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Next Generation HIV Testing

Human immunodeficiency virus (HIV) is a communicable retrovirus that leads to a progressive disease with a long asymptomatic period. CDC estimates that approximately 1.1 million adults and adolescents were living with HIV infection in the United States and that approximately 56,000 persons are newly infected with HIV each year. Without treatment, most persons develop acquired immunodeficiency syndrome (AIDS) within 10 years of HIV infection. Antiretroviral therapy delays this progression and increases the length of survival, but is most effective when initiated during the asymptomatic phase. It is estimated that on average, an HIV-positive person aged 25 years who receives high-quality care will survive an additional 39 years. Identifying persons early in the course of infection reduces morbidity and mortality, prevents new infections, and can reduce health-care expenditures.

CDC recommends routine HIV screening between the ages of 13 and 64 years in all health-care settings. Persons at high risk for HIV infection should be screened at least annually. The burden of HIV is greatest among gay, bisexual, and other men who have sex with men (MSM). The disproportionately high rates of diagnoses among African Americans and Latinos, suggest that adults from these subpopulations might benefit from more frequent testing to facilitate early diagnosis. Other groups identified as potentially high risk include teenagers and senior citizens. CDC estimates that people over 60 account for 19% of all newly diagnosed AIDS cases.

HIV can be transmitted during pregnancy, labor & delivery, or breastfeeding. The CDC has recommended that all pregnant women be counseled and encouraged to be tested for HIV infection. HIV testing should be included in the routine prenatal panel. Substantial progress has been made in reducing perinatal HIV transmission rates from 25-30% in 1991 to the current <2% transmission rate. This reduction is attributed to HIV screening of pregnant women, use of

antiretroviral drugs, and elective cesarean deliveries.

Human immunodeficiency virus exists as two distinct viral species, designated HIV-1 and HIV-2. Each species is further subdivided into subgroups, including M, N, & O for HIV-1, and subgroups A-G for HIV-2. The vast majority (99.6%) of HIV infections worldwide are caused by HIV-1, group M. The less prevalent viral types are largely confined to West Africa.

The interval between infection and detection of HIV antibody is called the window period. Improvements in HIV-1 antibody tests have steadily reduced the window period as seen in the following table.

ELISA Generation	Window Period (days)
First	42
Second	36
Third	22
Fourth	16

Several years ago, HIV-1 antibody tests were replaced by newer combination tests for HIV-1 and HIV-2, which did not distinguish between HIV-1 and HIV-2. Specimens that tested reactive to HIV-1/2 antibody were automatically forwarded for confirmatory testing by Western blot.

Improvements in sensitivity of newer generation HIV-antibody screens created the dilemma of falsely-negative Western blots, which may not show reactivity until 4 weeks or more. Therefore, since 2013, the confirmation test for reactive results is the HIV-1/HIV-2 differentiation immunoassay. This confirmation immunoassay, also known as Multispot, detects seroconversion earlier than Western blot and eliminates most indeterminate results that occur due to nonspecific reactivity from alloantibodies.

Beginning in mid-September, Saint Luke's Laboratories will change to a fourth generation HIV assay for initial screening. As noted, this assay decreases the detection window to 16 days post-infection. In addition to HIV-1 group M & O and

HIV-2, this new generation test detects HIV p24 antigen. Results will be reported as HIV Ag/Ab and either presumptive reactive or non-reactive. The test does not distinguish between HIV types or whether p24 antigen or antibody is detected. All reactive results will be forwarded to a reference laboratory for confirmation by Multispot testing. Specimens that do not confirm positive by Multispot may require further analysis by HIV PCR.

Rapid Malaria Antigen Test

Four species of Plasmodium are responsible for the majority of human malaria cases, including Plasmodium falciparum (*P. falciparum*), *P. vivax*, *P. malariae* and *P. ovale*. A fifth species, *P. knowlesi*, has been recognized as causing disease similar to *P. falciparum* infection in Southeast Asia, particularly Malaysia.

Rapid identification of malaria infections and differentiation of *P. falciparum* from other malarial parasites is a time-critical diagnosis. Traditional diagnosis depends upon microscopic identification of malarial organisms in peripheral blood. Although microscopy is sensitive, the timing of specimen collection is vital for optimal results, it is labor-intensive, and requires maintenance of expertise.

Recently, an immunochromatographic assay became available for testing of blood specimens for malaria antigen. The test detects histidine-rich protein II (HRP II) antigen, which is specific to *P. falciparum*, as well as a pan-malarial antigen common to all four major species. The clinical limit of detection for *P. falciparum* is 1000-1500 parasites/uL. The test distinguishes between *P. falciparum* and non-falciparum species. Because lower levels of parasitemia may not be detected, follow-up testing of negative results is recommended when suspicion for infection is high. Follow-up testing may include malarial smears, additional malaria antigen testing or malaria PCR. The test may not detect *P. knowlesi*.

The malaria antigen test will be available through Saint Luke's Microbiology in September 2015, and testing will be performed daily. Specimen requirement is one EDTA tube of blood.

Hereditary Pancreatitis Gene Panel

Hereditary pancreatitis (HP) is a rare autosomal dominant disorder that is characterized by early onset of acute pancreatitis during childhood or early

adolescence and progression to chronic pancreatitis by adulthood. Patients with HP have a higher risk of developing pancreatic cancer. The diagnosis of hereditary pancreatitis is based upon clinical history and recognition of an inheritance pattern.

Mutations in the protease serine 1 or cationic trypsinogen (*PRSS1*) gene are present in up to 80% of patients with hereditary pancreatitis unrelated to cystic fibrosis. The absence of a mutation does not eliminate the possibility of positive carrier status or the diagnosis of HP.

Chronic pancreatitis may also be inherited as an autosomal recessive disorder. Mutations in the cystic fibrosis transmembrane conductance regulator gene (*CFTR*) gene are most common cause of pancreatitis with or without the other manifestations of cystic fibrosis. Nearly 2000 different genetic variants in *CFTR* have been identified. Complete gene sequencing should be considered, especially if the patient has recurrent sinusitis or male infertility. Multiple family members may be affected.

Mutations in the serine protease inhibitor Kazal type 1 (*SPINK1*) gene are also associated with autosomal recessive pancreatitis. Patients with pancreatitis are often homozygous or compound heterozygous, possibly with a *CFTR* mutation. Mutations in *SPINK1* increase the risk for chronic pancreatitis about 12-fold over the general population.

Genetic testing is most commonly limited to the *PRSS1*, *CFTR* and *SPINK1* genes. Testing should be considered in patients with pancreatitis and one or more of the following criteria

- Unexplained pancreatitis as a child
- Idiopathic chronic pancreatitis, especially with onset before age 25
- Family history of recurrent pancreatitis or childhood pancreatitis
- Relatives with known mutations associated with hereditary pancreatitis
- Recurrent acute attacks of pancreatitis with no identifiable cause

Specimen requirement is a lavender top (EDTA) or yellow top (ACD) containing at least 3 mL of blood.