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The Crux

BIMONTHLY FORUM FOR THE LABORATARIANS

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Editorial

The Crux has served its purpose more than adequately. We are a proud team and a proud company to have initiated an interesting CME plan that has been appreciated even far beyond the borders of its country of birth - INDIA. “Made in India” is a symbol that now inherently commands respect and tremendous following.
The INDIAN sun never sets. What's more you don't have to leave your premises to be able to participate in this novel exercise. We reach your doorstep. Thanks for being with us thus far. With every issue we have to keep on significantly increasing the print order. We'll do whatever it takes to serve you as we have always done with a sincere heart and intentions.

Though a little expensive, neonatal screening protocol to a great extent reduces morbidity and mortality in affected children. As they say - catch them young! To be more specific - catch when born! Many nations have made it mandatory and almost all newborns are assessed for the usual neonatal diseases prevalent in that area and the race. These disorders being genetic or God given, there is nothing much that we can do at this juncture but by taking proper precautions (dietary or otherwise) we can definitely ease their pain and provide them a relatively prolonged and healthy life.
If parental screening or ante-natal screening are conducted, many of these disorders can be totally eliminated. Gene therapies are still a little while away, it has been successfully tried in cases of cystic fibrosis. Though still in infancy, these therapeutic modalities are just around the corner and waiting in the wings to take off. The spillover of INTERPRETATION portion from the last edition has been continued.

The DISEASE DIAGNOSIS segment of the issue brings to you Infectious Mononucleosis, a disease that we all suffer from (clinical or sub-clinical) at some stage of our lives. Caused by Epstein-Barr virus, IM is usually a benign disease but sometimes can have a fatal outcome.
All clinico-diagnostic aspects are discussed in ample detail. The risk of clinical complications is rather long and must be kept in mind. A detailed understanding of EBV serologic studies is appended too.

TROUBLE SHOOTING brings to the fore the importance of specimen quality . How certain sample deteriorations can affect quality of analyses is revealed. A relatively common problem that is often overlooked.

The BOUQUET has embraced haematology as its brain teaser for the issue. Rest is same but enticingly different.

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DISEASE DIAGNOSIS

INFECTIOUS MONONUCLEOSIS

DESCRIPTION
- Viral illness caused by Epstein-Barr virus (EBV), affecting mainly adolescents and young adults
- Characterized by classic clinical triad of lymphadenopathy, fever, and sore throat, occasionally with exudates. Malaise, splenomegaly, and occasionally a maculopapular rash also occur
- Relative and absolute lymphocytosis, atypical lymphocytes present. Acute course is prolonged, lasting up to 4 weeks, with full recovery taking several months.

SYNONYMS
- Glandular fever, Epstein-Barr virus infection, EBV infection
- Popular terms: 'kissing disease', 'mono'

CLINICAL ALERT
- If splenic rupture is suspected or rupture appears to be imminent, the patient should have urgent vascular access established and an immediate splenectomy should be considered
- If airway obstruction is threatened, corticosteroids are indicated and immediate intubation or tracheotomy may be needed.

CLINICAL HALLMARKS
- Viral illness caused by primary infection with Epstein-Barr virus (EBV), affecting mainly adolescents and young adults
- Characterized by classic triad of lymphadenopathy, fever, and sore throat; sometimes accompanied by malaise, splenomegaly, a maculopapular rash
- Relative and absolute lymphocytosis, atypical lymphocytes present, and diagnosis often made by heterophile antibody
- Despite a prolonged acute course lasting up to 4 weeks, with full recovery taking several months, most subjects fully recover from primary EBV infection with supportive care only.

CARDINAL FEATURES
- Characterized by classic clinical triad of lymphadenopathy, fever, and sore throat, occasionally with exudates
- Malaise, splenomegaly, and occasionally a maculopapular rash also occur
- Afflicts mainly adolescents and young adults
- Primarily lymphoreticular involvement
- Involvement of hematologic, pulmonary, cardiovascular, and central nervous systems also possible
- Relative and absolute lymphocytosis
- Positive heterophile agglutination test
- Specific serology for Epstein-Barr virus: Epstein-Barr nuclear, early antigen, and viral capsid antigen useful when serologic confirmation necessary
- Atypical large lymphocytes in blood smear
- Incubation period of 2-8 weeks
- Acute course lasts 2-4 weeks
- Full recovery can take several months

CAUSES
Common causes Epstein-Barr virus, a double-stranded DNA virus of the herpes virus family, transmitted primarily in saliva through oral contact.

Rare causes Transmission through sharing of food or drink, through blood transfusions, and through transplants of bone marrow.

Contributory or predisposing factors Seronegative status, immunosuppressive conditions or drugs, Possibly communal living, e.g. in camps, college dormitories etc.

EPIDEMIOLOGY
Incidence
- Incidence in general population is approx. 50/100,000/year
- Incidence in most vulnerable populations (adolescents and young adults) can be up to 100 times greater

Prevalence
This is a common viral infection, and the virus has a latent phase of infection lasting the life of the patient. Therefore the disease is highly prevalent in adult populations throughout the world.

Frequency
Increases gradually over first two decades of life; 85-90% of adults are seropositive.

Demographics
Age
- Most symptomatic cases occur between 15 and 30 years of age
- Epstein-Barr virus infection in young children is usually asymptomatic
- Infectious mononucleosis in those >35 years of age is rare, typically more severe, and characterized by different presenting symptoms

Gender
- Incidence is roughly equal in males and females
- Peak incidence occurs about 2 years earlier in females than in males

Race
Although striking differences in incidence of infectious mononucleosis are sometimes observed, no differences in rate of Epstein-Barr virus infection exist. Racial differences observed are, therefore, believed to be related to earlier, asymptomatic infection in lower socioeconomic groups.

Genetics
Individuals who suffer from a rare X-linked genetic lymphoproliferative disease called Duncan's syndrome are especially susceptible to developing severe infectious mononucleosis complications, with a survival rate of only 50%.

Geography
Infectious mononucleosis has a much higher incidence in developed countries. Infection with Epstein-Barr virus, however, is universal. Observed differences in disease incidence are believed to be related to earlier, asymptomatic infection in lower socioeconomic groups.

Socioeconomic status
- Lower socioeconomic groups have much lower rates of clinical disease since up to 85% of this population, owing to poor hygiene and more crowded living conditions, have seroconverted asymptomatically) by 4 years of age
- Occupational differences in disease incidence have been observed; but these are believed to be the result of socioeconomic factors.

CLINICAL PRESENTATION
Infectious mononucleosis is characterized by the classic triad of lymphadenopathy, fever, and sore throat

Symptoms
Severity of symptoms is variable, in general, young patients have mild or inapparent infection whereas older patients have more severe symptoms
Prolonged malaise, which may recur for several months
Prolonged and pronounced fatigue, which may recur for several months
High fever, usually peaking in afternoon, which lasts a few days and then Improves but can recur for up to 3 weeks
Pronounced sore throat, often described as the worst in patient's experience
Rash rarely occurs but can be macular, petechial, scarlatiniform, urticarial, or erythema multiforme
Anorexia, beginning early in illness, with or without loss of taste for cigarettes
Myalgia, beginning early in illness
Abdominal pain occurs rarely and is usually an indication of possible splenic rupture

Signs
Lymphadenopathy, with posterior cervical nodes most common submandibular and anterior cervical nodes are frequent; axillary and inguinal nodes may also occasionally occur
Erythematous pharyngitis and tonsillitis, with mucopurulent exudates on tonsils and soft palate. Tonsils occasionally so enlarged as to meet at midline ('kissing tonsils')
Splenomegaly, with tenderness in upper left quadrant, which peaks about 7 days into illness
Hepatomegaly, with tenderness over liver common
Fever is often higher during the first days of illness, then becomes low-grade or resolves over the following 2 weeks

Petechiae on palate, multiple lesions approx. 1-2 mm, seen at junction of throat and soft palate
Periorbital edema occurs occasionally
Jaundice occurs rarely
Immune-mediated thrombocytopenia or hemolytic anemia may occur
A variety of neurologic syndromes may occur (meningoencephalitis, cranial neuropathy - Bell's palsy)

ASSOCIATED DISORDERS

Infectious mononucleosis may be accompanied by streptococcal pharyngitis.
Epstein-Barr virus infection is associated with certain malignant disorders.
Burkitt's lymphoma, prevalent in Africa, also associated with malaria infection.
X-linked lymphoproliferative syndrome in susceptible families.
Nasopharyngeal cancer, prevalent in some parts of Asia.
Epstein-Barr virus-associated lymphoproliferative syndrome in bone marrow or organ transplant recipients.

DIFFERENTIAL DIAGNOSIS

- Streptococcal pharyngitis
- Cytomegalovirus mononucleosis
- Pharyngitis and tonsillitis
- Toxoplasmosis
- Rubella
- Diphtheria
- Lymphoma, leukemia
- Acute retroviral syndrome
- Mycoplasma infection
- Carbamazepine hypersensitivity
- Viral hepatitis A and B
- Human herpes virus 6 (HHV-6)

WORKUP

Diagnostic decision

- In adolescents or young adults, a prolonged fever, accompanied by exudative pharyngitis that does not respond to treatment; by marked lymphadenopathy; and possibly by splenomegaly and/or hepatomegaly, jaundice, and a transient erythematous maculopapular rash, indicate a likely diagnosis of infectious mononucleosis.
- In patients over 35 years of age, a prolonged fever with hepatomegaly and elevated liver enzymes, with or without lymphadenopathy, pharyngitis, or rash indicates a diagnosis of infectious mononucleosis
- Acute EBV infection should also be considered in cases of autoimmune haemolytic anemia, immune-mediated thrombocytopenia, aseptic meningitis/encephalitis etc.

Never miss!

- Epstein-Barr virus may be a very serious disease in immunocompromised patients. Epstein-Barr virus-induced lymphoproliferative syndrome, oral hairy leukoplakia, lymphomas 'runaway acute mononucleosis', and Epstein-Barr virus associated hemophagocytic syndrome may occur from infections in immunocompromised patients.
  While fatalities from mononucleosis are rare, they do occur. The most common causes of mortality are neurologic complications, splenic rupture, airway closure, and hematologic complications (severe thrombocytopenia). These complications of infection require immediate intervention when possible
  Severe acute mononucleosis occasionally occurs in older adults. This is often not considered in older adults since mononucleosis is usually a disease of children and adolescents.

INVESTIGATIONS

1) Complete blood count (CBC) with differential

Normal

Atypical lymphocytes absent
Relative lymphocyte percentage: 15-40%
Absolute lymphocyte count: 800-2200/mm^3

Abnormal

Keep in mind the possibility of false-positive results: atypical lymphocytes are seen in a variety of systemic viral illnesses; reactive lymphocytes can be confused with lymphoblasts
Atypical lymphocytes as high as 90% may occur
Absolute lymphocytosis as high as 50,000 leukocytes/mm^3
Relative lymphocytosis as high as 70%

Cause of abnormal result

Infectious mononucleosis.

Medications, disorders and other factors that may alter results: Multiple other causes: cytomegalovirus, HHV-6, rubella, hepatitis, toxoplasmosis, others.

2) Heterophile antibody test

Advantage

Rapid, inexpensive

Disadvantages:

Not always accurate, some false-positive results

- Antibodies may not be detectable until 2-3 weeks into illness Antibodies not usually detectable in young children
- Antibodies last for months or even lifelong, so does not prove acute infection
- Antibody titer does not correlate with severity of illness
- Normal result may be misleading in immunocompromised patients.

Normal

No heterophile antibodies present.

Abnormal

Heterophile antibodies present (Keep in mind the possibility of a false-negative or false-positive result)

Cause of abnormal result

Infectious mononucleosis.

Medications, disorders and other factors that may alter results: Immunocompromised patients may not produce antibodies even when suffering from disease.

3) Rapid streptococcal antigen test

Throat swab.

Advantage

Rapid, inexpensive

Disadvantage:

Not always accurate, false-negative results possible

Normal

No evidence of bacterial antigen.

Abnormal

Evidence of group A streptococcal antigen
Keep in mind the possibility of false-positive results

Cause of abnormal result

Bacterial infection.

4) Chest X-ray

Advantage

Can demonstrate possibly life-threatening splenomegaly in absence of physical findings.

Abnormal

Appearance of splenomegaly. Keep in mind the possibility of imaging artifacts

Cause of abnormal result

Splenomegaly.

5) Liver function tests

Advantage

Can be useful in differential diagnosis, may be useful in older patients or those with severe disease

Normal

- Aminotransferase: 0-35 international units/L (method dependent)
- Total bilirubin: 0-1.0 mg/dL
- Alkaline phosphatase: 30-120 international units/L (method dependent)

Abnormal

- Elevated liver enzymes
- Keep in mind the possibility of a false-positive result (nonspecific - elevated with other hepatitis infections, variety of hepatic illnesses)

Cause of abnormal result

Infectious mononucleosis, Viral hepatitis, Heart failure, Hepatocellular disorders, other liver disease

Medications, disorders and other factors that may alter results

Alcohol and many other drugs (e.g. anabolic steroids, isoniazid, rifampin, cephalosporins, ketoconazole, acetaminophen, chlorpromazine, allopurinol, carbamazepine, halothane) can cause liver function test elevation.

6) Epstein-Barr virus (EBV) serologic profile

Advantages

Very accurate, specific, Serologic profile correlates with type, stage of infection

Disadvantages

Expensive, Normal result may be misleading in immunocompromised patients

Normal

IgG titer toward viral capsid antigen (VCA) negative
IgM titer toward VCA absent
No titer toward Epstein-Barr virus early antigen (EA)
No titer toward Epstein-Barr nuclear antigen (EBNA)

Abnormal

IgG VCA titer >160
IgM VCA titer present
Epstein-Barr virus EA titer present
EBNA titer absent (if acute infection), positive (if remote infection)
Keep in mind the possibility of a false-positive result

Cause of abnormal result

- Acute **infectious mononucleosis** (2-6 weeks): high IgG VCA titer (as high as 640), high IgM VCA titer (as high as 160), high Epstein-Barr virus EA titer (as high as 160), no EBNA titer
- Recent infection with **mononucleosis** (6-16 weeks): moderate IgG VCA (10-640),moderate IgM VCA titer (as high as 160), moderate EA titer (as high as 40), and moderate EBNA titer (as high as 40)
- Remote infection with **mononucleosis** (3 months to years): IgG VCA positive (10-160); IgM VCA (negative); EA (negative); EBNA positive (10-40)
- No prior infection with Epstein-Barr virus: no titers to any antigens

CLINICAL HALLMARKS

Epstein-Barr virus specifically infects B cells: atypical lymphocytes are reactive T cells in response to systemic viral infection. Atypical lymphocytes are commonly seen in infectious mononucleosis but are not specific for mononucleosis

Because of the ubiquitous presence of Epstein-Barr virus in the population and frequent asymptomatic shedding of the virus in oral secretions, it is often difficult to determine the origin of new infections. The long and variable incubation period further obscures the source of the infection in most newly infected patients

Epstein-Barr virus is a potentially serious infection in immunocompromised patients. It causes oral hairy leukoplakia of the tongue in AIDS patients, lymphocytic interstitial pneumonitis in pediatric AIDS patients, and Epstein-Barr virus-associated lymphoproliferative syndromes in transplant patients

PROGNOSIS

- 95% of patients recover uneventfully, although resolution of all symptoms may take several months
  Fever subsides in about 10 days
- Adenopathy and splenomegaly subside in about 4 weeks
- Although many complications are possible (some severe), most patients with complications will recover
- Death is uncommon but usually due to splenic rupture, severe hemolytic anemia, central nervous system (CNS) involvement, encephalitis, thrombocytopenic purpura, blood dyscrasias, or contribution to malignancy
- Immunocompromised patients or patients with lymphoproliferative disease may have a much higher mortality rate
- Full recovery can take several months
- Mononucleosis confers significant immunity, and repeat episodes of acute Epstein- Barr virus infection do not occur

Factors affecting prognosis

Negative:

- Immunocompromised state
- X-linked lymphoproliferative syndrome (Duncan's syndrome)
- Severe blood dyscrasias/thrombocytopenia
- CNS involvement

CLINICAL COMPLICATIONS

CNS complications:

- Seizures
- Cerebellar syndrome
- Bell's palsy
- Subacute sclerosing panencephalitis
- Meningoencephalitis, optic neuritis
- Transverse myelitis
- Retrobulbar neuritis
- Coma, Guillain-Barré syndrome
- Reye's syndrome
- Psychosis
- There is no evidence that Epstein-Barr virus infection is associated with chronic fatigue syndrome (this is controversial)

Respiratory complications:

- Airway obstruction (secondary to tonsillar hypertrophy)
- Streptococcal pharyngitis
- Pneumonitis, pleural effusion
- Pulmonary hemorrhage
- Pneumonia

Hematologic complications:

- Hemolytic anemia
- Thrombocytopenic purpura
- Coagulopathy
- Aplastic anemia
- Hemophagocytic syndrome
- Granulocytopenia (rare)

Cardiac complications:

- Pericarditis
- Myocarditis
- ECG changes

Renal complications (rare):

- Glomerulonephritis
- Nephrotic syndrome
- Hematuria/proteinemia

Other complications:

- Splenic rupture (can be spontaneous and without clinical evidence)
- Hepatitis, liver necrosis
- Mycoplasma infection
- Monoarticular arthritis
- Jaundice, malformation, dermatitis (rare)
- Erythema multiforme
- Conjunctivitis

PREVENTION

Primary prevention

Risk factors:

Negative Epstein-Barr virus serologies (susceptible)
Age 15-25 years

- Communal living, especially in dormitories, camps
- Oral contact where saliva is mixed
- Sharing food and drinks
- Blood transfusion
- Transplants

Avoid above risk factors where possible; however, because the effects of the illness are more severe in older patients, it is possible that efforts at prevention are ill-founded, except in certain immunologically susceptible individuals (X-linked immunodeficiency).

Secondary prevention

Infection with Epstein-Barr virus, clinical or subclinical, confers substantial lifetime immunity to **infectious mononucleosis.**

Reactivation of Epstein-Barr virus can occur in the setting of immunosuppression but does not cause **infectious mononucleosis.**

INTERPRETATION

NEONATAL SCREENING TEST (....contd)

SOME OF THE ETHICAL QUESTIONS RAISED FOR NEONATAL SCREENING PROGRAMME ARE

1. Will presymptomatic diagnosis benefit the baby?
2. Will the benefit out - weigh the possible harm?
3. Is there an effective test?
4. Can we afford it?
5. Whether screening tests can be made available to all?
6. Whether they should be made mandatory?
7. And if not, to what extent informed consent is needed?
8. How far the screening laboratory's responsibility extends in ensuring that the patient receives appropriate management?

Babies diagnosed earlier by Neonatal Screening have better anthropometric indices as they grow.

When a diagnosis of metabolic disorder is made in one member of the family, a survey of siblings and parents is indicated.

Other relatives should be included when their medical history suggests that they may be similarly affected

It should be emphasized that when all siblings are mentally retarded and no biochemical abnormality can be found in any of them, it is important to screen the parents, particularly the mother, for any metabolic abnormalities, since maternal PKU as a cause of neonatal retardation and congenital anomalies is well recognized.

A facility to which patients can be referred for further study, treatment, and genetic counseling is an integral part of a screening programme without which purpose of neonatal screening would be defected.

The remarkable progress in the control of infectious diseases has led to the emergence of Genetic and Metabolic diseases as important causes of morbidity and mortality.

The socio-economic burden makes a couple desire one or two children, free from handicaps. They would readily accept screening tests during pregnancy or in the neonatal period to ensure normality of the child.

In the table below are some of the values of the analytes (normal ranges and alert ranges) in a neonatal screening test.

Some of the Normal Values in relation to Neonatal Screening Programme

No.	Analytes	Normal ranges	Alert ranges
1	Phenyl alanine	< 4.00 mgm / dL	> 6.00 mgm / dL
2	Leucine	< 4.00 mgm / dL	> 4.00 mgm / dL
3	Methionine	< 2.00 mgm / dL	> 4.00 mgm / dL
4	Tyrosine	< 6.00 mgm / dL	> 6.00 mgm / dL
5	Gal - 1 - PUT	100 % fluorescence	Low or no fluorescence
	GALT quantitative assay (Units/gm of Hb.)	> 2.4 (2.4 - 1.3 = ±)	< 1. 3
	Gal - 1 Phosphate	< 11.0 mgm / dL	> 12.0 mgm / dL
6.	T4 (Thyroxine hormone)		
	a). for < 1wk. age baby	> 7.5 ugm / dL	< 7.5 ugm / dL
	b. for > 1 wk age baby	> 5.4 ugm / dL	< 5.4 ugm / dL
	c). for L.B.W*. baby (< 2500gms)	> 4.5 ugm / dL	< 4.5 ugm / dL
7	T.S.H**.		
	Normal range < 48 hrs. age	up to 30 µ I.U. / ml	
	Normal range > 48 hrs. age	up to 25 µ I.U. / ml	

L.B.W - Low Birth Weight*

*T.S.H** - Thyroid Stimulating Hormone*

SOME OF THE INTERNATIONALLY SIGNIFICANT DISORDERS ARE DISCUSSED BELOW

Phenylketonuria (PKU) and other amino acid metabolism disorders

- These are a group of inherited health problems related to defects in the breakdown of amino acids (building blocks of protein).
- PKU is the most common one. The baby cannot break down the amino acid called phenylalanine.
- High levels of phenylalanine and other chemicals formed from it will cause damage to the brain.
- A baby with the problem is normal at birth, but within a few months will have obvious brain damage.
- If they are fed a special diet from birth these babies will have normal intelligence and be healthy. The mother should stop breastfeeding.
- Dr Robert Guthrie invented the Guthrie test in the USA to find PKU. The Guthrie test is convenient to perform.
- As well Phenylketonuria (PKU), other genetic problems (such as maple syrup urine disease and homocystinuria) can affect the way proteins are changed into amino acids.
- These conditions are rare, but can be life threatening.
- In almost all cases, if children with these conditions are fed a special diet from soon after birth, they will be healthy and have normal intelligence.

Galactosaemia

- Galactose is a sugar (carbohydrate). In the body lactose (one of the sugars in milk) is changed into galactose and glucose.
- In Galactosaemia, galactose cannot be properly broken down, and the high levels cause brain and liver damage, cataracts and other health problems.
- If the problem is found very early, most of the health problems can be prevented with a special diet.

Congenital hypothyroidism

- Congenital hypothyroidism arises when a baby does not make enough thyroid hormone. The baby's thyroid gland may make a little of the hormone, or may make none.
- The health problems are not usually obvious at birth, but with time there is a delay in brain development which usually does not improve with late treatment.
- If treatment with extra thyroid hormone is started early, children with congenital hypothyroidism grow and develop normally.

Cystic fibrosis

- Cystic Fibrosis (CF) is an inherited problem which mostly affects the lungs (sticky mucous) and gut (affecting the way food is absorbed).
- Children and young people with CF usually get a lot of severe chest infections, and digestion problems.
- CF does not affect brain development.
- Many people carry a gene which can cause CF (they are called 'carriers'), but a person needs two genes to have the disease.
- The blood test will find about 96% of children who have two genes for CF (i.e., they have health problem) and also many children who have only one gene (the 'carriers' who do not have health problems). An extra test (a sweat test) is needed to find out which children have the disease. About one in 12 of the children who need this extra test will have CF.
- Finding the disease early has been shown to improve the life of children with CF, although it does not prevent all of the problems.

BOUQUET

IN LIGHTER VEIN

- What's the difference between a general practitioner and a specialist?
  One treats what you have, the other thinks you have what he treats.

- What is a double-blind study?
  Two orthopaedists reading an electrocardiogram.

- Three doctors are in the duck blind and a bird flies overhead. The general practitioner looks at it and says, "Looks like a duck, flies like a duck... it's probably a duck," shoots at it but misses and the bird flies away.
  The next bird flies overhead, and the pathologist looks at it, then looks through the pages of a bird manual, and says, "Hmmmm...green wings, yellow bill, quacking sound...might be a duck." He raises his gun to shoot it, but the bird is long gone.
  A third bird flies over. The surgeon raises his gun and shoots almost without looking, brings the bird down, and turns to the pathologist and says, "Go see if that was a duck."

- A guy walks into a bar and orders a drink. After a few more he needs to go to the can. He doesn't want anyone to steal his drink so he puts a sign on it saying, "I spat in this beer, do not drink!". After a few minutes he returns and there is another sign next to his beer saying, "So did I!"

- There's this drunk standing out on the street corner, and a cop passes by, and says, "What do you think you're doing?" The drunk says, "I heard the world goes around every 24 hours, and I'm waiting on my house. Won't be long now, there goes my neighbor."

- A man walks into a bar, orders the bartender for two beers. He continues this for several nights and the bartender got a bit curious
  . The bartender walks up to him and asks "Sir, why do you always ask for two drinks?" the man replies, "I used to come here with my best friend but now he's dead. And I'm drinking the second beer on his behalf." A few days later, the man orders only for one beer. Curious, the bartender asks him," why only 1 beer now sir?" man replies, "I have given up drinking!"

- "Doctor, doctor, will I be able to play the violin after the operation?'
  "Yes, of course".
  "Great! I never could before!".

TROUBLE SHOOTING

SPECIMEN QUALITY

Hemolysis

Some analytes may be reported erroneously if the serum is not promptly removed from the clot, or if the barrier tube is not centrifuged after the clot has formed.

Major discrepancies are low glucose, high potassium and LD. Additionally, if hemolysis takes place during initial processing and venipuncture, or if prolonged contact with the clot takes place, elevation in cholesterol, creatinine, iron, phosphorus, calcium and most enzymes will be found. Hemolyzed hematological specimens are unsuitable for testing.

Quantity Not Sufficient (QNS)

Most hematology tests require that a full tube of blood be obtained. This is because there is a defined quantity of anticoagulant in each tube and the ratio of this to the blood volume has to be exact to ensure quality results. Particularly important are blue-top tubes used for Blood Coagulation tests. For prothrombin time, activated partial thromboplastin time and fibrinogen determinations exactly 4.5 mL of blood must be obtained (a full tube). The ratio is 1 part of 3.2% buffered sodium citrate added to 9 parts of blood. For CBCs a "short draw" lavender tube will result in red cell crenation, reduced MCV and hematocrit, and possible changes in leukocyte morphology, platelets and total leukocyte counts.

Clotted Specimens

All hematological testing utilizes anticoagulated blood.

For blood counts, a lavender top tube containing the anticoagulant EDTA is required. All specimens should be collected and the tube filled to the limit of the vacuum.Clotted samples, either macroscopic or microscopic in nature, cannot be processed for CBC testing, as such results will produce false leukopenia, lower red cell counts, and aberrant red cell indices.

As the equipment used to test blood counts incorporates a clot detector, it is occasionally possible that specimens that appear macroscopically normal will have small microscopic clots that are detected which will produce incorrect results. Similarly, small clots found in blue top tubes (for coagulation tests) will result in falsely prolonged test results.

Icteric Specimens

If the specimen is deeply icteric, falsely elevated cholesterol results may be obtained. It also interferes with usual creatinine estimations.

Lipemic Specimens

Lipemia can falsely elevate ALT and AST. Additionally, it can indicate that the patient did not adequately fast for 12-18 hours before having the specimen collected. In this situation, glucose and triglycerides will be elevated.

Decreased Bilirubin

Bilirubin is photodegradable. Prolonged exposure of the specimen to bright light will produce depressed results.

Decreased CO_2 Levels

Carbon dioxide levels are decreased if the specimen is not tested promptly. CO_2 escapes from red cells *in vitro*, at a rate proportional to time. This can be minimized by keeping the stopper on the tube and by refrigeration.

Poor Cell Preservation

Blood cells, particularly leukocytes become fragile and can be distorted morphologically if the specimen is older than 24 hours. In such situations, a reliable differential white cell count cannot be performed

Old Specimens

Blood specimens older than 24 hours cannot be adequately tested for some analytes. Particularly sensitive are most Hematology tests including Blood Coagulation procedures. In one of our earlier editions (Vol I, Issue IV) we had given half-life of usually tested for analytes and also suggested preservation temperatures and additives.

WISDOM WHISPERS

- You know a dream is like a river, ever changing as it flows.
  And a dreamer's just a vessel that must follow where it goes.
  Trying to learn from what's behind you and never knowing what's in store
  makes each day a constant battle just to stay between the shores.
  And I will sail my vessel 'til the river runs dry.
  Like a bird upon the wind, these waters are my sky.
  I'll never reach my destination if I never try,
  So I will sail my vessel 'til the river runs dry.
  Too many times we stand aside and let the water slip away.
  To what we put off 'til tomorrow has now become today.
  So don't you sit upon the shore and say you're satisfied.
  Choose to chance the rapids and dare to dance the tides

- There's a miracle of friendship that dwells within the heart
  And you don't know how it happens
  or where it gets its start
  But the happiness it brings you
  always gives a special lift
  Any you realize that friendship
  Is God's most perfect gift.

- The friends I made have slipped and strayed.
  And who's the one that cares
  A trifling lot and best forgot -
  And that's my tale, and theirs.
  Then if my 'friendships break and bend
  There's little need to cry
  The while I know that every foe
  Is faithful till I die.'

BRAIN TEASERS

1. Plummer Vinson/ Paterson-Kelly syndrome is related to which of the following?
   A. Folic acid deficiency B. Iron deficiency C. Zinc deficiency
   D. Cobalt deficiency

2. In which anemia do we observe pencil shaped RBCs ?
   A. Macrocytic anemia B. Hypochromic anemia C. Aplastic anemia
   D. Spherocytosis

3. Polymacrocytes and hypersegemented neutrophils are often found in which of the following anemias?
   A. Megaloblastic B. Hypochromic C. Hemolytic D. Aplastic

4. What is the type of RBCs usually seen in orotic aciduria?
   A. Microcytic B. Microspherocytic C. Normocytic D. Macrocytic

5. Which anemia would you suspect in a five - year old patient with gall stones?
   A. Hereditary spherocytosis B. Hypochromic anemia C. Drug induced
   D. Angiopathic

6. Which of the following is not an RBC membrane defect?
   A. Spherocytosis B. Elliptocytosis C. Stomatocytosis D. Unstable Hb

Answers: 1. B, 2. B, 3. A, 4. D, 5. A, 6. D.

TULIP NEWS

We at TULIP GROUP strive to get you all the relevant latest biomarkers for various diseases. In keeping with our tradition of providing economically priced pertinent RDTs (Rapid Diagnostic Tests), we present to you **the most important marker to diagnose Acute Myocardial Infarction.**

AMICHECK-TROP I WB

Rapid test for Detection of cardiac Troponin I in human serum/ plasma/ whole blood

Unlike Troponin T, Troponin I is specifically produced in the myocardium. The specificity of Troponin T vis-a-vis AMI is questionable as it can be produced from other organs too

Cardiac troponin I: An excellent marker

- For more than one decade cardiac form of TnI (cTnI) is known as a reliable marker of cardiac tissue injury.
- cTnI is considered to be more sensitive and significantly more specific in diagnosis of myocardial infarction than the golden marker of last decade CK-MB, as well as myoglobin, LDH isoenzymes and cTnT.
- Cardiac Troponin I (cTnI) meets all the criteria laid down by National Academy of Clinical Biochemistry (NACB) for an ideal cardiac biomarker in early identification and risk stratification of patients with chest pain suggestive of ischaemia and identification of patients that present after infarction.

Amicheck Trop I WB: An excellent diagnostic test

Rapid, Reliable and helps in early diagnosis of myocardial infarction.

Sensitivity adjusted to 0.1ng/ml, indicating even minor myocardial infarction.

Correlates with CHEMILUMNISCENCE assay

Enables sequential testing at baseline, 6 hours and 12 hours for effective triaging.

Convenience in choice of samples, whole blood, serum or plasma

Only kit to have a reference band of 1ng/ml of cTnI for differentiation between AMI and adverse cardiac events.

FOR SAFE DECISION MAKING AND COST EFFECTIVE USE OF INTENSIVE CARE FACILITIES!

AMICHECK-TROP I WB

Rapid test for Detection of cardiac Troponin I in human serum/ plasma/ whole blood

INTERPRETATION OF RESULTS

Positive
If intensity of the Test band is equal to or greater than the Reference band - cTnI concentration is 1.0 ng/ml

Positive
If intensity of the Test band is less than the Reference band - cTnI concentration is between 0.1-1.0 ng/ml

Negative
Presence of two coloured bands at Reference(R) and Control (C) regions indicate absence of cTnI or the concentration of cTnI in the specimen is below 1.0 ng/ml

Invalid
The test is invalid if Control band and/or Reference band is not visible at fifteen minutes . Verify the test procedure and repeat the test with a new device

Truely... ... The New Gold Standard!

IMMUTEX

Test for Infectious Mononucleosis

For further information contact:

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