Results

The data in the Table and the Chart indicate that up to the fifteenth day after the administration of tetanus antitoxin all mice possessed sufficient antitoxin to neutralize the

Effect of Previous Administration of Horse Serum on Duration of Protective Ability of Tetanus Antitoxin

Group	On Day 0	On Day 11	No. of Mice Surviving Challenge (Survivors/Total) with Approximately 1 M.L.D. of Tetanus Toxin				
			Days After Administration of Antitoxin*				
			3	7	15	19	24
I	0.1 ml. pertussis vaccine + 0.05 ml. horse serum	0.2 ml. tetanus antitoxin (300 units)†	12/12	12/12	9/11	4/13‡	2/12
II	0.1 ml. pertussis vaccine	"	12/12	12/12	12/12	11/12‡	2/12
III	"	—	2/12	1/12	2/11	0/12	0/12

* Note that the mice in group III received no antitoxin; they served as controls for the potency of the toxin.

† Two mice died of anaphylactic shock; 4 showed symptoms of severe anaphylaxis and recovered.

‡ The difference in the percentage of survivors in these two groups is statistically significant ($P < 0.01$).

Duration of prophylactic effectiveness of tetanus antitoxin in mice inoculated with horse serum and in mice not so inoculated.

challenge dose of toxin. Of the mice challenged on the fifteenth day, two deaths occurred among the animals of group I which had been inoculated with horse serum 11 days prior to antitoxin. No deaths occurred among the animals which had no previous experience with horse serum (group II). Of the mice challenged on the nineteenth day after the administration of antitoxin, only 4 of 13 (30%) of the animals inoculated with horse serum survived the challenge dose of tetanus toxin, as compared with 11 of 12 (91%) of the mice which had not previously received horse serum. The difference between the percentage of survivors in the two groups is a significant one ($P < 0.01$). In a second experiment conducted in a similar manner, comparable results were obtained. Of 23 mice inoculated with horse serum and challenged with tetanus toxin on the seventeenth day after the administration of tetanus antitoxin, only 7 survived. In contrast, of 24 mice with no previous experience with horse serum, 22 survived challenge doses of toxin administered on the seventeenth day after injections of antitoxin. The difference between the percentage of survivors in the two groups is a significant one ($P < 0.01$).

Discussion

The data presented here support the contention of Littlewood *et al.* that previous experience with horse serum may

result in failure of antitoxin to protect. However, we agree with Beeson (1955-6) that an alternative explanation of the fatal case of tetanus cited by the aforementioned authors may be that the conventional prophylactic dose of tetanus antitoxin (1,500 units) was insufficient to neutralize the toxin present. Beeson cites other cases of prophylactic failure of 1,500 units of tetanus antitoxin and suggests that 10,000 units should be used for adequate passive immunization.

An increase in the prophylactic doses of tetanus antitoxin from 1,500 to 10,000 units would thus seem to be advantageous for two reasons. Ten thousand units would offer better protection in cases in which unusually large amounts of toxin were being produced. Ten thousand units of tetanus antitoxin might also be more effective in cases in which the antitoxin was being rapidly eliminated because of the patient's previous experience with horse serum.

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A SIMPLE QUICK TEST FOR GLUCOSE IN URINE

REPORT ON USE OF CLINISTIX

BY

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Two extremely simple enzyme tests have been developed which are highly specific for glucose in urine. These are "tes-tape" and "clinitest," but the present paper is concerned only with the latter. The method consists in dipping a specially treated thick paper stick approximately the size of a book-match, the last half-inch of which is impregnated with reagents containing an enzyme system, into a specimen of urine. The stick turns blue in the presence of glucose, and the blue colour should have developed in one minute. If the stick remains colourless there is no significant glucose in the specimen.

Application of the Test

This paper reports on a field trial in which clinitest was used for detecting glucose in urine and the effectiveness of the test compared with "clinitest" reagent tablets as standard. The trial was limited to patients over the age of 11 years attending the Birmingham Chest Clinic for the first time. Nursing staff were responsible for obtaining a specimen of urine from all new patients in the specified group. This was normally done in the interval between the taking of the chest radiograph and the clinical examination, so that the tests were completed before the patient was seen by the physician. Nurses performed the actual tests after being trained in the technique, and recorded the results. The technique is simple, no special apparatus or boiling is required, and specificity is beyond doubt. Hunt, Gray, and Thorogood (1956) have already stressed that the test is essentially an ultra-micro-method in the strictest sense and requires all the standards of chemical cleanliness such methods demand.

In the small number of patients whose specimens gave a positive result, blood-sugar estimations were carried

out in the pathological laboratory within 10 minutes of the positive finding. The details of the further management of patients with positive findings in the urine depended on whether any pulmonary abnormality was present in addition or not. All cases of glycosuria, however, were fully investigated either as out-patients, if their lungs were normal, or as in-patients if pulmonary disease was present.

Results

During a period of five months, from June 1, 1956, to October 31, 1956, 942 patients (593 males and 349 females) attended for examination. Positive findings on clintest or clinistix, or both, were found in only 26 (2.76%). These are set out in Table I. Of the 26 with positive findings on urine examination, 20 were males and 6 were females, and these are discussed below.

TABLE I.—Results of Tests in 26 Cases with Positive Findings

Case No.	Age	Sex	Urine Test		Blood Sugar mg./100 ml.	Remarks
			Clintest	Clinistix		
1	41	M	Positive	Positive	280	Diabetic
2	62	M	"	Negative	100	Non-diabetic
3	74	M	"	Positive	300	Diabetic
4	40	M	"	Negative	85	Non-diabetic
5	21	M	"	Positive	75	Renal glycosuria
6	46	M	Negative	"	100	"
7	47	M	Positive	"	260	Diabetic
8	53	M	"	"	290	"
9	17	F	"	"	270	"
10	50	M	"	"	170	"
11	44	F	"	Negative	124	Non-diabetic
12	60	M	"	Positive	120	Renal glycosuria
13	72	F	"	Negative	110	Non-diabetic
14	25	M	"	Positive	340	Diabetic
15	26	M	"	"	90	Renal glycosuria
16	34	M	"	"	220	Diabetic
17	55	M	"	Negative	100	Non-diabetic
18	65	M	Negative	Positive	130	Renal glycosuria
19	48	M	Positive	"	125	"
20	47	F	"	Negative	100	Non-diabetic
21	51	F	"	Positive	270	Diabetic
22	22	F	"	"	104	Renal glycosuria
23	67	M	"	Negative	183	Diabetic
24	35	M	Negative	Positive	90	Renal glycosuria
25	21	M	"	"	190	Diabetic
26	52	M	"	"	210	Post-gastrectomy hyperglycaemia

Six were known diabetics referred with chest symptoms and found to have active tuberculosis (Cases 7, 9, 14, 16, 21, and 25). Clintest and clinistix were positive in five, but in one (Case 25) clinistix only was positive. Blood-sugar levels were 260, 270, 340, 220, 270, and 190 mg. per 100 ml. respectively.

In five cases diabetes was diagnosed without the patients being aware of their diabetic symptoms (Nos. 1, 3, 8, 10, and 23); three of these had tuberculosis and the other two had carcinoma of the lung. Clintest and clinistix were both positive in the first four but clintest only in the fifth, whilst blood-sugar estimations at the time of the positive findings were 280, 300, 290, 170, and 183 mg. per 100 ml. respectively.

In eight cases renal glycosuria was present (Nos 5, 6, 12, 15, 18, 19, 22, and 24). Clintest and clinistix were both positive in all but three (Cases 6, 18, and 24), in which clinistix only was positive. The blood-sugar levels in these eight cases were 75, 100, 120, 90, 130, 125, 104, and 90 mg. per 100 ml. respectively. Oral glucose-tolerance tests confirmed the presence of a low renal threshold for glucose in the eight cases. The lowest threshold was 75 mg. per 100 ml. (Case 5).

In the six non-diabetics clintest gave a positive result owing to the presence of reducing substances, but clinistix gave a negative result, indicating that there was no glucose present (Cases 2, 4, 11, 13, 17, and 20). The blood-sugar levels were 100, 85, 124, 110, 100, and 100 mg. per 100 ml. respectively, and the reducing substances giving a "trace" reaction with clintest in these six cases were accounted for by the drugs being taken by the patients at the time.

In one patient clintest was negative and clinistix positive, with a blood-sugar level of 210 mg. per 100 ml. (Case 26). This patient, a non-diabetic, was found to have a post-gastrectomy hyperglycaemia.

Discussion

Clinistix was used specifically for detection purposes, and is extremely accurate and reliable. It is more specific than clintest for detecting glucose in that there are fewer false positives, and from the point of view of detecting diabetics clinistix is more dependable than clintest. In 930 out of 942 cases the results of the two tests were identical (Table II)—916

TABLE II.—Results of Urine Tests in 942 Cases

	Clinistix		Total
	Positive	Negative	
Clintest { Positive ..	14	7	21
Negative ..	5	916	921
Total ..	19	923	942

being negative and 14 positive. In seven instances clintest was positive and clinistix negative. Further investigation showed that in all these cases the positive result was due to reducing substances other than glucose. It is worth emphasizing that there have been only a few false positives, although the tests have been carried out by nurses outside the laboratory. In five cases clinistix was positive and the clintest negative (Cases 6, 18, 24, 25, and 26): these included three renal glycosurics, one diabetic, and one patient with a post-gastrectomy hyperglycaemia. In all these the trace of glucose present was detected by clinistix but failed to be seen on clintest.

A number of factors such as variations in the temperature and pH of the specimen of urine, and also variations in the amount of ascorbic acid present, affect the sensitivity of the enzyme test and the intensity of the colours, thus making the test unreliable for quantitative use. Warnings about the unreliability of the enzyme test as a quantitative test have already been given by Hunt *et al.* (1956), and Tunbridge, Paley, and Coulson (1956).

The test is, however, of great value in detecting glycosuria and may be used for screening purposes in any busy clinic, such as a chest clinic, medical, surgical, and ophthalmological out-patient departments, and antenatal and post-natal clinics. It should prove invaluable to the general practitioner both in his surgery and during domiciliary consultations. The test has little place in the day-to-day management of diabetic patients having insulin.

Conclusion

This study has shown the reliability of clinistix in detecting glucose. The simplicity of applying and interpreting the test has been substantiated during the course of this trial.

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The University of London has authorized the expenditure of the total amount of money necessary for completing the School of Pharmacy in Brunswick Square, Professor W. H. Linnell, Dean of the School, told the council of the Pharmaceutical Society recently. In 1935 the cost was put at £350,000. To-day it would be £1,300,000. Although the official date for the completion of the new building was next December, teaching, he said, would begin in October.