
# SESSION 5 | WEDNESDAY, AUGUST 25, 2021

**Session Moderator:** Dr. Auwaerter
**Session Panelists:** Drs. Alexander, Bennett, Marr, and Mitre

## 61 | POWASSAN | AUWAERTER

In late August, a 19-year-old male hailing from northern Minnesota was transported to his local emergency department for two days of headache and a generalized seizure. He had been working as a landscaper before starting college a few days ago in September. His health has been excellent, though he vaped and used marijuana.

At presentation, he had a temperature of 38.1°C and was slightly groggy but had no focal neurological deficits or meningismus. No rash was present.

A head CT without contrast was unremarkable.

A lumbar puncture yielded clear fluid, CSF findings: protein 56 mg/dL (normal 14-45 mg/dL), glucose 66 mg/dL (50-80 mg/dL), RBC 4 (0-5), WBC 188 with 12% lymphocytes and 88% PMNs. A CSF Gram stain was negative.

Fevers persisted, and mental status declined over the next three days while on vancomycin, ceftriaxone, and acyclovir. CSF cultures are negative, as was a CSF HSV PCR.

Which of the following would be the most likely?

A. **Powassan virus**
B. West Nile virus
C. Rickettsia rickettsii
D. Listeria monocytogenes
E. Naegleria fowleri

Correct Answer: **Powassan virus**

Powassan virus (POWV) can cause encephalitis. POWV has two distinct lineages, antigenically indistinguishable but genetically distinct and transmitted by different ticks. Most clinical cases are now thought to be caused by lineage II, also called Deer Tick virus (DTV), transmitted by *Ixodes scapularis* in North America. Lineage I is transmitted by Ixodes cookei, a tick which prefers to feed on woodchucks and rarely bites humans. Cases of DTV have most been frequently reported in Minnesota, Wisconsin, and New York. Unlike the situation posed here, most patients with DTV infection are infected in Spring and summer. Even brief tick attachment can transmit DTV. Diagnosis requires a high index of suspicion given its rarity and the need to send testing to state health departments for POWV detection by IgM assays, plaque reduction neutralization assays or PCR.

West Nile virus (WNV) can infect any age; however, neuroinvasive disease in non-immunocompromised adults is almost exclusively seen in patients over the age of 50.

Rocky mountain spotted fever, caused by Rickettsia rickettsii would be extremely unlikely in Minnesota and the absence of rash after several days of illness is atypical.

Listeria meningitis is most frequently seen in newborns and older adults, while adolescents and young adults are most prone to the bacterial infections *S. pneumoniae* and *N. meningitidis*. The negative bacterial culture and relatively low pleocytosis is against the diagnosis.

The free-living amoeba, Naegleria fowleri, may cause meningoencephalitis seen chiefly in young boys participating in water activities. Human infections have only been described in 15 southern-tier states where the very warm waters likely contribute to higher densities of the organism that arise from colonized cattle's excreta. Given this patient's older age and exposure in Minnesota, naegleria infection is unlikely. Pleocytosis is typically much higher than this patient.

## 62 | Pertussis Prophylaxis | Auwaerter

A 2-year-old child is admitted to a pediatric hospital with pertussis.

What preventive therapy should be given to the mother?

A. Treat only if the mother becomes symptomatic
B. Culture the oropharynx and treat only if positive
C. Administer pertussis immune globulin only
D. Administer Tdap only if the mother was never immunized
E. **Treat with a 5-day course of azithromycin**

Correct answer: **Treat with a 5-day course of azithromycin**

Prior vaccination with Tdap should not be considered sufficiently protective to eliminate the need for chemoprophylaxis in the setting of an active household infection.

Administration of postexposure therapy to an asymptomatic contact within 21 days of onset of cough in the index patient can potentially prevent symptomatic infection.

Postexposure immunization, either passive with immunoglobulin or active with pertussis vaccine, does not protect contacts from infection and thus C and D are incorrect.

Postexposure antibiotic prophylaxis is appropriate for individuals with close contact with a person with pertussis. Close contact is defined as face-to-face exposure within 3 feet of a symptomatic patient. Individuals with direct contact with respiratory, nasal, or oral secretions may also be considered close contacts. Thus, this mother certainly qualifies.

The threshold to administer postexposure antibiotics should be lower in certain groups with high risk for morbidity and mortality, including infants and individuals with chronic lung disease or immunodeficiency.

The antibiotic regimens for postexposure prophylaxis are identical to those used for the treatment of pertussis: 5 days of azithromycin or 7 days of clarithromycin should suffice.

Patients with pertussis infection should avoid contact with children and infants until they have completed five days of appropriate antibiotic therapy. Also, infected individuals working in schools, daycare centers, or health care facilities should not return to work until completing at least five days of appropriate antibiotic therapy.

## 63 | CMV Prophylaxis | Alexander

A CMV seronegative renal transplant recipient received his allograft from a CMV seropositive donor.

The recommended post-transplant antiviral prophylaxis is:

A. No prophylaxis unless a CMV PCR test on blood returns positive
B. Acyclovir intravenously during the transplant hospitalization, then step down to valacyclovir for 6 months
C. **Ganciclovir until tolerating orals then stepdown to valganciclovir for 6 months**
D. Ganciclovir until tolerating orals then stepdown to valganciclovir for life

Correct answer: **Ganciclovir until tolerating orals then stepdown to valganciclovir for 6 months**

This kidney transplant recipient is at high serologic risk for CMV (donor positive, recipient negative). Accordingly, universal prophylaxis against CMV is recommended for the first 6 months post-transplant.

While acyclovir and valacyclovir have excellent activity against VZV and HSV, the activity against CMV is limited and requires high doses. Thus, ganciclovir and valganciclovir are standard of care prophylactic agents for CMV.

The duration of antiviral therapy generally ranges from 3 to 12 months and depends on the type of organ transplanted, the specific risk status of the patient, and individual institutional practice. A decrease in CMV disease was seen in donor positive/recipient negative kidney transplant recipients given 200 days compared with those given 100 days of prophylaxis, but in another study, extending CMV prophylaxis from 6 to 12 months did not prevent CMV infection or disease. Further, long courses of prophylaxis with valganciclovir are associated with higher rates of leukopenia and greater cost.

Thus, in high-risk kidney recipients, 6months of prophylaxis with ganciclovir /valganciclovir is generally recommended.

## 64 | CMV Resistance | Alexander

A lung transplant recipient developed fatigue, fevers, and diarrhea seven months post-transplant.

She had been receiving valganciclovir prophylaxis since transplant based on her high CMV serologic risk status (donor seropositive, recipient seronegative), but in the context of improving renal function without adjustments in her valganciclovir dosing.

At the time of presentation with fever and fatigue, her CMV viral load on blood was positive at 135,000 IU/ml and her WBC, hemoglobin, platelets, and creatinine clearance were within normal limits.

You recommend:

A. Hold on treatment pending a colonoscopy with colon biopsy to document invasive CMV colitis
B. Increase valganciclovir to prophylactic dosing appropriate for current renal function and recheck CMV viral load in one week
C. **Send blood for CMV resistance genotyping and start ganciclovir treatment, double dose**
D. Start letermovir

Correct Answer: **Send blood for CMV resistance genotyping and start ganciclovir treatment, double dose**

This patient is at high serologic risk for CMV and with risks for valganciclovir resistance including prolonged and potentially underdosed valganciclovir in the setting of her improving renal function. Taken together, and the fact that her viral load is now high with associated symptoms compatible with CMV syndrome and possibly CMV colitis, there is an urgent need to treat.

Should the diarrhea not improve after approximately 7 to 10 days of treatment, a colonoscopy would be warranted. Treatment with high dose ganciclovir can be attempted pending the resistance testing results, as some of the UL97 mutations which are typically the first to arise may be overcome with high dose ganciclovir.

Letermovir does have activity against some ganciclovir resistant strains, but letermovir is not approved for CMV treatment (only prophylaxis in stem cell transplant populations) and there is concern that letermovir has a low barrier for resistance as well.

If ganciclovir resistance is documented, foscarnet is typically considered first line treatment for ganciclovir resistant CMV disease.

## 65 | Trypanosomiasis | Mitre

A 23-year-old college student is seen for intermittent fevers, headaches and arthralgias.

He came to the US from the Central African Republic (central Africa) two months ago to attend college.

He says his symptoms have been present for at least the last four months, and it is hard for him to concentrate on his studies.

On exam his temperature is 100.6F; he has a soft, moveable posterior cervical node 3cm by 3cm; and his liver and spleen are palpable.

Which one of the following is the most likely diagnosis?

A. Malaria
B. Rift Valley Fever
C. Rickettsia africae infection
D. Typhoid Fever
E. **African trypanosomiasis**

Correct answer: **African trypanosomiasis**

West African trypanosomiasis due to Trypanosoma brucei gambiense is seen in West and Central Africa and is more chronic in presentation than the East African form due to Trypanosoma brucei rhodesiense.

- Patients may have intermittent fevers, headaches, and arthralgias for months before developing CNS infection (sleeping sickness).

- Posterior cervical adenopathy is common in the West African form. Patients may have hepatosplenomegaly.

Malaria may cause hepatosplenomegaly but is not associated with adenopathy.

This illness is too long in duration for Rift Valley Fever, Rickettsia africae infection, or Typhoid Fever.

## 66 | CRS | MARR

A 24 y/o male has acute pre-B cell lymphoblastic leukemia that has been refractory to multiple courses of conventional therapy. After an unsuccessful allogeneic stem cell transplant from his brother, his bone marrow biopsy is packed with blasts and peripheral smear show relapsed pre-B cell leukemia.

He is referred for CD19 CAR T cell therapy (Chimeric antigen receptor T cells), which he received following a preparative regimen consisting of fludarabine plus cyclophosphamide.

On day 10 following CAR T cell infusion, the patient developed fever to 39C on several serial measurements, and capillary leak syndrome with hypoxia and diffuse pulmonary infiltrates on chest xray. He has been receiving prophylaxis with acyclovir 800 mg po twice daily and micafungin 100 mg IV once daily.

He is transferred to the ICU where his is administered 2 liters of saline, given low dose norepinephrine to bring his mean blood pressure to >60mm/Hg, and placed on supplemental oxygen because his O2 saturation on room air was 90%.

Labs reveal that he is profoundly neutropenic (Absolute neutrophil count < 100), with serum creatinine rising from 1.3mg/dl to 2.4mg/dl, and transaminases rising from 1.5 x normal to 3x normal. Blood cultures are drawn and piperacillin-tazobactam begun.

What is the most likely cause of his abrupt deterioration?

A. Bacterial sepsis
B. Pneumocystis pneumonia
C. **Cytokine release syndrome**
D. GI bleed
E. Cardiogenic shock

Correct answer: **Cytokine release syndrome**

When a neutropenic patient develops fever and shock, the first consideration must be septic shock, and the patient should promptly receive broad spectrum antimicrobials. Shock would be an unusual presentation for a respiratory virus or pneumocystis pneumonia. There is no a priori reason for this

patient to develop cardiogenic shock. High fever would be unusual for a GI bleed. The cytokine release syndrome is a well described complication of CD19 CAR T cell therapy of lymphoid malignancies, particularly with high tumor burdens, like this patient.

Chimeric antigen receptor (CAR) T cells are genetically modified T cells engineered to express a chimeric antigen receptor (CAR) targeting antigen (CD19, CD22) expressed on the surface of, in this case, B cells. Recognition of a specific cell surface antigen activates T cell response independently of MHC recognition.

A cytokine release syndrome does occur 1-14 days following cell infusion. This syndrome can present with dysfunction of virtually any organ: fever and myalgias are common, but distributive shock, ARDS, respiratory failures, renal failure, and hepatic failure can occur.

There is interest in treating this syndrome with corticosteroids, tocilizumab (IL 6 blocker) or siltuximab (also IL6 blocker) but these are not standard therapies and could not be on the boards.

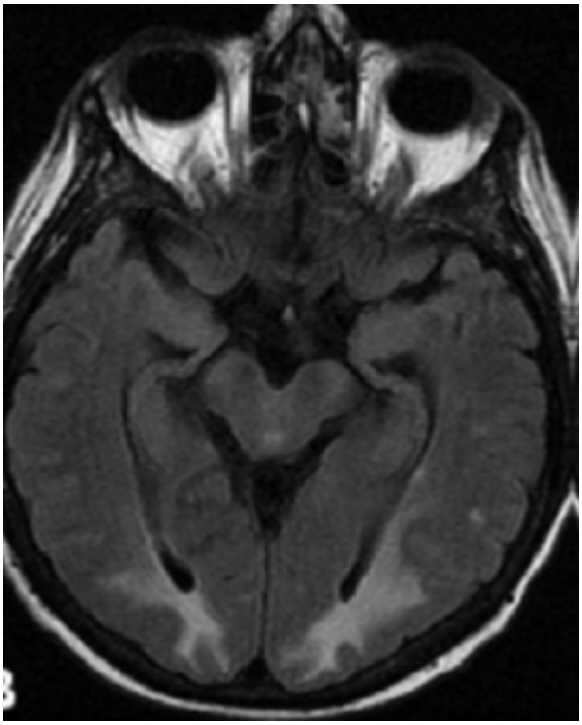
## 67 | PRES | Marr

A 28-year-old woman who is 9 days post receipt of allogeneic HSCT for acute myeloid leukemia presents with 2 days of altered mental status.

Last night, her nurse witnessed what may have been a self-limited focal seizure.

MRI with FLAIR imaging is shown below.

She is lethargic and confused but complains of headache. She is still severely neutropenic.



She is from Haiti and has a history of latent TB, which was treated for 9 months prior to transplant with INH.

Post-transplant, she is not yet engrafted, and her current serum creatinine is 3.2.

Her blood pressures have been increasingly high, now ranging from 140–170 systolic. Her current medications include tacrolimus (her last level was within the therapeutic range), and prednisone at 10 mg.

She is receiving fluconazole and valacyclovir prophylaxis.

Which of the following is the best explanation of her current process?

A. Tuberculosis
B. HHV-6
C. Cryptococcosis
D. **Tacrolimus toxicity**
E. Polyoma virus

Correct Answer: **Tacrolimus toxicity**

While reactivation TB is possible in a transplant recipient, it is less likely in people who have been treated for latent disease. The radiographic image is very atypical for tuberculosis or cryptococcosis.

She is receiving fluconazole, making cryptococcosis even less likely. Neutropenia is not predisposing to either infection.

Lesions in the white matter may be seen with polyoma virus and HHV6. Polyoma virus encephalitis (usually JC virus) is much more indolent and would be rare in this setting. HHV6 can cause limbic encephalitis but rarely confined to this cortical distribution or prior to engraftment.

The patient has posterior reversible encephalopathy, which has many possible causes but can result from tacrolimus neurotoxicity post-transplant. Tacrolimus levels may or may not be elevated. Diagnosis is made by the rapid onset of CNS symptoms, confusion, seizures and visual loss, plus subcortical edema which includes the parietal or occipital cortex, best seen on MRI by FLAIR (fluid-attenuated inversion recovery) imaging (Br. J. Haematol 2003: 122;128-134). Azotemia and acute hypertension, both of which she had, are predisposing factors.

## 68 | TOXO HSCT | MARR

A 20-year-old patient from Jamaica with aplastic anemia received a cord blood transplant 5 months ago in Bethesda. He pretransplant serology was CMV IgG positive, toxo IgG positive and HSV positive. He has had excellent engraftment, and is maintained on tacrolimus plus prophylactic antimicrobials.

Two weeks before admission (4 months post-transplant) he developed progressive fever, shortness of breath, and a slight cough. He has bilateral crackles on lung exam but no wheezes. There is significant hypoxemia (pO2=90mmHg on room air) but no skin rash or diarrhea.

He has not taken his trimethoprim-sulfamethoxazole, fluconazole, or acyclovir because he thinks they made him nauseated, but he did take his tacrolimus.

- His chest CT scan showed diffuse, bilateral ground glass infiltrates.
- WBC=5000 cells/uL (90% polys)
- Bronchoalveolar lavage: Direct stains negative for pneumocystis by DFA, bacteria by Gram stain, fungi by calcofluor, and AFB by auramine-rhodamine. Lavage fluid was negative on respiratory film array for RSV, coronavirus, influenza and human metapneumovirus.
- BAL PCR was positive for CMV, but blood CMV PCR negative
- BAL PCR was positive for Toxoplasma

What is the most likely cause of his pulmonary process?

A. Cytomegalovirus
B. Engraftment Syndrome

C. Bronchiolitis obliterans
D. **Toxoplasmosis**
E. Candidiasis

Correct answer: **Toxoplasmosis**

All the processes or organisms in all answer choices cause pneumonia except Candida. This is pulmonary toxoplasmosis as documented by the BAL PCR, which is very specific for detection of toxoplasma. Pulmonary toxoplasmosis is not common, but this presents identically to PCP, and would not be identified by the usual direct tests or cultures. The diagnosis is established by PCR of BAL fluid, which is very specific but with variable sensitivity. Had he taken his trimethoprim-sulfamethoxazole for PCP prophylaxis, he would have been protected from pulmonary toxoplasmosis.

Toxoplasmosis in HSCT patients is usually from reactivating latent infection, in patients who are antibody positive pretransplant. Transfusion acquired toxoplasmosis is rare. Patients with cord transplants do not have an experienced T cell repertoire from their donor.

Engraftment syndrome occurs typically when the neutrophil count is returning. Thus, this syndrome occurring months after the return of neutrophils is too late for this.

Bronchiolitis obliterans is a late complication (>100 days post-transplant), usually in allogeneic transplants, occurring with other evidence of graft vs. host disease, and manifesting as airway obstruction (wheezing and restrictive disease), sometimes with diffuse infiltrates and fever.

This is not likely to be due to Candida since Candida almost never causes pulmonary disease. CMV is not likely to be the cause in view of the negative blood PCR. A positive CMV PCR on BAL lavage is not rare, possibly due to saliva contamination, and often of no clinical significance. One does not see pneumonitis without signs of peripheral reactivation as well.

## 69 | Fusarium | Bennett

A 47-year-old male from Maryland with myelodysplastic syndrome and prolonged neutropenia underwent an allogeneic bone marrow transplant after myeloablative chemotherapy. Post bone marrow transplant he was placed on prophylactic acyclovir and fluconazole.

Two years ago, he spent 3 months on an island off the coast of Venezuela.

On day 5 following transplant, with an absolute neutrophil count of zero, he became febrile to 40°C with hypotension. Piperacillin-tazobactam and vancomycin were begun. The next day, new necrotic skin lesions were noted. The lesions were 2 to 3 cm in diameter and deep in the subcutaneous tissue and reddish purple in color. Chest CT showed a small peripheral consolidation in right lower lobe. Voriconazole was added.

On day 6 the laboratory reported two routine blood cultures positive for septated hyphae.

The most likely diagnosis is:

A. Disseminated aspergillosis
B. Disseminated mucormycosis
C. Disseminated paracoccidioidomycosis
D. Disseminated Talaromyces marneffei
E. **Disseminated fusariosis**

Correct answer: **Disseminated fusariosis**

The skin lesion could be caused by a variety of invasive bacteria or fungi, but the report of hyphae growing from blood should strongly suggest fusariosis.

Fusarium can cause skin or corneal disease in normal hosts, albeit rarely. With prolonged neutropenia, or following bone marrow transplantation, dissemination can occur, probably from skin or lungs in most cases. Necrotic skin lesions occur in 60-80% of cases.
For aspergillosis, or mucormycosis, blood cultures are almost always negative; in contrast, positive blood cultures are seen in 40-50% of cases of fusariosis. Thus, this case is far more likely to represent fusariosis than aspergillosis.

If this patient were in Southeast Asia, Talaromyces marneffei might be considered. The rapidly progressing skin lesions are atypical for talaromycosis or paracoccidioidomycosis and neither would grow in routine blood cultures in six days.

## 70 | Disseminated Histo | Bennett

A 34-year-old woman in Columbus, Ohio was admitted to the hospital because of high fever, prostration, and extreme malaise of increasing severity over the past week.

Her past history was notable for Crohn's disease being treated with adalimumab (Humira) for the past two months. Prior prednisone therapy had been discontinued.

She was born in Nicaragua but had lived in the United States with her husband and children for the past five years, working in a daycare center.

On examination, she was flushed and dyspneic, with pulse oximetry at 92% saturation. Chest x-ray showed a faint diffuse infiltrate.

Admission studies found her long standing anemia has worsened, with a hematocrit of 25%, platelet count 30,000, WBC 2,500 with a normal differential, alkaline phosphatase 250, ALT 120, AST 89 and creatinine 2.0.

She was transferred to intensive care and given intravenous cefepime and levofloxacin plus oral doxycycline. Admission and subsequent daily blood cultures remained negative. At the end of the first week, micafungin was begun because yeast cells were seen in her peripheral blood smear.

The most likely source of her infection was which of the following:

A. A human in Nicaragua
B. A human in her day care center
C. Her intestinal tract
D. Pigeon droppings
E. **Soil**

Correct answer: Soil

Patients receiving TNF-alpha inhibitors are at increased risk of disseminated, severe intracellular infections, including tuberculosis and histoplasmosis. Histoplasma is the most likely organism to be seen in a peripheral smear: this is likely from soil that contains bird or bat droppings, is aerosolized, and inhaled.

Although the clinical picture is compatible with either infection, yeasts in the peripheral blood smear provide strong evidence for acute disseminated histoplasmosis.

Candidemia and Cryptococcus can rarely be seen as yeast on smear, but would have grown from routine blood cultures and would not explain her pancytopenia. Viral associated lymphocytic hemophagocytosis can present as fever and pancytopenia, but would not explain yeasts in the blood stream.

An echinocandin such as micafungin is not effective and immediate institution of amphotericin B is indicated.

Azotemia, probably from her histoplasmosis, would suggest use of liposomal amphotericin B (AmBisome) would be better tolerated than conventional amphotericin B.

## 71 | Latent TB in SOT | Alexander

A 62-year-old with end stage renal disease and on hemodialysis is under consideration for kidney transplantation. He immigrated to the U.S. from South Africa 40 years prior. He notes that his mother died with tuberculosis when he was 12 years old and that he and his father cared for her in their two-room home during her illness.

He has never been treated for tuberculosis. He currently denies cough, weight loss and night sweats. A chest radiograph is clear.

You recommend:

A. **Treatment for latent tuberculosis**
B. Treatment for latent tuberculosis only if a Tuberculin Skin Test (TST) reactivity is ≥ 10 mm
C. Treatment for latent tuberculosis only if an interferon-gamma release assay (IGRA) for tuberculosis is positive
D. No treatment since his exposure was more than 25 years ago

Correct answer: **Treatment for latent tuberculosis**

The patient has a history of close contact with an individual with active pulmonary TB. He does not currently have active signs or symptoms of tuberculosis and his CXR is negative. While a tuberculin skin test or IGRA can be used to screen for latent tuberculosis, sensitivity of both tests may be lower in the setting of renal failure.

Therapy for latent tuberculosis should be provided for solid organ transplant candidates with the following specific indications:

- Tuberculin reactivity of ≥5 mm before transplantation
- History of tuberculin reactivity without adequate prophylaxis
- Recent conversion of TST to positive
- Radiographic evidence of old TB without prior prophylaxis; a chest computed tomographic scan should be performed in these patients to look for disseminated disease and to serve as a baseline study
- History of inadequately treated TB
- Close contact with an individual with active pulmonary TB
- Receipt of an allograft from a donor with a history of untreated TB

## 72 | Syphilis Uveitis | Auwaerter

A 30-year-old HIV-infected man who has sex with men (CD4 count 780 cells/mm3 with an undetectable HIV RNA) with no significant past medical history complains of pain and decreased vision in his right eye.

He was well until three days prior to presentation when he developed discomfort in his eye and blurry vision.

He denied any history of trauma. He had just returned from a 10-day trip to North Africa and Western Europe one week prior to the onset of symptoms.

On examination, he has a maculopapular rash on his trunk and diffuse lymphadenopathy. He is referred to an ophthalmologist and is diagnosed with panuveitis. A CBC, complete metabolic panel, RPR, and chest radiograph are unremarkable.

He had a negative ppd three months earlier.

Which of the following tests is most likely to be abnormal?

A. Toxoplasma serum IgG
B. Cerebrospinal fluid JC virus PCR
C. Cerebrospinal fluid TB PCR
D. **Serum treponemal EIA**
E. Serum Quantiferon

Correct answer: **Serum treponemal EIA**

This patient had a negative RPR because of a prozone effect. Diluted serum found a RPR titer of 1:2048. EIA is not affected by the prozone. The patient has secondary syphilis with ocular involvement. Panuveiutis is one of the most common ocular manifestations of syphilis- particularly, early-stage syphilis.

Approximately 70% of patients with ocular syphilis will have one or more CSF abnormalities. Of those who have CSF abnormalities, most will have CSF pleocytosis but only about half will have an abnormal CSF VDRL. Keep in mind that the 2021 CDC Treatment Guidelines no longer recommend a CSF examination in persons suspected of having ocular symptoms if they only have ocular signs and symptoms.

Among patients with secondary syphilis, nearly 100% should have reactive serum treponemal and non-treponemal antibodies (barring a prozone reaction).

The history does not provide any clues that he is at risk for TB infection. Uveitis could be caused by TB but is not likely here.

Toxoplasmosis could explain the uveitis but it not the most likely cause.

JC virus is the cause of JC virus encephalitis, which would be unlikely to cause uveitis and unlikely to cause any disease in a patient with such a high CD4 count.

Ocular syphilis is treated the same as CNS syphilis with a 14-day course of intravenous penicillin G.

A 58 y/o man developed a decline in mental status and "sepsis-like picture" 16 days following bilateral lung transplantation. He had never travelled outside of the US and worked in an office as an accountant.

Blood cultures were negative and his only remarkable laboratory finding was an elevated ammonia level (490 µmol/L).

Which of the following would be the most likely cause of this "sepsis like picture" occurring in this setting?

A. *Mycoplasma genitalium*
B. ***Ureaplasma parvum***
C. *Streptobacillus moniliformis*
D. *Brucella melitensis*
E. *Bacteroides thetaiotaomicron*

Correct answer: ***Ureaplasma parvum***

Hyperammonemia syndrome is a condition of previously unknown cause affecting approximately 4% of lung transplant recipients early after transplantation.

Despite maximal supportive therapy directed at suppressing ammonia production and augmenting its excretion, most with this condition have historically progressed to cerebral edema and died.

Recently, *Ureaplasma urealyticum* and *Ureaplasma parvum,* bacteria which produce large amounts of urease, have been associated with hyperammonemia syndrome in lung transplant recipients.

Diagnosis can be achieved using *U. urealyticum/parvum* culture and/or PCR of respiratory secretions and/or blood. With treatment directed against *U. urealyticum/parvum,* most with this condition survive.

## 74 | Artesunate | Mitre

A 27 yr old African-American female was hospitalized with severe malaria after returning to the U.S. from a trip in Ghana. She had a peak parasitemia of 7% and exhibited rapid improvement after initiation of artesunate. Nine days after discharge she presents to the Emergency Department with shortness of breath. Oxygenation on room air is 95%, BP 101/55, pulse 92. Hemoglobin is 4.1 gm/dl, compared to her discharge value of 8.3 mg/dl. Serum lactate dehydrogenase level is elevated and haptoglobin is below the level of detection. Chest x-ray is normal.

The most likely cause of this deterioration is which of the following:

A. Glucose-6 phosphate dehydrogenase deficiency (G6PD)
B. Methemoglobinemia

C. Pulmonary embolism
D. Delayed post-artesunate hemolysis
E. Drug resistant malaria

Correct answer: Delayed post-artesunate hemolysis

Although intravenous artesunate is the drug of choice for severe malaria, a few patients will develop dramatic hemolysis one to four weeks post treatment that may be accompanied by weakness, dyspnea, confusion, or kidney injury. Transfusion may be required. While the exact mechanism by which this delayed anemia occurs is not yet fully understood, a likely mechanism is hemolysis of erythrocytes that were previously infected with malarial parasites. Artesunate has been observed to kill intraerythrocytic parasites without causing immediate death of infected red blood cells. This can result in damaged (pitted) erythrocytes with reduced half-lives that lyse and are removed by the spleen, resulting in a delayed onset anemia. Artemisinin derivatives are not affected by G6PD and don't cause methemoglobinemia. Drug resistance of artesunate is rare in Africa and would not explain her original response. Pulmonary embolism would not explain the hemolysis

## 75 | Naegleria | Mitre

A 23-year-old, previously healthy man was seen in an emergency room in Kentucky in August for a severe headache that had been present for one day.

He eats homemade cheese made from raw cow's milk. Two days before he became ill, he had a Jet Ski accident on a man-made lake, ingested a fair amount of lake water, and sustained a minor injury to his leg; there was no head trauma. He was awake, alert, and oriented but had a stiff neck. The rest of the examination was unremarkable.

His CSF showed the following:

- WBC: 1740 (82% neutrophils)
- RBC: 30
- Glucose: 18
- Protein: 420
- Gram stain: negative

Dexamethasone, vancomycin, and ceftriaxone were begun for suspected bacterial meningitis. The following day he was worse with confusion and vomiting.

Cultures of the blood and CSF had no growth at 72 hours.

Pending further studies which one of the following would be the most likely etiology as suggested by his history?

A. Acanthamoeba castellanii
B. Balamuthia mandrillaris
C. Pythium insidiosa
D. **Naegleria fowleri**
E. Paracapillaria philippinensis

Correct answer: **Naegleria fowleri**

This patient has a clinical picture most consistent with the diagnosis of primary amebic meningoencephalitis. This rare, almost always fatal infection is due to Naegleria fowleri, a thermophilic freshwater ameba. Infection occurs when water enters the nose; amebae migrate along the olfactory nerves into the brain. Most cases occur in Southern states during July through September. Symptom onset is typically 1 to 14 days after water exposure; disease progresses rapidly. The CSF findings mimic those of bacterial meningitis.

Diagnosis is made by seeing actively moving trophozoites in a fresh wet-mount of centrifuged CSF. Trophozoites may be seen on Giemsa or Wright stain of CSF but are not seen with Gram stain.

Balamuthia mandrillaris and Acanthamoeba castellanii are free living amoeba that cause granulomatous encephalitis and present as focal neurologic deficits of subacute onset. Paracapillaria is an intestinal nematode that causes diarrhea. Pythium, sometimes referred to as a water mold, is an oomycete – a fungus-like eukaryotic organism that some scientists place in the Chromista life kingdom. Most often found in moist soil, it is a frequent cause of root rot that can destroy agricultural crop yields. Pythium is a rare infection of humans, but has been reported to cause deep tissue and vascular infection after trauma, most often in Thailand and other tropical regions.