With this issue we complete two years of our relationship with you. Trust you enjoyed reading what we enjoyed writing and editing for your consumption. We do hope that our genuine efforts assisted you in your day-to-day clinical practice. We discussed Dengue fever, Malaria, HIV/AIDS, Enteric fever, Hepatitis C, G6PD deficiency and many such issues of current relevance. These diseases were discussed under the heading DISEASE DIAGNOSIS. Our presentation comes under three technical write-ups to you; namely DISEASE DIAGNOSIS, INTERPRETATION and TROUBLE SHOOTING. Under INTERPRETATION we have interpreted many issues of clinical importance starting from trace elements in the first issue and cancer markers in the last issue. Efforts were made to clearly interpret investigations so that various out of the book clinical scenarios could be appropriately interpreted and proper understanding presented to the concerned clinician. TROUBLESHOOTING brought to you ways of eliminating problems while reporting peripheral smears, studying AFBs or conducting coagulation studies. This section confronted you with the various problems faced by the clinical laboratories. It also identified the remedial measures. Implementation of suggested ways would eliminate reports that the clinicians call us “not matching with the clinical picture”. However, clinicians are not always correct and they are not well conversed with the limitations of the procedures that are available to the Laboratarians as on date. Hope you could shoot off a few queries of your referring clinicians and ward off unpalatable situations. Each issue brought a few moments of laughter, a few words of wisdom and a few brainteasers to titillate gray matter. Trust, BOUQUET deepened the sulci / ravines of the brain. The monotony and seriousness of the technical articles was sought to be broken by BOUQUET. This issue follows up Hepatitis C of the previous issue with Hepatitis B. Ways of preventing self contamination/ infection is presented along with Hepatitis B has been known to exist for a long time and the virus is several times more infectious and hardy than the HIV/AIDS virus. Many of the Laboratarians have accidentally been infected while working with samples. The DISEASE DIAGNOSIS section discusses Hepatitis B in all its clinico-diagnostic details along with therapeutic and preventive aspects.

The diagnostic and classification criteria of diabetes mellitus have undergone a sea change of late. Under the INTERPRETATION portfolio we bring to you the very latest diagnostic and classification principles that are in use today as recommended by the World Health Organization. Nobody recommends a Glucose Tolerance Test anymore. Change your ways of diagnosing diabetes mellitus after reading “INTERPRETATION”. Normal Fasting Plasma Sugar level is now 110 mg/dL and PP Plasma sugar level is 140 mg/dL. You do not need a GTT, two fasting plasma glucose levels of over 126 mg/dL or more are sufficient to label a person as a diabetic.

TROUBLE SHOOTING portion outlines the Quality Control/ Assurance aspects of a clinical biochemistry laboratory. Follow the ways recommended and become a conscientious Laboratarian. If everything is followed to the hilt, you should manage accreditation from the concerned departments / organizations. Peep inside, BOUQUET is still very much there. Happy reading!
HEPATITIS B

Introduction
Hepatitis B is an infectious liver disease. It is caused by the hepatitis B virus (HBV). Infections of hepatitis B occur only if the virus is able to enter the bloodstream. To combat the disease, the body has several defenses. White blood cells, which protect the body from infections, attack and destroy the infected liver cells. The body also produces antibodies which circulate in the blood to destroy the virus and protect against future infections of hepatitis B. During the infection and recovery process, the liver may not function normally causing illness that affects the entire body.

For reasons that are not completely understood, 10 percent of people who develop hepatitis B become carriers of the disease. Their blood remains infected for months, years, sometimes for life. Seventy percent of carriers develop chronic persistent hepatitis B. Most do not appear to be ill. The remaining 30 percent of carriers experience continuous liver disease. This condition often progresses to cirrhosis and then, after 30 to 40 years, possibly to liver cancer. At present, there is no way of curing carriers.

Definition
The hepatitis B virus (HBV) is a double-stranded hepatotropic DNA virus belonging to the family Hepadnaviridae. It is a 42 nm spherical particle with a 27 nm diameter, electron-dense, nucleocapsid core and a 7 nm thickness outer lipoprotein envelope. The viral genome is 3.2 kb in length, and possesses 4 partially overlapping open-reading frames that encode various antigens. The virus only infects humans and some other non-human primates. Viral polymerase enzyme that is linked to a single molecule of double-stranded HBV DNA.

Prevalence
Hepatitis B is spread predominantly parenterally, through intimate personal contact, and perinatally. Individuals at risk are intravenous drug users, children of mothers with HBV, men who have sex with men, patients on hemodialysis and those exposed to blood or blood products. Approximately 5% of the world’s population are carriers of HBV, defined as being positive for hepatitis B surface antigen. HBV is endemic in many areas of the world, such as Asia, Micronesia, and sub-Saharan Africa as well as in certain populations in Australia, New Zealand, South America, the Middle East and the Arctic. There are 4 antigenic subtypes of HBV (adw, ayw, adr, ayr), with geographic variation in the distribution of these subtypes, but little clinical significance is associated with infection by these different subtypes.

Transmission
Sexual transmission
You may become infected if you have unprotected vaginal, anal or oral sex with an infected partner whose blood, saliva, semen or vaginal secretions enter your body. You can also become infected from shared sexual devices if they’re not washed or covered with a condom. The virus is present in the secretions of someone who’s infected and enters your body through small tears that can develop in your rectum or vagina during sexual activity.

Transmission through needle sharing
HBV is easily transmitted through needles and syringes contaminated with infected blood. That’s why sharing IV drug paraphernalia puts you at high risk of hepatitis B. Your risk increases if you inject drugs frequently or also engage in high-risk sexual behavior. Although avoiding the use of injected drugs is the most reliable way to prevent infection, you may not choose to do this. If so, one way to reduce your risk is to participate in a needle exchange program in your community. These programs allow you to exchange used needles and syringes for sterile equipment. In addition, consider seeking counseling or treatment for your drug use.

Transmission through accidental needle sticks
Hepatitis B is a concern for health care workers and anyone else who comes in contact with human blood. If you fall into one of these categories, get vaccinated against hepatitis B in addition to following routine precautions when handling needles and other sharp instruments.

Transmission from mother to child
Pregnant women infected with HBV can pass the virus to their babies. If you have hepatitis B, having your baby receive a shot of hepatitis B immune globulin at birth, along with the first in a series of three hepatitis B vaccines, will greatly reduce your baby’s risk of getting the virus. For you to become infected with HBV, infected blood, semen, vaginal secretions or saliva must enter your body.

You can’t become infected through casual contact hugging, dancing or shaking hands with someone who has hepatitis B. You also can’t be infected in any of the following ways:
- Coming into contact with the sweat or tears of someone with HBV
- Sharing a swimming pool, telephone or toilet seat with someone who has the virus
- Donating blood

Anyone of any age, race, nationality, sex or sexual orientation can be infected with HBV. But you’re at greatest risk if you:
- Have unprotected sex with more than one partner. You’re at risk whether you’re heterosexual, homosexual or bisexual. Unprotected sex means having sex without using a new latex or polyurethane condom every time.
- Share needles with someone infected with HBV.
- Have received a diagnosis of a sexually transmitted disease such as gonorrhea or chlamydia.
- Share needles during intravenous (IV) drug use.
- Share a household with someone who has a chronic HBV infection.
- Have a job that exposes you to human blood.
- Received a blood transfusion or blood products before 1970 - the date the blood supply began to be tested for HBV. Today, the risk of contracting HBV per unit of donated blood is approximately one in 250,000. Furthermore, new methods of blood screening promise to make the blood supply even safer.
- Older tests screen donor blood for antibodies substances produced by the immune system in response to invading organisms such as viruses. Nucleic acid testing, on the other hand, screens for the virus itself. This means tiny amounts of the virus can be detected before an antibody response ever occurs in a donor’s immune system.
- Travel to regions with high infection rates of HBV, such as sub-Saharan Africa, Southeast Asia, the Amazon Basin, the Pacific Islands and the Middle East.
- Are an adolescent or young adult residing in correctional facility.

Newborns whose mothers are infected with HBV also are at high risk. The same is true of infants and children whose parents were born in areas where HBV infection is widespread. In many developing countries, the most common method of transmission of the virus is between mother and child or among children living in the same household. In parts of sub-Saharan Africa, Asia and the Pacific, nearly all children are infected. Sometimes you may become infected with HBV even if you have no known risk factors for the disease.

Pathophysiology
The incubation period of HBV ranges from 45 to 160 days (mean = 100 days). The acute illness is usually mild. The risk of developing chronic infection (or the carrier state), defined as the presence of HBsAg in the blood for more than 6 months, is dependent on the age and immune function of the patient. Ninety percent of infected newborns, 30% of children under the age of 5 and 10% of adults progress to chronic infection. Patients with chronic infection will spontaneously clear surface antigen at a rate of 0.5% a year.

Viral and immune markers are detectable in blood and specific antigen-antibody patterns allow us to characterize hepatitis B infection. (Figure 1) The first detectable viral marker is HBsAg followed by HBeAg and HBV DNA. Titers may be high during the incubation period but HBV DNA and HBeAg begin to fall at

...
the onset of illness and may be undetectable at the time of peak clinical illness. Core antigen does not appear in blood but antibody to this antigen (anti-HBc) is detectable with the onset of clinical symptoms. The immunoglobulin M (IgM) fraction is an important diagnostic assay for acute hepatitis B infection. It is detectable at a time between when HBsAg disappears and Anti-HBs appears and for an interval is the only marker of acute infection. This is known as the window period (Figure 1).

Patients who clear the virus lose HBsAg and develop anti-HBsAb. Anti-HBsAb is a long-lasting antibody and is associated with immunity. The presence of anti-HBsAb and anti-HBcAb (IgG) indicates recovery and immunity in a previously infected individual. HBsAg is another viral marker detectable in blood and correlates with active viral replication (Figure 2).

The antigen is synthesized from a strand of DNA immediately preceding the area that codes for the core antigen. A mutation in this area can occur, preventing the production of the HBeAg. Such affected viruses are known as precore mutants. Liver injury in chronic hepatitis B is believed to be immunologically mediated, so the severity and course of disease do not correlate well with the level of virus in serum or the amount of antigen expressed in the liver. Antigen-specific cytotoxic T cells are believed to mediate the cell injury in hepatitis B and account for ultimate viral clearance. Specific cytokines produced by cytotoxic and other T cells also have antiviral effects on hepatocytes, contributing to viral clearance without cell death. The progression of acute to chronic hepatitis B is attributed to the lack of a vigorous cytotoxic T-cell response to hepatitis B antigens. Similarly, spontaneous seroconversion from HBsAg to anti-HBsAb during chronic hepatitis B may also be immunologically mediated, as is suggested from the transient flare of disease that often immediately precedes clearance of HBeAg. Viral factors may also affect outcome: Some HBV strains may be more pathogenic and more likely to lead to chronic infection, because they are less immunogenic or more resistant to T-cell attack.

Signs And Symptoms
Acute hepatitis B infection shares similar clinical and biochemical features with other acute viral hepatitides and a spectrum of severity ranging from asymptomatic, subclinical infection to fulminant, fatal disease. An insidious onset of nausea, anorexia, malaise and fatigue; flu-like symptoms, such as pharyngitis, cough, coryza, photophobia, headache, and myalgias; precedes the onset of jaundice. Fever is uncommon, unlike HAV infection. About 75% of adults have a subclinical infection. Symptoms abate or disappear with the onset of jaundice, although anorexia, malaise, and weakness may persist. Physical examination reveals mild enlargement and slight tenderness of the liver, mild splenomegaly, and posterior cervical lymphadenopathy in 15% to 20% of patients. Fulminant disease (acute liver failure) presents as a change in mental status (encephalopathy) and coagulopathy. Arthritis is a common extrahepatic manifestation of chronic hepatitis B. Mucocutaneous vasculitis, glomerulonephritis, and polyarteritis nodosa are less common. The glomerulonephritis of hepatitis B occurs more commonly in children than adults and is usually characterized by nephrotic syndrome with little decrease in renal function. Polymyositis nodosa occurs primarily in adults and is marked by a sudden and severe onset of hypertension, renal disease, and systemic vasculitis with arteritis in the vessels of the kidney, gallbladder, intestine, or brain. Other rare extrahepatic manifestations are mixed essential cryoglobulinemia, periarteritis and pancreatitis.

Diagnosis
Understanding the hepatitis B virus structure and the antibody response the virus evokes is crucial in diagnosing patients with HBV infection. This is discussed, in part, under pathophysiology. Antibody-antigen patterns allow us to determine if infection has occurred, whether chronic or acute disease is present, if immunity has developed and the nature of the illness in those chronically infected (Figure 1 & 2). Detecting HBsAg and IgM core antibody, or core antibody alone in blood and correlates with active viral replication. The transaminase increase persists at levels between 1 and 10 times the upper limit of normal in chronic infection. In acute infection, serum bilirubin level seldom increases above 10 mg/dL, alkaline phosphatase and prothrombin time are usually normal or mildly elevated (1-3 seconds) and serum albumin is normal or minimally depressed. Peripheral blood counts may show mild leukopenia with or without relative lymphocytosis.

Complications
Having a chronic HBV infection eventually may lead to serious liver diseases such as cirrhosis, liver failure and liver cancer. Having had HBV infection as an infant or child gives you a greater chance of developing these illnesses as an adult. Cirrhosis causes permanent scarring of the liver. It can also lead to a number of other complications, including esophageal bleeding and severe fluid retention in the abdomen (ascites). Toxins that accumulate in the blood can affect mental functioning, leading to confusion and even coma (hepatic encephalopathy). Hepatitis B-related acute liver failure - a condition in which all the vital functions of the liver shut down can be responsible for mortality. When that occurs, a liver transplant is necessary to sustain life.

The risk of chronic infection and death from cirrhosis, liver failure and liver cancer varies with the age at which infection with HBV occurs. People who become chronically infected later in life have a 15 percent chance of dying of liver disease, while those chronically infected as infants and children have a 25 percent chance of dying of cirrhosis or liver cancer.

Anyone chronically infected with HBV is also susceptible to infection with another strain of viral hepatitis-B virus. Formerly known as delta virus, the hepatitis D virus needs the outside coat of HBV in order to infect cells. You can't become infected with hepatitis D unless you're already infected with HBV.

Injection drug users with hepatitis B are most at risk, but you can also contract hepatitis D if you have unprotected sexual contact with an infected partner or live with someone infected with hepatitis B. Having both hepatitis B and hepatitis D makes it more likely you'll develop cirrhosis or liver cancer.

Outcome And Natural History
The course of acute hepatitis B is typically self-limited. Symptoms are mild and non-specific, and jaundice is rare. Indeed, the appearance of jaundice during the course of acute infection is highly predictive of eventual recovery. Fulminant disease with liver failure is an unusual complication. Factors associated with a severe outcome include advanced age, female sex, and perhaps some strains of virus. In chronic hepatitis, serum ALT levels fall after the acute phase of infection but persist at levels ranging from 1 to 10 times the upper limit of normal. Levels of HBV DNA are usually in the range of 107 to 1011 genome copies/mL; levels readily...
detectable by hybridization techniques. Spontaneous loss of HBeAg occurs at a rate of 8% to 12% per year, associated with a decrease in HBV DNA below levels detected by hybridization techniques, normalization of transaminases and a decrease in necro-inflammatory changes in the liver (the inactive carrier state). Loss of HBeAg occurs less frequently (1% per year).

The course of chronic hepatitis B is variable. Chronic carriers without active liver disease or viral replication (healthy carriers) generally have a benign course with very little chance of progressing to cirrhosis. Patients who continue to have active viral replication with high levels of HBV DNA and HBeAg in serum have progressive liver injury, and cirrhosis and end-stage liver disease may develop. A transient flare of disease often precedes remission. Loss of HBeAg is not always followed by permanent resolution of disease and disease flares may occur. Patients with hepatitis B should avoid immunosuppressive medications if possible. Chronic hepatitis B is still an important cause of cirrhosis and liver cancer. Chronic HBV infection is associated with a 10-fold increase in the incidence of cancer. Chronic HBV infection is associated with a 10-fold increase in the risk of developing hepatocellular carcinoma (HCC). Older males with cirrhosis and coinfection with hepatitis C are at greatest risk. The mechanism of oncogenesis is unknown. In regions where HBV is endemic, HCC is the leading cause of cancer-related deaths. HBV carriers, particularly those at highest risk should be screened, probably every 6 months, for HCC, with ultrasound and alpha-fetoprotein.

**Treatment**

If you know you've been exposed to HBV, call your doctor immediately. Receiving an injection of hepatitis B immune globulin within 24 hours of coming in contact with the virus may help protect you from developing hepatitis B. You should also receive the first in a series of three shots of the hepatitis B vaccine.

Once you've developed chronic hepatitis B, few treatment options exist. In some cases, especially if you don't have signs and symptoms or liver damage, your doctor may suggest monitoring, rather than treating, your condition. In other cases, your doctor may recommend treatment with antiviral medications. When liver damage is severe, liver transplantation may be the only option.

**Drug therapies**

Clinicians use three drugs to treat chronic HBV infection:
- Interferon
- Lamivudine (Epivir) T
- Adefovir dipivoxil (Hepsera) T

**Liver transplant**

When your liver has been severely damaged, a liver transplant may be an option. The encouraging news is that these transplants are increasingly successful. Today, more than 90 percent of people who have this procedure are alive a year later. Unfortunately, not enough donor organs are available for everyone who needs a transplant.

**How can the spread of hepatitis B be prevented in the workplace?**

The risk of hepatitis B can be significantly reduced by:
- Implementing infection control guidelines suitable for the specific workplace.
- Immunizing workers at risk.

**Infection Control**

Infection control precautions are the first line of defense to protect workers from hepatitis B and other blood-borne diseases. For this reason, the Laboratory Centre for Disease Control at Health Canada and the United States Department of Health and Human Services have developed a uniform approach called "universal precautions."

Originally developed for hospitals, universal precautions have been adapted to a wide range of workplaces. They apply to all situations where workers have risk of exposure to blood or certain body fluids.

The purpose of universal precautions is to prevent exposure to blood-borne diseases transmitted by needlestick accidents or fluid contact with an open wound, non-intact skin, or mucous membranes. Universal precautions are to be used in conjunction with other control measures. An example is washing hands whenever gloves are removed or whenever the skin contacts potentially infectious fluids.

Universal precautions recommend the use of engineering controls, safe work practices, and personal protective equipment to suit the specific task and workplace.

Engineering controls include the use of equipment to isolate or contain the hazard, such as puncture-resistant containers for disposing of used sharps, or biological cabinets for certain procedures in laboratories.

Safe work practices are required for all tasks involving possible exposure to blood or certain body fluids. They include:
- Safe collection of fluids and tissues for disposal in accordance with local and national regulations
- Safe removal and disposal or decontamination of protective clothing and equipment
- Procedures to follow in the event of spills or personal exposures such as needlestick injuries
- Specific and detailed procedures to observe when using and disposing of needles and other sharp objects

**Personal protective equipment**

Provides a barrier to blood and certain body fluids.

**Equipment recommended:**
- Gloves to protect the hands and skin
- Masks and eye protection to protect from splashes of blood or body fluids
- Aprons to protect clothing from splashes with blood, or gowns if large quantities of blood are present or anticipated

**Specific universal precautions have been developed for:**
- Health care workers
- Emergency personnel, firefighters, and police
- Laboratory personnel
- Pathology personnel
- Dentists and dental assistants
- Workers in correctional institutions
- People required to perform CPR
- Embalmers and morgue attendants

**Immunization**

Two recombinant DNA hepatitis B vaccines are available. Both provide safe, reliable protection from hepatitis B when used either before or immediately after exposure to the virus. Tests show 90 to 95 percent of vaccinations of healthy people result in the development of resistance against hepatitis B. At present, vaccination is the surest way to avoid acquiring hepatitis B as an occupational disease.

**Immunization Before Contact**

International medical fraternity recommends the vaccination of people who are at increased risk of contracting hepatitis B because of exposure to the virus in their work. They also recommend vaccination for people who are sexual or household contacts of carriers of hepatitis B.

Since the risk varies from workplace to workplace, institutions should review their situations and develop their own vaccination priorities. Hospital employees who have no contact with blood, blood products, or blood-contaminated body fluids and who are not at risk of needlestick injuries, are at no greater risk of hepatitis B than the general population.

**Immunization After Contact**

Workers who experience needlestick injuries, splash exposures to blood from carriers, or bite injuries should immediately seek medical attention.

If the blood is known to contain the hepatitis B virus, and the exposed worker has not been vaccinated or does not have antibodies against hepatitis B, post-exposure immunization is strongly recommended to prevent the development of hepatitis B.

International immunization guidelines recommend post-exposure vaccination when the source of blood is unknown. Vaccination against Hepatitis B is usually recommended within seven days of exposure. Depending on the specific circumstance, hepatitis B immunoglobulin is sometimes recommended also.

**For Routine Diagnostic Purposes the Rapid Immunochromatographic and Visual ELISA Formats are Often Enough. For Detailed Investigations Complete Hepatitis B Profile Tests Are Available in Various Immunological Formats.**
Change the Classification System

The new classification system identifies four types of diabetes mellitus: type 1, type 2, "other specific types" and gestational diabetes. Arabic numerals are specifically used in the new system to minimize the occasional confusion of type "I" as the number "11." Each of the types of diabetes mellitus identified extends across a clinical continuum of hyperglycemia and insulin requirements.

Type 1 diabetes mellitus (formerly called type I, IDDM or juvenile diabetes) is characterized by beta cell destruction caused by an autoimmune process, usually leading to absolute insulin deficiency. The onset is usually acute, developing over a period of a few days to weeks. Over 95 percent of persons with type 1 diabetes mellitus develop the disease before the age of 25, with an equal incidence in both sexes and an increased prevalence in the white population. A family history of type 1 diabetes mellitus, gluten enteropathy (celiac disease) or other endocrine disease is often found. Most of these patients have the "immune-mediated form" of type 1 diabetes mellitus with islet cell antibodies and often have other autoimmune disorders such as Hashimoto's thyroiditis, Addison's disease, vitiligo or pernicious anemia. A few patients, usually those of African or Asian origin, have no antibodies but have a similar clinical presentation; consequently, they are included in this classification and their disease is called the "idiopathic form" of type 1 diabetes mellitus.

Type 2 diabetes mellitus (formerly called NIDDM, type II or adult-onset) is characterized by insulin resistance in peripheral tissue and an insulin secretory defect of the beta cell. This is the most common form of diabetes mellitus and is highly associated with a family history of diabetes, older age, obesity and lack of exercise. It is more common in women, especially women with a history of gestational diabetes. Insulin resistance and hyperinsulinemia eventually lead to impaired glucose tolerance. Defective beta cells become exhausted, further fueling the cycle of glucose intolerance and hyperglycemia. The etiology of type 2 diabetes mellitus is multifactorial and probably genetically based, but it also has strong behavioural components.

The etiologic classifications of diabetes mellitus are listed in Table 1 on the next page. Types of diabetes mellitus of various known etiologies are grouped together to form the classification called "other specific types." This group includes persons with genetic defects of beta-cell function (this type of diabetes was formerly called MODY) or maturity-onset diabetes in youth) or with defects of insulin action; persons with diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; persons with dysfunction associated with other endocrinopathies (e.g., acromegaly); and persons with pancreatic dysfunction caused by drugs, chemicals or infections.

The definition and diagnosis of gestational diabetes mellitus was not altered in these new recommendations. Gestational diabetes mellitus is an operational classification (rather than a pathophysiologic condition) identifying women who develop diabetes mellitus during gestation. (Women with diabetes mellitus before pregnancy are said to have "pregestational diabetes" and are not included in this group.) Women who develop type 1 diabetes mellitus during pregnancy and women with undiagnosed asymptomatic type 2 diabetes mellitus that is discovered during pregnancy are classified with gestational diabetes mellitus. However, most women classified with gestational diabetes mellitus have normal glucose homeostasis during the first half of the pregnancy and develop a relative insulin deficiency during the last half of the pregnancy, leading to hyperglycemia. The hyperglycemia resolves in most women after delivery but places them at increased risk of developing type 2 diabetes mellitus later in life.

New Diagnostic Criteria for Diabetes Mellitus

The new diagnostic criteria for diabetes mellitus have been greatly simplified (Table 2). The oral glucose tolerance test previously recommended by the National (American) Diabetes Data Group has been replaced with the recommendation that the diagnosis of diabetes mellitus be based on two fasting plasma glucose levels of 126 mg per dL (7.0 mmol per L) or higher.
**TABLE 1**

**Etiologic Classifications of Diabetes Mellitus**

<table>
<thead>
<tr>
<th>Infections</th>
<th>Congenital rubella</th>
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<tbody>
<tr>
<td></td>
<td>Cytoomegalovirus</td>
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<tr>
<td>Other specific types</td>
<td>Others</td>
</tr>
<tr>
<td>Genetic defects of beta-cell function</td>
<td></td>
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<tr>
<td>Genetic defects in insulin action</td>
<td></td>
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<tr>
<td>Diseases of the exocrine pancreas</td>
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<tr>
<td>Pancreatitis</td>
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<tr>
<td>Trauma/pancreatectomy</td>
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<td>Neoplasia</td>
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<tr>
<td>Cystic fibrosis</td>
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<tr>
<td>Hemochromatosis</td>
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<tr>
<td>Others</td>
<td></td>
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<tr>
<td>Endocrinopathies</td>
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<tr>
<td>Acromegaly</td>
<td></td>
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<td>Cushion's syndrome</td>
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<tr>
<td>Glucocorticoids</td>
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<tr>
<td>Pheochromocytoma</td>
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<tr>
<td>Hyperthyroidism</td>
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<td>Somatostatinoma</td>
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<tr>
<td>Albosteronoma</td>
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<tr>
<td>Others</td>
<td></td>
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<tr>
<td>Drug- or chemical-induced</td>
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<tr>
<td>Venor</td>
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<tr>
<td>Pentamidine</td>
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<td>Nicotinic acid</td>
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<tr>
<td>Glucocorticoids</td>
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<td>Thyroid hormone</td>
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<td>Diazoxide</td>
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<tr>
<td>Beta-adrenergic antagonists</td>
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<tr>
<td>Thiazides</td>
<td></td>
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<tr>
<td>Phenytoin</td>
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</table>

**TABLE 2**

**CRITERIA FOR THE DIAGNOSIS OF DIABETES MELLITUS AND IMPAIRED GLUCOSE HOMEOSTASIS**

<table>
<thead>
<tr>
<th>Diabetes Mellitus</th>
<th>Positive findings from any two of the following tests on different days:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a) Symptoms of diabetes mellitus* plus casual† plasma glucose concentration 200 mg per dL (11.1 mmol per L) or</td>
</tr>
<tr>
<td></td>
<td>b) FPG 126 mg per dL (7.0 mmol per L) or</td>
</tr>
<tr>
<td></td>
<td>c) 2 hr PPG 200 mg per dL (11.1 mmol per L after a 75-g glucose load)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Impaired Glucose Homeostasis</th>
<th>a) Impaired fasting glucose:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FPG from 110 to &lt;126 (6.1 to 7.0 mmol per L)</td>
</tr>
<tr>
<td></td>
<td>b) Impaired glucose tolerance:</td>
</tr>
<tr>
<td></td>
<td>2 hr PPG from 140 to &lt;200 (7.75 to &lt;11.1 mmol per L)</td>
</tr>
<tr>
<td></td>
<td>c) Normal</td>
</tr>
<tr>
<td></td>
<td>FPG &lt;110 mg per dL (6.1 mmol per L)</td>
</tr>
<tr>
<td></td>
<td>2 hr PPG &lt;140 mg per dL (7.75 mmol per L)</td>
</tr>
</tbody>
</table>

↑Casual is defined as any time of day without regard to time since last meal.
*--Symptoms include polyuria, polydipsia or unexplained weight loss.
†--Casual is defined as any time of day without regard to time since last meal.

**Other options for diagnosis include two 2-hour postprandial plasma glucose (2 hr PPG) readings of 200 mg per dL (11.1 mmol per L) or higher after a glucose load of 75 g (essentially, the criterion recommended by WHO) or two casual glucose readings of 200 mg per dL (11.1 mmol per L) or higher. Measurement of the fasting plasma glucose level is the preferred diagnostic test, but any combination of two abnormal test results can be used. Fasting plasma glucose was selected as the primary diagnostic test because it predicts adverse outcomes (e.g., retinopathy) as well as the 2 hr PPG test but is much more reproducible than the oral glucose tolerance test or the 2 hr PPG test and easier to perform in a clinical setting.**

The choice of the new cutoff point for fasting plasma glucose levels is based on strong evidence from a number of populations linking the risk of various complications to the glycemic status of the patient. As per the study on the risk of diabetic retinopathy based on the glycemic status of 40- to 74-year-old participants in the National Health and Nutritional Epidemiologic Survey (NHANES III) the risk of retinopathy greatly increases when the patient’s fasting plasma glucose level is higher than 109 to 116 mg per dL (6.05 to 6.45 mmol per L) or when the result of a 2 hr PPG test is higher than 150 to 180 mg per dL (8.3 to 10.0 mmol per L). However, the committee decided to maintain the cutoff point for the 2 hr PPG test at 200 mg per dL (11.1 mmol per L) because so much literature has already been published using this criterion. They selected a cutoff point for fasting plasma glucose of 126 mg per dL (7.0 mmol per L) or higher. This point corresponded best with the 2 hr PPG level of 200 mg per dL (11.1 mmol per L). The risk of other complications also increases dramatically at the same cutoff points.

A normal fasting plasma glucose level is less than 110 mg per dL (6.1 mmol per L) and normal 2 hr PPG levels are less than 140 mg per dL (7.75 mmol per L). Blood glucose levels above the normal level but below the criterion established for diabetes mellitus indicate impaired glucose homeostasis. Persons with fasting plasma glucose levels ranging from 110 to 126 mg per dL (6.1 to 7.0 mmol per L) are said to have impaired fasting glucose, while those with a 2hr PPG level between 140 mg per dL (7.75 mmol per L) and 200 mg per dL (11.1 mmol per L) are said to have impaired glucose tolerance. Both impaired fasting glucose and impaired glucose tolerance are associated with an increased risk of developing type 2 diabetes mellitus. Lifestyle changes, such as weight loss and exercise, are warranted in these patients. The committee chose not to address the current controversies surrounding the diagnosis of gestational diabetes mellitus and did not alter the diagnostic criteria in this area. Screening for gestational diabetes mellitus is generally accomplished with administration of a 50-g glucose load one hour before determining a plasma glucose level. A positive screen (defined as a plasma glucose level of 140 mg per dL [7.75 mmol per L] or higher) should prompt a diagnostic test: fasting plasma glucose levels should be measured after a 100-g glucose load at baseline and at one, two and three hours after the glucose load. Two of the four values must be abnormal (105 mg per dL [5.8 mmol per L] or higher; 190 mg per dL [10.5 mmol per L] or higher; 165 mg per dL [9.15 mmol per L] or higher; and 145 mg per dL [8.05 mmol per L] or higher) for a patient to be diagnosed with gestational diabetes mellitus. The WHO criteria use a glucose load of 75 g with a test two hours after the glucose load, using the same criterion for the diagnosis of gestational diabetes mellitus.

**Glycated Hemoglobin**

Measurements of glycated hemoglobin have commonly been used to monitor the glycemic control of persons already diagnosed with diabetes mellitus. Measurements of this hemoglobin, also called glycosylated hemoglobin, glycocromoglobin, hemoglobin A₁c, or hemoglobin A₁, are in the evaluation of the stable linkage of glucose to minor hemoglobin components. There is currently no agreement on standardization, so a variety of measurement methods and normal ranges are being used. Some experts argue that a glycated hemoglobin test could be used for the diagnosis of diabetes mellitus. Glycated hemoglobin levels are as highly correlated to adverse clinical outcomes (e.g., retinopathy) as are fasting plasma glucose or postprandial plasma glucose levels and are as reproducible as fasting plasma glucose levels. The major advantage of measuring glycated hemoglobin is that the specimen can be collected without regard to when the patient last ate.

(... To be continued)
In Lighter Vein

Dad, can you write in the dark?"

"I think so. What is it you want me to write?"

"Your name on this report card."

A little girl came home from school and said to her mother, "Mommy, today in school I was punished for something that I didn't do."

The mother exclaimed, "But that's terrible! I'm going to have a talk with your teacher about this . . . by the way, what was it that you didn't do?"

The little girl replied, "My homework."

A teacher was having trouble teaching arithmetic to one little boy. So she said, "If you reached in your right pocket and found a nickel, and you reached in your left pocket and found another one, what would you have?"

"Somebody else's pants."

Teacher: "Sam, what is the outside of a tree called?"

Sam: "I don't know."

Teacher: "Bark, Sam, bark."

Sam: "Bow, wow, wow!"

The teacher came up with a good problem. "Suppose, " she asked the second-graders, "there were a dozen sheep and six of them jumped over a fence. How many would be left?"

"None," answered little Norman.

"None? Norman, you don't know your arithmetic."

"Teacher, you don't know your sheep. When one goes, they all go!"

Wisdom Whispers

If I speak in the tongues of men and of angels, but have not love, I am only resounding gong or a clanging cymbal.

If I have the gift of prophecy and can fathom all mysteries and all knowledge, and if I have a faith that can move mountains, but have not love, I am nothing.

If I give all I possess to the poor and surrender my body to the flames, but have not love, I gain nothing.

Love is patient, love is kind. It does not envy, it does not boast, it is not proud.

Love does not delight in evil but rejoices with the truth.

Love always protects, always trusts, always hopes, always perseveres.

Love never fails. But where there are prophecies, they will cease; where there are tongues, they will be stilled; where there is knowledge, it will pass away.

Brain Teasers

1. An increase of what amount of blood urea indicates acute renal failure?
   A. > 20 mg/dL
   B. > 40 mg/dL
   C. > 60 mg/dL
   D. > 100 mg/dL

2. What is the upper normal level of CA19-9 in blood in U/mL?
   A. 20 B. 37 C. 60 D. 100

3. What is the upper critical level of total calcium for human beings in mg/dL?
   A. 10 B. 12 C. 14 D. 16

4. Which of the following constituents has the highest concentration in a normal CSF?
   A. Albumin B. Beta Globulin C. Alpha globulins D. Prealbumin
Tulip Group offers the latest range in Biochemistry instruments

As discussed in the last issue, the Instrumentation Division of Tulip Group of Companies is on an expansion spree. Evolving, Developing, Upgrading techniques and Keeping up with the latest in the market is the focus of the Tulip Instrumentation Division.

Moving ahead with this trend, Tulip Group has recently launched the latest brand in the range of semiautomatic Clinical Chemistry Analysers

2000 Evolution

Simple and user friendly, both the analysers are facilitated to give accurate estimation of enzymes, substrates, metabolites, electrolytes, trace elements, plasma protein and immunoglobins. Another advantage is that the analysers can be operated on wide range of operational modes such as Absorbance, Endpoint, Kinetic, Fixed time kinetic, Multistandard and Differential and are coupled individually with built in thermal printer for direct print out of results.

3000 Evolution has an additional advantage of the flow cell operating system. And most importantly both 2000 Evolution & 3000 Evolution are CE certified. A complete Clinical Chemistry Analyser!

Salient Features

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<th>2000 Evolution</th>
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<tr>
<td>90 programming locations</td>
<td>120 programming locations</td>
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<td>Automatic microcontroller based filter selection</td>
<td>Life long iodine lamp 12V, 5W</td>
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<td>Long life iodine lamp 12V, 5W</td>
<td>LCD backlit display</td>
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<td>LCD backlit display</td>
<td>Low reagent consumption - 500 µl</td>
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<td>Facility to store K Factor</td>
<td>Facility to store K Factor and blank</td>
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<td>Display of results on screen</td>
<td>On line real time graph for all kinetic tests</td>
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<tr>
<td>Built-in 10 position dry block incubator for both square and round cuvettes</td>
<td>Facility to print patient name and ID</td>
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<td>Acoustic signalling of erroneous entries</td>
<td>Built-in, 10 position dry block incubator for both square and round cuvettes</td>
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<td>120 programming locations</td>
<td>400 Test result memory</td>
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<td>Life long iodine lamp 12V, 20W with lamp save facility</td>
<td>Easy programmable software</td>
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<td>7 filter with one optional free position</td>
<td>400 Test result memory</td>
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<td>18 µl Flowcell low reagent consumption</td>
<td>Compact Chemistry Analyser with Printer</td>
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Follow the Evolution, Follow the Progress