A STUDY TO DETERMINE THE EFFECT OF DRUGS ON GLUCOSE URINE TESTING

by

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A THESIS

Presented to
the University of Oregon School of Nursing
and the Graduate Council
of the University of Oregon Medical School
in partial fulfillment
of the requirements for the degree of
Master of Science

June 11, 1971

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This study was supported by traineeships from the United States Public Health Service Grant Numbers NT-35-C 12 and 3 A11 NU 00035 13S1.

ACKNOWLEDGEMENTS

The writer expresses her sincere gratitude to Miss Lucile Gregerson, Associate Professor, University of Oregon School of Nursing, for her kind assistance in the preparation of this thesis.

The writer also wishes to express her thanks to David S. Phillips, Ph.D., for his assistance and support in the statistical analysis of the data.

Appreciation is also expressed by the writer to the thesis readers, Dr. Maxine Patrick, Professor, University of Oregon School of Nursing and Miss Evelyn Schindler, Associate Professor, University of Oregon School of Nursing, for their help in preparing this thesis.

Acknowledgement is extended to those consulted and mentioned in the study.

The writer wishes to express her appreciation to the patients from the Out Patient Clinics, whose participation made this study possible.

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CHAPTER I

INTRODUCTION

Introduction to the Problem

Most hospitals use the copper-reducing method to do the routine urine testing on their diabetic patients. It is the nurse's responsibility to carry out this function within the hospital and to decide how much, if any, Insulin needs to be given to the patient.

Dr. Wolfgang Wirth and Richard Thompson, in "The Effects of Various Conditions and Substances on the Results of Laboratory Procedures", which appeared in The American Journal of Clinical Pathology of June 1965 state

> We believe that alertness and knowledge of possible actions of medications are the responsibility of the laboratory workers. (23)

Sister Mary Paulette Elking and Hugh F. Kabat, in "Drug Induced Modifications of Laboratory Test Values" found in The American Journal of Hospital Pharmacy, September 1968, reflect on the aforementioned article and state

> Their contention hardly seems tenable in the light of laboratory personnel's lack of a systematic and intimate knowledge of drugs and drug therapy. Would not this role more logically fall to the pharmacist functioning in the clinical environment? (9)

It is true that the laboratory workers and pharmacists should

work together on the problem of drugs interfering with the laboratory tests and their true value, but nurses should also be involved. It is the nurse's responsibility to know the medications she administers to her patients, their expected results and side effects. Beland states that

> the safety of the patient depends on all those who participate in his care. They must assume responsibility for the identification of threats to his well-being and for the institution of appropriate measures to anticipate, forestall, and control harmful agents or conditions. This is both a legal and a moral responsibility. (1)

It is the nurse who will be administering medications such as Insulin to the patient and if the urine test reacts positively, she should then be aware that a false positive may occur if the patient is taking a medication that will also reduce the Clinitest tablet as glucose does. If a nurse were to administer Insulin to a patient who had a false positive reading she could thus induce a hypoglycemic reaction which would cause unnecessary concern.

Statement of the Problem

The literature (4, 6, 11, 27) indicates that certain medications will cause the urine to react positively to the copper-reducing method (Clinitest) when in fact there is no glucose present in the urine. Some of the drugs listed are ascorbic acid, chloral hydrate, chloramphenicol, chlortetracycline, oxytetracycline, corticosteroids, isoniazid, nicotinic acid, penicillin, probenecid, salicylates, streptomycin, sulfonamides

and the thiazide diuretics. For this study the effect of the salicylates, isoniazid, and the thiazide diuretics were studied.

Diabetic patients usually have their urine tested with the clinitest method at home and in the hospital to determine the state of their disease and amount of medication needed to control it. They may be taking some of the above listed medications. It is therefore, important to find out if false positives do in fact occur when certain medications are taken. The literature (3, 4, 6, 11, 27) indicates that since the oxidase enzyme method (Tes-Tape) is specific for glucose, copper-reducing substances other than glucose will not react giving false positives. Other testing processes may result in false positives.

Purposes of the Study

The purposes of the study were:

1. To determine if specific drugs do reduce the Clinitest Tablet when there is no glucose present in the urine.
2. To determine if there is a relationship between the age of the patient and medications in reducing the Clinitest Tablet when there is no glucose present in the urine.
3. To determine the relationship that differences in dosages of medication may make in reducing the Clinitest Tablet when there is no glucose present in the urine.

Hypotheses

The following null hypotheses were formulated:

1. Urine samples of patients not taking medications will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose.
2. Urine samples of patients taking salicylates will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose wheb age of the patient is a variable.
3. Urine samples of patients taking thiazide diuretics will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
4. Urine samples of patients taking Isoniazid will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
5. Urine samples of patients taking salicylates will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in

testing urine for glucose when the dosage of the medication is a variable.

6. Urine samples of patients taking thiazide diuretics will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

7. Urine samples of patients taking Isoniazid will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

Explanation of Terms

Terms used in this study include the following:

Copper-reducing method, (Clinitest Reagent Tablet): a tablet containing:

a. anhydrous copper sulfate that fixes the peak of color at two percent glucose in a given volume of urine.

b. sodium hydroxide which gives an excess of alkali after reacting with citric acid, and supplies heat for the reaction.

c. citric acid which is neutralized by the sodium hydroxide producing heat and forming sodium citrate which keeps the

divalent copper in solution by forming a complex.

d. sodium carbonate which yields the carbon dioxide essential to the proper functioning of the test by excluding atmospheric oxygen. (16, 19, 28)

Oxidase enzyme method, (Tes-Tape): a roll of paper impregnated with reagents:

a. glucose oxidase which reacts with glucose in the urine to remove two hydrogen ions, forming gluconolactone which is promptly hydrated to gluconic acid. The removed hydrogen ions are then combined with atmospheric oxygen to form hydrogen peroxide.

b. peroxidase in the presence of hydrogen peroxide oxidizes orthotolidine which in its oxidized state turns blue. (25)

False positive: results where the Clinitest Tablet is reduced chemically showing a positive reaction, the same as by glucose, but there is no glucose in the urine.

Limitations

This study was limited to:

1. data collected in the Medicine and Rheumatology Out Patient Clinics of the University of Oregon Medical School and the Out Patient Clinic of the State Tuberculosis Hospital in Portland, Oregon.

2. data collected on each patient, specifically age, medication and dosage.
3. data collected on forty non-diabetic patients.
   a. Ten patients who had taken no medications.
   b. Ten patients who had taken only salicylates.
   c. Ten patients who had taken only thiazide diuretics.
   d. Ten patients who had taken only Isoniazid.

Steps of the Study

The steps in the development of this study were as follows:

1. Relevant literature was reviewed with reference to medications, their effect on glucose urine testing and the nurse's responsibility in testing urine and administering medications.
2. The problem was defined.
3. The purpose and the scope of the study were formulated.
4. The limitations were determined.
5. The hypotheses were formulated.
6. Unstructured interviews were held with individuals knowledgeable in the field of medications to obtain suggestions for developing the study.
   a. Edward E. Rosenbaum, M. D., of Rheumatology Clinic
   b. Marian L. Krippaehne, M. D., of Medicine Clinic

c. Clifford A. Fratzke, M. D., of Tuberculosis Clinic

7. A form was developed for recording the data. (Appendix A)

8. Administrative clearance for collecting the data from patients in the Out Patient Clinic at the Medical School was obtained from Mrs. P. Hunsaker, R. N., Supervisor and at the University State Tuberculosis Hospital Out Patient Clinic from Mrs. B. Hiatt, R. N., M. S., Hospital Administrator.

9. The Medicine Out Patient Clinics were attended in the morning and the Rheumatology and Tuberculosis clinics in the afternoon.

10. The patients' charts were read to establish what medications they were taking.

11. The patients were questioned about the medications they were taking to ascertain frequency and size of dosage and to verify that they actually were taking the medication.

12. A fresh urine sample was obtained from the patient.

13. The urine sample was tested with Tes-Tape and Clinitest at once in the Out Patient Clinic. (Appendix B)

14. The findings were recorded. (Appendix A)

15. The data were tabulated and interpreted. Tables were constructed from the tabulated data and the report was written.

16. The findings were summarized, conclusions were drawn, and recommendations for further study were made.

Overview of the Study

This study is presented in four chapters. Chapter I presents an introduction to the problem, a statement of the problem, the purposes of the study, hypotheses, explanation of terms and the steps in the development of the study. Chapter II presents a review of related literature concerning drugs, their effect on glucose urine testing and the nurse's responsibility in collecting and testing urine and administering medications. Chapter III describes the methodology and statistical analysis of the data and the interpretations of the findings of the study. Chapter IV includes a summary of the study, the conclusions drawn and recommendations for further study.

CHAPTER II

REVIEW OF RELATED LITERATURE

Introduction

In 1827, Richard Bright of Guy's Hospital first introduced urine testing as part of the doctor's routine in examination of the patient. In the early 1960's, a survey demonstrated that the practice of routine urine examinations was being done only by a few physicians. (14) With the development of new rapid, simple, modern urine tests and new interpretations of the old urine tests, repetitive urine testing once again has become a rewarding examination for both the patient and the doctor. (16) Although the new tests are rapid and simple, the classic urine tests have an advantage in that they have been used for so long that their limitations and usefulness in examining patients' urine are readily recognized. Their disadvantages still remain that some of the tests are cumbersome, require a laboratory, need to have someone make up chemical solutions accurately and cannot be run by the patient or by the physician at the bedside or in the patients' home. (16) The advantage of the modern tablet, tape or dipstick is that they require no laboratory and they can be run and read correctly by intelligent patients as well as by the physician at the bedside. (16)

History of Urine Testing for Glucose

Procedures for the detection of sugar in urine are among the oldest tests known in clinical chemistry. During the sixth Century A. D., Indian doctors tested urine of pathological cases and found it to be sweet to taste and sticky to touch and so named it "Madhumeha", meaning urine of honey. (24)

The Japanese and the Chinese in the third Century A. D. observed that urine was sweet and attracted dogs. (24) Paracelsus (1493-1541) noticed that when the urine of a diabetic person evaporated, a white powder was left and he called it salt but R. H. Major later was correct when he said it was sugar. (24) Francis Home and Johann Peter Frank (1780-90) proposed a yeast test for the detection of sugar in urine. (24) In 1815 Chevreul identified sugar in the urine as glucose. (9) In 1838, Bouchardat proved that diabetic urine has grape-sugar in it and he used a fermentation test, the polariscope and copper solutions for detecting the sugar. (24) Trommer in 1841 introduced a test for grape-sugar in urine and in 1848 Hermann Von Fehling introduced a quantitative test for sugar in urine. (24) In 1908, S. R. Benedict introduced his copper-reduction test for sugar in the urine and this test became one of great popularity. (12)

Clinitest Reagent Tablet

Glucose, a fermentable, dextrorotatory, copper-reducing sugar is found in the urine when the venous blood sugar level exceeds the renal threshold, usually between 160 and 180 mg. per 100 cc. of blood. (7, 15)

Since 1947, the Clinitest Reagent Tablet, a self-heating alkaline copper-reduction test, has been used in this country and in many parts of the world, to test urine for glucose. (9) The Clinitest Tablet is convenient and permits a qualitative, and crudely quantitative test for sugar in urine. (12) Clinitest Reagent Tablets detect clinically significant amounts of sugar in the urine in concentrations of 0.25 percent to 2 percent. (19, 22, 24) A special procedure can be used for obtaining rough estimations of quantities of sugar in excess of 2 percent. (24)

Each tablet contains anhydrous copper sulfate, anhydrous sodium hydroxide, citric acid and sodium carbonate. The amount of copper sulfate fixes the peak of color at 2 percent glucose in a given volume of urine. Sodium hydroxide is calculated to give an excess of alkali after reacting with citric acid, as well as to supply just sufficient heat for completing the reaction. The citric acid present is neutralized by the sodium hydroxide producing heat and forming sodium citrate which keeps the divalent copper in solution by forming a complex. The small quantity of sodium carbonate yields the carbon dioxide essential to the proper functioning of the test by excluding atmospheric oxygen which

may cause degradation of the sugar and cause negative readings in specimens containing as high as 0.25 percent glucose. (16, 19, 28)

The color changes of precipitates in the copper-reducing tests are believed to be influenced by the colloidal nature of the precipitate and the degree of hydration of the cuprous oxide. A color chart supplied with the tablets has six color blocks representing urine sugar levels of 0.25 percent, 0.5 percent, 0.75 percent, 1.0 percent, 2.0 percent, and over. (16, 19, 28) The colors range from blue to green, greenish yellow, orange or brick red. (9) Since the tablets contain anhydrous sodium hydroxide, they are very hygroscopic and deteriorate in the presence of moisture, even to the humidity of the air or the amount in cotton. The tablets are also sensitive to heat. The appearance of the tablets reflect their condition. Tablets which are bluish-white and slightly spotted react satisfactorily but if the tablets show dark blue discoloration in spots or in over-all appearance, they will not give an accurate result. (15)

False positives to tests for glycosuria can occur as the copper used may be slightly reduced and the reaction may be mistaken for sugar when large quantities of conjugated glycuronates occur in the urine. Glycuronates appear in decomposing urine and may be avoided by examining freshly voided specimens. (7, 8). The glycuronates appear in the urine in considerable quantities and give a mildly positive reaction when the copper-reducing test is used after the ingestion

of salicylates, menthol, chloral hydrate, morphine and aminopyrine. As a group, the glycuronates reduce the copper but unlike glucose, are nonfermentable. (4, 9) False positives may also occur when urine contains sugars other than glucose such as galactose, lactose, fructose, maltose and pentose. (5) (14)

The reliability of the Clinitest method for testing urine has been studied by different researchers. (1, 6, 23) One of the studies was done by Cook, Free and Giordano (6) who performed a series of tests using the Benedict's solution and the Clinitest method. Testing was done on six hundred and ninety urines from hospital patients and the data showed that every urine that was negative with Benedict's was also negative with Clinitest and every urine that was positive with Clinitest was positive with Benedict's test. Cook, Free and Giordano (6) repeated their study using urine from three hundred and seventy-six healthy subjects and the findings were the same as with hospital patients.

Tes-Tape

The enzyme, glucose oxidase, was first identified by D. Muller in 1927. (12) Tes-Tape is a strip of paper that is impregnated with three reagents, glucose oxidase, peroxidase, and orthotolidine. Glucose oxidase reacts with the glucose in the urine to remove two hydrogen ions, forming gluconolactone which is promptly hydrated to gluconic

acid. The removed hydrogen ions are then combined with atmospheric oxygen to form hydrogen peroxide. The peroxidase, in the presence of hydrogen peroxide, oxidizes the orthotolidine which, in its oxidized state, turns blue. (25)

It is recommended that the user of Tes-Tape lay the strip flat against a white background as that prevents light from diffusing through the tape and blanching a color response. If the observer reads a 0.5 percent (3+) or below, the instructions state to wait two full minutes for maximal color development signifying 2.0 percent or more (4+) concentration. Correct reading is usually the higher concentration.

In 1956, results reported by Comer (5) indicated that Tes-Tape had an over-all accuracy of ninety-six percent in the testing of one thousand, five hundred urine samples with glucose concentrations of zero to two percent. In 1957, Leonards (17) found Tes-Tape satisfactory as a quantitative indicator only for testing urine containing 0.25 percent glucose or less. Urine specimens that contained 0.5 percent glucose or more were often found to give readings that were deceptively low. This means that patient's may be spilling more sugar than the test indicates and thus not given enough insulin.

Since a rapid, easily performed quantitative examination for urinary sugar is of obvious value to the patient, the physician and a laboratory, a study by Bell and Jumper was undertaken in June 1958 (3) to re-evaluate the reliability of Tes-Tape. The accuracy was

investigated by testing one hundred and four samples of urine with predetermined amounts of glucose added. The test discriminated correctly among these possibilities except in six cases, four 0.25 percent samples being misread as 0.5 percent and two 0.1 percent samples being misread as 0,25 percent.

Eli Lilly & Company improved their product, Tes-Tape, by changing the method of processing and packaging in October 1956. (25) As the material was formerly packaged, exposure to excessively hot or humid environments promoted deterioration of the enzymes impregnated on Tes-Tape resulting in a reduction of its quantitative reliability. An improvement also in the spectrum of color development pictured on the reference chart on each dispenser was matched more closely with the actual hues and intensities which developed on the Tes-Tape. In addition, prompt packaging of the material after impregnation with the enzymes, together with individual foil-wrapping of each dispenser, minimizes deterioration from exposure to warm or moist conditions. (25) In August 1958, Seltzer and Loveall (22, 25) tested the improved product and concluded that when used as recommended, Tes-Tape was a convenient and reliable semiquantitative estimate in urinary glucose.

Medications and Their Effects

Drugs may alter laboratory tests through a variety of

pharmacological, physical or chemical mechanisms. Through its pharmacological activity, a drug may affect the normal physiological levels, in the blood or urine, of the particular substance being measured. (9)

Through physical or chemical interference, a drug may not only alter a test's value but actually prevent its determination by a particular method. Reducing agents excreted in the urine may enter into chemical reactions with test reagents to invalidate a particular procedure. Intermediate or end products of drug metabolism may also add to the complexity of the problem. (9)

In May 1962, W. T. Caraway (4) after reviewing the literature presented a comprehensive report which provided a wealth of information pertaining to the effect of a large variety of factors, chemical as well as physical in nature, on laboratory procedures.

Caraway states

> It is desirable that clinical laboratory procedures have a high degree of diagnostic specificity. Chemical analysis of biologic material is based upon the presence of functional groups in organic compounds or upon the separation and measurement of ions. Such analyses are inherently complicated and are becoming more so with the introduction of chemotherapeutic agents that are analogs of normal intermediary metabolites. (4)

Wirth and Thompson (27) in 1964 extracted the data collected by Caraway and put them into tabular form for easier use. For each laboratory test they listed the normal value, drugs affecting the test

and results, either false positive or false negative.

Elking and Kabat (11) in 1968 added to the data tabulated by Wirth and Thompson. The added citations were condensed from various drug compendia, abstracts and journals spanning the interval from 1965 to early 1968. Three of the many drugs or drug groups listed in the report that interfere with urine testing for glucose when using a copper-reducing test are the salicylates, thiazide diuretics, and Isoniazid.

Salicylates: The salicylates are excreted mainly by the kidney. Practically all of a given dose can be recovered in the urine as free-unaltered salicylate. Free salicylate is extremely variable and is chiefly dependent on urine pH, alkaline urine having more free salicylate in it than acid urine. Excretion of the salicylates is relatively slow. Approximately fifty percent of a given dose is eliminated in twenty-four hours. (13)

Thiazides: These drugs are absorbed rapidly in the gastro-intestinal tract and show effect within one hour after ingestion. All thiazides probably undergo active secretion in the proximal tubule. The extent of this process may vary, as may the degree of subsequent reabsorption. The renal clearance of the drugs is therefore high and may be either above or below the rate of filtration. Most compounds are rapidly excreted within three to six hours. Chlorothiazide does not undergo metabolic alteration in the body and the other thiazides

have not been systematically studied. (13)

Isonicotinic Acid Hydrazide (Isoniazid): This drug is readily absorbed with fifty to seventy percent of a dose being excreted in the urine in twenty-four hours. Part of the drug is present in the urine in unchanged form. (13, 18)

Patient's taking Isoniazid are divided into two groups according to the manner in which they metabolize the drug. The first group has all the drug present in the urine as free Isoniazid and it's hydrozones, acetyl Isoniazid and isonicitonic acid. In the second group, free Isoniazid, acetyl Isoniazid and isonicitonic acid represent thirty-eight to forty-eight percent of the dose of the agent but the quantity of free Isoniazid is greater and acetyl Isoniazid is lower than in the first group. (13, 18)

The Responsibility of the Nurse

The nurse has a responsibility whenever a test is performed or medication given to know what is the expected value and side effects. (2) Performing and recording urine tests accurately is essential if the patient's physician is to keep informed about his condition, prevent complications and maintain nutritional balance. (20) It is the nurse's responsibility to know how to collect urine specimens, and whether the container need be clean or sterile. The nurse should also know whether the specimen should be the first or second voided specimen, clean catch or sterile specimen, timed or single specimen. (21)

The nurse needs to be aware of the fact that contamination of the urine need not only be from unclean containers. Hydrogen peroxide or some other strong oxidizing agent such as hypochlorite in a container can cause Tes-Tape to give a false positive reading. This can occur also if catheters have been soaked in hydrogen peroxide as autoclaving does not inactivate hydrogen peroxide. (4)

Urine should be examined as quickly as possible after collection because after urine stands at room temperature for a few hours, the formed elements deteriorate, bacteria multiply, and chemical changes, such as glycuronate, destroy its usefulness for examination. If a test must be delayed, refrigeration is essential. (21) Specimens of urine for enzyme assay are preferably collected without a preservative. When a preservative is used, glacial acetic acid, 5 ml., can be added to prevent decomposition and mask unpleasant odors. (4)

Manuafacturer's directions should be observed carefully because improper handling or deterioration of test material may produce a false result. Touching the indicator end of a dipstick or tape, or exposing the test material to moisture or light can make test results inaccurate. (21)

The nurse should also be aware that when testing with Clinitest or with Benedict's solution, there is the possibility of false positive reactions to a number of so-called saccharoids such as glutathione, ergothionine, cystine, creatinine and fructose. Clinitest is less

sensitive than the glucose oxidase strips (Tes-Tape), an advantage because fewer false positive tests for diabetes are apt to occur. It can however be a disadvantage as Clinitest may yield a positive test with the nonglucose reducing substances present in the urine. (7, 15)

Summary

A review of the literature and related studies reveals that urine testing for glucose is an old practice but with the introduction of chemotherapeutic agents, testing accurately is becoming more complex.

Studies have shown that two of the most widely used methods for testing urine for glucose Tes-Tape and Clinitest are reliable, efficient and convenient when used according to the directions of the manufacturer.

The literature indicates the nurse has responsibility for not only testing the urine correctly but for knowing how the urine should be collected. The nurse also needs to know the possibility of false readings, positive and negative, and their causes.

CHAPTER III

REPORT OF THE STUDY

Introduction

This study was undertaken to determine if specific drugs or drug groups do reduce the Clinitest Reagent Tablet when there is no glucose present in the urine. The literature states (4, 11, 27) that there are medications that will reduce the copper as does glucose. Since the nurse often has the responsibility in the hospital of testing the patient's urine for glucose and for administering medication as indicated by the test, it is important that she be aware of the possibility of false positives. The study followed the steps and tested the hypotheses as listed in Chapter I.

Report of the Study

The Out Patient Clinics at the University of Oregon Medical School were visited when they were in session, Medicine Clinic during the morning, Rheumatology in the afternoon. The Tuberculosis Clinic at the University State Tuberculosis Hospital was also visited in the afternoon. The purpose of the study and procedures were explained to the Head Nurse in each Clinic.

It had been pre-determined that forty patients would be selected

to participate in the study. These forty patients were non-diabetics and divided into four groups: ten patients not taking any medications; ten patients taking salicylates selected from the Rheumatology Clinic; ten patients taking thiazide diuretics selected from the Medicine Clinic and ten patients taking Isoniazid selected from the Tuberculosis Clinic.

The patients meeting the criteria were selected in the order in which they attended the clinic. The patient's charts were then read to obtain information concerning what medications they were taking and the dosage of each. The patients selected were taking sixty grains or more of the salicylates, five hundred milligrams of chlorthiazide or the equivalent of the thiazide group, or three hundred to four hundred milligrams of Isoniazid. The first ten patients coming to the Clinic meeting the specific criteria; non-diabetic, only taking the medications being studied and predetermined dosages of medication, were selected.

An explanation of the study was given separately to each individual asked to participate. If the individual agreed to participate, his name, age, Out Patient Clinic number, were recorded on the report form. Each patient was questioned as to what medications he was taking, how many tablets and how often he was taking them to check with what was ordered by the physician and this then was recorded on the report form. The date, time and sex were also recorded for ease of identification. Frequency of medication was recorded to verify that the patients were all taking the same dosage at the same time of day. The patient's

statements were accepted as being accurate. The report form may be found in Appendix A.

After receiving a fresh urine sample from each patient in a clean disposable cup the urine was immediately tested, first with the Tes-Tape to determine if there was any glucose present. If the Tes-Tape gave a negative response for glucose, the urine was next tested with the Clinitest Reagent Tablet to determine if there was a copper-reducing substance, such as the medication being taken by the patient, present. (5) These results were then recorded on the report form in the appropriate box. (Appendix A) The steps used for testing the urine with Tes-Tape and Clinitest Reagent Tablet may be found in Appendix B.

Analysis of Data

The data obtained from testing the urine of each individual were tabulated according to medication the patient was taking. The age, dosage of medication, and response to Tes-Tape and Clinitest was recorded. These data may be found in Tables 1, 2, 3, and 4.

The first group to be studied were patients not taking any medication and whose urine was free from glucose according to the response of Tes-Tape. Table 1 shows the comparison of patients taking no medication, their age and the response of Tes-Tape and Clinitest to urine testing. It was found that the urine gave a negative response to

both Tes-Tape and Clinitest Reagent Tablet when the patient was taking no medication and had no glucose present in the urine.

No statistical analysis was necessary since all of the responses were negative; hence the following null hypothesis was accepted: Urine samples of patients not taking medications will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose.

Table 1. Comparison of Patients Taking No Medication, Their Age, and the Response of Tes-Tape and Clinitest Reagent Tablet to Urine Testing.

	Age in years	Tes-Tape	Clinitest
	(1)	(2)	(3)
1.	15	negative	negative
2.	33	negative	negative
3.	37	negative	negative
4.	37	negative	negative
5.	39	negative	negative
6.	40	negative	negative
7.	43	negative	negative
8.	45	negative	negative
9.	50	negative	negative
10.	66	negative	negative

Table 2 shows the comparison of patients taking salicylates, their age, dosage of salicylates, and the response of Tes-Tape and Clinitest Reagent Tablet to urine testing.

Table 2 shows that there were three trace responses to the Clinitest Reagent Tablet when testing the urine for glucose when the

patients were taking sixty grains or more of salicylates. These three responses were lifted out of the table and the mean age and dosage was determined for each group. Group I was the three trace responses and Group II were the remaining seven negative responses.

The age of Group I ranged from 62 years to 66 years with a mean age of 63.3 years. The age of Group II ranged from 36 years to 68 years with a mean age of 53.3 years.

The dosage of Group I ranged from 80 grains to 90 grains with a mean dosage of 83 grains. The dosage of Group II ranged from 60 grains to 80 grains with a mean dosage of 68 grains.

The student's t-test was used to analyze the data, as it compares the differences between the means of two groups, thus testing the null hypothesis of no significant differences among the responses. The assumption that the variances of two population groups do not differ was tested by using the F test and was found to be significant. To correct for this difference, a new table value for t was computed using the formula of Cochran and Cox. (Appendix C) The computed value for t concerning dosage was smaller than the new table t so the null hypotheses were accepted at the five percent level:

1. Urine samples of patients taking salicylates will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.

2. Urine samples of patients taking salicylates will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

Table 2. Comparison of Patients Taking Salicylates, Their Age, Dosage of Salicylates, and the Response of Tes-Tape and Clinitest Reagent Tablet to Urine Testing.

	Age in years	Dosage per day	Tes-Tape Response	Clinitest Response
	(1)	(2)	(3)	(4)
1.	32	75 grains	negative	negative
2.	36	60 grains	negative	negative
3.	53	60 grains	negative	trace
4.	57	60 grains	negative	negative
5.	62	90 grains	negative	negative
6.	62	80 grains	negative	negative
7.	63	60 grains	negative	negative
8.	64	80 grains	negative	trace
9.	66	80 grains	negative	negative
10.	68	80 grains	negative	trace

Table 3 shows the comparison of patients taking thiazide diuretics, their age, dosage of thiazide and the response of Tes-Tape and Clinitest to urine testing.

The age of the patients tested ranged from 39 years to 66 years. All patients were taking 500 milligrams of chorthiazide or the equivalent daily.

One patient out of the ten patients studied had a trace response to the Clinitest Reagent Tablet. The remaining nine patients had a negative response to both Tes-Tape and Clinitest Reagent Tablet. Since only one trace response appeared, no statistics were computed and the following null hypotheses were accepted:

1. Urine samples of patients taking thiazide diuretics will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
2. Urine samples of patients taking thiazide diuretics will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

Table 3. Comparison of Patients Taking Thiazide Diuretics, Their Age, Dosage of Thiazide, and the Response of Tes-Tape and Clinitest Reagent Tablet to Urine Testing.

	Age in years	Dosage per day	Tes-Tape Response	Clinitest Response
	(1)	(2)	(3)	(4)
1.	39	50 mg. E. *	negative	negative
2.	54	50 mg. E. *	negative	negative
3.	56	50 mg. E. *	negative	negative
4.	57	50 mg. E. *	negative	negative
5.	58	500 mg. D**	negative	negative

Table 3. Continued

	Age in years	Dosage per day	Tes-Tape Response	Clinitest Response
	(1)	(2)	(3)	(4)
6.	59	50 mg. H. D. ***	negative	negative
7.	60	50 mg. H. D. ***	negative	negative
8.	61	50 mg. H. D. ***	negative	negative
9.	61	50 mg. H. D. ***	negative	negative
10.	66	50 mg. H. D. ***	negative	trace

* Esidrex
** Diuril
*** Hydrodiuril

Table 4 shows the comparison of patients taking Isoniazid, their age, dosage of Isoniazid and the response of Tes-Tape and Clinitest to urine testing. The age of the patients tested ranged from 28 years to 64 years. All patients stated they were taking 300 to 400 milligrams of Isoniazid daily. All responses to urine testing by Tes-Tape and Clinitest Reagent Tablet were negative and thus no statistical analysis was necessary. The following null hypotheses were accepted:

1. Urine samples of patients taking Isoniazid will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method when age of the patient is a variable.
2. Urine samples of patients taking Isoniazid will show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in

testing urine for glucose when the dosage of the medication is a variable.

Table 4. Comparison of Patients Taking Isoniazid, Their Age, Dosage of Isoniazid, and the Response of Tes-Tape and Clinitest Reagent Tablet to Urine Testing.

	Age in years	Dosage per day	Tes-Tape Response	Clinitest Response
	(1)	(2)	(3)	(4)
1.	28	400 mg.	negative	negative
2.	36	300 mg.	negative	negative
3.	44	300 mg.	negative	negative
4.	44	400 mg.	negative	negative
5.	45	300 mg.	negative	negative
6.	46	400 mg.	negative	negative
7.	46	400 mg.	negative	negative
8.	56	400 mg.	negative	negative
9.	58	300 mg.	negative	negative
10.	64	300 mg.	negative	negative

Summary of Data

This study was undertaken to determine if specific drugs or drug groups do reduce the Clinitest Reagent Tablet when there is no glucose present in the urine. The age of the patient and the dosage of medication were considered as variables.

It was found that no significant relationship existed between age of the patient and dosage of medication. No statistical analysis was necessary except in one instance. That was not significant, hence all null hypotheses were accepted. Large dosages of salicylates do at times affect the response to the Clinitest Reagent Tablet.

CHAPTER IV

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary of the Study

This study was undertaken for the purpose of determining if specific drugs or drug groups do reduce the Clinitest Reagent Tablet when there is no glucose present in the urine. The age of the patient and the dosage of medication were considered as variables.

Following a review of the related literature concerning the effect of drugs on laboratory testing, unstructured interviews were held with individuals who were knowledgeable in the field of medications. A report form was constructed and steps for testing the urine determined.

Permission to obtain data using the patients in the Out Patient Clinic at the University of Oregon Medical School and the Out Patient Clinic at the University State Tuberculosis Hospital was obtained.

Forty patients were selected to participate in this study. These forty patients were divided into four groups: ten patients taking no medications; ten taking only salicylates; ten taking a thiazide diuretic; and ten taking Isoniazid.

Information about each patient, such as their age, medication taken, dosage and frequency of medication taken, along with the data and time of testing, was recorded on the report form.

A fresh urine sample from each individual was tested first with Tes-Tape to determine if any glucose was present. If the Tes-Tape gave a negative response for glucose, the urine was next tested with the Clinitest Reagent Tablet to determine if there was a copper-reducing substance, such as the medication being taken by the patient, present.

The data obtained by testing the urine from each individual were tabulated according to medication. Patients taking no medications had a range of age from fifteen to sixty-six years. The data showed that the responses to Tes-Tape and Clinitest were all negative. The patients taking salicylates ranged in age from thirty-two to sixty-eight years and the dosage of medication ranged from sixty to ninety grains per day. The data showed there were three trace responses out of the ten to the Clinitest method while all ten responses to Tes-Tape were negative. The data were analyzed using the student's t, F test and Cochran and Cox formula. (Appendix C) Patients taking thiazide diuretics had a range of age from thirty-nine to sixty-six years. All patients were taking 500 mg. of chlorthiazide or equivalent medication. The data showed that all responses to both Tes-Tape and Clinitest were negative with the exception of one trace response to Clinitest. The patients taking Isoniazid ranged in age from twenty-eight to sixty-four years and the dosages of medication were 300-400 mg. daily. All responses to Tes-Tape and Clinitest were negative. No statistical analysis was necessary on the data collected.

Conclusions

A study of this size should be regarded as a pilot to further study. The findings apply only to the forty participants; however the following is concluded:

1. There was no significant difference when testing urine for glucose with Tes-Tape or Clinitest Reagent Tablet when the patient is taking salicylates, thiazide diuretics, or Isoniazid and when age of the patient is a variable.
2. There was no significant difference when testing urine for glucose with Tes-Tape or Clinitest Reagent Tablet when the patient is taking salicylates, or thiazide diuretics, or Isoniazid and when dosage of the medication is a variable.
3. There appeared to be the possibility of false positive reactions to Clinitest Reagent Tablet when patients were taking larger than the usual dosage of salicylates.
4. The findings of this study challenge the conclusions of Caraway, Wirth and Thompson and Elking and Kabat and point out the need for empirical studies to test theoretically derived conclusions.

Recommendations for Further Study

A replication of this study might yield information not obtained

in this small study. It is recommended that a series of studies be done that:

1. involve a larger number of patients.
2. use Benedict's solution as well as Clinitest and Tes-Tape for urine testing.
3. compare findings derived from the study of hospital patients and those attending the Out Patient Clinics.
   a. it is recognized that the patient's illness establishes a variable which complicates the study, but because of the illness, the findings could have greater pertinence.
   b. it is recognized that an advantage of studying hospital patients is that the investigator could control the administration of medications, the collecting and testing of urine.
4. use aliquot urine samples to check the urine collected over a longer period of time. It is not known if this would result in a more accurate reading.
5. compare controlled known diabetics taking medications such as salicylates, thiazide diuretics and Isoniazid, with non-diabetics taking the same medications to determine if the diabetic's urine would react differently than that of the non-diabetic when tested with Tes-Tape, Clinitest and Benedict's Solution.

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APPENDICES

APPENDIX A

Report Form

COMPARATIVE STUDY OF CLINITEST & TES-TAPE

NAME_____ O.P. NO._____

DATE_____ TIME_____

AGE_____ SEX_____

MEDICATION TAKING_____

DOSAGE_____ FREQUENCY_____

TES-TAPE	CLINITEST

APPENDIX B

Steps Used in Testing Urine

APPENDIX B

Steps Used in TESTING URINE

1. Test urine first with Tes-Tape to check for the presence of glucose:
   a. Tear off strip of Tes-Tape approximately one and one-half inches long.
   b. Dip one end into the urine.
   c. Remove and wait one minute.
   d. Compare with color chart on Tes-Tape container.
   e. Record findings.
   f. If Tes-Tape is negative for glucose, then test same urine sample with Clinitest Tablet.

2. Test urine with the Clinitest Tablet;
   a. Place five drops of urine in a clean test tube.
   b. Rinse dropper thoroughly with clean water.
   c. Place ten drops of water in same test tube.
   d. Place one Clinitest Tablet in same test tube.
   e. Wait fifteen seconds after solution has stopped boiling.
   f. Shake test tube gently.
   g. Compare with color chart accompanying Clinitest tablets.
   h. Record findings.

APPENDIX C

Statistical Analysis

Student's t test:

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{EX_1^2 - (EX_1)^2/N_1 + EX_2^2 - (EX_2)^2/N_2}{N_1 + N_2 - 2}\left(\frac{1}{N_1} + \frac{1}{N_2}\right)}} \quad (22)$$

F test:

$$F = \frac{s_1^2}{s_2^2}$$

where s_1^2 = the larger of the two sample variances

s_2^2 = the smaller of the two sample variances. (6)

Cochran and Cox formula:

$$t_{.05} = \frac{S\bar{X}_1^2 (t_1) + S\bar{X}_2^2 (t_2)}{S\bar{X}_1^2 + S\bar{X}_2^2}$$

where t_1 is the 5% value for t at N_1-1 degrees of freedom

where t_2 is the 5% value for t at N_2-1 degrees of freedom (6)

AN ABSTRACT OF THE THESIS OF

ALICE L. DAHLEN

For the MASTER OF SCIENCE in NURSING EDUCATION

Date of receiving this degree: June 11, 1971

Title: A STUDY TO DETERMINE THE EFFECT OF DRUGS ON GLUCOSE URINE TESTING

Approved: [redacted]

(Associate Professor in Charge of Thesis)

This study was undertaken for the purpose of determining if specific drugs or drug groups do reduce the Clinitest Reagent Tablet when there is no glucose present in the urine. The age of the patient and the dosage of medication were considered as variables.

Following a review of the related literature concerning the effect of drugs on laboratory testing, unstructured interviews were held with individuals who were knowledgeable in the field of medications. A report form was constructed and steps for testing the urine determined.

Forty patients were selected to participate in the study from the Out Patient Clinics at the University of Oregon Medical School and from the University State Tuberculosis Hospital.

The data obtained by testing the urine from each individual were tabulated and analyzed by using the student's t test of significance.

Findings

On the basis of this study, the following null hypotheses were accepted:

1. Urine samples of patients not taking medications show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose.
2. Urine samples of patients taking salicylates show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
3. Urine samples of patients taking thiazide diuretics show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
4. Urine samples of patients taking Isoniazid show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when age of the patient is a variable.
5. Urine samples of patients taking salicylates show no

significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

6. Urine samples of patients taking thiazide diuretics show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

7. Urine samples of patients taking Isoniazid show no significant difference between the reactions obtained by the copper-reducing method and the oxidase enzyme method in testing urine for glucose when the dosage of the medication is a variable.

It was found that three out of the ten responses demonstrated a trace response with the Clinitest Reagent Tablet and a negative response with the Tes-Tape when the patients were taking salicylates. The data were analyzed using the student's t test. Although statistically there is no significant difference between testing with Tes-Tape and Clinitest when patients are taking salicylates, large dosages do appear to have some affect on the response when the urine is tested with Clinitest Reagent Tablet.

Conclusions

A study of this size should be regarded as a pilot to further study. The findings apply only to the forty participants; however they do lead to the following conclusions:

1. There was no significant difference when testing urine for glucose with Tes-Tape or Clinitest Reagent Tablet when the patient is taking either salicylates, thiazide diuretics, or Isoniazid and when age of the patient is a variable.
2. There was no significant difference when testing urine for glucose with Tes-Tape or Clinitest Reagent Tablet when the patient is taking either salicylates, thiazide diuretics, or Isoniazid and when dosage of the medication is a variable.
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in this small study. It is recommended that a series of studies be done that:

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4. use aliquot urine samples to check the urine collected over a longer period of time. It is not known if this would result in a more accurate reading.
5. compare controlled known diabetics taking medications such as salicylates, thiazide diuretics and Isoniazid, with non-diabetics taking the same medications to determine if the diabetic's urine would react differently than that of the non-diabetic when tested with Tes-Tape, Clinitest and Benedict's Solution.