The examination of urine has been standard medical practice for several centuries. Many 17th and 18th century paintings exist showing a woman standing or sitting next to a man who is examining a flask of golden liquid (figure 1). Because the surroundings often include various pieces of chemical apparatus, these paintings have often been historically misidentified as representing alchemists when in fact they represent medical doctors or, at best, iatrochemists, examining a sample of the woman’s urine. From its clarity, color, the presence or absence of sediments, etc. the physician hoped to discern the nature of the woman’s disease. Such examinations were crude, to say the least, and the period author, Robert Burton (1577-1640), rather colorfully characterized the practitioners of this art as “piss prophets.”

As is apparent from figures 2 and 3, visual and microscopic examination of urine continued well into the 20th century. However, as the 19th century pro-

Figure 1. An 18th century painting of a “Uroscopy” by Franz Janneck (1703-1761), often misidentified as a painting of an alchemist or, at best, of a “medical chemist.”

Figure 2. A colored plate from a 1905 textbook of medical chemistry showing the appearance and sediments associated with the urine of patients suffering from various medical conditions (1).

Figure 3. Sedimentation glasses for urine analysis. The sediment actually collects in a small cavity in the stopcock at the base of the glass from which it can later be removed for microscopic examination. (Oesper Collections).
gressed, there was an increasing shift away from visual characterization as more and more specific chemical tests were developed. This, in turn, gave rise to the appearance of urine testing kits that individual physicians could use in their offices. Some of these were quite elaborate (figures 4 and 5), whereas others were quite specific, such as the ureometer testing kit in figure 6.

Figure 4. A circa 1900 Pilling testing kit for urine analysis (Oesper Collections).

Figure 5. A period ad for the urine testing kit in figure 4.

Figure 6. A circa 1900 ureometer kit (Oesper Collections).

Figure 7. A ureometer for the quantitative determination of urea in urine.
The ureometer (figure 7) consisted of a bulb with an attached vertical tube that was graduated and sealed at one end. The tube and bulb were filled with a freshly prepared alkaline solution of sodium hypobromite \([\text{Na(BrO)}]\):

\[
4\text{OH}^- (\text{aq}) + \text{Br}_2 (\text{l}) \rightarrow 2\text{OBr}^- (\text{aq}) + 2\text{H}_2\text{O}(\text{l}) \quad [1]
\]

A measured volume of the urine to be tested was then added using the graduated eye dropper, whereupon any urea present was oxidized to dinitrogen gas and carbonate:

\[
(\text{NH}_2)_2\text{CO(aq)} + 3\text{BrO}^- (\text{aq}) + 2\text{OH}^- (\text{aq}) \rightarrow \text{N}_2(g) + 3\text{H}_2\text{O}(\text{l}) + \text{CO}_3^{2-} (\text{aq}) + 3\text{Br}^- (\text{aq}) \quad [2]
\]

The released dinitrogen gas would displace part of the liquid in the graduated vertical tube and from its measured volume one could estimate the amount of urea present in the urine sample.

The clinical detection and estimation of sugar in urine is, of course, of great importance in diagnosing and monitoring diabetes. The earliest reliable test for glucose in urine was developed by the German chemist, Hermann von Fehling (figure 8), in 1849 (2). It consisted of mixing solutions of copper sulfate and of a sodium hydroxide/sodium potassium tartrate mixture with the urine sample. If glucose was present, the resulting blue copper tartrate complex was reduced to form a red precipitate of dicopper oxide (figure 9):

\[
\text{RCHO(aq)} + 2\text{Cu(L)}_2^{2-} (\text{aq}) + 5\text{OH}^- (\text{aq}) \rightarrow \text{Cu}_2\text{O(s)} + \text{RCOO}^- (\text{aq}) + 4\text{L}^{2-} (\text{aq}) + 3\text{H}_2\text{O(l)} \quad [3]
\]

where RCHO represents the reducing aldehyde group on glucose and L represents the bidentate tartrate ligand. By the early 20th century this test had given rise to small reagent/test tube racks (figures 10 and 11) containing the necessary reagents and apparatus for performing the Fehling test directly in a physician’s office.
In 1909 the American clinical chemist, Stanley Rossiter Benedict (figure 12), proposed an alternative reagent for glucose consisting of a copper citrate complex dissolved in a mildly alkaline sodium carbonate solution. This is now universally known as Benedict’s solution (3). Since the citrate ligand, like the tartrate ligand, is bidentate, equation 3 still applies, where the necessary hydroxide ion is now supplied by the hydrolysis of the carbonate ion. Whereas in Fehling’s original test the reagent must be freshly prepared before each trial by mixing equal parts of the copper (II) sulfate solution (called Fehling’s solution A) and the tartrate/sodium hydroxide solution (called Fehling’s solution B), in sharp contrast, Benedict’s copper citrate complex/carbonate mixture is quite stable and can be prepared ahead of time and stored a single bottle.

Yet a third, unnamed alternative chemical test, using glycerin as the complexing agent, was also sometimes used (1). Since glycerin also acts as a bidentate ligand with respect to the copper (II) cation, equation 3 can once again be used to represent the resulting reaction with glucose.

Another approach to the detection of sugar in urine involved a device known as a saccharometer (figure 13) (1). This was essentially identical to the ureometer described earlier. Ten mL of urine was shaken with some compressed yeast and the mixture placed in the saccharometer such that the vertical tube was completely filled. The device was then set in a warm room for 24 hours. If glucose was present, fermentation would occur, leading to the displacement of liquid in the vertical tube by the resulting carbon dioxide gas:

\[ C_6H_{12}O_6(aq) \rightarrow 2C_2H_5OH(aq) + 2CO_2(g) \]  

Attempts to quantify this test using a graduated vertical tube were only approximate due to the finite solubility of carbon dioxide in water.

References and Notes

1. J. W. Holland, A Text-Book of Medical Chemistry and Toxicology, Saunders: Philadelphia, 1905, plate VII.