Papers and Originals

Five-year Follow-up Report on the Birmingham Diabetes Survey of 1962

Report by the Birmingham Diabetes Survey Working Party*

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Summary: In a diabetes survey 630 persons who had glycosuria or were age- and sex-matched were given a 50-g. oral glucose tolerance test (G.T.T.). Five years later the test was repeated in 527 (83.6%) cases. The original G.T.T.s were classed as normal or showing "G.T.T. diabetes," "lag storage," "renal glycosuria," or "miscellaneous abnormalities." Compared with the normal group in the first test those with G.T.T. diabetes showed a higher rate of conversion to "florid diabetes," but many others with G.T.T. diabetes remained unchanged or became normal. The more abnormal the first test the more likely it was to progress to florid diabetes. Most lag storage curves remained unchanged or became normal, but a significant number converted to a diabetic abnormality. Renal glycosuria was an innocent peculiarity compared with other categories. The various "miscellaneous abnormalities" tended to change, and showed an excessive conversion to diabetes.

The best separation between non-diabetic and diabetic at the follow-up test occurred at 135 mg./100 ml. Those in the diabetic categories at the original test showed a mortality slightly above that in the general population, comparable to that found in diabetics in general. New cases of florid diabetes appeared in the population which screened negative for glycosuria at the rate of 0.3 per 1,000 per annum.

Introduction

In 1960 and 1961 a diabetes survey was carried out in the practices of 10 family doctors in different parts of Birmingham (Diabetes Survey Working Party, 1962), and including all social classes. The population of these practices was 19,412, and urine tests were obtained on 18,532 (95.5%), the glucose oxidase paper strip (Clinistix) being used on specimens passed after the largest meal of the day. Those who reported glycosuria proceeded to a 50-g. oral glucose tolerance test (G.T.T.) and 464 such tests were performed. In addition, 343 G.T.T.s were carried out on an age-matched group taken at random from those who had not found glycosuria. Categories of the G.T.T. were arbitrarily defined (see Definitions) and the criteria for "normal" glucose tolerance, "florid diabetes," and "G.T.T." or chemical diabetes became those accepted by the British Diabetic Association (FitzGerald and Keen, 1964). Other categories were "lag storage," "renal glycosuria," and "miscellaneous abnormality." Examples of all abnormalities were found both in those who reported glycosuria and in those who did not.

Those found to have florid diabetes were advised to have treatment. The many subjects in other categories were told that they were normal and no treatment was advised. In 1966

and 1967 as many as possible from all categories, including those whose tests were normal, were examined and subjected again to the oral G.T.T. Their morbidity in the intervening years was assessed. During this period some of the original survey population developed clinical diabetes and these new cases were recorded.

This paper is mainly concerned with the significance of abnormalities of the oral G.T.T. and the meaning of single blood glucose estimations, whether they showed glycosuria or not. The observations on the value and limitations of diabetes surveys expressed in our earlier papers are confirmed and amplified.

Method

The 807† subjects subjected to a G.T.T. in the original survey were included in the follow-up study (Table I). Only 55 who had shown florid diabetes and had been advised to take treatment were not asked to have a repeat test.

The G.T.T.s were carried out in the morning after overnight fast. The 50 g. of glucose was given in 200 ml. of orange-flavoured drink. Most tests took place on Sunday mornings at the practitioners' consulting-rooms, 15 or 20 subjects at a time; they remained seated throughout the tests and did not smoke. Those who had moved to other doctors in the West Midlands were tested at the Birmingham General Hospital and the infirm were tested at home. The 17 (3%) who had left the district had repeat tests in laboratories in other parts of the country. Nearly all (97%) of the blood samples, however, were tested in the same laboratory (Birmingham General Hospital) as that in which the original test took place and the blood was analysed within three hours of taking the specimen. Blood glucose was determined on finger-prick capillary samples taken fasting and $\frac{1}{2}$, 1, 1½, and 2 hours after glucose, Hoffman's (1937) method being used with a Technicon Autoanalyzer run at 30 readings an hour.

Definitions

The categories used in the interpretation of the G.T.T. were defined as follows:

G.T.T. Diabetes: All tests in which the 1-hour capillary blood glucose figure exceeded 180 mg./100 ml. and the 2-hour figure 120 mg./100 ml.

Florid Diabetes: As for G.T.T. diabetes, but where the fasting value exceeded 130 mg./100 ml.

Lag Storage Curves: Level over 180 mg./100 ml. at $\frac{1}{2}$ or 1 hour with fasting levels under 110 mg./100 ml., 1½-hour figures under 160 mg./100 ml., and 2-hour figures under 120 mg./100 ml.

Renal Glycosuria: Glycosuria found by Clinistix, no blood sugar being above normal values (see below).

Miscellaneous Abnormality: These tests have been divided into the following:

Group A, where the fasting value exceeded 110 mg./100 ml. but the 2-hour figure was below 120 mg./100 ml.

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† The discrepancy of three between this figure and the 810 in the already published totals is due to a subsequently discovered numerical error in original data.

Group B, where the 1½-hour figure exceeded 160 mg./100 ml. and the ½ or 1 hour, or both, exceeded 180 mg./100 ml., while the fasting level was below 110 mg./100 ml. and the 2-hour figure was below 120 mg./100 ml.

Group C, where the 2-hour figure exceeded 120 mg./100 ml. while the fasting and 1-hour values were normal.

Normal: No glycosuria on using Clinistest, though the enzyme test might have been positive. All blood values normal—that is, below 110 mg./100 ml. fasting, 180 mg./100 ml. at ½ hour, 180 mg./100 ml. at 1 hour, 160 mg./100 ml. at 1½ hours, and 120 mg./100 ml. at 2 hours.

Unclassifiable: Results not conforming to any of the above categories.

Results

The extent to which the follow-up was complete, and the reasons for failure to repeat the test, are shown in Table I. The deliberate exclusion of 47 control subjects was because of the excessive weighting of the younger age groups had they been included.

There were 630 subjects available for a second G.T.T., which was carried out in 527 cases (83.6%) (Table II). Those

TABLE I.—Follow-up by Age Group

	Age at First Test				Total
	0-29	30-49	50-69	70+	
Original No. . . .	140 (100)	259 (100)	300 (100)	108 (100)	807 (100)
Refused	13 (9.2)	28 (10.8)	39 (13.3)	22 (20.3)	102 (12.6)
Emigrated . . .	5 (3.5)	4 (1.5)	1 (0.3)	0	10 (1.2)
Untraced . . .	2 (1.4)	2 (0.7)	3 (1.0)	0	7 (0.9)
Dead	0	4 (1.5)	30 (10.0)	43 (39.8)	77 (9.5)
Deliberately excluded (see text) . .	14 (10)	27 (10.4)	5 (1.6)	1 (0.9)	47 (5.8)
No. followed up .	106 (75.7)	194 (74.9)	222 (73.7)	42 (38.8)	564 (69.9)

Figures in parentheses are percentages.

TABLE II.—Percentage Retested (By G.T.T.)

Original Category	Available for Retest	No. Retested
G.T.T.	74 (100)	57 (77.0)
Lag	141 (100)	121 (85.8)
Renal	52 (100)	46 (88.5)
Miscellaneous A	29 (100)	19 (65.5)
Miscellaneous B	27 (100)	21 (77.8)
Miscellaneous C	63 (100)	50 (79.4)
Unclassified	13 (100)	13 (100)
Normal	231 (100)	200 (86.6)
Total	630 (100)	527 (83.6)

This table excludes those from the Normal Category deliberately not followed up, Deaths, and Emigrations. Figures in parentheses are percentages.

TABLE III.—Age Distribution by Category at First G.T.T. (Retests Only)

Original Category	Total	0-29	30-49	50-69	70+
Normal	200	56 (28)	67 (33.5)	68 (34)	9 (4.5)
G.T.T.	57	4 (7)	16 (28.1)	29 (50.9)	8 (14)
Lag	121	8 (6.6)	54 (44.6)	52 (43)	7 (5.8)
Renal	46	17 (37)	22 (47.8)	7 (15.2)	0
Miscellaneous A	19	2 (10.6)	7 (36.8)	7 (36.8)	3 (15.8)
Miscellaneous B	21	2 (9.5)	0	16 (76.2)	3 (14.3)
Miscellaneous C	50	14 (28)	19 (38)	13 (26)	4 (8)
Unclassified	13	1 (7.7)	6 (46.2)	4 (30.8)	2 (15.3)
Total	527	104 (19.7)	191 (36.2)	196 (37.2)	36 (6.8)

Figures in parentheses are percentages.

TABLE IV.—Changes of Category on Retesting

First Test Category	Retest Category									
	Total	Normal	Florid	G.T.T.	Lag	Renal	Misc. A	Misc. B	Misc. C	Unclass.
Normal	200 (100)	120 (60)	0	11 (5.5)	21 (10.5)	12 (6)	6 (3)	4 (2)	22 (11)	4 (2)
G.T.T.	57 (100)	7 (12.3)	10 (17.5)	23 (40.3)	7 (12.3)	1 (1.8)	2 (3.5)	1 (1.8)	5 (8.8)	1 (1.8)
Lag	121 (100)	28 (23.1)	1 (0.8)	15 (12.4)	44 (36.4)	11 (9.1)	7 (5.8)	7 (5.8)	6 (4.9)	2 (1.7)
Renal	46 (100)	14 (30.4)	0	1 (2.2)	7 (15.2)	18 (39.1)	1 (2.2)	2 (4.4)	3 (6.5)	0
Misc. A	19 (100)	3 (15.8)	2 (10.5)	1 (5.3)	7 (36.8)	0	2 (10.5)	2 (10.5)	2 (10.5)	0
Misc. B	21 (100)	3 (14.3)	0	6 (28.6)	4 (19.0)	0	1 (4.8)	2 (9.5)	3 (14.3)	2 (9.5)
Misc. C	50 (100)	16 (32)	0	13 (26)	5 (10)	4 (8)	3 (6)	2 (4)	5 (10)	2 (4)
Unclass.	13 (100)	1 (7.7)	0	2 (15.4)	3 (23.1)	2 (15.4)	0	1 (7.7)	4 (30.7)	0
Total	527 (100)	192 (36.4)	13 (2.5)	72 (13.7)	98 (18.6)	48 (9.1)	22 (4.2)	21 (4.0)	50 (9.5)	11 (2.1)

Figures in parentheses are percentages.

within the florid diabetes category had been excluded on the assumption that their diabetes had not improved.

The age groups at the time of the first test of those who were retested are given in Table III. There were considerable variations with age of the numbers in each category of the original population having glycosuria and of the controls, and these variations are reflected in the retested population.

The extent of the changes in G.T.T. category is shown in Table IV. The total number of individuals in each category who had a further test is given in the first column. Those on the diagonal (in italics) are unchanged. In spite of many individual changes the total numbers in each category, with the exception of the florid, G.T.T. diabetes, and lag storage groups, remain remarkably constant after five years.

As regards the follow-up of the G.T.T. diabetes category and the validity of the two-hour figure of 120 mg./100 ml. as a divisor between diabetes and non-diabetic curves, the most clear separation was achieved with a figure of 135 mg./100 ml. after testing other values (Table V).

A similar assessment of the lag storage category with the likelihood of conversion to a diabetic abnormality on follow-up is given in Table VI. Maximum half-hour and one-hour values of blood glucose other than 180 mg./100 ml. were tested, but none produced such a clear-cut separation between those who showed a diabetic abnormality on follow-up and those who did not.

The original categories were set aside and the results were recorded in three groups: (1) two-hour blood glucose below 120 mg./100 ml., (2) two-hour blood glucose between 120 and

TABLE V.—Follow-up of Original G.T.T. Diabetic Category, Separated According to Whether the 2-Hour Glucose at First Test was in Excess of 135 mg./100 ml. or not

First Test	Retest				
	Normal and Renal	Florid and G.T.T.	Lag	Others	Total
2-hour value below 135 mg./100 ml.	4 (2.8)	7* (11.6)	5 (2.4)	4 (3.2)	20
2-hour value over 135 mg./100 ml.	4 (5.2)	26† (21.4)	2 (4.6)	5 (5.8)	37
Total	8	33	7	9	57

The figures in parentheses are the "expected" numbers according to the χ^2 and the differences between "actual" and "expected" are not significant. *Includes 2 florid diabetics. †Includes 8 florid diabetics.

TABLE VI.—Follow-up of Original Lag Storage Category Separated According to Whether ½ or 1-Hour Blood Glucose at First Test Exceeded 200 mg./100 ml. or not

First Test	Retest				
	Normal and Renal	Florid and G.T.T.	Lag	Others	Total
Highest ½ or 1-hour value: 180-199 mg./100 ml. . .	27 (20.0)	4 (8.2)	23 (22.5)	8 (11.3)	62
Over 200 mg./100 ml. . .	12 (19.0)	12 (7.8)	21 (21.5)	14 (10.7)	59
Total	39	16	44	22	121

The figures in parentheses are the "expected" numbers according to the χ^2 test and the differences are significant ($P < 0.05$).

199 mg./100 ml., and (3) two-hour blood glucose over 200 mg./100 ml. (Table VII).

The original categories were again set aside and results recorded in the following three groups: (1) two-hour blood glucose below 135 mg./100 ml., (2) two-hour blood glucose between 135 and 199 mg./100 ml., and (3) two-hour blood glucose over 200 mg./100 ml. (Table VIII).

The age-specific death rates for the 77 subjects who died, calculated from the expected death rate for England and Wales, are given in Table IX.

Discussion of the Glucose Tolerance Test

Normal

Two hundred of the tests in the original survey were normal and 120 (60%) were again normal after five years (Table IV). None of the subjects had developed florid diabetes, but 11 were now G.T.T. diabetics. Substantial numbers had moved into the lag storage (21), renal (12), and miscellaneous C (22) groups. Apart from the shifts of category which might accompany ageing during the five-year period, the possibility of day-to-day changes in the test has to be considered. The reproducibility of the oral G.T.T. has been examined many times (Hale-White and Payne, 1926; Kosaka *et al.*, 1966). McDonald *et al.* (1965) repeated a 100-g. oral test (venous blood) six times in a year on 334 male prisoners of various ages. They found a wide variation, from those whose blood sugar readings were very reproducible to those who showed striking differences between the tests. The range of individual deviations was 4-47 mg./100 ml. at one hour and 2-43 mg./100 ml. at two hours after glucose with median values of 17 mg. and 12 mg. respectively. Fasting values were more constant. Subjects with the highest overall blood glucose readings were generally the most variable, but there were numerous exceptions. Nine per cent. of the men had two or more readings of

the test which would be classed as mildly diabetic by the criteria of the U.S. Public Health Service (1960).

These results, allowing for differences in technique and the fact that our subjects had only one repeat test, suggest that the changes in category in the normal group after five years are explained by the day-to-day variability of the G.T.T. rather than by a secular change in glucose tolerance. In some of the other categories, however, there are more changes than could be expected to a florid or G.T.T. diabetic abnormality and fewer than expected to normal glucose tolerance (Table IV). This represents a true secular change, and the behaviour of the normal group can be used as a baseline for comparison.

G.T.T. Diabetes

Most of those who developed florid diabetes in the whole follow-up (10 out of 13) came from the 57 who were originally in the G.T.T. diabetic category. Twenty-three remained unchanged, 15 now showed lag storage abnormality, 13 miscellaneous C abnormality, and 11 had reverted to normal. Those with G.T.T. diabetes were older than the normal group (Table III), but enough elderly subjects were retested to show that the difference between them and the G.T.T. diabetics could not be explained by age alone.

Since divisions between categories are arbitrary, small differences between the two tests might be enough to change a category. For this reason we have divided this category into those whose blood glucose in the original test was in excess of 135 mg./100 ml. and those in whom it was below this. Those with the higher figures were more likely to change to florid diabetes or remain unchanged and less likely to revert to normal or lag storage categories (Table V).

Lag Storage Effect

This aberration of the glucose tolerance test is common and in the original survey accounted for 21.5% of the positive results. We estimated that it would be found in 9.26% of the normal population. The peak occurs between half and one hour from the start of the test, and minor rises of the blood glucose above 180 mg./100 ml. 30 to 60 minutes after glucose may easily be missed in the half-hourly sampling. Glycosuria in such a case would be attributed to renal glycosuria. If venous samples are used the rise after glucose may not be detected, since the A-V difference at one hour may be as great as 70 mg./100 ml., and this cause of glycosuria has in the past been largely overlooked.

It is assumed that the immoderate rise of blood glucose after the test dose is related to rapid emptying of the stomach, since this type of curve is very common after operations in which the stomach is joined to the jejunum (Zollinger and Hoerr, 1947). The sharp fall which brings the blood glucose to normal levels by the end of two hours is presumably related to brisk secretion of insulin; but the factors which provoke this are complex and include the stimulation of intestinal glucagon, which in turn provokes insulin production.

There is little reason to expect that the lag storage curve would be related to impending diabetes, and that has been the general view in the past (Mosenthal and Barry, 1950). The results of our follow-up show that most of these subjects continue to show the lag storage effect or have changed to more normal categories, but the proportion who have converted to a diabetic glucose tolerance (13.2%) is significantly high. If the curves are divided into those which rose above 200 mg./100 ml. and those which did not (Table VI) it appears that the tests which originally showed the highest peaks are those most likely to convert to a diabetic abnormality. The lag storage cannot, therefore, be regarded as entirely innocent, and those in whom it is recorded should be reviewed every five years. No explanation can be offered for the diabetic tendency, but it may be that one form of

TABLE VII.—Predictive Value of a Single 2-Hour Blood Glucose at First Test, Separated at 120 and 199 mg./100 ml. Regardless of G.T.T. Category

First Test 2-Hour Blood Glucose (mg./100 ml.)	Total	Florid	G.T.T.	Lag	Renal	A	B	C	Uncl.	Normal
< 120	414	3	34	86	42	17	17	38	8	169
120-199	118	17	37	12	6	5	4	11	3	23
200+	32	30	1	0	0	0	0	1	0	0
Total	564	50	72	98	48	22	21	50	11	192

TABLE VIII.—Predictive Value of a Single 2-Hour Blood Glucose at First Test, Separated at 135 and 199 mg./100 ml. Regardless of G.T.T. Category

First Test 2-Hour Blood Glucose (mg./100 ml.)	Total	Florid	G.T.T.	Lag	Renal	A	B	C	Uncl.	Normal
< 135	466	5	46	93	46	21	18	44	10	183
135-199	66	15	25	5	2	1	3	5	1	9
200+	32	30	1	0	0	0	0	1	0	0
Total	564	50	72	98	48	22	21	50	11	192

These tables include 37 florid follow-up single blood glucose tests.

TABLE IX.—Age-specific Death Rates

Category at First Test	0-29	30-49	50-69	70+	Total
G.T.T.	0	0	5	17	22 (19.38)
Florid	0	2	6	5	13 (8.96)
Lag	0	0	6	4	10 (13.08)
Renal	0	0	0	1	1 (1.54)
Misc. A	0	0	1	0	1 (2.53)
Misc. B	0	0	1	2	3 (4.82)
Misc. C	0	1	4	3	8 (5.06)
Unclass.	0	0	1	2	3 (1.75)
Normal	0	1	6	9	16 (17.20)
Total	0	4	30	43	77 (74.32)

Actual Deaths (Expected Deaths)

Source of Expected Deaths: Abridged Life Table, 1962, England and Wales.

abnormal insulin response to a glucose load is responsible as a prediabetic phenomenon in some cases of lag storage. We cannot produce any evidence to show whether those who develop lag storage after gastric operations are unduly liable to develop diabetes.

Renal Glycosuria

We have followed the definition of Lawrence (1947) which includes those who show glycosuria during a test in which the blood glucose levels all lie within the normal range. Marble (1959) required glycosuria in all specimens, and this criterion makes renal glycosuria a very rare condition, since fasting urine is nearly always sugar-free to Benedict's test. We took as our minimum standard for significant glycosuria a trace on Clinitest, and this makes renal glycosuria fairly common in the original survey, accounting for 54 (8.1%) of the 464 positive results on self-testing.

The follow-up shows clearly that there is no tendency for those who show renal glycosuria to develop diabetes. Most of the tests were either unchanged or had become normal, a result which might be expected in view of the known tendency for renal glycosuria to diminish with advancing age. An appreciable number were now classed as lag storage curves. It is possible that these were really lag storage curves initially, the peak being missed between the half-hour and the one-hour reading.

The findings confirm the impression of most authorities (Graham, 1950; Robbers and Rübelin, 1953) that renal glycosuria is an innocent abnormality. In a few instances the condition is familial, but we have not recorded any such families in the survey.

Miscellaneous Abnormality

In the original survey certain glucose tolerance curves did not fit into any recognized category and were classified as miscellaneous abnormality of three types. Ninety-three patients from the positive and control groups with these abnormalities have been retested: 22 miscellaneous A, 21 miscellaneous B, and 50 miscellaneous C. In all three categories there has been considerable shift on retesting, but 2 out of 22 (11%) of the miscellaneous A tests have converted to florid diabetes, while 6 out of 21 (28.6%) miscellaneous B and 13 out of 50 (26%) miscellaneous C have changed to the G.T.T. diabetic category.

These changes in the direction of diabetes cannot be dismissed as unimportant and are more frequent than in the normal group. Mosenthal and Barry (1950) recorded the miscellaneous C curve in 3 out of 50 tests on normal active subjects, using a 100-g. glucose load, but considered it "obviously normal," while Fajans (1960) was at pains to point out that a false diagnosis of diabetes should not be made on the strength of such a test. Nevertheless, we consider that the conversion to diabetes is abnormally high in this category and we take the view that when curves of miscellaneous A, B, or C type are recorded the test should be repeated at intervals of one year for several years.

Predictive Value of Single Blood Glucose Reading

The standard glucose tolerance test is arduous for the subject tested and for the laboratory staff who carry out the test. For this reason some workers have relied on the result of a single blood glucose estimation two hours after a test dose of glucose for the diagnosis of diabetes. In the Bedford Survey (Butterfield, 1964; Keen, 1964; Sharp, 1964) three categories were distinguished: (1) normal when the figure was below 121 mg./100 ml., (2) borderline when the figure lay between 121 and 199 mg./100 ml., and (3) diabetic when the figure was above 199 mg./100 ml. We have therefore reclassified all

our original tests according to these three categories and shown the results of the repeated tests five years later (Tables VII and VIII). It is apparent that those in category 3 are almost certain to have significant diabetes and that those in category 1 are unlikely to develop diabetes after five years, but the situation of the 118 in category 2 is uncertain. It may be noted that though 17 subjects moved into the florid category 23 had become normal.

We therefore attempted to find a blood glucose level between 120 and 200 mg./100 ml. which would give the best predictive division between those likely to be normal and those likely to be diabetic if re-examined five years later. The figure of 135 mg./100 ml. emerged as the best for the purpose, as shown in Tables VII and VIII, for it appears that 14 of the 15 subjects with florid diabetes originally had two-hour blood glucose levels between 136 and 199 mg./100 ml. and only six had become normal.

We therefore suggest the following classification of blood glucose levels two hours after a 50-g. glucose load: (1) below 135 mg./100 ml., probably normal; (2) 135-199 mg./100 ml., a high risk of florid diabetes; and (3) over 200 mg./100 ml. certainly florid diabetes. A full G.T.T., however, is superior to a single reading because it elucidates the cause of glycosuria, does not rely on a single figure, and ensures more accurate two-hour timing.

Mortality Rates

In Table IX are shown the deaths in each category during follow-up by age at the time of the first test. The actual deaths are put alongside the deaths expected in the population of the same age and sex in 1962-8, calculated from the figures of the Registrar General for England and Wales. The mortality rate for the West Midland conurbation is somewhat higher than that for England and Wales, so that the difference between actual and expected deaths has been slightly exaggerated. The excess in those with florid and G.T.T. diabetes is small, but is comparable to that found in a diabetic population in Birmingham by Hayward and Lucena (1965).

New Cases of Diabetes in Survey Population

During the follow-up new cases of florid diabetes have been appearing in that large majority of the original survey population in whom no glycosuria was reported and therefore no investigation was made at the time. In the eight years 1962-9 inclusive there have been 35 such cases, or 4.5 in each year. We estimate that during this time the original practice population of 20,000 has dwindled by death and movement to about 11,000, giving an estimated rate for the appearance of florid diabetes in a previously screened population of about 0.3 per 1,000 per annum. There were 12 men and 23 women, 2 being under the age of 40, 20 between 40 and 69, and 13 over 70. Twenty-three were diagnosed because of diabetic symptoms and 12 were picked up on routine medical examination. Four are now on insulin, 16 on oral treatment, and 13 on diet alone.

Diabetes Surveys

In spite of the large number of diabetes surveys in different parts of the world few attempts have been made to assess the significance for the future of minor abnormalities of the G.T.T. Wilkerson and Krall (1953) followed up their pioneer whole population survey of 1946 in Oxford, Massachusetts (Wilkerson and Krall, 1947). Of 161 persons who had been included in a "blood sugar suspect" group, 18 had died and only 118 were available for retesting. Of this group, 17 were considered to be diabetic (14.4%) compared with 4 out of 225 (1.8%) of an age-matched control group. These results accord with our own figures, but different criteria of abnormalities

preclude direct comparison. Walker and Brown (1964) retested the whole population of Ibstock (5,406) for glycosuria five years after a similar screening test. They found that new clinical and "intermediate" diabetics as well as non-diabetic glycosuria had arisen in the previously tested population. Seven cases of symptomatic diabetes had been reported during follow-up.

Survey Method

The starting point of this study was general practice under the National Health Service in the United Kingdom. We believe that this has great advantages in population survey work for the following reasons. (1) The entire population can be studied regardless of occupation, age and infirmity, or financial consideration. (2) Practical details of testing can be planned to cause the least inconvenience to those who participate. (3) The relationship normally existing between doctor and patient encourages co-operation of individuals, which is the largest factor in achieving a high rate of follow-up. (4) The continuous morbidity from all cases and the mortality in the population are easily studied. (5) Close involvement of the hospital consultants with the participating family doctors ensures a definite policy in the management of those individuals discovered to have a diabetic or incidental abnormality. Advice and treatment can be administered firmly and consistently.

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Resistant Urinary Infections Resulting from Changes in Resistance Pattern of Faecal Flora Induced by Sulphonamide and Hospital Environment*

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Summary: The faecal flora was studied in eight children admitted to hospital for treatment of a first urinary infection with sulphonamides. The original, sulphonamide-sensitive *Escherichia coli* organisms were found to disappear, to be replaced by other *E. coli* serotypes that were almost invariably resistant to sulphonamides. Some of these serotypes carried R-factors for multiple antibiotic resistance.

Possibly some urinary infections with antibiotic-resistant organisms may be due to faecal organisms whose resistance has been changed by previous antibiotic treatment. Hence it is important to study the effects of individual antibiotics on the faecal flora.

Introduction

Primary urinary tract infections are usually caused by sulphonamide-sensitive bacteria, while those recurring after treatment with sulphonamides are often caused by sulphon-

amide-resistant ones. Re-evaluation of the figures from our earlier study (Bergström *et al.*, 1968) show that the shorter the interval between treatment and recurrence the more frequently sulphonamide resistance occurs (Table I). Most of the

TABLE I.—*Sulphonamide Resistance in Primary Infections and Recurrences Appearing Within a Year of Sulphonamide Therapy for 10 Days (151 Girls) or 60 Days (128 Girls)*

Type of Infection	Days After Start of Therapy	Frequency of Sulphonamide-resistant Infections Before and After Treatment	
		For 10 Days	For 60 Days
Primary infections	Before	15/151 (10%)	13/128 (10%)
Recurrences	1-13	5/5 (100%)	7/7 (100%)
	14-60	12/24 (50%)	14/15 (93%)
	61-365	7/23 (30%)	8/19 (42%)

recurring infections recorded in that study were reinfections, not relapses (Bergström *et al.*, 1967). Thus the appearance of resistant strains could not usually be ascribed to their development within the urinary tract. Since urinary bacteria commonly originate in the intestinal flora (Vahlne, 1945; Turck *et al.*, 1962), treatment with sulphonamides may have caused a change in the resistance pattern of the intestinal flora, which then played a part in a subsequent urinary infection. The present study was undertaken to test this hypothesis.

Infants who had been admitted consecutively to hospital with non-obstructive, acute, febrile urinary tract infections

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