NON MAJOR ELECTIVE

HEALTH AND DISEASES **SUB.CODE: 16SNMEBC1**

UNIT- I

BLOOD SAMPLE COLLECTION PROCEDURE

Blood sample collection procedure plays a vital part in the efficiency of patient treatment in hospitals around the world. We often hear about the importance of phlebotomy practice as well as the significance of accurate laboratory results; however, the blood tube transportation process between the point of collection and the laboratory is often neglected although it is critical to a successful diagnosis.

Blood sample collection procedure consists of a chain of events and no portion of this sequence is trivial in order to maintain high-quality clinical results, and more importantly, consistent and repeatable clinical results. Studying the chain of events of the blood sample collection procedure, we will understand that it is typically designated into three major activities: phlebotomy, transportation, and analysis.

Traditional blood sample collection procedure

Focusing on the transportation part in the blood sample collection procedure, let us think about how it is done today. The classical approach is “batch and deliver”; a familiar process we can easily relate to from a factory environment, where the technician collects up to several samples in a transportation device (for example a cooler or pneumatic tube system (PTS)) and then transports the aggregated samples in one delivery at a certain time interval.

The disadvantage of this method is that there is the creation of wasted time which has a negative downstream impact into the whole blood sample collection procedure such as inconsistency of ToTAT (Total Turnaround Time), creating capacity spikes in laboratory equipment, and undocumented freshness of blood samples leading to unreliable results due to poor blood sample condition (for example hemolysis, coagulation).

Focus on FIFO

Blood sample transportation is a vital part of the blood sample collection procedure and it should not be overlooked; due attention and investments need to be in place. By using the Tempus600 Blood Transportation System the hospitals get a reliable platform to fill the blood tube transportation gab in the blood sample collection procedure.

The Tempus600 system allows FIFO and real-time clinical sample delivery between phlebotomy and laboratory without compromising on quality while logistically, creates a single-piece workflow that will dramatically improve hospital efficiency, and overall patient

satisfaction. A single job but a big process and a very important part of the complete treatment of the patient.

URINE

Urine has a long, rich history as a source for measuring health and well-being and remains an important tool for clinical diagnosis. The clinical information obtained from a urine specimen is influenced by the collection method, timing and handling. A vast assortment of collection and transport containers for urine specimens are available. Determining which urine collection method and container should be used depends on the type of laboratory test ordered.

Types of Collection

Laboratory urine specimens are classified by the type of collection conducted or by the collection procedure used to obtain the specimen. Random Specimen This is the specimen most commonly sent to the laboratory for analysis, primarily because it is the easiest to obtain and is readily available. This specimen is usually submitted for urinalysis and microscopic analysis, although it is not the specimen of choice for either of these tests.

Random specimens can sometimes give an inaccurate view of a patient's health if the specimen is too diluted and analyte values are artificially lowered. Pediatric specimens, which routinely undergo chemistry and microscopic analysis, are generally of this type. As the name implies, the random specimen can be collected at any time. Although there are no specific guidelines for how the collection should be conducted, avoiding the introduction of contaminants into the specimen is recommended. This requires explicit instructions to patients so that they do not touch the inside of the cup or cup lid.

First Morning Specimen This is the specimen of choice for urinalysis and microscopic analysis, since the urine is generally more concentrated (due to the length of time the urine is allowed to remain in the bladder) and, therefore, contains relatively higher levels of cellular elements and analytes such as protein, if present. Also called an 8-hour specimen, the first morning specimen is collected when the patient first wakes up in the morning, having emptied the bladder before going to sleep. Since the urine can be collected over any eight-hour period, collection is practical for patients who have atypical work/sleep schedules. Proper collection practices and accurate recording of the collection time are important criteria of a first morning specimen.

Note: Any urine that is voided from the bladder during the eight-hour collection period should be pooled and refrigerated, so that a true 8-hour specimen is obtained. Midstream Clean Catch Specimen This is the preferred type of specimen for culture and sensitivity testing because of the reduced incidence of cellular and microbial contamination. Patients are required to first cleanse the urethral area with a castile soap towelette. The patient should then void the first portion of the urine stream into the toilet. These first steps significantly reduce the opportunities for contaminants to enter into the urine stream. The urine midstream is then collected into a clean container (any excess urine

should be voided into the toilet). This method of collection can be conducted at any time of day or night.

Timed Collection Specimen Among the most commonly performed tests requiring timed specimens are those measuring creatinine, urine urea nitrogen, glucose, sodium, potassium, or analytes such as catecholamines and 17-hydroxysteroids that are affected by diurnal variations. A timed specimen is collected to measure the concentration of these substances in urine over a specified length of time, usually 8 or 24 hours. In this collection method, the bladder is emptied prior to beginning the timed collection. Then, for the duration of the designated time period, all urine is collected and pooled into a collection container, with the final collection taking place at the very end of that period. The specimen should be refrigerated during the collection period, unless otherwise requested by the physician. Accurate timing is critical to the calculations that are conducted to determine analyte concentrations and ratios. Interpretations based on faulty calculations can result in improper diagnoses or medical treatment.

Catheter Collection Specimen This assisted procedure is conducted when a patient is bedridden or cannot urinate independently. The healthcare provider inserts a foley catheter into the bladder through the urethra to collect the urine specimen. (Specimens may also be collected through an existing foley catheter.) Specimens may be collected directly from a foley into an evacuated tube or transferred from a syringe into a tube or cup. Suprapubic Aspiration Specimen This method is used when a bedridden patient cannot be catheterized or a sterile specimen is required. The urine specimen is collected by needle aspiration through the abdominal wall into the bladder.

Pediatric Specimen For infants and small children, a special urine collection bag is adhered to the skin surrounding the urethral area. Once the collection is completed, the urine is poured into a collection cup or transferred directly into an evacuated tube with a transfer straw. Urine collected from a diaper is not recommended for laboratory testing since contamination from the diaper material may affect test results.

Urine Collection Products

There are many different manufacturers of urine collection containers. Information on a specific product's uses, features and claims should be obtained from that device's manufacturer.

Urine Collection Containers (cups for collection and transport) Urine collection container cups come in a variety of shapes and sizes with lids that are either snap on or screw on. To protect healthcare personnel from exposure to the specimen and protect the specimen from exposure to contaminants, leak-resistant cups should be utilized. Some urine transport cup closures have special access ports that allow closed-system transfer of urine directly from the collection device to the tube. Urine Collection Containers (24-hour collection) Urine collection containers for 24-hour specimens come in a variety of shapes and colors, but most are of 3 liter (L) capacity[1] and are amber colored (to protect light-sensitive analytes such as porphyrins and urobilinogen).

Closure types vary and some have a port for ease of specimen transfer into a tube. When a preservative is required, it should be added to the collection container before the urine collection begins and warning labels should be placed on the container. If there is more than one acceptable preservative for the analyte being tested, the least hazardous one should be selected. A corresponding Material Safety Data Sheet (MSDS) should be given to the patient, and the healthcare provider should explain any potential hazards. Some common 24-hour preservatives are hydrochloric acid, boric acid, acetic acid and toluene.

Urinalysis Tubes Urine specimens are poured directly into urinalysis tubes with screw- or snap-on caps. Additionally, there are evacuated tubes similar to those used in blood collection that are filled by using a straw device, from cups with integrated transfer devices built into their lid, or from direct sampling devices that are used to access catheter sampling ports. Urinalysis tubes come in an array of tube shapes: conical bottom, round bottom, or flat bottom. Conical bottom tubes provide the best sediment collection for microscopic analysis. Some tubes are specially designed to be used with a pipetter that allows for standardized sampling. The tubes you select should be able to withstand centrifugation and, if used with an automated instrument system, should be compatible with the corresponding racks and carriers.

Fill volumes of urinalysis tubes usually range from 8 to 15 mL. Preservatives for Urinalysis NCCLS Guidelines recommend testing urine within two hours of its collection. However, refrigeration or chemical preservation of urine specimens may be utilized if testing or refrigeration within a two-hour window is not possible. A variety of urine preservatives (tartaric and boric acids being the most common) are available that allow urine to be kept at room temperature while still providing results comparable to those of refrigerated urine.

Generally, the length of preservation capacity ranges from 24 to 72 hours. Claims for the length of specific analyte preservation should be obtained from the manufacturer. When a specimen is directly transferred from a collection cup into a preservative tube, it provides a stable environment for the specimen until testing can be conducted and reduces the risk of bacterial overgrowth or specimen decomposition. Non-additive tubes (those not containing any chemical preservatives) can be used for urinalysis, but must be handled following strict timing and refrigeration guidelines. Preservatives for Culture and Sensitivity (C&S) Testing The most common preservative used for culture and sensitivity is boric acid, which comes in tablet, powder or lyophilized form.

There is clinical evidence to suggest that non-buffered boric acid may be harmful to certain organisms and that buffered boric acid preservatives can reduce the harmful effects of the preservative on the organisms.[2] C&S preservatives are designed to maintain the specimen in a state equivalent to refrigeration by deterring the proliferation of organisms that could result in a false positive culture or bacterial overgrowth. Preserved urine specimens can be stored at room temperature until time of testing. Product claims regarding duration of preservative potency should be obtained from the particular manufacturer.

Specimen Collection and Transport Guidelines

As with any type of laboratory specimen, there are certain criteria that need to be met for proper collection and transportation of urine specimens. This will ensure proper stability of the specimen and more accurate test results.

- All urine collection and/or transport containers should be clean and free of particles or interfering substances.
- The collection and/or transport container should have a secure lid and be leak-resistent. Leak-resistent containers reduce specimen loss and healthcare worker exposure to the specimen while also protecting the specimen from contaminants.
- It is good practice to use containers that are made of break-resistant plastic, which is safer than glass.
- The container material should not leach interfering substances into the specimen.
- Specimen containers should not be reused.
- The NCCLS guidelines for urine, GP-16A2, recommend the use of a primary collection container that holds at least 50 mL, has a wide base and an opening of at least 4 cm.[1] The wide base prevents spillage and a 4 cm opening is an adequate target for urine collection. The 24-hour containers should hold up to 3L.[1]
- The NCCLS guidelines recommend sterile collection containers for microbiology specimens.[1] The containers should have secure closures to prevent specimen loss and to protect the specimen from contaminants.
- Transport tubes should be compatible with automated systems and instruments used by the lab.
- Collection containers and/or transport tubes should be compatible with the pneumatic tube system if one is used for urine specimen transport in the facility. A leak-proof device in this situation is critical.
- NCCLS recommends the use of an amber colored container for specimens being assayed for light sensitive analytes, such as urobilinogen and porphyrins.[1] The colorant prevents the degradation of certain analytes.
- Proper labeling should be applied to the collection container or tubes.

Specimen Preservation Guidelines

- NCCLS guidelines for microbiological urine testing recommend the use of chemical preservatives if the specimen cannot be processed within 2 hours of collection. Otherwise, these specimens should be refrigerated at 2-8°C.[1] For urinalysis, NCCLS recommends the evaluation of urine preservation systems by the laboratory before being utilized in the facility.[1]
- The proper specimen-to-additive ratio must be maintained when using a chemical preservative to ensure accurate test results. Maintaining the correct ratio is especially important when transferring samples into a preservative tube. Use the indicated fill lines on the tube to ensure proper fill. Underfilling the tube will leave a high concentration of preservative in the specimen, while overfilling the tube will overly dilute the preservative. In either case, the function of the preservative may be compromised.

- An evacuated tube system is designed to achieve proper fill volume to ensure the proper specimen-to-additive ratio and proper preservative function. Evacuated systems also reduce the potential exposure of the healthcare worker to the specimen.
- Chemical preservatives should be non-mercuric and environmentally friendly.
- The EPA cites mercuric oxide used in urinalysis preservatives as a source of mercury in medical laboratories. The American Hospital Association and the EPA have issued a Memorandum of Understanding for the "virtual elimination of mercury containing waste from the health care industry waste stream" by the year 2005.[3] Certain states have already established a zero tolerance mandate for mercury waste generation and improper disposal. The EPA website, http://www.epa.gov/mercury offers additional information on mercury that is pertinent to medical environments and safety.

Urine Specimen Handling Guidelines

Labels Include the patient name and identification on labels. Make sure that the information on the container label and the requisition match. If the collection container is used for transport, the label should be placed on the container and not on the lid, since the lid can be mistakenly placed on a different container. Ensure that the labels used on the containers are adherent under refrigerated conditions. Volume Ensure that there is sufficient volume to fill the tubes and/or perform the tests. Underfilling or overfilling containers with preservatives may affect specimen-to-additive ratios.

Collection Date and Time Include collection time and date on the specimen label. This will confirm that the collection was done correctly. For timed specimens, verify start and stop times of collection. Document the time at which the specimen was received in the laboratory for verification of proper handling and transport after collection. Collection Method The method of collection should be checked when the specimen is received in the laboratory to ensure the type of specimen submitted meets the needs of the test ordered. An example of an optimum specimen/test match would be a first morning specimen for urinalysis and microscopic examination. Proper Preservation Check if there is a chemical preservative present or if the specimen has not been refrigerated for greater than two hours post collection.

After accepting the test request, ensure that the method of preservation used is appropriate for the selected test. If the correct preservative was not used the test cannot be conducted. Light Protection Verify that specimens submitted for testing of light-sensitive analytes are collected in containers that protect the specimen from light. This is a glimpse into the complexity of proper urine collection and handling. Since a variety of urine collection procedures and applications exist today, it becomes critical to understand how, when and where things can go wrong. As the trend toward more home-based testing and less invasive methods continues, urine will become one of the most useful specimen types collected for clinical assessment.

Concentration Terms

Concentration is a very common concept used in chemistry and related fields. It is the measure of how much of a given substance there is mixed with another substance. This can apply to any sort of chemical mixture, but most frequently is used in relation to solutions, where it refers to the amount of

solute dissolved in a solvent. To concentrate a solution, one must add more solute, or reduce the amount of solvent (for instance, by selective evaporation). By contrast, to dilute a solution, one must add more solvent, or reduce the amount of solute. There exists a concentration at which no further solute will dissolve in a solution.

At this point, the solution is said to be saturated. If additional solute is added to a saturated solution, it will not dissolve. Instead, phase separation will occur, leading to either coexisting phases or a suspension. The point of saturation depends on many variables such as ambient temperature and the precise chemical nature of the solvent and solute. Concentration may be expressed both qualitatively ('informally') and quantitatively ('numerically').

1. Qualitative notation
2. Quantitative notation
   - 2.1. Mass percentage
   - 2.2. Mass-volume percentage
   - 2.3. Volume-volume percentage
   - 2.4. Molarity
   - 2.5. Molality
   - 2.6. Normality
   - 2.7. Formal
   - 2.8. "Parts-per" notation
3. Techniques used to determine concentration
4. Table of concentration measures

1. Qualitative notation: Qualitatively, solutions of relatively low concentration are described using adjectives such as "dilute," or "weak," while solutions of relatively high concentration are described as "concentrated," or "strong." As a rule, the more concentrated a chromatic solution is, the more intensely coloured it is.
These glasses containing red dye demonstrate qualitative changes in concentration. The solutions on the left are "weaker" (or more dilute), compared to the "stronger" (or more concentrated) solutions on the right.

2. Quantitative notation: Quantitative notation of concentration is far more informative and useful from a scientific point of view. There are a number of different ways to quantitatively express concentration; the most common are listed below. Note: Many units of concentration require measurement of a substance's volume, which is variable depending on ambient temperature and pressure. Unless otherwise stated, all the following measurements are assumed to be at standard state temperature and pressure (that is, 25 degrees Celsius at 1 atmosphere).

2.1. Mass percentage: denotes the mass of a substance in a mixture as a percentage of the mass of the entire mixture. For instance: if a bottle contains 40 grams of ethanol and 60 grams of water, then it contains 40% ethanol by mass. Commercial concentrated aqueous reagents such as acid and bases are often labeled in concentrations of weight percentage with the specific gravity also listed. In older texts and references this is sometimes referred to as weight-weight percentage (abbreviated as w/w).

2.2. Mass-volume percentage, (sometimes referred to as weight-volume percentage and often abbreviated as % m/v or % w/v): denotes the mass of a substance in a mixture as a percentage of the

volume of the entire mixture. Mass-volume percentage is often used for solutions made from solid reagents. It is the mass of the solute in grams multiplied by one hundred divided by the volume of solution in milliliters.

2.3. Volume-volume percentage or % (v/v): describes the volume of the solute in mL per 100 mL of the resulting solution. This is most useful when a liquid – liquid solution is being prepared. For example, beer is about 5% ethanol by volume. This means every 100 mL beer contains 5 mL ethanol (ethyl alcohol).

2.4. Molarity (M): denotes the number of moles of a given substance per litre of solution. For instance: 4.0 litres of liquid, containing 2.0 moles of dissolved particles, constitutes a solution of 0.5 M. Such a solution may be described as "0.5 molar." (Working with moles can be highly advantageous, as they enable measurement of the absolute number of particles in a solution, irrespective of their weight and volume. This is often more useful when performing stoichiometric calculations.). See molar solution for further information.

2.5. Molality (m): denotes the number of moles of a given substance per kilogram of solvent. For instance: 2.0 kilograms of solvent, containing 1.0 moles of dissolved particles, constitutes a molality of 0.5 mol/kg. Such a solution may be described as "0.5 molal." The advantage of molality is, it does not change with the temperature, as it deals with the mass of solvent rather than the volume of solution. Volume increases with increase in temperature resulting in decrease in molarity. Molality of a solution is always constant irrespective of the physical conditions like temperature and pressure.

2.6. Normality (N): Normality is a concept related to molarity, usually applied to acid-base solutions and reactions. For acid-base reactions, the equivalent is the mass of acid or base that can accept or donate exactly one mole of protons (H+ ions). Normality is also used for redox reactions. In this case the equivalent is the quantity of oxidizing or reducing agent that can accept or furnish one mole of electrons. Whereas molarity measures the number of particles per litre of solution, normality measures the number of equivalents per litre of solution. In practice, this simply means one multiplies the molarity of a solution by the valence of the ionic solute. A bit more complex for redox reactions. Note: The normality is always equal to, or greater than the molarity for acid-base reactions. However, for redox reactions the normality is typically equal to or less than the molarity.

2.7. Formal (F): The formal (F) is yet another measure of concentration similar to molarity. It is used rarely. It is calculated based on the formula weights of chemicals per litre of solution. The difference between formal and molar concentrations is that the formal concentration indicates moles of the original chemical formula in solution, without regard for the species that actually exist in solution. Molar concentration, on the other hand, is the concentration of species in solution. For example: if one dissolves sodium carbonate (Na_2CO_3) in a litre of water, the compound dissociates into the Na^+ and CO_3^{2-} ions. Some of the CO_3^{2-} reacts with the water to form HCO_3^- and H_2CO_3. If the pH of the solution is low, there is practically no Na_2CO_3 left in the solution. So, although we have added 1 mol of Na_2CO_3 to the solution, it does not contain 1 M of that substance. (Rather, it contains a molarity based on the other constituents of the solution.) However, one can still say that the solution contains 1 F of Na_2CO_3.

2.8. "Parts-per" notation: The parts-per notation is used for extremely low concentrations. This is often used to denote the relative abundance of trace elements in the Earth's crust, trace elements in forensics or other analyses, or levels of pollutants in the environment.

2.8.1. Parts per hundred (denoted by '%' and very rarely 'pph'): -denotes one particle of a given substance for every 99 other particles. This is the common percent. 1 part in 10^2.

2.8.2. Parts per thousand (denoted by '‰' [the per mil symbol], and occasionally 'ppt'): denotes one particle of a given substance for every 999 other particles. This is roughly equivalent to one drop of ink in a cup of water, or one second per 17 minutes. 'Parts per thousand' is often used to record the salinity of seawater. 1 part in 10^3.

2.8.3. Parts per million ('ppm'): denotes one particle of a given substance for every 999,999 other particles. This is roughly equivalent to one drop of ink in a 40 gallon drum of water, or one second per 280 hours. 1 part in 10^6.

2.8.4. Parts per billion ('ppb'): denotes one particle of a given substance for every 999,999,999 other particles. This is roughly equivalent to one drop of ink in a canal lock full of water, or one second per 32 years. 1 part in 10^9.

2.8.5. Parts per trillion ('ppt'): denotes one particle of a given substance for every 999,999,999,999 other particles. This is roughly equivalent to one drop of ink in an Olympic-sized swimming pool, or one second every 320 centuries. 1 part in 10^{12}.

2.8.6. Parts per quadrillion ('ppq'): denotes one particle of a given substance for every 999,999,999,999,999 other particles. This is roughly equivalent to a drop of ink in a medium-sized lake, or one second every 32,000 millennia. There are no known analytical techniques that can measure with this degree of accuracy; nevertheless, it is still used in some mathematical models of toxicology and epidemiology. 1 part in 10^{15}.

UNIT - 2

CARBOHYDRATE DISORDERS

Introduction Carbohydrates are important energy stores, fuels and metabolic intermediates Routine biochemistry tests e.g. lactate, glucose and second-line metabolic tests e.g. amino acids are essential for the investigation of disorders of carbohydrate metabolism. However, definitive diagnosis is usually achieved by measurement of the activity of the affected enzyme. The easiest sample type to obtain is blood (erythrocytes, leucocytes, lymphocytes) but the choice of tissue depends on the pattern of expression of the enzyme in question. For some assays, cultured skin fibroblasts (from a punch biopsy) or liver/muscle biopsies are required.

INBORN ERRORS OF CARBOHYDRATE METABOLISM

- Galactosaemia
- Glycogen storage diseases
- Pyruvate carboxylase deficiency
- Fructose-1,6-bisphophatase deficiency
- Hereditary fructose intolerance
- Glucose-6-phosphate dehydrogenase deficiency
- Galactosaemia Lactose from milk is hydrolysed by intestinal lactase to produce glucose and galactose.

There are three inborn errors of galactose metabolism:

- Galactokinase deficiency
- Galactose-1-phosphate uridyltransferase (Gal-1-PUT) deficiency
- Uridine diphosphate-galactose 4-epimerase deficiency

The Pyrophosphorylase Pathway is an alternative route for production of UDP-galactose (essential for incorporation of galactose into proteins and lipids). The generation of galactose-1-

phosphate by this pathway explains why galactose-1-phosphate can still be synthesised in patients with galactosaemia who are on strict dietary galactose restriction Galactokinase Galactose-1-ph

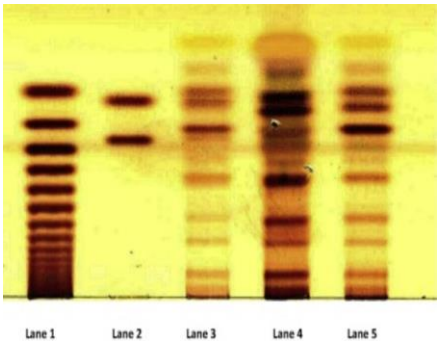
Classical Galactosaemia

- This disorder is due to galactose-1-phosphate uridyltransferase deficiency .
- There is accumulation of galactose-1-phosphate and galactose and secondary formation of galactitol.

- It typically presents by the end of the first week of life with poor feeding, vomiting, lethargy, jaundice, hepatomegaly, neonatal cataracts and renal tubular disease and is often associated with E. coli septicaemia.

- Biochemically there is hyperbilirubinaemia, raised alanine aminotransferase (ALT), generally elevated plasma and urine amino acids, albuminuria, glycosuria and galactosuria.
- A positive urine Clinitest® for reducing substances with a negative Clinistix® test (specific for glucose) may provide a clue to the diagnosis but is not specific. However in galactosaemia a negative Clinitest® may occur if there has been insufficient galactose intake due severe vomiting or reduced milk intake. Furthermore the Clinitest® and Clinistix® may be positive due to the glycosuria due to the renal tubular dysfunction. Urine sugars can be identified by Thin Layer Chromatography (TLC).

2D Urine amino acid TLC plate showing a generalised aminoaciduria



Urine galactose on a TLC plate

CLASSICAL GALACTOSAEMIA

- Milk feeds should be stopped whist awaiting the definitive test results.

- The definitive test is quantitative assay of galactose-1-phosphate uridyltransferase ('Gal-1-PUT') activity in red cells or the qualitative Beutler test which is a fluorescent spot test for 'Gal-1-PUT'.

BEUTLER TEST

- Whole blood and a reaction mixture (UDP-glucose, galactose-1-phosphate, NADP) is spotted onto filter paper at 0 minutes, after 60 minutes incubation & after 120 min incubation

- Normal transferase activity results in the production of NADPH, which is fluorescent under UV light.

- No fluorescence indicates galactose-1-phosphate uridyltransferase deficiency

- False negative results may occur if the patient has a had a blood transfusion up to 6 weeks before the sample was taken. False positive results may occur if the patient has glucose-6-phosphate dehydrogenase deficiency as the endogenous activity of this enzyme is used to generate NADPH.

- This can be confirmed with the quantitation of galactose-1-phosphate in erythrocytes or DNA analysis for common European mutation: Q188R (77% of mutant alleles in UK).

TREATMENT:

- If galactose is excluded from diet then life-threatening illness usually resolves quickly.
- Long-term complications e.g. low IQ, growth delay, ovarian dysfunction, still occur despite early diagnosis and treatment possibly due to endogenous galactose production.
- Partial enzyme deficiencies occur and several variant alleles exist e.g. Duarte; usually benign

GALACTOKINASE DEFICIENCY

- This is a rare disorder where there is an inability to phosphorylate galactose and galactose and galactitol are excreted in urine
- Neonatal (but not congenital) cataracts occur-often bilateral due to the accumulation of galactitol in the lens.
- There is a positive urine reducing substances due to galactose in urine usually with a negative Clinistix®.
- Diagnosis is by measurement of galactokinase activity in red cells. Treatment is with a galactose- free diet. The cataracts are reversible if milk excluded in first few weeks of life

UDP-GALACTOSE 4- EPIMERASE DEFICIENCY

MILD FORM

- A partial enzyme deficiency due to reduced protein stability and more pronounced in cells with long lifespan e.g. erythrocytes.
- Normal growth and development
- No treatment appears necessary

SEVERE FORM

- Very rare
- A similar presentation to classical galactosaemia.
- Accumulation of UDP-galactose & galactose-1-phosphate.
- The Beutler test is normal and red cell galactose-1-phosphate is increased.
- The definitive test is assay of UDP-galactose-4- epimerase activity in erythrocytes.

GLYCOGEN STORAGE DISEASES

PATHWAY

- Glucose is stored in the form of glycogen, mainly in liver and muscle
- Glycogen is made up of straight chains of glucose residues with α-1,4 linkages, branched at intervals with α-1,6 linkages
- Glycogen metabolism is highly regulated by several amplifying reaction cascades.
- Adrenaline and glucagon stimulate glycogen breakdown.
- Glycogen synthesis is increased by insulin.

GSD I

- GSD I accounts for approximately 25% of GSD cases
- Glucose-6-phosphatase deficiency (GSD Ia) is a defect in the release of glucose from glucose-6-phosphate and affects both glycogenolysis and gluconeogenesis.
- It presents with hepatomegaly, short stature and truncal obesity
- Biochemically there is hypoglycaemia, lactic acidaemia, hyperuricaemia and hyperlipidaemia
- Histological analysis shows excess of fat and glycogen in hepatocytes
- GSD Ib is a defect in a transporter protein and has the above features plus neutropaenia, recurrent bacterial infections and inflammatory bowel disease
- The diagnosis is nowadays confirmed by DNA analysis in the majority of patients
- It is also possible to measure the activity of glucose-6-phosphatase and the transporter protein function in a fresh liver biopsy with comparison of fresh and frozen results to distinguish type Ia from Ib

HEREDITARY FRUCTOSE INTOLERANCE

- Fructose is a monosaccharide found in fruit, honey and many vegetables. The disaccharide sucrose, composed of glucose and fructose, is found in many foods. Sorbitol (also from fruit and vegetables) can be converted into fructose by the liver.

- Hereditary Fructose Intolerance (HFI), a defect in fructose metabolism (deficiency of aldolase B), only presents after ingestion of foods containing fructose, sucrose or sorbitol. When an infant with HFI is weaned, they suffer from nausea, vomiting, gastrointestinal discomfort and lethargy. They are at risk of liver and kidney failure and death, if fructose is not withdrawn.
- Affected individuals may reach adulthood undiagnosed due to development of an aversion to fructose- containing foods. Around 50% of adults with HFI have no dental caries, so occasionally the diagnosis has been made by dentists.
- Biochemical features include hypoglycaemia (accumulated fructose-1-phosphate inhibits glucose production), hypophosphataemia, elevated plasma lactate, positive urine reducing substances, hyperuricaemia and a generalised aminoaciduria.
- Diagnostic clues include a rapid improvement on withdrawal of fructose from the diet and a compatible nutritional history. Definitive diagnosis is by mutation analysis (there is one relatively common mutation in northern Europeans: A149P) or measurement of enzyme activity in a liver biopsy. An intravenous fructose tolerance test can be done but this needs to be done in a specialist centre and is not recommended in young children. In affected patients there is a decrease in plasma glucose and phosphate.

DIABETES

Diabetes mellitus, commonly known as diabetes, is a metabolic disease that causes high blood sugar. The hormone insulin moves sugar from the blood into your cells to be stored or used for energy. With diabetes, your body either doesn't make enough insulin or can't effectively use the insulin it does make.

Untreated high blood sugar from diabetes can damage your nerves, eyes, kidneys, and other organs.

There are a few different types of diabetes:

- Type 1 diabetes is an autoimmune disease. The immune system attacks and destroys cells in the pancreas, where insulin is made. It's unclear what causes this attack. About 10 percent of people with diabetes have this type.
- Type 2 diabetes occurs when your body becomes resistant to insulin, and sugar builds up in your blood.
- Prediabetes occurs when your blood sugar is higher than normal, but it's not high enough for a diagnosis of type 2 diabetes.
- Gestational diabetes is high blood sugar during pregnancy. Insulin-blocking hormones produced by the placenta cause this type of diabetes.

A rare condition called diabetes insipidus is not related to diabetes mellitus, although it has a similar name. It's a different condition in which your kidneys remove too much fluid from your body.

Each type of diabetes has unique symptoms, causes, and treatments. Learn more about how these types differ from one another.

SYMPTOMS OF DIABETES

Diabetes symptoms are caused by rising blood sugar.

General symptoms

The general symptoms of diabetes include:

- increased hunger
- increased thirst
- weight loss
- frequent urination
- blurry vision
- extreme fatigue
- sores that don't heal

SYMPTOMS IN MEN

In addition to the general symptoms of diabetes, men with diabetes may have a decreased sex drive, erectile dysfunction (ED), and poor muscle strength.

SYMPTOMS IN WOMEN

Women with diabetes can also have symptoms such as urinary tract infections, yeast infections, and dry, itchy skin.

Type 1 diabetes

Symptoms of type 1 diabetes can include:

- extreme hunger
- increased thirst
- unintentional weight loss
- frequent urination
- blurry vision
- tiredness

It may also result in mood changes.

Type 2 diabetes

Symptoms of type 2 diabetes can include:

- increased hunger
- increased thirst
- increased urination
- blurry vision
- tiredness
- sores that are slow to heal

It may also cause recurring infections. This is because elevated glucose levels make it harder for the body to heal.

GESTATIONAL DIABETES

Most women with gestational diabetes don't have any symptoms. The condition is often detected during a routine blood sugar test or oral glucose tolerance test that is usually performed between the 24th and 28th weeks of gestation.

In rare cases, a woman with gestational diabetes will also experience increased thirst or urination.

The bottom line

Diabetes symptoms can be so mild that they're hard to spot at first. Learn which signs should prompt a trip to the doctor.

CAUSES OF DIABETES

Different causes are associated with each type of diabetes.

Type 1 diabetes

Doctors don't know exactly what causes type 1 diabetes. For some reason, the immune system mistakenly attacks and destroys insulin-producing beta cells in the pancreas.

Genes may play a role in some people. It's also possible that a virus sets off the immune system attack.

Type 2 diabetes

Type 2 diabetes stems from a combination of genetics and lifestyle factors. Being overweight or obese increases your risk too. Carrying extra weight, especially in your belly, makes your cells more resistant to the effects of insulin on your blood sugar.

This condition runs in families. Family members share genes that make them more likely to get type 2 diabetes and to be overweight.

GESTATIONAL DIABETES

Gestational diabetes is the result of hormonal changes during pregnancy. The placenta produces hormones that make a pregnant woman's cells less sensitive to the effects of insulin. This can cause high blood sugar during pregnancy.

Women who are overweight when they get pregnant or who gain too much weight during their pregnancy are more likely to get gestational diabetes.

The bottom line

Both genes and environmental factors play a role in triggering diabetes. Get more information here on the causes of diabetes.

Diabetes risk factors

Certain factors increase your risk for diabetes.

Type 1 diabetes

You're more likely to get type 1 diabetes if you're a child or teenager, you have a parent or sibling with the condition, or you carry certain genes that are linked to the disease.

Type 2 diabetes

Your risk for type 2 diabetes increases if you:

- are overweight
- are age 45 or older
- have a parent or sibling with the condition
- aren't physically active
- have had gestational diabetes
- have prediabetes
- have high blood pressure, high cholesterol, or high triglycerides
- have African American, Hispanic or Latino American, Alaska Native, Pacific Islander, American Indian, or Asian American ancestry

Gestational diabetes

Your risk for gestational diabetes increases if you:

- are overweight
- are over age 25
- had gestational diabetes during a past pregnancy
- have given birth to a baby weighing more than 9 pounds

- have a family history of type 2 diabetes
- have polycystic ovary syndrome (PCOS)

The bottom line

Your family, environment, and preexisting medical conditions can all affect your odds of developing diabetes. Find out which risks you can control and which ones you can't.

Diabetes complications

High blood sugar damages organs and tissues throughout your body. The higher your blood sugar is and the longer you live with it, the greater your risk for complications.

Complications associated with diabetes include:

- heart disease, heart attack, and stroke
- neuropathy
- nephropathy
- retinopathy and vision loss
- hearing loss
- foot damage such as infections and sores that don't heal
- skin conditions such as bacterial and fungal infections
- depression
- dementia

Gestational diabetes

Uncontrolled gestational diabetes can lead to problems that affect both the mother and baby. Complications affecting the baby can include:

- premature birth
- higher-than-normal weight at birth
- increased risk for type 2 diabetes later in life
- low blood sugar
- jaundice
- stillbirth

The mother can develop complications such as high blood pressure (preeclampsia) or type 2 diabetes. She may also require cesarean delivery, commonly referred to as a C-section.

The mother's risk of gestational diabetes in future pregnancies also increases.

The bottom line

Diabetes can lead to serious medical complications, but you can manage the condition with medications and lifestyle changes. Avoid the most common diabetes complications with these helpful tips.

Diabetes and diet

Healthy eating is a central part of managing diabetes. In some cases, changing your diet may be enough to control the disease.

Type 1 diabetes

Your blood sugar level rises or falls based on the types of foods you eat. Starchy or sugary foods make blood sugar levels rise rapidly. Protein and fat cause more gradual increases.

Your medical team may recommend that you limit the amount of carbohydrates you eat each day. You'll also need to balance your carb intake with your insulin doses.

Work with a dietitian who can help you design a diabetes meal plan. Getting the right balance of protein, fat, and carbs can help you control your blood sugar. Check out this guide to starting a type 1 diabetes diet.

Type 2 diabetes

Eating the right types of foods can both control your blood sugar and help you lose any excess weight.

Carb counting is an important part of eating for type 2 diabetes. A dietitian can help you figure out how many grams of carbohydrates to eat at each meal.

In order to keep your blood sugar levels steady, try to eat small meals throughout the day. Emphasize healthy foods such as:

- fruits
- vegetables
- whole grains
- lean protein such as poultry and fish
- healthy fats such as olive oil and nuts

Certain other foods can undermine efforts to keep your blood sugar in control.Discover the foods you should avoid if you have diabetes.

Gestational diabetes

Eating a well-balanced diet is important for both you and your baby during these nine months. Making the right food choices can also help you avoid diabetes medications.

Watch your portion sizes, and limit sugary or salty foods. Although you need some sugar to feed your growing baby, you should avoid eating too much.

Consider making an eating plan with the help of a dietitian or nutritionist. They'll ensure that your diet has the right mix of macronutrients. Go here for other do's and don'ts for healthy eating with gestational diabetes.

Diabetes diagnosis

Anyone who has symptoms of diabetes or is at risk for the disease should be tested. Women are routinely tested for gestational diabetes during their second or third trimesters of pregnancy.

Doctors use these blood tests to diagnose prediabetes and diabetes:

- The fasting plasma glucose (FPG) test measures your blood sugar after you've fasted for 8 hours.
- The A1C test provides a snapshot of your blood sugar levels over the previous 3 months.

To diagnose gestational diabetes, your doctor will test your blood sugar levels between the 24th and 28th weeks of your pregnancy.

- During the glucose challenge test, your blood sugar is checked an hour after you drink a sugary liquid.
- During the 3 hour glucose tolerance test, your blood sugar is checked after you fast overnight and then drink a sugary liquid.

The earlier you get diagnosed with diabetes, the sooner you can start treatment. Find out whether you should get tested, and get more information on tests your doctor might perform.

Diabetes prevention

Type 1 diabetes isn't preventable because it's caused by a problem with the immune system. Some causes of type 2 diabetes, such as your genes or age, aren't under your control either.

Yet many other diabetes risk factors are controllable. Most diabetes prevention strategies involve making simple adjustments to your diet and fitness routine.

If you've been diagnosed with prediabetes, here are a few things you can do to delay or prevent type 2 diabetes:

- Get at least 150 minutes per week of aerobic exercise, such as walking or cycling.
- Cut saturated and trans fats, along with refined carbohydrates, out of your diet.
- Eat more fruits, vegetables, and whole grains.
- Eat smaller portions.

GLUCOSE TOLERANCE TEST(GTT)

What Is Gtt?

GTT short for Glucose Tolerance Test is a test designed to assess the body response to glucose. In GTT, the patient is given a glucose solution and blood samples are drawn afterword at intervals to measure how well the body cells are able to absorb glucose. There are several variations to the glucose tolerance test used in different conditions but, the most common one of them is the Oral glucose tolerance test or OGTT.

The OGTT is mainly used in the diagnosis of gestational diabetes. For OGTT the patient is required to fast for 8 hours and then a fasting plasma glucose is tested, after that oral glucose solution is given. After that blood samples can be drawn up to 4 times at different intervals to measure the blood glucose. A OGTT is usually performed in the morning as glucose levels usually fall by afternoon.

OGTT used to be the gold standard in the diagnosis of diabetes type 2 but, is now being replaced with other GTT methodology. The GTT is primarily used for the diagnosis of diabetes, insulin resistance, impaired beta cell function, carbohydrate metabolism disorder and also reactive hypoglycaemia and acromegaly.

Who Is Given Glucose Tolerance Test (Gtt)?

The GTT is usually given to pregnant women during 24th and 28th week of pregnancy. This test is also given to pregnant who has diabetes symptoms or have the risk of developing diabetes prior to the pregnancy.

Besides that the GTT is also given to other patients who are experiencing symptoms of varied diseases that can cause high glucose levels in the blood stream or restrict the proper absorption of glucose by the body cells.

What Are The Preparations Needed For Gtt?

GTT is an elaborate blood test, that requires frequent testing and as the special requirements need for GTT are as follows;

- Have a normal diet like any other day.
- Inform the doctor about the varied prescription drugs you are taking, as certain drugs like corticosteroids, diuretics and anti- depressants can cause false results.
- Fasting is required for 8 to 10 hours prior to the test and only water is allowed during this period.
- You might want to avoid using the washroom prior to testing as urine samples might be needed
- On the morning of the test do not smoke or have coffee or caffeine based product.
- The GTT is not to be done on a sick person

Glucose Tolerance Test Procedure

The GTT procedure is as follows;

- At first a zero -time or baseline blood sample is drawn.
- Then the patient is given a specific dose of glucose solution to drink

- After that the blood samples are drawn at regular intervals to measure the blood sugar levels and also insulin levels in certain cases. The blood sampling can be done as requested by the doctor and could involve up to 6 hours of testing.

GTT SIDE EFFECTS

There is a slight risk attach with Glucose tolerance test which are as follows;

People with high levels of sugar have the following side effect in response to drinking the glucose solution, like;

- Nausea
- Stomach discomfort
- Diarrhoea
- Constipation

Risks attached to drawing out blood samples include the following;

- Swelling and redness at the puncture side
- Haematoma
- Fever
- Dizziness
- Infection at the puncture site

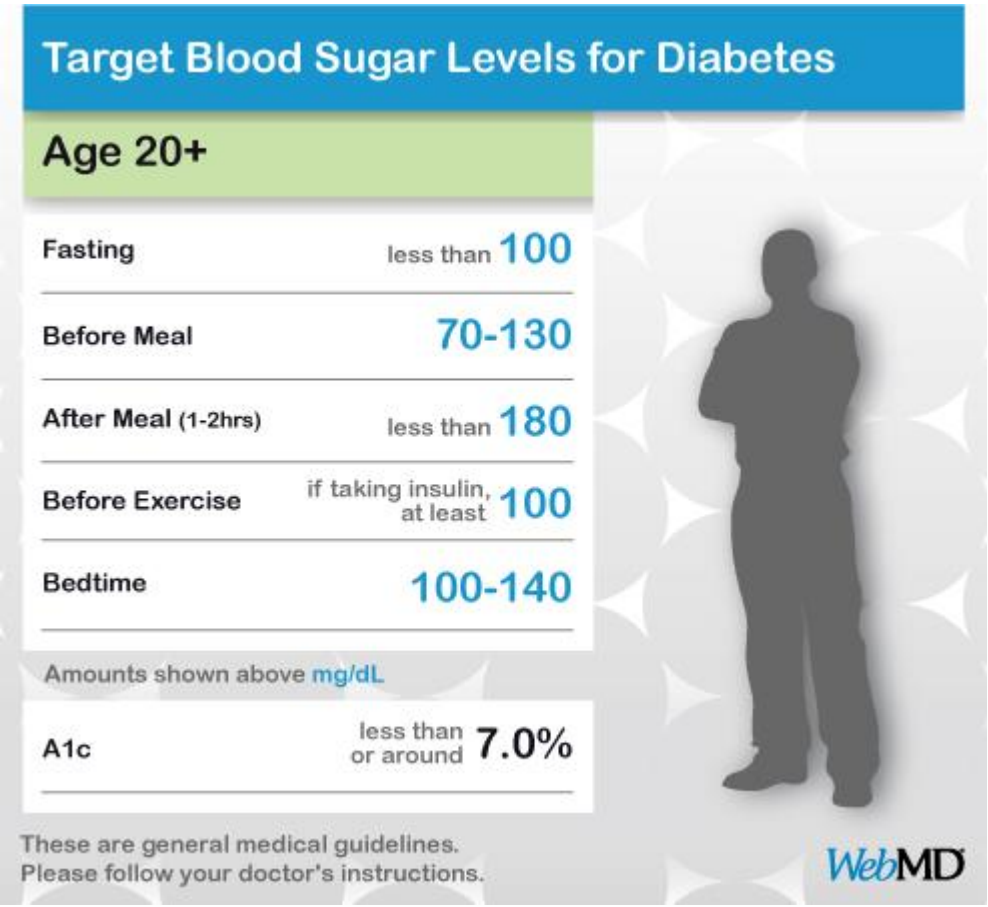
GTT NORMAL VALUE

The GTT normal value is lower than 140 mg/dL and if the blood glucose level is between 140 and 199 mg/dL then it is a strong indication of prediabetes.

The OGTT normal range for fasting results is between 100 – 125 mg/dL for prediabetes, 126 mg/dL or greater for diabetes and greater than 92 mg/dL for gestational diabetes.

The OGTT normal range for after 2 hour test results is between 140 – 199 mg/dL for pre diabetes, 200 mg/dL or greater for diabetes and greater than 153 mg/dL for gestational diabetes.

Normal Blood Sugar Levels for Adults With Diabetes



factors influence blood glucose levels?

Thong Le Jan 17, 2019 1min read
Factors rise your blood glucose levels

- Eating too much food
- Not being active
- Side effects of steroids or anti-psychotic medications
- Illness
- Stress
- Pain
- Menstrual periods
- Dehydration

Factors lower your blood glucose levels

- Eating too little food
- Too much alcohol or alcohol on an empty stomach
- Too much insulin or too many diabetes pills
- Skipping or delayed meals
- Too much exercise without enough food

UNIT – 3

Lipid Metabolism Disorders

- Metabolism is the process your body uses to make energy from the food you eat. Food is made up of proteins, carbohydrates, and fats. Chemicals in your digestive system (enzymes) break the food parts down into sugars and acids, your body's fuel. Your body can use this fuel right away, or it can store the energy in your body tissues. If you have a metabolic disorder, something goes wrong with this process.

- Lipid metabolism disorders, such as Gaucher disease and Tay-Sachs disease, involve lipids. Lipids are fats or fat-like substances. They include oils, fatty acids, waxes, and cholesterol. If you have one of these disorders, you may not have enough enzymes to break down lipids. Or the enzymes may not work properly and your body can't convert the fats into energy. They cause a harmful amount of lipids to build up in your body. Over time, that can damage your cells and tissues, especially in the brain, peripheral nervous system, liver, spleen, and bone marrow. Many of these disorders can be very serious, or sometimes even fatal.

- These disorders are inherited. Newborn babies get screened for some of them, using blood tests. If there is a family history of one of these disorders, parents can get genetic testing to see whether they carry the gene. Other genetic tests can tell whether the fetus has the disorder or carries the gene for the disorder.

Plasma lipoproteins: genetic influences and clinical implications

- Plasma lipids — such as cholesterol and triglycerides, and plasma lipoproteins such as low-density lipoprotein (LDL) and high-density lipoprotein (HDL) — are among the most important risk factors for cardiovascular disease.

- Progress in understanding the genes determining plasma lipoprotein levels has rapidly accelerated owing to high-throughput automated DNA sequencing and genome-wide association analysis.

- Phenomic analysis (or deep phenotyping) allows lipoprotein phenotype data to be analysed as part of a continuum that includes biochemical and molecular data.

- Genetic determinants of plasma lipoprotein levels seem to conform to a mosaic model, involving contributions from multiple DNA sequence variants, both rare and common, with a range of effect sizes.

- Many of the same genes in which rare mutations cause extreme and uncommon syndromes or diseases of lipoprotein metabolism also contain common variants with more subtle effects on plasma lipoprotein levels in the normal range.

- In addition to increasing our understanding of plasma lipoprotein metabolism, the identification by genetics of new pathways and targets is likely to inform new drug design and could eventually lead to evidence-based changes in practice.

CHOLESTROL

What is cholesterol?
Cholesterol is a waxy, fat-like substance that's found in all the cells in your body. Your body needs some cholesterol to make hormones, vitamin D, and substances that help you digest foods. Your body makes all the cholesterol it needs. Cholesterol is also found in foods from animal sources, such as egg yolks, meat, and cheese.

If you have too much cholesterol in your blood, it can combine with other substances in the blood to form plaque. Plaque sticks to the walls of your arteries. This buildup of plaque is known as atherosclerosis. It can lead to coronary artery disease, where your coronary arteries become narrow or even blocked.

What are HDL, LDL, and VLDL?
HDL, LDL, and VLDL are lipoproteins. They are a combination of fat (lipid) and protein. The lipids need to be attached to the proteins so they can move through the blood. Different types of lipoproteins have different purposes:

- HDL stands for high-density lipoprotein. It is sometimes called "good" cholesterol because it carries cholesterol from other parts of your body back to your liver. Your liver then removes the cholesterol from your body.
- LDL stands for low-density lipoprotein. It is sometimes called "bad" cholesterol because a high LDL level leads to the buildup of plaque in your arteries.
- VLDL stands for very low-density lipoprotein. Some people also call VLDL a "bad" cholesterol because it too contributes to the buildup of plaque in your arteries. But VLDL and LDL are different; VLDL mainly carries triglycerides and LDL mainly carries cholesterol.

What causes high cholesterol?

The most common cause of high cholesterol is an unhealthy lifestyle. This can include

- **Unhealthy eating habits,** such as eating lots of bad fats. One type, saturated fat, is found in some meats, dairy products, chocolate, baked goods, and deep-fried and processed foods. Another type, trans fat, is in some fried and processed foods. Eating these fats can raise your LDL (bad) cholesterol.
- **Lack of physical activity,** with lots of sitting and little exercise. This lowers your HDL (good) cholesterol.
- **Smoking,** which lowers HDL cholesterol, especially in women. It also raises your LDL cholesterol.

Genetics may also cause people to have high cholesterol. For example, familial hypercholesterolemia (FH) is an inherited form of high cholesterol. Other medical conditions and certain medicines may also cause high cholesterol.

What can raise my risk of high cholesterol?

A variety of things can raise your risk for high cholesterol:

- **Age.** Your cholesterol levels tend to rise as you get older. Even though it is less common, younger people, including children and teens, can also have high cholesterol.
- **Heredity.** High blood cholesterol can run in families.
- **Weight.** Being overweight or having obesity raises your cholesterol level.
- **Race.** Certain races may have an increased risk of high cholesterol. For example, African Americans typically have higher HDL and LDL cholesterol levels than whites.
- **Weight.** Being overweight or having obesity raises your cholesterol level.

What health problems can high cholesterol cause?

If you have large deposits of plaque in your arteries, an area of plaque can rupture (break open). This can cause a blood clot to form on the surface of the plaque. If the clot becomes large enough, it can mostly or completely block blood flow in a coronary artery.

If the flow of oxygen-rich blood to your heart muscle is reduced or blocked, it can cause angina (chest pain) or a heart attack.

Plaque also can build up in other arteries in your body, including the arteries that bring oxygen-rich blood to your brain and limbs. This can lead to problems such as carotid artery disease, stroke, and peripheral arterial disease.

Hyperlipidemia

ou call it high cholesterol. Your doctor calls it hyperlipidemia. Either way, it's a common problem.

The term covers several disorders that result in extra fats, also known as lipids, in your blood. You can control some of its causes; but not all of them.

Hyperlipidemia is treatable, but it's often a life-long condition. You'll need to watch what you eat and also exercise regularly. You might need to take a prescription medication, too.

The goal is to lower the harmful cholesterol levels. Doing so can reduce your risk of heart disease, heart attack, stroke, and other problems.

Causes

Cholesterol, a waxy substance, is a type of fat your body makes. It can also come from what you eat.

Foods that have cholesterol, saturated fat, and trans fats can raise your blood cholesterol level. These include:

- Cheese
- Egg yolks
- Fried and processed foods
- Ice cream
- Pastries
- Red meat

Don't exercise much? That can lead to putting on extra pounds, which can raise your cholesterol.

As you get older, your cholesterol levels often creep up, too.

Hyperlipidemia can run in families. People who inherit the condition can get very high cholesterol. That means they have a much greater chance of having a heart attack, even when they're young.

Symptoms and Risks

Most people with hyperlipidemia can't tell that they have it at first. It's not something you can feel, but you may notice the effects of it someday.

Cholesterol, along with triglycerides and other fats, can build up inside your arteries. This makes the blood vessels narrower and makes it more difficult for blood to get through. Your blood pressure could go up.

The buildup can also cause a blood clot to form. If a blood clot breaks off and travels to your heart, it can cause a heart attack. If it goes to your brain, it can cause a stroke.

How It's Diagnosed

Your doctor should check your lipid levels regularly. It is a blood test called a lipoprotein panel. The results show the levels of:

LDL cholesterol : The "bad" cholesterol that builds up inside your arteries

HDL cholesterol : The "good" cholesterol that lowers your risk for heart disease

Triglycerides : Another type of fat in your blood

Total cholesterol: A combination of the other three numbers

The American Heart Association recommends that adults 20 and older have their cholesterol checked every 4 to 6 years. You may have to fast 9 to 12 hours before the test.

Total cholesterol of 200 mg/dL or more is out of the normal range. Your doctor will consider things like your age, whether you smoke, and whether a close family member has heart problems to decide whether your specific test numbers are high and what to do about them.

UREA AND AMMONIA METABOLISM AND THE CONTROL OF RENAL NITROGEN EXCRETION

Nitrogen metabolism is necessary for normal health. Nitrogen is an essential element present in all amino acids; it is derived from dietary protein intake, is necessary for protein synthesis and maintenance of muscle mass, and is excreted by the kidneys. Under steady-state conditions, renal nitrogen excretion equals nitrogen intake. Renal nitrogen excretion consists almost completely of urea and ammonia. (To note, ammonia exists in two distinct molecular forms, NH_3 and NH_4^+, which are in equilibrium with each other. In this review, we use the term *ammonia* to refer to the combination of both molecular forms.

When referring to a specific molecular form, we state either NH_3 or NH_4^+.) Other nitrogen compounds (*e.g.,* nitric oxide metabolites, and nitrates) and many nitrogen-containing compounds (*e.g.,* uric acid, urinary protein, *etc.*), comprise <1% of total renal nitrogen excretion. The two major components of renal nitrogen excretion, urea and ammonia, are regulated by a wide variety of conditions and play important roles in normal health and disease, including roles in the urine concentrating mechanism and in acid-base homeostasis. In this review, we discuss the mechanisms and regulation of both urea and ammonia handling in the kidneys, their roles in renal physiologic responses other than nitrogen excretion, and the clinical uses of urea production and metabolism.

UREA INTRODUCTION

Proteins throughout the body are continually turning over but at vastly different rates: consider the short half-lives of transcription factors versus the longer half-lives of structural proteins of muscle. To achieve such differences, there must be biochemical mechanisms that precisely identify proteins to be degraded plus mechanisms that efficiently degrade doomed proteins. The consequence is that these processes do not interfere with the turnover of proteins that are required to maintain cellular functions.

The “how” and “why” of the biochemical reactions that are required for maintenance of cellular functions are being uncovered . Here, we will examine the overall metabolism and functions of urea. Knowledge of urea functions and metabolism is important because urea is the major circulating source of nitrogen-containing compounds and it plays important roles in regulating kidney function.

Foods rich in protein are converted to the 9 essential and 11 nonessential amino acids, as shown in the summary of overall protein metabolism. The difference between the two groups is that the essential amino acids cannot be synthesized in the body and, hence, they must be provided in the diet or proteins cannot be synthesized.

Amino acids have two fates: (*1*) they can be used to synthesize protein, or (*2*) they are degraded in a monotonous fashion in which the *α*-amino group is removed and converted to urea in the liver. Not surprisingly, the production of urea is closely related to the amount of protein eaten; therefore, urea can be used to estimate whether a patient with CKD is receiving the required amounts of protein (3,4). In addition, urea production serves as an estimate of the accumulation of putative uremic toxins and, thus, as a guideline for management of the diets of patients with CKD.

COMA

coma is a deep state of prolonged unconsciousness in which a person cannot be awakened; fails to respond normally to painful stimuli, light, or sound; lacks a normal wake-sleep cycle; and does not initiate voluntary actions.Coma patients exhibit a complete absence of wakefulness and are unable to consciously feel, speak or move.Comas can be derived by natural causes, or can be medically induced.

Clinically, a coma can be defined as the inability consistently to follow a one-step command.It can also be defined as a score of ≤ 8 on the Glasgow Coma Scale (GCS) lasting ≥ 6 hours. For a patient to maintain consciousness, the components of *wakefulness* and *awareness* must be maintained.

Wakefulness describes the quantitative degree of consciousness, hereas awareness relates to the qualitative aspects of the functions mediated by the cortex, including cognitive abilities such as attention, sensory perception, explicit memory, language, the execution of tasks, temporal and spatial orientation and reality judgment.From a neurological perspective, consciousness is maintained by the activation of the cerebral cortex—the gray matter that forms the outer layer of the brain and by the reticular activating system (RAS), a structure located within the brainstem.

Etymology

The term 'coma', from the Greek κῶμα *koma*, meaning deep sleep, had already been used in the Hippocratic corpus (*Epidemica*) and later by Galen (second century AD). Subsequently, it was hardly used in the known literature up to the middle of the 17th century. The term is found again in Thomas Willis' (1621–1675) influential *De anima brutorum* (1672), where lethargy (pathological sleep), 'coma' (heavy sleeping), *carus* (deprivation of the senses) and apoplexy (into which *carus* could turn and which he localized in the white matter) are mentioned. The term *carus* is also derived from Greek, where it can be found in the roots of several words meaning soporific or sleepy. It can still be found in the root of the term 'carotid'. Thomas Sydenham (1624–89) mentioned the term 'coma' in several cases of fever (Sydenham, 1685).

Signs and symptoms

Image of a man unresponsive to stimuli

General symptoms of a person in a comatose state are:

- Inability to voluntarily open the eyes
- A non-existent sleep-wake cycle
- Lack of response to physical (painful) or verbal stimuli

- Depressed brainstem reflexes, such as pupils not responding to light
- Irregular breathing
- Scores between 3 and 8[10] on the Glasgow Coma Scale

Causes

Many types of problems can cause a coma. Forty percent of comatose states result from drug poisoning.Certain drug use under certain conditions can damage or weaken the synaptic functioning in the ascending reticular activating system (ARAS) and keep the system from properly functioning to arouse the brain.[12] Secondary effects of drugs, which include abnormal heart rate and blood pressure, as well as abnormal breathing and sweating, may also indirectly harm the functioning of the ARAS and lead to a coma. Given that drug poisoning is the cause for a large portion of patients in a coma, hospitals first test all comatose patients by observing pupil size and eye movement, through the vestibular-ocular reflex.

The second most common cause of coma, which makes up about 25% of cases, is lack of oxygen, generally resulting from cardiac arrest. The Central Nervous System (CNS) requires a great deal of oxygen for its neurons. Oxygen deprivation in the brain, also known as hypoxia, causes sodium and calcium from outside of the neurons to decrease and intracellular calcium to increase, which harms neuron communication.Lack of oxygen in the brain also causes ATP exhaustion and cellular breakdown from cytoskeleton damage and nitric oxide production.

Twenty percent of comatose states result from the side effects of a stroke.During a stroke, blood flow to part of the brain is restricted or blocked. An ischemic stroke, brain hemorrhage, or tumor may cause restriction of blood flow. Lack of blood to cells in the brain prevents oxygen from getting to the neurons, and consequently causes cells to become disrupted and die. As brain cells die, brain tissue continues to deteriorate, which may affect the functioning of the ARAS.

The remaining 15% of comatose cases result from trauma, excessive blood loss, malnutrition, hypothermia, hyperthermia, abnormal glucose levels, and many other biological disorders. Furthermore, studies show that 1 out of 8 patients with traumatic brain injury experience a comatose state.

Unit 4

JAUNTICE

Jaundice is a term used to describe a yellowish tinge to the skin and the whites of the eye. Body fluids ay also be yellow.

The color of the skin and whites of the eyes will vary depending on levels of bilirubin. Bilirubin is a waste material found in the blood. Moderate levels lead to a yellow color, while very high levels will appear brown.

About 60 percent of all infants born in the United States have jaundice. However, jaundice can happen to people of all ages and is normally the result of an underlying condition. Jaundice normally indicates a problem with the liver or bile duct.

Fast facts on jaundice

- Jaundice is caused by a buildup of bilirubin, a waste material, in the blood.
- An inflamed liver or obstructed bile duct can lead to jaundice, as well as other underlying conditions.
- Symptoms include a yellow tinge to the skin and whites of the eyes, dark urine, and itchiness.
- Diagnosis of jaundice can involve a range of tests.
- Jaundice is treated by managing the underlying cause.

Fatty Liver

Fatty liver is also known as hepatic steatosis. It happens when fat builds up in the liver. Having small amounts of fat in your liver is normal, but too much can become a health problem.Your liver is the second largest organ in your body. It helps process nutrients from food and drinks and filters harmful substances from your blood.Too much fat in your liver can cause liver inflammation, which can damage your liver and create scarring. In severe cases, this scarring can lead to liver failure.When fatty liver develops in someone who drinks a lot of alcohol, it's known as alcoholic fatty liver disease (AFLD).

Symptoms of fatty liver

In many cases, fatty liver causes no noticeable symptoms. But you may feel tired or experience discomfort or pain in the upper right side of your abdomen.

Some people with fatty liver disease develop complications, including liver scarring. Liver scarring is known as liver fibrosis. If you develop severe liver fibrosis, it's known as cirrhosis.

Cirrhosis may cause symptoms such as:

- loss of appetite
- weight loss
- weakness
- fatigue

- nosebleeds
- itchy skin
- yellow skin and eyes
- web-like clusters of blood vessels under your skin
- abdominal pain
- abdominal swelling
- swelling of your legs
- breast enlargement in men
- confusion

Cirrhosis is a potentially life-threatening condition. Get the information you need to recognize and manage it.

Causes of fatty liver

Fatty liver develops when your body produces too much fat or doesn't metabolize fat efficiently enough. The excess fat is stored in liver cells, where it accumulates and causes fatty liver disease.This build-up of fat can be caused by a variety of things.For example, drinking too much alcohol can cause alcoholic fatty liver disease. This is the first stage of alcohol-related liver disease.In people who don't drink a lot of alcohol, the cause of fatty liver disease is less clear.

One or more of the following factors may play a role:

- obesity
- high blood sugar
- insulin resistance
- high levels of fat, especially triglycerides, in your blood

Less common causes include:

- pregnancy
- rapid weight loss
- some types of infections, such as hepatitis C

- side effects from some types of medications, such as methotrexate (Trexall), tamoxifen (Nolvadex), amiodorone (Pacerone), and valproic acid (Depakote)
- exposure to certain toxins

Certain genes may also raise your risk of developing fatty liver.

CARDIAC ARREST

Diagnosis

If you survive sudden cardiac arrest, your doctor will try to learn what caused it to help prevent future episodes. Tests your doctor may recommend include:

Electrocardiogram (ECG)

During an ECG, sensors (electrodes) that can detect the electrical activity of your heart are attached to your chest and sometimes to your limbs. An ECG can reveal disturbances in heart rhythm or detect abnormal electrical patterns, such as a prolonged QT interval, that increase your risk of sudden death.

Blood tests

A sample of your blood might be tested to check the levels of potassium, magnesium, hormones and other chemicals that can affect your heart's ability to function. Other blood tests can detect recent heart injury and heart attacks.

Imaging tests

These might include:

- **Chest X-ray.** This allows your doctor to check the size and shape of your heart and its blood vessels. It might also show whether you have heart failure.
- **Echocardiogram.** This test uses sound waves to produce an image of your heart. It can help identify whether an area of your heart has been damaged by a heart attack and isn't pumping hard enough or whether there are problems with your heart valves.

  This test and others, including a nuclear scan, MRI, CT scan and cardiac catheterization, can all determine your heart's pumping capacity by measuring what's called the ejection fraction, one of

the most important predictors of your risk of sudden cardiac arrest. Ejection fraction refers to the percentage of blood that's pumped out of a filled ventricle with each heartbeat.

A normal ejection fraction is 50 to 70 percent. An ejection fraction of less than 40 percent increases your risk of sudden cardiac arrest.

- **Nuclear scan.** This test, usually done with a stress test, helps identify blood flow problems to your heart. Tiny amounts of radioactive material, such as thallium, are injected into your bloodstream. Special cameras can detect the radioactive material as it flows through your heart and lungs.
- **Coronary catheterization (angiogram).** During this procedure, a liquid dye is injected into the arteries of your heart through a long, thin tube (catheter) that's advanced through an artery, usually in your arm, to arteries in your heart. As the dye fills your arteries, the arteries become visible on X-ray and videotape, revealing areas of blockage.

Treatment

Sudden cardiac arrest requires immediate action for survival.

CPR

Immediate CPR is crucial for treating sudden cardiac arrest. By maintaining a flow of oxygen-rich blood to the body's vital organs, CPR can provide a vital link until more-advanced emergency care is available.

If you don't know CPR and someone collapses unconscious near you, call 911 or emergency medical help. Then, if the person isn't breathing normally, begin pushing hard and fast on the person's chest — at a rate of 100 to 120 compressions a minute, allowing the chest to fully rise between compressions. Do this until an automated external defibrillator (AED) becomes available or emergency personnel arrive.

Defibrillation

Advanced care for ventricular fibrillation, a type of arrhythmia that can cause sudden cardiac arrest, generally includes delivery of an electrical shock through the chest wall to the heart. The procedure, called defibrillation, momentarily stops the heart and the chaotic rhythm. This often allows the normal heart rhythm to resume.

Defibrillators are programmed to recognize ventricular fibrillation and send a shock only when it's appropriate. These portable defibrillators are increasingly available in public places, including airports, shopping malls, casinos, health clubs, and community and senior citizen centers.

At the emergency room

Once you arrive in the emergency room, the medical staff will work to stabilize your condition and treat a possible heart attack, heart failure or electrolyte imbalances. You might be given medications to stabilize your heart rhythm.

Long-term treatment

After you recover, your doctor will discuss with you or your family what other tests might help determine the cause of the cardiac arrest. Your doctor will also discuss preventive treatment options with you to reduce your risk of another cardiac arrest.

Treatments might include:

- **Drugs.** Doctors use various anti-arrhythmic drugs for emergency or long-term treatment of arrhythmias or potential arrhythmia complications. A class of medications called beta blockers is commonly used in people at risk of sudden cardiac arrest. As a side effect, an anti-arrhythmia drug might cause your arrhythmia to occur more frequently — or even cause a new arrhythmia.

  Other possible drugs that can be used to treat the condition that led to the arrhythmia include angiotensin-converting enzyme (ACE) inhibitors and calcium channel blockers.

- **Implantable cardioverter-defibrillator (ICD).** After your condition stabilizes, your doctor is likely to recommend an ICD, a battery-powered unit that's put into your body near your left collarbone. One or more electrode-tipped wires from the ICD run through veins to your heart.

  The ICD constantly monitors your heart rhythm. If it detects a rhythm that's too slow, it paces your heart as a pacemaker would. If it detects a dangerous heart rhythm change, it sends out low- or high-energy shocks to reset your heart to a normal rhythm.

- **Coronary angioplasty.** This procedure opens blocked coronary arteries, letting blood flow more freely to your heart, which might reduce your risk of serious arrhythmia. A long, thin tube (catheter) is passed through an artery, usually in your leg, to a blocked artery in your heart.

This catheter is equipped with a special balloon tip that briefly inflates to open the blocked artery.

At the same time, a metal mesh stent might be inserted into the artery to keep it open long term, restoring blood flow to your heart. Coronary angioplasty can be done at the same time as a coronary catheterization (angiogram), a procedure that doctors do to locate narrowed arteries to the heart.

- **Coronary bypass surgery.** Also called coronary artery bypass grafting, bypass surgery involves sewing veins or arteries in place at a site beyond a blocked or narrowed coronary artery (bypassing the narrowed section), restoring blood flow to your heart. This can improve the blood supply to your heart and reduce the frequency of racing heartbeats.
- **Radiofrequency catheter ablation.** This procedure can be used to block a single abnormal electrical pathway. One or more catheters are threaded through your blood vessels to inside your heart. They're positioned along electrical pathways identified by your doctor as causing your arrhythmia.

  Electrodes at the catheter tips are heated with radiofrequency energy. This destroys (ablates) a small spot of heart tissue and creates an electrical block along the pathway that's causing your arrhythmia to stop your arrhythmia.

- **Corrective heart surgery.** If you have a congenital heart deformity, a faulty valve or diseased heart muscle tissue due to cardiomyopathy, surgery to correct the abnormality might improve your heart rate and blood flow, reducing your risk of fatal arrhythmias.

UNIT - 5

CANCER

- Cancer is the name given to a collection of related diseases. In all types of cancer, some of the body's cells begin to divide without stopping and spread into surrounding tissues.

- Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and divide to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place.

- When cancer develops, however, this orderly process breaks down. As cells become more and more abnormal, old or damaged cells survive when they should die, and new cells form when

they are not needed. These extra cells can divide without stopping and may form growths called tumors.

- Many cancers form solid tumors, which are masses of tissue. Cancers of the blood, such as leukemias, generally do not form solid tumors.

- Cancerous tumors are malignant, which means they can spread into, or invade, nearby tissues. In addition, as these tumors grow, some cancer cells can break off and travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor.

- Unlike malignant tumors, benign tumors do not spread into, or invade, nearby tissues. Benign tumors can sometimes be quite large, however. When removed, they usually don't grow back, whereas malignant tumors sometimes do. Unlike most benign tumors elsewhere in the body, benign brain tumors can be life threatening.

- **Differences between Cancer Cells and Normal Cells**

- Cancer cells differ from normal cells in many ways that allow them to grow out of control and become invasive. One important difference is that cancer cells are less specialized than normal cells. That is, whereas normal cells mature into very distinct cell types with specific functions, cancer cells do not. This is one reason that, unlike normal cells, cancer cells continue to divide without stopping.

- In addition, cancer cells are able to ignore signals that normally tell cells to stop dividing or that begin a process known as programmed cell death, or apoptosis, which the body uses to get rid of unneeded cells.

- Cancer cells may be able to influence the normal cells, molecules, and blood vessels that surround and feed a tumor—an area known as the microenvironment. For instance, cancer cells can induce nearby normal cells to form blood vessels that supply tumors with oxygen and nutrients, which they need to grow. These blood vessels also remove waste products from tumors.

- Cancer cells are also often able to evade the immune system, a network of organs, tissues, and specialized cells that protects the body from infections and other conditions. Although the immune system normally removes damaged or abnormal cells from the body, some cancer cells are able to "hide" from the immune system.

- Tumors can also use the immune system to stay alive and grow. For example, with the help of certain immune system cells that normally prevent a runaway immune response, cancer cells can actually keep the immune system from killing cancer cells.

How Cancer Arises

- Cancer is caused by certain changes to genes, the basic physical units of inheritance. Genes are arranged in long strands of tightly packed DNA called chromosomes.
- Credit: Terese Winslow

- Cancer is a genetic disease—that is, it is caused by changes to genes that control the way our cells function, especially how they grow and divide.

- Genetic changes that cause cancer can be inherited from our parents. They can also arise during a person's lifetime as a result of errors that occur as cells divide or because of damage to DNA caused by certain environmental exposures. Cancer-causing environmental exposures include substances, such as the chemicals in tobacco smoke, and radiation, such as ultraviolet rays from the sun. (Our Cancer Causes and Prevention section has more information.)

- Each person's cancer has a unique combination of genetic changes. As the cancer continues to grow, additional changes will occur. Even within the same tumor, different cells may have different genetic changes.

Gallstones (Cholelithiasis)

What Are Gallstones?

Gallstones are pieces of solid material that form in your gallbladder, a small organ under your liver. If you have them, you might hear your doctor say you have cholelithiasis.

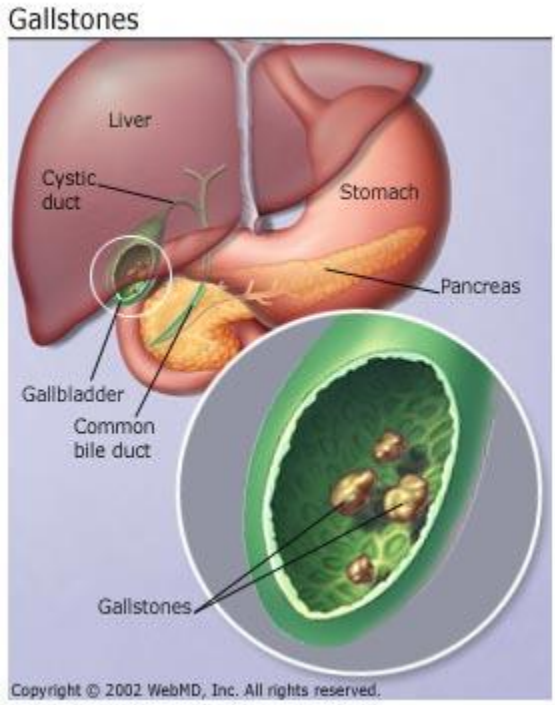
Your gallbladder stores and releases bile, a fluid made in your liver, to help in digestion. Bile also carries wastes like cholesterol and bilirubin, which your body makes when it breaks down red blood cells. These things can form gallstones.

Gallstones can range from the size of a grain of sand to that of a golf ball. You might not know that you have them until they block a bile duct, causing pain that needs treatment right away.

Gallstone Types

The two main kinds of gallstones are:

- **Cholesterol stones.** These are usually yellow-green. They're the most common, making up 80% of gallstones.
- **Pigment stones.** These are smaller and darker. They're made of bilirubin..



Signs and Symptoms of Gallstones

Symptoms may include:

- Pain in your upper belly, often on the right, just under your ribs
- Pain in your right shoulder or back
- An upset stomach
- Vomiting
- Other digestive problems, including indigestion, heartburn, and gas

See your doctor or go to the hospital if you have signs of a serious infection or inflammation:

- Belly pain that lasts several hours
- Fever and chills
- Yellow skin or eyes
- Dark urine and light-colored poop

Causes of Gallstones

Doctors aren’t sure exactly what causes gallstones, but they might happen when:

- **There's too much cholesterol in your bile.** Your body needs bile for digestion. It usually dissolves cholesterol. But when it can't do that, the extra cholesterol might form stones.
- **There's too much bilirubin in your bile.** Conditions like cirrhosis, infections, and blood disorders can cause your liver to make too much bilirubin.
- **Your gallbladder doesn't empty all the way.** This can make your bile very concentrated.

Gallstone Risk Factors

You're more likely to get gallstones if you:

- Have a family history of them
- Are a woman
- Are over age 40
- Are of Native American or Mexican descent
- Are obese
- Have a diet high in fat and cholesterol but low in fiber
- Don't get much exercise
- Use birth control pills or hormone replacement therapy
- Are pregnant
- Have diabetes
- Have an intestinal disease like Crohn's
- Have hemolytic anemia or cirrhosis of the liver
- Take medicine to lower your cholesterol
- Lose a lot of weight in a short time
- Are fasting