Questions:

1. Can neurosyphilis present as unilateral paresthesias of the mouth and tongue?
   - Yes, it can. Please refer to full response on the webinar recording.

2. Are the CSF tests only VDRL?
   - The only CSF tests referred to in the surveillance case definitions (CSTE position statement) are a reactive VDRL (for verified neurologic manifestations) or elevated CSF protein or leukocyte count (for likely neurologic manifestations). No other CSF test would meet the surveillance case criteria for neurologic manifestations. The CDC treatment guidelines also mention a CSF FTA-ABS test, which is more sensitive but less specific than a CSF VDRL test (i.e., a negative CSF FTA-ABS test can help to rule out neurosyphilis, but a positive CSF FTA-ABS test does not necessarily indicate neurosyphilis). The clinical significance (sensitivity, specificity, and predictive value for neurosyphilis) of other CSF treponemal tests and CSF PCR tests for neurosyphilis have not been validated.

3. When a HIV patient has a high titer and received 7.2 BIC, 3 to 6 months later, tested again, titer did not decrease. The Dr. will say "treatment failure", then want patient to be treated again with 7.2 BIC. As a DIS, what would be our next step? Patient would not have s/s, admits to no other sex partners.
   - Because optimal management of this scenario is unclear, the role of a DIS in this situation would depend on your health department’s policies and standard operating procedures.
   - CDC Treatment Guidelines state that persons with HIV infection and primary or secondary syphilis should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy; those who meet the criteria for treatment failure (i.e., signs or symptoms that persist or recur or persons who have a sustained (>2 weeks) fourfold increase or greater in titer) should be managed in the same manner as HIV-negative patients (i.e., a CSF examination and retreatment guided by CSF findings). In addition, CSF examination and retreatment can be considered for persons whose nontreponemal test titers do not decrease fourfold within 12-24 months of therapy. If CSF examination is normal, treatment with benzathine penicillin G administered as 2.4 million units IM each at weekly intervals for 3 weeks is recommended. Serologic titers might not decline despite a negative CSF examination and a repeated course of therapy. In these circumstances, the need for additional therapy or repeated CSF examinations is unclear, but is not generally recommended. Serologic and clinical monitoring should be provided.
   - Similarly, for persons who are not known to be infected with HIV, optimal management of persons who have less than a fourfold decline in titers after treatment of syphilis is unclear. At a minimum, these persons should receive additional clinical and serologic follow-up and be evaluated for HIV infection. If additional follow-up cannot be ensured, retreatment is recommended. Because treatment failure might be the result of unrecognized CNS infection, CSF examination can be considered in such situations.

4. If you have HIV, but your viral load is undetectable, do you have the same increased risk of HIV positive with a viral load or low CD4?
   - Certain studies have demonstrated that among persons with HIV infection and syphilis, CSF abnormalities are associated with a CD4 count of ≤350 cells/mL and/or an RPR titer of ≥1:32.
However, the clinical significance of CSF abnormalities in the absence of neurologic signs and symptoms is unclear. **All** persons with HIV infection and syphilis should be screened for neurologic signs and symptoms and should have a careful neurologic exam. Neurosyphilis should be considered in persons with HIV infection and neurologic signs and symptoms, and further testing (i.e., CSF examination) is warranted for such persons.

5. **Isolated blurry vision not uncommon, LP invasive and difficult if uninsured, would appreciate other guidance on such cases.**
   - The diagnosis of neurosyphilis, ocular syphilis, and otosyphilis can be challenging and requires clinical judgment. Persons who have syphilis and symptoms or signs suggesting neurologic disease or ophthalmic disease should have an evaluation that includes CSF analysis, ocular slit-lamp opthalmologic examination, and otologic examination. Treatment should be guided by the results of this evaluation. Admittedly, the decision about which symptoms or signs merit further evaluation can be subjective and difficult. Clinicians must use their best judgement to decide which signs and symptoms should be evaluated further.

6. **Is it possible for someone that has been having blurriness and cloudy vision and has commenced treatment to see these symptoms resolve quickly after treatment? Other than a referral to eye specialist what other recommendations would you make?**
   - Patients with ocular syphilis vary in their response to treatment for ocular syphilis. Symptoms can improve relatively quickly, but typically the rate of improvement (or likelihood of improvement) depends on the duration of symptoms prior to initiating treatment. Patients who are treated relatively soon after onset of symptoms tend to improve more quickly than patients who have had symptoms for a long time. Persons who have syphilis and symptoms or signs suggesting neurologic disease or ophthalmic disease should have an evaluation that includes CSF analysis, ocular slit-lamp ophthalmologic examination, and otologic examination. For a patient diagnosed with ocular syphilis, would defer to the ophthalmologist for further follow up of the ocular manifestations.

7. **Should we then recommend to Providers to screen for Neuro if the client/patient has syphilis?**
   - Yes, we would recommend that providers screen patients with syphilis for symptoms or signs suggesting neurologic, ocular, or otic disease. Persons who have syphilis and symptoms or signs suggesting these manifestations should be evaluated further as described above.

8. **In written answers, please consider also providing additional guidance on expected drop in RPR in HIV+ patients at 3, 6, 9 months.**
   - Interpretation of treponemal and nontreponemal serologic tests for persons with HIV infection is the same as for the HIV-uninfected patient. Although rare, unusual serologic responses have been observed among persons with HIV infection who have syphilis, including post-treatment serologic titers that are higher than expected (high serofast).
   - CDC Treatment Guidelines state that persons with HIV infection and primary or secondary syphilis should be evaluated clinically and serologically for treatment failure at 3, 6, 9, 12, and 24 months after therapy; those who meet the criteria for treatment failure (i.e., signs or symptoms that persist or recur or persons who have a sustained (>2 weeks) fourfold increase or greater in titer) should be managed in the same manner as HIV-negative patients (i.e., a CSF examination and retreatment
9. **Is it possible to use positive PCR results on CSF to meet verified criteria for neurosyphilis?**
- No, CSF PCR results are not included in the verified or likely criteria for neurosyphilis. See also the response to question #2.

10. **Since nontreponemal titers can decline and even disappear in late latent disease, you could have a positive treponemal test but negative nontreponemal titer, AND late clinical manifestations, no?**
- Yes, it is theoretically possible that a patient with late clinical manifestations (and late syphilis) would have a nonreactive nontreponemal test result and a reactive treponemal test result. These patients would not meet the surveillance case criteria for late clinical manifestations (or for Unknown Duration or Late Syphilis). We elected to include reactive nontreponemal and treponemal tests as part of the late manifestations criteria, because (1) this is likely a rare scenario for persons with late manifestations of syphilis, and (2) it was felt that the case definition would lack sufficient specificity (i.e., could include cases that weren’t truly cases) if it included persons with nonreactive nontreponemal tests. Please keep in mind that this determination is for surveillance purposes only. Clinically, it is possible that it might be appropriate to diagnose and treat a patient with a nonreactive nontreponemal result for tertiary syphilis (late clinical manifestations of syphilis), regardless of the surveillance categorization.

11. **Is the treatment modality different for the verified, possible and likely clinical manifestations?**
- No, these classifications are for surveillance purposes only. Clinically, any patient diagnosed with neurosyphilis, ocular syphilis, otosyphilis, or tertiary syphilis (late clinical manifestations) should be managed according to CDC Treatment Guidelines. The recommended regimen for neurosyphilis/ocular syphilis/otosyphilis is Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days. The recommended regimen for tertiary syphilis with normal CSF examination (and no neurosyphilis) is Benzathine penicillin G 7.2 million units total, administered as 3 doses of 2.4 million units IM each at 1-week intervals.

12. **Patient has +rpr/+tppa, otic sx, no lp, no exam by ophth. Should patient be coded as otic=possible AND neuro=possible?**
- Yes, otic symptoms are also neurologic symptoms, so this is a case that would be coded as Otic Manifestations = Possible and also Neurologic Manifestations = Possible.
13. How is this increased, more detailed surveillance being presented to providers?
   - These changes to surveillance are not expected to significantly alter clinical practice. However, providers that diagnose, manage, and report a substantial number of syphilis cases might benefit from knowing about the expanded surveillance for clinical manifestations and which pieces of data are of potential interest to the health department (e.g., whether CSF examination was performed and results, or whether patient was evaluated/diagnosed by an ophthalmologist or otolaryngologist). We have discussed and continue to discuss these surveillance changes with providers in the National Network of STD Clinical Prevention Training Centers, who will also help to publicize these changes to the pertinent providers. In addition, we hope health departments will share these webinars and slides with key providers as well. We would welcome suggestions or other ideas for reaching STD providers with the appropriate information.

14. Has there been any communication about reporting changes for NETSS related to this?
   - Yes, we have been discussing the logistics of data transmission for the case definitions and variables on the STD Surveillance Coordinators calls. We anticipate that there will be a period of transition as health department implement these changes to their data systems, so we will be accepting data transmissions in their current format for the time being (at least the next year or two).

15. Does the titer also have to increase by at least two dilutions in previously treated individuals in order to qualify again for neuro if they are showing signs/symptoms?
   - Clinically, no. Neurosyphilis should be considered in persons with syphilis who have neurologic signs or symptoms. In addition, treatment failure (i.e., failure of nontreponemal test titers to decline fourfold within 6-24 months after therapy) might be the result of unrecognized CNS infection. Serologic response to treatment appears to be associated with several factors, including stage of infection at treatment and initial nontreponemal titer, and optimal management for persons with less than a fourfold decline in titers after treatment for syphilis is unclear. However, because lack of a fourfold decrease in titer might be a sign of treatment failure, and because treatment failure might be the result of unrecognized CNS infection, CSF examination (and evaluation for neurosyphilis) can be considered in such situations.
   - For surveillance purposes, it sounds like you are referring to a case that was previously treated and reported, and now the case has been diagnosed/treated for neurosyphilis without evidence of re-infection (i.e., no signs/symptoms of primary or secondary syphilis and no fourfold increase in titer since treatment). For surveillance purposes, if this case was initially reported in the current reporting year, the initial case report should be updated to include the clinical manifestations using the clinical manifestations variables. If the case was initially reported in a previous reporting year and this seems to be a failure of the initial treatment (i.e., no evidence of re-infection), AND if the case meets the likely or verified criteria for neurologic, ocular, otic, or late clinical manifestations, then the case should be reported as a new Unknown Duration or Late Syphilis case and the likely or verified clinical manifestations should be noted using the appropriate variables. Although this latter scenario is expected to be exceedingly rare, the revisions to the Unknown Duration or Late Syphilis case definition included addition of criteria to allow for reporting of this type of case.
16. What is the treatment for ocular or neuro syphilis, shots or IV?

- The recommended regimen for neurosyphilis/ocular syphilis/otosyphilis is Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 million units IV every 4 hours or continuous infusion, for 10-14 days.