48 per cent., 10 were double tertian, nearly 20 per cent., 16 were estivo-autumnal, 32 per cent., one was estivo-autumnal and tertian, and one was estivo-autumnal and double tertian, 4 per cent., and among these, four showed the Widal at the time the malarial parasite was found. In two of these the parasite occurred during the convalescence from their typhoid, one on the fourteenth and one on the eighteenth day of normal temperature. The other two cases had had typhoid two and four months previously.

I hope I have brought before you clearly the great value, and, in fact, the necessity of careful systematic examination of the blood in obscure fevers, by not only the Widal method but also by that of the fresh blood. The greatest care is taken to furnish good operating sets and good operators to every camp, but when we compare the mortality from surgical cases and that from camp fevers (preventable fevers if early recognized), it must be admitted that even the surgical sets and the expert surgeons are not any more important to the army than the bacteriological set and the expert hematologist.

In conclusion I wish to acknowledge my indebtedness to General Sternberg, Surgeon-General of the Army, not only for permission to use the army records but for his personal encouragement in this work, and the opportunities he has given me for study. I also wish to thank Major-Surgeon Walter Reed, Pathologist to Army Medical Museum and President of the Army Typhoid Investigation Board, and the commanding officers of the United States General Hospitals at Savannah, Ga., and Fort Myer, Va., Major-Surgeons, United States Army, Drs. D. M. Appel and Wm. B. Davis.

THE PHENYLHYDRAZIN TEST FOR SUGAR IN THE URINE.

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So many and so varied are the statements made in the text-books in describing this important test for sugar, that an attempt has been made in this paper to bring order out of chaos. As a reagent, both for laboratory and clinical work, phenylhydrazin possesses exceptional value and advantages — not only on account of its delicacy, but, as will be subsequently shown, as a positive test for the detection of sugar in the urine, even when present in minute quantities. As is well known, the reducing sugars possess the following chemical properties, which, although well marked, yet other substances are present at times in the urine which possess one or more of these properties, and thereby give rise to confusion:

(1) In alkaline solutions they reduce the salts of certain metals to their oxides, suboxides or the metals themselves — such as copper, bismuth and silver. This is shown in Fehling's, Trommer's, Nylander's and the silver tests.

(2) They decolorize and deoxidize solutions of indigo blue.

(3) They undergo fermentation with yeast — some of them, it is true, with difficulty.

(4) They turn the plane of polarized light either to the right or the left.

(5) They form with phenylhydrazin definite crystalline compounds possessing a fixed formula.

It is upon one or more of these properties that the clinical and laboratory tests for sugar depend.

Phenylhydrazin ($C_6H_5N_2$ —HN—NH₂) is derived from the group II, N —NH₂ by the substitution of a phenyl radical for one of the hydrogen atoms. It is strongly basic, and unites with acids to form salts, of which the best known is the hydrochlorate. It is but sparingly soluble in water, but readily soluble in acids, alcohol and ether, and combines with aldehydes to form hydrazones, and with sugars to form osazones. It reduces Fehling's solution in the cold with the evolution of nitrogen.¹ It was first brought to the notice of the medical profession, as a test for sugar, through the researches of E. Fischer.²

In order to test the delicacy of this reagent, and also to ascertain if it formed crystalline compounds with other basic bodies in the urine, so as to interfere with its accuracy, the following experiments were undertaken: One-half gramme each of the following carbohydrates was taken, dissolved in a test-tube in 10 cubic centimetres water, and to each solution was added one-half gramme sodium acetate and one-tenth gramme phenylhydrazin. They were all heated for one hour in the water bath, and allowed to cool, with the following results:

TABLE I.

Substance used.	Amount of precipitate.	Color of precipitate.
Lactose.	Heavy crystalline.	Yellow.
Glucose (dextrose).	" "	" "
Levulose.	" "	" "
Maltose.	Large "	" "
Saccharose (cane sugar).	Small "	" "
Glycogen.	Slight amorphous.	Dark brown.
Potato starch.	Very slight (amorphous).	Light yellow.
Amylodextrin.	" "	" "
Soluble starch.	" "	" "
Inosite.	Slight.	" "
Control blank (phenylhydrazin and sodium acetate).	No.	" "

Under the microscope it was seen that some of these possessed a definite crystalline form, as tabulated.

TABLE II.—CRYSTALS.

Substance used.	Description of crystals.
Lactose.	Yellow needle-like crystals radiating from a centre.
Glucose.	Sheaves of long yellow needles.
Levulose.	Very long yellow needles, irregularly grouped.
Maltose.	Broad, radiating yellow flakes.
Cane sugar.	Very small fine needles and spicules.
Glycogen.	Dark-brown oily globules.
Potato starch.	Nothing.
Amylodextrin.	A few oily globules.
Soluble starch.	Nothing.
Inosite.	A few oily globules.
Control blank.	Nothing.

As will be seen from the above tables, all of the reducing sugars, including cane-sugar (which, however, will not reduce until it is split up), form definite crystalline compounds. In regard to cane sugar, it would seem at first as though the crystalline combination were due to the splitting up of the cane sugar into dextrose and levulose by the prolonged heating. However, a close study of these crystals shows that they possess a definite morphology, and in no way resemble the crystals derived from either dextrose or

¹ A. H. Allen: Chemistry of Urine, p. 60.

² E. Fischer: Berichte der deutschen chemischen Gesellschaft, 17, 579, 1884.

levulose. In spite of statements to the contrary, it seems that cane sugar does form an independent compound with phenylhydrazin, as is seen both by the form and grouping of the crystals. Although no attempt was made to determine the melting point, such a test would have undoubtedly greatly aided their identification as a separate compound.

As dextrose (or glucose) is by far the most important of these sugars, and is what is meant in medicine by the generic name of sugar, the delicacy of the reagent with this carbohydrate was next determined, with the following results (amount used in each case was 10 cubic centimetres) :

TABLE III.

Percentage.	Appearance of precipitate.	Crystals by microscope.
1	Very heavy.	Crystals.
0.1	Heavy.	Crystals.
0.01	Slight.	A few crystals.
0.001	Very slight.	Very few crystals, but well defined.
0.0001	No.	No crystals.

From the above it is evident that the limit of the delicacy of the test is about 0.0001, but this limit far exceeds that which would be necessary for practical purposes, as so small an amount of sugar in the urine has no clinical importance. The writer had occasion to examine a suspected urine for sugar in which Fehling's test was doubtful. Nylander's test gave but a faint brown coloration after standing, while phenylhydrazin gave well-defined crystals.

For the proper recognition of these crystals, and of the sugars from which they are formed, much stress has been laid upon their melting points. This, however, is of minor importance, because, as has been shown, the combination of each sugar with phenylhydrazin forms crystals which in every case have a definite morphology, and therefore each sugar can be recognized by these crystals alone without reference to their melting points. As applied to the urine, this would be of great clinical value. As it is well known that basic or other substances might occur in the urine which interfere with the usual clinical tests for sugar, the following substances were also tried with phenylhydrazin in the proportion that they exist in the urine.

TABLE IV.

Name.	Precipitate.
Urea.	None.
Uric acid.	Slight, a few oily globules.
Hippuric acid.	None.
Kreatinin.	None.

Neither the above bodies nor xanthin gives rise to crystals; the only substance that might cause confusion is glycuronic acid, which in alkaline or neutral solutions gives a yellow crystalline compound resembling phenylglucosazone, but whose melting point is lower. In von Jaksch's modification of the test in an acid solution, there is found only a brown resinous mass. This substance not only reacts positively with Fehling's solution, but also reduces bisnuth and silver in alkaline solutions and is dextrorotary, but, however, it does not undergo fermentation with yeast.³ This shows that we have in phenylhydrazin a reagent

³ Halliburton: Phys. and Path. Chemistry, p. 793-4.

of great accuracy and delicacy, which not only enables us to detect sugar with certainty, but even to determine the kind of sugar present. Nothing else occurs in the urine, except the sugars, which gives rise to these crystalline compounds, each of which has a definite form and a definite melting point.

Outside of the sugars, Fehling's and Nylander's tests are interfered with by the following bodies — either existing in the urine as such, or following their ingestion. The principal ones are as follows:

Fehling's test. — Chloral, chloroform, sulphonal, glycosuric, hippuric, salicylic, benzoic, glycuronic and uric acids, kreatinin, kreatin, xanthin, pyrocatechin, hydrochinon, albumin.

Nylander's test. — Albumin, free sulphuretted hydrogen, rhubarb pigment, melanin, kairin, glycosuric and glycuronic acids, turpentine, quinine, eucalyptus, and the presence of large amounts of uric acid.

To apply the phenylhydrazin test to the urine, take 25 cubic centimetres urine in a small beaker, add one gramme phenylhydrazin and two grammes sodium acetate. Heat over the water bath from thirty minutes to an hour, and then cool by plunging the beaker in cold water. A yellow crystalline deposit is thrown down, which on examination by the microscope is found to consist of the yellow crystals of phenylglucosazone if this sugar be present. The reaction takes place according to the following equations:

From the above equation it will be seen that an excess of phenylhydrazin must be present in order that the crystals may be formed.

The experiments set forth in this paper seem to justify the following conclusions:

- (1) Phenylhydrazin forms with the reducing sugars, crystalline chemical compounds, each having an individual and definite morphology.
- (2) Albumin need not be removed.
- (3) It is possible to recognize any of the sugars by their crystalline forms alone, with recourse to their melting points.
- (4) Substances that interfere with Fehling's or Nylander's reagents do not interfere with this test, or form anything that would in any way be misleading.
- (5) The test is an extremely delicate one, and of undoubted accuracy.

Clinical Department.

AN INSTANCE OF URTICARIA OCCURRING AS AN INITIAL RASH IN TYPHOID FEVER.

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ON April 10th I was called to see Mr. L. R., married, forty-three years of age, by occupation a special officer of one of our principal hotels, who gave the following history of his illness: He had been in his usual health and, in fact, felt perfectly well until five