

Basic Laboratory Tests Basic Urine Tests (Urinalysis)

				Examples of conditions in
	Alternative		Usual	which abnormal values
Test	Names	Units	Normal Range	occur
pH, urine	рН	pH units	4.5 – 7.8	Various acid-base disorders, medications, prolonged urine sample storage
Glucose, urine	UGluc	g% or g/dL	Negative	Diabetes mellitus, low renal glucose threshold, kidney tubule diseases
Protein, urine	UProt	mg% or mg/dL	0-30 mg/dL	Exercise, fever, various types of kidney disease
Bilirubin, urine	UBili		Negative	Hemolysis
Ketones, urine	UKetone		Negative	Prolonged fasting or starvation; diabetes mellitus
Leukocyte esterase, urine	LE		Negative	Urinary tract infection or inflammation
Hemoglobin, urine	UHb		Negative	Hemolysis, kidney glomerular disease, any cause of bleeding from the kidney or urinary tract
White blood cells, urine	UWBC	(#/HPF)	0-9 per HPF	Kidney or urinary tract infection or inflammation
Red blood cells, urine	URBC	(#/HPF)	0-4 per HPF	kidney glomerular disease, any cause of bleeding from the kidney or urinary tract
Red Cell Casts, urine	RBC Casts		None	Kidney glomerular disease
Granular casts, urine	Gran Casts	(#/40LPF)	0-10 per 40 LPF	Normal finding and also seen in various types of kidney diseases
Hyaline casts, urine	Hyaline Casts	(#/40LPF)	0-10 per 40LPF	Normal, dehydration
Specific gravity, urine	SpG	Degrees Fahrenheit	1.003-1.035	Diluted or substituted urine specimen
Creatinine, urine	UCr	(mg/dL)	27-260 mg/dL	Diluted or substituted urine specimen.
Temperature, urine	Temp	90.5-99.6		Diluted or substituted urine specimen
Protein/Creatinine ratio, urine	UP/Cr	mg/mgCr or mg/gCr	0.00-0.20 mg/mgCr or 0-200 mg/gCr	Exercise, fever, various types of kidney disease
Microalbumin, urine	MA	mg/dL	3-30 mg/dL	Kidney glomerular disease including diabetes
Microalbumin/Creatinine ratio, urine	MA/Cr	mg/gCr	0-30 mg/g Cr	Kidney glomerular disease including diabetes
Nitrites, urine	UNitrate		Negative	Urinary tract infection
Crystals, urine	UCrystals		Negative	Kidney stone disease, various medications, various amino acids and other biologic compounds
Fat, urine	UFat		Negative	Various kidney diseases
Bacteria, urine	UBacteria			Urinary tract infection, prolonged urine sample storage
Adulterants, urine	Adult		Negative	Adulteration of urine specimen
Diuretic agents, urine	DIU Thiazides		Negative	Blood pressure medications
Beta Blockers, urine	BB		Negative	Blood pressure medications
Cotinine, urine	UCot (Nic)	micrograms/mL	Negative	Tobacco use or exposure. Use of nicotine replacement products.
Cocaine, urine	UCoc		Negative	Cocaine use or exposure

Urine Tests (Urinalysis)

The analysis of the urine for protein, other chemical substances and formed elements is termed urinalysis. The presence of protein and other substances is determined by using chemical methods. The presence of formed elements, like blood cells, crystals and casts, is determined by microscopic examination.

Urine pH (pH)

One major function of the kidney is to regulate acid-base balance by excreting excess acid or base into the urine. The normal urine pH is between 4.5 and 7.8. But by itself, urine pH provides little useful information. Furthermore, prolonged storage of urine samples before analysis can result in the overgrowth of bacteria leading to a high urine pH. For these reasons, urine pH determinations are usually not done on insurance urine specimens.

Urine Bilirubin and Urobilinogen

Bilirubin is produced from the normal metabolism of <u>hemoglobin</u>. In its native form, bilirubin is insoluble in water. In the liver, glucuronic acid molecules are attached (conjugated) to bilirubin to make it water soluble. Some conjugated bilirubin may be filtered by the kidney <u>glomeruli</u> and pass into the urine where it can be detected with chemical tests. The presence of bilirubin in the urine (bilirubinuria) may be seen in conditions that produce elevated blood concentrations of conjugated bilirubin including various liver diseases, bile duct obstruction, medications and some inherited disorders. Hemolysis, which can produce elevated blood levels of unconjugated bilirubin, typically does not cause bilirubinuria. However, with hemolysis, a related compound, urobilinogen, is often present in the urine.

Urine Glucose

Glucose is normally filtered by the kidney <u>glomeruli</u>. Filtered glucose is then completely reabsorbed into the blood stream by the kidney tubules and normally glucose is not present in the urine. However, there is a limit to the amount of glucose the tubules can reabsorb. This limit, termed the renal threshold for glucose, is normally equivalent to a blood glucose concentration in the range of 160 to 180 mg/dL. Thus, the presence urine glucose (glycosuria) usually indicates a blood glucose level above 180 mg/dL and is presumptive evidence of diabetes mellitus. However, some individuals have a lower renal glucose threshold resulting in the glycosuria despite a normal blood glucose concentration. Although urine glucose testing was once commonly done to screen for diabetes mellitus and as a way to monitor the effectiveness of diabetes treatment, finger-stick blood glucose measurements and HbA1c levels are most often used today for these purposes. However, glycosuria, if found, should prompt an evaluation for diabetes mellitus.

Urine Ketones

Ketones in the urine (ketonuria) may occur with prolonged fasting or starvation. They may also be seen in alcoholic intoxication and type 1 diabetes mellitus.

Urine hemoglobin and myoglobin

The destruction of red blood cells is termed hemolysis. Hemolysis releases hemoglobin into the blood stream. Initially free hemoglobin is bound to the protein, haptoglobin. But if the capacity of haptoglobin to bind hemoglobin is exceeded, unbound hemoglobin may be filtered by the kidney glomeruli and appear in the urine (hemoglobinuria). Another cause of hemoglobinuria is the rupture of red blood cells that may have entered the urine in a variety of ways. See hematuria. When red blood cells are in prolonged contact with urine, they may rupture, releasing free hemoglobin in the urine. This is frequently seen with prolonged storage of urine samples.

Myoglobin is a protein released as a result of muscle destruction (rhabdomyolysis). Myoglobin may be filtered by the kidney glomeruli and may appear in the urine. Rhabdomyolysis is an uncommon but serious condition often having significant mortality implications.

Proteinuria: Urine Protein, Urine Protein/Creatinine ratio, Microalbuminuria, Urine Microalbumin/Creatinine ratio

The presence of protein in the urine is termed proteinuria. Normally, little protein is filtered through the kidney glomeruli and most of the protein that passes through the glomeruli is reabsorbed by the kidney tubules. Therefore urine protein concentrations are normally quite low and in the range of 0-30 mg/dL or 30 to 150 mg protein per day.

There are three major categories of diseases that result in proteinuria: <u>Glomerular</u> disease (glomerular proteinuria); kidney tubular disease (tubular proteinuria); and overproduction proteinuria (light chain proteinuria).

The hallmark of <u>glomerular proteinuria</u> is the presence of increased amounts of albumin in the urine (albuminuria). Normal glomeruli prevent almost all blood albumin from being filtered. Most of what little albumin that passes through the glomeruli is reabsorbed by the kidney tubules and only a small amount of albumin (<3 mg/dL or <30 mg/day) is normally present in the urine. Depending on the amount of albumin that is present, albuminuria is classified as microalbuminuria (3- 30 mg/dL or 30-300 mg/24 hours) or gross albuminuria (>30 mg/dL or > 300 mg/24 hours). Although small amounts of albuminuria may be seen transiently following exercise and with fever, persistent albuminuria, whether it is microalbuminuria or gross albuminuria, usually indicates glomerular damage. Since kidney glomeruli are composed of capillaries, microalbuminuria or gross albuminuria often indicates the presence of generalized arterial disease and increased mortality risk. Diabetes mellitus is a common cause of glomerular proteinuria and regular screening of diabetic patients for the presence of microalbuminuria has been recommended by various medical societies in order to detect early diabetic kidney disease (diabetic nephropathy).

Proteinuria may also occur if there are defects in or damage to the kidney tubules preventing them from reabsorbing protein passing through the glomeruli. This is called <u>tubular proteinuria</u>. Tubular proteinuria is usually mild and characterized by the presence of globulins in the urine. But the characterization of the kind of proteins present in the urine requires specialized testing, not usually done as part of insurance underwriting. Tubular proteinuria is often associated with other abnormal urine chemistry results such as glycosuria (glucose in the urine) and phosphaturia (increased urine concentrations of phosphate). Various toxins and some congenital kidney diseases can result in tubular proteinuria.

Another uncommon cause of proteinuria is <u>the overproduction of small proteins</u> called light-chains by plasma cells and lymphocytes. These light chains are small enough to be filtered by the glomeruli. If a large amount of light chains is produced and pass through the glomeruli, the ability of the kidney tubules to reabsorb them may be overwhelmed and light-chain proteinuria may occur. Light chain proteinuria is seen with hematologic malignancies like multiple myeloma, Waldenstroms macroglobulinemia, and some leukemias and lymphomas. Light chain proteinuria can also be seen with benign and malignant plasmacytomas, benign monoclonal gammopathy, and amyloidosis

Concentrated urine that is otherwise normal, as might occur in dehydrated individuals, will result in increased urinary protein concentration without there being an increased amount of protein excretion over a 24 hour period. Conversely a dilute urine, as might occur in an individual who has consumed an excessive amount of water, will result in lower concentrations of urinary protein and might lead to the erroneous conclusion that significant proteinuria does not exist when in fact over a 24 hour period excessive urinary protein excretion may be present. For that reason and since <u>urinary creatinine excretion</u> is relative constant, urinary protein concentration is often adjusted for urine concentration by dividing the urine protein (or albumin) concentration by the urine creatinine concentration to arrive at a urine <u>protein/creatinine</u> ratio or a <u>urine albumin/creatinine</u>. The normal values for urine albumin/creatinine ratio are <3 mg albumin/g creatinine. Albumin/creatinine concentration ratios in the range of 3-30 mg albumin/g creatinine are termed <u>gross albuminuria</u>.

Tests for hematuria (blood in the urine): Urine Red Cells and Red Cell Casts,

The presence red blood cells in the urine (hematuria) is abnormal and often indicates the presence of kidney or urinary tract disease. <u>Glomerular</u> disease can result in red blood cells passing through the glomeruli, into the tubules and then into the urine. Sometimes when red blood cells come into contact with proteins in the tubules, they stick together forming a mold (cast) of the inside of the kidney tubules. Such <u>red cell casts</u>, detected on microscopic analysis of urine specimens, are indicative of glomerular damage. However, red cell casts may eventually fall apart in the urine, leaving only multiple individual red blood cells. The presence urinary red blood cells detected on microscopic analysis is non specific and can be due to glomerular disease or other disease processes involving the kidneys, ureters, bladder, or urethra. Not uncommonly, the presence of red cells in the urine may be due to the contamination of the urine specimen by blood from other sources, often from the vagina.

However, the presence of persistent hematuria in multiple urine specimens should in most cases prompt an evaluation for the source of the blood, sometimes requiring an evaluation for kidney or urinary tract tumors and other disease processes.

Red blood cells in the urine may eventually rupture (lyse) releasing hemoglobin into the urine. The presence of hemoglobin in the urine <u>(hemoglobinuria)</u> usually has the same implications as the presence of red cells in the urine (hematuria).

Tests for pyuria (white cells in urine): <u>Urine White Cells, Leukocyte Esterase</u>, and <u>Urine Nitrites</u> Urinary tact infections are infections involving the urethra, bladder, ureters or kidneys. Bacterial urinary tract infections produce inflammation and cause white blood cells to migrate from the blood stream to the site of infection. In the presence of urinary tract inflammation and infection, white cells may be seen in the urine with a microscope. This is termed pyuria. If pyuria is present, a urine culture is often done to confirm the presence of a urinary tract infection and determine the type of bacteria causing the infection. Other methods are also available to screen for urinary tract infections.

White blood cells liberate an enzyme called <u>leukocyte esterase</u> which can be detected in the urine by chemical methods. The presence of leukocyte esterase in the urine is presumptive evidence of pyuria. But false positive urine leukocyte esterase results can occur with vaginal contamination and false negative results can occur with high levels of urine glucose, albumin and in the presence of vitamin C and various antibiotics and other substances.

Since bacteria convert chemicals termed nitrates into nitrites, the presence of urine nitrite is presumptive evidence of a urinary tract infection. False negative urine nitrite results are common and may be due to high urine specific gravity, low dietary consumption of nitrates, prolonged urine sample storage and infection with some bacteria that do not produce nitrites.

Tests for urine concentrating ability: Specific Gravity and Urine Creatinine

A major function of the kidney is the regulation of salt and water balance. When required to conserve water, the kidney is able to concentrate urine 20 fold. One measure of the kidney's concentrating ability is the urine specific gravity which is the density of urine compared to pure water. The normal range for urine specific gravity is 1.003 of 1.030. In the past, specific gravity was measured by physical chemical methods using a refractometer or hygrometer. Today, more commonly it is measured by chemical reagents that depend on the ionic strength of the urine. The reagent method is less accurate than physical chemical methods. And both methods are less useful than directly measuring urine osmolality.

Urine creatinine concentration is another indicator of how concentrated or dilute a urine specimen is. Creatinine is a chemical substance that is a normal product of muscle metabolism. It is filtered by the kidney <u>glomeruli</u> and also secreted into the urine by the renal tubules. Since an individual's daily production of creatinine is fairly constant, urine creatinine concentration reflects how concentrated or dilute the urine is: concentrated urines have higher urine creatinine concentrations and dilute urines have lower creatinine concentrations. The normal urine creatinine concentration varies from 2 mg/dL to over 19 mg/dL.

There are many clinical uses for urine specific gravity and urine creatinine measurements. In insurance medicine, the two main uses of urine specific gravity and creatinine concentration are to help interpret the significance of proteinuria and to aid in the detection of adulterated or substituted urine specimens. The use of urine creatinine concentration to help determine the significance of proteinuria is discussed in the proteinuria section.

A urine specific gravity or urine creatinine concentration that is outside the physiologic limits (<1.001 or <2 mg/dL) suggests the possibility that the urine has been substituted or diluted, possibly with the intent of preventing certain substances from being detected in the urine.

Tests for other formed elements: Hyaline Casts, Granular Casts, Crystals, Fat, and Bacteria

Microscopic examination of the urine occasionally reveals other abnormalities. Hyaline casts are cylindrical molds (casts) of the inside of kidney tubules formed from the aggregation of normal tubular protein. Zero to two hyaline casts per low power microscope field is considered normal. Dehydration and low urine flow states often result in increased numbers of hyaline casts. The presence of hyaline casts is usually of little significance.

Cellular casts may occur when various types of cells become trapped in the protein matrix of what would otherwise be a hyaline cast. These cellular casts include <u>red cell casts</u>, white cell casts and tubular epithelial cell casts, among others. White cell casts are seen in kidney infections (pyelonephritis) and in conditions producing kidney tubular inflammation. Tubular epithelial cell casts are seen in acute renal failure (acute tubular necrosis), some viral infections, and with exposure to various drugs and toxins. Granular casts are the remnants of degenerating cellular casts. Their significance depends on they type of cells forming the casts.

Crystals, fat and bacteria may also be seen on microscopic examination of urine specimens. Many types of crystals can form in the urine due to kidney stones, various medications, and other biologic compounds like bilirubin and various amino acids. The presence of fat in the urine (lipiduria) is abnormal. When accompanied by proteinuria, lipiduria suggests the presence of the nephrotic syndrome. Bacteria in the urine may or may not be pathological depending on whether the urine specimen was collected in a sterile manner and whether examination of the urine specimen was delayed, potentially allowing the overgrowth of bacteria.

Occasionally, fungi, parasites, tumor cells, and other abnormalities may be seen on microscopic examination of the urine.

Urine drug tests and tests for urine adulteration (contamination):

Many other substances can be detected in the urine including nicotine metabolites and a variety of medications and illicit drugs. Chemical tests for nicotine metabolites (cotinine) are often done on urine specimens obtained in the course of insurance underwriting in order to determine if the proposed insured is using tobacco products or nicotine replacement products. Tests for blood pressure medications (diuretics or thiazides and beta blockers) are also often performed. In addition, insurance companies often request that tests be done to detect the presence of metabolites of <u>cocaine</u> and other illicit substances.

Similar urine tests for illicit substances are commonly done in the course of pre-employment evaluations. However, since it is commonly known that urine tests are done for these purposes, some individuals attempt to foil these urine tests by intentionally diluting their urine hoping to dilute the urinary concentration of illicit substances to a level below the detection threshold. Other individuals attempt to substitute water or other liquids for their urine. For that reason <u>urine temperature</u> is often measured at the time of urine collection to determine if the urine specimen temperature is the same as body temperature. <u>Urine specific gravity</u> and <u>urine creatinine concentrations</u> are usually performed to verify that the urine specimen has not been diluted or substituted. Other individuals sometimes add chemicals to (adulterate) their urine sample to interfere with the chemical methods used to detect the substance in question. For that reason, the laboratory usually performs additional chemical tests to detect the presence of <u>adulterants</u>.