which gave a high incidence of efficacy against Gram-negative bacilli, including *Pseudomonas pyocyanea*, also gave better results when the higher concentrations were used; of 61 different Gram-negative bacilli, 37 were sensitive to tests with 30 $\mu\text{g.}$; with tablets containing 150–750 $\mu\text{g.}$, another 17 organisms proved sensitive, leaving 7 out of 61 unresponsive. The same trend is seen with polymyxin. While none of the eight strains of *Ps. pyocyanea* studied was sensitive to disks containing 10 $\mu\text{g.}$, six responded to 50 $\mu\text{g.}$, and all the eight responded to 100 $\mu\text{g.}$

These observations help to explain why occasionally a satisfactory result is obtained clinically by the use of massive doses of penicillin subconjunctivally when the organism is reported as penicillin-insensitive. Likewise, control by neomycin of experimental infection by pneumococci is explained by the fact that the dose used (0.5 g. subconjunctivally) gives high concentrations which would be effective against pneumococci which on the ordinary testing might well be reported as insensitive to neomycin.

At present the agents suitable for subconjunctival injection are penicillin, streptomycin, neomycin, and polymyxin (and there is promise in soframycin, of which, however, we have no experience). Streptomycin has distinct limitations in that it is not well tolerated locally and is productive of sensitization. Polymyxin has a limited range of action and is not free from local irritative effects. Penicillin and neomycin are the two agents that can be used readily as a subconjunctival injection, but neomycin is a toxic substance that has to be used with care. Chloramphenicol would be almost ideal for subconjunctival injection, if it were not so insoluble that it has to be used as a suspension of its micronized form, with a maximum possible injection of 0.75 ml. of 15% suspension containing in all some 100 mg. The tetracyclines are entirely unsuitable for subconjunctival use, as they are both insoluble and locally irritative. Information on the relative efficacy of the higher concentrations of these different agents, while it helps in making a choice in any particular case, therefore still leaves considerable problems.

It would seem desirable to establish the following simple routine in reports on the sensitivity of organisms in eye swabs—possibly in all cases, but certainly in infected eyes. One Petri dish should carry six disks or tablets containing the standard strengths for the commonly used antibiotics in ophthalmology: penicillin 10 units, streptomycin 20 $\mu\text{g.}$, chloramphenicol 30 $\mu\text{g.}$, tetracycline 30 $\mu\text{g.}$, neomycin 30 $\mu\text{g.}$, and polymyxin 10 $\mu\text{g.}$ A second and third Petri dish would contain the same agents in 5 times and 25 times the concentration. The results so obtained can easily be set out in three columns, giving the clinician clear guidance on the relative efficacy of the different antibiotics in different concentrations for the organism under consideration. A simpler procedure would be to use one Petri dish for penicillin and neomycin, each agent in the three strengths suggested; a second Petri dish would complete tests on other antibiotics in one strength only.

We are indebted to Dr. F. S. Gorrill and Messrs. Evans Medical Supplies for their interest and generosity in supplying specially prepared sensitivity tablets for this study. Dr. S. T. Cowan, of the National Collection of Type Cultures, and Dr. R. I. N. Greaves, of the University Pathology Department at Cambridge, have helped with cultures. We are obliged to Dr. L. Hewlett, of the Royal Eye Hospital, and to Dr. J. Ungar, of Glaxo Laboratories, for advice.

INCIDENCE OF GLYCOSURIA AND DIABETES MELLITUS IN A GENERAL PRACTICE*

BY

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The importance of diagnosing diabetes mellitus early has been recognized for some years, yet many cases are not discovered until the onset of one of the complications of the disease. Joslin *et al.* (1946) stated that the only way to diagnose the disease in its early stages was by more frequent examination of the urine, not only of patients attending for consultation but also of persons who were supposedly healthy. The magnitude of the undiagnosed diabetic population will not be known until attempts have been made to find the true incidence of the disease. Diabetes is not notifiable, hence little information is available regarding its incidence. Tunbridge (1953) estimated that there were 150,000 diabetics in this country, and, because the proportion of the population over 40 years old was rapidly increasing, he estimated that within 20 years there would be half a million diabetics, or nearly 1% of the population. Andrews (1957), in a survey in West Cornwall, found an incidence of known cases of 5.6 per 1,000. In the United States also the disease is not notifiable, but several estimates have been made using data from death certificates which varied from 0.71% (Joslin *et al.*, 1946) to 0.48% (Marks, 1946).

Canvassing a population for cases of the disease gives only the prevalence of those that are known. An estimate of the true incidence depends entirely upon searching for cases as yet undiagnosed. Two surveys have been carried out which demonstrated that in the population there is a reservoir of undiagnosed diabetes (Blotner *et al.*, 1943; Blotner, 1946). In these surveys 45,000 and 69,000 men respectively had their urine tested for sugar, but, as these surveys were limited to men entering the Armed forces, no estimate could be made of the true incidence of diabetes in the population as a whole. The first systematic attempt to estimate the true incidence of the disease in a community was made by Wilkerson and Krall (1947) in Oxford, Massachusetts. Using postprandial blood and urine specimens, they tested 70.6% of the total population of 4,983. The incidence of the disease in the population tested was found to be 1.4%.

The second comprehensive diabetes-detection drive was carried out by Kenny *et al.* (1951) in Newmarket, Ontario. Using postprandial blood and urine specimens, they tested 81% of the population of 4,419 and found 54 cases of diabetes, 21 of them previously undiagnosed; the incidence of the disease was therefore 1.2%. In neither this survey nor in that of Wilkerson and Krall was there any attempt to classify the cases of non-diabetic glycosuria. Other diabetes-detection drives have been reported (Ford, 1949; MacBryde, 1949; Cauley, 1949; Sharkey *et al.*, 1950; Getting *et al.*, 1952; Fox, 1952; Loube and Alpert, 1954; Burn, 1956). Several of these were concerned with particular sections of the population, and in none was it possible to draw any definite conclusions on the true incidence of diabetes.

*From material presented as a thesis for the degree of M.D. in the University of St. Andrews.

The object of the present survey was to search for glycosuria in a general practice and to report the incidence of diabetes and non-diabetic glycosuria. An attempt was made to classify the causes of the latter.

Material and Methods

The practice is situated in Newcastle upon Tyne and is entirely urban. There are four doctors in partnership, and the total number of persons on the practice list at the time of the survey was 9,940. The first 1,000 patients tested were selected by making an alphabetical list of those whose surnames began with the first six letters of the alphabet. These patients were divided geographically and urine specimens were collected as described below. The remaining 991 patients were selected by taking every thirtieth card from the practice filing system and testing the urine of that person and all the members of his or her household. A total of 1,991 (20% of the total persons on the practice list) had specimens of urine tested for glucose. The reason for the change in the method of collection was that initially it had been the intention to test the whole practice, but this proved to be taking too long, and significant results could not be obtained without making allowance for the shifting population to and from the practice.

Urine specimens only were tested. Ideally, blood samples should have been examined also, but the practical difficulties of performing almost 2,000 blood-sugar estimations were too great. It was hoped that the disadvantages of urine-testing alone would be overcome by the method of urine analysis chosen for the survey.

Samples of urine were collected as follows. Specimen bottles were delivered personally to each household selected. Instructions were given to fill the bottle one hour postprandially next day. All specimens were then collected and tested. The possibility of patients testing their own urine specimens was considered, but this method was rejected on the evidence of Cauley (1949) and Getting *et al.* (1952), who reported the failure of diabetes-detection drives due to apathy of the public and its inability to carry out simple testing procedures.

For each person whose urine was examined a record card was filled in giving name, age, address, housing conditions, social group, general health, occurrence of obesity, and whether or not there was a family history of diabetes. For females a note was made of the obstetric history, with particular reference to birth difficulties and foetal gigantism.

In testing urine specimens "clintix" was used as the screening procedure, and "clintest" as a recheck if the result had proved positive with clintix. The latter is a glucose-oxidase test, the limit of sensitivity being 0.1 g. of glucose per 100 ml. of urine (Hunt *et al.*, 1956). Clintest is a modification of Benedict's qualitative test for sugar in urine. All those who gave a positive reaction to clintix were offered a blood-sugar estimation. In most cases a glucose-tolerance test was performed, but in certain instances a single two-hour postprandial blood-sugar estimation was made instead. This applied to persons under 14 years and to adults who presented with symptoms of diabetes. The standard oral 100 g. glucose-tolerance test was performed with urine and blood samples taken with the patient fasting and at $\frac{1}{2}$, 1, $1\frac{1}{2}$, 2, and $2\frac{1}{2}$ hours. Patients were instructed to eat a full diet during the week prior to the test except for the 12 hours immediately preceding.

The test was performed in ambulant persons only. These tests were done in the pathological laboratory at the Newcastle General Hospital. The blood-sugar estimation used was the colorimetric method for true sugar first described by Haslewood and Strookman (1939) and modified by King (1946).

Diagnostic Criteria

Single Blood-sugar Estimations

Persons under 14 years of age who were found to have a two-hour postprandial blood-sugar level greater than 100 mg./100 ml. were referred for a glucose-tolerance test. If the reading was less than 100 mg./100 ml. they were assumed not to have diabetes and no further tests were performed. Persons over 14 years of age with symptoms suggestive of diabetes whose two-hour postprandial blood-sugar level was over 250 mg. were diagnosed as diabetic. Those with levels less than 250 mg. were referred for a glucose-tolerance test.

Glucose-tolerance Test

The interpretation of this test used in the survey was based on the criteria advocated by Harrison (1957).

Normal Curve.—Fasting level 80–120 mg./100 ml. of blood, peak level less than 180 mg. reached within 60 minutes, return to below 100 mg. within two hours, and no glucose in any urine specimen.

Diabetic Curve.—Fasting level greater than 120 mg. and glucose in one or more urine specimens: diabetes diagnosed. Peak level greater than 190 mg., time taken for return to below 100 mg. more than two hours even though fasting level normal, and glucose in one or more specimens of urine: diabetes diagnosed.

LAG-Storage Curve.—Fasting level normal, peak level greater than 180 mg., time taken for return to below 100 mg. two hours or less, 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 without Glycosuria.—Fasting level 80–120 mg., peak level greater than 180 mg., and no glucose in any urine specimen.

Results of the Survey

During the survey, 1,991 persons (20% of the practice list) had a specimen of urine tested for glucose; 993 (49.9%) were males and 998 (50.1%) were females. A comparison of the age distribution of the practice sample tested and the age distribution of the population of the City of Newcastle (General Register Office, 1954) shows that the sample tested was fairly representative of the city as a whole (Table I).

TABLE I.—Age Distribution of Population of Practice Tested in Relation to Age Distribution of Population of Newcastle. Age and Sex Distribution of Cases of Diabetes Encountered During the Survey

Age in Years	Newcastle		Practice		No. of Diabetics in Each Group					
	Total Persons	%	Total Tested	%	New Cases		Known Cases		Total Cases	
					M	F	M	F	M	F
0-9	46,476	15.94	347	17.43						
10-19	38,214	13.11	284	14.26						
20-29	43,280	14.84	284	14.26						
30-39	43,197	14.81	323	16.22	1		1		2	
40-49	42,511	14.58	285	14.32		1				
50-59	35,202	12.07	218	10.96	1	1	1	4	2	5
60-69	25,349	8.69	143	7.18		5		1		6
70-79	14,432	4.95	92	4.62		1		1		2
80-89	2,951	1.01	15	0.75			1		1	
Total	291,612	100.00	1,991		2	8	3	6	5	14

Age distribution of males and females in population of practice tested in relation to age distribution of population of Newcastle upon Tyne.

Taking the sexes separately, the similarity remains apparent (see Chart). The maximum difference in any one decade between the percentage of males in the practice sample tested and that of the city was 2.64% (0-9 years). For females the maximum difference was 2.33% (30-39 years).

An analysis of the social groupings of the population of the practice tested compared with the social groupings in the County of Northumberland (including Newcastle) shows that there was a higher percentage of persons in the practice sample in social groups IV and V than in the county and a smaller percentage in social group III (Table II).

TABLE II

Social Group	% Practice Sample in Each Group	% Population of County in Each Group
I	4.9	2.8
II	15.2	12.1
III	34.0	53.0
IV	26.1	19.7
V	19.8	12.4

Glycosuria.—Of the 1,991 persons tested 105 were found to have glycosuria—an incidence of 5.27%. Only 49 (46.7%) of these gave a positive result with clintest. However, 62 of the 105 cases showed an abnormal blood-sugar reading on subsequent examination. Of the remaining 43 cases, 34 (32.4%) had a normal blood-sugar reading. These comprised 27 adults with normal tolerance tests and 7 children who had a single postprandial blood examination only. Nine cases (8.6%) had no blood examination performed. Of the 105 glycosurias 58 (55.2%) were males and 47 (44.8%) were females. Glycosuria was uncommon in the age-groups 0-19 and 70-89. The highest incidence occurred in age-group 30-39.

Blood-sugar Estimations.—Seventy-five glucose tolerance tests and 11 single postprandial blood-sugar estimations were performed. Nineteen glycosurias did not have blood-sugar values estimated. Nine of these were known diabetics and one was a known case of lag-storage glycosuria. All these cases had been investigated previously at the diabetic clinic of the Newcastle General Hospital, and the results were available. Nine subjects had no blood examination—six refused the test, one was suffering from mental illness, one was senile, and one died from a dissecting aneurysm of the aorta before the test could be performed.

Diabetes.—Nineteen cases of diabetes were encountered during the survey—an incidence of 0.95%. Nine of these were known previously—an incidence of 0.45%. The remaining 10 were diagnosed as a result of the survey. Thus 52.6% of the total diabetics encountered were newly discovered. Fourteen of the nineteen cases were female and five were male. Thirteen were found in age-group 50-69 years (Table I). Six cases (31.6%) gave a family history of diabetes compared with only 6.34% of the total practice sample tested. Nine patients (47.4%) were either obese at the time of the survey or gave a history of having been so at some time. Four gave a history of obstetric difficulty—three of them with a history of foetal gigantism (birth weight over 10 lb.).

Previously Known Cases.—The ages of these patients ranged from 37 to 82 years, the mean age being 58.7 years. The highest incidence (five cases) occurred in age-group 50-59 years. The average duration of the disease was six years. Insulin treatment was being given in four cases; the remainder were being treated by diet alone.

Newly Discovered Cases.—The ages of these cases ranged from 35 to 70 years, the mean age being 57.5 years. The highest incidence (five cases) was found in age-group 60-69 years. All cases gave a positive reaction to both clintestix and clintest; therefore no case would have escaped detection if clintest alone had been used as the screening method. The diagnosis was made by glucose-tolerance test in eight cases and by a single postprandial blood-sugar estimation in two. Only one patient had complained of symptoms of diabetes prior to the survey; seven had symptoms on inquiry and three had no symptoms even after leading questions. Only one case subsequently required treatment with insulin, the remainder being treated successfully with diet alone.

Lag-Storage Glycosuria.—The incidence of this condition in the population tested was 0.85%, a total of 17 patients (15 males and 2 females). They were fairly evenly distributed throughout the age-groups 20 to 79, the mean age being 49.0 years. All gave a positive reaction to clintestix, but 10 gave a negative result with clintest, of whom six had a peak blood-sugar value greater than 200 mg./100 ml. in the glucose-tolerance curve. None had symptoms suggestive of diabetes, but seven were considered to be borderline cases biochemically. The doubtful cases fell into two categories: those with a fasting blood-sugar value of 110-120 mg./100 ml., a peak greater than 180 mg. but with a curve falling to below 100 mg. within two hours; and those with a fasting blood-sugar of less than 110 mg./100 ml., but after a peak greater than 180 mg. the hyperglycaemia was prolonged, reaching about 100 mg. at two hours. Only one case gave a family history of diabetes.

Renal Glycosuria.—Twenty-five cases (15 males and 10 females) were diagnosed as cases of renal glycosuria, an incidence of 1.26%. The ages of these patients ranged from 15 to 70 years, with a mean of 38 years. All gave a positive reaction to clinistix, but only 14 were positive to clinitest. None had a family history of diabetes.

Transient Glycosuria.—Twenty-seven cases of glycosuria were subsequently found to have normal glucose-tolerance tests.

Hyperglycaemia Without Glycosuria.—One case was found to have hyperglycaemia according to the tolerance test, but no glucose was detected in any of the urine specimens except in the initial screening sample. After a peak of 194 mg./100 ml. the curve fell to less than 100 mg. at two hours.

Children with Glycosuria.—Only seven cases (4 males and 3 females) of glycosuria were found in persons tested under the age of 15 years. None had a two-hour postprandial blood-sugar value greater than 100 mg./100 ml., and, as all were symptom-free, none was subjected to a glucose-tolerance test.

Discussion

The sample of the population tested seemed to be fairly representative of Newcastle as a whole from the point of view of age and sex. The method of collection of the urine samples worked well but was rather laborious. However, the two great enemies of diabetes-detection drives—namely, apathy of the public and its inability to perform the simplest of testing procedures (Gettling *et al.*, 1952)—were overcome by using this system. It was hoped that the possibility of human error had been reduced to a minimum.

Clinistix was found to be an excellent method for the mass detection of glycosuria. Only 49 out of the total of 105 cases of glycosuria gave a positive reaction to clinitest. Twenty-four of those which gave a negative reaction to clinitest had an abnormal glucose-tolerance curve subsequently. All the cases of diabetes found as a result of the survey gave a positive reaction to both tests, but the results indicate that the extreme sensitivity of the glucose-oxidase test was necessary to uncover many cases of glycosuria, including some that have been classified as borderline cases of diabetes. The reason for this may have been that many persons submitted fasting urine specimens and not postprandial as instructed.

Over half the diabetics encountered were discovered as a result of the survey, suggesting that a large number of undiagnosed diabetics are present in the population. A total incidence of 0.95% is a smaller figure than those found in the two previous comprehensive surveys. Wilkerson and Krall (1947) found an incidence of 1.4% using slightly different criteria in the diagnosis of the disease. It is possible that five cases diagnosed as lag-storage glycosuria in the present survey would have been diagnosed as diabetes by Wilkerson and Krall. Kenny *et al.* (1951) found an incidence of 1.2%, but again the criteria of diagnosis used were not the same.

The diagnosis of frank cases of diabetes presented no problems. The association of symptoms, glycosuria, and hyperglycaemia made up a classical picture. Others had the typical diabetic type of tolerance curve. The difficulties of diagnosis were confined to the borderline cases.

Most of the newly discovered diabetics were in the upper age-groups; indeed, half of them were aged 60–69. All were mild cases except one, a man, aged 35 who was of low intelligence and also was found to be suffering from severe pulmonary tuberculosis. This was the only case that required insulin.

The incidence of lag-storage glycosuria was surprisingly high; but, unfortunately, no figures are available for comparison, mainly because many workers, especially in the United States, do not recognize the condition as a separate entity. Indeed, it seems likely that several of these cases would have been classified as diabetics by some authorities. The relatively high incidence of the condition found in the present survey seemed to justify its use in the classification of glycosuria.

There are two problems associated with both lag-storage glycosuria and renal glycosuria: first, they must be differentiated from diabetes; and, secondly, it must be decided whether or not they are prediabetic states. Joslin *et al.* (1946) stated that in their experience renal glycosuria never progressed to diabetes. However, Wilkerson and Krall (1953) in a follow-up study of their earlier survey suggested that allegedly harmless glycosuria may often precede frank diabetes.

Conclusions

The survey has demonstrated that there is a reservoir of undiagnosed diabetes in the practice population. There may be as many as one undiagnosed case for every one already known. The results have confirmed the importance of routine testing of urine for glucose. It would seem desirable to test the urine of all patients attending the surgery for consultation, regardless of their complaints. The ages of the newly discovered diabetics indicate that routine testing is of greater importance in persons over 40 years old, and it is suggested that they should have their urine tested annually.

The survey has indicated the value of diabetes-detection drives. The presence of so many undiagnosed cases of diabetes in an ageing population warrants the institution of large-scale detection campaigns similar to those already being carried out in the United States. These could be organized by individual diabetic clinics, but would require the co-operation of public health authorities and general practitioners.

The importance of the large number of cases of non-diabetic glycosuria uncovered by the survey is difficult to assess at the present time. All these cases, and especially those labelled as borderline cases of diabetes, will require careful follow-up.

Lastly, the survey has demonstrated once again the desirability of having a standardized method of performance and generally accepted interpretation of the glucose-tolerance test.

Summary

A survey to find the incidence of glycosuria and diabetes mellitus in a general practice in Newcastle upon Tyne is reported. Some 1,991 persons (20.03% of the total practice) had their urine tested for glucose. 105 cases of glycosuria were found—an incidence of 0.95%. Nine cases had been previously known and 10 were discovered as a result of the survey. The latter were found mainly in the older age-groups and the disease was mild in severity in most cases.

Seventeen cases of lag-storage glycosuria were found—an incidence of 0.85%. Seven were adjudged to be

borderline cases of diabetes and will require careful follow-up. Of the other cases of non-diabetic glycosuria 25 were classified as renal glycosuria, 27 as transient glycosuria, seven were children and were unclassified, and nine did not have blood examinations performed. One case was found to have hyperglycaemia without glycosuria on a glucose-tolerance test. The significance of these cases is discussed, and it is concluded that all will require reassessment at a later date.

The inference drawn from the study is that the number of undiagnosed diabetics present in the population is large enough to warrant the routine testing of urine for glucose, especially in the older age-groups. It is suggested that large-scale diabetes-detection drives should be started in this country on the same lines as in the United States.

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The Ministry of Health booklet, *The Feeding of Children from One to Five Years*, which has sold over 3,000 copies a year since it was first issued in 1942, is now available in a revised edition (H.M.S.O., price 1s.). It has been designed mainly to help those in charge of groups of young children to plan and prepare balanced, attractive, and varied meals. For this purpose, recipes in it are based on ingredients for ten children. There is, however, much general advice on the feeding of the under-fives, and on their emotional as well as their nutritional needs in the building of good health and good habits.

DEVELOPMENT OF CHEST PAIN IN MUNCHAUSEN'S SYNDROME

BY

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Pain in the chest of cardiac distribution is one of the less common symptoms of patients with Munchausen's syndrome. When, however, it has occurred, electrocardiographic changes indicating myocardial ischaemia have sometimes been found (Davidson, 1953; J. C. Barker, 1959, personal communication). In the case of a patient with Munchausen's syndrome reported below, the diagnosis of an acute myocardial infarction was repeatedly made on the basis of recurrent attacks of cardiac pain and certain electrocardiographic changes, though, in fact, the electrocardiographic pattern was that of the sickle-shaped R-T plateau type (Bedford and Thomas, 1954), a physiological variant usually associated with perfectly good health.

Case History

The patient was born in 1918. At different times he claims to be employed either as a clerk or as a publican. Since 1953, using one of two names, he has attended at least 16 hospitals in England and Scotland. His usual story is that of severe gripping pain situated across the front of the chest on both sides and often radiating up to the neck and down the left arm. The pain develops about half to one hour beforehand while he is walking or lifting heavy weights, etc. Physical examination is usually negative apart from showing an emphysematous type of chest. At times, however, he has sweated profusely, and on one occasion there was a fall in blood-pressure to 95/60 mm./Hg. Almost always electrocardiography is performed, after which a diagnosis of an acute myocardial infarction is often made and he is treated accordingly in hospital with bed rest, sedatives, and anticoagulants. Sometimes the electrocardiographic changes are not considered to be typical of acute coronary artery disease, but in view of the history of chest pain he is admitted to hospital for further observation. On one occasion, however, the casualty officer at a certain hospital did not accept his story of pain in the chest even though he was dyspnoeic; after a complete physical examination, which was negative, the patient was discharged from hospital without electrocardiography or any further ado.

When the patient is admitted he is at first extremely plausible (he often gives a graphic account of his wartime exploits in the R.A.F., claiming to have taken part in the Moehe Dam raids), but subsequently he becomes very objectionable, especially towards the nursing staff, and almost invariably takes his own discharge against medical advice within a period of several days to a few weeks. While residing in one hospital he had several bouts of chest pain associated with sweating and hypotension for which he received numerous injections of morphine until it was realized that he was becoming addicted to this drug. At the same hospital he cut his wrists with a razor-blade, but his wounds were superficial and it was considered that the gesture was a psychopathic one rather than a true suicidal attempt. During all his visits to hospital he has remained afebrile (except on two occasions), and the white-cell count and erythrocyte sedimentation rate have been normal.

Occasionally he presents at hospital with other symptoms such as headache, vertigo, or pain in the right testis (recently he was explored for a supposed torsion of the testis but no abnormality was detected apart from the presence of a hydrocele). In February, 1959, he attended the out-patient department of Charing Cross Hospital with