Background

Recognition of the presence of disease is based to some extent on the existence of objective signs or recognizable abnormalities known as symptoms. Groups of sign and symptoms occurring in a characteristic pattern (referred to as syndromes) are of value in diagnosis and in determining the distribution as well as the cause, or etiology, of diseases.

The process of diagnosing a disease involves several steps. First, the patient will consult with the physician and describe any particular symptoms that he or she has previously noticed. The physician will then examine the patient and note any signs that may be further indicative of the problem. Based on this initial assessment and the patient’s medical history, the physician may then make a diagnosis of the disorder. However, in some cases it may be necessary to go a step further and order various laboratory tests, possibly including X-ray examinations. This serves not only to arrive at a correct diagnosis, but also to rule out any other disorders which may share the same signs and/or symptoms.

There are many different types of specimens used in laboratory diagnosis, including blood, feces, sputum, stool, urethral and vaginal secretions, and cerebrospinal fluids. Urine testing is another very important diagnostic tool that involves the physical, chemical, and visual examination of a urine sample. A thorough urinalysis may provide more information about the general condition of the body than any other set of tests. Urinary tract infections, kidney malfunction, diabetes, and liver disease are just some of the medical problems that can be diagnosed through urinalysis.

Urinalysis is often used for the screening of drugs. A urine sample can be tested for drug overdose and toxicity, or for the presence of abused drugs, commonly including amphetamines, barbiturates, cannabinoids, cocaine, methadone, benzodiazepines, methaqualone, and opiates. This test is very useful as a pre-employment drug screen. One limitation, however, is that this test provides only qualitative detection of drugs. Quantitation of drug levels is not recommended because urine levels are time and clearance dependent and are not directly related to toxic symptoms seen clinically.

Another important use of urinalysis is for pregnancy testing. When a woman becomes pregnant, a hormone known as human chronic gonadotropin begins to be secreted by the embryonic tissues shortly after fertilization. HCG secretion then increases until it reaches a peak in about 50 to 60 days; thereafter, the HCG concentration drops to a much lower level and remains relatively stable throughout the pregnancy. Because HCG is excreted in the urine, urinalysis is used to detect this hormone, thereby indicating the
presence of an embryo. Such a pregnancy test may give positive results as early as 8 to 10 days after fertilization.

Several factors are examined when analyzing a urine sample. These include appearance of the urine, odor, pH, specific gravity, and microscopic observations.

**Appearance:**
The color of normal urine can range from pale yellow to amber, depending on the concentration of the pigment urochrome, which is the end product of hemoglobin breakdown. The appearance of the urine may serve as an indication of a pathological condition. For instance, pale yellow urine may indicate diabetes insipidus, granual kidney, or may simply be dilute due to ingestion of copious amounts of water. A milky color may signify fat globules or pus corpuscles, the latter possibly indicating a urogenital tract infection. Reddish colors may be due to food pigments (such as beets), certain drugs, or blood in the urine. Greenish colors indicate either bile pigment (jaundice) or certain bacterial infections, such as those caused by several species of Pseudomonas. Lastly, brown-black urine can indicate phenol or metallic poisonings r'or hemorrhages due to conditions such as renal injury or malaria.

**Odor:**
The odor or urine can vary greatly according to both diet and pathology. An ammonia smell may result from certain foods, while a fishy smell may indicate cystitis. A fecal smell could be due to an intestinal-urinary tract fistula. Other distinctive smells could be indicative of disorders such as acetonuria, which has an overripe apple smell, or diabetes, the urine of which can also be noted to be sweet-smelling.

**pH:**
The pH of normal urine ranges from 4.5 to 8.0, the acidity or alkalinity of which can fluctuate depending on the type of food ingested. Pathological conditions can also affect the pH of urine. Fevers and acidosis lower the pH, whereas anemia, vomiting, and ischuria (urine retention) raise the pH.

**Specific Gravity:**
Yet another component of urinalysis is the determination of specific gravity. This is a measure of the density of a substance in g/ml as compared to the density of water, which has a specific gravity of 1.00 g/ml. The specific gravity of urine usually ranges between 1.015 and 1.025, although numbers slightly higher or lower may be normal for people with diets either very high or low in fluid content. Specific gravity is generally inversely proportional to urinary volume. A pathological low specific gravity indicates nephritis, whereas a pathological high specific gravity indicates either nephritis or diabetes mellitus.

**Microscopic Observations:**
The microscopic examination of urine is a vital aspect of routine urinalysis. Urine is made up primarily of water, with some salts and organic materials dissolved in it. Inorganic substances normally found in the urine include sulfates, chlorides, phosphates, and ammonia. Casts, cells, crystals, and microorganisms are some of the significant elements found in the urine sediment.
Casts:
Casts in the urine are particularly significant because they represent cylindrical molds formed in the renal tubular lumina. They are formed by the precipitation of proteins and agglutination of cells within the renal tubules. Casts are classified into several major types: hyaline, epithelial, granular (coarse and fine), fatty, waxy, red-blood cell, and white-blood cell. Because casts originate within the renal parenchyma, their presence in the urinary sediment often provides important diagnostic clues as to the underlying renal pathology. For example, the presence of red blood-cell casts is always indicative of renal parenchymal disease, especially glomerulonephritis. The formation of casts is favored in a number of pathological conditions in the nephrons. These include: (1) the presence of protein constituents in the tubular urine, (2) increased acidification, and (3) increased osmolar concentration. A reasonable conclusion, then, is that casts will be formed principally within the distal convoluted tubules and the collecting ducts because the urine becomes maximally acidified and concentrated in this segment of the nephrons.

Cells:
Cells are exfoliated from different parts of the genitourinary tract for various reasons, including normal "wear and tear", degenerative and inflammatory processes, or secondary processes due to infarction or tumor formation. The metabolic activity of the cells found in a urine sample has been impaired to varying degrees, resulting in membrane changes in permeability and selectivity, and causing variations of hydration, intracellular osmolality, density, and microscopic characteristics. Swelling, shrinking, or intracellular structural changes may also occur due to exposure for ill-defined periods of time to wide variations in urine osmolality and pH, toxic substances, excreted drugs, and metabolites, and bacterial actions. Cell types include urothelial (transitional), columnar epithelial, prostatic, seminal vesicle, decoy, multinucleated giant, squamos, tubular epithelial, oval fat, red-blood cell, and white-blood cell. Microscopic evaluation of cells in urinary sediment may help in the diagnosis of neoplastic disease (carcinoma) and some non-neoplastic diseases of the urinary tract.

Crystals:
The variety of crystals and amorphous compounds found in the normal urinary sediment may represent both the end product of tissue metabolism and the excessive consumption of certain foods or drugs. The type of crystal or amorphous compound depends to some extent on the pH and osmolality of the urine. The presence of some crystals are of little or no significance while others constitute a positive diagnostic test. Common crystals may be present normally in acid, neutral, or alkaline urine. However, abnormal types of crystals are almost always associated only with acid or neutral urine.
<table>
<thead>
<tr>
<th>URINE TYPE</th>
<th>CRYSTAL TYPE</th>
<th>POSSIBLE INDICATIONS</th>
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<tbody>
<tr>
<td>Alkaline</td>
<td>Calcium phosphate</td>
<td>Calculi (stone) formation</td>
</tr>
<tr>
<td>Alkaline</td>
<td>Triphosphate</td>
<td>- calculi formation</td>
</tr>
<tr>
<td>Alkaline</td>
<td>Calcium carbonate</td>
<td>- obstructive uropathy</td>
</tr>
<tr>
<td>Acid</td>
<td>Calcium oxalate</td>
<td>- urinary tract infection</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- Proteus mirabilis infection</td>
</tr>
<tr>
<td>Acid</td>
<td>Hippuric acid</td>
<td>- gout</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- leukemia</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- high purine metabolism</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- chronic nephritis</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- severe liver disease (leucine and tyrosine may occur together)</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>- calculi, congenital cystinosis, congenital cystinuria (cystine present)</td>
</tr>
<tr>
<td>Acid</td>
<td>Uric acid</td>
<td>No clinical significance</td>
</tr>
</tbody>
</table>

### Albumin, glucose, and ketones:

The presence of various substances in the urine that are not normally there can, in some cases, be an indication of a disorder. For example, the presence of albumin (a plasma protein that helps regulate the osmotic concentration of the blood) in a urine sample may indicate a kidney malfunction since kidneys are supposed to filter albumin and glucose out of the waste material and return them to the body. And as such, the presence of glucose in urine may also be a positive indication of a disorder, namely diabetes mellitus. The hallmark of diabetes is an increase in the concentration of blood sugar (hyperglycemia). When the blood sugar reaches a certain high concentration, it exceeds the renal threshold and the kidneys begin to excrete the excess. At this point, glucose appears in the urine (glycosuria). Another substance that might be found in the urine to indicate diabetes is ketones. These occur when fats are metabolized at abnormally high rates, thus causing ketone bodies to accumulate faster than they can be oxidized. Ketones may also appear in the urine when carbohydrate metabolism is inadequate. So
a person may also have ketonuria when he or she suddenly begins a very low carbohydrate diet. Other symptoms of diabetes mellitus include the classical triad, that is, excessive urine output (polyuria), dehydration accompanied by great thirst (polydipsia), and increased appetite (polyphagia). The person is also likely to lose weight and the ability to grow or repair damaged tissues is increased.

**Phenylketonuria:**
Urinalysis is also useful in assisting the detection of a condition known as phenylketonuria. PKU is a failure of the body to produce the enzyme necessary to oxidize phenylalanine to tyrosine, namely, phenylalanine hydroxylase. PKU is a recessive genetic trait whose incidence is somewhat over 1:11,000 in the United States. PKU cause nerve and brain damage, accompanied by mental retardation if left untreated. However, by reducing or eliminating phenylalanine from the diet, retardation does not occur. Because the phenylketones appear in the urine, infants with PKU often have diapers with distinctive odors; this observation by Swedish mothers ultimately led to the conclusion by scientists that PKU may be detected by checking the urine. However, urinalysis is not used as an initial screening for PKU. Ideally, newborns should be screened via a blood test when they are between 48 to 120 hours of age and have been on a milk (protein) feeding for at least 24 hours. After birth, 2 – 6 weeks may pass before phenylpyruvic acid is excreted in the urine. After PKU has been diagnosed, urine screening type tests may be used to make sure the diseases is being controlled properly. (Look at the nutrition label of carbonated drinks. Some state that they contain phenylketonurics, namely phenylalanine). State laws require PKU testing of infants within 28 days or less; in some states, testing is required prior to hospital discharge regardless of age.

**Case Studies**

**CASE 1 – Jeff Jones** is 19 years old. He notices that he has increased urine output (polyuria), increased appetite (polyphagia), and great thirst (polydipsia). He has also experienced unexplained weight loss.

**CASE 2 – Mr. Thompson** is 60 years old and has been unusually tired for several weeks. He occasionally feels dizzy and lately finds it increasingly difficult to sleep at night. He has swollen ankles and feet and his face looks puffy. He experiences a burning pain in his lower back, just below the rib cage. He also notices that his urine is dark in color. He goes to see his physician, who finds that he has elevated blood pressure, and that the kidney region is sensitive to pressure.

**CASE 3 – Ms. Smith** is 27 years old and has been experiencing painful and difficult urination (dysuria), frequency of urination and urgency. Her urine has a milky color. She also has fever and malaise, which is evidence of infection. Upon seeking treatment, she is given antibiotic therapy. After a few days of antibiotics, her symptoms disappear.

**CASE 4 – Normal sample (control)**