceptible age groups where the prevalence of diabetes mellitus is highest. Another possibility is that in addition to the above factors, certain important changes took place in the social and economic structure of most countries during this period, which tended to intensify these changes. One such effect is probably the growing respect in which women are held at the present time throughout the world. This, to all intents and purposes, had its origin only at the turn of the century, as is evident from the statistical data available on the subject. The fact that they are subjected to greater medical supervision has already been referred to, and it is a well-known fact that females generally live longer than males, so that there is a

greater possibility of larger numbers of females surviving to that age zone when diabetes is most likely to have its onset, than in the case of males.

Age at Onset of Diabetes Mellitus.

The average age at onset of diabetes, as determined for 957 patients for whom the data was available, was 53.6 years. This is a little higher than that reported by Andrews for his group of patients in 1957, viz. 52 years. Tables 42 and 43 give the ages at onset and the sex incidence of the two groups of diabetic patients included in our study.

Table 42. / -

Table 42.

Age at onset and Sex Incidence of 379* diabetic patients - 1939/1940 group.

Age group	Male		Female		M. + F.	
	Number	%	Number	%	Number	%
0 - 9 years	2	1.4	-	-	2	0.5
10 - 19 "	9	6.2	6	2.6	15	3.9
20 - 29 "	11	7.6	9	3.8	20	5.3
30 - 39 "	17	11.8	11	4.7	28	7.4
40 - 49 "	25	17.4	37	15.7	62	16.35
50 - 59 "	30	20.8	81	34.5	111	29.2
60 - 69 "	35	24.3	64	27.2	99	26.3
70 - 79 "	13	9.0	27	11.5	40	10.6
80 - 89 "	2	1.4	-	-	2	0.5
TOTAL	144*		235		379	
Average Age at Onset	50.1 yrs.		55.3 yrs.		53.3 yrs.	

* Data relating to one patient was not available.

Table 43. / -

Table 43.

Age at onset and Sex Incidence of 578* diabetic patients - 1949/1950 group.

Age group	Male		Female		M. + F.	
	Number	%	Number	%	Number	%
0 - 9 years	-		3	0.8	3	0.5
10 - 19 "	9	4.6	11	2.9	20	3.5
20 - 29 "	11	5.6	16	4.2	27	4.7
30 - 39 "	24	12.2	22	5.8	46	7.9
40 - 49 "	33	16.8	55	14.4	88	15.2
50 - 59 "	50	25.5	125	32.7	175	30.3
60 - 69 "	43	21.9	106	27.7	149	25.8
70 - 79 "	23	11.7	44	11.5	67	11.6
80 - 89 "	3	1.7	-	-	3	0.5
TOTAL	196		382		578	
Average age at onset	52.3 yrs.		54.6 yrs.		53.8 yrs.	

* Data relating to one patient was not available.

It will be observed that there is a considerable difference in the age at onset of diabetes among males and females in both groups; males in general seem to have an earlier onset in both groups. This is particularly evident in the case of the 1939/1940 group where the male diabetic appears to acquire diabetes mellitus at the age of 50.1 years. This is advanced to 52.3 years for the male diabetic in

FIG. 4

PERCENTAGE DISTRIBUTION OF DIABETIC PATIENTS ACCORDING TO AGE AT ONSET 1939—1940

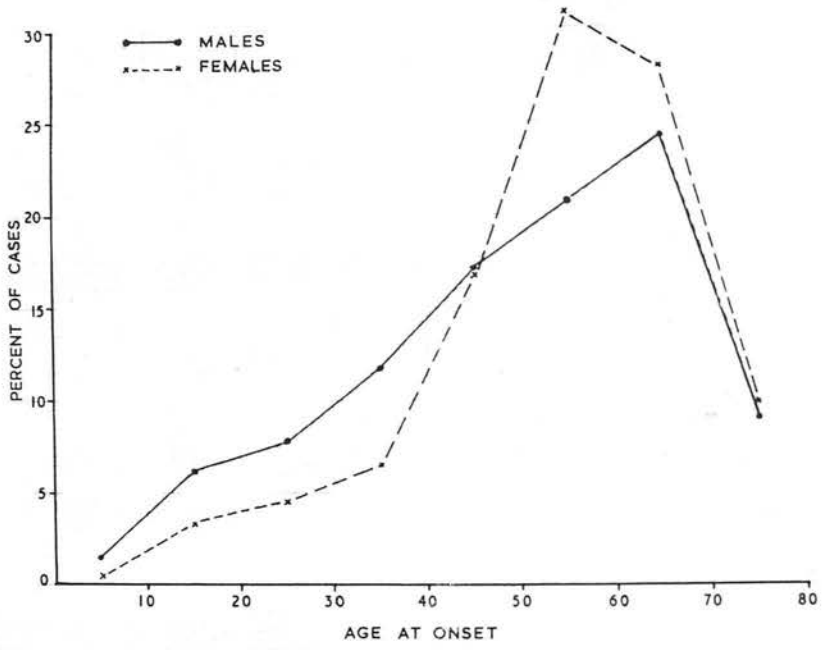
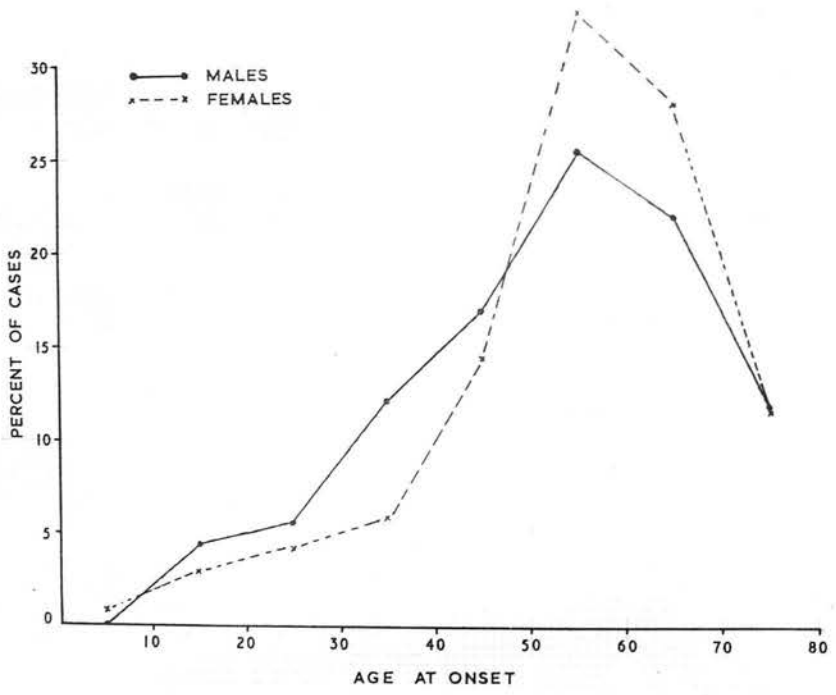


FIG. 5

PERCENTAGE DISTRIBUTION OF DIABETIC PATIENTS ACCORDING TO AGE AT ONSET 1949—1950



the 1949/1950 group. On the other hand, there is a characteristic reduction in the age at onset of diabetes mellitus among female diabetics of the 1949/1950 group as compared with the 1939/1940 group.

Furthermore, the age at onset in relation to sex shows a striking difference between male and female diabetics. (Vide Figures 4 and 5). The curve for the female diabetics of the 1939/1949 group rises to a peak in the sixth decade, whereas that for the males is somewhat flatter and the peak is reached in the seventh decade.

Somewhat similar curves are obtained for the male and female diabetics in the 1949/1950 group, although the peaks in both instances are reached in the sixth decade; the maximum female incidence of diabetes is apparently slightly less than that of the 1939/1940 group, but the general shape of the curve is not much altered. Of considerable interest is perhaps the relative preponderance of male diabetics in the first five decades. This is considerably more pronounced in the 1949/1950 group of diabetics.

Type of Diabetes.

Classification of diabetes into different types is believed by some authors to be a formidable task.(213) Joslin believes that there is no satisfactory method available at present, either for the classification of diabetes mellitus or for the purpose of determining the severity of the disease. He has repeatedly stressed the fact that the nature of the disease may frequently undergo modification in the same individual at different periods.

Following the lead given by Falta and his colleagues,(214)(215)

Himsworth[216][217] has differentiated two types of diabetes, viz:

(1) "The "Insulin-sensitive" type - which requires little insulin to prevent the excretion of many grammes of urinary sugar, tolerates little or no increase of insulin dosage without showing hypoglycaemic symptoms, and reacts to withdrawal of treatment by profuse glycosuria; and,

(2) The "Insulin-resistant" type, which requires many units of insulin to deal with each gramme of urinary sugar, tolerates many units of insulin above the dose required to keep the urine free of sugar, and on cessation of treatment, shows little or no glycosuria."

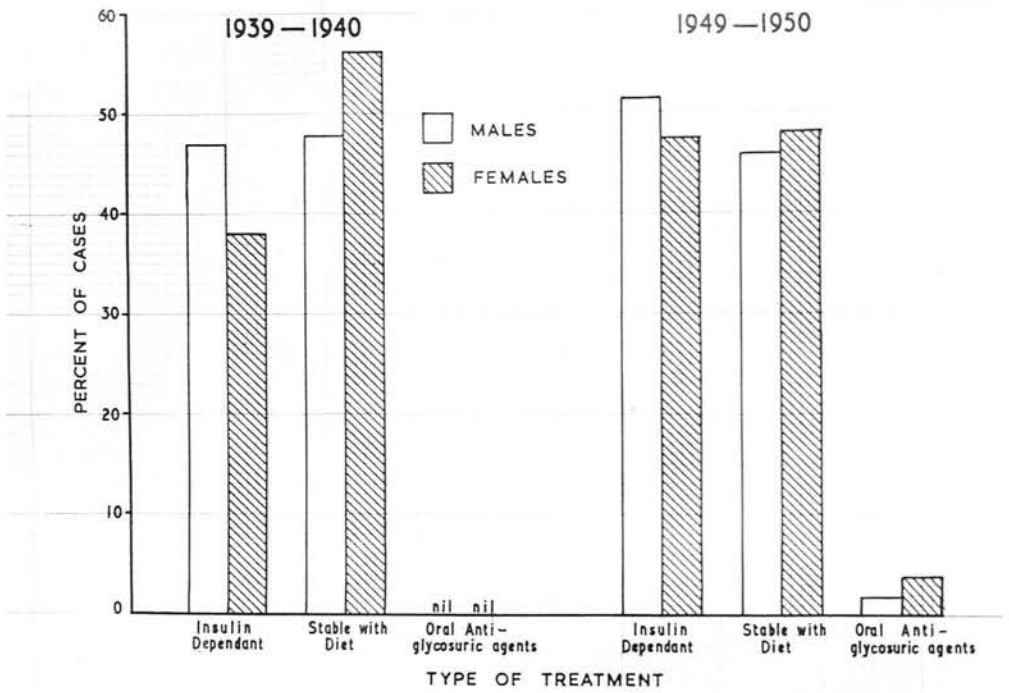
The insulin-sensitive patients tend to be young and thin, with healthy arteries and a normal blood pressure. The onset is usually sudden and tends to be severe, although it responds readily to insulin. Ketosis develops rapidly if treatment is withheld, and even a slight excess of insulin over the ideal dosage produces symptoms of hypoglycaemia.

The insulin-resistant diabetics, on the other hand, tend to be older and are generally obese; the disease is milder and the onset is often insidious. Arteriosclerosis and hypertension are commonly associated with this type. The condition is insusceptible to insulin and the patients can generally tolerate very large amounts of insulin without exhibiting adverse reactions. Ketosis is a very infrequent occurrence among this group of diabetics.

The above classification has been modified to some extent by Lawrence,[216] who has further sub-divided the insulin-resistant type

FIG. 6

PERCENTAGE DISTRIBUTION OF DIABETIC PATIENTS ACCORDING TO TYPE OF TREATMENT



into two groups based on the absence of stores of body fat. This subject has been discussed in considerable detail in Part II of the thesis.

For the purpose of the present study, the patients have been divided into three main groups, viz:

(1) Those who were dependant on insulin;

(2) Those who could be stabilised by dietetic restriction alone; and

(3) Those who required oral antiglycosuric agents for stabilisation.

The last category of patients should actually be considered along with the first group as those patients were originally stabilised with the aid of insulin at the commencement of treatment, and were put on the antiglycosuric agent at a considerably later date.

The distribution of patients according to the different types is shown in Table 44.

Table 44.

The distribution of 959 Diabetic Patients according to Sex and Type of Diabetes Mellitus

Type of Diabetes Mellitus	1939 - 1940				1949 - 1950				Total	
	Male		Female		Male		Female			
	Number	%	Number	%	Number	%	Number	%	Number	%
Insulin-dependant	68	46.9	89	37.9	101	51.3	180	47.1	438	45.7
Stable with diet	69	47.6	132	56.2	90	45.7	183	47.9	474	49.4
Other drugs	-	-	-	-	3	1.5	14	3.6	17	1.8
Not known	8	5.5	14	5.9	3	1.5	5	1.4	30	3.1
TOTAL	145		235		197		382		959	

When both groups are considered together there appears to be a slight preponderance of diabetics who were stabilised on diet alone, although certain differences become evident when the two sexes are considered separately. In the 1939/1940 group, the proportion of insulin-dependant to "diet-stable" diabetics appears to correspond more or less to the general pattern observed for the combined groups, although the latter type seems to predominate to a greater extent among the female diabetics than among the males.

A considerable change appears to have occurred in the distribution of the two major types of diabetes mellitus among the males and females in the succeeding 10 years, as shown by the proportion of diabetics belonging to the two sexes in the 1949/1950 group. We note here an equal distribution of the two types of diabetes among the females, whereas the insulin-dependant type seems to be commoner among the male diabetics in this group. There appears to be no obvious reason as to why this change should have occurred in the type of diabetes mellitus, as no similar changes seem to have occurred in the two groups as far as their body weight was concerned.

The results obtained in the present study seem to differ considerably from what has been observed elsewhere. For example, in the series of patients studied by C.T. Andrews, only 18 percent of the patients were found to require no insulin, whereas 37 percent of all patients required one type of insulin and the remaining 45 percent had to receive two types of insulin to maintain adequate control.

Experiences in other countries too, indicate that a considerably larger proportion of patients require insulin for their

management than those who could be controlled by diet alone. Joslin believes that approximately 60 percent of his patients require insulin for stabilisation. The proportion of patients receiving insulin treatment in the Scandinavian countries appears to be even greater, as reported by Jørgen Christenson[217] for Denmark; approximately 82 percent of all diabetics were reported by him to be on insulin treatment in 1950. Vartianen and Vartianen[218] reported that 76.6 percent of the male diabetics and 68.7 percent of all female diabetics in Finland were taking insulin at the end of 1942. The figures reported for some tropical countries seem to indicate even a higher preponderance of insulin-dependant cases, for example, in the group of patients reported by Cosnett,[219] only 29 (15.3 percent) out of a total of 189 patients treated at a medical unit in Natal were controlled by diet alone. The remaining 84.7 percent required varying amounts of insulin to maintain adequate control. A characteristic feature observed among these Indian diabetics was that a considerably large proportion of them were relatively insulin-resistant, and required large amounts of insulin in order to maintain adequate control (vide Table 45), whereas the majority of the diabetic patients in England and Wales require less than fifty units of insulin per day to maintain adequate control (Stocks, P. (1949).[220]

Table 45. / -

Table 45.

Daily Insulin requirements in 189 patients.

Number of Units	Number of Patients	Percent
0 (controlled on diet)	29	15.3
1 - 49 units	58	30.6
50 - 99 "	76	40.2
100 - 149 "	19	10.1
150 - 199 "	4	2.1
200 and over	3	1.6

Source: Cosnett, J.E. Brit. M. J. 1, 187 - 192, 24 Jan. 1959.

Weight at Onset of Diabetes.

Most authors believe that obesity is a very important factor in the development of diabetes. It has been proved by insurance statistics that the heavier an individual is at the time of his insurance examination, the more likely he is to develop diabetes in later life.(221)(222) The mortality among men with diabetes who are overweight is believed to be more than three times that of a corresponding group of male diabetics who are of normal weight.(223) (Vide Table).

Amount overweight	Increase in Diabetic Mortality over that of men of normal weight.
5 - 15%	$1\frac{1}{2}$
15 - 24%	3 1/5
25% and over	$8\frac{1}{3}$

Table 46 gives the data for one thousand successive cases of diabetes for whom the age, date of onset of the disease, weight and height were known.

Table 46.

Variation from Normal of Maximum Weights at or prior to onset of 1000 cases of true Diabetes, calculated for height, age and sex.

Age (years)	No. of cases	Percentage of each decade		
		Percentage in normal average zone (+5 or -5 percent)	Below Standard Weight	Above Standard Weight
0 - 10	43	37	44	19
11 - 20	84	39	29	32
21 - 30	112	19	10	71
31 - 40	172	6	5	89
41 - 50	244	12	3	85
51 - 60	252	12	1	87
61 - 70	79	10	6	84
71 - 80	14	14	7	79

Source: Joslin, E.P., et al: Treatment of Diabetes Mellitus 10th Edition, Henry Kimpton, London p. 64.

This table illustrates clearly that the maximum weights of only 8 percent were below the standard weights, whereas 15 percent were in that zone, and almost 70 percent of the patients were above it.

Joslin states further, that among 2000 of his own cases of diabetes mellitus no case occurred in persons more than 30 percent underweight. Other authors[224][225] have found the same relationship between obesity and diabetes mellitus. Travie has noted that in his own series of 1500 cases, obesity preceded the onset of diabetes mellitus in 83 percent of cases; moreover, in the remaining 17 percent too, the body weight was observed to increase prior to the onset of the disease. He also observed that hyperglycaemia was often preceded by hypercholesterolemia and hyperuricaemia. Fineberg[225] has observed that "Although diabetes is basically a disease of heredity in which carbohydrate metabolism is disturbed by a relative insufficiency of insulin, still obesity is by far the most important of its precipitating and aggravating factors. Diabetes appears to be largely a penalty of obesity, and the greater the obesity, the more likely the penalty to be inflicted."

Joslin, Dublin and Marks[226] have demonstrated convincingly that a high incidence of diabetes occurs in occupations which favour the development of obesity. In an analysis of the case records of 4596 diabetic patients for whom data were available, they found that 78.5 percent of the males and 83.3 percent of the females were overweight (i.e. 5 percent or more above the average weight for age) at the time of their maximum weight. The weight at onset of diabetes however, gave somewhat lower figures. Of the 3094 for whom these data

were available, 62.7 percent of the males and 67.4 percent of the females were found to be overweight. Moreover, one-half of the men and approximately 60 percent of the women were observed to be at least 20 percent overweight at their maximum weight.

The actual percentage of individuals with obesity among diabetics may vary as reported by different authors; e.g. Parkhurst and Betsch[227] found that obesity was present in 66 percent and 50 percent of two groups of patients reviewed by them.

The beneficial influence of the food shortage which occurred in the Second World War, reducing the incidence of obesity in Japan with its consequent reduction in the incidence of Type I diabetes (viz: the mild type of diabetes not requiring insulin therapy, which commonly occurs in obese elderly people), is commented on by Yoshio Goto et al[228] in Japan.

Pyke and Please[229] have noted that diabetics were generally heavier than non-diabetics; that obesity was observed earlier in women than in men, and that it generally occurred at or about the age of 30. Among females the weight was observed to increase with parity among diabetics more than among non-diabetics.

The obesity that occurs in women between the second and fourth decades of life is believed by some authors[230] to be caused exogenously by diencephalohypophyseal dysfunction and that exogenous factors such as polyphagia play only a secondary part in the causation of obesity. They suggest that the observation that the anterior pituitary lobe in women weighs more than men, together with the fact that the weight of the anterior pituitary lobe of the pituitary increases by 20 percent during pregnancy, may explain in part the

predisposition of women to obesity. Other workers[231] have proved experimentally that overnutrition does in fact predispose to diabetes in certain strains of mice. The same is believed to hold true for man too, by some workers.[232]

Of great clinical importance is the observation that reduction in body weight may restore the glucose tolerance in obese diabetics.[233][234][235] In spite of the overwhelming evidence presented, the exact nature of the relationship between diabetes mellitus and obesity is not very clear. Some people[236] believe that obesity is probably an hereditary trait which accompanies diabetes. Long[237] has offered a plausible theory based upon the participation of insulin in the metabolism of fat. Assuming that an individual who maintains a constant and normal body weight requires a certain daily production of insulin, it follows that one who has a calorie intake in excess of daily needs will require an additional daily production of insulin to be utilised in the deposition of fat. When this persists over a period of many years, the pancreas becomes partially exhausted and fails to provide an adequate supply of insulin. How long it takes for this to occur is probably a function of the degree of excess of intake of food, and the inherent capacity of the pancreas. At first a state of relative insulin-deficiency occurs. At this stage a reduction in the demand for insulin by immediate correction of the caloric intake, and eventual reduction of body weight is believed to re-establish an equilibrium between supply and demand. The diabetes is considered to be reversible at this stage. If, however, the condition is allowed to persist, the pancreas becomes exhausted, and an irreversible stage of diabetes mellitus is said to develop. Once

this has occurred diabetic symptoms become gradually manifest and the condition is no longer controlled by diet restriction alone.

A somewhat similar, but different approach to this problem is based on the numerous experimental investigations conducted by Young.(238) These lead one to assume that the pre-diabetic increase in height in children, and the increase in weight in the adult are simply reactive or protective mechanisms for the storage of carbohydrates, of which the oxidation is suppressed and of the nitrogen which is retained under the influence of anterior pituitary action. The expansive capacity of adults is definitely limited, and unless the child is capable of sustained excessive growth, this reaches a stage when the body can no longer store up excess carbohydrates in the form of extra body tissue. Sugar then leaks into the bloodstream, and despite a subsequent and complete subsidence of pituitary overactivity, permanent stigmata may remain in the form of islet-cell lesions in the pancreas associated with permanent diabetes.

Although a great deal of evidence has been presented and many theories promulgated to explain and illustrate the association between obesity and diabetes, there is sufficient evidence to indicate that it may not be of such importance in the aetiology of diabetes mellitus, at least as far as some of the tropical countries are concerned.(239) Tulloch affirms that although obesity is of primary importance as an aetiological factor in diabetes mellitus in several countries in the tropics, it is however of minor importance in countries such as India, Ghana, Ceylon and Uganda, and that it is of no importance at all in countries like Vietnam, Thailand, Congo and Zanzibar, etc. De Soyza(240)

has observed that obesity is not an outstanding feature of the Sinhalese and Muslim diabetics in Ceylon. Nearly 68 percent of all diabetics examined were observed to be underweight. Table 47 shows the analysis of the weights of two groups of diabetic patients seen in a Diabetic Clinic and as observed in a diabetic survey, respectively.

Table 47.

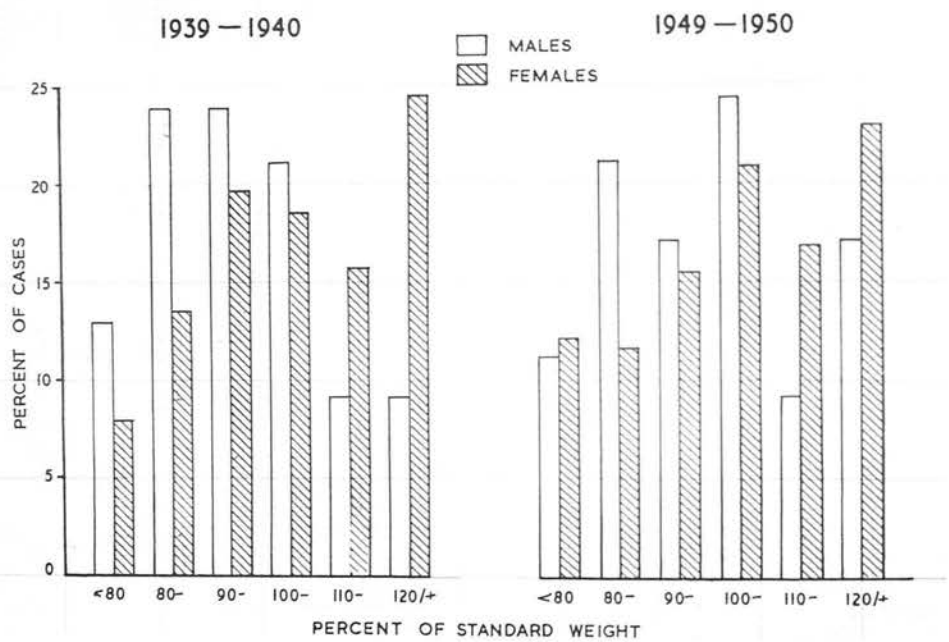
Weights	Clinic Patients		Diabetic Survey	
	Males %	Females %	Males %	Females %
Underweight: 5%	40.0	45.0	45.0	61.0
" 10%	15.0	24.2	23.0	17.0
Normal Weight	15.0	12.0	13.0	11.0
Overweight 5%	18.0	12.4	13.0	6.0
" 10%	12.0	6.4	6.0	5.0
Total number examined	600	500	47	64

Source: De Soyza, V.P. "An Investigation into the aetiological factors of diabetes". Ceylon Govt. Press. 1946.

The analysis of the data relating to weight at onset of diabetes mellitus in the two groups of patients considered in the present study is given in Table 48. It should be noted that due to incompleteness of the records, particulars regarding the weight history of patients were available only for 736 patients; 109 (75.1 percent)

FIG. 7

PERCENTAGE DISTRIBUTION OF DIABETIC PATIENTS ACCORDING TO STANDARD WEIGHT AT ONSET



of the male and 178 (75.7 percent) of the female diabetics in the 1939/1940 group and 152 (77.1 percent) of the male and 297 (77.8 percent) of the female diabetics in the 1949/1950 group respectively.

Table 48.

Percentage of Standard Weight	1939 - 1940				1949 - 1950			
	Male		Female		Male		Female	
	Number	%	Number	%	Number	%	Number	%
80	14	12.8	14	7.9	17	11.2	36	12.1
80 - 89	26	23.8	24	13.5	32	21.1	35	11.8
90 - 99	26	23.8	35	19.6	26	17.1	46	15.5
100 - 109	23	21.1	33	18.5	37	24.3	62	20.9
110 - 119	10	9.2	28	15.7	14	9.2	50	16.8
120+	10	9.2	44	24.8	26	17.1	68	22.9
TOTAL	109*		178		152		297	

It will be observed that obesity as such is not so important a factor among the male diabetics in both the 1939/1940 and 1949/1950 groups, as shown by the fact that the percentage of individuals who were 10 percent or more above their standard weights in the two groups were only 18.4 percent in the 1939/1940 group and 26.3 percent for those in the 1949/1950 group. On the other hand, as many as 36.6 percent of the males in the former and 32.3 percent in the latter group were found to be 10 percent or more below their standard weights.

On the other hand, approximately 40 percent of the female diabetics in both groups were 10 percent or more above their standard weight at the onset of illness.

Marital State.

The incidence of diabetes mellitus has been shown to be higher in married women than in single women. This difference is not found in men,[241][242] among whom single males appear to have a higher mortality rate from diabetes than married males. Divorced males seem to have the highest mortality rate among males, whereas widows seem to have the highest rate among females.

Table 49.

Age adjusted* Death Rates per 100,000 from Diabetes Mellitus by Sex and Marital Status, White Persons, aged 20 - 74 (United States 1949 - 1951).

Marital Status	Males	Females
Single	18.2	12.6
Married	13.4	22.4
Widowed	19.6	25.3
Divorced	22.8	21.2

* Adjusted on the basis of the age distribution of the total population residing in the United States on April 1, 1950.

Source: Metropolitan Life Insurance Company, Statistical Bulletin, Vol. 38, p.5, Feb. 1957. - Joslin, E.P. et al; Treatment of Diabetes Mellitus - 10th Edition. p.34.

The variations in the mortality from diabetes mellitus according to marital status in the United States has also been analysed for the years 1949 - 1957 by the National Office of Vital Statistics of the United States, and are shown in Table 50.(243)

Table 50.

Death Rates/100,000 from Diabetes Mellitus by Race, Sex and Age - United States, 1949 - 1951.

Age	White Males				White Females			
	Single	Married	Widowed	Divorced	Single	Married	Widowed	Divorced
20-24 years	1.3	0.5			1.6	1.1		
25-34 "	4.9	1.3		6.5	3.9	1.5		3.5
35-44 "	9.6	2.8		12.6	4.7	2.5	4.2	4.2
45-54 "	17.5	8.9	19.7	19.6	9.4	11.5	16.1	10.5
55-59 "	30.0	22.6	31.1	33.2	20.9	38.1	43.5	33.5
60-64 "	45.9	38.8	52.7	53.8	32.2	74.7	81.2	65.0
65-69 "	63.8	60.8	78.9	84.6	47.3	111.6	120.7	86.9
70-74 "	85.6	95.6	108.4	124.4	71.9	162.1	163.2	170.8
75+	112.9	139.9	153.5	182.9	114.5	193.9	195.4	269.5

Source: National Office of Vital Statistics, Special Reports; Selected Studies, Vol. 39. No.7, May 8, 1956.

The above table shows that single men up to the age of 70 experienced higher rates than married men at corresponding age periods; at ages above 70 years, married men had comparatively higher rates. The differences between the two groups were proportionately greater at

ages under 45. The widowed and divorced males generally had rates higher than either the single or the married groups, and of the two groups, the divorced males apparently seemed to be the worse off among the two.

The pattern of mortality for women according to marital status appeared to be somewhat similar to that of men up to the age of 45; but at ages above that, the picture was completely different. Above this age married women seemed to have consistently higher rates than single women; the differences between the groups was quite large and this tended to increase with age. At ages between 60 and 74 years, the rates for married women were almost double those for single women. The rates for the widowed were correspondingly higher than the rates for the married women. A very significant feature in the series is the relatively low rate obtained for the divorced women at all age groups.

It is suggested that the higher rates among single persons at the younger age groups reflect the lower marriage rates among young diabetics as compared with non-diabetics. The relatively lower mortality rates among married women compared to single men may be due to several factors; such as the fact that single men who become diabetic during their working life are less likely to seek and carry out treatment than married women. This effect may well be supplemented by the various socio-economic differences that exist between the two groups. The differences that exist between the single and married women is still more significant in that at all ages above 45 years, married women have correspondingly higher rates than single women; in fact, at ages above 60 years, their rates are almost double

that of single women. Of the factors that are possibly responsible for these differences are the fact that single women at all age groups are more likely to keep their body weight under control than married women. Perhaps of even greater significance are the various endocrine factors relating to repeated pregnancies and cessation of menstruation that possibly play a major role in bringing about these changes. Joslin has commented on the possible role of menopause as an important factor which tends to increase the incidence of diabetes mellitus between the ages of 40 - 50 years by attempting to correlate the increase in the rates with the onset of menopause in women. It has been stated that pregnancy in itself does not tend to produce diabetes, but it does bring about an increased demand of insulin as pregnancy advances and that these requirements fall off rapidly after delivery.(244) Mosenthal and Boldnan(245) had earlier commented on the injurious effect of pregnancy upon the carbohydrate tolerance almost twenty years before. Joslin et al(246) confirmed this observation, but believed that the difference was mainly due to the greater tendency of married women than single women to become fat. A similar view was also expressed by Munro and his colleagues (1949)(247) who observed that the large excess of married women over men among their group of patients with diabetes mellitus was confined to multiparous rather than nulliparous women. They believed that the difference was - "related at least in part to previous child-bearing." Pyke(248) has observed that the tendency to develop diabetes among women rises with increasing parity, and that a woman who has had five children apparently had about three times as great a chance of

developing diabetes as a woman who had no children.

These observations are corroborated by the studies of Joseph P. Hoet (1954),[249] who has put forward both clinical and experimental evidence to show that certain abnormalities in the glucose tolerance curve appear about the fourth month of gestation in those patients who have a diabetic trait, or who have a latent weakness of insulin production; this disordered glucose regulation is apparently transient and tends to disappear after delivery. He expresses the view that hypercorticism that occurs as a result of pregnancy is the most obvious of the several hormonal factors which may be involved in the production of hyperglycaemia which occurs commonly in pregnancy.

The marital status at the onset of diabetes of the two groups of diabetic patients in our present study are shown in Tables 51 and 52.

Table 51.

Marital Status at the onset of Diabetes Mellitus of 380 patients first seen in 1939/1940.

Marital Status	Males		Females		M. & F.	
	Number	Percent	Number	Percent	Number	Percent
Married	95	65.5	189	80.4	284	74.7
Single	33	22.7	24	10.2	57	15.0
Widowed	8	5.6	16	6.8	24	6.3
Not known	9	6.2	6	2.6	15	4.0
TOTAL	145		235		380	

Table 52.

Marital Status at the onset of Diabetes Mellitus of 579 patients first seen in 1949/50.

Marital Status	Males		Females		M. & F.	
	Number	Percent	Number	Percent	Number	Percent
Married	150	76.1	288	75.4	438	75.6
Single	28	14.2	56	14.7	84	14.5
Widowed	10	5.1	32	8.4	42	7.3
Separated	1	0.5	2	0.5	3	0.5
Not known	8	4.1	4	1.0	12	2.1
TOTAL	197		382		579	

On the whole, approximately 75 percent of all diabetic patients in both groups appear to be composed of married individuals. Minor differences become evident, however, when the two sexes are considered separately.

In the 1939/1940 group, the proportion of married to single male diabetics is 95:33, whereas the corresponding figure for the female diabetics of the same group is 189:24. In the 1949/1950 group the ratio of married to single male diabetics is 150:28, and the corresponding figure for females is 288:56. Both these values approximate quite closely the average observed for the group as a whole. Also the proportion of married to single persons in both the male and female diabetics is almost identical. An analysis of the marital status of all individuals over the age of 20 years in the South-Eastern region of Scotland[250] shows that 70.0 percent of all

males and 61.2% of all females were married, whereas 23.3 percent of all males and 24.3 percent of all females were single. This proves that the proportion of married to single females is significantly higher among diabetics than in the normal population.

Tables 53 and 54 show the present marital status of the two groups of patients. As mentioned earlier, almost 90 percent of the patients in the first group have died subsequently, and thus this table gives us an approximate idea of the proportion of individuals in the different marital groups which one would expect to find in an analysis of death certificates for an identical group of patients. On the other hand, only 51.8 percent of the patients in the 1949/1950 group have died, so that the picture presented by this group is considerably different.

Table 53.

Present Marital Status of 380 diabetic patients first seen in 1939/1940.

Marital Status	Males		Females		M. & F.	
	Number	Percent	Number	Percent	Number	Percent
Married	80	55.2	94	40	174	45.8
Single	23	15.9	24	10.2	47	12.4
Widowed	32	22.1	108	45.9	140	36.8
Divorced	-	-	2	0.9	2	0.5
Not known	10	6.8	7	3.0	17	4.5
TOTAL	145	100.0	235	100.0	380	100.0

Table 54.

Present Marital Status of 579 Diabetic Patients first seen in 1949/1950.

Marital Status	Males		Females		M. & F.	
	Number	Percent	Number	Percent	Number	Percent
Married	131	66.5	177	46.4	308	53.2
Single	17	8.6	44	11.5	61	10.5
Widowed	32	16.3	135	35.3	167	28.8
Separated	-	-	3	0.8	3	0.5
Not known	17	8.6	23	6.0	40	7.0
TOTAL	197	100.0	382	100.0	579	100.0

It will be observed that among the 145 male diabetics, almost 112 (77.3 percent) were married or widowed and only 23 (15.9 percent) were single. On the other hand the proportion of married and widowed females to single females was even greater as shown by the fact that there were 202 (85.9 percent) married or widowed females and only 24 (10.2 percent) single females in this group.

Social Class Distribution.

Very little data are as yet available on the influence of occupational and socio-economic status on the incidence and mortality from diabetes mellitus; even such data as are now available is probably not very reliable, due to various errors that are commonly introduced in the process of collection and tabulation of the

requisite data. Information with regard to matters such as one's occupation or marital status are obtained generally from the information supplied in the census returns and death certificates. The usual experience has been a significant lack of conformity between the data obtained from these two sources. Another major drawback is the presence of a considerable amount of bias in the method of assessment of this problem. It is a well-known fact that diabetes mellitus is commoner among persons who have passed middle-age. Therefore one would, perforce, be faced with the issue of having to deal with only a minority of all deaths from diabetes during the period of active working life of people. This is particularly so in the higher socio-economic groups, where people generally retire from active work only at quite an advanced age.

Not much information is available on the place of the diabetic in the labour pattern of a country. It has been stated that there is some reluctance on the part of the employers to take known diabetics into permanent situations, although this problem does not arise in the case of those seeking temporary employment.[+] It is believed that the disability caused by diabetes mellitus forces such individuals to take employment which does not involve extremes of physical exertion or long and variable hours of work. These limitations would have their greatest impact in Social Classes III and IV, and to a lesser extent in other social groups. One would imagine that the general tendency would be for the diabetic to change his occupation from that of a highly-skilled to a less skilled job or else, from a manual to a non-

[+]Tunbridge, R.E. Lancet. 2, 893. Oct. 31, 1953.

manual employment group within his own particular social group. Our study however, does not throw any new light on this subject.

The best recent data on the subject are based on the mortality rates for England and Wales during 1949 - 1953, the five-year period centred around the census carried out in 1951.(251)

Table 54a gives the summary of mortality data accumulated for this period.

Table 54a.

Mortality from Diabetes Mellitus by Social Class.
Ages 20-64, England and Wales, 1949 - 1953.

Social Class	Standard Mortality Rates		
	Men	Women	
		Married+	Single
I Professional, managerial etc. occupations	134	60	X
II Intermediate	100	80	78
III Skilled	99	100	82
IV Partly skilled	85	122	77
V Unskilled	105	119	75

+Classified according to the husband's socio-economic status.

X Less than 10 deaths.

Source: The Registrar-General's Decennial Supplement, England and Wales, 1951. Occupational Mortality, Part 2, Vol. 1, Commentary, HMSO, 1958.

In the above table, the Standard Mortality Ratio, viz, the number of observed deaths from diabetes in each classification,

expressed as a percentage of the number of expected deaths on the basis of the age specific mortality for the sex from the disease in the general population, has been calculated for each of the three groups of individuals, viz. men, married women and single women, in each of the five social classes.

It will be evident that the mortality rate among males was highest in Social Class I, and lowest among Social Class IV, which consists primarily of semi-skilled workers. The ratios for the three remaining groups did not vary a great deal from the average for all males. In contrast to this, mortality among married women was lowest in Social Class I, and there was a noticeable increase in the ratios from Class I to Class IV; Class V had a slightly lower rate than Class IV. The mortality ratios among single women were significantly lower than in the other two categories, but there was hardly any significant variation with the social class. It has been suggested that the high ratio among males in Class I is in part due to the high proportion of persons engaged in sedentary occupations among this group, which is generally accepted as a factor which tends to produce obesity; - this in turn precipitates the onset of diabetes mellitus in the susceptible individual. It is also possible that the total deaths in Class I includes those whose true socio-economic status was in fact Social Class II.

The trend in mortality according to social class among married women probably illustrates the beneficial effect produced by greater attention paid to personal health and more frequent medical examinations by married women in better financial and social

circumstances, than their poorer counterparts.

Table 55 gives the Standard Mortality Ratios for the different occupation groups. Relatively high ratios are recorded for men in higher administrative posts, clerical workers (Social Class III), shop-keepers (Social Class II), personal service workers (Social Class III), shop-assistants (Social Class III) and non-commissioned men in the armed forces who were classified under Social Class III. In contrast, mine-workers, semi-skilled workers, building and dock-workers (Social Class V), and agricultural workers have relatively low rates.

Table 55. / -

Table 55.

Mortality from Diabetes Mellitus in Selected Socio-Economic Groups or Social Sub-classes. Ages 20-64, England and Wales 1949-53.

Socio-economic group or social sub-class X	Social Class	Standard Mortality Ratio	
		Men	Married women *
Higher administrative etc.	I	134	60
Clerical workers	III	126	75
Shop-keepers	II	124	70
Armed forces - non commissioned men	III	123	133
Personal service	III	120	85
Shop assistants	III	118	79
Unskilled workers	V	104	119
Transport workers	III	100	113
Farmers	II	98	127
Skilled workers	III	95	107
Other administrative etc.	II	91	72
Drivers of goods vehicles	III	89	-
Builders, labourers	V	86	95
Foreman	III	86	85
Agricultural workers	IV	82	132
Building and dockworkers	V	81	100
Semi-skilled workers	IV	79	124
Mine workers	III	67	205

X Classified according to occupation.

* Classified according to husband's socio-economic status.

Source: The Registrar-General's Decennial Supplement. England & Wales 1951, Occupational Mortality, Part II, Vols. 1 and 2, H.M.S.O. 1958.

Somewhat similar conditions have been reported from Italy.(252) A statistical survey on mortality from diabetes mellitus in Italy over the period 1888 through 1952 revealed that the highest figures corresponded to the richest categories, viz. manufacturers and traders, men of property and well-to-do people etc. These data are shown in Table 56.

Table 56.

Mortality from Diabetes according to occupation. (Per 100,000 population).

	Average/year for the 5 year period 1929 - 1933	Average/year for the 5 year period 1934 - 1938
All types of agricultural workers	6.42	6.16
Merchants and industrialists	83.71	94.36
Sellers of agricultural produce and other merchandise	13.98	18.47
Carpenters and polishers, etc.	6.38	8.94
Those attached to making of bread and confectionery etc.	8.43	7.77
Tanners of hides and leather; shoe-makers	8.19	6.60
Metallurgists, mechanics, electricians	5.81	4.80
Asphalt workers, furnace-workers, ceramic & glass workers	7.69	7.25
Tailors	6.87	3.91
Coachmen and car-drivers etc.	4.95	5.15
Domestic servants	7.63	6.41
Clergymen	62.77	79.89
Teachers	14.34	11.10
Doctors & others associated with the medical profession	27.92	19.93
Other professions	49.65	56.76
Landlord, proprietors, etc.	156.96	89.63
Household attendants	11.95	18.24

The social class distribution of the two groups of patients in our present study is given in Table 57. Of the patients belonging to the 1939/1940 group, the social class distribution was not determined for 8 (5.5 percent) males and 14 (6 percent) females. The distribution of patients among the different social classes was very similar in the two groups. The greater proportion of the patients -(74 (51 percent) of the males and 126 (53.6 percent) females) belonged to Social Class III. This is probably to be expected as the Social Class III is presumably the largest social group found in Great Britain. The second largest category was Social Class IV and this was followed by Class II. Only 4 (2.7 percent) of the male diabetics and 5 (2.1 percent) of the female diabetics belonged to Social Class I.

Table 57.

Social Class distribution of 959 Diabetic Patients.

Social Class	1939 - 1940						1949 - 1950					
	Male		Female		M. + F.		Male		Female		M. + F.	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
I	4	2.7	5	2.1	9	2.4	10	5.1	6	1.6	16	2.7
II	21	14.5	21	8.9	42	11.1	42	21.3	62	16.2	104	17.9
III	74	51.0	126	53.6	200	52.6	93	47.2	155	40.6	248	42.8
IV	30	20.7	49	20.9	79	20.7	32	16.2	91	23.8	123	21.2
V	8	5.5	20	8.5	28	7.4	6	3.0	28	7.3	34	5.9
Not known	8	5.5	14	6.0	22	5.7	14	7.2	40	10.4	54	9.5
TOTAL	145	99.9	235	100.0	380	99.9	197	100.0	382	99.9	579	100.0

Table 58.

The Distribution of Patients according to Employment Group.

Employment Group	1939 - 1940						1949 - 1950					
	Male		Female		M. & F.		Male		Female		M. & F.	
	Number	%	Number	%	Number	%	Number	%	Number	%	Number	%
Manual	85	58.6	156	55.4	241	68.4	89	45.2	201	52.6	290	50.1
Non-manual	45	31.0	47	20.0	92	24.2	85	43.1	107	28.0	192	33.2
Agricultural	7	4.9	18	7.6	25	6.6	9	4.6	33	8.6	42	7.2
Not known	8	5.5	14	6.0	22	5.8	14	7.1	41	10.8	55	9.5
TOTAL	145	100.0	235	100.0	380	100.0	197	100.0	382	100.0	579	100.0

Minor differences in the Social Class distribution of patients are found in the 1949 - 1950 group when the two sexes are considered separately. However, in this group too, Social Class III is the largest group with 248 (42.8 percent) patients. The second highest number of patients are found in Social Class II in the case of males with 42 (21.3 percent) patients, and Social Class IV in the case of females with 91 (23.8 percent) patients. Male diabetics of Social Class IV come next followed by those of Social Classes I and V respectively. The sequence is slightly different in the case of the female diabetics, where Social Class IV is followed by Social Classes II, V and I respectively.

Table 58a shows the Social Class distribution of a control group of 554 individuals who have been matched for age and sex with

an identical number of diabetic patients from our study, who had since died and whose death certificates were available. The sample was drawn from among individuals who at the time of death, were residing in Edinburgh.

Table 58a.

Social Class Distribution of a group of 554 individuals.

Social Class	Males		Females		M. & F.	
	Number	Percent	Number	Percent	Number	Percent
I	5	2.48	13	3.68	18	3.24
II	20	9.99	48	13.59	68	12.27
III	104	51.74	165	46.74	269	48.55
IV	31	15.42	62	17.56	93	16.78
V	29	14.42	31	8.78	60	10.83
D.K.	12	5.97	34	9.63	46	8.48
TOTAL	201	100.02	353	99.98	554	100.15

It will be observed that the largest number of individuals are drawn up from Social Class III. This is more so in the case of male than female persons. The second largest group is Social Class IV, and this is followed by Social Class V and I. It has been mentioned earlier that the two largest social groups from which our diabetic patients had been drawn up were Social Classes III and IV, which therefore corresponds to the normal Social Class distribution in the population. Slight differences are, however, evident in respect to

Social Classes V and I. The normal distribution in the population of Edinburgh as shown in our control group, shows that 14.42 percent of males and 8.78 percent of females belonged to Social Class IV, although only 5.5 percent of males and 8.5 percent of female diabetics of the 1939/40 group were drawn up from this Social Class. The proportions appear to be even less in the 1949/50 group.

The distribution of patients according to their employment group is shown in Table 58. It will be observed that as many as 241 (63.4 percent) of the patients in the 1939 - 1940 group belonged to the manual group and only 92 (24.2 percent) belonged to the non-manual group. The employment group of 22 (5.8 percent) of the patients could not be ascertained. There is no significant difference in the distribution between male and female diabetics. The position is somewhat different in the case of the 1949 - 1950 group in that there is a slight variation in the distribution when the two sexes are considered separately, An approximately equal number of patients seem to have been drawn from the two main categories, viz. manual and nonOmanual workers in the case of the male diabetics, whereas the distribution of female diabetics seems to correspond more to what was observed in the 1939 - 1940 group, viz. a preponderance of manual workers as compared to the other two categories.

ANALYSIS OF DEATH CERTIFICATES

As mentioned earlier, of the total of 959 patients in our study, 632 patients had died and their death certificates were traced and analysed. Table 59 shows the extent to which diabetes mellitus was mentioned either as the primary or as a secondary cause of death in the death certificates.

Table 59.

The extent to which "Diabetes Mellitus" was mentioned in the Death Certificates of 632 patients dying with Diabetes Mellitus.

	Males		Females		M & F.	
	Number	%	Number	%	Number	%
Diabetes as primary cause of death	62	27.9	112	27.3	174	27.5
Diabetes as secondary cause of death	61	27.5	138	33.6	199	31.5
Diabetes not mentioned	99	44.6	160	39.1	259	41.0
TOTAL	222	100.0	410	100.0	632	100.0

It is evident from this table that of the total of 632 patients, only 174 (27.5 percent) would have been classified as dying from diabetes; 199 (31.5 percent) would be classified as dying of other diseases although diabetes mellitus would be mentioned in the death certificate as a contributory cause of death. 259 (41 percent) of the total failed to have the disease mentioned in the death certificate.

In a study carried out by Lombard and Joslin(253)(254) in which the death certificates of 714 diabetic patients in the year 1936, and 1000 patients in 1946 were analysed, 63 percent of all patients in the first study and 65.7 percent in the second study were found to have been classified as dying of diabetes, while 13 percent of the patients in the first study and 9.9 percent in the second, although dying of diabetes, were otherwise classified. Of the two groups, 24 percent of the first study and 24.6 percent of the second failed to have the word "diabetes" mentioned in the death certificate.

In a more recent study carried out in 1958, it was shown that only 33 percent of individuals dying with diabetes have been so classified, while 44.2 percent have been certified as dying of other diseases although diabetes was mentioned in the death certificate.

The analysis of our own figures indicates that the extent to which diabetes fails to be mentioned in the death records is even greater. It will also be evident that the rate of omission is considerably greater for the male diabetics than that for the female.

In an attempt to elucidate the possible causative factors which might have led to this considerable underdiagnosis of diabetes, the data was subjected to further analysis in order to find out whether there was any significant relationship between the accuracy of diagnosis and factors such as - the number of items mentioned in the death certificate, the place of death, age at death, social class and employment group of the patient, etc.

Table 60 shows the number of items recorded on the death certificates of the 632 diabetic patients.

Table 60.

Number of items recorded in the Death Certificates of 632 patients dying with Diabetes Mellitus.

Type of Diagnosis	Number of Items in the Death Certificate						Total
	1	2	3	4	5	Not known*	
Diabetes as primary cause of death	29	81	52	11	1	-	174
Diabetes as secondary cause of death	-	89	86	22	2	-	199
Diabetes not mentioned	97	109	36	7	-	10	259
Total	126	279	174	40	3	10	632

* Sudden deaths.

It will be seen that of the total, 126 (19.9 percent) death certificates had only one item, 279 (44.1 percent) had two items and 174 (27.5 percent) had three items on the death certificates. Of the first group, viz. those certificates that had only one item mentioned, more than 75 percent failed to have the word "diabetes" mentioned in the records, whereas in those that had two items, the percentage that did not have diabetes mentioned dropped to only 39 percent. The extent to which diabetes mellitus is omitted in the death certificates appears to lessen with the increase in the number of items in the death certificate. As pointed out by Lombard and Joslin, it is possible that where only one condition was mentioned, the

the underlying cause of death was some severe catastrophe such as coronary thrombosis, accident or cancer, which were found to account for a considerable number of omissions in their series of cases.

Place of Death.

Table 61 shows the place of death for the 632 patients according to the manner in which the deaths were certified as to whether diabetes was mentioned as the primary or secondary cause of death, or whether it was omitted in the death certificate.

Table 61.

Place of death according to type of diagnosis.

Type of Diagnosis	Hospital	Other Institution	Home	Nursing Home	Others	Total
Diabetes as primary cause of death	73	5	85	-	11	174
Diabetes as secondary cause of death	96	4	93	1	5	199
Diabetes not mentioned	103	9	122	-	25	259
TOTAL	272	18	300	1	41	632

Of the total, 300 (47.4 percent) deaths took place in the home, whereas 272 (43.0 percent) deaths took place in a hospital. Relatively few deaths occurred in nursing homes and other institutions. Of the 300 deaths that occurred in the home, 122 (40.6 percent) did not have the term "diabetes" mentioned in the death

certificate, whereas only 103 (37.8 percent) of the patients who died in a hospital failed to have diabetes mentioned in death certificates.

Influence of Age at Death on Type of Diagnosis.

Table 62 gives the ages at death of the 632 patients and the manner in which the deaths were certified in each case.

Table 62.

Type of Diagnosis according to age at Death.

Type of Diagnosis	Age Group (years)					Total
	0-19	20-39	40-59	60-79	80+	
Diabetes as primary cause of death	2	13	38	111	10	174
Diabetes as secondary cause of death	2	7	25	152	13	199
Diabetes not mentioned	1	7	34	180	34	256
TOTAL	5	27	97	443	57	629*

3
632

Average age at death of 410 female diabetics = 67.6 years.

" " " " " 222 male " = 64.2 "

*The ages at death of three patients were not recorded.

It is clear from the above data that the younger the age at death of the patient, the greater was the likelihood of having diabetes entered, either as the primary or secondary cause of death in

the death records. For example, only one out of five persons who died with diabetes mellitus before the age of 19 failed to have diabetes mentioned in the certificate. 7 out of the 27 patients who died between the ages of 20 and 39 years did not have diabetes mentioned. Thus the percentage rate of omission is seen to increase gradually with the advance in age of death of the patient, until, among those individuals dying at ages above 80 years, almost 60 percent fail to have 'diabetes' mentioned in the death certificate.

Influence of Type of Diabetes Mellitus on Death Certification.

The association between the type of daibetes mellitus and the manner in which the deaths were certified is shown in Table 63.

Table 63.

Type of Diagnosis according to Type of Disease.

Type of Diagnosis	Insulin dependant*	Stabilised with diet	Not known	Total
Diabetes mentioned as primary cause of death	101	64	9	174
Diabetes mentioned as secondary cause of death	102	90	4	196
Diabetes not mentioned	55	191	13	259
TOTAL	258	345	26	629

* Three patients who had originally been treated with oral anti-glycosuric agents have been included among this group of cases.

The above data shows that 55 (21.3 percent) out of 258 patients who had been on insulin treatment while yet alive failed to have diabetes mentioned in the death certificate, whereas 191 (55.3 percent) out of 345 patients who had been stabilised on diet alone were so diagnosed.

Association between Social Class Distribution and Type of Diagnosis.

The breakdown of the data by social class and type of diagnosis as found in the death record is illustrated in Table 64.

Table 64.

Type of Diagnosis according to Social Class of patient.

Type of Diagnosis	Social Class						Total
	I	II	III	IV	V	Not known	
Diabetes as primary cause of death	4	13	93	51	10	3	174
Diabetes as secondary cause of death	2	38	95	42	19	3	199
Diabetes not mentioned	6	40	125	54	18	16	259
TOTAL	12	91	313	147	47	22	632

It will be observed that the proportion of individuals dying with diabetes who did not have diabetes mellitus mentioned in their death certificates was highest (50 percent) in Social Class I. The

percentage rate of omission is observed to diminish considerably as one goes down the social scale, and the best results, as far as accuracy of death certifications are concerned, are obtained in Social Class IV, where the rate of omission of diabetes in death certificates is only 36.1 percent. There is however, a slight increase in the rate of omission in Social Class V as compared to Social Class IV.

The breakdown of the data to show the association between the type of diagnosis and the three main employment groups, viz. manual, non-manual and agricultural, shows some very interesting results. (Vide Table 65).

Table 65.

Type of Diagnosis according to the employment group of the patient.

Type of Diagnosis	Employment Group				Total
	Manual	Non-manual	Agricultural	Not known	
Diabetes as primary cause of death	109	46	16	3	174
Diabetes as secondary cause of death	130	52	14	3	199
Diabetes not mentioned	161	70	12	16	259
TOTAL	400	168	42	22	632

The table illustrates clearly the significant difference observed in the manner of death certification in the case of

agricultural workers as compared with manual and non-manual workers. Only 12 (28.6) percent individuals in the former group failed to have diabetes mentioned in the death certificate in contrast to 161 (40.2 percent) and 71 (41.7 percent) respectively for the other two groups.

PRIMARY CAUSES OF DEATH AMONG DIABETIC PATIENTS

Of the total of 632 death certificates of diabetic patients which were analysed the primary causes of death were determined for 612 cases and are shown in Table 66. The classification adopted for allocating the primary cause of death is based on the "abbreviated list of 50 Causes of Diseases, injuries and causes of death" given in the latest International Classification available, with the difference that, in the case of malignant tumours, further analysis has been made as regards the system of organs involved.

Table 66. / -

Table 66

Primary Causes of Death among 612 Diabetic Patients

Primary Cause of Death	Males		Females	
	Number	Percent	Number	Percent
Diabetes - coma not mentioned	57	25.5	103	25.9
Diabetes - with coma	4	1.0	8	2.0
Tuberculosis	7	3.3	5	1.3
Arteriosclerotid and degenerative heart disease	50	23.2	82	20.6
Chronic rheumatic heart disease	1	0.5	3	0.8
Other diseases of heart	4	1.9	13	3.3
Hypertension with heart disease	3	1.4	12	3.0
Hypertension without heart disease	3	1.4	4	1.0
Vascular lesions of the C.N.S.	11	5.1	54	13.6
Influenza	1	0.5	2	0.5
Pneumonia and bronchitis	7	3.3	10	2.6
Gastritis and other intestinal infections	2	0.9	2	0.5
Nephritis and nephrosis	1	0.5	3	0.8
All other infections	-	-	3	0.8
Senility and other ill-defined causes	5	2.3	8	2.0
Other accidents	3	1.4	5	1.3
Simple prostatic hypertrophy	3	1.4	-	-
Suicides	2	0.9	-	-
All carcinomas	24	12.2	39	10.1
Carcinoma of the oesophagus & stomach	3	1.4	10	2.6
" " " large intestine	3	1.4	3	0.8
" " " genito-urinary organs	1	0.5	7	1.8
" " " pancreas	3	1.4	2	0.5
" " " lungs	6	3.8	4	1.0
" " " prostate	2	0.9	-	-
" " " breast	-	-	5	1.3
" " " liver & biliary system	1	0.5	2	0.5
" " " other organs	5	2.3	6	1.6
Intestinal obstruction, etc.	1	0.5	-	-
Anaemias	-	-	1	0.2
All other diseases	26	12.0	40	10.4
TOTAL	215		397	

It will be observed that diabetes mellitus was mentioned as the primary cause of death in 61 (28.4 percent) male and 111 (27.9 percent) female diabetics. The incidence of deaths from diabetic coma was only 1.9 percent in the case of males and 2.0 percent in females. It will be noted that these figures are almost twice as high as those observed for the group of 325 diabetic patients in the experience of Joslin's clinic, which has already been mentioned (255) in Part I.

The commonest cause of death among both the male and female diabetics was atherosclerotic and degenerative heart disease which accounted for 23.2 percent of all deaths among males and 20.6 percent of the deaths among females. The female diabetics thus seem to have a lesser incidence of arteriosclerotic and degenerative heart disease, in spite of the fact that they tend to survive longer and die at a more advanced age than the male diabetics.

The second most frequent cause of death was the group attributed to vascular lesions of the central nervous system. This group of diseases accounts for 5.1 percent of all deaths among male diabetics and 13.6 percent, in the case of female diabetics. Thus the female diabetics appear to die more frequently from cerebro-vascular lesions than the male diabetics.

Deaths from all malignant tumours on the other hand, appear to be considerably higher among the males than in the case of females. They accounted for 12.2 percent of all deaths among males and 10.8 percent of deaths among females. Detailed analysis of data in relation to deaths from malignant tumours as shown in Table 66

indicate that the higher incidence of malignant tumours in the males is due, mainly to the greater proportion of deaths from carcinoma of the lungs, the pancreas and the large intestine. The female diabetics on the other hand appear to have a higher mortality from carcinoma of the oesophagus and stomach as opposed to male diabetics.

The numbers of patients dying from the other causes are too few to draw any firm conclusions.

In order to see whether there was any significant difference in the percentage of deaths from the various causes among diabetics as compared with those for the general population from which our group of diabetic patients had been obtained, the percentage of deaths occurring from the various causes have been calculated for a control group of individuals from the City of Edinburgh and are presented in Table 67. The control group has been matched for sex, age at death and year of death with the original group. However, the control group includes only 554 cases as it was drawn up at a time when only 554 death certificates of the original group of diabetic patients had been obtained. The discrepancy in numbers in the control group should however, not invalidate the comparability of the two groups to any considerable extent, as shown by the fact that the age and sex distribution of the control group bears a close similarity to the diabetic group. (Vide Table).

Table. / -

Table.

Age and sex distribution of the Diabetic Patients as compared with the control group.

AGE GROUP	DIABETIC GROUP						CONTROL GROUP					
	Male		Female		M. & F.		Male		Female		M. & F.	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent	Number	Percent
0 - 19 years	3	1.37	2	0.49	5	0.79	3	1.49	3	0.85	6	1.08
20 - 39 "	16	7.30	11	2.68	27	4.29	13	6.47	9	2.55	22	3.97
40 - 59 "	38	17.35	59	14.39	97	15.42	42	20.98	52	14.73	94	16.96
60 - 79 "	139	63.47	304	74.14	443	70.42	130	64.67	269	76.20	399	72.02
80 +	23	10.50	34	8.29	57	9.06	13	6.46	20	5.66	33	5.95
TOTAL	219	99.99	410	99.99	629	99.98	201	100.07	353	99.99	554	99.98

Table 67. /-

Table 67

Primary Causes of Death of 554 Individuals.

PRIMARY CAUSE OF DEATH	Males		Females	
	Number	Percent	Number	Percent
Diabetes	2	0.99	4	1.13
Tuberculosis	13	6.47	11	3.14
Arteriosclerotic and degenerative heart disease	56	27.86	90	25.49
Chronic Rheumatic heart disease	9	4.48	8	2.27
Other diseases of heart	1	0.49	2	0.57
Hypertension with heart disease	6	2.98	13	3.68
Hypertension without heart disease	2	0.99	3	0.85
Vascular lesions of the C.N.S.	21.	10.45	39	11.05
Influenza	2	0.99	1	0.28
Pneumonia and Bronchitis	10	4.98	18	5.09
Nephritis and nephrosis	1	0.49	5	1.42
Appendicitis	-	-	1	0.28
Other infections	3	1.49	-	-
Senility and other ill-defined causes	4	1.99	14	3.96
Other accidents	6	2.98	10	2.83
Simple Prostatic Hypertrophy	3	1.49	-	-
Ulcer of stomach and duod enum	3	1.49	1	0.28
Suicides	1	0.49	2	0.57
All carcinomas	35	17.41	73	20.68
Carcinoma of oesophagus and stomach	10	4.98	14	3.96
" " large intestine	7	3.48	12	3.39
" " genito-urinary organs	1	0.49	15	4.25
" " lungs	8	3.98	4	1.13
" " prostate	3	1.49	-	-
" " breast	-	-	10	2.83
" " liver and biliary system	1	0.49	3	0.57
" " other organs	5	2.49	15	4.25
Intestinal Obstructions	2	0.99	3	0.85
Anaemias	-	-	2	0.57
All other diseases	21	10.45	53	15.01
TOTAL	201		353	

The control group shows a slightly greater percentage of deaths occurring from arteriosclerotic and degenerative heart disease. The incidence of carcinoma too, is considerably higher in the control group, particularly so among females who have a rate which is almost double that of the corresponding group of diabetic females. It will be noted however, that 28.4 percent of all male diabetics and 27.9 percent of all female diabetics had their deaths attributed to diabetes mellitus and this makes it somewhat difficult to utilize these tables for the purpose of comparing the incidence of deaths attributed to conditions such as cardio-vascular disease, which have been shown in previous studies to be commoner among diabetic individuals than among the normal population.

We have therefore, compared the incidence of the five main causes of death among diabetic patients, viz. diabetes mellitus, cardio-vascular, cerebro-vascular, cancer and other causes, with those of the control group, in order to observe whether there was indeed any significant difference between diabetics and the general population, when due allowance had been made for age and sex distribution. Tables 67a and 67b show the "Primary Causes of Death" for the diabetic patients and the control group respectively.

Table 67a. / -

Table 67a.

Primary Causes of Death.

Cause of Death	Diabetic Group				Control Group			
	Males		Females		Males		Females	
	Number	Percent	Number	Percent	Number	Percent	Number	Percent
Diabetes Mellitus+	64	-	118	-	2	-	4	-
Cardio-vascular	80	52.98	132	47.14	83	41.71	140	40.11
Cerebro-vascular	12	7.95	57	20.35	21	10.55	41	11.75
Cancer	22	14.47	40	14.28	35	17.59	73	20.92
Others	37.	24.50	51	18.21	60	30.15	95	27.22
TOTAL	215		398		201		353	

+Deaths attributed to diabetes mellitus have been excluded for the purpose of calculating the percentages.

Table 67b.

Combined Primary and Secondary Causes of Death.

CAUSE OF DEATH	DIABETIC GROUP								CONTROL GROUP							
	Male				Female				Male				Female			
	Prim.	Sec.	Total	% of 215 certs.	Prim.	Sec.	Total.	% of 398 certs.	Prim.	Sec.	Total.	% of 201 certs.	Prim.	Sec.	Total.	% of 353 certs.
Diabetes Mellitus	64	58	122	57.6	118	128	246	61.8	2	0	2	1.1	4	6	10	3.1
Cardio-vascular	80	32	112	51.2	132	75	207	52.0	83	23	106	52.7	146	46	186	52.4
Cerebro-vascular	12	15	27	12.5	57	38	95	23.9	21	8	29	14.4	41	27	68	18.7
Cancer	22	6	28	13.0	40	2	42	10.6*	35	1	36	17.9	73	4	77	22.1*
Others	37	56	93	43.3	51	85	136	34.2	66	32	98.	45.8	95	77	172	49.9

+ The difference observed is significant

In order to make the two groups more comparable, in Table 67a, we have excluded those cases which had diabetes mellitus mentioned as the Primary cause of death in calculating the percentages. When this was done it became evident that cardio-vascular causes accounted for the greatest number of deaths in both the diabetic and the control groups. Furthermore, there appears to be a considerable excess of cases attributed to cardio-vascular causes among both males and females in the diabetic group, as compared with those of the control group. This is more evident in the case of the male than the female individual. The differences, though they appear to be large, are not significant.

Deaths attributed to cerebro-vascular causes are greater among the female diabetics, as compared to females of the control group. On the other hand, fewer male diabetics appeared to have cerebro-vascular diseases mentioned as a primary cause of death as compared to males in the control group.

Deaths from cancer appear to be commoner among the control group than among the diabetics, the difference being considerably greater among the females than in the case of the males.

In a further attempt to make the two groups more comparable and also to minimize any adverse effect that the occurrence of "Diabetes Mellitus" as a Primary cause of death in the death certificate, may have in vitiating the assessment of the incidence of conditions such as cardio-vascular diseases, we have combined the Primary and Secondary causes

of death as they appeared on the death certificates in the two groups and have presented them in Table 67b.

This table illustrates one very important fact, viz. that cardio-vascular causes appear either as the primary or as the secondary cause of death, as often in the death certificates of the control group as they do among those of diabetic patients. This observation leads one to conjecture whether there is indeed any greater prevalence of cardio-vascular diseases among diabetic patients as compared with the normal population, when suitable adjustments have been made for the age and sex distribution. This would therefore appear to be a field in which further research is indicated, and would certainly prove profitable.

The incidence of cerebro-vascular disease appears to be somewhat similar to what has already been described above, although the difference observed between the diabetic females and the females of the control group appear to be considerably less when both the primary and secondary causes are considered together.

The same appears to be true for deaths due to cancer in the case of males, although in the case of females, diabetic patients now appear to have cancer mentioned in the death certificates less frequently than in the control group.

DURATION OF DIABETES MELLITUS

The average duration of diabetes for the whole group was approximately 9.3 years as shown in Table 67a.

Table 67a

Average duration of life from the onset of Diabetes Mellitus in 629 patients.*

Group	Average Duration (Years)		
	Males	Females	M + F
1939 - 1940	10.2	10.5	10.6 (approx)
1949 - 1950	7.3	8.1	7.8
Both Groups	9.05	9.36	9.25

Of the figures quoted above, those for the 1939 - 1940 group would approximate more closely to what would normally be expected in the case of diabetic patients as a whole, because approximately 90 percent of this group of patients are dead. The figures for the 1949 - 1950 groups are considerably low. This is to be expected as only some 51.8 percent of this group of patients had died; 221 (38.16 percent) patients were visited, and the majority of these patients were found to be enjoying reasonably good health, with several years of life yet before them. It is possible that these figures would be substantially different (perhaps even better than those for the 1939 - 1940 group), if the investigation were extended for a further 10 - 15 years.

The Association between Sex and Duration of Diabetes

The relationship between the duration of diabetes mellitus and sex, for our group of 632 patients is shown in Table 68.

Table 68

Duration of Diabetes Mellitus of 632 Diabetic Patients according to Sex.

Duration of Diabetes Mellitus (Years)	1939 - 1940		1949 - 1950	
	Males	Females	Males	Females
1	5	8	6	4
1 - 4	28	40	29	54
5 - 9	27	56	44	69
10 - 14	22	51	15	52
15 - 19	25	35	3	6
20 - 24	6	18	3	7
25 - 29	1	6	3	3
30 +	2	1	-	-
Not known	1	-	2	-
Total number of patients	117	215	105	195

The longest duration of life achieved by any patient in the 1939 - 1940 group was 40 years for a male and 30 years for a female. The corresponding figures for the 1949 - 1950 group were 28 years for the male and 27 years for the female.

Influence/

Influence of the age at Onset on the Duration of Diabetes

It has been mentioned earlier that the severity and type of the disease depend to some degree on the age at which the symptoms first begin to manifest themselves. In general, the lower the age at onset, the more severe is the disease likely to be. Consequently, the early onset diabetic has to face all the fatal complications that severe diabetics generally succumb to. Table 69 shows the association between duration of life and the age at which the symptoms first became manifest.

Table 69

Duration of Diabetes of 632 Diabetic Patients According to the Age at onset of the Disease.

Age at Onset (Years)	Duration of Diabetes (Years)			
	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
0 - 9	5.0	-	-	-
10 - 19	10.0	7.4	7.5	7.0
20 - 29	4.2	13.5	7.5	9.0
30 - 39	13.2	15.0	14.0	12.0
40 - 49	15.7	14.2	8.8	12.9
50 - 59	11.6	11.9	10.1	9.3
60 - 69	8.4	8.7	4.9	7.2
70 - 79	4.07	5.0	5.9	4.2
80 +	0.5	-	1.0	-

The feature which appears to be common to all four groups is that the maximum duration of life is achieved when the disease begins sometime between the ages of thirty years and fifty years. The optimum ages at onset varies between the different groups; e.g. among the male diabetics in the 1939 - 1940 group, the longest duration of life was experienced by those who developed the disease sometime between 40 and 50 years. This age group enjoyed an average longevity of over two years more than the next best age group which is that between 30 and 39 years. The shortest duration of life is experienced by those who developed symptoms for the first time after the age of 70 years. This of course is to be expected as the average life expectancy at the age of 70 is only 9.1 years in Scotland. Even so, the diabetic male appears to live for less than half this period.

Another very interesting feature observed in this group of patients is the extremely short duration of life of the individual who acquires diabetes between the ages of 20 and 29. Their duration is only 4.2 years from the onset of first symptoms. It is therefore imperative that this group should receive maximum amount of attention in all programmes directed at increasing the longevity of the diabetic. The factors that have probably contributed towards shortening the life of the juvenile diabetic are multiple; psychological, social and educational factors may all interfere with the satisfactory control of the diabetic during this critical period. These problems have been studied in great detail by numerous authors whose works have been already referred to earlier in Part II of this thesis.

This feature is surprisingly absent in the female diabetic. The duration of life of the female diabetic improves gradually with increase in the age at onset up to the age group 30 - 39 years. Thereafter it diminishes gradually. The shortest duration of life (5 years) is experienced by the 70 - 79 year group.

On the whole, it will be observed that the duration of life of patients in the 1949 - 1950 group are considerably shorter than those of the 1939 - 1940 group. The general pattern is however, similar to what has already been described. The only difference is that, whereas in the 1939 - 1940 group the duration of diabetes increases gradually with increase in age up to a certain point and thereafter gradually declines, there is no such uniformity or smoothness in the curve obtained for the male diabetics of the 1949 - 1950 group. The maximum duration is experienced by those whose onset was between 30 - 39 years. The duration is then shortened to only 8.8 years for the 40 - 49 year group. Thereafter the duration increases to 10.1 years for the 50 - 59 year group. No explanations can be offered to clear up these peculiar fluctuations, besides the fact that the proportion of patients in the 1949 - 1950 group for whom these data were available represent only about 50 percent of the whole group, and is therefore not representative of the group.

Influence of the Type of Disease on Duration

The type of diabetes is the most important factor which determines the prognosis of the diabetic patient. The thin, young individual whose

disease is usually of sudden onset suffers from the more severe type of disease as already explained in Part II; whereas the middle-aged, obese individual who generally develops the symptoms of diabetes insidiously, acquires the milder form of the disease which has a more favourable prognosis than the former.

Table 70

Duration of Diabetes according to the Type of Disease.

Type of Diabetes	1939 - 1940		1949 - 1950	
	Duration (Years)		Duration (Years)	
	Male	Female	Male	Female
Insulin Dependant	10.3	10.6	7.0	8.1
Stable with Diet	10.5	10.5	6.7	7.8
Not known	6.5	9.2	15.0	7.2

The data accumulated for our group of diabetics however, do not appear to conform to this view altogether, as these features are true only for the male diabetics in the 1939 - 1940 group. Insulin-dependant diabetics seem to carry a better prognosis as evidenced by a longer duration in all the other categories. The shorter durations for both sexes in the 1949 - 1950 group are probably due to the same reasons enumerated earlier.

Association between Marital Status and Duration

It has been observed that the incidence of diabetes was considerably

greater among the married than among single persons; and the proportion of married to single persons is greater for the female than for the male diabetic. It has already been shown that single men up to the age of seventy years experienced higher mortality rates from diabetes than married men at the corresponding ages, and that married men had higher rates for ages above seventy. The widowed and divorced males had higher rates than either the single or married groups. For the female diabetics, the pattern of death rates was identical to that of the males up to the age of forty-five; above this age, married women had considerably higher rates than single women.

With a view to determining whether there was any correlation between the marital status of the diabetic and the duration of the disease, the data accumulated for our group of 632 diabetic patients have been analysed as regards the duration of diabetes corresponding to marital status, both at the onset of illness and also at the time of death. The results are presented in Table 71.

Table 71

Duration of Diabetes in 632 Diabetic Patients According to Marital Status.

Marital Status	Marital Status at Onset				Marital Status at Death			
	1939 - 1940		1949 - 1950		1939 - 1940		1949 - 1950	
	Duration (Yrs.)		Duration (Yrs.)		Duration (Yrs.)		Duration (Yrs.)	
	Male	Female	Male	Female	Male	Female	Male	Female
Married	10.5	11.2	7.7	8.2	10.3	9.3	7.4	7.9
Single	10.0	9.3	7.3	7.3	9.2	9.3	6.8	7.3
Widowed	8.1	4.8	2.1	2.2	10.7	11.3	7.2	7.9
Divorced	-	-	-	-	-	10.0	-	-
Not known	10.3	6.3	7.7	6.5	-	24.6	9.0	11.2

It should be noted that the figures illustrated above are subject to two limitations as far as their accuracy is concerned. First, the calculations have been made without taking into consideration the appropriate group of individuals, viz. all age groups have been considered for the purpose of calculating the duration instead of taking only those between 20 and 75+ years. Secondly, the data regarding the marital status of a considerable proportion of patients were not available.

However, the following points are of considerable interest :-

1) The pattern of duration of diabetes for the males in the 1939 - 1940 group is different from that for the females in the same group and for both males and females in the 1949 - 1950 group.

2) Married males have a longer duration than the single males.

3) Married female diabetics of the 1939 - 1940 group have the longest duration of diabetes as compared to either the single or widowed females.

4) Single females appear to have a shorter duration than the single males, while widowed females seem to be the worst affected, with a duration of life only half that of the single female.

5) The durations of life enjoyed by both sexes in the 1949 - 1950 group are considerably shorter than those of the 1939 - 1940 group, for the reasons enumerated earlier. However, in this case too, we observe that married women have the longest

duration, followed by those for single women. The widowed females appear to live only one-third the duration of the single female.

6) In contrast to what has been stated above, the durations corresponding to marital status at death, shows that the widowed persons among both males and females in practially all groups enjoy a longer duration of life than either married or single persons. The only exception is the married female in the 1949 - 1950 group, who apparently has a slightly longer duration.

Association between Social Class and Employment Group, and Duration

The relationship between the social class distribution and the duration of life of our group of diabetic patients is illustrated in Table 72.

Table 72

The duration of diabetes of 631 diabetic patients according to their social class at the time of death.

Social Class	Duration of Diabetes (Years)			
	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
I	16.0	7.0	9.5	6.0
II	13.2	12.1	7.3	8.2
III	9.1	10.5	7.0	6.0
IV	10.3	9.7	7.2	8.4
V	10.1	9.8	10.5	8.4

Male diabetics of Social Class I apparently have the longest duration among all other categories; this group is closely followed by Social Class II. Social Class III has the shortest duration, viz. 9.1 years. Among the females, women in Social Class II seem to fare better than any of the other Social Classes; however the duration achieved by this group is considerably less than that achieved by males in Social Class I. The comparability of these results are however open to question as the number of diabetics in the upper Social Classes were relatively small (vide Table 57).

The association between duration of life and the employment group of 631 diabetics is shown in Table 73.

Table 73

The Duration of Diabetes of 632 Diabetic Patients According to their Employment Group.

Employment Group	Duration of Life (Years)			
	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
Manual	9.6	10.4	7.2	7.8
Non-manual	11.2	10.5	7.1	8.3
Agricultural	9.6	9.0	9.1	7.4
Not known*	16.0	14.3	11.0	10.0

* The relevant data for 1 male and 9 female diabetics of the 1939 - 1940 group and 1 male and 9 female diabetics of the 1949 - 1950 group were not available.

Influence of the Weight at Onset of Diabetes on Duration

The close association that exists between obesity and diabetes mellitus has been discussed in some detail in Part II. Table 74 shows the average duration of diabetes of 632 diabetic patients according to their body weights as recorded at the onset of the disease. In those instances where this was not available the weight recorded on the first visit to the Diabetic Clinic has been taken for making the calculations.

Table 74

The Duration of Diabetes According to Weight at Onset of the Disease.

Weight at Onset of Diabetes expressed as a percentage of Standard Weight.	Duration of Diabetes (Years)			
	1939 - 1940		1949 - 1950	
	Male	Females	Male	Female
< 80	6.8	7.8	6.7	5.2
80 - 89	8.8	8.3	8.3	8.7
90 - 99	13.0	10.8	9.4	6.1
100 - 109	12.8	10.3	5.4	9.0
110 - 119	13.1	11.8	7.5	8.2
120 +	10.2	13.1	7.3	7.4
Not known	7.7	9.2	7.4	8.5

It will be observed that the longest duration of life was experienced by the male diabetic patients in the 1939 - 1940 group who were between 90 and 119 percent of their standard weights. Patients less than 80 percent

of their standard weight had only about half this duration; A slightly less significant reduction was observed for those who were 20 percent above their standard weights. The duration of diabetes of the female diabetics however appear to increase steadily with the gradual increase in body weight. For example, the longest duration of diabetes among females is achieved by those females who were 20 percent or more above their standard weight at the time of diagnosis. The figures obtained for the 1949 - 1950 group of diabetics are not discussed as they do not appear to present any consistent changes corresponding to changes in the weight at onset of diabetes.

Duration of Diabetes in Relation to Place of Death.

The data accumulated for the group of 629 diabetic patients who died subsequent to diagnosis have been analysed with a view to ascertaining whether there was any significant association between the duration of diabetes and the place of death. The data are presented in Table 75.

Table 75

Duration of Diabetes According to Place of Death

Place where Death Occurred.	1939 - 1940				1949 - 1950			
	Male		Female		Male		Female	
	Number	Duration (Years)	Number	Duration (Years)	Number	Duration (Years)	Number	Duration (Years)
Hospital	55	9.9	83	10.0	46	6.5	88	7.7
Other Institution	4	5.2	9	8.3	2	9.0	3	4.6
Nursing Home	-	-	-	-	-	-	1	1.0
Home	49	10.9	107	10.3	46	8.2	98	8.2
Others	8	5.8	16	14.8	9	6.6	5	10.2
TOTAL	116		215		103		195	

It will be observed that the majority of deaths occurred either in the home or in a hospital. A slightly greater number of male diabetics had died in hospital while the majority of female patients had died at home. The duration of diabetes has been on the average longer for the male diabetic than for the female in both groups. Among the male diabetics in the 1939 - 1940 group, the longest duration has been experienced by those who died at home. This group is closely followed by those who had died in hospitals. Those who had died in other institutions such as homes for the ages, convalescent homes, etc. (3 in number) had a duration which was less than half that of patients who had died at home. The last category includes those whose deaths occurred away from home and more particularly, those whohad met with sudden deaths. This group too experienced a comparatively short duration as compared with the other two groups.

Among the female diabetics of the 1939 - 1940 group too, the longest duration of diabetes was experienced by those who had died at home, although this figure (viz. 10.3 years) was considerably less than that for males in the corresponding group (11.8 years).

The duration of diabetes experienced by both sexes in the 1949 - 1950 group were considerably less than those for the other group, but the pattern was more or less identical.

Duration of Diabetes in Relation to the Registration District

Table 76 shows the distribution of diabetic patients and their duration of diabetes among the different registration areas of Scotland.

Table 76

	1939 - 1940				1949 - 1950			
	Male		Female		Male		Female	
	Number	Duration	Number	Duration	Number	Duration	Number	Duration
Edinburgh	64*	10.1	103	10.4	54	7.7	91	8.1
Midlothian	12	15.3	38	10.2	18	6.6	34	8.2
East Lothian	5	11.6	12	11.8	11	6.7	7	3.8
West Lothian	12	9.0	20	10.6	5	8.4	24	8.0
Clackmannan	3	9.0	5	8.7	-	-	2	13.0
Stirling	1	6.0	7	13.8	3	9.0	3	10.0
Peebles	4	12.0	4	6.2	1	20.0	1	5.0
Berwickshire	3	4.5	6	7.6	5	3.9	11	6.5
Selkirk	2	5.5	2	3.5	2	-	3	5.0
Roxburgh	2	10.5	8	11.2	2	9.5	4	9.2
Lanark	2	12.0	5	14.0	2	3.0	11	9.5
Rest of Scotland	6	7.0	5	11.1	2	6.0	4	4.0
	116		215		105		195	

* Duration of Diabetes was not available for 1 patient.

It will be observed that approximately 50 percent of the patients who had died were residents of Edinburgh, and between 20 and 30 percent were from the counties of Mid Lothian and West Lothian. Among the male diabetic patients in the 1939 - 1940 group the longest duration (viz.15.3 years) was experienced by those patients living in the Mid Lothian area, while the shortest duration was experienced by two patients from Selkirk,

who survived for an average duration of only $5\frac{1}{2}$ years from the onset of symptoms. It is of considerable interest to note that the male diabetic living in the county of Midlothian experienced the longest duration among all other groups. In the case of females, the longest duration of diabetes was experienced by patients who lived in Lanark (viz. 14 years) with Stirling coming a close second with an average duration of 13.8 years for only one patient. The lowest duration for the females is again experienced by two diabetic patients from Selkirk who survived for only $3\frac{1}{2}$ years from the onset of first symptoms.

It is however, evident that the groups that have been considered are not strictly comparable and as such the relative "durations" of their diabetes as illustrated above are open to correction. To begin with, the numbers included in the different groups are not equal and far too small to make direct comparison between them. It is also possible that the patients who survived the shortest duration, viz. those from Selkirk, belonged to a somewhat different class of patients in comparison to those from Edinburgh, and the Midlothian districts. It is quite likely that these patients were suffering from a more severe type of diabetes mellitus and probably had other associated complications which necessitated their being referred to the Diabetic Clinic at the Royal Infirmary, whereas, had they belonged to the milder type unassociated with other complications, the chances are that they would have continued to be supervised by their own general practitioners, as is usually the case in remote areas. On the other hand, diabetic patients from Edinburgh and its suburbs tend to be drawn up from all categories of patients (both mild and severe) as it is more

convenient for the patient and the general practitioner alike to make use of a specialised clinic near at hand. Furthermore, the number of patients from these areas are comparatively large when compared with those from the more remote regions. Thus, the durations of life of the diabetic patients from these regions would tend to approximate nearer to the average duration for the whole group than other areas.

CALCULATION OF A LIFE TABLE FOR THE DIABETICS AND IN COMPARISON WITH THE SCOTTISH LIFE TABLE.

The expectation of life of the diabetic patient as calculated from a consideration of all deaths alone as was frequently done in the past, does not give a true picture regarding the actual expectation of life experienced by them because of the fact that the contribution to the total life expectancy made by the surviving diabetics at the time such a calculation was made, have not been properly calculated in making such an estimation. In the past it was customary to consider the further expectancy of life of a diabetic as approximately two-thirds - three-quarters the life expectancy of a normal individual of the same age.(258)

For the purpose of the present study, we have considered both the duration of life lived up to date by the dead as well as the survivors, and have also made an allowance for the further expectation of life that the survivors would, under normal circumstances and on the basis of past experience, be expected to achieve in the future. This latter estimation was calculated as follows :-

The further expectations of life of a surviving diabetic was taken as the period of further life expectancy which he would have achieved under normal circumstances multiplied by the proportion of survivors to total number of diabetics in that particular age group. This factor viz. $\left(\frac{\text{Survivors}}{\text{Total number of Diabetic Patients}}\right)$ would give us an approximate idea of the chances of survival that this particular groups of diabetics had been subjected to in the past, and which therefore could also be expected to hold true for the future.

The following instance is given as an illustration of the method

in which the calculation was made.

e.g. A diabetic patient who was 25 years old in 1939, would have survived 22 years by 1961, and his age would then be 47 years. The further expectation of life for this individual is then obtained by referring to the Scottish Life Table for 1960. This figure, however does not give us the true estimate for this particular individual, and only gives us an approximate idea of how long a person aged 47 years in 1960 would be expected to live. In order to calculate the true expectation of life for this particular individual, we refer to a graph showing the "percentage expectancy of life" for the cohort of people aged 25 years at the subsequent age groups. This graph is drawn by making use of the l_x column in the Abridged Life Table, 1960 for Scotland. Thus the true expectation of life for this individual would be his expectation of life as shown in the Life Table multiplied by the "Percentage of life expectancy" at the age of 47 years obtained by referring to the graph showing the "percentage life expectancy" for the cohort aged 25 years.

The diabetic patient however does not have the same chances of survival as the normal individual. Therefore, in estimating his chances of survival we make use of the experience derived by his particular age group of diabetics as observed in our follow-up. In this particular instance, out of a total of 7 diabetic patients who were aged 25 years in 1939, four patients had died and only three were alive. Therefore we consider that for this particular age group of diabetics, the chances of survival, based on past experience would be 3/7. Thus in order to estimate the future life expectancy for this patient, we have to multiply

FIG. 8

EXPECTATION OF LIFE OF MALE DIABETIC PATIENTS COMPARED WITH THE LIFE EXPECTANCY OF NORMAL MALES IN SCOTLAND 1960

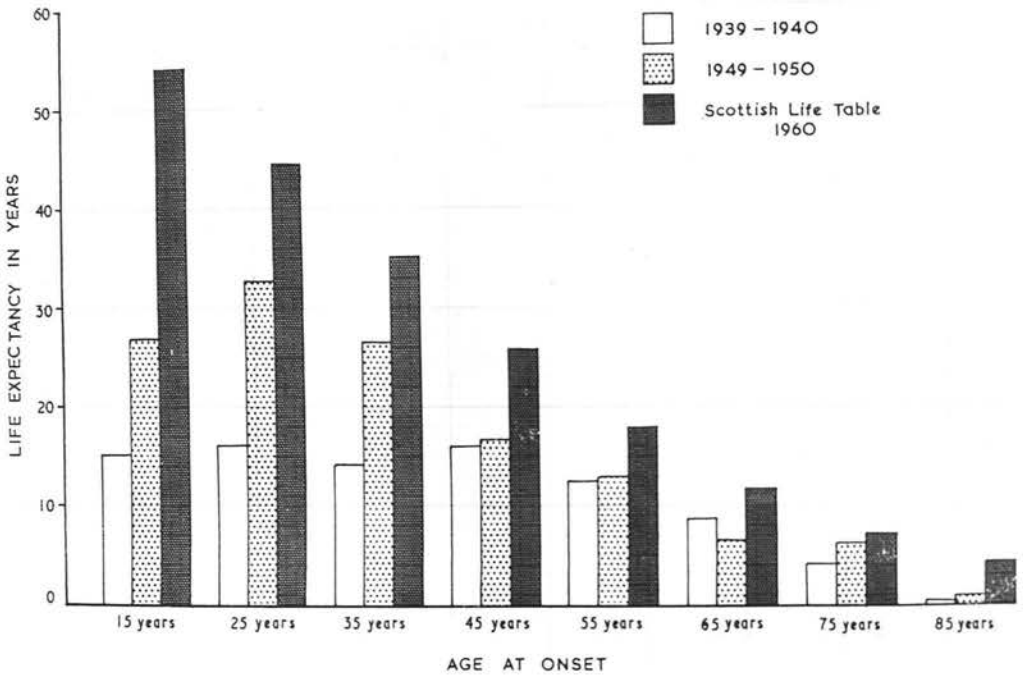
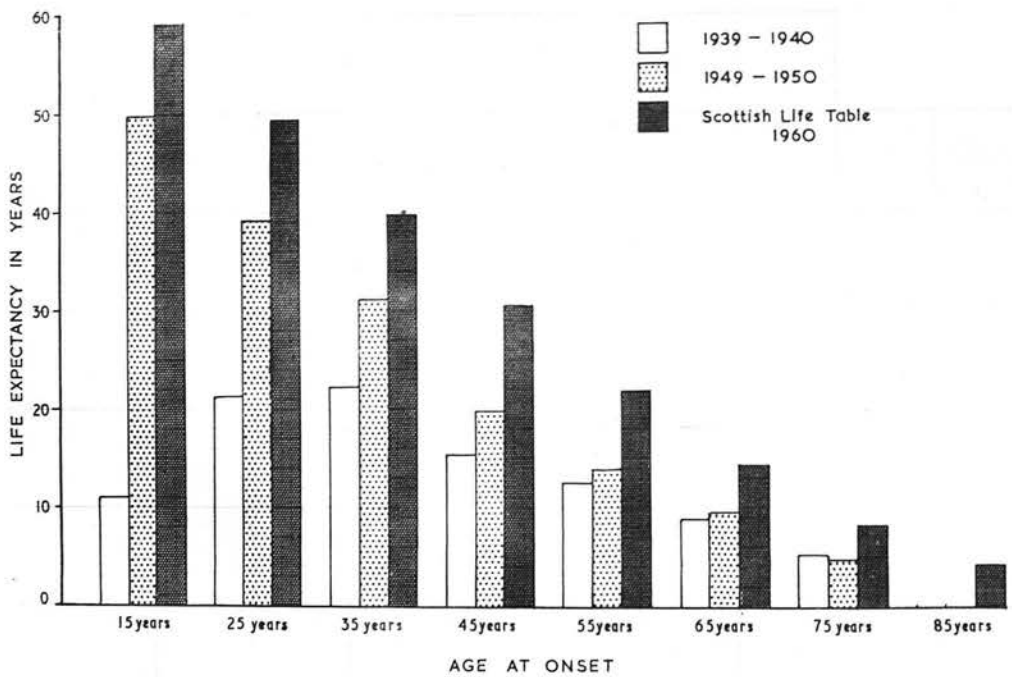


FIG. 9

EXPECTATION OF LIFE OF FEMALE DIABETIC PATIENTS COMPARED WITH THE LIFE EXPECTANCY OF NORMAL FEMALES IN SCOTLAND 1960



the original figure obtained earlier by 3/7. This would give us the true expectation of life for this diabetic patient.

The life table constructed in this manner for our two groups of diabetic patients have been compared with the Scottish Life Table 1960 and is shown in Table 77 and Figures 8 and 9.

Table 77

Life Table for the Two Groups of Diabetic Patients Compared with the Scottish Life Table, 1960.

Age (Years)*	Males			Females		
	Diabetics 1939/40	Diabetics 1949/50	Life Table 1960	Diabetics 1939/40	Diabetics 1949/50	Life Table 1960
15	15.15	26.91	54.06	11.0	49.76	59.09
25	16.17	32.95	44.52	21.28	39.09	49.33
35	14.09	26.69	35.09	22.08	31.11	39.70
45	16.01	16.77	25.98	15.33	19.88	30.48
55	12.50	12.93	17.91	12.39	13.73	21.83
65	8.85	6.55	11.63	8.93	9.48	14.14
75	4.07	6.32	7.04	5.09	4.58	8.15
85	0.5	1.00	4.26	-	-	4.19

* Age at onset of Diabetes in the case of Diabetic patients.

Figure 7, which shows the trend in the expectation of life for male diabetics of the two groups 1939 - 1940 and 1949 - 1950, illustrates the remarkable improvement achieved as regards the prognosis of the diabetic

individual during the last decade. There has been a considerable improvement in the expectation of life of male diabetics, up to the age of forty-five and again after the age of seventy years. The greatest improvement is shown at the age of twenty-five years, where the increase in the expectation of life in the 1949 - 1950 group is almost double that of the 1939 - 1940 group. Thereafter, the improvement observed becomes less well marked until the two groups have identical expectations of life at about the age of 45 - 46 years. From the age of forty-five up to seventy years, we observe the unusual phenomenon of a diminished expectation of life for the 1949 - 1950 group as compared with the 1939 - 1940 group. The difference is most marked at the age of sixty-five years. From the age of seventy years onwards, the 1949 - 1950 group shows an increasing life expectancy as compared with the other group. The prognosis of the diabetic at this period is so good that his life expectancy is only slightly less than that of the normal individual at the age of eighty-five years.

The expectation of life of the female diabetic in the 1939 - 1940 group has been on the whole better than that for the male in the same group except at ages up to fifteen years and again around forty-five years. The life expectancy at the age of fifteen years in particular is extremely low (viz. 11 years). The improvement in the life expectancy achieved by this group in the ten year period is remarkable in that it is almost four-times that of the 1939 - 1940 group. The gap between the two groups narrows to some extent as the age advances, until after the age of seventy years the 1949 - 1950 group has a lower life expectation, than the 1939 - 1940

female diabetic!

When we compare the male diabetic of the 1949 - 1950 group with the average Scottish male subject, we observe that the expectation of life of the diabetic is well below that of the latter except at the latter extreme of life when the difference is negligible. This difference, as could be well expected, is greatest at the younger age groups. For example, at the age of fifteen years, the diabetic individual at present has a life expectation of only half that of a normal individual of the same age. The position however improves as the age at onset of diabetes increases, so that a diabetic individual who develops symptoms at the age of twenty-five years would have approximately about two-thirds the normal life expectancy for his age, and at thirty-five years it would be almost three-quarters of the normal.

The prognosis of the female diabetic appears to have improved enormously in comparison with that of the males. For example, the female diabetic who develops symptoms at the age of fifteen years, has an expectation of life of 49.76 years, which is more than 80 percent of the normal life expectation for an individual of that age. Unlike in the case of the male, this favourable position is noted only among the younger age groups as shown by a gradual diminition in the expectation of life when compared with the normal for their age (Table 78).

Table 78/

Table 78

Expectation of Life of Diabetic Patients Expressed as a Percentage of that of the Corresponding Age Groups in the Scottish Life Table - 1960.

Age at Onset of Diabetes Mellitus	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
15	28 %	18 %	49 %	84 %
25	36 "	43 "	74 "	79 "
35	40 "	55 "	76 "	78 "
45	62 "	50 "	64 "	65 "
55	70 "	56 "	72 "	62 "
65	76 "	63 "	56 "	67 "
75	57.8 "	62 "	89 "	56 "

The extremely short expectation of life of the female diabetic of the 1939 - 1940 group who developed diabetic symptoms between the ages of 10 - 19 years, has been commented upon earlier. It is difficult to understand as to why this particular age group should have such a low expectation of life. Out of the six patients who were originally included in this group only one has survived up to now; and the average duration of diabetes for the five patients who had died was only 7.4 years as compared with the group average of 10.5 years.

On the other hand, out of seven male diabetics who developed diabetes between the ages of 10 and 15 years, three have survived up to now and have lived an average of 22.6 years. The four patients who had

died, lived for an average period of 10 years. This compares favourably with the average duration for all males in this group.

With a view to ascertaining whether there were any other reasons as to why these young female diabetics showed a lower life expectancy than was generally expected, we have analysed the Primary Causes of Death of the 325 diabetic patients in the 1939 - 1940 group by sex and also as to whether they died before or after the age of forty years. The data are presented in Table 79.

Table 79/

Table 79

Analysis of the Primary Causes of Death of 325 Diabetic Patients According to whether the death occurred Before or After the age of 40 Years - (1939 - 1940 Group).

PRIMARY CAUSE OF DEATH	MALES		FEMALES	
	< 40 Years	40+ Yrs.	< 40 Yrs.	40+ Years
Diabetes	6	30	2	55
Diabetic Coma	1	2	2	4
Tuberculosis	2	1	1	2
Arteriosclerotic & Degenerative Heart Disease	1	23	-	38
Chronic Rheumatic Heart Disease	-	-	-	2
Other diseases of the Heart	-	2	-	9
Hypertension with Heart Disease	-	1	-	8
Hypertension without Heart Disease	-	1	-	2
Vascular lesions of C.N.S.	-	5	1	25
Influenza	-	-	-	2
Pneumonia & Bronchitis	1	2	-	6
Gastritis & Other Intestinal Infections	-	-	-	2
Nephritis & Nephrosis	-	1	-	1
All other infections	-	-	1	1
Senility & other ill-defined causes	-	3	-	6
Other accidents	-	1	1	1
Suicides	1	-	-	-
Simple Prostatic Hypertrophy	1	1	-	-
Malignant tumours	1	12	-	18
All other diseases	1	16	1	19
TOTAL	14	101	9	201

The numbers involved in the above analysis are too small to supply any conclusive evidence, but it will be seen that almost 77 percent of the female diabetic patients whose death occurred before the age of forty years died of some acute catastrophe such as acute exacerbation of the diabetic state, tuberculosis, infections or accidents. On the other hand, among the female diabetics whose deaths occurred after the age of forty years, these causes accounted for only 36.3 percent of the deaths. Among the male diabetics of the same group, the percentage of individuals dying from the above conditions was only 71.2 percent for the "below forty" group as compared with 36 percent for those above forty years.

PART IV

ANALYSIS OF SURVIVING DIABETICS

The data relating to those diabetics who are yet alive and those whose whereabouts are not known will be described in the following chapter. It has already been mentioned earlier that out of the total of 959 patients considered in this study, 632 patients were known to have died; of the remaining 327 patients, 249 were alive and were visited; 35 were known to be alive but were not visited as they lived too far away. No information was available regarding the remaining 43 patients. The distribution of this group of patients according to the year of first visit to the Diabetic Clinic is shown in Table 80.

Table 80

Status	1939	1940	1949	1950	Total
Alive & Visited	13	14	108	114	249
Alive - not visited	5	4	15	11	35
No Trace	6	6	15	16	43
Total	24	24	138	141	327

The sex distribution of the patients among the different groups was characteristic in that there were more males than females in the 1939 - 1940 group, whereas the proportion of female to male patients was greater in the 1949 - 1950 group. (Table 81).

Table 81/

Table 81

Sex Distribution

Status	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
Alive and Visited	15	12	67	155
Alive - not visited	5	4	12	14
No Trace	8	4	13	18

The ages at onset of diabetes mellitus among the different groups are shown in Table 82.

Table 82

Age at Onset of Diabetes Mellitus.

STATUS	Age at Onset (Years)										TOTAL
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80 +	D.K.	
1939 - 1940											
Alive & Visited :											
Males	1	3	3	4	2	1	1	-	-	-	15
Females	-	1	2	4	2	2	1	-	-	-	12
Alive - Not Visited:											
Males	-	1	1	-	-	2	1	-	-	-	5
Females	-	-	1	-	2	1	-	-	-	-	4
No trace:											
Males	-	1	3	2	1	-	-	-	-	1	8
Females	-	-	-	2	2	-	-	-	-	-	4
1949 - 1950											
Alive & Visited:											
Males	-	5	6	15	16	17	7	1	-	-	67
Females	1	9	11	16	31	57	28	2	-	-	155
Alive - Not Visited:											
Males	-	2	3	3	1	3	-	-	-	-	12
Females	1	-	1	2	1	3	6	-	-	-	14
No trace:											
Males	-	-	-	1	5	3	4	-	-	-	13
Females	1	1	2	-	3	7	1	3	-	-	16

It will be observed that male diabetics in both the 1939 - 1940 and 1949 - 1950 groups appeared to develop diabetes at a somewhat earlier age than female diabetics. Among the diabetic patients belonging to the 1939 - 1940 group who were visited, the peak incidence of diabetes had occurred in the third decade, whereas in the case of the male diabetic in the same group, the number of cases were more evenly spaced out between the first and the third decades. The same phenomenon was observed in the case of female diabetics belonging to the 1949 - 1950 group, although, in this instance, the peak incidence of diabetes was observed to occur in the fifth decade. The high incidence among the male diabetics was observed to be evenly spread over the 3rd, 4th and 5th decades without any such characteristic peak.

Type of Diabetes Mellitus

The distribution of the 249 diabetic patients who were visited according to the type of disease, viz. whether they were dependant on insulin for stabilization or whether they were controlled by diet alone or required oral antiglycosuric agents, is shown in Table 83.

Table 83

Group	Insulin Dependent	Stabilized with diet	Stabilized with other drugs.	Not Known	Total
1949 - 1950					
Males	46	19	2	-	67
Females	85	60	10	-	155
1939 - 1940					
Males	7	6	-	2	15
Females	5	7	-	-	12
TOTAL	143	92	12	2	249

When both groups are taken together, we can observe that the majority of patients (57.43%) required insulin for stabilization of their diabetes at the onset of illness, whereas only 36.94 percent were stabilized by dietetic restriction alone. When the two groups are studied separately and the two sexes considered individually, it is observed that, in general, male diabetics were more dependant on insulin for stabilization than the female diabetics. Also the proportion of insulin dependant diabetics seemed to be greater than those who could be stabilized on diet restriction alone for both males and females in the 1949 - 1950 group.

This feature, however, was not present in the case of the 1939-1940 group, where the proportion of female diabetics who could be stabilized by diet, etc., restriction alone, exceeded those who required insulin for stabilization. The male diabetics, however, showed the same relationship as observed for those in the 1949 - 1950 group.

Obesity

The important part played by obesity in the aetiology of diabetes mellitus has been discussed in some detail in the preceding chapters. The beneficial effect produced by reducing the weight of the obese individual in improving his glucose tolerance and to some small extent by reducing their chances of developing premature degenerative cardio vascular changes is well known.

In order to assess how far these observations were true for our own group of patients, we have compared the present weights of the patients

who were alive and visited with their corresponding weights at the onset of the disease. For the sake of conformity and more accurate comparison we have taken the weights as a percentage of the standard weight for the individual based on his or her age and height at the time of examination.

These findings are summarised in Table 84.

Table 84

Percentage of Standard Weight of 249 Diabetic Patients.

% of Standard Weight	Weight at Onset of Diabetes M.						Weight at Present					
	1939-1940		1949-1950		Total		1939-1940		1949-1950		Total	
	M.	F.	M.	F.	No.	%	M.	F.	M.	F.	No.	%
< 80	4	1	5	20	30	12.04	-	1	2	8	11	4.41
80 - 89	4	1	20	16	41	16.46	5	-	10	22	37	14.86
90 - 99	0	2	10	26	38	15.26	3	1	18	41	63	25.30
100 - 109	1	4	16	26	47	18.87	1	4	21	43	69	27.71
110 - 119	3	1	4	27	35	14.05	1	2	5	19	27	10.84
120 +	0	2	6	27	35	14.05	0	2	3	15	20	8.03
Not Known	3	1	6	13	23	9.23	5	2	8	7	22	8.83
TOTAL	15	12	67	155	249		15	12	67	155	219	

Data relating to weight at onset of disease for 23 patients and for the present weight in 22 patients were not available. However it will be observed that, at the time the diagnosis was first made, only 34.13 percent of the 249 patients were found to be within 10 percent of their standard weights while 28.5 percent were less than 10 percent of their standard weights, and a further 28.1 percent, more than 10 percent of their standard weight. The degree of control maintained by way of proper dietetic control is shown by the fact that almost 53 percent of all patients were at the time of interviewing within 10 percent of their standard weights. A further 19.27 percent were 10 percent or below the standard weight and only 18.87 percent were 10 percent or more above the standard weight. When the sexes are considered separately we observe an overall improvement in the weights of patients of both sexes. However the greatest improvement has been shown by patients belonging to the 1949 - 1950 group, e.g. the proportion of patients who were 10 percent (above or below their standard weight) at onset of diabetes was 38.8 percent for males and 33.54 percent for females. 37.31 percent of the male diabetics and 23.33 percent of the females were 10 percent or more below the standard weight while 14.85 percent of males and 34.84 percent of the female diabetics were 10 percent or more above their standard weights.

At the time these patients were visited, 58.2 percent of the males and 54.19 percent of the female diabetics were found to be within 10 percent of their standard weights, while 17.9 percent of the male and 19.35 percent of the female diabetics were 10 percent or more

below their standard weights. The proportion of female diabetics weighing 10 percent or more above the standard weight was 21.92 percent whereas only 19.4 percent of the males were in this category. In general, there has been a diminution of both the underweight and overweight diabetics among both sexes in our surviving diabetics.

The number of diabetics studied in the 1939 - 1940 groups are too few to draw any firm conclusions; these too, however, tend to show in general, the same picture as illustrated by the 1949 - 1950 group.

Degree of Medical Supervision.

In an effort to find out the amount of medical supervision maintained over the control of their diabetic state, the patients who were interviewed were asked to state the frequency with which they attended either the diabetic clinic or their own general practitioner for supervision of their diabetic state. The results are summarised in Tables 85 and 86 respectively.

Table 85

Attendance at the Diabetic Clinic

Group	Regularly	Irr-egularly	None	Not known	Total
1949 - 1950					
Males	39	22	6	-	67
Females	83	70	2	-	155
1939 - 1940					
Males	3	9	2	1	15
Females	2	5	4	1	12
Total	127	106	14	2	249

It will be observed that as many as 127 patients (51 percent) attended the clinic regularly for supervision of their diabetic state and a further 106 patients (42.57 percent) attended the clinic at sometime or another, although not so regularly as the former group. Only 14 patients (5.62 percent) failed to report at the diabetic clinic after the initial diagnosis of their diabetic state.

When the two groups (viz. the 1949 - 1950 and the 1939 - 1940) are studied separately, it is observed that the percentage of patients who defaulted from attending the diabetic clinic was greater in the 1939 - 1940 group than in the 1949 - 1950 group. The percentage of defaulters in this group was greater among female diabetics (viz. 33.33 percent) than among the male diabetics (13.33 percent). The number of defaulters among the 1949 - 1950 diabetics was considerably lower and hardly significant.

Table 86

Supervision by General Practitioner

Group	Regularly	Irr-egularly	None	Not known	Total
1949 - 1950					
Males	3	14	47	3	67
Females	26	35	93	1	155
1939 - 1940					
Males	2	3	9	1	15
Females	1	2	8	1	12
TOTAL	32	54	157	6	249

As illustrated in the above table, relatively fewer diabetics (34.53 percent) availed themselves of the services of their family doctor in keeping their diabetic state under control. The degree to which such supervision was sought for, differed between the two sexes in the two groups of patients; e.g. whereas 40 percent of the female diabetics in in 1949 - 1950 group sought the help of their family doctor in keeping their disease under control, only 29.9 percent of the male diabetics in the same group availed themselves of their help. This position is found to be reversed in the case of the 1939 - 1940 group of diabetics. In this group 40 percent of the male diabetics stated that they paid regular visits to their family doctor, while only 33.4 percent of the female diabetics affirmed that they did so.

Frequency of Urine Tests

Some idea of the degree of attention shown by the patients towards maintaining satisfactory control of their diabetic state could be obtained by ascertaining the frequency with which such patients carry out the routine testing of their urine. With this idea in mind, the 249 patients who were visited, were asked to state whether they carried out such urine tests regularly (i.e. at least once a fortnight), or irregularly or not at all. The results obtained from this questionnaire are given in table 87.

Table 87/

Table 87

Frequency of Urine Tests

Group	Regular	Irregular	None	Unknown	Total
1949 - 1950					
Males	37	23	4	3	67
Females	78	62	12	3	155
1939 - 1940					
Males	5	7	2	1	15
Females	5	1	5	1	12
Total	125	93	23	8	249

Data relating to 8 patients could not be ascertained. Of the 249 patients, 125 (50.2 percent) stated that they examined their urine at regular intervals and a further 37.34 percent were found to examine their urine at some time or another, although not so regularly as the former group. Only 23 patients (9.23 percent) stated that theynever tested their urine. A considerably larger proportion of male diabetics as compared to females stated that they tested their urine at some time or another. This tendency was more marked particularly in the 1939 - 1940 group where almost 80% of the male diabetic patients examined their urine samples at regular or irregular intervals, whereas only 50 percent of female diabetics in the corresponding group stated that they ever did so.

Present Treatment

The method of treatment of diabetes followed by the patients at the time of the interview is shown in Table 88.

Table 88

Treatment of Diabetes in 249 Diabetic Patients

Group	Insulin	Oral Drug	Diet	No Treatment	Unknown	Total
1949 - 1950						
Males	43	5	11	7	1	67
Females	79	30	31	14	1	155
1939 - 1940						
Males	6	2	2	2	3	15
Females	4	1	1	5	1	12
Total	132	38	45	28	6	249

Of the 249 diabetic patients who were visited, accurate particulars regarding the present mode of treatment was not available for 6 patients (2.4 percent). 132 patients (53.01 percent) were being treated with insulin while a further 38 patients (15.26 percent) required oral antiglycosuric drugs for control of their diabetic state. 45 patients (18.07 percent) maintained adequate control with the aid of dietetic restriction alone, while 28 patients (11.24 percent) received no form of treatment at all.

Of the 12 female diabetics who were followed up from 1939 - 1940 only 4 (33.3 percent) were taking regular insulin while one patient was being treated with an oral antiglycosuric agent. One patient was maintaining adequate control by diet restriction alone. Five patients (41.66 percent) were not following any form of treatment. The position

was more or less similar for the male diabetics in the same group. 6 patients (40 percent) were stabilised on insulin, while 2 (13.3 percent) were being controlled by diet restriction. Only 2 patients were not following any form of treatment.

The proportion of patients who were dependant on insulin among the 1949 - 1950 group appeared to be considerably larger as shown by the fact that 43 male diabetics (64.17 percent) were regularly taking insulin injections, whereas only 11 (16.41 percent) were being treated by diet restriction alone. Only 7 patients (10.44 percent) were not taking any form of treatment.

A correspondingly fewer number of female diabetics (viz. 79 50.96 percent) were found to take regular insulin injections, whereas a slightly larger percentage, viz. 20 percent were maintaining adequate control with dietetic restriction. 14 patients (9.03 percent) followed no form of therapy.

Marital State

Table 89 shows the marital status of 327 diabetic patients at the time of diagnosis and Table 90 shows the present marital status of the 249 diabetic patients who were interviewed.

Table 89/

Table 89

Marital Status at Onset of Diabetes

Status	Marital State					Total
	Married	Single	Widowed	Separated	Not Known	
1939 - 1940						
Alive & Visited:						
Males	6	8	-	-	1	15
Females	8	2	2	-	-	12
Alive - not Visited:						
Males	2	2	1	-	-	5
Females	3	1	-	-	-	4
No Trace:						
Males	2	4	-	-	2	8
Females	3	1	-	-	-	4
1949 - 1950						
Alive & Visited:						
Males	52	10	4	1	-	67
Females	101	27	25	2	-	155
Alive - not Visited						
Males	7	4	-	-	1	12
Females	10	3	1	-	-	14
No Trace:						
Males	10	1	-	-	2	13
Females	13	5	-	-	-	18

Table 90

Present Marital State of 249 Diabetic Patients

STATUS	Marital State					TOTAL
	Married	Single	Widowed	Separated	Not Known	
1949 - 1950						
Males	57	4	6	-	-	67
Females	82	17	53	3	-	155
1939 - 1940						
Males	6	5	3	-	1	15
Females	5	2	4	1	-	12
	150	28	66	4	1	249

It will be observed that there were more single than married individuals among males at the onset of diabetes unlike that in the case of females of the 1939 - 1940 group among whom there was a greater preponderance of married persons. In the 1949 - 1950 group, however, the proportion of married to single individuals appears to be identical for both males and females; e.g. the married, widowed or separated males accounted for 85.07 percent of the total as opposed to 14.92 percent for single males, while the relative percentages for the female diabetics were 82.58 percent and 17.42 percent respectively. The changes that have occurred with regard to marital status during the years between the onset of diabetes and the present time is shown in Table 90. This shows a reduction in the proportion of single individuals among both males and females of both groups. The total married, widowed or separated individuals have increased among both sexes belonging to both groups.

Social Class Distribution

The distribution of patients according to their social class and employment group is shown in Table 91.

Table 91/

Table 91

Social Class and Employment Group of 327 Diabetic Patients.

STATUS	I	II			III			IV			V	Not known	TOTAL
		Non-manual	Manual	Agricultural	Non-manual	Manual	Agricultural	Non-Manual	Manual	Agricultural	Non manual		
Alive & Visited: 1949-1950													
Males	3	1	13	-	19	14	-	6	4	2	3	2	67
Females	3	1	22	4	57	18	1	14	10	11	8	6	155
1939-1940													
Males	1	-	3	-	4	3	-	2	-	-	1	1	15
Females	1	-	2	-	6	1	-	-	-	-	1	1	12
Alive & Not Visited: (Both groups & Both sexes).	4	-	3	3	2	1	-	-	-	2	-	20	35
No Trace: (Both groups & Both sexes).	1	-	2	1	3	6	-	2	1	1	2	24	43
TOTAL	13	2	45	8	91	43	1	24	15	16	15	54	327

Of the 249 patients who were alive and visited, the majority of patients belonged to Social Class III. Social Class IV was the next most common group, and this was followed by Social Classes II, V and I respectively. When the different social classes were further subdivided into the three major employment groups, viz. non-manual, manual and agricultural workers, certain interesting features revealed themselves.

As one would normally expect, the greatest number of individuals in Social Class III appeared to be drawn up from among non-manual workers. They were followed by the manual worker, while there was only one diabetic patient drawn from among agricultural workers. The same situation was seen among the patients belonging to Social Class IV; although, in this group however, the proportion of diabetic patients who were taken from among agricultural workers was considerably higher than in any of the other groups.

There is also an interesting sex distribution among the diabetics belonging to the different Social Classes, e.g. among the male diabetics the largest number seem to be drawn up from among the non-manual workers belonging to Social Class III. They are followed by the manual workers of the same Social Class. The next most frequent category is the manual group in Social Class II. They are in turn followed by the non-manual of Social Classes IV and V respectively. The situation is different in the case of the female diabetics. Here we observe that the largest number of female diabetics are drawn up from among the non-manual workers in Social Class III as was seen in the case of male diabetics. The second largest group, however is the normal group in Social Class II. This is closely followed by the manual workers in Social Class III. Non-manual workers in Social Class IV occupy the fourth place and they are followed by the agricultural and non-manual workers of Social Class IV and non-manual workers of Social Class V respectively.

The patients belonging to the different Social Classes in the 1939 - 1940 group are too few in number to draw any valid conclusions.

Occupations and Socio-Economic Group

The distribution of patients according to their socio-economic groups is shown in Table 92.

Table 92

Distribution of Patients According to their Socio-Economic Groups.

Socio-Economic Group	1939 - 1940		1949 - 1950	
	Male	Female	Male	Female
1. Employers, Managers, etc. (Large establishments)	1	-	5	7
2. Employers, Managers, etc. (Small establishments)	2	2	7	8
3. Professional Workers (Self employed)	-	-	-	1
4. Professional Workers (Employees)	1	1	3	2
5. Intermediate non-manual workers	-	1	2	7
6. Junior non-manual workers	3	1	16	21
7. Personal Service workers	-	1	-	8
8. Foreman & Supervisors - Manual	-	-	1	6
9. Skilled manual workers	1	1	3	8
10. Semi-skilled Manual workers	2	-	6	15
11. Unskilled manual workers	1	1	3	8
12. Own account workers (other than Professional)	1	-	2	3
13. Farmers - Employers & Managers	-	-	-	4
14. Farmers - Own account	-	-	-	-
15. Agricultural workers	-	-	2	12
16. Members of Armed Forces	-	-	-	-
17. Not known	1	1	2	6

The largest number of diabetic patients appeared to have been drawn from among skilled manual workers. The second largest group was that of junior non-manual workers. Of considerable interest is the fact that wives of agricultural workers and semi-skilled manual workers appeared to be more prone to diabetes mellitus than those of managers and other employers.

Effect of Diabetes Mellitus on Occupation

The presence of a large number of female diabetics among our group of diabetic patients who were interviewed who had not engaged in any remunerative occupation other than the role of housewife, has tended to diminish the validity of our data relating to any deleterious effect if any, that diabetes mellitus may have produced on the stability of their employment status.

The relevant data accumulated for these 249 diabetic patients are shown in Table 93.

Table 93

Effect of Diabetes Mellitus on Occupation

Group	Retired or changed because of Diabetes M.	Retired or changed because of other causes.	No change	Not Known	Total
1949 - 1950					
Males	7	22	36	2	67
Females	7	10	136	3	155
1939 - 1940					
Males	2	4	7	2	15
Females	1	1	10	-	12
TOTAL	17	37	189	7	249

Of the total of 249 patients, data relating to 7 (2.8 percent) were not ascertained. 189 (75.9 percent) had not changed their occupation since the diagnosis of diabetes. Only 17 patients (6.82 percent) had to change their occupation or retire due to diabetes, whereas 37 patients (14.85 percent) changed or retired from their occupations for other reasons. Only 6 (40 percent) of the 15 male diabetics had changed or retired from their occupations and only one-third of this number had changed or retired from their occupation primarily as a result of diabetes. The percentage of male diabetics who either changed or retired from their occupations in the 1949 - 1950 group too, was similar to that of the 1939 - 1940 group (viz. 43.2 percent). The percentage of those whose retirement or change of occupation was attributed to diabetes,mellitus, was however slightly smaller (viz. 10.4 percent).

SUMMARY AND CONCLUSIONS

An attempt has been made in the preceding study to evaluate the present position with regard to the prognosis and the longevity of individuals suffering from diabetes mellitus, and also to determine the extent to which mortality data could be relied upon to supply useful information regarding their status. The study was based primarily upon the follow-up of two cohorts of individuals who had come to the Diabetic Clinic at the Royal Infirmary, Edinburgh, during the years 1939/1940 and 1949/1950 for diagnosis and treatment of glycosuria. The total number of patients included in the study was 959. Of these, 380 patients (145 males and 235 females) belonged to the 1939/1940 group, and 579 patients (179 males and 382 females) belonged to the 1949/1950 group. The proportion of males to females in our group of patients closely resembles those observed for other studies that have been made before, in this country and elsewhere.

Of the total, 632 patients (410 females and 222 males) had died subsequently and their death certificates were analysed. Of the remainder, 249 patients were alive and were subsequently visited. A further group of 35 patients were known to be alive but were not visited for reasons given in the detailed text. Whatever conclusions we have drawn from this study will therefore be based on these 916 cases.

The average age at onset calculated for 957 patients was 53.6 years, which is slightly higher than that reported by Andrews in 1959, viz. 52 years. The age at onset of diabetes has not varied in

the case of females in the 1939/1940 and the 1949/1950 groups, although that for the male diabetic had increased from 50.1 years to 52.3 years during this ten year period. The classification of patients into the two types, according to whether they required insulin for stabilisation or whether they were controlled by diet alone, showed that there were 45.7 percent of the former and 49.4 percent of the latter. The remaining 4.9 percent were stabilised with the aid of oral antiglycosuric agents. These values are considerably different from the experiences observed in other clinics both in Great Britain as well as in other countries; e.g. in the series of patients studied by Andrews, only 18 percent of the patients were observed to require no insulin. Joslin has observed that 60 percent or more of the patients under his care required insulin for stabilisation. The proportion of insulin-dependant cases seem to be even greater in the Scandinavian countries.

Analysis of the data with regard to the conjugal status of the patients showed a marked preponderance of married individuals among our group of patients. Approximately 80 percent of all patients were either married or widowed and only 15 percent were single. The marital status of the remainder was not known. The Social Class distribution of patients seemed to show a preponderance in Social Class III, which is not unexpected, as it is the largest social group in Great Britain. This is followed by Social Class IV. The least number of patients appears to be drawn from Social Class I. The percentage distribution of males and females among the different

social classes appears to be similar in both groups except for the fact that male diabetics of Social Class II occupy the second place in the 1949/1950 group, whereas among the females, the second largest group is Social Class IV.

The analysis of death certificates showed that 27.5 percent of cases had diabetes mentioned as the primary cause of death. A further 31.5 percent had diabetes mentioned elsewhere, while the remainder (41.0 percent) had no mention of diabetes. The percentage rate of omission of diabetes as a cause of death appears to be greater than that observed in the United States of America where it is believed to vary from 24.0 to 24.6 percent. Our data also show that the rate of omission is considerably greater for the male diabetic than for the female, and also when multiple causes of death were mentioned in the certificate. It was clear that those certificates which failed to have diabetes mentioned, referred to deaths which resulted from the more acute conditions such as cerebro-vascular catastrophes and coronary occlusion. The milder cases of diabetes which required no insulin failed to have the diagnosis of diabetes mellitus mentioned more frequently than the insulin-dependant cases; also, the older the patient was at the time of death, the greater was the likelihood of not having diabetes mentioned in the certificate. Similarly, patients dying in hospitals and other institutions had a greater chance of having the correct diagnosis entered up than those who died at home or elsewhere.

It is therefore obvious that studies made from the death records of patients who have presumably died from diabetes will reflect

the status of only a fraction of all patients who had died with the disease; and this group will be made up of a sample of individuals who were chiefly drawn up from among the young, thin and insulin-dependant diabetics. Numerous epidemiological studies have been made in the past using mortality statistics to show the relationship between obesity, diet and the trend in mortality statistics during different periods. Our study however, indicates that all conclusions derived from such studies were in effect applicable only to a biased sample of diabetic individuals who suffered from the severe type of diabetes and who finally succumbed to one of its many complications in a hospital or some other large institution at a comparatively young age. In view of our findings, it seems that one should be extremely cautious in interpreting the results obtained from surveys based on mortality data.

The commonest cause of death among both male and female diabetic patients was arteriosclerotic and degenerative heart diseases. These accounted for 23.2 percent of all deaths among males and 20.6 percent among females, when only the primary cause of death was considered. On the whole the incidence of cardio-vascular disease was in effect very much greater, as shown on further analysis of our data. For example, it was seen that in those cases where diabetes mellitus was mentioned as the primary cause of death, 47.1 percent of cases had cardio-vascular disease mentioned elsewhere. Where diabetes mellitus was mentioned as a secondary or contributary cause of death, 51.2 percent of all such cases had cardio-vascular disease mentioned as the primary cause of death. Among these cases where

there was no mention of diabetes mellitus, 48.0 percent had cardio-vascular disease as the primary cause of death.

The female diabetic however, appeared to have a lesser incidence of arteriosclerotic and degenerative heart disease, in spite of the fact that they survive longer and die at a later age than the male diabetic - vascular lesions of the central nervous system was the second commonest cause of death and seemed to affect the female diabetic patients rather more than the males.

The incidence of deaths from infection and diabetic coma are comparatively low among our group of patients. Only 1.9 percent of the males and 2.0 percent of the females died as a result of diabetic coma. The figures are however, almost twice those observed for the group of 235 diabetic patients in the experience of the Joslin clinic. The incidence of deaths from carcinoma was 12.1 percent for males and 10.1 percent for females, both of which are higher than the figure obtained by Andrews for his group of patients, viz. 7.9 percent. On the other hand, the incidence of deaths from carcinoma for the whole population of Edinburgh and the Mid-, East-, and West Lothians were 20.2 percent and 17.9 percent for males and females respectively.

The close association that exists between arteriosclerotic and degenerative heart disease, and diabetes mellitus, has been commented upon by numerous writers in the past. Our study too, shows that there is indeed a close relationship between the two conditions in spite of the slightly younger age group of the patients. This is a field where further research would seem to be profitable, and it is quite likely that much light may be thrown on the aetiology of both

diabetes mellitus and cardio-vascular diseases by concentrating our attention on this problem.

An analysis of the death certificates according to the duration of diabetes mellitus showed that the females had a duration of 10.5 years as compared to 16.2 years for the males; also the male diabetic patients who developed the disease between 40 - 49 years experienced the longest duration, viz. 15.7 years, whereas the shortest duration, viz. 4.2 years, was experienced by the male diabetic who developed the disease between 20-29 years. The duration of diabetes mellitus among the female diabetics ranged from 5 to 15 years. The 20 - 29 years age-group however, did not experience the same adverse prognosis as the corresponding group of male diabetic patients. Also the type of diabetes does not appear to influence the prognosis to any significant extent, although a slightly longer duration was experienced by the insulin-dependant female diabetic patients, and the male diabetics of the insulin-independant group.

The conjugal state of the patients appeared to exert some influence on the prognosis as evidenced by the fact that widowed persons had a shorter duration than either the married or single persons. Also persons who were 10 percent or more above their standard weight apparently experienced the longest duration, whereas those who were 10 percent or more below their standard weight experienced the shortest duration.

The distribution of patients according to the different registration districts does not provide any conclusive evidence in support of a possible regional variation in the prognosis of the disease.

However, patients living in Edinburgh and the Mid-Lothians appear to experience a longer duration than others; whereas patients from Berwickshire and Selkirk experienced the shortest duration.

Our calculations of the expectations of life for the different age groups, taking into account the time elapsed between the onset of the disease and death in some cases, and the onset of the disease and the present time plus an allowance for further expectation of life for the survivors, show that a great deal of improvement has occurred as regards the life expectancy of the diabetic patient during the ten-year period between 1939/1940 and 1949/1950. The improvement has been most marked in the case of the female diabetic who now enjoys a life expectancy of 49.76 years at the age of 15 years, which is nearly 84 percent of the normal life expectancy at that age. The expectations of life at other age-groups too, compare very favourably with that of the average female, and ranges from 56 percent of the normal life expectancy at the age of 75 years to 79 percent at the age of 25 years. The male diabetic on the other hand, does not appear to have benefited to the same extent as the female diabetic, particularly among the younger age group, e.g. the life expectancy of the 15 year old male diabetic patient is only 26.91 years, which is only 49 percent of the normal life-expectancy at that age. Male diabetics however, appear to have a more favourable chance of survival at the age of 65 years and again at ages over 75 years, than the female diabetic of the corresponding age groups.

In view of our above findings, we are able to conclude that the prognosis of the diabetic patients have improved considerably

during the last ten years and that the chances are that they will now live considerably longer and lead more active and useful lives than a decade or two ago. Possible reasons for these changes are the improvement in the general medical care introduced through the National Health Services in 1948, and perhaps the introduction of the chemotherapeutic and other antibiotic agents which also came into effect about the same period.

The comparatively greater longevity of the young female diabetic as compared to the male diabetic is of particular interest. It would be useful to know whether young women are more careful than young men in their attention to dietary control and insulin, or whether some other unknown factor or factors are responsible for this characteristic difference in longevity between the two sexes in the younger age groups.

The information obtained in this section about survivorship after diabetes has been diagnosed, is, we fell, an advance on previous information about the effect of treatment in this condition, and shows more accurately than some of the previous studies as to how the outlook for diabetic patients has improved in recent years. It shows how the diabetic individual has a life expectancy, which although appreciably reduced, is nevertheless sufficient to give him many years of satisfactory life and work. This information should prove useful in assessing the employment prospects of diabetics in general, and whether or not it would be profitable to give them a special training prior to engaging them in suitable occupations. A minor but still important consideration is the possibility that our

findings may induce insurance companies to give more generous terms to diabetic patients than are available at the present time.

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APPENDIX A (Questionnaire)

DIABETES MELLITUS FOLLOW-UP

Name _____ D O P D No. _____

Address _____

	Column	Code
Number	1	
	2	
	3	
	4	
Year of 1st visit to clinic 1 1939 2 1940 3 1949 4 1950	5	
Duration of illness Don't know X	6	
X	7	
Age at onset	8	
	9	
Status 1 Dead 2 Alive and visited 3 Alive and not visited 4 DK	10	
Sex 1 M 2 F	11	
Marital State (Present) 1 M 2 S 3 W 4 D 5 Sep. 6 DK	12	
Marital State (at onset) 1 M 2 S 3 W 4 D 5 Sep. 6 DK	13	
Age Now or at Death	14	
	15	
Occupation	16	
	17	
Social Class 1 I 2 II 3 III 4 IV 5 V 6 DK	18	
Employment Group 1 Manual 2 Non-manual 3 Agricultural 4 DK	19	
Employment Status 1 Employed 2 Retired 3 H.W. 4 School 5 Student 6 Unoccupied 7 DK	20	

Appendix A (Contd.)

	Column	Code
Type of Diabetes 1 Insulin Dependent 2 Diet Alone 3 Other Drugs 4 DK	21	
Effect of D.M. on occupation 1 Retired or changed because of DM 2 Other causes 3 No change 4 DK	22	
Attended Clinic 1 Regularly 2 Irregularly 3 Not at all 4 DK	23	
G.P. supervision 1 Regular 2 Irregular 3 None 4 DK	24	
Tested Urine 1 Regularly 2 Irregularly 3 None 4 DK	25	
Present Treatment 1 Insulin 2 Oral drugs 3 Diet 4 DK	26	
Percentage of Standard Weight 1 80 2 80+ 3 90+ 4 100+ 5 110+ 6 120+ 7 DK	27	
Diet 1 Strict 2 Strict at first 3 Free 4 DK	28	
Control, Hypoglycaemia 1 Good 2 Fair 3 Poor 4 DK	29	
Ketotic 1 Good 2 Fair 3 Poor 4 DK	30	
Retinopathy Present Absent DK	31	
Neuropathy Present Absent DK	32	
Albuminuria Present Absent DK	33	
Cause of Death Primary 1 Diabetes 2 Cardiovascular 3 Cerebro V. 4 Cancer 5 Other 6 NA	34	
Cause of Death Secondary 1 Diabetes 2 Cardiovascular 3 Cerebro V. 4 Cancer 5 Other 6 NA	35	
Cause of Death Abbreviated List B	36	
	37	
Area 01 Edinburgh 02 Midlothian 03 East Lothian 04 West Lothian 05 Fife	38	
06 Clackmannan 07 Stirling 08 Peebles 09 Berwickshire 10 Selkirk	39	
11 Roxburgh 12 Lanark 13 Rest of Scotland 14 England 15 Abroad		

Appendix A (Contd.)		Column	Code
Change of Address	1 Same County 2 Farther 3 No change	40	
Place of Death	1 Hospital 2 Other Institution 3 Nursing Home 4 Home 5 NA	41	
Month of Death	1 Jan. 2 Feb. 3 Mar. 4 April 5 May 6 June 7 July 8 Aug. 9 Sept. 10 Oct. 11 Nov. 12 Dec.	42	

APPENDIX B.

Standard weights, according to sex, age and height.

1) MEN.

Age period		15 - 19	20 - 24	25 - 29	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 -
Height		lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.
Ft.	ins.									
4	11	111	117	122	125	127	130	132	133	134
5	0	113	119	124	127	129	132	134	135	136
5	1	115	121	126	129	131	134	136	137	138
5	2	118	124	128	131	133	136	138	139	140
5	3	121	127	131	134	136	139	141	142	143
5	4	124	131	134	137	140	142	144	145	146
5	5	128	135	138	141	144	146	148	149	150
5	6	132	139	142	145	148	150	152	153	154
5	7	136	142	146	149	152	154	156	157	158
5	8	140	146	150	154	157	159	161	162	163
5	9	144	150	154	158	162	164	166	167	168
5	10	148	154	158	163	167	169	171	172	173
5	11	153	158	163	168	172	175	177	178	179
6	0	158	163	169	174	178	181	183	184	185
6	1	163	168	175	180	184	187	190	191	192
6	2	168	173	181	186	191	194	197	198	199
6	3	173	178	187	192	197	201	204	205	206

Appendix B (Contd.)

2) WOMEN.

Age period		15 - 19	20 - 24	25 - 29	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 -
Height		lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.	lbs.
Ft.	ins.									
4	11	110	113	116	119	122	126	129	131	132
5	0	112	115	118	121	124	128	131	133	134
5	1	114	117	120	123	126	130	133	135	136
5	2	117	120	122	125	129	133	136	138	140
5	3	120	123	125	128	132	136	139	141	143
5	4	123	126	129	132	136	139	142	144	146
5	5	126	129	132	136	140	143	146	148	150
5	6	130	133	136	140	144	147	151	152	153
5	7	134	137	140	144	148	151	155	157	158
5	8	138	141	144	148	152	155	159	162	163
5	9	141	145	148	152	156	159	163	166	167
5	10	145	149	152	155	159	162	166	170	173
5	11	150	153	155	158	162	166	170	174	177
6	0	155	157	159	162	165	169	173	177	182

Height: (with shoes).

Weight: Indoor clothes (with shoes).

APPENDIX C.

SOCIAL CLASS.

I - Professional etc., occupations.

II - Intermediate occupations.

III - Skilled occupations.

IV - Partly skilled occupations.

V - Unskilled occupations.

SOCIO-ECONOMIC GROUPS.

(1) Employers and managers in central and local government, industry, commerce, etc. - large establishments.

(Persons who employ others or generally plan and supervise in non-agricultural enterprises employing 25 or more persons).

(2) Employers and managers in industry, commerce, etc. - small establishments.

(As in "(1)" but in establishments employing fewer than 25 persons).

(3) Professional workers - self-employed.

(Self-employed persons engaged in work normally requiring qualifications of university degree standard).

(4) Professional workers - employees.

(Employees engaged in work normally requiring qualifications of university degree standard).

(5) Intermediate - non-manual workers.

Appendix C (Contd.)

(Employees, not exercising general planning or supervisory powers, engaged in non-manual occupations ancillary to the professions but not normally requiring qualifications of university degree standard; persons engaged in artistic work and not employing others thereat; and persons engaged in occupations otherwise included in Group (6) who have an additional and formal supervisory function.

(6) Junior non-manual workers.

(Employees not exercising general planning or supervisory powers, engaged in clerical, sales and non-manual communications and security occupations, excluding those who have additional and formal supervisory functions).

(7) Personal service workers.

(Employees engaged in service occupations caring for food, drink, clothing and other personal needs).

(8) Foremen and supervisors - manual.

(Employees "other than managers" who formally and immediately supervise others engaged in manual occupations, whether or not themselves engaged in such occupations).

(9) Skilled manual workers.

(Employees engaged in manual occupations which require considerable and specific skills).

(10) Semi-skilled manual workers.

(Employees engaged in manual occupations which require

Appendix C (Contd.)

slight but specific skills).

(11) Unskilled manual workers.

(Other employees engaged in manual occupations).

(12) Own account workers (other than professional).

(Self-employed persons engaged in any trade, personal service or manual occupation not normally requiring training of university degree standard and having no employees other than family workers).

(13) Farmers - employers and managers.

(Persons who own, rent or manage farms, market gardens or forests, employing people other than family workers in the work of the enterprise).

(14) Farmers - own account.

(Persons who own or rent farms, market gardens or forests and having no employees other than family workers).

(15) Agricultural workers.

(Employees engaged in tending crops, animals, game or forests, or operating agricultural or forestry machinery).

(16) Members of armed forces.

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