

# Review on Pathology of Blood and Urine

**Shubhangi S. Pawar, Sanjay K Bais, Revansiddha Prabhakar Mane**

Fabtech College of Pharmacy, Sangola, Solapur, Maharashtra, India

**Abstract:** *Pathology is being important now a days Since the major pandemic like COVID 19 where seen although it is very essential in some conditions like diabetes, kidney stones, High blood pressure conditions to take precautions to avoid Major damage and life treating events. In this review article we get to know what the pathophysiology actually include and what is pathogenesis in turn of pharmacy. In this overview report of overview of the blood and urine through which various the disease conditions or the body behaviour is depend, if their is variation of the normal count of the constituents of these takes place it causes dysfunction of the body organs or biochemical reactions. In the further overall studies we will discuss about the what are major components of the blood and urine as well Their Major role in the clinical signs and symptoms. Further we come to know that what are the actual analytical methods of the testing, recognising, classify gread and stages of the different components and classify them and various types of maliganancy. Also let you know that is the contribution of the pathological analysis in the disease oriented surveillance and the evaluation, treatment as well.. at the end we will go through some report samples of pathological laboratori.*

**Keywords:** Blood and Urine

## I. INTRODUCTION

Pathology is the study of the causes and effects of disease or injury. The word pathology also refers to the study of disease in general, incorporating a wide range of biology research fields and medical practices. However, when used in the context of modern medical treatment, the term is often used in a narrower fashion to refer to processes and tests that fall within the contemporary medical field of "general pathology", an area which includes a number of distinct but inter-related medical specialties that diagnose disease, mostly through analysis of tissue, cell, and body fluid samples. Idiomatically, "a pathology" may also refer to the predicted or actual progression of particular diseases (as in the statement "the many different forms of cancer have diverse pathologies", in which case a more proper choice of word would be "pathophysiologies"), and the affix pathy is sometimes used to indicate a state of disease in cases of both physical ailment (as in cardiomyopathy) and psychological conditions (such as psychopathy). [1] A physician practicing pathology is called a pathologist.

Pathology includes the knowledge regarding the diagnosis of the disease through the different analytical techniques that are implemented on the biological sample material and compared with standard results, it includes the examination of blood, urine and other different body fluids and whole bodies i.e. autopsies. [1]

Early systematic human dissections were carried out by the Ancient Greek physicians Herophilus of Chalcedon and Erasistratus of Chios in the early part of the third century BC. The first physician known to have made postmortem dissections was the Arabian physician Avicenna (980–1037). Rudolf Virchow (1821–1902) is generally recognized to be the father of microscopic pathology. Most early pathologists were also practicing physicians or surgeons. [2]

In common medical practice, general pathology is mostly concerned with analyzing known clinical abnormalities that are markers or precursors for both infectious and non-infectious disease, and is conducted by experts in one of two major specialties, anatomical pathology and clinical pathology. Further divisions in specialty exist on the basis of the involved sample types. [2]

The term pathology has its different types as general pathology, anatomic pathology, clinical pathology, forensic pathology, veterinary pathology, pathology as a medical speciality. Their are different analytical techniques for every type of diagnosis and identify the error.

As a field of general inquiry and research, pathology addresses components of disease: cause, mechanisms of development (pathogenesis), structural alterations of cells (morphologic changes), and the consequences of changes (clinical manifestations). [3]

### 1.1 Clinical Chemistry of Blood

Blood is one of the important body fluids which carry the nutrients and the Drug material to treat or to provide the supplies to cells Our blood is made up of liquid and solids. The liquid part,called plasma, is made of water, salts, and protein. Over half of your blood is plasma. The solid part of your blood contains red blood cells, white blood cells, and platelets.[4,5]

Red blood cells (RBC) deliver oxygen from your lungs to your tissues and organs. White blood cells (WBC) fight infection and are part of your immune system. Platelets help blood to clot when you have a cut or wound. Bone marrow, the spongy material inside your bones, makes new blood cells. Blood cells constantly die and your body makes new ones. Red blood cells live about 120 days, and platelets live about 6 days. Some white blood cells live less than a day, but others live much longer.[4,5]

Red blood cells (RBCs), also referred to as red cells, red blood corpuscles (in humans or other animals not having nucleus in red blood cells), haemats, erythroid cells or erythrocytes(from Greek erythros for "red" and kytos for "hollow vessel", with -cyte translated as "cell" in modern usage), are the most common type of blood cell and the vertebrate's principal means of delivering oxygen ( $O_2$ ) to the body tissues—via blood flow through the circulatory system. RBCs take up oxygen in the lungs, or in fish the gills, and release it into tissues while squeezing through the body's capillaries. RBC's cytoplasm is rich of hemoglobin the hemoglobin is the component which play major function of the RBC that is transport of gases from lungs to body and body to lungs. When it carries oxygen from the lungs to body it is known as the "oxyhemoglobin", and when it carries carbon dioxide from body parts to the lungs for purification they know as "carboxyhemoglobin". Each human RBC contain approximately 270 million hemoglobines.[4,5] There are four blood types: A, B, AB, or O. Also, blood is either Rh-positive or Rh-negative.

So if you have type A blood, it's either A positive or A negative. Which type you are is important if you need a blood transfusion. And your Rh factor could be important if you become pregnant an incompatibility between your type and the baby's could create problems.

Blood tests such as blood count tests help doctors check for certain diseases and conditions. They also help check the function of your organs and show how well treatments are working. Problems with your blood may include bleeding disorders, excessive clotting and platelet disorders. If you lose too much blood, you may need a transfusion. Also the life threatening disease like blood cancer can be determined by Pathology studies.[4,5]

#### Erythrocytes:

Erythrocytes are nothing but RBC'S these are the major component of the body around 40 to 45% of erythrocytes is their inside the blood, A type of blood cell that is made in the bone marrow and found in the blood. Erythrocytes contain a protein called hemoglobin, which carries oxygen from the lungs to all parts of the body. Checking the number of erythrocytes in the blood is usually part of a complete blood cell (CBC) test. It may be used to look for conditions such as anemia, dehydration, malnutrition, and leukemia. Also called RBC and red blood cell. If there is variation in no. Of the erythrocytes in the CBC test report then it shows different physiological changes in body.[6]

A red blood cell (RBC) count is typically done as part of a complete blood count. This is a screening test to check for a variety of medical conditions. We need to take these CBS testing on Specific duration of time to avoid certain erythrocytic problem. symptoms such as weakness or tiredness during a general checkup. look for specific health problems, such as internal bleeding, anemia, kidney disease, and certain cancers. You may also need this test if your healthcare provider wants to watch any of these health problems. Your healthcare provider may also want this test done to determine if your RBC count is too high.

A red blood cell count is often part of a complete blood count (CBC). This means that other components of blood are also measured. These include white blood cells, your hemoglobin level, and platelets.[6]

If healthcare provider suspects that you have a particular illness, they may also order other tests needed for making a diagnosis.

An RBC count is measured in millions per cubic millimeter (million/mm<sup>3</sup>). Normal values may vary slightly among different labs. One example of normal values is:

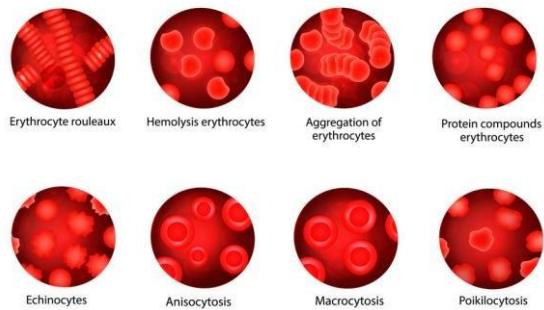
3.6 to 5 million/mm<sup>3</sup> for females

4.2 to 5.4 million/mm<sup>3</sup> for males[6]

When a pathogen invades the human body, it infects the blood and organs, causing infection and sepsis-related symptoms. Pathogens change the internal environment, increasing the levels of reactive oxygen species, influencing erythrocyte morphology, and causing erythrocyte death, i.e., eryptosis. Characteristics of eryptosis include cell shrinkage, membrane blebbing, and surface exposure of phosphatidylserine (PS). Eryptotic erythrocytes increase immune cell proliferation, and through PS, attract macrophages that remove the infected erythrocytes. Erythrocyte-degraded hemoglobin derivatives and heme deteriorate infection; however, they could also be metabolized to a series of derivatives. The result that erythrocytes play an anti-infection role during sepsis provides new perspectives for treatment. This review focuses on erythrocytes during pathogenic infection and sepsis. During infection, pathogens require iron to maintain survival; thus, they may invade erythrocytes leading to membrane structure changes and eryptosis, which causes erythrocyte shrinkage, membrane blebbing, and phosphatidylserine (PS) exposure, resulting in degraded and reduced amounts of erythrocytes, thereby inducing anemia. In vivo studies indicate multiple protruding spikes on the surface during septic shock and RBC aggregation. In vivo studies revealed similar results; in mouse models of cecal ligation and puncture (CLP)-induced sepsis, plasma-derived extracellular vesicles (EVs) increase RBC rigidity and influence RBC deformability. In rat models of CLP-induced sepsis, oxidative stress alters the rheology of blood-influenced RBC deformability [6].

The following image showing the different size and shape of erythrocytes:

#### **Pathology erythrocytes**



#### **Anemia:**

It is the disease conditions in which there is less no of the erythrocytes than that of the normal count. Anemia is defined by WHO by a hemoglobin level that is less than 13 g/dL in male adults, and less than 12 g/dL in female adults. This definition is the most commonly used one in both clinical and research settings. Anemia will lead to decreased capacity of RBCs to carry oxygen, eventually causing significant morbidities and mortalities. Anemia presents initially with non-specific symptoms like fatigue, weakness, or even impaired cognitive functions. Elderly with anemia are at a higher risk of hospitalization with higher mortality rates. Anemia can be present in up to 17% of congestive heart failure cases worsening capacity and survival significantly. In children anemia has been shown to cause a decline in psychomotor and cognitive development. Moreover, the risks of preterm labor, low birth weight, and maternal mortality, were all found to significantly increase with the presence of iron deficiency [7,8]. To summarize, children, young women, pregnant women, and elderly have the highest risk of morbidity and mortality associated with anemia. Other important factors include racial and ethnic disparities; African Americans have a 3-fold increase in the prevalence of anemia when compared to whites. The most important cause of anemia is iron deficiency. However, chronic diseases and other causes that lead to decreased RBCs count, have been dramatically increasing lately [7,8].

Anemia is usually subdivided according to its pathophysiology into: insufficient production, or bleeding/hemolysis causing loss of RBCs. Therefore, the main two types of anemia are hyporegenerative and regenerative. In hyporegenerative anemia, there is impaired bone marrow function that causes decreased production of precursor. This can occur due to abnormal infiltration of bone marrow or malnutrition. On the other hand, regenerative anemia involves proper response of bone marrow to the decrease of RBCs by a compensatory increase in production [7,8].

There are different types of anemia classified on basis of their causes as the anemia due to deficiency of nutritional supplies known as nutritional anemia, deficiency of the folic acid and another one type is their i.e. due to deficiency of cobalamin the disease and their treatment are discussed below.[7,8]

Treatment for nutritional deficiency anemia Normal blood counts can normally be achieved following a regimen of oral iron for eight weeks. However, it is recommended to keep patients on treatment for several months later, as this will replenish body stores of iron, and will lead to a significant decrease in recurrence rates. Intravenous iron is preserved for severe cases or cases with continuous blood loss, noncompliance, or malabsorption. It is also essential to correct the underlying cause of iron deficiency.

When it comes to cobalamin deficiency treatment, eight weeks are usually enough for anemia to resolve. However, it is essential to periodically administer vitamin B12 injections to prevent recurrence especially in cases of malabsorption. Irreversible cases will require lifelong therapy. Oral vitamin B12 is not associated with good outcomes due to low bioavailability. [7,8] When folic acid deficiency is confirmed, treatment will mainly depend on oral supplementation which has a relatively high bioavailability. It is also essential to consider alcoholism and malabsorption as possible etiologies, as nutritional folic acid deficiency is very rare. When oral folic acid supplementation fails, raise the doses or give folic acid injections. Before administering folic acid by any route, cobalamin deficiency must be ruled out. Otherwise, severe exacerbation of neurological manifestation may occur.

### **White Blood cells: (Leucocytes)**

WBC is one of the blood components having major percentage in their count it acts as the physiological protective system they produce antibodies for every antigen entering into the body and the antibodies destroy the antigen this reaction causing to increase the fever weakness sometime.

White blood cell disorders occur when you have too many or too few white blood cells. White blood cells, also known as leukocytes, are one of four types of cells that make up blood. They are produced in the bone marrow and play an important role in your immune system.[5]

The reference range for the total white blood cell (WBC) count can vary from one lab to the next but is typically described as follows::

**Males:** 5,000 to 10,000 cells per microliter of blood (cells/mL)

**Females:** 4,500 to 11,000 cells/mL

**Newborns under two weeks of age:** 9,000 to 30,000 cells/mL

**Children and adolescents:** 5,000 to 10,000 cells/mL

Doctors can measure these cells with a test called a white blood cell (WBC) count. When white blood cells are abnormally high, it usually suggests that your immune system is fighting a disease or infection. When they are too low, it suggests that a disease, autoimmune disorder, or other condition has weakened your immune system.[,10]

A disorder refers to any condition that disrupts the normal functioning of the body.

### **White blood cell disorders fall into two categories:**

- **Leukopenia:** A decrease in white blood cells, which can be caused by cells being destroyed or by not enough cells being made
- **Leukocytosis:** An increase in white blood cells, which can be a normal response of the immune system but also caused by certain cancerous or non-cancerous diseases.

Symptoms of white blood cell disorders can vary based on the underlying cause, although some people may be asymptomatic (without symptoms). If symptoms develop, they can often be non-specific. There can even be an overlap in symptoms between leukopenia and leukocytosis.[9,10]

There are also five major types of white blood cells, each of which has a specific function:

- **Monocytes:** Frontline defenders that attack anything the immune system considers abnormal
- **Lymphocytes:** Blood cells that produce immune proteins called antibodies that target and fight specific disease-causing organisms
- **Neutrophils:** Blood cells that mainly fight bacterial infections
- **Eosinophils:** Blood cells that mainly fight parasitic infections

- **Basophils:** Blood cells that help trigger inflammation to fight infections, diseases, or toxins.[9,10,11]

Some of the white blood cell disorders associated with **leukopenia include:**

- **Aplastic anemia:** A rare condition in which the body stops producing enough new bloodcells.[10]
- **Autoimmune neutropenia:** A condition in which your immune system mistakenly attacks and destroys neutrophils..
- **Cyclic neutropenia:** A rare genetic disorder in which neutrophil production drops every 21days or so
- **Chronic granulomatous disease:** An genetic disorder that causes certain white blood cells to malfunction and behave abnormally
- **Leukocyte adhesion deficiencies:** A group of rare genetic disorders that affect the white bloodcells' ability to fight infection. [9,10]

Some of the white blood cell disorders associated with **leukocytosis include:**

- **Chronic idiopathic neutrophilia:** A condition in which neutrophils remain persistently elevated for no apparent reason.[10]
- **Hemolytic anemia:** A disorder in which red blood cells die faster than they are made, often due to an underlying genetic or autoimmune cause
- **Idiopathic thrombocytopenia:** A condition in which your immune system mistakenly attacks and destroys blood-clotting cells called platelets
- **Lymphoma:** A group of cancers that start in cells of the lymphatic system
- **Lymphocytic leukemia:** A type of blood cancer that starts in lymphocytes
- **Myeloproliferative disorders:** Includes six types of slowing-growing cancers that cause the overproduction of white blood cells (chronic eosinophilic leukemia, chronic myelogenous leukemia, chronic neutrophilic leukemia, essential thrombocytophenia, polycythemia vera, and primary myelofibrosis)[10,11]

### **Lymphocyte**

Lymphocytes are a type of white blood cell. They help your body's immune system fight cancer and foreign viruses and bacteria. Your lymphocyte count can be taken during a normal blood test at your healthcare provider's office.

T, B, and NK cells and their respective subsets (Table I) originate from the bone marrow-derived progenitors. Progenitors that migrate to the thymus and receive signals through the Notch receptor commit to the T-cell lineage.<sup>1</sup> In human beings, lineage development is critically dependent on IL-7 for T cells<sup>2</sup> and IL-15 for NK cells.<sup>3</sup> Lymphocyte specificity and diversity are gained during the process of T-cell receptor (TCR) or B-cell receptor (BCR) generation, key events in the adaptive immune. [12,13]

Lymphocyte levels vary depending on your age, race, sex, altitude and lifestyle.

A type of immune cell that is made in the bone marrow and is found in the blood and in lymph tissue. The two main types of lymphocytes are B lymphocytes and T lymphocytes. B lymphocytes make antibodies, and T lymphocytes help kill tumor cells and help control immune responses. A lymphocyte is a type of white blood cell.[12,13]

There are two main types of lymphocytes::

- **T lymphocytes (T cells):** T cells control your body's immune system response and directly attack and kill infected cells and tumor cells.
- **B lymphocytes (B cells):** B cells make antibodies. Antibodies are proteins that target viruses, bacteria and other foreign invaders.

### **1.2 Functions of Lymphocytes**

Lymphocytes help your body's immune system fight cancer and foreign viruses and bacteria (antigens). Lymphocytes help your immune system remember every antigen it comes in contact with. After an encounter, some lymphocytes turn into memory cells. When memory cells run into an antigen again, they recognize it and quickly respond. This is why you don't get infections like measles or chickenpox more than once. It's also the reason getting vaccinated can prevent certain diseases.[12,13]

T- cells and B-cells work together for inducing the immune system in our body as:

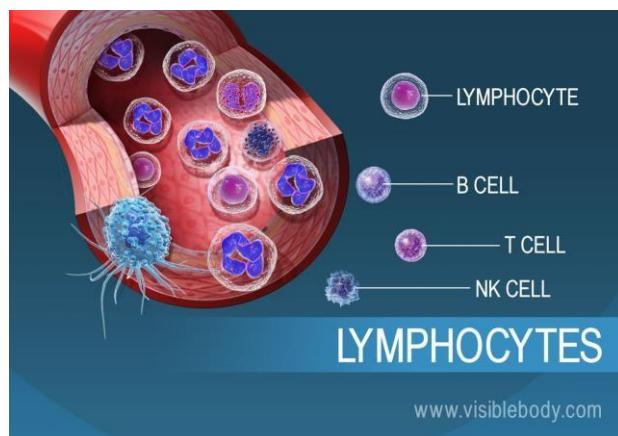
**T cells:**

T-cells help kill infected cells and control your body's immune response to foreign substances. Most of your T cells need the help of another immune cell to become activated. After your T cells are activated, they multiply and specialize into different types of T cells. These types include.[12,13]

**NK cells**

NK cells are lymphocytes of the innate immune system, because they do not rearrange their germline DNA to gain specificity. They do not express TCR or immunoglobulin genes, but instead use a variety of germline-encoded receptors to induce their functions.<sup>26</sup> These CD16. The ligands for some of these

- **Cytotoxic (killer) T cells:** Cytotoxic T cells attach to antigens on infected or abnormal cells. Then, they kill the infected cells by making holes in their cell membranes and inserting enzymes into the cells.
- **Helper T cells:** Helper T cells help your other immune cells. Some helper T cells help B cells make antibodies against foreign invaders. Others help activate cytotoxic T cells.[12,13]
- **Regulatory (suppressor) T cells:** Regulatory T cells make substances that help end your immune system's response to an attack. Sometimes, they prevent harmful responses from occurring.
- B cells have receptors on their surfaces where antigens attach. B cells learn to recognize the different antigens and produce specific antibodies to attack each one. The B cells respond to antigens in two ways.
- **Primary immune response:** When an antigen attaches to a receptor, your B cells are stimulated. Some B cells change into memory cells. Other B cells change into plasma cells. Plasma cells make an antibody specific to the particular antigen that stimulated it. Production of enough of that specific antibody can take several days.[12,13]
- **Secondary immune response:** If your B cells encounter that antigen again, the memory cells remember it and multiply. They change into plasma cells and quickly produce the correct antibody.



**Fig: Lymphocytes**

**Platelets:**

Platelets are tiny blood cells that help your body form clots to stop bleeding. If one of your blood vessels gets damaged, it sends out signals to the platelets. The platelets then rush to the site of damage and form a plug (clot) to fix the damage.

The process of spreading across the surface of a damaged blood vessel to stop bleeding is called adhesion. This is because when platelets get to the site of the injury, they grow sticky tentacles that help them stick (adhere) to one another. They also send out chemical signals to attract more platelets. The additional platelets pile onto the clot in a process called aggregation.[14,15]

Under a microscope, a platelet looks like a tiny plate. Your healthcare provider may do a blood test called a complete blood count to find out if your bone marrow is making the right number of platelets.[14,15]

A normal platelet count is 150,000 to 450,000 platelets per microliter of blood.

- Your risk for bleeding develops if a platelet count falls below 10,000 to 20,000. When the platelet count is less than 50,000, bleeding is likely to be more serious if you're cut or bruised.
- Some people make too many platelets. They can have platelet counts from 500,000 to more than 1

million.[14,15]

These are health conditions linked to abnormal platelets or abnormal platelet counts:

#### **Thrombocytopenia:**

In this condition, your bone marrow makes too few platelets. Or your platelets are destroyed. If your platelet count gets too low, bleeding can occur under the skin as a bruise. Or it can happen inside the body as internal bleeding. Or it can happen outside the body through a cut that won't stop bleeding or from a nosebleed. Thrombocytopenia can be caused by many conditions. These include several medicines, cancer, liver disease, pregnancy, infections, and an abnormal immune system.

#### **Essential thrombocythemia:**

In this condition, your bone marrow makes too many platelets. People with this condition may have platelet counts of more than 1 million, which can lead to bleeding. Other symptoms can include blood clots that form and block blood supply to the brain or the heart. Doctors don't fully know what causes this type of thrombocythemia, but changes in bone marrow cells (called mutations) can lead to some cases.[14,15]

#### **Secondary thrombocytosis:**

This is another condition caused by too many platelets. Secondary thrombocytosis is more common. It's not caused by a bone marrow problem. Instead, another disease or condition stimulates the bone marrow to make more platelets. Causes include infection, inflammation, some types of cancer,

Many rare diseases are linked to poor platelet function. This means the number of platelets is normal, but the platelets don't work as they should. Medicines such as aspirin can cause this. It's important to know which medicines affect platelets. Know that while taking these medicines you have an increased risk of bleeding. [14,15]

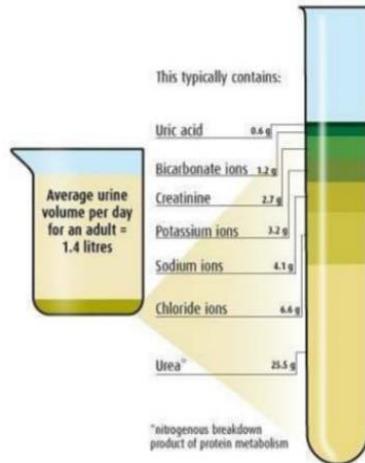
#### **Urine:**

The kidneys remove waste products from the blood through small filtering units called nephrons.

- Each nephron consists of a ball of small blood capillaries, called a glomerulus, and a small tube called a renal tubule.
- The kidneys form urine, which passes through the ureters to the bladder for storage prior to excretion.
- Waste products of protein metabolism are excreted, electrolyte levels are controlled and pH (acid-base balance) is maintained by excretion of H<sup>+</sup> ions.

## Composition of Normal Urine

- Water 96%
  - Urea 2%
  - Uric acid
  - Creatinine
  - Ammonia
  - Sodium
  - Potassium
  - Chloride
  - Phosphate
  - Sulphate
  - Oxalate
- 2%



#### **Normal Constituents of Urine:**

#### **Urea: Nitrogenous Constituents:**

1. Urea is the main end product of catabolism of protein in mammals. Its excretion is directly proportional to the protein intake. It consists of 80-90% of the total urinary nitrogen.
2. In fever, diabetes, or excess adrenocortical activity, urea excretion is increased due to increased protein catabolism.

3. Decreased urea excretion is due to decreased urea production in the last stages of fatal liver disease.
4. In acidosis, there is decreased urea excretion.[17,18]

**Ammonia:**

1. Ammonia is formed by the kidney from glutamine or amino acids in acidosis.
2. There is a high ammonia output in the urine in uncontrolled diabetes mellitus in which renal function is unimpaired.

**Creatinine**

1. Creatine is excreted by children and pregnant women and much smaller amounts in men. The excretion in men is 6% of the total excretion of creatinine.
2. Creatinine is formed from creatine. It is excreted in relatively constant amounts regardless of diet.
3. The creatinine coefficient is the ratio between the amount of creatinine excreted in 24 hours and the body weight in kg. It is usually 20-26 mg/kg/day in normal men and 14-22 mg/kg/day in normal women.
4. Creatinine excretion is decreased in many pathological conditions.
5. Creatine excretion is also found in pathological states such as starvation, hyperthyroidism, impaired carbohydrate metabolism and infections.
6. Creatine excretion is decreased in hypothyroidism.[17,18]

**Uric Acid:**

1. It is the end product of the oxidation of purines in the body. It is not only formed from dietary nucleoprotein but also from the breakdown of cellular nucleoprotein in the body.
2. It is slightly soluble in water and precipitates readily from acid urine on standing.
3. Uric acid excretion is increased in leukemia, severe liver disease and various stages of gout.
4. The concentrated urine on cooling forms a brick-red deposit which is mainly acid urate.
5. Pure uric acid is colourless. Deposits of uric acid and urates are coloured by absorbed urinary pigments, particularly the red uroerythrin.
6. The specificity of the analysis of uric acid is increased by treatment with uricase, the enzyme (from hog kidney) which converts uric acid to allantoin.[17,18]

**Amino Acids:**

1. About 150-200 mg of amino acid nitrogen is excreted in the urine of adults in 24 hours.
2. The infant at birth excretes about 3 mg amino acid nitrogen per pound of body weight, and up to the age of 6 months the value reaches to 1 mg/pound which is maintained throughout childhood. Premature infants excrete 10 times amino acid nitrogen than that of full-term infant.
3. The low excretion of amino acid nitrogen is due to its high renal threshold value.
4. Increased amounts of amino acids are excreted in liver disease and in certain types of poisoning.
5. In cystinuria, 4 amino acids-arginine, cystine, lysine and ornithine are excreted in urine.[17,18]

**Allantoin:**

1. It is the partial oxidative products of uric acid. Small quantities of the allantoin are excreted in human urine.
2. In other sub-primate mammals, allantoin, the principal end product of purine metabolism, is excreted.[17,18]

**Sulphates:**

1. The urine sulphur is derived from sulphur containing amino acids such as methionine and cysteine and therefore, its output varies with protein intake.

**Abnormal constituent of urine****Urinalysis**

Urinalysis (UA) simply means analysis of urine, it is a laboratory test done to detect problems with your body that can appear in your urine.

The abnormal constituents found in urine are as follows

- Proteins
- Sugar(Glucose & others)
- Ketone bodies
- Bile salts
- Bile pigments
- Blood[17,18]

**A. Proteins:**

Normal- upto 150 mg/24 hours or 10mg/100ml in single sample

**Tests (Qualitative )**

**Heat Coagulation and acetic acid test-** The test is based on the principle of heat coagulation and precipitation of proteins by acetic acid.

**Sulphosalicylic acid test-** Sulphosalicylic acid neutralizes protein cation, resulting in precipitation.

**Heller's Nitric Acid Ring test** is a chemical test that shows that strong acids cause the denaturation of precipitated proteins. Concentrated nitric acid is added to a protein solution from the side of the test tube to form two layers. A white ring appears between the two layers if the test is positive Heller's test is commonly used to test for the presence of proteins in urine.[17,18]

***Abnormal Conditions of Protein*****Proteinuria:****Pre-renal**

Symptoms of the disease Addison's disease, Fever, Eclampsia, Hypertension, Haemoglobinuria, Rhabdomyolysis.

**Renal:**

All cases of glomerulonephritis, Nephrotic syndrome, Pyelonephritis.

**Post renal:**

Symptoms of post renal Lesions of renal pelvis, urethra (cystitis, prostatitis), Severe UTI.

**Minimal Proteinuria (<0.5gm/day)**

Exercise, Fever, Emotional stress, HTN, Renal tubular dysfunction, Polycystic kidneys, Lower UTI.

**Moderate proteinuria (0.5-3 gm/day)**

Chronic glomerulonephritis, CCF, Pyelonephritis, Pre-eclampsia, Multiple myeloma.

**Marked Proteinuria (>3gm/day)**

Acute glomerulonephritis, Chronic glomerulonephritis, severe, Nephrotic syndrome, Diabetic nephropathy, severe, Renal amyloidosis, Lupus nephritis.

**B. Sugar:**

This is a non-specific test useful for semiquantitation of marked glucosuria. Normally the Sugar is detected in the urine sample of the diabetes patients if they have more Sugar in body. [17,18]

***Abnormal Conditions Of Sugar*****GlycosuriaDefinition**

The condition in which abnormal quantities of glucose are excreted in urine is called Glycosuria. Normal urine contains traces of glucose which cannot be detected by Benedict's test. Beyond the renal threshold value- 160-180 mg/100ml, the tubules can not reabsorb glucose which escapes absorption and is excreted in urine.

Occurs in two conditions

- In normal blood glucose level Leads to,
- Alimentary Glycosuria
- Emotional Glycosuria
- In pregnancy & Lactation
- Renal (hereditary) Glycosuria
- In hyperglycemia Leads to,

Occurs due to increased blood glucose level in Diabetes Mellitus.

Blood glucose level becomes very high and Glucose is excreted in the urine.

In this renal threshold value for glucose is normal.[17,18]

#### **C. Ketone Bodies:**

It is condition when ketone bodies are excreted in urine. In This condition it Causes- Diabetes Keto Acidosis, Fever, Anorexia, Gastrointestinal disturbances, Fasting, Starvation, Severe vomiting, ketourea etc. [17,18]

#### **D. Bile Salt:**

##### **Primary bile acids**

Cholic acid and chenodeoxycholic acid (CDCA)- synthesized from cholesterol in the liver, conjugated with glycine or taurine, and secreted into the bile.

##### **Secondary bile acids**

- Deoxycholate and lithocholate, are formed in the colon as bacteria metabolites of the primary bile acids.
- Bile salts- Sodium taurocholate and sodium glycocholate are found in urine.
- In Normal urine: Urochrome, Traces of Urobilin
- In Abnormal Urine- Bilirubin, Urobilinogen, Biliverdin, Urobilin

#### **E. Blood**

In the lesion of kidney or urinary tract blood is excreted in the urine.

Free haemoglobin is also found in urine after quick hemolysis e.g. in black water fever( a complication of malaria) or after severe burns.[17,18]

#### **Abnormal Conditions of blood**

**Hematourea** - when 5 or more intact RBCs/HPF.

##### **Symptoms:**

Renal Neoplasms, Calculi, TB, Pyelonephritis, Hydronephrosis, Oxaluria, Acute GN, Polycystic kidney disease.

#### **Light Microscopy**

Although the light microscope remains a central modern biomedical sciences, light

Microscopy is often regarded as an old technique. While light microscopy is indeed over 400 years old, the technique continues to evolve and its full potential in the biomedical sciences may not yet be fully realised.

The purpose of light microscopy is to provide magnified images of specimens illuminated or emitting light in the visible range of the spectrum, or that of the adjacent ultraviolet or near-infrared regions of the spectrum. Optical magnification is achieved by passing light through lenses. With modern digital imaging technologies, a digital photomicrograph can be easily magnified. After a certain point, magnification reveals no further details and the image becomes highly pixelated. This shows that magnification has increased without increasing the resolution. This is a simplistic illustration of how resolution is more important than magnification in most of the applications.

A light microscope is a biology laboratory instrument or tool, that uses visible light to detect and magnify very small objects and enlarge them.

They use lenses to focus light on the specimen, magnifying it thus producing an image. The specimen is normally placed

close to the microscopic lens.[20]

Microscopic magnification varies greatly depending on the types and number of lenses that make up the microscope. Depending on the number of lenses, there are two types of microscopes i. e Simple light microscope (it has low magnification because it uses a single lens)and the Compound light microscope (it has a higher magnification compared to the simple microscope because it uses at least two sets of lenses, an objective lens, and an eyepiece). The lenses are aligned in that, they can be able to bend light for efficient magnification of the image.[20] viewed by passing it through one or two lenses. The transparency of the specimen allows easyand quick penetration of light. Specimens can be vary from bacterial to a cells and other microbial particles.

#### **Principle of a light microscope (optical microscope)**

As mentioned earlier, light microscopes visualize an image and it uses a glass lens, and magnification is determined by, the ability of lenses to bend light and focus it on the specimen,it results in formation an image. When a ray of light passes through one medium into another, the ray bends at the interface causing refraction. The refractive index is used to determine bending of light, which is a measure of how great a substance slows the speed of light. The refractive indexes of the two mediums that form the interface, the direction and magnitude of bending of the light are determined. [20]

#### **Different types of Light Microscope:**

There are different types of light Microscope are used as they are of two types i.e. Simple light Microscope and Compound light Microscope where as in simple light Microscope only one lens is used and in compound light Microscope two or more lenses are used.

#### **Types of light Microscope**

- Bright field Light Microscope
- Phase Contrast Light Microscope
- Dark-Field Light Microscope
- Fluorescence Light Microscope

#### **Bright field Microscope:**

It is type of the most basic optical Microscope used in microbiology laboratories in this laboratory the dark image against bright background is produced. It is of two lenses, and widelyused to view plant and animal cell organelles and also it includes parasites such as Paramecium by staining with basic stains. Its functionality is based on to provide a high-resolution image, which fully depends on the perfect use of the microscope. This means that an sufficient amount of light will enable sufficient focusing of the image, to give a quality image. It is also known as a compound light microscope.[20]

#### **Phase contrast light Microscope:**

This is a type of optical microscope in this small light deviations known as phase shifts takes place during light penetration into the unstained specimen. These phase shifts are get converted into the image to mean, when light passes through the opaque specimen, the phase shifts brighten and the specimen forming an illuminated (bright) image in the background.[20]

The principle behind the working of the phase-contrast microscope is based on the use of an optical method of transform a specimen into an amplitude image, that's can be viewed by theeyepiece of the microscope which locates at upper side of Microscope.

natural state, at a high contrast and efficient clarity. This is done because if the specimens arestained and fixed, they kill most cells, it is a characteristic that is uniquely undone with the brightfield light microscope.

#### **Applications of Phase-Contrast Microscope**

- Determine morphologies of living cells such as plant and animal cells

- Studying microbial motility and structures of locomotion
- To detect certain microbial elements such as the bacterial endospores

### **Dark-Field Light Microscope**

This is a specialized type of bright field light microscope it has several similarities towards the Phase-Contrast Microscope. For making of a dark field Microscope, place a darkfield stop underneath and a condenser lens which produces a hollow cone beam of light, the beam of light enters the objective only, from the specimen.[20,21]

This technique is used to visualize the living unstained cells. This is affected by the way illumination is done on the specimen in that, when a hollow cone beam of light is transmitted to the specimen, deviated light (unreflected/unrefracted) rays do not pass through the objectives but the undeviated (reflected/refracted) light passes through the objectives and it results to the specimen forming an image.[20,21]

This makes the surrounding field of the specimen appear black while their the specimen will appear illuminated. This is enabled by the dark background this the name, dark-field Microscopy.

### **Applications of the Dark Field Microscope**

- It is used to visualize the internal organs of larger cells such as the eukaryotic cells.
- Identification of bacterial cells with distinctive shapes such as *Treponema pallidum*, a causative agent of syphilis.

### **The Fluorescent Microscope**

The above-discussed microscopes will normally produce images after a light has been transmitted and passed through the specimen.

In the case of the fluorescent Microscope, the specimen emits light. How? By adding a dye molecule to the specimen. This dye molecule will normally become excited when it absorbs light energy, hence it releases any trapped energy as light. The light energy that is released by the excited molecule has a long wavelength compared to its radiating light. The dye molecule is normally a fluorochrome, that fluoresces when exposed to the light of a certain specific wavelength. The image formed is a fluorochrome-labeled image from the emitted light.[20,21]

The principle behind this working mechanism is that the fluorescent microscope will expose the specimen to ultra or violet or blue light, which forms an image of the specimen that is emanated by the fluorescent light. They have a mercury vapor arc lamp that produces an intense beam of light that passes through an exciter filter. The exciter filter functions to transmit

a specific wavelength to the fluorochrome stained specimen, producing the fluorochrome- labeled image, at the objective.[20,21]

### **Applications of the Fluorescent Microscope**

Used in the visualization of bacterial agents such as *Mycobacterium tuberculosis*.

Used to identify specific antibodies produced against bacterial antigens/pathogens in immunofluorescence techniques by labeling the antibodies with fluorochromes.

Used in ecological studies to identify and observe microorganisms labeled by the fluorochromes.

It can also be used to differentiate between dead and live bacteria by the color they emit when treated with special stains.[21]

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