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Editorial

What do the terms “Pastia lines and Forchheimer spots” remind you of? LOST?? Scarlet Fever, isn't it. **Scarlet fever** is a disease caused by erythrogenic toxin (a bacterial exotoxin) released by *Streptococcus pyogenes*. Once a major cause of death, it is now effectively treated with antibiotics. The term *scarlatina* may be used interchangeably with *scarlet fever*, though it is most often used to indicate the less acute form of scarlet fever seen since the beginning of the twentieth century.

Scarlet fever was feared in the pre-antibiotic era, as it was associated with the late post-streptococcal complications of glomerulonephritis and endocarditis leading to heart valve disease, all of which were protracted and often fatal afflictions at the time.

This disease is most common in 4-8 year olds with males and females being equally affected. By the age of 10 years most children have acquired protective antibodies and scarlet fever at this age or older is rare.

It is usually spread by the aerosol route (inhalation) but may also be spread by skin contact or by fomites.

Asymptomatic carriage may occur in 15-20% of school-age children.

The incubation period is 1-4 days. Go on, turn this page to acquire in-depth knowledge about this disease entity in the “**DISEASE DIAGNOSIS**” section.

Rheumatic fever is an inflammatory disease that occurs following *Streptococcus pyogenes* infection, such as streptococcal pharyngitis or scarlet fever. Believed to be caused by antibody cross-reactivity that can involve the heart, joints, skin, and brain, the illness typically develops two to three weeks after a streptococcal infection. Acute rheumatic fever commonly appears in children between the ages of 6 and 15, with only 20% of first-time attacks occurring in adults. The illness is so named because of its similarity in presentation to rheumatism. “**INTERPRETATION**” segment outlines for you clear cut understanding of various diagnostic tests performed to diagnose Rheumatic disorders.

“**TROUBLE SHOOTING**” enumerates the various steps that need to be taken after having been exposed to HIV. IT is called PEP or Post exposure prophylaxis.

Very serious stuff above and within? “**BOUQUET**” hasn't been forgotten!

DISEASE DIAGNOSIS

SCARLET FEVER

Background

Scarlet fever (known as scarlatina in older literature references) is a syndrome characterized by exudative pharyngitis, fever, and scarlatiniform rash. It is caused by toxin-producing group A beta-hemolytic streptococci (GABHS) found in secretions and discharge from the nose, ears, throat, and skin. Scarlet fever may follow streptococcal wound infections or burns, as well as upper respiratory tract infections, but food-borne outbreaks have been reported. Ordinarily, scarlet fever evolves from a tonsillar/pharyngeal focus, although the rash develops in less than 10% of cases of "strep throat." The site of bacterial replication tends to be inconspicuous compared to the possible dramatic effects of released toxins. Exotoxin-mediated streptococcal infections range from localized skin disorders (eg, bullous impetigo) to the systemic rash of scarlet fever to the uncommon but highly lethal streptococcal toxic shock syndrome.

Pathophysiology

As the name "scarlet fever" implies, an erythematous eruption is associated with a febrile illness. The circulating toxin, produced by GABHS and often referred to as erythemogenic or erythrogenic toxin, causes the pathognomonic rash as a consequence of local production of inflammatory mediators and alteration of the cutaneous cytokine milieu. This results in a sparse inflammatory response and dilatation of blood vessels, leading to the characteristic scarlet color of the rash. Usually, the sites of GABHS replication in scarlet fever are the tonsils and pharynx. Clinically indistinguishable, scarlet fever may follow streptococcal infection of the skin and soft tissue, surgical wounds (ie, surgical scarlet fever), or the uterus (ie, puerperal scarlet fever).

Etiology

Scarlet fever is a streptococcal disease. Streptococci are gram-positive cocci that grow in chains. They are classified by their ability to produce a zone of hemolysis on blood agar and by differences in carbohydrate cell wall components (A-H and K-T). They may be alpha-hemolytic (partial hemolysis), beta-hemolytic (complete hemolysis), or gamma-hemolytic (no hemolysis). Group A streptococci are normal inhabitants of the nasopharynx. Group A streptococci can cause pharyngitis, skin infections (including erysipelas pyoderma and cellulitis), pneumonia, bacteremia, and lymphadenitis. Most streptococci excrete hemolyzing enzymes and toxins. The erythrogenic toxins produced by GABHS are the cause of the rash of scarlet fever. The erythema-producing toxin was discovered by Dick and Dick in 1924. Scarlet fever is usually associated with pharyngitis; however, in rare cases, it follows streptococcal infections at other sites. Although infections may occur year-round, the incidence of pharyngeal disease is highest in school-aged children (5-15 years) during winter and spring and in a setting of crowding and close contact. Person-to-person spread by means of respiratory droplets is the most common mode of transmission. It can rarely be spread through contaminated food, as seen in an outbreak in China. The organism is able to survive extremes of temperature and humidity, which allows spread by fomites. Geographic distribution of skin infections tends to favor warmer or tropical climates and occurs mainly in summer or early fall in temperate climates. The incubation period for scarlet fever ranges from 12 hours to 7 days. Patients are contagious during the acute illness and during the subclinical phase.

Epidemiology

As many as 10% of the population contracts group A streptococcal pharyngitis. Of this group, as many as 10% then develop scarlet fever. In the past century, the number of cases of scarlet fever has remained high, with marked decrease in case-mortality rates secondary to widespread use of antibiotics. Transmission usually occurs via airborne respiratory particles that can be spread from infected patients and asymptomatic carriers. The infection rate increases in overcrowded situations (eg, schools, institutional settings). Immunity, which is type specific, may be induced by a carrier state or overt infection. In adulthood, incidence decreases markedly as immunity develops to the most prevalent serotypes. Complications (eg, rheumatic fever) are more common in the developing world. Scarlet fever predominantly occurs in children aged 5-15 years, though it can also occur in older children and adults. By the time children are 10 years old, 80% have developed lifelong protective antibodies against streptococcal pyrogenic exotoxins. Scarlet fever is rare in children younger than 2 years because of the presence of maternal antiexotoxin antibodies and lack of prior sensitization. Leslie et al suggest from a case-control study that antecedent streptococcal infection can increase the likelihood of children developing certain neuropsychiatric disorders, including Tourette syndrome, attention-deficit/hyperactivity disorder, and major depressive disorder. Males and females are affected equally. No racial or ethnic predilection is reported for group A streptococcal infection.

History

The cutaneous eruption of scarlet fever accompanies a streptococcal infection at another anatomic site, usually the tonsillopharynx. The illness generally has a 1- to 4-day incubation period. Its emergence tends to be abrupt, usually heralded by sudden onset of fever associated with sore throat, headache, nausea, vomiting, abdominal pain, myalgias, and malaise. The characteristic rash appears 12-48 hours after onset of fever, first on the neck and then extending to the trunk and extremities. In the untreated patient, fever peaks by the second day (temperature as high as 103-104°F) and gradually returns to normal in 5-7 days. Fever abates within 12-24 hours after initiation of antibiotic therapy. A recent history of exposure to another individual with a "strep" infection may aid in the diagnosis.

Physical Examination

The patient usually appears moderately ill. Fever may be present. The patient may have tachycardia. Tender anterior cervical lymphadenopathy may be present. The

mucous membranes

usually are bright red, and scattered petechiae and small red papular lesions on the soft palate are often present. On day 1 or 2, the tongue is heavily coated with a white membrane through which edematous red papillae protrude (classic appearance of white strawberry tongue). By day 4 or 5, the white membrane sloughs off, revealing a shiny red tongue with prominent papillae (red strawberry tongue). Red, edematous, exudative tonsils (see the image below) are typically observed if the infection originates in this area. The exudative pharyngitis typical of scarlet fever. Although the tongue is somewhat out of focus, the whitish coating observed early in scarlet fever is visible. Generally, the rash



Oral lesions

develops 12-48 hours after the onset of fever, first appearing as erythematous patches below the ears, chest, and axilla. Dissemination to the trunk and extremities occurs over 24 hours. Typically, the rash consists of scarlet macules over generalized erythema (boiled lobster appearance). **The characteristic exanthem** consists of a fine erythematous punctate eruption that appears within 1-4 days after the onset of the illness. The eruption imparts a dry rough texture to the skin that is reported to resemble the feel of coarse sandpaper. The erythema blanches with pressure. The skin can be pruritic but usually is not painful.

The eruption first appears on the upper trunk and axillae and then becomes generalized, though it is usually more prominent in flexural areas (eg, axillae, popliteal fossae, and inguinal folds). It may also appear more intense at dependent sites and sites of pressure, such as the buttocks. **Capillary fragility** is increased, and rupture may occur. Often, transverse areas of hyperpigmentation with linear arrays of petechiae in the axillary, antecubital, and inguinal areas (Pastia lines, or the Pastia sign) can be observed. These arrays may persist for 1-2 days after resolution of the generalized rash. **Another distinctive facial finding** is a flushed face with circumoral pallor. In severe disease, small vesicular lesions termed miliary sudamina may appear on the abdomen, hands, and feet. **The cutaneous rash**, shown below, lasts for 4-5 days, followed by fine desquamation, one of the most distinctive features of scarlet fever. The desquamation phase begins 7-10 days after resolution of the rash, with flakes peeling from the face. Peeling from the palms (see the image below) and around the fingers occurs about a week later and can last up to a month or longer. The extent and duration of this phase are directly related to the severity of the eruption.



Skin lesions

Desquamation of the palms is a frequently observed self-limited manifestation of scarlet fever present in the healing period following resolution of the infection and acute eruption.

Complications

Complications of scarlet fever may include the following: Cervical lymphadenitis, Otitis media and/or mastoiditis, Ethmoiditis, Peritonsillar abscess, Sinusitis, Bronchopneumonia, Meningitis, Brain abscess, Intracranial venous sinus thrombosis, Septicemia, meningitis, osteomyelitis, and septic arthritis. Acute renal failure from poststreptococcal glomerulonephritis, Hepatitis, Vasculitis, Uveitis.

Of these, otitis media, pneumonia, septicemia, osteomyelitis, rheumatic fever, and acute glomerulonephritis are the most common. Appropriate evaluation and early intervention with antibiotics are essential to prevent these disorders. **Rare but lethal** early toxin-mediated sequelae include myocarditis and toxic shock like syndrome. A lethal form of streptococcal infection is capable of producing the toxic streptococcal syndrome. **Late complications** of group A streptococcal infection include rheumatic fever and poststreptococcal glomerulonephritis. Risk of acute rheumatic fever following an untreated streptococcal infection has been estimated at 3% in epidemic situations and approximately 0.3% in endemic scenarios. If a nephritogenic strain of group A beta-hemolytic streptococci causes infection, the individual has a 10-15% chance of developing glomerulonephritis. **Weeks to months after the illness**, transverse grooves (ie, Beau lines) may appear on the nail plates and hair loss

(telogen effluvium) may occur.

Diagnostic Considerations

The overwhelming majority of cases of scarlet fever are caused by group A beta-hemolytic streptococci (GABHS). Other bacteria can cause a pharyngitis and similar rash, such as *Staphylococcus aureus*, *Haemophilus influenzae*, *Arcanobacterium haemolyticum*, and *Clostridium* species. The differential diagnosis includes other causes of fever accompanied by erythematous eruptions. Recurrent cases of scarlet fever have been reported from reinfection with strains unrelated to *Streptococcus pyogenes*. **The cutaneous eruption** of fifth disease may be confused with that of scarlet fever, but the affected child is usually well and afebrile. **Rubella and rubeola** may appear similar, but the presence of conjunctivitis, purulent rhinitis, and cough are helpful clues to the diagnosis of rubeola. In addition, the eruption of rubeola usually begins behind the ears and on the scalp and forehead, not on the torso. Rubella typically begins on the head and face. **Other viral exanthemata**, such as those caused by Epstein-Barr virus (infectious mononucleosis), enterovirus, hepatitis B infection, HIV, and *Streptobacillus moniliformis* infection (rat bite fever), may also have to be considered. **Other bacteria-associated syndromes** with cutaneous eruptions (eg, toxic shock syndrome, secondary syphilis) may appear similar to scarlet fever, but the presence of vasomotor instability and ischemic necrosis of digits in the former and palmoplantar involvement with positive serology in the latter should suffice to differentiate them from scarlet fever. **Noninfectious diseases** that should be considered include Kawasaki disease, acute lupus erythematosus, morbilliform drug eruption, and juvenile rheumatoid arthritis. **Other problems to be considered include the following:** *Arcanobacterium haemolyticum*, Atropine toxicity, Enteroviral infection and nonspecific viral infection, Fifth disease, Epstein-Barr virus (infectious mononucleosis), Hepatitis B infection, HIV, Juvenile rheumatoid arthritis, Pediatric cellulitis, Plant allergic reactions, Roseola, *S moniliformis* infection (rat bite fever), Severe sunburn, Viral exanthema.

Differentials

Abortion Complications, Drug Eruptions, Erythema Multiforme, Exfoliative Dermatitis, Fifth Disease or Erythema Infectiosum, Lupus Erythematosus, Acute, Measles, Rubeola, Mononucleosis in Emergency Medicine, Pediatric Erythema Toxicum, Pediatric Kawasaki Disease, Pediatric Pharyngitis, Pediatric Pneumonia, Pityriasis Rosea in Emergency Medicine, Rubella, Scabies in Emergency Medicine, Staphylococcal Scalded Skin Syndrome in Emergency Medicine, Syphilis, Toxic Epidermal Necrolysis in Emergency Medicine, Toxic Shock Syndrome,

Histologic Findings

The microscopic findings of the eruption of scarlet fever are nonspecific and have an appearance similar to that of other exanthematous eruptions. A sparse perivascular infiltrate is present, usually consisting primarily of lymphocytes with a slight amount of spongiosis in the epidermis. Slight parakeratosis may be present, which probably correlates with the sandpaper like texture of the skin.

Approach Considerations

In addition to standard blood and urine tests done as part of a complete medical workup, the following studies are indicated in scarlet fever: **Throat culture** or rapid streptococcal test, **Anti-deoxyribonuclease B and antistreptolysin-O titers** (antibodies to streptococcal extracellular products), **In most cases**, no imaging studies are indicated.

Blood and Urine Studies

The complete blood count (CBC) commonly reveals a leukocytosis. The white blood cell (WBC) count in scarlet fever may increase to 12,000-16,000/ μ L, with a differential of up to 95% polymorphonuclear lymphocytes. During the second week, eosinophilia, as high as 20%, can develop. **Urinalysis and liver function tests** may reveal changes associated with complications of scarlet fever. Said tests are part of a complete medical workup. **Patients whose bacterial source** may suggest another process (eg, a patient with a suppurative leg wound who may have osteomyelitis) should be evaluated accordingly.

Throat Culture

Throat culture remains the criterion standard for confirmation of group A streptococcal upper respiratory infection. International guidelines for prevention and treatment of rheumatic fever state that group A streptococci virtually always are found on throat culture during acute infection. **Throat cultures** are approximately 90% sensitive for the presence of group A beta-hemolytic streptococci (GABHS) in the pharynx. However, because a 10-15% carriage rate exists among healthy individuals, the presence of GABHS is not proof of disease. **To maximize sensitivity**, proper obtaining of specimens is crucial. Vigorously swab the posterior pharynx, tonsils, and any exudate with a cotton or Dacron swab under strong illumination, avoiding the lips, tongue, and buccal mucosa. **Direct antigen detection kits** (ie, rapid antigen tests [RATs], strep screens) have been proposed to allow immediate diagnosis and prompt administration of antibiotics. Kits are latex agglutination or a costlier enzyme-linked immunosorbent assay (ELISA). Several studies of RAT kits report results of 95% specificity but only 70-90% sensitivity. Operator technique can also significantly influence the results of the test.

Antideoxyribonuclease B and Antistreptolysin O Titers

Streptococcal antibody tests (eg, antideoxyribonuclease B [ADB] and antistreptolysin O [ASO] titers) are used to confirm previous group A streptococcal infection. The most commonly available streptococcal antibody test is the ASO test. An increase in ASO titers can sometimes be observed but is a late finding and usually of value only in retrospect. **Streptococcal antibody tests** can provide confirmatory evidence of recent infection but have no value in acute infection and currently are not indicated in this setting. They may be of value in patients with suspected acute renal failure or acute glomerulonephritis.

Prognosis

When the condition is identified in a timely fashion, the prognosis is excellent. Most patients recover fully after 4-5 days, with resolution of skin symptoms over several weeks. Attacks may recur. **In the preantibiotic era**, infections due to GABHS were major causes of mortality and morbidity. Historically, scarlet fever resulted in death in 15-20% of those affected. However, scarlet fever is no longer associated with the deadly epidemics that made it so feared in the 1800s. Since the advent of antibiotic therapy, the mortality rate for scarlet fever has been less than 1%. **Today, as a result** not only of antibiotic therapy but also of enhanced immune status of the population and improved socioeconomic conditions, scarlet fever usually follows a benign course. Any undue morbidity and mortality are more likely to arise from suppurative complications (eg, peritonsillar abscess, sinusitis, bronchopneumonia, and meningitis) or problems associated with immune-mediated sequelae, rheumatic fever, or glomerulonephritis. Very rare complications, such as septic shock with multisystem organ failure, have been reported. **Known complications**, such as septicemia,

vasculitis, hepatitis, or rheumatic fever, should be considered on a case-by-case basis as determined by the presence of clinical history and examination findings suggestive of those diseases. Localized soft tissue infections may suggest the presence of underlying osteomyelitis, but scarlet fever may occur from cellulitis alone. When scarlet fever has been determined to be due to a soft tissue infection over or near bone, evaluation for bony involvement should be considered.

Approach Considerations

The goals in the treatment of scarlet fever are (1) to prevent acute rheumatic fever, (2) to reduce the spread of infection, (3) to prevent poststreptococcal glomerulonephritis and suppurative sequelae (eg, adenitis, mastoiditis, ethmoiditis, abscesses, cellulitis), and (4) to shorten the course of illness. **Antibiotic therapy** is the treatment of choice for scarlet fever. Whether antibiotics prevent poststreptococcal glomerulonephritis is still debated in the literature.

Medical Care

Penicillin remains the drug of choice (documented cases of penicillin-resistant group A streptococcal infections still do not exist). A first-generation cephalosporin may be an effective alternative, as long as the patient does not have any documented anaphylactic reactions to penicillin. If this is the case, erythromycin may be considered as an alternative. **Cultures should be obtained** where organisms other than streptococcal bacteria are suspected. The desquamating rash that follows is self-limited, with only emollients necessary for care. **If odynophagia** accompanying streptococcal pharyngitis is especially severe, hospitalization may be warranted for intravenous hydration and antibiotics.

Prevention

At this time, a vaccine for group A streptococci does not exist. To minimize contagion, children with scarlet fever should not return to school or day care until they have completed 24 hours of antibiotic therapy.

Long-Term Monitoring

Follow-up evaluation is recommended to ensure resolution of the primary infection. Some patients report pruritus associated with the desquamating rash. Oral antihistamines and emollients usually are sufficient to control the pruritus.

Medication Summary

Treatment is aimed at providing adequate antistreptococcal antibiotic levels for at least 10 days. **Treat patients who have scarlet fever** with a standard 10-day course of oral penicillin VK or erythromycin. Patients can also be treated with a single intramuscular injection of penicillin G benzathine. These regimens may prevent acute renal failure if antibiotics are initiated within 1 week of the onset of acute pharyngitis. First-generation or later generation cephalosporins may also be used. Erythromycin should be considered in patients allergic to penicillin. Tetracyclines and sulfonamides should not be used.

Patient Education

Patients must be instructed to complete the entire course of antibiotics, even if symptoms resolve. They should be advised to follow general good hygiene precautions, especially in households with other small children. **Patients should be warned** that they will have generalized exfoliation over the next 2 weeks. In particular, they should be warned about signs of complications of streptococcal infection, like persistent fever, increased throat or sinus pain, and generalized swelling.

INTERPRETATION

INTERPRETATION OF LABORATORY TESTS IN RHEUMATIC DISEASE

Laboratory tests are an important adjunct in the clinical diagnosis of rheumatic diseases and are sometimes helpful in monitoring the activity of a disease.

Interpretation of laboratory tests is not always straightforward, as the presence of a laboratory abnormality does not always imply the presence of disease, and a single test generally does not confirm (or exclude) a diagnosis. This means that understanding the sensitivity (the proportion of patients with the disease who have a positive test) and the specificity (the proportion of patients without the disease who have a negative test) of tests is critically important. A test with both a high sensitivity and specificity is useful in diagnosis. Positive and negative predictive values are often more helpful in decision-making. The positive predictive value of a particular test reflects the proportion of patients with a positive test who truly have the disease, and a negative predictive value reflects the proportion of patients with a negative test who truly do not have the disease. Predictive values are dependent on the background prevalence of the disease and are disease specific (Table I).

Table I. Sensitivity, specificity and predictive value

	Disease present	Disease absent
Positive test	a (true positive)	b (false positive)
Negative test	c (false negative)	d (true negative)

Sensitivity = $a/a+c$

Specificity = $d/b+d$

Positive predictive value = $a/a+b$

Negative predictive value = $d/c+d$

GENERAL TESTS OF INFLAMMATION: General tests of inflammation are not diagnostically specific, but are helpful in determining the presence and intensity of an inflammatory process. They are useful for monitoring disease activity. **The acute phase response** is determined by proteins produced by the liver in response to the pro-inflammatory cytokines IL-1, IL-6 and TNF- α . The most commonly measured protein is C-reactive protein (CRP). The platelet count is also often raised in the presence of inflammation due to stimulation of megakaryocytes by the pro-inflammatory cytokines. The level of some plasma proteins may even be reduced in inflammatory states, e.g. albumin. The acute phase response is seen in a wide variety of acute and chronic disorders including infection, infarction, inflammatory arthritis and certain neoplastic disorders. **General tests of inflammation** are not diagnostically specific, but are helpful in determining the presence and intensity of an inflammatory process.

ERYTHROCYTE SEDIMENTATION RATE (ESR): The ESR has been used for many years as an indicator of nonspecific inflammation. It is a measure of rouleaux formation, which is dependent on the concentration of fibrinogen and immunoglobulins. It is simple and cheap to perform. **Limitations** of the test are: **it is an indirect measurement of plasma acute phase response and can be influenced by conditions such as anaemia, it rises and falls slowly compared with the CRP, values increase with age, values are slightly higher in women, the range of abnormal values is less than that for the CRP.**

CRP: The CRP is a sensitive and early indicator of inflammation. The

level is not affected by age, sex or anaemia. This test is valuable in monitoring disease activity, particularly in rheumatoid arthritis (RA) and polymyalgia rheumatica. Some rheumatologists feel that the CRP levels correlate somewhat better with activity than does the ESR, and that the test is more sensitive. However the higher cost limits its popularity in some areas. Although helpful in determining the presence or absence of inflammation, 10% of patients with mild RA may have CRP values in the normal range. The level of acute phase reactants may have prognostic implications in RA, with time-integrated values (i.e. the elevation of CRP over a period of time) correlating with radiographic progression.

ANTINUCLEAR ANTIBODIES: Antinuclear antibodies (ANAs) are autoantibodies directed against various The immunofluorescent ANA test is useful as a first screening test in patients with suspected connective tissue disease. The results are expressed as the highest titre at which fluorescence is detected. Although titres of 1:20 or 1:40 are commonly reported as positive, titres of 1:320 or higher are usually considered more clinically meaningful. Patterns of staining by ANAs can be seen (homogenous, speckled, cleolar), and may provide a clue as to the specific autoantibody present, e.g. double-stranded DNA antibodies give rise to a homogenous pattern. However, interpretation of these patterns requires considerable experience and skill and has largely been replaced by the determination of specific antinuclear antibodies using ELISA in the evaluation of specific disorders. **The ANA test** is very sensitive for the diagnosis of systemic lupus erythematosus (SLE) (sensitivity 98%, specificity 90%) in an unselected population. This means that most people with SLE will have a positive result, and a negative result will make SLE very unlikely (negative predictive value 99%). The positive predictive value of the ANA test for SLE is low (30 - 40%) and is limited by the fact that the ANA is positive in a number of other conditions (rheumatoid arthritis 40%; scleroderma 90%; Sjögrens syndrome 70%). This means that two-thirds of patients with a positive ANA test may have a disease other than SLE. False positive ANAs are commonly found in the normal population, including family members of patients with rheumatic disorders. These are usually low in titre (1:40; 1:80). Higher titres are more likely to be associated with underlying illness. **The ANA test** should be performed when evaluating patients with photosensitive skin rashes, inflammatory polyarthritis, nephritis or cytopenias. The ANA is not a sensitive way of following disease activity and fluctuating titres do not correlate well with a change in clinical status.

ANTI-DNA ANTIBODIES: Only antibodies to double-stranded DNA are clinically useful. They are highly specific for SLE (specificity > 99%), i.e. very useful for diagnosis when positive. However, dsDNA antibodies are only present in 60% of patients with SLE, and their absence would not exclude the diagnosis of SLE. Anti-DNA testing should be reserved for patients with a positive ANA. Some studies have shown a modest correlation between the titre of dsDNA antibodies and clinical activity, particularly in patients with renal disease. This suggests that the test may be useful in monitoring as well as diagnosis. Therapeutic decisions should always be considered within the clinical context, rather than based solely on the change in titre.

ANTIBODIES TO EXTRACTABLE NUCLEAR ANTIGENS: Antibodies to extractable nuclear antigens (ENA) include ANAs directed at Sm, RNP, SS-A (Ro) and SS-B (La) antigens. **These are often present**, and may co-exist, in SLE and other connective tissue diseases. **Antibodies to Sm antigens** have a high specificity for SLE (99%) but only occur in 25% of patients with SLE. It is diagnostically useful to test for Sm antibodies when dsDNA antibodies are negative, as a positive result strongly suggests a diagnosis of SLE. **Antibodies to ribonuclear proteins (RNP)** bind to antigens that are different from, but related to, Sm. In SLE, RNP antibodies usually accompany a positive Sm antibody. However,

patients who are negative for Sm antibodies, but positive for RNP antibodies, would generally have U1 RNP antibodies. These are more specific for mixed connective tissue disease, which is a syndrome of arthritis, myositis, Raynaud's phenomenon and sclerodactyly.

ANTI-Ro/La: Antibodies to SS-A (Ro) and SS-B (La) usually co-exist and are found in approximately 50% of SLE patients and 75% of patients with primary Sjögren's syndrome. Anti-Ro antibodies are specifically associated with subacute cutaneous lupus and mothers of infants with neonatal lupus. Similarly, they may be positive in a small subset of patients with Sjögren's syndrome with a negative ANA. Antibodies to ENA should only be looked for in patients who have a positive ANA screening test, except for isolated clinical conditions where determination of anti-Ro antibody positivity may have diagnostic implications. Patients tend to maintain the same antibody profile over the course of their illness, thus testing for these antibodies on a single occasion is usually sufficient.

ANTI-CENTROMERE AND ANTITOPISOISOMERASE 1 ANTIBODIES:

The fluorescent patterns of ANA staining (centromeric, nucleolar) may suggest the possibility of scleroderma. Anti-centromere antibodies are found almost exclusively in patients with the limited cutaneous forms of the disease or CREST (calcinosis, Raynaud's, oesophageal dysmotility, sclerodactyly and telangiectasia) syndrome. They occur in 50 - 60% of patients. **Anti-topoisomerase 1** antibodies (previously known as Scl-70) are associated with the more diffuse form of scleroderma and are seen in 15 - 20% of patients. The presence of these antibodies is associated with a higher risk of pulmonary fibrosis. It is important to note that the

diagnosis of all forms of systemic sclerosis is still dependent on clinical evaluation, with the specific autoantibodies supporting the diagnosis and allowing distinction of clinical subgroups.

ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODIES (ANCA): ANCAs target antigens in the cytoplasm of the neutrophils. Two subtypes are recognised, namely pANCA (perinuclear) and cANCA (cytoplasmic) based on their patterns of staining on immunofluorescence. The specific antigens recognised by these antibodies are myeloperoxidase (MPO) and proteinase-3 (PR-3) respectively. cANCA are associated with Wegener's granulomatosis with a sensitivity of 60 - 80% and specificity of 98%. However, as Wegener's is a relatively rare disease in the general population, the positive predictive value is low. The diagnosis is usually made on clinical grounds, assisted by biopsy, with a positive cANCA supporting the diagnosis. The titre of cANCA may help in following disease activity in these patients. However, the correlation of titre and disease activity is weak and should not be used as the sole parameter to justify immunosuppressive therapy. pANCA are associated with microscopic polyangiitis and other forms of pauciimmune glomerulonephritis, including polyarteritis nodosa. These antibodies are also found in other disorders, including SLE, rheumatoid arthritis, and inflammatory bowel disease. For this reason their specificity is poor (60%) and sensitivity ranges from 60% to 90%. To improve diagnostic utility, these tests should only be requested when the level of suspicion of the associated disease (the pre-test probability) is high, e.g. in unexplained nephritis or pulmonary renal syndromes.

(To be continued...)

BOUQUET

In Lighter Vein

Three men were drunk and they stopped a taxi.....the taxi driver figured that they were not in their right minds.....so, he just switched on the engine and switched it off after a while and told them : "we have arrived".....

The first man gave him money..... the second one thanked him.....but the third one.....he slapped the taxi driver.....

The taxi driver was stunned because he was hoping that none of them must have realized that the car didn't move an inch...so, he asked the third man: "what was that for?"

The third man replied: "control your speed next time you got here so quick you almost killed us..."

Once upon a time there was a shepherd looking after his sheep on the side of a deserted road.

Suddenly a brand new Porsche screeches to a halt. The driver, a man dressed in an Armani suit, Cerutti shoes, Ray-Ban sunglasses, TAG-Heuer wrist-watch, and a Pierre Cardin tie, gets out and asks the Shepherd: "If I can tell you how many sheep you have, will you give me one of them?" The shepherd looks at the young man, and then looks at the large flock of grazing sheep and replies: "Okay."

The young man parks the car, connects his laptop to the mobile-fax, enters a NASA Webster, scans the ground using his GPS, opens a Database and 60 Excel tables filled with logarithms and pivot tables, then prints out a 10 page report on his high-tech mini-printer. He turns to the shepherd and says, "You have exactly 1,586 sheep here."

The shepherd cheers, "That's correct, you can have your sheep." The young man makes his pick and puts it in the back of his Porsche.

The shepherd looks at him and asks: "If I guess your profession, will you return my animal to me?" The young man answers, "Yes, why not".

The shepherd says, "You are a Management Consultant from a top-notch consultancy like McKinsey, etc..".

How did you know?" asks the surprised young man.

"Very simple," answers the shepherd. "First, you came here without being called. Second, you charged me a fee to tell me something I already knew, And third, you don't understand anything about my business... Now can I have my DOG back?"

A taxi passenger tapped the driver on the shoulder to ask him a question. The driver screamed, lost control of the car, nearly hit a bus, went up on the footpath, and stopped centimeters from a shop window.

For a second everything went quiet in the cab, and then the driver said "Look mate, don't ever do that again. You scared the daylight out of me!"

The passenger apologized and said, "I didn't realize that a little tap would scare you so much."

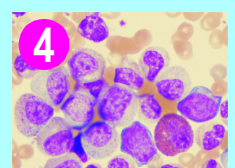
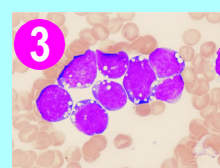
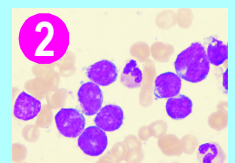
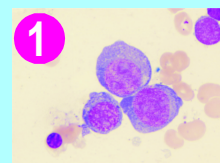
The driver replied, "Sorry sir, it's not really your fault. Today is my first day as a cab driver. I've been driving a van carrying dead Bodies for the last 25 years.....you can imagine what went into my mind when u tapped my back!!"

Wisdom Whispers

- To appear wise, one must talk;
To be wise, one must listen.
- To appear to do good, one must be busy;
To do good, one must know when to stand aside.
- To appear to lead, one must put oneself first;
To lead, one must put oneself last.
- To appear caring, one must give advice;
To be caring, one must give space.
- To appear to love, one must know how to give;
To love, one must know also how to receive.
- To appear happy, one must smile;
To be happy, one must be free with tears.

Brain Teasers

Try and diagnose the following hematological pathologies.



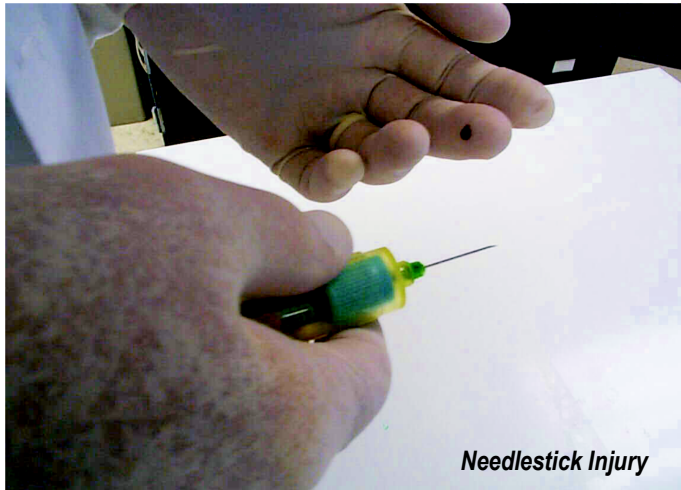
Answers: 1. AML M6 2. ALL L1 3. ALL L3 (B CELL) 4. CML

TROUBLESHOOTING

TREATING HIV EXPOSURE

DECREASING HIV RISK WITH POST-EXPOSURE PROPHYLAXIS

Treating HIV exposure has been shown to decrease the risk of HIV infection. Workers in health care settings are constantly exposed to occupational hazards; wet floors that lead to slip and falls, toxic chemicals that cause burns to the hands or face. But there is one hazard that people in the health care field fear most, the needle stick. Occupational exposure to blood borne infections, including HIV infection, via the needle stick occurs all too often. Some sources report that nearly 1 million healthcare workers suffer needle stick injuries each year. As a result, hundreds of workers are infected with diseases such as Hepatitis B, Hepatitis C and HIV. But treating HIV exposure with HIV medications has been shown to decrease the incidence of sero-conversion and HIV infection. **Because of the increasing problem of HIV infection from needle sticks, Internationally institutions now recommend treating HIV exposure with what they call as post-exposure prophylaxis (PEP) for those workers thought to be exposed to HIV in the workplace.**



What is Post Exposure Prophylaxis (PEP)?

PEP is just what the name suggests; prophylaxis (preventative) medications given after an HIV or suspected HIV exposure in hopes of decreasing the likelihood of HIV infection from the exposure. The PEP medication combinations used depends on the degree of exposure and the HIV status of the source of the exposure. But before any medications are prescribed, it has to be determined if PEP is indicated and appropriate.

WHEN IS PEP INDICATED?

The following scenarios warrant PEP.

Two drug PEP recommended when

- exposure to asymptomatic HIV+ person by solid needle stick or superficial injury that break the skin
- a mucous membrane exposure to a large volume of HIV infected blood that's source is asymptomatic (consider for a lesser volume, a few drops)
- a mucous membrane exposure to a small volume of HIV infected blood that's source is symptomatic.

Three drug PEP recommended

- exposure to asymptomatic HIV+ person via deep puncture from a

large bore hollow needle

- a puncture from a needle with visible blood on the needle
- a puncture from a needle used in a patient's vein or artery.

Three or More Drug PEP Recommended

- any needle stick exposure from any type needle used on a symptomatic HIV+ person
- a mucous membrane exposure to a large volume of HIV infected blood whose source is symptomatic.

Possibility of Two Drug PEP under Certain Circumstances

- needle stick with any type needle and any degree of exposure if the source has an unknown HIV status but has HIV risk factors
- needle stick with any type needle and any degree of exposure if the source has an unknown HIV status and unknown risk factors but a setting in which exposure to HIV+ persons is likely
- a mucous membrane exposure to any volume of blood whose source has an unknown HIV status but has HIV risk factors
- a mucous membrane exposure to any volume of blood whose source has an unknown HIV status but is in a setting where where HIV exposure is likely

No PEP Warranted

- any needle stick injury involving a known HIV negative source
- a mucous membrane exposure to any volume of HIV negative blood

WHAT MEDICATION COMBINATION IS USED?

PEP regimens are chosen depending on the type of exposure. Typically regimens are prescribed for a four week period. PEP should be started within hours of the potential exposure not days. The sooner PEP is began the better.

Preferred Two-Drug Regimen

Option 1 - (Zidovudine, AZT)+ (Lamivudine) twice daily. (Retrovir + Epivir) twice daily is typically substituted for ease of administration. This twice a day regimen is a bit harder to take but is recommended in pregnancy.

Option 2 - (Tenofovir + Emtricitabine) taken once daily. This one drug regimen is easier to take but does have the risk of liver toxicity.

Preferred Three-Drug Expanded Regimen

Basic two drug regimen option 1 or 2 above with the addition of (Lopinavir + Ritonavir) twice daily.

CONCERNS ASSOCIATED WITH PEP

While the benefits of PEP have been documented, there are some concerns as well. It's these concerns that cause practitioners to consider the need for PEP thoroughly before prescribing it. PEP is not without risk and should only be given in those people that absolutely need it. That being said concerns associated with PEP include: **Adherence Issues and the Problem of Resistance** - It's no secret that HIV medications have some unpleasant side effects. Because of these side effects the people who have been exposed find it difficult to take their PEP regimen as prescribed and/or complete the four week course. Both of these barriers result in poor adherence. And as in the case of HIV+ people on medication, poor adherence leads to viral resistance and poor control of HIV. That could make the difference between the PEP being successful or not.

THE LAST WORD ON PEP

PEP is a viable option for occupational exposures to HIV. While it is not without it's downfalls, it is effective in reducing the risk of HIV infection from a needle stick. But, without addressing the problem of needle sticks, more people are going to become infected by this route, health care cost will continue to rise and the epidemic will continue to grow.

TULIP NEWS**Glycated Albumin (GA) Assay..... a *PREVIEW***

When GA only ?

- GESTATIONAL DIABETES
- DIABETIC NEPHROPATHY
- PREMENOPAUSAL WOMEN
- DIABETICS WITH ANEMIAS
- DIABETICS ON HEMODIALYSIS
- DIABETICS ON PERITONEAL DIALYSIS
- THERAPEUTIC OUTCOMES IN POSTPRANDIAL HYPERGLYCEMIA

***ALL CASES REQUIRING IMMEDIATE & INTERMEDIATE GLYCEMIC CONTROL STATUS**

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