

A COMPREHENSIVE SURVEY  
INTO THE INCIDENCE OF  
GLYCOSURIA AND DIABETES MELLITUS  
IN AN URBAN COMMUNITY

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Diabetes Mellitus, of all the chronic diseases, is the one condition which can most readily be detected. Unfortunately the interval between the onset of the condition and its diagnosis is far too great and this will be lessened only by more frequent routine examination of the urine. The only way in which an early diagnosis of diabetes will ever be made is to search for it. Various estimates of the incidence of diabetes have been made. Marks (1947) estimated the incidence of diabetes to be 0.48% and that there were 670,000 diabetics in the United States. Stocks in this country from an examination of Food Office Registers estimated that the incidence was 0.23%. In Cornwall, Andrews completed a survey into the incidence of diabetes and investigated almost 40% of the population. This work was done in conjunction with fifty general practitioners and they found 593 diabetics and of these 579 were confirmed which gave a rate of 5.6 per 1,000 and this was considered high compared with previously published figures. During the War in the United States Beardwood conducted a house-to-house canvass with the aid of civil defence personnel in Philadelphia and interviewed 34,633 people and found 357 diabetics, all of whom were known cases. This gave a rate of 1% of the population.

All these figures dealt with the incidence of cases which were known to be diabetics and any real estimate of the incidence must include not only the known cases but also the cases which are not yet diagnosed. Gates (1942) published an account of a survey in industry which covered 1,800 employees, all of whom were routinely examined as part of the work's medical service. He found 8 known diabetics - an incidence of 0.44% and 20 previously unrecognised cases - an incidence of 1.1%. No mention is made in the report of the method of urine testing or of the diagnostic criteria used to establish a diagnosis.

Elotner's (1943) survey at the Boston induction centre showed how many diabetics largely symptomless could be brought to light. He tested 45,560 consecutive inductees for the armed forces between the ages of 15 and 45 years. Benedict's qualitative test was used for the initial screening and all those who gave a positive reaction were re-tested after a meal. If the post-prandial specimen gave a positive reaction they were referred for a glucose tolerance test. Glycosuria was found in 367 cases (0.8%) and 208 of these were diagnosed as diabetics, 126 as cases of transient glycosuria and 33 as renal glycosuria. His

diagnostic criteria were a blood sugar level of more than 180 mgm/100 ml. after 100 gms. of glucose and one or more urine specimens showing evidence of sugar. He described transient glycosuria as showing evidence of glycosuria on the initial screening but not in subsequent tests.

Spellberg and Leff (1945) performed a similar study on 32,033 consecutive inductees in New Orleans and found 9 cases of diabetes out of 37 cases of Glycosuria. This gave rates of 1.15 per 1,000 for Glycosuria and 0.3 Diabetics per 1,000.

	<u>Number Examined</u>	<u>Glycosuria</u>	<u>Diabetes</u>
Blotner	45,650	367 (0.8%)	208 (0.45%)
Spellberg	32,033	37 (0.12%)	9 (0.03%)

Suggestions were made to explain the large differences between these figures. There was a difference in the age groups tested. Blotner's age groups went up to 45 years while Spellberg's went up to 35 years and it is well known that diabetes is more common in the older age groups. There were also differences in the geographical areas of the two groups. There was a low incidence in the rural south which was the source of most of Spellberg's inductees and a high incidence in the industrial north from where most of Blotner's recruits came. The Journal of the American Medical Association (1944) said that Blotner's survey was not representative as it was largely an urban community and included a larger proportion of Jewish stock among whom diabetes is considered to be more prevalent. Spellberg's group included more negroes among whom diabetes was considered to be less prevalent. However, as Joslin (1952) says "Negroes appeared at one time to be almost immune to diabetes but the falsity of this concept has long been evident."

This statement differs from the experience of Politzer (1960) who found a very low incidence of diabetes among a primitive African negro group and he has suggested that it may be due to differences in the mode of life, particularly in connection with dietary habits. This view is supported by Seftel (1960) who found striking differences in the incidence of diabetes in two groups of rural and urban female Africans. It may be that Diabetes is less prevalent among primitive communities but as the march of civilization overtakes them, that they

lose, through changes in diet and habits, their racial immunity to Diabetes. The differences between Blotner's and Spellberg's surveys have never been satisfactorily explained by racial or geographical variations but there were differences in their diagnostic criteria which probably played some part in the differences.

Blotner (1946) was stimulated by the discussion caused about these differences and tested another group of recruits and in all included 69,088 men between the ages of 18 and 37 years. He used Galatest as a screening test and all people who were positive were retested with Benedict's Qualitative Solution. The blood sugar was measured by the method of Folin and Wu. He found 1,383 cases of Glycosuria which gave a rate of 2.0%. He performed 479 glucose tolerance tests and found 251 Diabetics. His diagnostic criteria were as follows:-

1. Normal Curve - Fasting Blood sugar below 130 mgm/100 ml  
Peak level below 165 mgm/100 ml.
2. Potential Diabetes - Peak level 165 mgm/100 ml. in  $\frac{1}{2}$  - 1 hour  
and some or all specimens containing sugar.
3. Diabetes - Peak level greater than 170 mgm. and some or all  
specimens containing sugar.

Using these criteria for his glucose tolerance tests he found 190 normal curves, 38 potential diabetics and 251 cases of Diabetes. Blotner thus discovered an even higher proportion of cases of glycosuria than he found in his first series but a similar proportion had diabetes. It has been suggested that the high incidence of diabetes in Blotner's series was due to his reliance on the height of the curve to establish the diagnosis and he paid no diagnostic significance to the fasting level or to the return of the curve to normal or otherwise after two hours. Some of the cases he diagnosed as diabetics would no doubt have been considered to be cases of lag curve in this country. However, this emphasis on the height of the curve did not explain the differences in the incidence of glycosuria in his series and other series.

Fox (1952) tested 19,358 students at the University of Minnesota between the ages of 14 and 37 years but the vast majority were between the ages of 17 and 27 years. He found 155 cases of glycosuria (0.8%) and 70 cases of Diabetes. It has been said that the incidence of glycosuria in Blotner's series may have been high because of emotional

factors causing glycosuria. This may well have been an important factor as the induction of civilians into the armed forces seems to me to be of sufficient stress to cause glycosuria, that such emotional stress can cause glycosuria has been shown by the work of Edwards (1931).

A similar study was carried out by Burn (1956) in Salford. His aim was to search for cases of diabetes not yet diagnosed. His scheme was run in conjunction with a Mass Radiography programme. There was considerable previous publicity and leaflets were distributed round the town explaining the aim of the survey and asking people to bring a specimen of urine to the centre when they attended for their Mass Radiography Examination. 4,549 attended for X-ray and of these 2,165 (47%) brought urine specimens. Clinitest was used for the initial screening, one tablet being dropped in 1 ml. urine. If this test was positive the standard Clinitest method was used. All the cases which were positive with the standard test were referred for further investigation. 150 people were positive to the screening test and of these 31 were positive to the standard test. This was an incidence of 1.4% of those who submitted specimens. 29 people were further investigated by the laboratory and glycosuria confirmed in 16 people. 6 newly discovered diabetics were found (0.28%) and 7 cases of renal glycosuria.

All these surveys showed that there was a reservoir of undiagnosed diabetes in the countries concerned but all of the surveys were limited in scope as only selected groups of the community were examined and it was impossible to give an estimate of the true incidence of diabetes mellitus.

The first comprehensive survey to ascertain the true incidence of diabetes in a community was carried out by Wilkerson and Krall (1947). They tested 3,516 (70.6%) people out of the total population of 4,983 in Oxford, Mass. The age composition of Oxford closely paralleled the age composition of the country as a whole and the survey was thus considered to be of particular value in assessing the incidence of diabetes in the United States. Wilkerson and Krall tested specimens of urine passed one hour after the midday or evening meal and special centres were set up for the testing procedures. Blood samples were also taken when the people attended, venous samples were taken from

adults and capillary from children. The blood sugar was measured by the method of Folin and Wu. The urines were tested by Benedict's qualitative method and those that gave a positive reaction were retested by Benedict's quantitative method.

The screening criteria used were as follows:-

1. Those cases having a venous blood sugar level of 160 mgm per 100 ml, or a capillary blood sugar level above 190 mgm per 100 ml, were selected for further tests.
2. Those cases with blood sugar levels below the above figures and no glycosuria were considered to be normal.
3. People with Glycosuria with or without Hyperglycaemia as defined above were given a second test.

The second tests were carried out 1-1½ hours after a meal and if the blood sugar level was above 170 mgm/ 100 ml, (Venous) or 200 mgm/100 ml, (Capillary) the patient was considered to have diabetes. If the second test was not in accord with the screening test a glucose tolerance test was performed. Glucose tolerance tests were also done in border line cases, in people with persistent hyperglycaemia without glycosuria and in people with persistent glycosuria without hyperglycaemia. In cases with a history of known diabetes further tests were performed if the records did not show blood sugar levels considered to be diagnostic in the survey. Emphasis was placed on the height of the curve in the glucose tolerance test and no account was taken of the initial blood sugar level or the duration of hyperglycaemia.

The cases were classified thus:

1. Normal. Non-Diabetic.
2. Known Diabetics.
3. Newly discovered Diabetics.
4. Unclassified Glycosuria. Those cases with glycosuria without hyperglycaemia.
5. Hyperglycaemia without glycosuria.

There were 231 people with glycosuria or hyperglycaemia or both. 40 (0.8%) known cases of diabetes and 30 (0.6%) newly discovered cases were found in the survey. This gave a total incidence of 1.4% of those tested. The most common finding was glycosuria without hyperglycaemia. 123 people had glycosuria, without hyperglycaemia

on screening and 104 were negative when subjected to a second test. 17 of these people with glycosuria were considered to have unclassified glycosuria. There were 43 people with hyperglycaemia without glycosuria and of these 8 were considered to have diabetes when retested. The authors comment that fasting blood sugar tests were unreliable as a means of excluding diabetes. They also considered that both blood and urine tests were necessary and supported their opinion by pointing out that if they had used urine tests only, 8 cases of diabetes would have been missed while if they had used blood tests only, 6 cases of diabetes would have been missed. The border line cases found in their survey were considered to require follow up and perhaps serial blood sugar tests before a firm diagnosis could be made.

Four years later, Wilkerson and Krall (1953) returned to Oxford for a progress study to discover what had happened to the 70 originally classified as diabetics and to the 118 with border line blood sugar levels (above 140 mgm per 100 ml, and below 170 mgm per 100 ml, (venous blood)).

In addition a control group of 225 were selected to match the above group on the basis of age and sex distribution. This group had normal blood sugar levels in the original study. In the intervening four years 16 of the original diabetics had died. In the suspect group (those with border line blood sugar levels in the original study) a total of 17 new cases of diabetes (14.4%) were found while in the control group only 4 new cases (1.8%) were found. In other words those with slightly elevated blood sugar levels became diabetic about eight times more frequently than those with normal blood sugar levels. A further progress report by Wilkerson and Krall (1959) has shown that in general the suspect group are still becoming diabetic eight times faster than the matched control group while the persisting glycosuria cases are not becoming diabetic unless they originally also had hyperglycaemia.

Following this report mass screening surveys have been carried out on a large scale in the United States. In 1949 McBryde tested 17,451 people in the course of a detection drive in St. Louis and using Galatest as a screening procedure found 3.5% of those tested to have glycosuria. Sharkey (1950) reported the results of a continuous diabetes detection drive in Dayton, Ohio. There was considerable



previous radio and newspaper publicity and numerous voluntary bodies were acquainted with the aims of the drive. Galatest powder was used for testing the urine specimens which were collected 1-3 hours after a meal rich in carbohydrate. Suitable menus for such meals were described in the newspapers. All cases which had a positive urine test were referred for blood sugar tests. The two principal groups co-operating in the drive were schools and industrial firms. No details were described of the numbers refusing to be tested. A total of 69,159 people were tested and 2,991 (4.7%) gave a positive result with Galatest. Among this number were 151 known cases of diabetes and 148 newly discovered cases. This was a total incidence of 0.43%.

In the following year Loubé (1951) reported on 19,828 people tested during a detection drive in Washington. Using Galatest for screening purposes he found 866 people (4.4%) to have glycosuria. A further finding in his survey was that nearly one-third of the patients had taken no action even though they had been told that their urine contained sugar and that they should contact their own doctor. Olmstead (1953) described a survey in which he used the St. Louis Dreyapak, which is a filter paper strip which is dipped in the specimen of urine and allowed to dry, as a screening test. They distributed these Dreyapak strips to 270 chemists shops in the town and to several large industrial firms. Only 12% of those distributed to the public through chemists' shops and only 14% of those given out by industrial firms were returned. 1.75% of those tested were found to be suffering from diabetes. More recently Bouton (1960) described the results of the Schenectady Diabetes Detection programme. 6,000 people are tested annually, blood sugar tests being measured by the Wilkerson-Heftman method for true glucose. Capillary blood is used and taken  $1\frac{1}{2}$  -  $2\frac{1}{2}$  hours after a meal and 160 mgm. per 100 ml, is the screening level. They have found 237 cases above the screening level and of these 100 (0.9%) were newly discovered cases of diabetes.

Since 1947 a total of 109 surveys have tested over one million people in the United States (Joslin 1959). About three-quarters of these surveys used blood tests alone or in combination with urine tests. The most commonly used screening level was 130 mgm. per 100 ml. of venous blood without regard to previous food intake. The doubtful cases

are usually referred to their own doctors who made the final diagnosis. The average survey result appeared to vary from 1.0% to 1.5% diagnosed as diabetic depending on the type of population, the thoroughness of the testing technique and the effectiveness of the organisation of the survey. The smallest yield is reported as being 0.1% among 3,547 industrial workers in Peabody, Mass. while the largest percentage found was 8.3% among 156 Indians over the age of 14 years who were tested in Ignacio, Colorado.

The second comprehensive community diabetes drive was carried out by Kenny, Chute and Best (1951) in Newmarket, Ontario, and tested 4,419 (81%) of the population over school age. They used blood and urine tests about 1-hour after breakfast or lunch. The urines were tested with Clinitest which is a modification of Benedict's qualitative method. Capillary blood samples were taken and the blood sugar was measured by a modified Somogyi-Nelson method which was said to be effective in preventing the passage of non-glucose reducing substances, mainly glutathione and thus was a measure of the true glucose present. These levels were thus lower than those using the Folin and Wu method.

The screening criteria used by these authors were as follows:-

1. A blood sugar level greater than 160 mgm per 100 ml,  $\frac{1}{2}$  -  $1\frac{1}{2}$  hours after a meal.
2. A blood sugar level greater than 150 mgm. per 100 ml,  $1\frac{1}{2}$  - 2 hours after a meal.
3. A blood sugar level greater than 120 mgm. per 100 ml, 2 hours after a meal.
4. Glycosuria.

If any of the above criteria were present the person was re-examined. The re-examination consisted of a glucose tolerance test and the diagnostic criteria were:-

Glycosuria together with any one of the following -

1. A fasting blood sugar level greater than 120 mgm. per 100 ml. - Diabetes diagnosed.
2. A peak blood sugar level greater than 200 mgm. per 100 ml, and a 2-hour blood sugar level above 120 mgm. per 100 ml, - Diabetes diagnosed.
3. A blood sugar during the initial screening of greater than 200 mgm. for 100 ml, - Diabetes diagnosed.

The authors also said that diabetes would be diagnosed if the levels were markedly in excess of the above values even though no glycosuria was discovered. It will be seen that the diagnostic criteria are more stringent than those adopted by Wilkerson and Krall. In the Newmarket survey 54 cases of diabetes were found, 1.2% of those tested and this included 21 previously undiagnosed cases. The incidence of glycosuria was 2.8% and no attempt was made to classify the cases of non-diabetic glycosuria. Kenny et al. comment on their survey that one case of glycosuria would have been missed if blood samples only had been taken and 5 cases of hyperglycaemia would have been missed if urine samples only had been tested.

Two years later Kenny and Chute (1953) carried out a further survey in two Ontario towns, Hawkesbury and South Porcupine. They used similar methods to those used in the Newmarket survey, testing post prandial blood and urine specimens. The urines were tested with Clinitest and the blood sugar measured by the modified Somogyi-Nelson technique. They tested 70% of the population over six years of age in South Porcupine and 60.5% of those over six years of age in Hawkesbury. The total number tested was 6,673 and 87 (1.3%) Diabetics were found. This included 35 newly discovered cases.

In other countries estimates have been made of the prevalence of diabetes and efforts are being made to discover undiagnosed cases. Albertsson (1953) tested 59% of the population of Akranes, Iceland and found one known case and three new cases. Nakayama (1956) tested 4,000 people over 40 years of age in Japan and found 146 diabetics - 3.7% of those tested. Von Schliack described the results of testing 12,389 people in Germany among whom he found 229 (1.84%) cases of diabetes. Mulder (1958) in Holland, Broch (1958) in Norway and Martensson (1958) in Sweden have described their programmes of diabetes detection which were carried out in conjunction with Mass Radiography Drives. The incidence of diabetes has been discovered to be approximately the same as that found in other countries. Czyczyk in Warsaw (1958) has said his first results show that the disease is much more prevalent than it was originally thought and that for every known case of diabetes there are about

two undiscovered cases.

In this country very few attempts have been made to ascertain the incidence of diabetes in the community and diabetes detection programmes have not yet been introduced. Cochrane and Miall (1956) reported on the results they had obtained during a Medical Research Council survey which was principally concerned with the investigation of pneumoconiosis and tuberculosis in South Wales. This is the first community survey in this country which I have been able to find in the literature. They tested 23,000 people in the Rhondda Fach and 8,000 people in the Vale of Glamorgan and found incidences of diabetes of 1.19% and 1.02% respectively. Details of their methods and diagnostic criteria were not described.

The second survey which was described was that of Redhead (1960). He tested a total of 1,991 people which was 20% of the people in the practice in which he worked. Urine samples were tested and the people were asked to fill the specimen bottles 1-hour post-prandially. The specimens were tested with Clinistix and if a positive reaction was obtained they were retested with Clinitest. All those who gave a positive reaction to Clinistix were offered a blood sugar estimation. In most cases a glucose tolerance test was performed but in certain instances a single two-hour post-prandial blood sugar estimation was made instead. The survey was the first survey which made an attempt to classify the cases of non-diabetic glycosuria. The diagnostic criteria used in the interpretation of the glucose tolerance test were as follows -

1. Fasting level greater than 120 mgm per 100 ml, and glucose in one or other urine specimens. Diabetes diagnosed.
2. Peak level greater than 190 mgm per 100 ml, and time taken to return below 100 mgm. per 100 ml, more than two hours and glucose present in one or other urine specimens: diabetes diagnosed.

3 The blood sugar estimation used was the colorimeter method for true sugar first described by Haslewood and Strookman (1938) and modified by King (1946).

Of the 1,991 people tested 105 were found to have glycosuria - 5.27%, 19 cases of diabetes were encountered during the survey - an incidence of 0.95%. Nine of these were known previously and the remaining 10 were diagnosed as a result of the survey. 14 of the 19 cases were female and five were male. 13 were found in the age

group of 50-69 years and six cases (31.6%) gave a family history of diabetes.

The sample of the practice that was tested was fairly representative of the City of Newcastle and the survey demonstrated that there was a reservoir of undiagnosed diabetes in the practice tested and Redhead suggested that diabetes detection drives should be carried out in this country. Redhead's survey though most valuable was not a community detection drive but was limited to the practice in which he worked.

Walker (1959) produced a preliminary report on her work in Ibstock, Leics. which was later more fully described (1961). In this rural parish of 5,406 inhabitants which was considered to be static 81% of the population over 5 years of age were tested. Field workers called at each house and left a specimen bottle for each person in the household. It was explained that the bladder should be emptied before the evening meal; four extra teaspoonsful of sugar (20 Gm. Carbohydrate) should be taken with that meal and the specimen of urine required should be passed one hour later, put into the bottle supplied, and named. The field worker called the next day and tested it with Clinistix in the presence of the family. Any positive urine was also tested with Testape and Clinitest. All the subjects with a positive reaction to Clinistix were requested to attend for a glucose tolerance test. Capillary blood samples were used during the tolerance test and the blood sugar was estimated by the true blood glucose method of Asatoor and King (1956) the results of which are closely correlated with the glucose oxidase method (Middleton and Griffiths 1957).

4,105 people were tested which represented 81% of the population over 5 years of age. 167 cases of glycosuria were discovered and 33 known diabetics were encountered during the survey. The diagnostic criteria used were based on those of Conn (1958) and the levels considered important during the tolerance tests were -

1. One hour level 160 mgm per 100 ml,
2.  $1\frac{1}{2}$  hour level 140 mgm per 100 ml,
3. 2 hour level 120 mgm per 100 ml.

These levels were taken to divide the intermediate and lower blood sugar curves and it was of interest that this level separated

the cases of transient or intermittent glycosuria from those constantly exhibiting glycosuria.

The cases of glycosuria were subdivided according to their blood sugar curves into -

- (a) Latent Diabetics with levels well above those described above - 25 people.
- (b) Intermediate Blood sugar levels up to or just above the levels described - 42 people.
- (c) Transient Glycosuria. Blood sugar levels below those described - 75 people.
- (d) A group of 25 people with glycosuria on whom no test was performed.

The total percentage of diabetics was 1.4% which consisted of 33 known diabetics (0.8%) and 25 newly discovered cases (0.6%).

It is hoped that a follow up survey will be carried out in Ibstock in about five years in order to find out exactly how much greater is the chance of developing diabetes in the cases of glycosuria than in the apparently normal population and also to try and find out more information about the pre-diabetic state.

It may be asked whether there is any advantage in detecting these mild symptomless cases of diabetes. The work of Wilkerson and Krall (1953) suggested that these mild cases tended to become more severe. It is also thought that the complications of diabetes are more common and severe in the undiagnosed diabetic. Lawrence (1960) says that septic lesions are more deep-seated and extensive in the undiagnosed or poorly controlled diabetic. This view is confirmed by Winter (1960) who states that there is adequate clinical evidence that early case finding and strict control will delay the onset of vascular complications and minimise their severity. The early detection and management of diabetes is said by Dunlop (1959) to be vital if the degenerative changes that so often accompany untreated diabetes are to be prevented. Joslin (1959) states that most diabetic patients who develop neuropathy have had antecedent periods usually of months or years duration of neglected or poorly managed and uncontrolled diabetes. This emphasis on the early detection and careful control in the prevention of complications is confirmed by other authors. (Lister, (1959) Keiding et al, (1952), Marble (1955) Root et al, (1959) ).

Though the importance of diagnosing diabetes has been realised for years, many cases are first discovered by the onset of one of these complications. The discovery of these mild symptomless cases should help to reduce the incidence of these complications.

The aim of this present survey was to ascertain the incidence of diabetes in Halstead, Essex and to discover any unknown cases and also whether diabetes detection drives were a practical reality as a routine public health measure in this country. An attempt was also made to classify the cases of non-diabetic glycosuria.

POPULATION TESTED

Halstead is a market and industrial town in North West Essex with a population of exactly 6,000 (1951 Census). There are two wards separated by the River Colne on whose banks the town is built. The inhabitants are mostly Halstead born and bred and there are comparatively few strangers. There is no strong racial element and in particular no Jewish element. The only outsiders in the town are 35 American Servicemen and their families making a total of about one hundred. There are two residential institutions in the town. One is an Essex County Council Old People's Home which has 30 residents with equal numbers of each sex. The other institution is a Residential School for Educationally Subnormal Children which has 90 pupils, all of whom are girls. Halstead is thus not a completely natural population unspoilt by artificial migration. The industries in Halstead consist of the manufacture of textiles, foundry work and the assembly of photo-electric instruments. The textile mill employs about 700 people, many of whom are women and young girls. This mill was acquired by the firm in 1828 but had been in existence before that date. The foundries of which there are four in the town produce oil fired boilers, general castings, non-ferrous castings and steel castings. The firm which assembles photo-electric instruments has only been in existence for 15 years but now employs over 100 people who are engaged in assembling instruments which are used in light measuring in numerous branches of science, technology, industry and medicine.

There are four general practitioners in the town working in two partnerships and the majority of the inhabitants are on the list of one or other of these partnerships.

The survey was not preceded by any preliminary publicity but after the first few weeks work it was well known that such a survey was in progress and in a small town like Halstead the feeling of community participation made a great deal of difference to the response to the survey. The field work was done by two people, one of whom was a recently retired health visitor who was very well known in the town and the other was the author of this thesis.

There are 2,236, houses in the town of which 795 are owned by the Council. There are two main Council house estates, the pre-war



estate of about 200 houses which are built in terraces and the post-war estate of some 500 houses which has been laid out on garden city lines.

#### SELECTION OF SCREENING TESTS.

The total number of new cases discovered must be the main objective in any screening programme. The tests selected should be sensitive and specific. Sensitivity requires a high proportion of diabetics to be positive and specificity requires a high proportion of non-diabetics to be negative to the screening tests (Wilkerson (1956)). Any screening test must be a compromise between the ideal and the practical. The tests which are well known in laboratories cannot necessarily be used as modifications have to be introduced to deal with the somewhat different conditions existing in a large scale field survey. The method must be rapid and inexpensive. Numerous studies have pointed out the advantages of obtaining blood as well as urine samples. (Wilkerson and Krall (1947), Kenny and Chute (1951)). Harting et al (1951) agreed that blood sugar measuring was more efficient than urine testing but said the differences were less marked in finding those with marked hyperglycaemia and glycosuria. Engelhardt et al (1953) confirmed this and said the ideal test would be blood and urine tests after carbo-hydrate loading. This was confirmed by Fitcher et al (1953). Wilkerson said if only one test was to be done it should be the blood sugar test as such a test was more specific as well as more sensitive for diabetes detection. In spite of the great advantages of testing blood and urine specimens it was considered to be impractical to do both tests as a greater number of people would have been necessary to do all the work. Olmstead (1953) said that it was his belief that few diabetics would fail to show glycosuria if tested about 2 hours after a large meal. It was hoped that the greater sensitivity and specificity of the enzyme urine test (Luntz (1957)) which had not been used by those workers advocating blood and urine tests would reduce the possibility of missing any cases with hyperglycaemia without glycosuria.

There are various types of urine tests available and which have been used for mass screening. There are two main groups.

1. Tests that measure reducing substances in urine.

(a) Benedict's qualitative test. Eight drops of urine are added to 5 ml. of Benedict's solution and boiled for two minutes. If "sugar is present a red or yellow precipitate of cuprous oxide is seen.

(b) Clinitest is a modification of Benedict's test in which a reagent tablet is dropped into a measured amount of diluted urine. Heat is generated by the sodium hydroxide which is present in the tablet and the colours produced if "sugar" is present are the same as in Benedict's test.

(c) Galatest in which a white alkaline powder containing bismuth is used. A drop or two of urine is placed on a small amount of the powder; the presence of sugar is indicated by the production of a grey or black colour. (Reduction of the bismuth). The reaction is complete in less than 30 seconds.

(d) St. Louis Dreyapak. This consists of a strip of filter paper which is sewn to a piece of polyethylene film. The filter paper is prepared by soaking it in 1% solution of sodium fluoride and drying it. The filter paper is dipped in a specimen of urine and allowed to dry. Dried "sugar" is said to be preserved for as long as 90 days. When the dried strips are collected they are suspended in a pan of boiling benedict's reagent and the colours produced by the presence of "sugar" are similar to those shown by Benedict's Test in a test tube.

2. Enzyme tests which are specific for glucose.

These tests consist of a strip of filter paper impregnated with glucose-oxidase, o-tolidine and with a second enzyme, a vegetable peroxidase. When the strip of paper is dipped in urine containing glucose and withdrawn, the glucose in the minute amount of urine absorbed on the strip is oxidised by atmospheric oxygen in the presence of the oxidase. Gluconic acid and hydrogen peroxide are formed and the latter then reacts with o-tolidine in the presence of the peroxidase to produce a blue pigment. There are two proprietary names of reagent using this reaction - Clinistix and Tes-Tape. Clinistix is provided in the form of separate strips of thin paper resembling a book-match; only the last half-inch is impregnated with the reagents. No colour scale is provided and the makers state that the test should not be used quantitatively.

Tes-Tape is provided as a roll of test paper and the paper is impregnated with an additional reagent - a yellow dye which gives colour changes ranging from light green through dark green to dark blue according to the concentration of glucose in the urine. A colour scale is provided. Various authors have investigated these enzymes tests, Hunt (1956), Tunbridge (1956), Jablokov et al (1957), Moran (1957) and Leonards (1957) and they report that Clinistix and Tes-Tape turn blue with glucose concentrations as little as 0.01 - 0.1% but their use as a quantitative test is inaccurate. The limit of sensitivity of these enzyme tests is greater than that of Benedict's test which reveals "sugar" in urine when it amounts to 0.15% or higher (Harrison, (1957)). It was decided to use Clinistix as a screening procedure and Clinitest as a quantitative test for further testing of those urines giving a positive result with Clinistix.

#### INVESTIGATION.

Labelled specimen bottles were delivered to each house in the town together with a duplicated letter signed by all the doctors in the town (Appendix A.). The explanatory letter described the aims of the survey, appealed for the co-operation of each person and included a form which was to be completed and returned with the bottles on the following day. The form required the householder to fill in the name, age and occupation of each person in the house. Instructions were given to fill the bottles one hour after the main meal of the day and put their names on the bottles. Details of any known diabetics in the house were obtained. In some cases these known diabetics submitted specimens for testing but the majority did not. It was found that some people had recently had a specimen of urine tested. These included life insurance and ante-natal examinations and investigations in hospital or by the general practitioner. It was decided that if the examination had been carried out within the last three months a further test was unnecessary. In doubtful cases a further sample was obtained. The bottles were collected on the following day together with the form. The electoral register was used as a basis for the survey but it was carried out street by street and it was occasionally found that a house did not appear on the register as it had been unoccupied when the register was compiled. In these cases the house was included in the survey. Consideration was given

to asking the people to test a specimen of their own urine but the experience of Getting et al (1952) decided against this method in the survey. He found that only 41% of the people who had obtained the self-test kit actually tested their urine. Burn (1956) found that only 47% of the people who attended for Chest X-Ray and had been asked to bring a urine specimen did so. This public apathy made it necessary for a more personal approach which was obtained by delivering the bottles and collecting the bottles on the following day.

#### URINE ANALYSIS.

The bottles were collected on the following morning and taken back to a centre where they were checked against the list of people to whom bottles had been given. They were then tested with Clinistix. The Clinistix was dipped in the specimen of urine, withdrawn and placed on top of the bottle to allow the colour change to take place. The colour is said by the manufacturers to develop in one minute but in this survey the sticks were left for two minutes before being discarded. The specimens were all tested on the same day that they were collected. All the urines which gave a positive reaction with Clinistix were tested with Clinitest which is a modification of Benedict's test and is an accurate quantitative test. All the people whose urines gave a positive reaction with Clinistix were offered a blood sugar test. It was hoped that they would all have a glucose tolerance test but this was not possible in every case. The known diabetics were not subjected to further blood sugar tests as all their records were available and it was not considered necessary to repeat the tests.

In the case of infants from whom it was impossible to obtain a specimen of urine the mothers were asked to press the end of a Clinistix between two folds of a wet nappy and note the colour change and return the Clinistix with the other specimens.

#### POSTAL SURVEY.

A certain number of people refused to accept the bottles or they were returned empty. Details of these refusals were collected and a letter signed by their own doctor was sent to each of these people (Appendix B). The letter contained a small envelope, containing a Clinistix and printed on the envelope was:

TICK COLOUR CHANGE

TICK COLOUR CHANGE

NO CHANGE

BLUE

OTHER COLOUR

A stamped addressed envelope was also enclosed for the return of the Clinistix and the form. The Clinistix was examined when it was returned as well as noting the colour change marked on the envelope. This is somewhat similar to the method described by Crombie (1959) which was used as a pilot survey by the College of General Practitioners. In their survey the Clinistix was contained in a glass vial with Silica-gel in the base and sealed by a plastic push-on cap. This was presumably done to ensure that the Clinistix would retain its ability to change colour when used. We carried out some tests prior to this survey and it was found that even after the Clinistix had been out of its container and been sent through the post, it retained its ability to change its colour when dipped in a specimen of urine containing glucose. It was also discovered in these tests that the blue colour of the positive Clinistix persisted for several days even if exposed to the air.

GLUCOSE TOLERANCE TEST.

The glucose tolerance test was a modification of the standard test as described by Panton and Marrack. A full diet was consumed up to 11 p.m. the night before the test. After a fasting blood sample had been taken, a dose of 50 gm. of glucose in water was taken by mouth and blood and urine samples taken after  $\frac{3}{4}$  hour and after 2 hours. Venous samples were taken.

The reasons that this test was used rather than the standard test with samples at half-one, one and a half and two hours were two-fold, Firstly this method was the one in common use by the laboratories doing the tests and secondly the large numbers involved and the fact that a large number of the tests had to be done in the patients' homes would have made the standard test very time consuming. The specimens were tested at the Pathological Laboratories at the Essex County Hospital, Colchester and St. John's Hospital, Chelmsford. The blood sugar was measured by a modification of the method of Folin and Wu as described by Varley (1958). This method was further modified by the dilution of the blood with an isotonic solution of sodium sulphate which removes glutathione which is the

chief substance other than glucose causing reduction. This method gives a result which is near the figure for true glucose.

### DIAGNOSTIC CRITERIA

#### Fasting Blood Sugar.

A fasting level greater than 120 mgm. per 100 ml. and glucose in the fasting specimen was considered to be diagnostic of diabetes.

#### Glucose Tolerance Test.

The interpretation of this test was similar to that used by Redhead and based on the criteria suggested by Harrison (1957).

#### Normal Curve.

Fasting level 80-120 mgm/100 ml. of blood,  $\frac{3}{4}$  hour level less than 180 mgm., return below 100 mgm. by 2 hours and no glucose in any urine specimen.

#### Diabetic Curve.

Fasting level greater than 120mgm. per 100 ml. and glucose in one or more urine specimens; diabetes diagnosed.  $\frac{3}{4}$  hour level greater than 190 mgm. per 100 ml; time taken for return to below 100 mgm. greater than 2 hours even though fasting level normal and glucose in one or more specimens of urine: diabetes diagnosed.

#### Lag-Storage Curve.

Fasting level is normal,  $\frac{3}{4}$  hour level greater than 180 mgm. Time taken for return to below 100 mgm. per 100 ml. less than 2 hours and glucose present in one or more urine specimens.

#### Renal Glycosuria Curve.

Normal curve as described above but glucose present in one or more urine specimens.

#### Hyperglycaemia sine Glycosuria.

Fasting level is above 120 mgm. per 100 ml.,  $\frac{3}{4}$  hour level is above 180 mgm., curve is much prolonged, and no glucose is present in any urine specimen.

The exception in these criteria to those advocated by Harrison (1957) is the substitution of the  $\frac{3}{4}$  hour level for the peak level. Harrison says that the highest point or peak of the curve is normally within the first hour. In the standard glucose tolerance test it is sometimes the half hour and sometimes the one hour level which is found to be the highest point of the curve. For practical purposes the  $\frac{3}{4}$  hour level should in most cases give a reading which is near to the peak of the curve.

Another difference from the criteria used by Redhead is in the hyperglycaemia sine glycosuria which he used for cases with a normal fasting level while I have retained the levels originally suggested by Harrison. The criteria for all these curves as described by Harrison are for capillary blood while I have used the same criteria for venous blood. The fasting levels of capillary and venous blood are approximately the same but after glucose the venous blood sugar may be lower than the capillary level.

RESULTS.

5,562 people had a specimen of urine tested for glucose. There were 2,655 males and 2,907 females. A further 104 had recently been tested and 137 people responded in the postal survey and tested themselves and returned the Clinistix. Details were obtained of 40 people who were reputed to be known diabetics and are not included in the previous figures. The total number covered by the survey was thus 5,843 which represents 97.38% of the population of 6,000 (1951 Census). However, details of the refusals were collected and of the 426 who refused initially only 137 replied to the postal survey and 289 refused. If this is added to the number covered by the survey the resident population of Halstead is found to be 6,132 and the percentage covered in the survey is 95.28%. The 289 people who refused represent 4.72% of the total population.

The details of the age groups tested and the total population are shown in the following tables. The known diabetics are excluded from the tables.



**TABLE I.** Age distribution of people tested in survey, recently tested and those who responded to postal survey (known diabetics excluded)

Age	Tested during Survey		Recently tested by own Doctor.		Postal Survey		Total covered by Survey.	
	M.	F.	M.	F.	M.	F.	M.	F.
0 - 9	377	423	1	2	1	-	379	425
10 -19	348	420	1	5	4	6	353	431
20 -29	311	284	7	15	6	3	324	302
30 -39	374	379	3	7	8	6	385	392
40 -49	385	362	5	10	5	7	395	379
50 -59	370	395	5	12	12	13	387	420
60 -69	281	348	4	15	17	21	302	384
70- 79	162	220	5	6	5	17	172	243
80 -89	44	70	1			6	45	76
90 -99	3	6					3	6
<b>TOTAL:</b>	<b>2,655</b>	<b>2,907</b>	<b>32</b>	<b>72</b>	<b>58</b>	<b>79</b>	<b>2,745</b>	<b>3,058</b>
								<b>2,745</b>
								<b>5,803</b>

**TABLE II.** Age distribution of people covered by survey compared with age distribution of population of Halstead (1951 Census).

Age	Total Population		Total covered by Survey	
	Male	Female	Male	Female
0 - 9	418	365	379	425
10 -19	337	406	353	431
20 -29	364	387	324	302
30 -39	398	399	385	392
40 -49	431	463	395	379
50 -59	365	415	387	420
60 -69	271	373	302	384
70 -79	179	274	172	243
80 -89	52	94	45	76
90 -100	2	7	3	6
<b>TOTAL:</b>	<b>2,817</b>	<b>3,183</b>	<b>2,745</b>	<b>3,058</b>
	<b>6,000</b>		<b>5,803</b>	

**TABLE III.** Percentage Age distribution of Population tested compared with that of England and Wales. (Mid. 1959)

Age in years	Percentage in Each Age Group England and Wales.		Percentage in Each Group covered by Survey	
	Male	Female	Male	Female
0 - 9	15.76	13.97	13.06	13.16
10 -19	15.38	13.79	12.17	13.37
20 -29	12.95	12.15	11.24	9.35
30.-39	14.68	13.90	13.27	12.16
40 -49	13.73	13.23	13.82	11.73
50 -59	13.29	13.33	13.41	13.15
60 -69	8.38	10.45	10.48	12.31
70 -79	4.52	6.74	6.00	7.58
80 and over	1.31	2.44	1.69	2.61
<b>TOTAL:</b>	100.00	100.00	95.14	95.42
			Refusals 4.86	4.58
			<b>Totals</b> 100.00	100.00

It will be seen from the Tables that in some age groups more people were tested than were present in that group in the 1951 Census. This anomaly is due to the increase in the population since then and the progression of the population from one age group to the next.

Table III shows the percentage of the population of Halstead in each group which was covered by the survey. The population was taken to be 6,123 which was the number discovered in the survey. Unfortunately it was impossible to place the refusals in their age groups as the information was not available. There were 141 males and 148 females who refused and the vast majority were adults.

Table III shows that the population covered by the survey was not a representative sample of the population of England and Wales. In the age groups under 40 years the population tested was much less than that of England and Wales. The difference in any one decade varied from 0.42% to 3.21%. In the age groups 40 - 49 and 50 - 59 there was a much closer comparison between those tested and of the population of the country as a whole. In the last three age groups the percentage tested was greater than that of the country as a whole. Thus it will be seen that the population tested could not be considered to be a national sample as the percentage tested was much less in the decades under 40 years reasonably representative in the fourth and fifth decades and not representative in the next three decades.

Glycosuria

Of the 5,562 people covered by the survey 148 were found to have glycosuria. Six of the people in the postal survey returned Clinistix stating that they had turned blue. Only four of these were blue when examined. Subsequent one hour post-prandial urine specimens of the remaining two people failed to show any evidence of glycosuria. This was similar to the findings of Crombie (1959) half of whose results were noted as blue but no colour change was seen when the Clinistix was examined by the practitioner. He assumed that these mildly positive tests were due to contamination of the Clinistix by the patient's fingers when testing. There were thus 152 cases of glycosuria and details were available of 40 reputed cases of diabetes with evidence of glycosuria on previous occasions. Therefore there was a total of 192 cases of glycosuria out of 5,843 people covered by the survey - an incidence of 3.28%. 150 specimens were tested with Clinitest, 64 specimens (42.1%) were positive and 86 were negative. The 40 "known" diabetics and two of the positive Clinistix in the postal survey did not have specimens tested with Clinitest. Of the 192 cases of glycosuria, 121 were in males and 71 in Females - 63.0% and 37.0% respectively. There were only five cases under the age of 20 years. The age distribution is shown in Table IV.

TABLE IV. Age distribution of people with Glycosuria.

Age in years	Males	Females	TOTAL
0 - 9	1	-	1
10 - 19	-	4	4
20 - 29	20	6	26
30 - 39	14	3	17
40 - 49	26	5	31
50 - 59	17	13	30
60 - 69	20	29	49
70 - 79	16	8	24
80 - 89	7	3	10
<b>TOTAL:</b>	<b>121</b>	<b>71</b>	<b>192</b>

Blood Sugar Examinations.

109 glucose tolerance tests were performed and 13 fasting blood sugars were done. Details were available of three other glucose tolerance tests which had been done previously. 27 cases of glycosuria did not have blood examinations done. The details of these are described later.

Diabetes.

73 cases of diabetes were discovered during the survey - an incidence of 1.19% of the population and 1.25% of those tested. 38 of these were previously known cases and 35 were discovered by this survey:- incidences of 0.62% and 0.57% of the population respectively. There were 34 cases in males and 39 in females. 38.02% of the cases of glycosuria were diabetics. Table V shows the distribution of these cases.

TABLE V. Distribution of known and "new" cases of Diabetes by age groups

Age in years	Known Cases		New Cases		Total Cases	
	Male	Females	Male	Female	Male	Female
0 - 9	-	-	-	-	-	-
10 - 19	-	1	-	-	-	1
20 - 29	2	-	-	-	2	-
30 - 39	-	1	-	-	-	1
40 - 49	6	-	3	-	9	-
50 - 59	2	3	2	5	4	8
60 - 69	2	14	7	8	9	22
70 - 79	2	2	4	3	6	5
80 - 89	1	2	3	-	4	2

Previously known cases.

Details of 40 people were obtained who said they were known diabetics. All their records were available and 38 satisfied the diagnostic criteria laid down. Of the two others one was a case of renal glycosuria and the other one had a single blood sugar estimation which was normal so no firm diagnosis could be made. The age of these 38 known diabetics varied from 11 years to 84 years with a preponderance of cases in the 60 - 69 age group. Of the 16 cases in this age group 14 were female. There was no marked difference in the other age groups.

New Cases.

35 previously unknown cases were discovered by this survey. There was no marked difference in incidence between the sexes, 16 cases occurring in females and 19 in males. All the new cases were above the age of 40 years and the maximum incidence, 15 cases, was in the age group 60-69 years. 33 cases gave a positive reaction to Clinitest, and only 2 cases gave a negative reaction to Clinitest. The diagnosis was made by a glucose tolerance test in 32 cases and by a fasting blood sugar in the other 3 cases. These three cases had high fasting levels, 185, 268 and 287 mgm per 100 ml. respectively which were all considerably above the diagnostic level of 120 mgm. per 100 ml.

Renal Glycosuria.

37 cases were diagnosed as cases of renal glycosuria. 28 cases were in males and 9 in females. 33 cases were diagnosed by Glucose tolerance tests done during the survey and 3 were known cases whose records were available. One other case was reputed to be diabetic, but her records showed her to be suffering from renal glycosuria. The age distribution is shown in Table VI.

TABLE VI. Age distribution of cases of renal Glycosuria.

Age	Male	Female	Total
20 - 29	2	3	5
30 - 39	7	2	9
40 - 49	5	2	7
50 - 59	5	2	7
60 - 69	3	-	3
70 - 79	4	-	4
80 - 89	2	-	2
TOTAL:	28	9	37

There were 26 cases negative to Clinitest and only 10 cases were positive to Clinitest. One case did not have a specimen tested. The incidence of renal glycosuria was 19.27% of the cases of glycosuria and 0.63% of those tested. There were two expectant mothers in this group. One man aged 67 years had a glucose tolerance test performed twenty-five years ago and the present test showed no change in the condition.

Normal curve.

34 cases of glycosuria were found to have normal curves after a glucose tolerance test. All the cases were positive to Clinitest and 6 were positive to Clinitest. The age distribution is shown in Table VII.

TABLE VII.      Age distribution of people with normal glucose tolerance tests.

Age	Male	Female
10 - 19	-	1
20 - 29	7	1
30 - 39	4	-
40 - 49	6	3
50 - 59	5	-
60 - 69	2	3
70 - 79	1	1
	25	9

There were 25 cases in males and 9 in females. The cases were distributed throughout the age groups.

Lag Storage Glycosuria.

There were only 6 cases of this condition, 5 in males and one in females. All gave a positive reaction to Clinistix and 3 to Clinitest. All of these had a fasting level below 103 mgm. per 100 ml: a  $\frac{3}{4}$  hour level of between 200 and 231 mgm. per 100 ml.: and all of them were well below 100 mgm. per 100 ml. after 2 hours. The ages of these six people were 24 years, 26 years, 29 years, 30 years and two people aged 57.

Hyperglycaemia sine Glycosuria.

There were no cases of this condition using the criteria described by Harrison.

Unclassified Cases.

There were 4 patients whose glucose tolerance curves did not satisfy the criteria of any of the conditions so far described. The details of their glucose tolerance curves are shown below. During the glucose tolerance test none of the specimens of urine showed any evidence of glycosuria.

TABLE VIII

Details of blood sugars (in mgm. per 100 ml.)  
of four patients with hyperglycaemia without  
glycosuria.

	<u>Fasting level</u>	<u><math>\frac{3}{4}</math> hour level</u>	<u>2 hour level.</u>
Male aged 68	113	221	144
Female " 67	110	205	140
Male " 63	122	217	103
Male " 54	123	152	129

One was positive to Clinitest and three negative in the initial screening. If they had showed glycosuria during the glucose tolerance test they would have all satisfied one or other of the criteria necessary to establish a diagnosis of diabetes. Three of these cases have a high threshold. Griffiths says that in long standing diabetes the threshold may rise and there may be no glucose in the urine at blood levels over 200 mgm. per 100 ml. Further he states that glycosuria is therefore not essential for the diagnosis of diabetes. Joslin however considers glycosuria essential for a diagnosis of diabetes. Most people would consider that these cases were mild diabetics. They will require careful observation and further tests at frequent intervals.

Single Blood Sugar Tests.

13 fasting blood sugar tests were done. Three people were diagnosed as suffering from diabetes. It was impossible to classify the remaining ten into any type of glycosuria. Five were positive to Clinitest and five were negative. Their ages varied from 8 years to 70 years and eight were males and two females. It is possible that very mild cases of diabetes may have been missed by not carrying out a full glucose tolerance test. 8 of the 35 diabetics discovered in this survey had fasting levels below 120 mgm. per 100 ml. though most of them were just below this figure. Most of the people who only had a fasting blood sugar done had levels below 100 mgm. but one lady of 70 years had a fasting level of 114 mgm. per 100 ml. and may have been a mild diabetic. She was unable to drink the glucose. All these cases will be kept under close observation.

No blood tests.

There were 27 people who had no blood tests done. Two died

from cerebral vascular accidents before the tests could be done. Four moved out of the district and failed to respond to letters. Two people had subsequent post-prandial tests which were negative. One was a 14 year old mentally retarded girl who resisted an attempt to perform a blood sugar test and the other was an expectant mother in the last stages of her pregnancy whose urine showed no evidence of glycosuria after delivery. 19 people refused to undergo a blood examination. 14 of these were negative to Clinitest and five positive. The five who were positive were aged 29 years, 58 years, 60 years, 71 years and 82 years. 4 were males and one female. The man of 82 years was a possible case of diabetes as he had gross glycosuria and this survey showed that two of his daughters aged 54 years and 58 years were suffering from previously undiagnosed diabetes. Their fasting blood sugar levels were 268 and 286 mgm. per 100 ml. This family incidence was demonstrated on several occasions though no effort was made to ascertain the incidence in families.

In one other family one of whom was a known diabetic two siblings were discovered to be suffering from diabetes. In another family two brothers were found to have renal glycosuria and two sons of one of them were also discovered to have renal glycosuria.

Table IX summarises the details of the blood tests done and the classification of all cases of glycosuria encountered during the survey.



TABLE IX  
 DETAILS OF BLOOD TESTS DONE AND CLASSIFICATION  
 OF ALL CASES OF GLYCOSURIA.

Diagnosis	Blood Tests done during Survey		Blood Tests done Previously	Other Blood Sugar Tests	No Blood Tests Done	TOTAL
	Glucose Tolerance Tests	Fasting Blood Sugar				
Diabetes - Confirmed known Cases			38			38
Diabetes - New cases	32	3				35
Renal Glycosuria	33		1	3		37
Lag Storage	6					6
Unclassified - Hyper-glycaemia	4					4
Normal Blood Sugar	34					34
No Diagnosis - Insufficient Tests		10	1		27	11
No Blood Sugar Tests Done					27	27
<b>TOTAL:</b>	109	13	40	3	27	192

## DISCUSSION.

The percentage of the population tested, 95%, is higher than any of the other community surveys. Wilkerson and Krall tested 70.6% in Oxford, Mass., Kenny and Chute tested 81% over six years of age in Newmarket, Canada and Walker in Ibstock, Leics., tested 81% over five years of age. The higher response obtained enables a more accurate estimate to be made of the incidence of glycosuria and diabetes mellitus in the country as a whole. The higher response was due to the method of collecting the specimens. Both the people doing the field work were well known in the town and the people were more amenable to the project when it was already identified in their minds with the Health Department. Consideration was given to employing a team to carry out the work but it was felt that a higher percentage response would be obtained by limiting the field work to people well known in the town. The distribution and collection of specimen bottles was extremely laborious and several visits had to be made to a large number of households before all the bottles were collected.

The response to the postal survey was disappointing, only 137 (32.1%) out of 426 people. However, it should be remembered that all of these people refused in the first instance. This response is similar to that found in the survey by Fuenning (1960) who circularised 1,600 University employees and only 584 replied (36.5%). Fuenning felt that most people would test a specimen with the Clinistix which was enclosed but if it was negative would not trouble to reply. I think that most people in Halstead, having heard so much about this survey from neighbours would be sufficiently curious to test their urine with the Clinistix which was sent to them and only a small minority would take no action. However, it must be conceded that a patient testing his own urine might have failed to report a positive reaction due to apprehension or fear.

The population of Halstead which was covered by the survey has been shown to be different in age structure from that of the country as a whole. The results of this survey therefore have to be applied cautiously if one is to calculate the incidence of diabetes in the whole country.

Clinistix was found to be excellent for the rapid testing of large numbers of specimens. It selected the people who required more detailed tests and obviated the necessity for blood tests on the whole population. 87 cases which were positive to Clinistix were negative when tested with Clinitest but 34 of these cases had abnormal blood sugar curves. These 34 cases would have been missed if the screening had been done with Clinitest but presumably would have been detected if blood tests had been done on the whole population. Only 2 cases of diabetes gave a negative reaction to Clinitest and subsequent enquiries and further tests showed that these two people had submitted early morning specimens. The one hour post prandial specimens of these two people gave a positive result with Clinitest. The greater sensitivity of Clinistix appeared to have made up for the impossibility of doing blood sugar tests on the whole population.

The difficulties in comparing the results of surveys are very great when the methods used vary so much and the populations tested differ according to the age and sex distribution. There will be differences depending on the initial screening test which is selected. Differences will occur between surveys in which urine only has been tested and those where blood sugar has been estimated. Variations are likely depending on the timing of the screening test whether it was fasting, post-prandial or after carbohydrate loading. Differences will occur depending on whether venous or capillary blood samples are taken and which method of blood sugar analysis is used. The initial surveys measured the total reducing substances and more recent surveys have measured the true glucose in the blood samples. Finally the diagnostic criteria used will cause differences between the results of the surveys. All these causes of variation will be discussed in turn but the first factor causing differences is the population tested and in the literature there are details of only four community surveys and of these only one, the original one in Oxford, Mass., included all age groups. The Canadian surveys excluded all children under six years and the survey in Istock excluded children under five years. Details of these are given in Table X.

TABLE X. COMMUNITY DIABETES SURVEYS.

Date	Place	Population	Included in Survey	Percentage Response
1946	Oxford, Mass. U.S.A.	4,983	3,516	70% of Population
1951	Newmarket, Canada	4,800	4,419	81% over 6 years
1953	Porcupine, Canada	5,058	} 6,673	70% over 6 years
1953	Hawkesbury, Canada	7,017		60% over 6 years
1958	Ibstock, England	5,406	4,105	81% of those over 5 years.
1960	Halstead, England	6,123	5,843	95% of total Population.

Comparison of the results of these surveys must be guarded as only the survey in Oxford, Mass., included the whole population and the percentage response, 70.6%, was considerably less than that in the present survey which was 95%. The results in the Canadian surveys and the survey in Ibstock must be compared with the present survey remembering that the youngest age group was excluded.

The incidence of glycosuria in this survey was 3.3%. Previous surveys have found incidences of glycosuria between 0.8% in Blotner's original survey among inductees in New Orleans and 5.27% found by Redhead in a sample of a general practice in Newcastle. The details of the community surveys and their screening methods are given in Table XI.

TABLE XI. INCIDENCE OF GLYCOSURIA IN COMMUNITY SURVEYS.

Place	Screening Test	Percentage Glycosuria
Oxford, U.S.A.	Benedict's	3.5%
Newmarket	} Clinitest	1.7%
Porcupine		
Hawkesbury	} Clinistix	4.8%
Ibstock		
Halstead	Clinistix	3.3%

The incidence of glycosuria is seen to be less than that found by Walker who used Clinistix as a screening test but she excluded the youngest age group. Even allowing for this she found a greater percentage than that found in the present survey. Redhead in

Newcastle found 5.3% of his practice sample to be suffering from glycosuria and he used Clinistix as a screening test. His sample was reasonably representative of the City of Newcastle but there were differences in the age structure between the sample and the national structure. The other surveys which have used Clinistix as a screening test are those in Noordwijk, Holland and in Geneva where incidences of 3.6% and 4.8% of Glycosuria were found. However, these surveys were not community surveys but depended on people coming forward and volunteering for tests. American community studies have reported incidences between 3.5 and 5.0%. The reasons for the quite large differences in the incidence of glycosuria are not clear and the differences apply only to non-diabetic glycosuria. Are there then real differences in the incidence of non-diabetic glycosuria or are these differences due to the use of non-representative samples?

Almost half the diabetics in the town were discovered as a result of the survey. The incidence, 1.2%, is similar to that found in other surveys. Walker found the incidence to be 1.3%, Redhead in Newcastle found it to be 0.95%. Kenny in Canada found it to be 1.2% and Wilkerson found the incidence to be 1.4%.

It has been mentioned that results will vary depending on the diagnostic criteria used, whether venous or capillary samples were taken and whether the total reducing substances or the true glucose in the blood were measured. After a night's fast, normal capillary and venous blood sugars are approximately the same but after glucose the venous may be lower than capillary blood sugar. In diabetes mellitus differences between capillary and venous blood sugar are often less or absent after administration of glucose (Harrison (1957)). In a normal person after glucose the capillary values are 20 - 50 mgm. higher than the corresponding figures in venous blood.

Numerous methods are available for the estimation of total reducing substances and for true glucose. The original Folin and Wu method is thought to give values about 20 mgm. per 100 ml. higher than those methods using true glucose, (Wilkerson (1956)). Mosenthal and Barry have done investigations on the differences between capillary and venous blood and different methods of blood sugar analysis and state that the most dependable results are

obtained by measuring true glucose in venous blood. The method of blood sugar analysis used in this survey gives results which are near to true glucose figures and were measured on venous blood. I suggest that this method was reliable for the diagnosis of diabetes but the use of venous blood may have prevented the accurate classifications of some cases of non-diabetic glycosuria.

Another factor which makes comparison between surveys difficult is the different diagnostic criteria used. Joslin states that patients with glycosuria whose venous blood sugar (original Folin and Wu) is either 130 mgm. per 100 ml. fasting or 170 mgm. per 100 ml. at any other time of the day are diagnosed as diabetics. Corresponding values for true glucose are 110 mgm. per 100 ml. and 150 mgm. per 100 ml. These levels may seem low but his results in tracing border-line cases over the years has justified their adoption. All 35 of the newly diagnosed cases of diabetes satisfy one or both of these criteria. However when the other results are examined no less than 41 of the other cases of glycosuria satisfy one or other of the criteria. 20 were classified as renal glycosuria, 7 as normal curves, 6 as lag curves, 4 as unclassified hyperglycaemia and four people only had a fasting blood sugar done. These cases must obviously be carefully followed up and grouped together as intermediate cases, potential or pre-diabetics. Moyer et. al. suggest that the standard oral test is the most valid test and that using venous blood and a true glucose method of blood sugar analysis, a level above 140 mgm. should be considered to be diagnostic of diabetes. Mosenthal considers that the height of the curve should be disregarded and emphasis placed on the value at the end of two hours which should be below 100 (true glucose) or 120 mgm. per 100 ml. (Folin and Wu) Chesrow and others have pointed out that the return to normal of the blood sugar curve may be prolonged in the elderly. Conn (1958) says in his experience the blood sugar levels (Somogyi-Nelson) of 160 at 1 hour, 140 at  $1\frac{1}{2}$  hours and 120 at two hours invariably indicates a potential diabetic and it is interesting that Walker (1961) who used these levels found that this division separated the cases of transient glycosuria from those of constant glycosuria. The main community surveys are shown in Table XII with details of the Methods used in diagnosis. Blood sugar levels are after the standard oral glucose tolerance test.

Place	Blood Samples	Blood Sugar Analysis	Blood sugar levels considered to be diagnostic of Diabetes (in mgm. per 100 ml.)
OXFORD, U.S.A.	Venous-Adults Capillary-Children	Original Folin & Wu	170 (venous) 200 (capillary)
NEWMARKET, Canada PORCUPINE, Canada HAWKESBURY, Canada	} Capillary	Modified Somogyi- Nelson	Fasting 120 or Peak 200 and 2 hours 120
IBSTOCK	Capillary	Asatoor and King	1 hour 160 1½ hour 140 1 hour 120
HALSTEAD	Venous	Modified Folin & Wu	Fasting 120 or ¾ hour 190 and 2 hour 120

TABLE XIII shows the main surveys with the known and newly discovered cases.

Place	Known Diabetics		Newly Diagnosed		TOTAL
OXFORD	40	0.8%	30	0.6%	1.4%
NEWMARKET	33	0.75%	21	0.5%	1.2%
PORCUPINE HAWKESBURY	52	0.75%	35	0.52%	1.3%
IBSTOCK	33	0.8%	25	0.6%	1.4%
HALSTEAD	38	0.62%	35	0.57%	1.2%

It will be seen from Tables XII and XIII that in spite of the considerably different methods of blood sugar analysis and different diagnostic criteria used there is a remarkably close grouping of the total incidence of diabetes in the surveys. When one considers that the population tested varied in age structure and in response to the survey the results are even more remarkable. The only other survey

which included all age groups was that in Oxford, Mass., and the incidence of diabetes in only slightly higher than that found in Halstead. If one uses the diagnostic criteria used by Wilkerson and Krall which are similar to those suggested by Joslin a further 41 cases of latent diabetes would have been found and the total incidence of diabetes in Halstead would be 1.9%. However, as Wilkerson (1959) points out, it is not advisable to interpolate from one method to another but each should have its own criteria for interpretation, It will be seen that the diagnostic criteria used in the other community surveys and in this survey are more stringent than those of Wilkerson and Krall and valid comparisons between any of these surveys cannot genuinely be made. Board (1959) and Silvestri-Lapenna (1959) have suggested that there should be an international organisation for research into diabetes and that there should be international standards for tests and for diagnosis. Such standards would greatly facilitate comparisons between surveys.

All the newly discovered cases were above the age of 40 years and the maximum incidence, 15 cases, was in the age group 60-69 years. This is similar to the findings in other surveys. No clinical history was taken from any of the newly discovered cases but not all the cases were mild symptomless cases and several had marked symptoms of diabetes mellitus.

The diagnostic criteria used may explain the differences in the incidence of other types of glycosuria in this survey and other surveys. There was a remarkably low incidence of lag storage glycosuria in this survey. Unfortunately there are very few figures for comparison mainly because many workers, particularly in the United States, do not recognise the condition as a separate entity. All the cases, 6 in all, giving an incidence of 0.1%, would have been diagnosed as cases of diabetes by some American workers. The only other figures are those given by Redhead who found an incidence of 0.85%. The reasons for this difference may have been due to one of two factors. The use of venous blood gives a peak level which may be from 20-50 mgm. less than the peak level using capillary blood. Secondly, the use of the  $\frac{3}{4}$  hour level may also in some cases have failed to give as high a peak level as would have been given using the  $\frac{1}{2}$  and 1 hour



levels.

There were 37 cases diagnosed as renal glycosuria. This is an incidence of 19% of the cases of glycosuria and 0.63% of those tested. American workers restrict the diagnosis to cases where all the urine specimens, including the fasting specimen, contain sugar. In doing so, many cases are placed in the unclassified group, which would be diagnosed as renal glycosuria in this country. Blotner (1943) made such a diagnosis in only 10% of the cases of glycosuria he discovered among inductees in New Orleans. It seemed important to me to classify the cases of glycosuria in the orthodox manner in use in this country so that by further tests in the future the basis of such classification could be upheld or exploded.

There were four cases of unclassified hyperglycaemia which would be considered to be cases of diabetes by most people. Joslin considers glycosuria to be essential for the diagnosis but other workers do not consider it to be essential (Harrison (1957)) (Loeb, (1956)). The renal threshold is often significantly raised in older diabetics. These four cases are being followed up as cases of diabetes.

The real problem of non-diabetic glycosuria is the differentiation from diabetes and the follow up to ensure that it does not develop into diabetes. Joslin (1959) says that in his experience renal glycosuria never progressed to diabetes and Dunlop and Stewart (1954) say they have followed cases of lag storage for years without noticing the development of diabetes.

It should be possible by following up the cases of glycosuria found in this survey to find out whether any of the cases of non-diabetic glycosuria develop diabetes or whether they persist as non-diabetic glycosurics. Such a follow up study similar to that performed in Oxford, Mass., should enable us to forecast the progress in all the various types of glycosuria and whether such a condition is reversible or permanent. Further information about the pre-diabetic state might be obtained and should enable us to give advice which might prevent the development of frank diabetes. A lot of information about diabetes is available but most of it has been obtained by studying cases of frank diabetes. It is likely that further information about the prevention of diabetes

will come from such community surveys as the present one.

CONCLUSIONS.

This survey has confirmed other studies and shows that there are a large number of undiagnosed diabetics in the community. If the incidence of 6 per 1,000 is applied to the country as a whole, it will be seen that there may be as many as 300,000 undiagnosed cases. When the other border line or pre-diabetic cases are added to this figure the enormity of the problem can be seen.

The reasons for treating such calculations with some reserve have already been discussed.

This survey has shown a method of detecting diabetes but such a method is unlikely to be practical for most Health Departments. It has been suggested (Leading Article, B.M.J. 1959) that the detection of cases of latent diabetes is a challenge to the family doctor. However, there are many people who never attend their doctor and this makes the challenge more formidable.

The institution of diabetic detection drives are a fresh avenue for the preventive medical services to explore. With the development of the Clinistix method of testing, the community detection drive becomes a practical reality. This survey has shown that the greater sensitivity of Clinistix makes it unnecessary for blood sugar samples to be obtained from the whole population. It has also been shown in this survey that under the age of 20 years only mild cases of glycosuria of no significance were discovered. A mass postal survey, area by area, should be confined to those over the age of 20 years. The electoral register should be taken as a target. Each two, or perhaps three years, a Clinistix would be posted to each person on the register giving instructions how to use it. The instructions would include directions for each positive reactor to take 1 hour post prandial specimen of urine to his own doctor or to a clinic set up for the purpose. This specimen should be tested with Clinitest and if it is positive a blood sugar examination should be done. The people whose urine was negative to Clinitest would be instructed to bring one hour post prandial specimens on two subsequent occasions. If either of these are positive a blood sugar examination would be done but if they were all negative the patient would be instructed to report back in six

months. I suggest that such a scheme is possible and very worth while.

Finally, this work has shown once again the desirability of standardising the methods of diabetes detection and for the introduction of a generally accepted interpretation of the glucose tolerance test.

It would have been impossible to do this work without the help of a great number of people. Dr. K. J. Atkinson, Dr. W.A.L. Collier, Dr. A. H. Rea and Dr. P. Train are the four general practitioners in Halstead without whose help the survey would not have been possible. I received great help and encouragement from Dr. Probert, Consultant Physician and Dr. Penfold, Consultant Pathologist to the Colchester Hospital Group.

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A COMPREHENSIVE SURVEY INTO THE INCIDENCE OF  
GLYCOSURIA AND DIABETES MELLITUS IN AN URBAN COMMUNITY.

1. The literature on diabetes detection drives is reviewed. Since 1947 such drives have tested over one million people in the United States and Canada. A few surveys have been reported in this country but have been limited in scope as they have been confined to special groups and there are no details in the literature of a complete community drive.
2. The results of the first complete community survey in this country are reported. 5,843 (95%) of the population of Halstead, Essex, were covered by the survey. Clinistix was used as the screening test and one hour post-prandial specimens were tested. A total of 192 cases of Glycosuria were encountered.
3. 38 known cases of Diabetes Mellitus and 35 newly discovered cases were found in a total incidence of 1.2%. The newly discovered cases were all over 40 years and the maximum incidence was in the 60-69 age group.
4. An attempt was made to classify the other cases of Glycosuria. The difficulties of such classifications are discussed.
5. If accurate comparisons are to be made of the incidence of diabetes in various countries it is essential that comparable methods of blood sugar analysis and comparable diagnostic criteria are used.
6. The survey confirmed the findings of other surveys that for every known diabetic there is another undiagnosed case. There may be as many as 300,000 undiagnosed cases in the country and some suggestions are made for the institution of large scale postal diabetes detection drives.



A P P E N D I X A.



# HALSTEAD URBAN AND RURAL DISTRICTS

JOHN HARKNESS

M.B.CH.B., D.P.H., D.I.M., D.OBST.R.C.O.G.

MEDICAL OFFICER  
OF HEALTH

COUNCIL OFFICES

MOUNT HILL

HALSTEAD, Essex

Dear Sir/Madam,

## Diabetic Survey.

Considerable interest has recently been aroused in comprehensive diabetic surveys among healthy populations. It has been found that 1% of the population suffer from diabetes. In Halstead, if this percentage is accurate, there are 60 people suffering from diabetes, of whom approximately 30 are unaware of their potential disability.

In order to carry out this survey we hope that every person in Halstead will have a specimen of urine tested.

We hope you will cooperate to make this medical survey a success.

If anything is discovered you will be immediately informed of the result. If you hear nothing you can be assured your result was satisfactory.

Yours faithfully,

*K. McKinnon*  
*M. L. Collins*  
*John Harkness*  
*A. R.*  
*Pelshaw.*

Please complete and return with specimen bottles.

	Name	Age	Occupation	Place of Employment
1.				
2.				
3.				
4.				
5.				
6.				

ple

John JONES.

27

Weaver

Courtauld's (Braintree)

BOTTLES SHOULD BE FILLED ONE HOUR AFTER THE MAIN MEAL OF THE DAY.

A P P E N D I X B.

Dr. Peter Train.

Chipping Hill House,  
Chipping Hill,  
HALSTEAD.

Dear

**DIABETIC SURVEY.**

I am hoping that you will help us to complete this survey. Will you please complete the enclosed form giving your name, age and occupation? Test a specimen of your urine by dipping in the stick which is in the small envelope, replace it in the small envelope, and send it with the completed form in the enclosed stamped addressed envelope. If the stick changes colour within 5 minutes, please note colour change on envelope.

Many thanks for your help.

Sincerely,

