The Pattern of DIABETES

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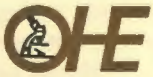

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Cover: An illustration of the pancreas from *De succo Pancreatico: or, a Physical and Anatomical Treatise of the Nature and Office of the Pancreatick Juice* by R. De Graaf, London, 1676. Print by courtesy of The Wellcome Historical Medical Museum and Library.

The Pattern of DIABETES

OVER the past 40 years, diabetes has changed from a progressive or rapidly fatal disease into a controlled chronic disorder with mortality confined mainly to old age. The new picture dates from the isolation of insulin by Banting and Best at Toronto University in 1922.

There are some 300,000 persons being treated for diabetes in England and Wales—either by dietary restriction or with an anti-diabetic preparation. There is also probably a similar number with undetected diabetes many of whom would benefit from treatment but who are receiving none. In the past four years, interest has grown in the detection of these unsuspected cases of diabetes and many local surveys have been undertaken. This paper examines recent trends in diabetes and discusses the issues involved in diabetes detection.

Knowledge of diabetes is of great antiquity. It was recognised in ancient Egypt and described in the Sanskrit Verdic literature of India as "the passing of urine with honey". Aretaeus in the first century A.D. gave the classical description of the disease, and laid emphasis on the large amounts of urine passed—hence the name diabetes from the Greek for syphon. Susruta, the Indian, in the fifth century A.D. and the Arabian physicians Rhazes, Avicenna and others gave good clinical descriptions as did Japanese and Chinese writers of the third century. Thomas Willis (1621–1675) recognised the importance of sugar in the urine and distinguished diabetes mellitus—from the Latin word honeyed—from the insipid variety.[1]

Gradually through the observations of Thomas Cawley in 1788, Richard Bright and others it became recognised that diabetes was associated with changes or malfunctioning of the pancreas. This was confirmed in 1889 by the German physiologist Oscar Minkowski (1858–1931). He and Von Merring found that removal of the pancreas caused sugar to appear in the urine of a

dog and produced a form of diabetes. Previously in 1869, Paul Langerhans (1859–1888) had identified specific cells, which appear as nests or islets in the pancreas; and in 1916, Sir Edward Shafer (1850–1935) suggested that these islets secreted some substance controlling the metabolism of carbohydrates: he gave this substance the name insulin—meaning something present in an islet.

Insulin is an essential hormone if the body is to use the various food elements, carbohydrates, protein and fat, in a normal manner for energy and growth. It promotes the formation and storage of glycogen (a polysaccharide, like starch), of fat and of protein; it increases the "burning" of sugar and decreases its excessive new formation from protein. In all these ways, it helps to regulate the metabolism. In addition, insulin counterbalances the effects of several other hormones on these processes.

Diabetes mellitus is a disease associated either with a breakdown of the body's own supply of insulin through damage to the pancreas, or with a change in the sensitivity of the body's response to insulin. Among the young, diabetes mellitus is usually the result of the breakdown of the body's own supply. In older people, it is more commonly the consequence of metabolic disturbance leading to interference with the activity of the body's insulin supplies.

The islets of Langerhans are an exception among the hormone-producing organs in that they can be overstrained and eventually exhausted. When this occurs, they are unlikely to make an effective recovery. When the body's supply of insulin is defective, the amount of sugar in the blood becomes very high (hyperglycaemia) and sugar appears in the urine (glycosuria). At a later stage, substances known as ketone bodies also appear in the blood and urine (ketonuria). These result chiefly from the incomplete oxidation of fatty acid. If they form in sufficient amounts, the patient passes into a coma. Death ultimately occurs either because of the failure of the body to use glucose, or through the toxic effects of ketone bodies. A person suffering from diabetes is particularly vulnerable to communicable diseases, especially tuberculosis and staphylococcal infections, and highly susceptible to degenerative conditions, such as arterial disease and cataract.

Once the relation between diabetes and insulin was recognised, repeated attempts were made to isolate the hormone. The failure of the body's own supply of insulin could be made good by insulin extracted from the pancreas of animals. Although this would not cure the disease in the sense of restoring the functioning of the pancreas, it would restore metabolic balance; it is a classic example

of replacement therapy. Before an "artificial" source of insulin was available, the only therapy for diabetes was rigorous dieting. This attempts to reduce body-weight and the "work-load" to match the capacity of the pancreas. It is still of value in milder cases, but the scope of this therapy is limited in severe cases.

For many years, attempts to extract insulin from the pancreas in carcases met with failure. Eventually, a young doctor with little previous research experience, Frederick Banting, working with a medical student, Charles Best, succeeded. The insulin producing islets are sited in the main digestive gland. Banting and Best considered that previous failures were due to the destruction of insulin in the pancreas of carcases by digestive juices. These destructive digestive juices are not present in the pancreas of a calf before birth and a solution was extracted from the foetal carcase which was able to produce a sharp fall in the blood sugar level of a diabetic dog. The discovery was announced in the autumn of 1922. British made insulin was first marketed in April 1923 and in the course of the following year production had expanded sufficiently to meet home demand.

The original form of insulin, now known as "unmodified" or "soluble" insulin, is rapidly absorbed and effective for a period of only eight to ten hours. On its own it could involve an inconvenient treatment regime since injections are needed at least twice a day. In 1936 and 1937 protamine insulin and protamine zinc insulin were developed by insulin manufacturers. These modified insulins remain in the body's tissues longer than soluble insulin, being slowly released into the blood stream over approximately 24 hours. Later, globin and isophane insulins were introduced with durations of action mid-way between soluble insulin and protamine zinc insulin; and more recently still insulin-zinc suspensions have been developed. In many cases, these modifications enable blood-sugar levels to be controlled by a single daily injection containing different mixtures to suit the particular needs of individual patients. All of these insulin preparations are derived from natural sources, from the pancreatic glands of pigs and cattle. It was not until 1963, that insulin was first synthesised in the laboratory by Claus Hoffman in Pittsburg.

Because insulin is destroyed by digestive juices, it cannot be given by mouth. An alternative way of treating diabetes orally has, therefore, been sought for many years. After unsatisfactory early attempts with rather toxic pharmaceuticals, the first clinical report of an oral anti-diabetic followed a chance observation. During the last war, Loubatieres observed a hypoglycaemic effect

with some of the sulphonamides. In 1945, Franke and Fuchs in Germany noticed that patients receiving a new sulphonamide developed symptoms of a low blood sugar similar to the effect of an overdose of insulin. Although this compound proved too toxic, chemical modifications developed by pharmaceutical manufacturers, notably tolbutamide and chlorpropamide, had similar anti-diabetic properties and proved safe for clinical use. The success of these compounds, known as the sulphonylureas, stimulated the re-examination of another chemical group, the biguanides which were also known to have had anti-diabetic properties, but to have been toxic. Chemical modification of these compounds, led to the development of phenformin and metformin. The mode of action of these compounds is still not fully understood. They are of value in milder cases of diabetes but are relatively ineffective in severe cases.

A vital part of a diabetic's regime is a convenient quantitative means of measuring to what extent the disease is under control, since treatment for diabetes does not cure the disease in the sense of removing the underlying disability. Also, as diabetes tends to develop insidiously, particularly in adults, and as damage or overstrain of the pancreas appears irreversible, early detection is essential. Chemical tests for glucose in the urine are long established: Pavy first produced tablets for testing urine in the second half of the 19th century. Currently two simple and convenient chemical tests have been widely adopted for urine testing. Clinitest, developed in 1942, enables diabetics to judge whether the sugar content of urine is rising or falling. Clinistix, a glucose oxidase strip, which was developed in 1955, simply and rapidly indicates whether or not the urine contains sugar. The introduction of Clinistix for simple diagnosis of glycosuria has opened up the possibility of large-scale detection of unsuspected cases of diabetes. The introduction of Dextrostix for testing blood sugar levels further extends the scope for pre-symptomatic detection.

Trends in Diabetes

TRENDS in mortality can give no more than a general impression of the rises and falls of the disease, partly because of technical problems associated with mortality statistics and partly because a change in treatment may reduce mortality but may leave the incidence of new cases unaltered.

Deaths are classified in mortality statistics according to the underlying cause, the conditions which initiated the train of morbid events leading directly to death.* Much of the mortality in diabetes is due to the infectious and degenerative diseases to which diabetics are particularly prone. A change in the mortality risk from these diseases either through their decline or through the development of effective treatment may thus be reflected in trends in diabetes mortality. Also, in the past, deaths from degenerative diseases brought on by diabetes would be certified as due to the degenerative disease if diabetes had not been diagnosed. Thus, diabetes statistics may not be true measures of the incidence or mortality of the disease.

More important, however, in attempting to measure the rise or fall of diabetes is the effect of treatment. With communicable diseases, such as tuberculosis, the cure or the control of the condition will itself reduce the incidence of new cases. Diabetes, however, is merely controlled. Insulin therapy in no way affects the incidence of new cases, and as it staves off mortality it increases the total population of diabetics. As there appears to be a hereditary factor in the development of diabetes the numbers vulnerable to diabetes increase from generation to generation. Finally, as

* Currently the selection of the underlying cause depends entirely on the judgment of the certifying doctor. Until the 1940's, however, underlying causes were selected according to arbitrary rules of procedure and diabetes had a high precedence. For those years, therefore, diabetes mortality tended to reflect the death rates of diabetics. The figures for the years before the 1940's have been brought into line with later figures by multiples calculated from a dual tabulation of deaths during the years prior to the change-over. This will alter the earlier levels of mortality generally, but will not affect relative changes between different years in the period prior to that in which the dual tabulation is available. This factor particularly affects death rates for those aged 55 or more.

death rates from general mortality fall and the number of elderly people rises, the incidence of diabetes will also rise since it becomes more common with age.

However, with these qualifications, the pattern of mortality from diabetes reveals some of the trends of the disease during recent years. The pattern of mortality has altered greatly since the early 1920's. (*Figs.* 1 and 2). Mortality in the younger ages has been substantially reduced, but has risen among the elderly. For ages up to 35 years, death rates are between one-tenth and one-fifth the levels of the early 1920's, while mortality from diabetes for females over 75 is nearly twice as high as its early 1920's level (*Table* A). This reduction of diabetes mortality among persons under 65 years old represents a saving of nearly 2,000 lives each year.*

The change in mortality from diabetes cannot be attributed simply to the introduction of insulin: the pattern is more complex. Diet plays an important part in the incidence of the disease. This is especially true with the older age groups where diabetes arises from an inability of the body's insulin to meet the demands placed on it.

There are periods when the relationship between diabetes and diet appear clear. There are significant declines soon after the outbreak of the First and Second World Wars, coinciding with restrictions in food supplies. Food rationing, by reducing the weight of and by preventing obesity in potential diabetics, reduced the incidence of new cases. From 1940–1947 there is a strong correlation between diabetes mortality and the consumption of fat.[2] There are other periods too where diet might appear to affect diabetes mortality particularly among young adult females. The sharp but brief fall for females aged 15 to 35 years in 1929–1930 coincided with the "skinny-look"; while a rise for this group early in the last war—an exception to the trends of other age groups—might reflect a new diet of factory canteen meals and the absence of a stimulus to slim.

Diet, however, cannot be the whole or even the main explanation of the trends in diabetes mortality. It is true that mortality rose following the relaxation of food restrictions after the First World War, but the end of rationing after the second war did not bring a rapid rise in mortality—nor has the rise in fat consumption since 1948. Also the greatest improvements were not in those ages where obesity is a major problem nor were they

* This figure is calculated by applying 1920–1922 diabetes mortality rates to the present population, and deducting from this the actual mortality which occurred.

FIG. 1

Diabetes. Death Rates per million by Age. Males. England and Wales 1911–1962.

Source: Registrar General Statistical Review (Various Years).

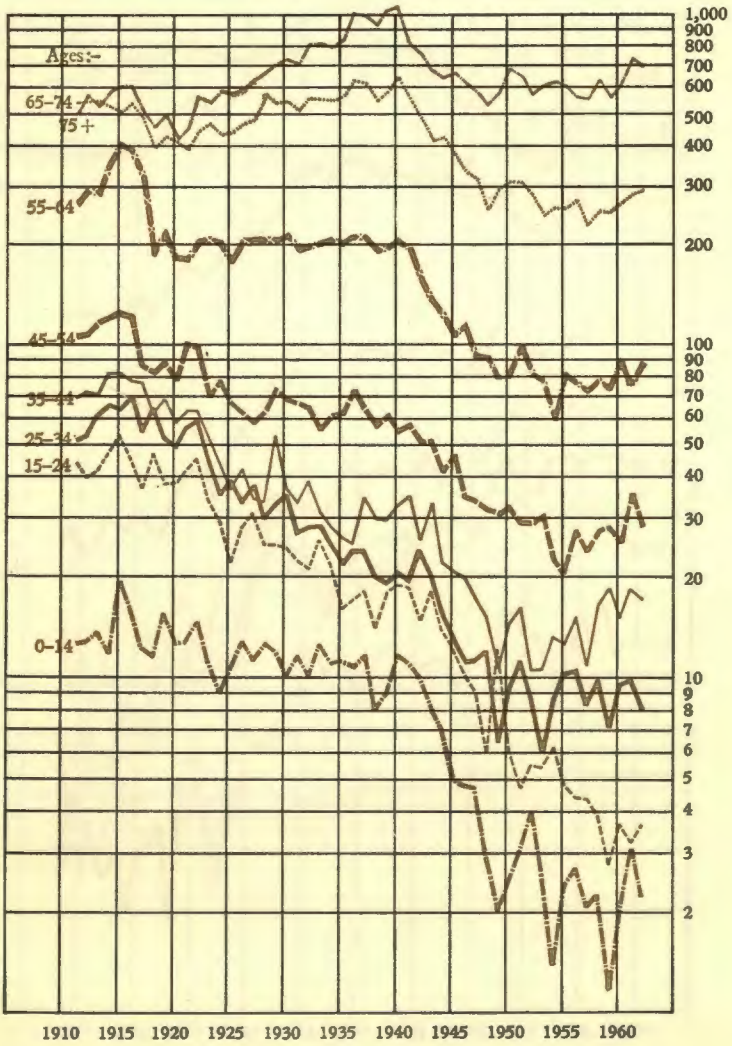


FIG. 2

Diabetes. Death Rates per million by Age. Females. England and Wales 1911–1962.

Source: Registrar General Statistical Review (Various Years).

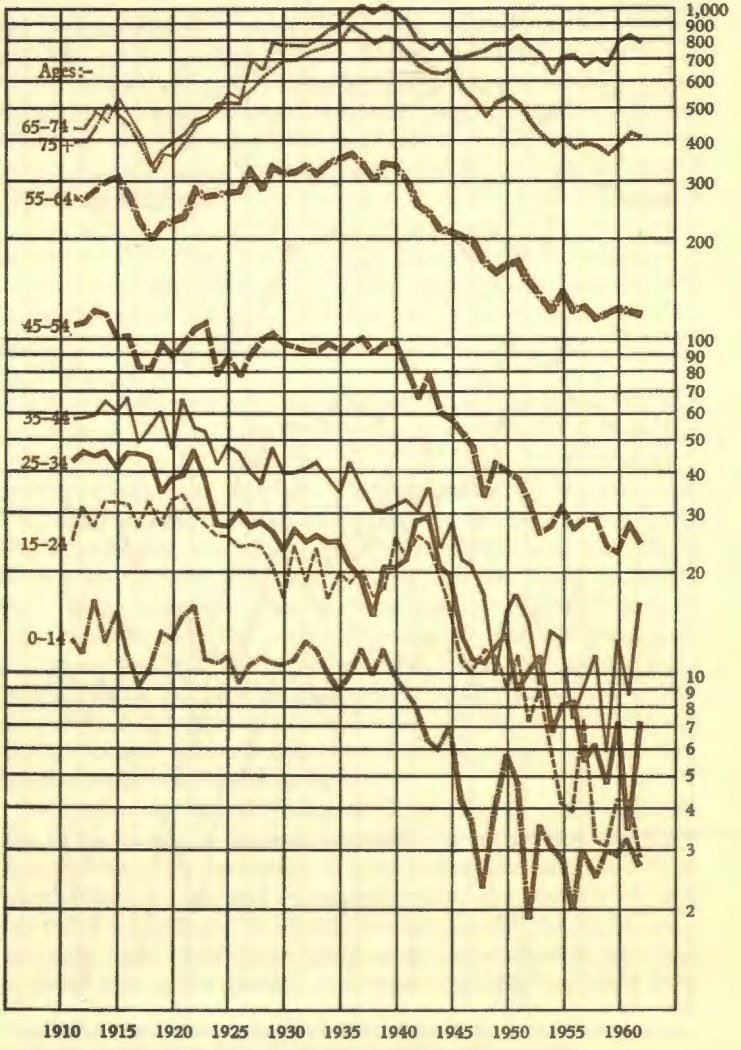


TABLE A

Diabetes 1962 Death Rates by Age as a Percentage 1920–1922 Rates.

	Ages							
	0—	15—	25—	35—	45—	55—	65—	75+
	%	%	%	%	%	%	%	%
Males	17	9	15	29	31	46	70	147
Females	18	9	17	29	25	48	96	196

confined to those ages which showed a similar change as a result of food rationing in the First World War. Sweet and sugar rationing ceased in 1953, but even among the young there was no increase in mortality from diabetes.

The period of most rapid decline in diabetes mortality is the decade 1940–1950. The start of the decline coincides with dietary changes, yet the pace and extent of the decline continued even after the stabilising of diet at war-time levels. Also the ages which obtained greatest relative benefit were not those where obesity tends to be most frequently found, or those to which the similar dietary conditions of the First World War brought the largest declines. There were probably other factors operating. This decade of decline also coincides with the introduction first of sulphonamides (from 1939), then of penicillin (from the mid–1940's), and eventually of the broad spectrum antibiotics. These provided effective therapy for the infections to which a diabetic is particularly susceptible and vulnerable. The danger to the diabetic from an infection lies in the resultant upset of metabolism as the body's defences against infection come into operation. This change will disturb the delicate balance which diabetic therapy seeks to maintain. If the infection is prevented or rapidly terminated, the chances of this occurring are greatly reduced. The substantial fall in mortality from diabetes during the 1940's could well, therefore, be due in part to the control over infections and a reduction in their particular danger to diabetics.

The point of greatest interest is the impact of insulin therapy since it was first made available in this country in 1923. Over the whole period there has been greater control in the diabetic conditions of younger persons, where generally the body's own supply of insulin has been reduced. The gains are less among the older groups where diabetes is associated with excessive demands for insulin.

The improvements obtained through insulin appear, however, to have been gained only slowly. It is true that immediately following the introduction of insulin the mortality rate for certain ages, particularly among males between 15 and 44 years, fell abruptly: between 1922 and 1925, it declined by one half for males aged 15 to 24 years. But after 1925 mortality fell away only slowly until the outbreak of the war. The rapid improvement thereafter completely overshadows the decline immediately following the introduction of insulin.

The question arises why this specific therapy, which undoubtedly proved life-saving, did not have a greater or a more immediate

effect on mortality. From the evidence on mortality of different social classes it appears that the benefits of insulin therapy were not uniformly shared by all social groups, and that the bulk of the community did not enjoy the full benefits of this therapeutic advance for many years.

Social class mortality is compiled from census returns. It is available for males over 16 years old, covering the years 1920–1922, 1930–1932 and 1949–1953 and for the last two periods for females. Mortality rates from diabetes of different age groups over 16 years during each of these periods are given in *Figs.* 3 and 4 for social classes I and II (Professional and managerial occupation), for social class III (skilled occupations) and for social classes IV and V (semi-skilled and unskilled occupations).

In 1920–1922, the years immediately preceding the introduction of insulin, social class mortality among males followed the pattern expected from class difference in diet. Mortality from diabetes was consistently higher for all ages among the professional and managerial classes. In the decade which saw the introduction of insulin all social classes benefited for ages below 55 years, but the speed of improvement was substantially greater for the professional and managerial groups. For men aged 25 to 34 years, diabetes mortality for social classes I and II fell by 62 per cent, for social class III by 38 per cent and for social classes IV and V by only 18 per cent. Thus in the first decade of insulin therapy in the younger ages the social class pattern had been reversed. With females too in 1930–1932 for most ages the pattern is the opposite to what might be expected from standards of diet.

In the 20 year period between the 1931 and 1951 census, the greatest improvement in diabetes mortality took place. Again, the relative improvement was greatest with social classes I and II. For men aged 35 to 44 years, diabetes mortality for social classes I and II fell by 70 per cent against 41 per cent fall for social classes IV and V.*

Generally, two explanations can be put forward for disparity in the benefits that different social classes obtain from medical care. The first concerns the cost of medical care, with lower income groups being unable before the advent of the National Health

* There is a further factor which might qualify this supposition, and this is the effect of relative changes in diet and nutrition between social classes during this period. However, it is doubtful whether a great part of the failure of mortality from diabetes to improve rapidly between 1920–1922 and 1930–1932 among unskilled and labouring occupations could be attributed to an improvement of nutrition among this section of the community. It compares the periods of the post First World War boom with the depth of the inter-war depression. Also, the period 1949–1953 came at the end of over ten years rationing which tended to bring uniformity of diet.

FIG. 3

Diabetes Mortality by Social Class for different ages—Males. 1920–1922, 1930–1932 and 1949–1953.

Source: Registrar General. Census Reports Supplement IIa. Occupational Mortality.

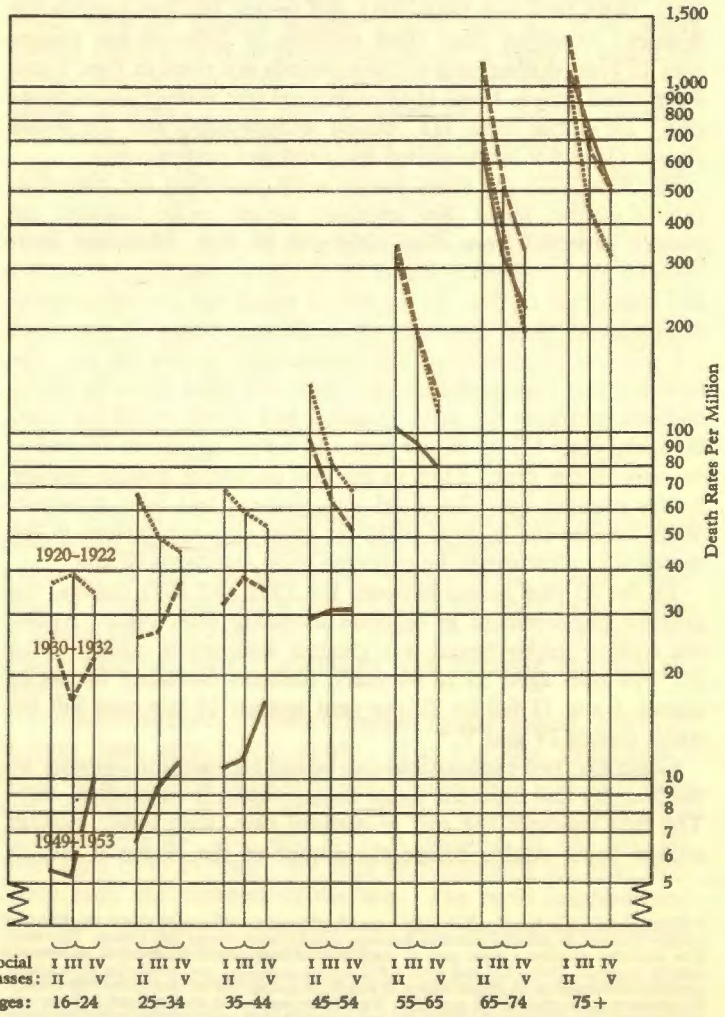
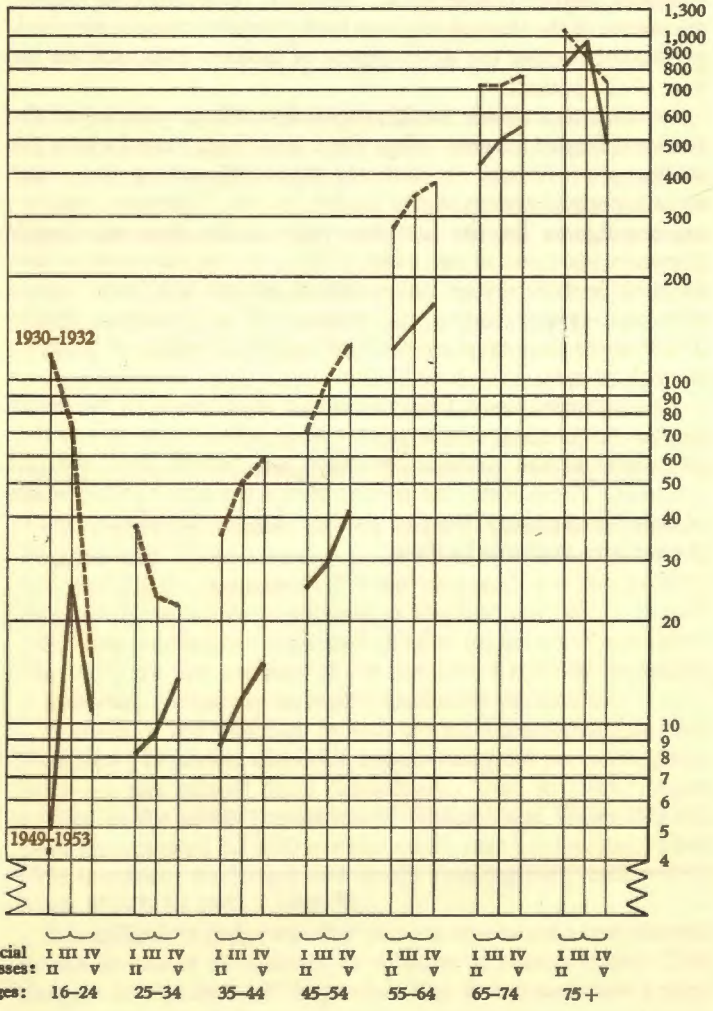


FIG. 4

Diabetes Mortality by Social Class for different ages—Females. 1930–1932 and 1949–1953.

Source: Registrar General. Census Reports Supplement IIa. Occupational Mortality.



Service to afford a proper standard of care. The second concerns differences of competence and skills between social classes, with the failure of lower socio-economic groups to take advantage of opportunities open to them generally irrespective of cost. With insulin therapy, either of these factors would be expected to operate to an exceptionally high extent. Firstly regarding costs, the therapy is continuous and thus, where the patient pays, the economic burden is substantial. Secondly regarding competence, the course of the therapy requires both extensive co-operation and, particularly before the development of modern tests, skill on the part of the patient.

Insulin was available for 25 years before the introduction of the National Health Service. Thus there was a long period where the slower improvement in diabetes mortality among the lower socio-economic groups might be due to cost. However, comparing the figures for the first five years of the National Health Service with those of the early 1930's, the pattern remains unchanged with a slower improvement among the lower socio-economic groups despite the removal of an economic barrier which might have impeded their taking full advantage of progress in medical care.

The principal lesson from this is that the removal of the direct charges for medical care is not by itself sufficient to ensure that all sectors of the community derive full benefit from medical progress. There is also the need to obtain the active participation of those whose competence or attitudes hinder the effective use of the services available to them.

The Incidence and Cost of Diabetes

DURING the days of rationing, diabetics were entitled to extra meat, fats, cheese and milk. The claims for these benefits indicate the number of known diabetics in these years. In England and Wales at the start of 1941, a total of 33,500 were registered. By mid–1942, registrations had risen to 58,300, reaching nearly 92,000 in 1945 and just over 98,000 in 1947. By 1945, the stringency of ordinary food and milk rations was such that most people suffering from diabetes were claiming the extra rations. The increase between 1941 and 1945 was probably due in part to an improvement in registration. The 1947 figure represented a rate of 2·3 per 1,000 population which was similar to the figure found in the Survey of Sickness. About two-thirds of these were receiving insulin, approximately the same proportion as in 1943 and 1945.[3]

During 1955, a study of 106 general practices throughout England and Wales revealed a consultation rate for diabetes of 3·7 per 1,000 population—2·9 for men and 4·4 for women.[4] Applied to the whole population of England and Wales in mid-1955, this produces an estimated 163,000 under care for diabetes. For 1955, the first estimate of the number of hospital in-patients is available, amounting to 26,000 discharges or deaths.[5]

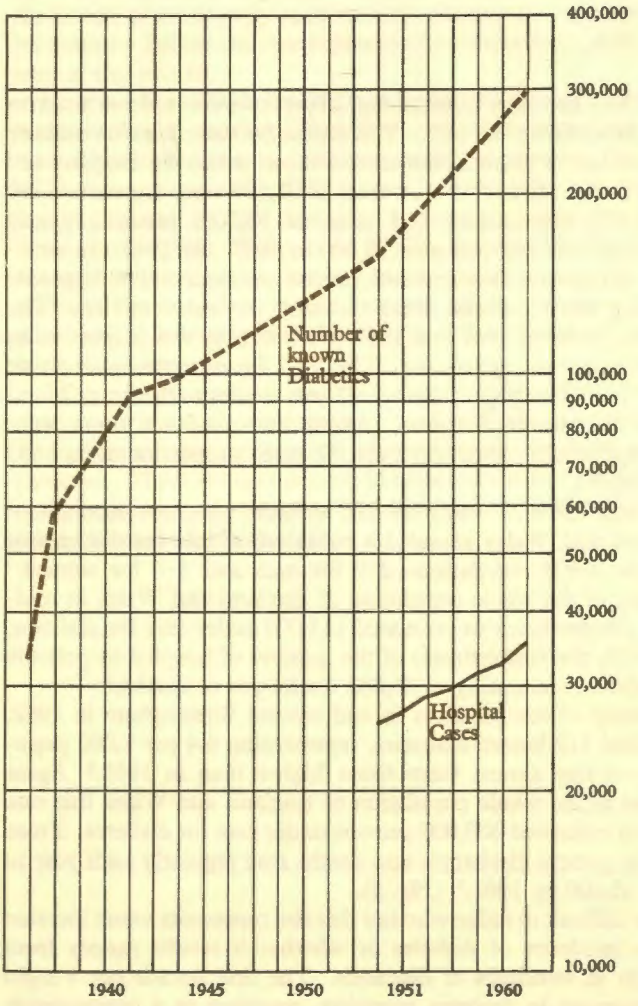
A study of ten practices in and around Birmingham in 1962, identified 119 known diabetics, representing 6.4 per 1,000 population—a rate almost three times higher than in 1945.[6] Again applied to the whole population of England and Wales this rate gives an estimated 300,000 persons under care for diabetes. From 1955 in-patient discharges and deaths rose regularly each year to reach 35,600 by 1961.[7] (*Fig.* 5).

It is difficult to judge whether this rise represents a true increase in the incidence of diabetes or whether it results mainly from changes in standards of diagnosis. The first decade saw a rapid improvement in diabetes mortality, resulting in a cumulatively

FIG. 5

Estimated numbers of "Known Diabetics" for various years 1940–1962, and numbers of hospital in-patients 1955–1961. England and Wales.

Sources: See text.



greater number of diabetics living their normal span of life. But in all, this cause would explain a rise of 30,000 in the number of diabetics—the number who would have died if there had been no decline in mortality rates since before 1940.* The second decade saw a rise in nutrition levels which would lead to a rise in the incidence of diabetes.† Added to this, the decline in general mortality has led to a rising proportion of middle-aged and elderly persons in the population: in 1938, persons over 45 years represented 31 per cent of the total population; by 1960, this had risen to 38 per cent. In absolute numbers, there has been an increase of 4.4 m. persons over 45 years, during the two decades which saw the estimated rise in the number of known diabetics. Assuming that the rates of patients aged over 45 years consulting their doctors for diabetes in the mid-1950's remained constant over the two decades from 1940, the rise in the number of persons aged 45 years and over would explain an increase of around 37,000 in the number of known diabetics.

On the side of diagnostic standards, the introduction of the National Health Service in 1948 increased contact between patients and doctors, particularly for women and the elderly, which increased the opportunity for making an early diagnosis, while the availability of Clinistix in 1956–1957 simplified the detection of glycosuria making it easier to identify likely diabetics as a routine part of general practice.

The cost of diabetes to the National Health Service, for hospital in-patients and for treatment in general practice, amounts to approximately £5·7m.[8] To this should be added in the region of a further £0·5m. for out-patient attendance of diabetic clinics. The largest part of the cost is for in-patient care, amounting to approximately £3·7m. or to just over £100 per hospital discharge or death following an average stay of 26 days. The cost of care outside hospitals is much lower amounting to an average of about £9 per diabetic each year. The year's supply of pharmaceutical preparations accounts for just over £5 and an allocation of the general practitioner's consultations for nearly £2, the balance being attributed to out-patient attendance.

* This figure is calculated by deducting the number of deaths due to diabetes over the years 1941–1960 from the number which would have occurred if the 1938–1940 mortality rates had remained constant. Allowance was then made for subsequent cohort mortality from all causes.

† The rise in numbers of diabetics registered for food allowances between 1941–1947 is on the surface not consistent with a lower nutritional standard reducing the incidence of diabetes. However, as rations become severer the incentive to registration is increased leading paradoxically to an apparent rise in the incidence of diabetes.

This estimate of the incidence and costs of diabetes refers to the number of known diabetics in the population. The problem of diabetes is far greater than these figures suggest. Diabetes detection surveys have found that for every known diabetic in the community there is probably another unsuspected case.

Until after the Second World War detection of diabetes, apart from normal contact between doctors and patients, depended on examination for such matters as life insurance, recruitment to the armed forces or ante-natal care. The introduction of Clinistix for detection of glycosuria stimulated public health investigators to survey the general population for diabetes as a public health measure comparable to mass radiography for tuberculosis. The first recorded survey was undertaken in the U.S.A. in 1946[9] followed by a study in Canada in 1950.[10] In the following ten years no fewer than 109 surveys covering a million people were undertaken in North America.[11]

The earliest recorded survey in Britain was conducted in a single general practice in Newcastle during 1960,[12] followed by a community study in Ibstock, Leicestershire.[13] At least 21 further surveys were conducted in 1961 and 1962 covering a minimum of 130,000 persons.[14]

The surveys vary widely in the method of selecting the population to be screened, the procedures in screening and in follow-up.

The screened populations include all patients on the lists of a group of general practices,[6] residents on the electoral roll of a small community,[15] selective age groups or relatives of diabetics in a community,[16] persons attending mass radiography units[17] while current surveys include populations drawn from persons resident in old people's homes, hospital admissions, persons visited by district nurses, employees at industrial concerns and pupils of schools.[14] There has been the suggestion that a survey could be mounted among the readers of a popular woman's magazine. The largest reported survey covered the population on the electoral roll of Bedford, to which about two-thirds, 25,701 persons responded.[18]

All these surveys have been based on urine testing for glycosuria by Clinistix and subsequent blood sugar testing for diagnosis of the diabetics among the glycosurics. The Bedford survey included in addition a control sample of 500 persons tested for blood sugar levels.

The methods of mounting the screening tests have differed widely. The principal difference is between self-testing and test-

ing of urine by the survey unit. The organisation problem with self-testing is the distribution of Clinistix, while with the survey unit testing, it is the collection of urine samples.

Clinistix for self-testing have been distributed to the survey population by post for return either in all cases to the survey unit, or only when found positive either to the unit or to the patient's own general practitioner. Volunteer workers have also been employed for house to house distribution and collection of Clinistix. Where the survey population is selective, such as persons attending mass X-ray units or those visited by district nurses, Clinistix have been distributed and collected concurrently with routine contact and administration.

To avoid the possibility of failure to follow instructions or to interpret results correctly, the alternative of collecting urine samples has been adopted in community surveys. Jars for samples have been distributed to houses by volunteer workers and collected the following day. Testing and subsequent action is then under the control of the survey unit.

The costs of seven surveys are given in *Table B*. They include only the direct expenses of conducting the screening for glycosuria, and exclude staff and professional costs of conducting the surveys.

Costs vary much as would be expected from the different ways in which the surveys were conducted. The costs of testing equipment are a small part of the total: at current trade prices, they would amount to approximately £50 per 10,000 screened for glycosuria.

Where, as in Rotherham and Cardigan, equipment is distributed as part of routine contact with those surveyed, screening costs are not substantially higher than costs of equipment. Even with volunteer labour, distribution of Clinistix to a whole local community, as in Basingstoke, involves substantially higher costs, covering printing, publicity and ancillary administrative expenditure. In rural Essex and Perth, the surveys were conducted by post and although they differed greatly in size, the costs of screening 10,000 come out remarkably similar.

In Birmingham and Forfar, costs include the collection of urine samples, which were self-tested before despatch in Birmingham. The Birmingham survey achieved the highest response rate. A large part of the cost was for follow-up of those who did not respond to the initial invitation. The average cost per diabetic detected for the three-quarters who responded immediately came to £6 but rose to £17·5 for those who required follow-

TABLE B

Direct Costs of Glycosuria Screening in Various Diabetes Surveys

Survey Area	*Survey Population*	*Survey Method*	*Direct Costs* £	*Costs per 10,000* £	*Cost per Diabetic Detected* £
Rotherham	17,508 self testing	Clinistix distributed to persons visiting mass X-ray unit for themselves and their families	95(a)	54	3·65
Cardigan	17,039 self testing	Clinistix distributed and collected from persons over 40 normally visited by District Nurses	112	66	1·13
Basingstoke	13,716 self testing	House to house volunteer worker distribution and collection Clinistix. 65% response.	250	182	n.a.
Rural Essex	1,700 self testing	Postal distribution and pre-paid return of Clinistix to over 25's in community. 66% response.	48	282	4·80
Perth	30,522 self testing	Postal distribution and pre-paid return of Clinistix all ages in community. 75% response	970	318	6·88
Birmingham	19,412 self testing	Surgery and postal distribution and pre-paid return of Clinistix and urine container to all patients in 10 practices. Postal follow-up. 95% response.	1,250	643	9·84
Forfar	10,758 unit testing	House to house volunteer worker collection of urine samples from whole population. 85% response	350	325	10·00
Totals	110,655		3,075	278	5·81(b)

(a) Excluding £30 costs of equipment not used.
(b) Including estimated 92 diabetics in Basingstoke (Rate of 0·67 per 1,000).

up.[19] If the figures from the Birmingham survey are applied to the whole population, it would cost £1·35m. to detect 225,000 unsuspected diabetics from those who respond without great prompting, but a further £1·31m. to detect the remaining 75,000 from the less co-operative members of the community.

The lowest average cost per diabetic detected was in Cardiganshire where the survey concentrated on those over 40 years old—the age groups which have the highest proportion of diabetics. Where all ages are screened, average cost per case detected rises, since a smaller proportion of those screened are found to be diabetic.

Using the average costs from these seven surveys, the direct costs for screening the population of England and Wales for glycosuria would amount to approximately £1·5m. For screening every five years, the cost would be £0·3m. a year.

But this is not the whole cost that diabetes detection would involve for the National Health Service. Expenditure on screening would no more than identify glycosurics. If the proportion of glycosurics in the community is the same as in the Birmingham survey there would, over a five year period, be revealed approximately 210,000 glycosurics a year. Each of these would need further screening by questioning for cardinal symptoms, estimating the postprandial blood sugar and, in doubtful cases, carrying out a full glucose tolerance test. The costs involved could be as much again as the primary glycosuria screening. This screening should reveal approximately 300,000 cases of undetected diabetes over a five year period, or 60,000 new cases a year.

At present these undiagnosed cases are making no demands on the National Health Service for their diabetic condition. Once a diagnosis has been made there will arise the need and the cost of continuing care. The cost of treating the present unsuspected cases of diabetes should not involve a direct duplication of the present expenditure on the disease. Much of the cost (£3·7m. out of £5·7m. a year) is for hospital care and it is reasonable to assume that the majority of diabetics needing hospital care already eventually receive it. At the present estimated expenditure outside hospitals, of about £9 a year for a known diabetic, the cost to the National Health Service for treating the cases at present undetected would amount to approximately £2·4m. a year.

In all, therefore, diabetes detection would involve an expenditure of from £2·5m. to £3·0m. a year bringing the total cost of diabetes to nearly £9m. This may be compared with an expenditure of £51m. on diseases of the teeth or £20m. on bronchitis.[8]

There is the possibility that this expenditure on diabetes surveys could lead to some saving to the National Health Service through reducing the number of hospital in-patients. On the extreme assumption that early diagnosis and care would eventually replace the need for in-patient care, savings would outweigh expenditure by £0·7m. a year. In addition, if early care through advice on dieting prevented the progress of early cases, this may lead to saving on anti-diabetic medicines. However, the chances of a saving to the National Health Service through early detection of diabetes requires a great reduction in the proportion of in-patients and successful control of the disease through early treatment of cases.

But apart from expenditure on the health services, there are wider economic considerations. The object of health expenditure is benefit for the patient. In consideration of the costs of diabetes detection and treatment, there are the broad economic benefits of better health, which might offset them. In 1960–1961 diabetes was responsible for a loss of 1·83m. working days,[20] which at average sickness benefits payments cost the insurance funds nearly £1·0m. and the employees or their firms perhaps twice or three times as much again.

In addition, the performance of many of the present undiagnosed diabetics may be impaired by the untreated symptoms of the disease.

The Implications of Diabetes Detection

In recent years greater emphasis has been laid on pre-symptomatic detection. This is a secondary form of preventive medicine —early diagnosis and prompt treatment, which contrasts with the conventional prophylactic concept. With modern medicines the pattern of disease in modern industrialised communities has changed out of all recognition. The control of infections has revealed a submerged layer of chronic diseases, which often are difficult to treat or to control successfully once symptoms have appeared; by then the impetus and direction of the condition have become irreversible. The conditions, therefore, need to be detected in their "silent" or pre-symptomatic stages. The early detection of diabetes illustrates this approach.

The simple and principal object of diabetes detection is to bring treatment in its broadest meaning to those who require it. Detection surveys have revealed the full range of the disease in people receiving no treatment, from cases which show no more

than abnormal glucose tolerance to florid diabetes with complications already developed. Diabetes screening can therefore be a life preserving measure. A secondary object is to obtain information on the epidemiology of the condition and to discover more about the early course of the disease. Diabetes detection surveys have raised many questions concerning the course of diabetes, the significance of which are still far from understood. The concept of the disease is slowly changing, as greater attention is focused on the pre-symptomatic or even on the pre-disease condition.

Against these considerations it needs to be remembered that diabetes is at present incurable. There is not yet conclusive evidence that early diagnosis and treatment can necessarily do more than postpone the onset of complications. However, personal preventive medicine, in contrast to control of communicable diseases, raises in a more acute form the issue of participation and response. A response of three-quarters of the community might be adequate to protect the whole in the control of communicable diseases such as poliomyelitis; but with personal preventive measures, the quarter who do not respond receive no benefit. If diabetes screening campaigns are to be as effective as possible considerable persuasion may be required, even though it is still difficult to be dogmatic about the full benefits of early treatment.

The method of detecting diabetes involves a number of important issues. Ideally a screening test should involve a simple laboratory procedure which separates all individuals likely to have the conditions: it should be sensitive providing positive results for a high proportion of those with the condition, as well as specific, giving negative results for those without the condition. It should also be rapid and inexpensive.[21]

The rapidity and economy of Clinistix has led to its adoption for mass surveys by urine testing. Although it identifies people with glycosuria, only about one-third of these have high blood sugar. Furthermore, among the random sample whose blood sugar levels were measured in Bedford it was found that a number who had high blood sugars provided negative results on urine tests.[22] This may suggest imperfect testing of the urine or, more interestingly, that the relationship between glycosuria, hyperglycaemia and diabetes is still imperfectly understood.[23] In the ten practices which took part in the Birmingham survey, 17 new cases of clinical diabetes have occurred since the survey was taken: sixteen of these were non-glycosuric two years previously.[19] Urine testing alone thus does not appear to identify a proneness to diabetes. Nevertheless, it has made possible community

surveys and through the detection of unsuspected cases contributed towards accomplishing the principal object of diabetes detection.

The recent introduction of Dextrostix, a simple blood sugar screening device affords the opportunity of adopting a screening technique more close to the ideal. It also provides a more effective means of studying the early causes of the disease. In Bedford, there was a large number with marginal blood sugar elevation not readily assignable to "normal" or to diabetic categories. The implications of this borderline state have yet to be revealed, but the widespread distribution of arterial disease and cataract might be related to it.[23]

What are the practical implications of all this? There is a substantial number of undetected diabetics in the population, many of whom would benefit from treatment. Screening methods, although far from ideal, have made possible detection of unsuspected cases. The surveys have raised many problems, the solution to which will throw some light on the early course and perhaps even on the initial causes of the disease. Screening methods have, partly as a response to these problems, been advanced and a combination of blood sugar and urine sugar screening is now feasible.

Diagnosis and treatment are parts of a whole in patient care and responsibility for this lies principally with a patient's general practitioner. Because diabetes is a chronic and potentially a progressive condition continuity of care is essential. Because of the greater chances of survival with long-term replacement therapy the problems of control have become of great importance. Disclosure of the fact that a person is diabetic may come as a shock. A major problem is one of adjustment and acceptance of a regime. Stability of family and home are important: strain produces a change in blood sugar and a rise in ketonaemia, while over-eating is a characteristic response to stress.[24]

The general practitioner is well situated, too, for the conduct of diabetes surveys. In the course of a year he sees probably two in every three patients on his list, and this perhaps involves contact with members of an even larger proportion of family groups. The economy of conducting surveys in conjunction with routine contacts is borne out by the costs listed in *Table* B. In addition, personal contact can reduce the incidence of errors in testing and should inspire a higher response.

The possibility of conducting diabetes surveys through general practices, however, raises a practical issue arising from the present problems involved in re-imbursing practice expenses. The cost

of conducting surveys would be borne individually by a general practitioner either as a loss of remuneration or by a curtailment of other services. At current trade prices, costs of equipment for glycosuria screening would amount to no more than £12 per practice but to £135 for blood sugar screening. To these expenses, however, must be added the costs of administration.

The drawback in continuing detection surveys entirely within the confines of general practice is that progress becomes fragmented. A single general practice could not provide either the variety or the size of diabetic population necessary to obtain a fuller understanding of the disease in the community. It may also face difficulties of administration and arranging follow-up work and, without co-ordination, overstrain local hospital and laboratory resources. This co-ordinating function could, however, be provided by the local Medical Officer of Health. Surveys carried out in general practice but administered by local Medical Officers of Health would also solve the practical difficulties of costs. In addition it provides the chance to consolidate results for a local community.

Although this arrangement would provide a suitable method of mounting surveys, it would not produce an effective organisation for subsequent research. There is need for a further body to undertake follow-up studies and research. It may be noted that in England and Wales a Local Authority requires to obtain the permission of the Ministry of Health before conducting a survey. The Ministry, however, do not undertake the responsibility for co-ordination of research. In other fields concerning the progress of therapy, there exist many influential bodies consolidating advances along disciplinarian lines, such as endocrinology or neurology. Among the large number of medical societies, there is not yet, however, a focal point for preventive medicine.

The Problem of Diabetes

PROGRESS in the past 40 years in the control of diabetes has exceeded the advances made in the many centuries before. In the first two decades the question of treatment was paramount: there was the hope that insulin might provide an effective response to the disease. But it provided only part of the solution and even then its full benefits were not obtained until advances had been made in the control of infections.

In the last two decades attention has turned to the early detection of the disease. Advances in diagnostic techniques made community screening feasible; but early detection is only a first step. The findings of the detection surveys have raised problems which before were concealed. It is probably true to say that there is less certainty in the understanding of diabetes today than there appeared to be when insulin was first isolated. It is only by working towards a full understanding of the complexity of diabetes through surveys of the community that there is hope of eventually finding the effective answer to the disease—its full prevention or cure. Meantime, early detection during the course of these diabetes surveys can bring the chance of treatment to many who would otherwise have continued as unrecognised victims of the disease.

REFERENCES

1. Papaspyros, N. S. 1964. *History of Diabetes Mellitus.* Thieme, Stuttgart.
2. Himsworth, H. P. 1948. *Proc. Roy. Soc. Med.* 62. 321, 330.
3. Stocks, P. 1949. *Sickness in the Population* 1944–1947 G.R.O.
4. Logan, W. P. D. and Cushion, A. A. 1958. *Morbidity Statistics from General Practice,* Vol. 1. G.R.O.
5. Registrar General Statistical Review 1955. *Supplement on Hospital In-patient Statistics,* 1959.
6. Coll. Gen. Prac. 1962. *Brit. Med. J.*, i. 1497.
7. Min. of Health and G.R.O. Report on In-patient Enquiry—1961. Pt. I. 1963.
8. O.H.E. 1964. *Costs of Medical Care.*
9. Wilkerson, H. L. C. and Krall, L. P. 1947. *J. Amer. Med. Ass.* 135. 209.
10. Kenny, A. J. and Best, C. H. 1951. *Canad. Med. Ass. J.* 65. 233.
11. Joslin, E. P. *et al.* 1959. *The Treatment of Diabetes,* 10th Ed. Kimpton, London.
12. Redhead, I. H. 1960. *Brit. Med. J.* i. 695.
13. Walker, J. B. and Kerridge, D. 1961. *Diabetes in an English Community,* Leicester Univ. Press.
14. British Diabetic Association. 1964. Private communication.
15. Harkness, J. 1962. *Brit. Med. J.* i. 1503.
16. Mills, G. A. and Campbell, A. J. M. 1964. *Med. Off.* 111, 315.
17. Dewar, J. 1964. *Med. Off.* 111, 313.
18. Sharp, C. L. 1964. *Proc. Roy. Soc. Med.* 57, 193.
19. Crombie, D. 1964. *J. Coll. Gen. Practit.* 7. 379.
20. M.P.N.I. Report for 1962. Cmnd. 2069.
21. Wilkerson, H. L. 1955. *J. Chron. Dis.* 2. 464.
22. Butterfield, W. J. H. 1964. *Proc. Roy. Soc. Med.* 57. 196.
23. Keen, H. 1964. *Proc. Roy. Soc. Med.* 57. 200.
24. Tunbridge, R. E. 1953. *Lancet* ii. 8. 95.

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