Congenital Syphilis Surveillance:

Case Classification Workshop

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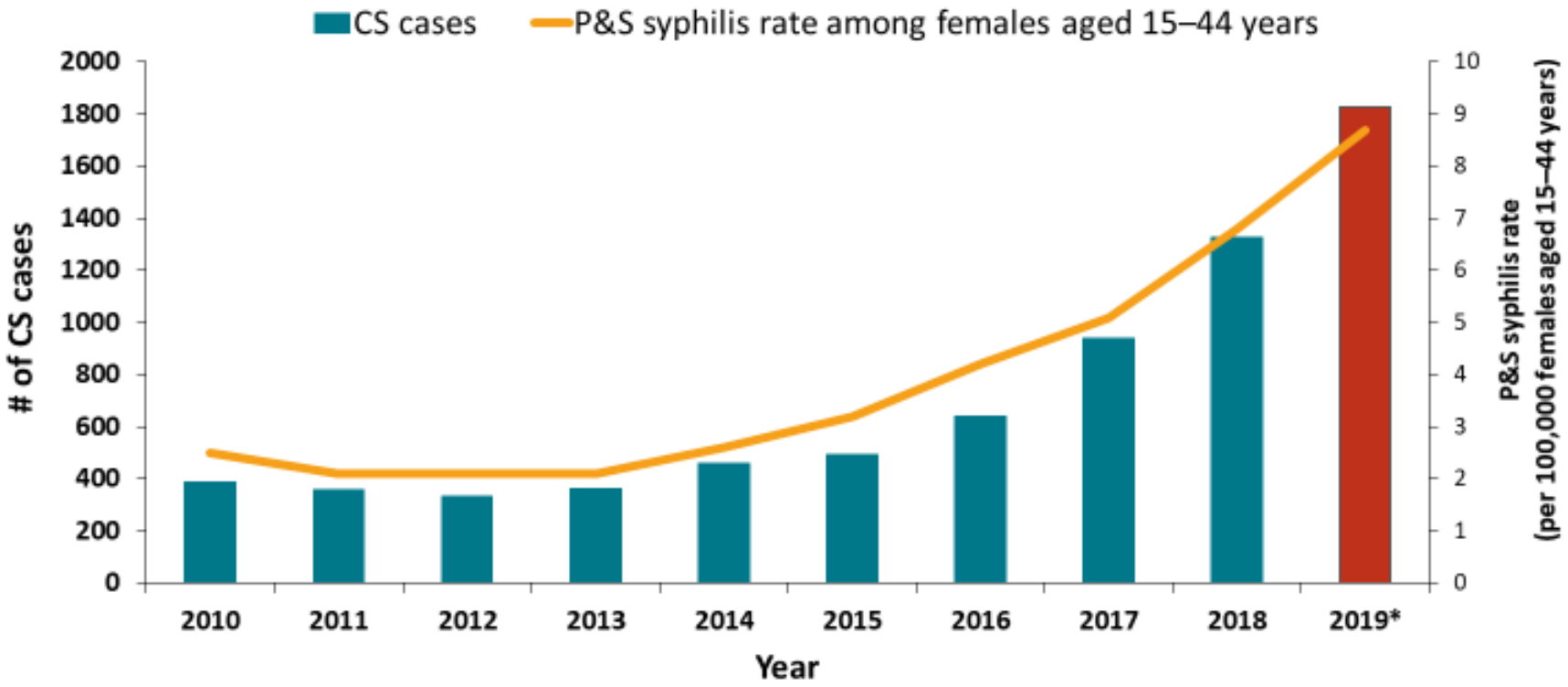
CDC Division of STD Prevention

October 23, 2020

Co-hosted by the Council of State & Territorial Epidemiologists

CS cases continue upward trajectory in 2019



*2019 CS case-counts are preliminary as of October 22, 2020

STD PCHD Strategy Area I: Conduct surveillance

4. Conduct CS Surveillance

- Conduct provider and mother follow-up and review medical records of all reported CS cases
- Manage, analyze, and disseminate date on reported CS cases, ensuring capture of epidemiologic core maternal, fetal, and neonatal variables

STD PCHD
Strengthening STD Prevention and Control for Health Departments

Poll Question #1: Pre-workshop Comfort

- **My current level of comfort with making CS case classifications is best described as:**

1) **Very comfortable**
   - I know the case definition well and get practice applying it
2) **Somewhat comfortable**
   - I know the case definition fairly well, but I don't get to practice applying it often
3) **Somewhat uncomfortable**
   - I could use a case definition refresher
4) **Very uncomfortable**
   - I'm brand new at this…help!

Fundamentals:
Making CS Case Classifications

There are 2 paths to being a reportable CS case…

Congenital Syphilis Case

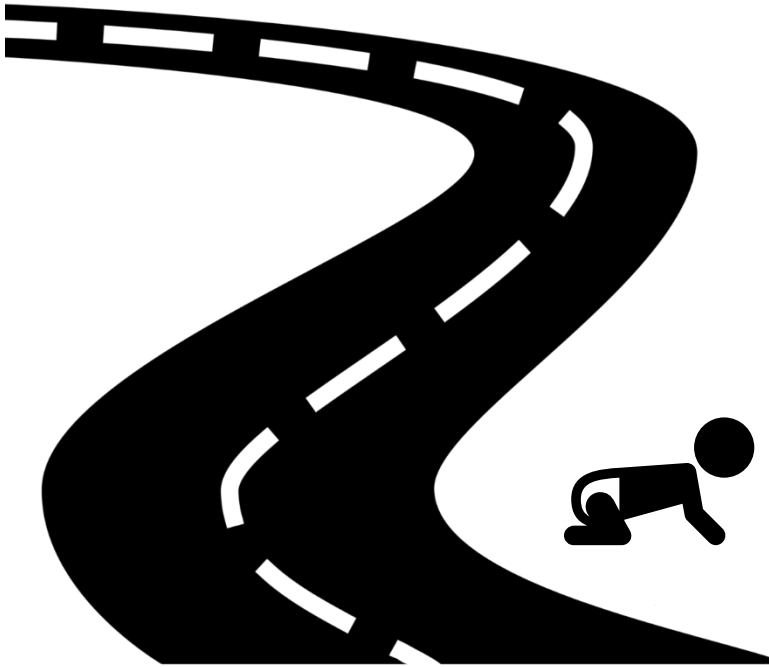
There are 2 paths to being a reportable CS case…

Congenital Syphilis Case

Maternal Criteria:
A Possible Path for Liveborn or Stillborn Infants

There are 2 paths to being a reportable CS case…

Congenital Syphilis Case

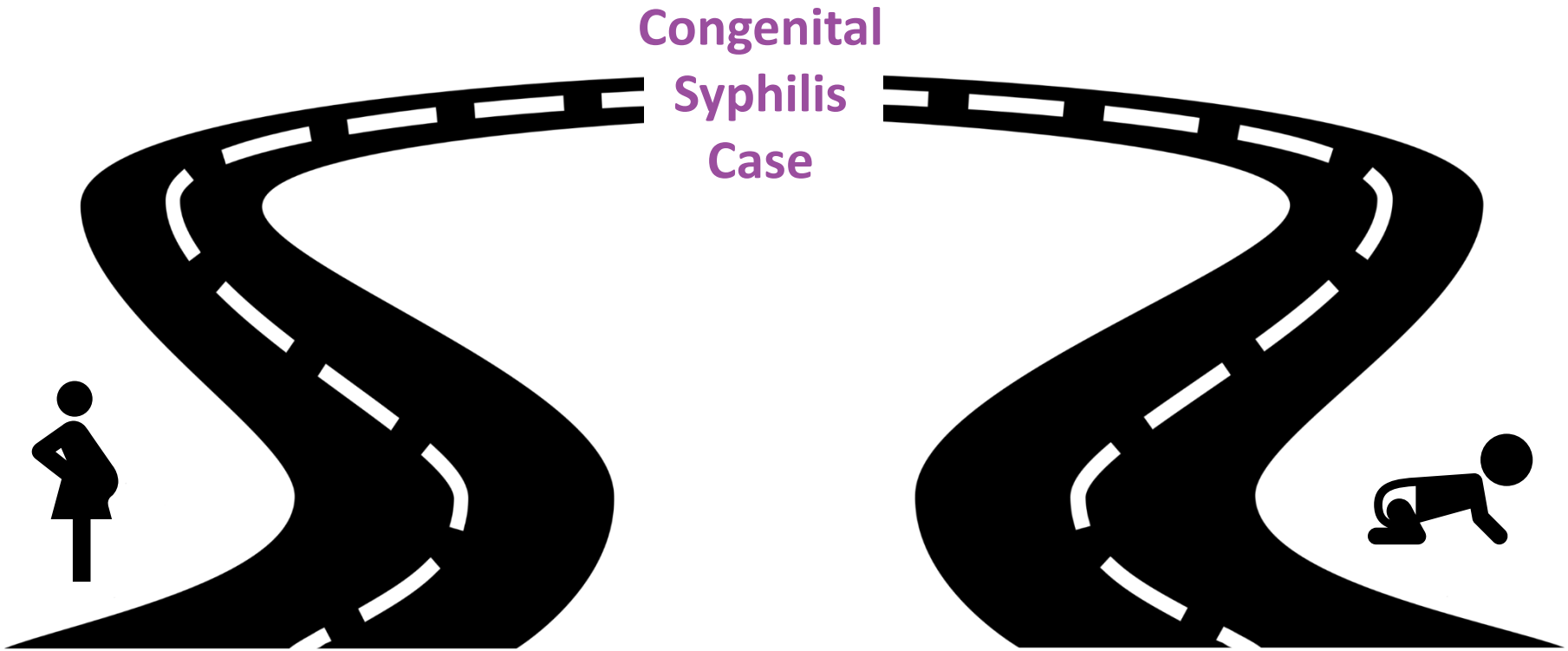


There are 2 paths to being a reportable CS case…

Congenital Syphilis Case

Infant Criteria:
A Possible Path for Liveborn Infants

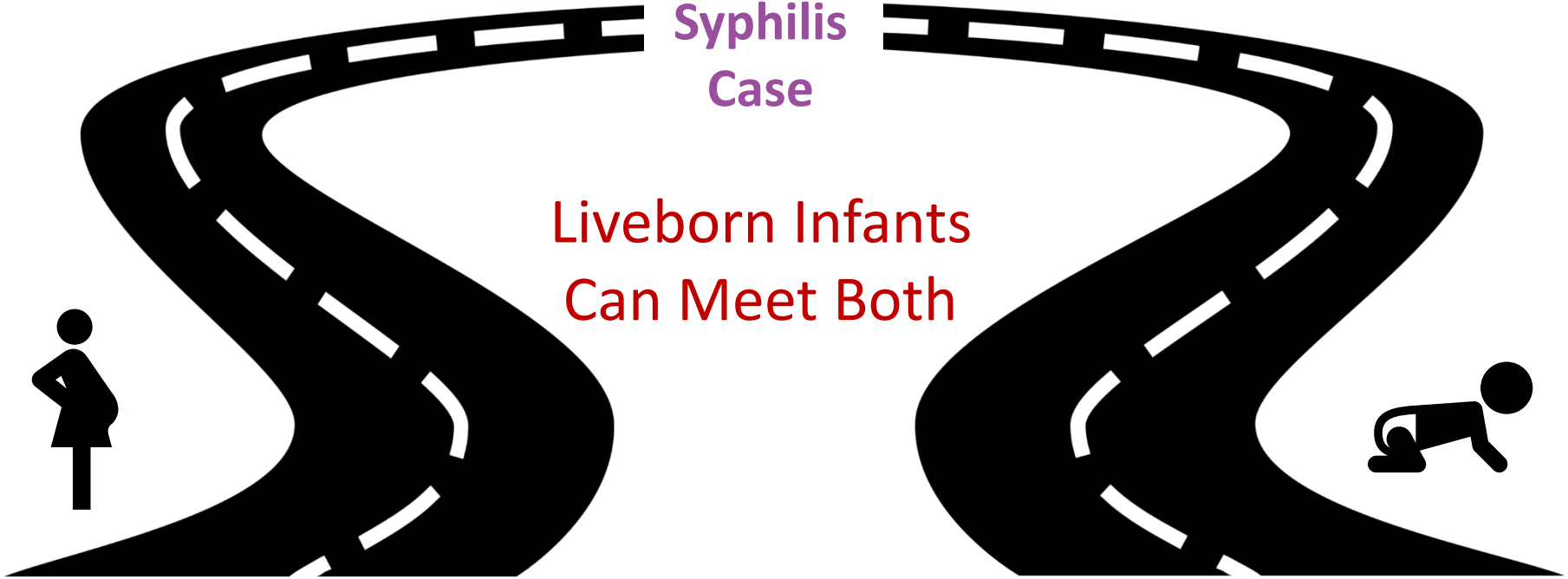
There are 2 paths to being a reportable CS case…

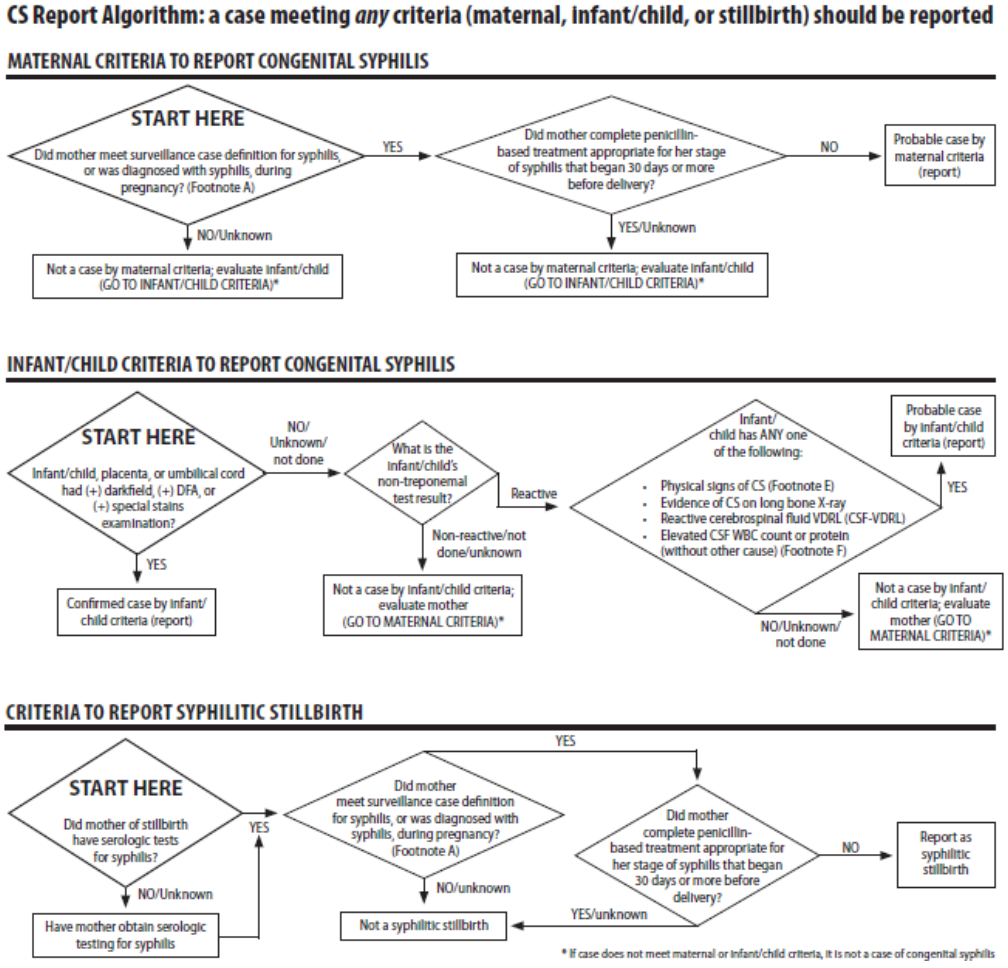


There are 2 paths to being a reportable CS case…

Congenital Syphilis Case

Liveborn Infants Can Meet Both





Page 4 of the old **CS 73.126 form** still contains one of the clearest algorithms for determining CS case status

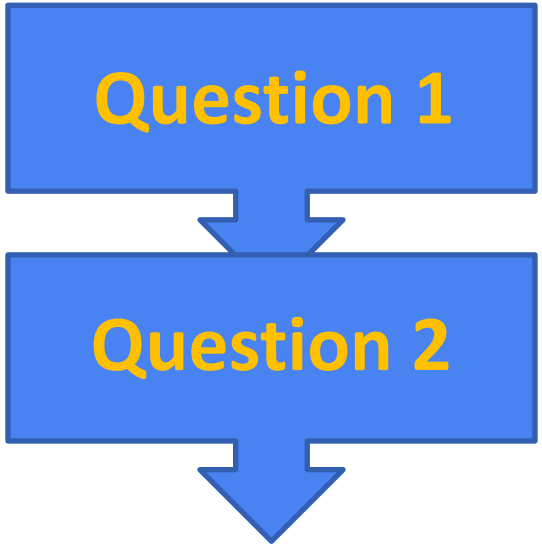
https://www.cdc.gov/std/program/Congenital-Syphilis-Form-2013.pdf

Terminology primer

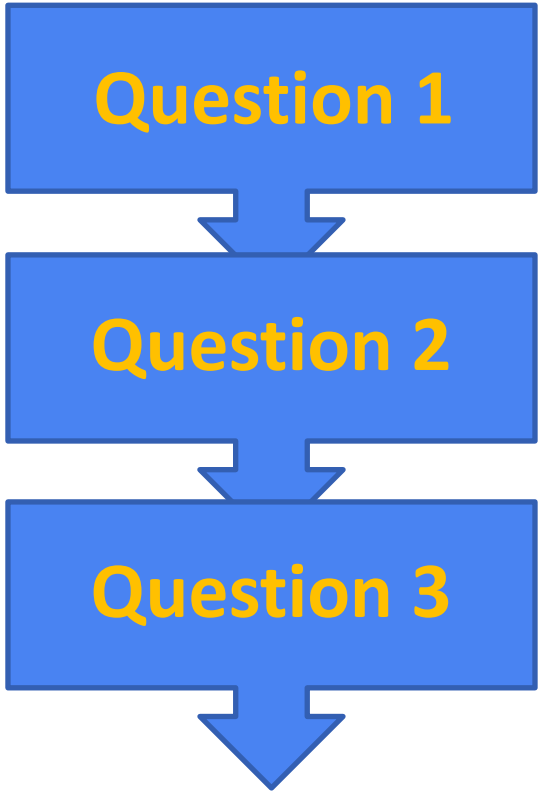
- **Infant vital status at birth**
  - Live-birth (LB)
  - Stillbirth (SB)
- **Specimens and tests**
  - Cerebrospinal fluid (CSF)
  - White Blood Cell (WBC)

Question 1

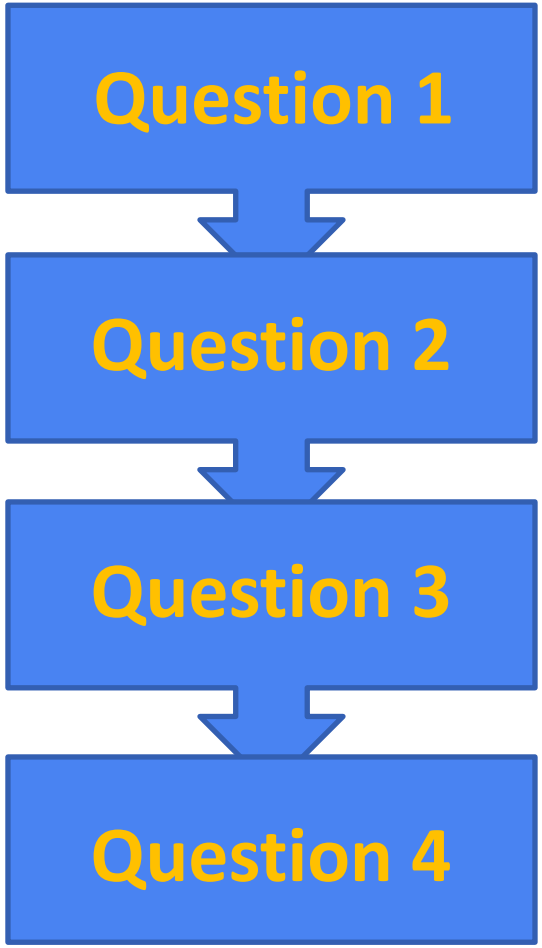
- **Did the infant's mother have syphilis during pregnancy?**



- Did the infant's mother have syphilis during pregnancy?
- Was she adequately treated for her syphilis with a regimen initiated at least 30 days prior to delivery?



- Did the infant's mother have syphilis during pregnancy?
- Was she adequately treated for her syphilis with a regimen initiated at least 30 days prior to delivery?
- Is there evidence of mother's re-infection prior to delivery?



- Did the infant's mother have syphilis during pregnancy?
- Was she adequately treated for her syphilis with a regimen initiated at least 30 days prior to delivery?
- Is there evidence of mother's re-infection prior to delivery?
- Does the infant meet criteria for CS reporting independent of its mother?

Question 1

- **Did the infant's mother <u>have syphilis during pregnancy?</u>**
  - Mother needs to meet one of the syphilis case definitions while pregnant
    - Look for test results
  - Does *not* need to be a new, reportable case
  - Syphilis identified post-partum *can* be relevant

Question 2

- **Was she adequately treated for her syphilis with a regimen initiated at least 30 days prior to delivery?**
  - Adequate treatment includes:
    - Only benzathine penicillin G (2.4mu IM)
    - Completion of treatment regimen appropriate for stage of syphilis
    - Appropriate spacing intervals
  - The first dose of the completed regimen must be given ≥30 days before delivery

Question 3

- **Is there evidence of mother's re-infection prior to delivery?**
  - Re-infection is captured as a 4-fold increase in titers after treatment
    - Do not look for a 4-fold increase until after mom has received her first dose of benzathine penicillin
  - Mother's titer does *not* need to decline before delivery

Question 4

- **Does the infant meet criteria for CS reporting independent of its mother?**
  - Infant needs to have a reactive RPR
  - Infant needs to have 1 or more signs, symptoms, or lab findings of CS:
    - Classic signs on the investigation form
    - Abnormal long bone X-rays
    - Elevated CSF protein or WBC
    - Reactive CSF-VDRL
    - Direct detection of *T. pallidum* in an appropriate specimen

Mother

Did mother have syphilis during pregnancy?

Mother

Did mother have syphilis during pregnancy?

This is the time to look for a reactive non-trep and trep test result. Most stages require both. Remember that **primary syphilis only requires one**!

Instead of nontrep/trep results, you may find direct detection of *T. pallidum* using an appropriate test & specimen.

Mother

Did mother have syphilis during pregnancy?

If you're leaning toward 'yes,' go ahead and confirm that mom's syphilis was staged appropriately. This will become important in a moment.

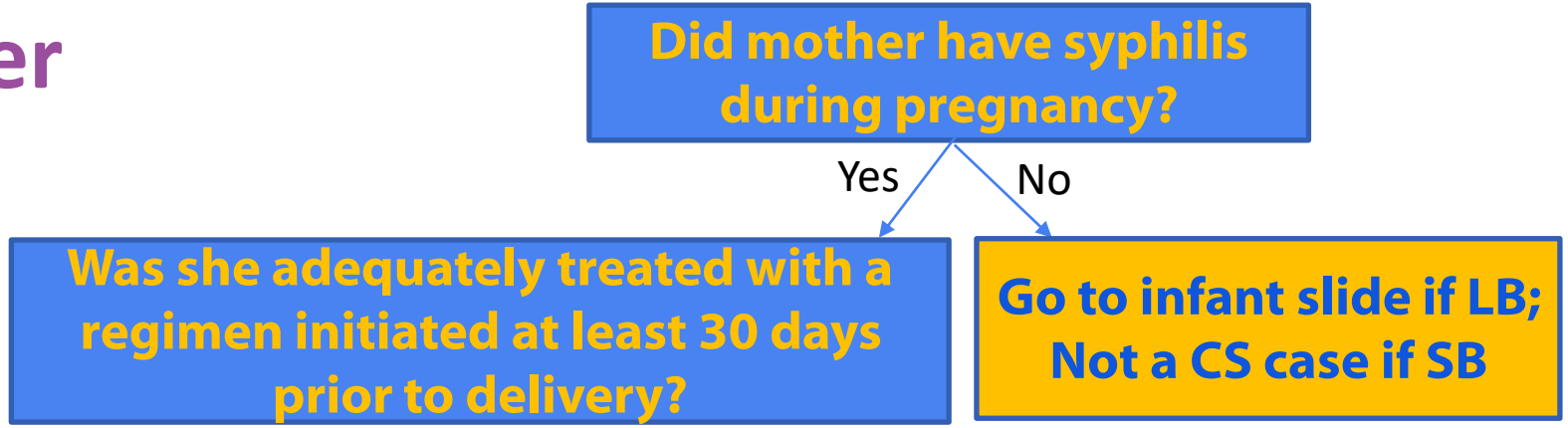
Mother

Did mother have syphilis during pregnancy?

No

Go to infant slide if LB; Not a CS case if SB

Mother


Did mother have syphilis during pregnancy?
Yes
No
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Go to infant slide if LB; Not a CS case if SB

Mother

Did mother have syphilis during pregnancy?

Yes

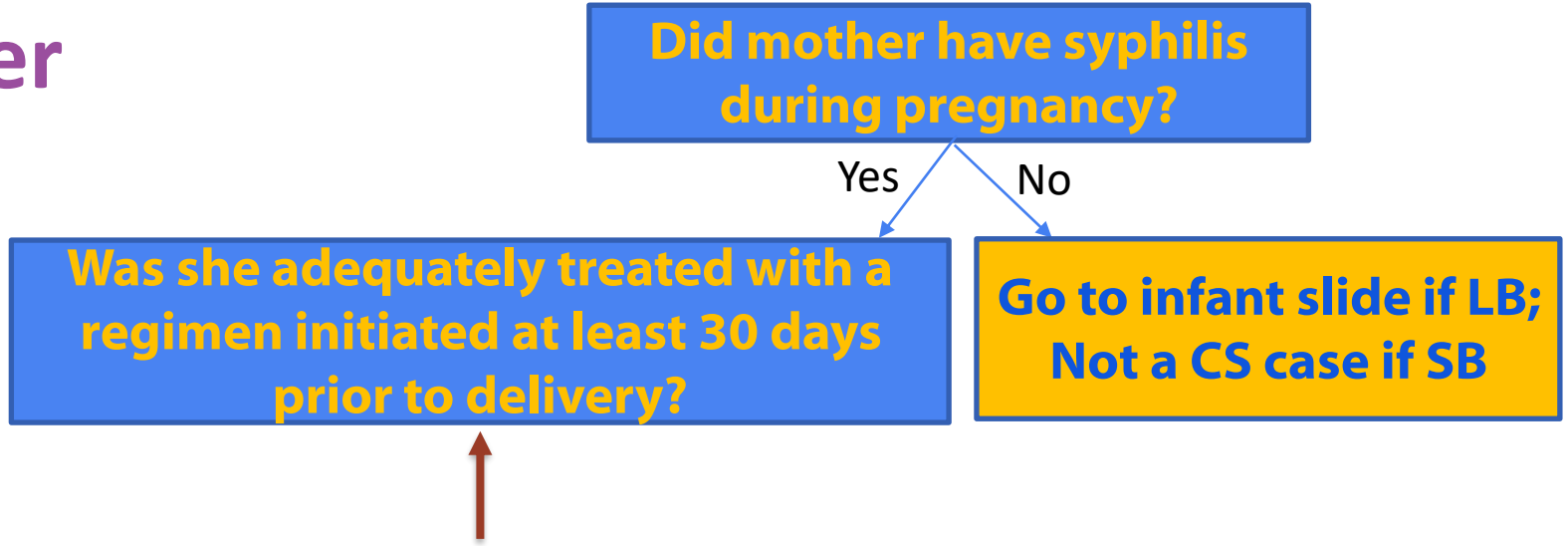
No

Was she adequately treated with a regimen initiated at least 30 days prior to delivery?

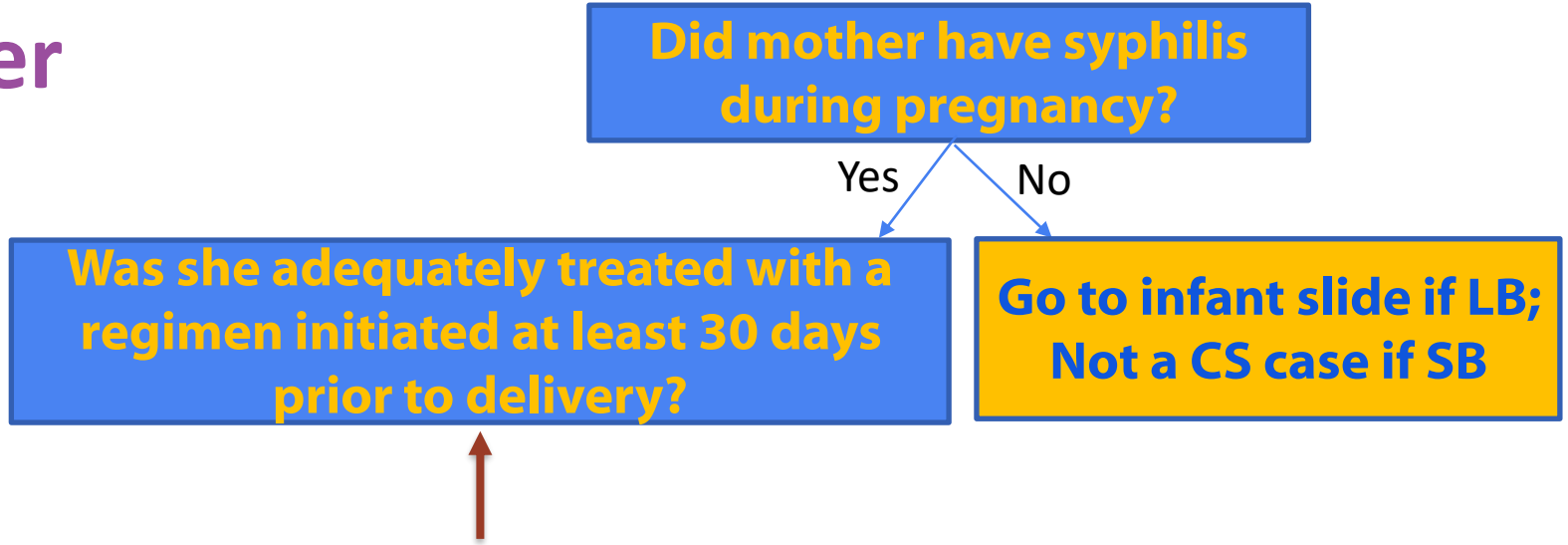
Go to infant slide if LB; Not a CS case if SB

Bicillin is imperative during pregnancy! Do not accept ‘penicillin allergy’ as an acceptable reason to forego bicillin.

Mother


Did mother have syphilis during pregnancy?
Yes
No
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Go to infant slide if LB; Not a CS case if SB
For mothers with unknown duration or late stage syphilis, 3 shots of bicillin are needed for adequate treatment.

Mother



For mother's with unknown duration or late syphilis, 3 shots of bicillin are required for adequate treatment.

Spacing of those shots is a very touchy subject—mostly because the 2015 Treatment Guidelines leave room for interpretation.

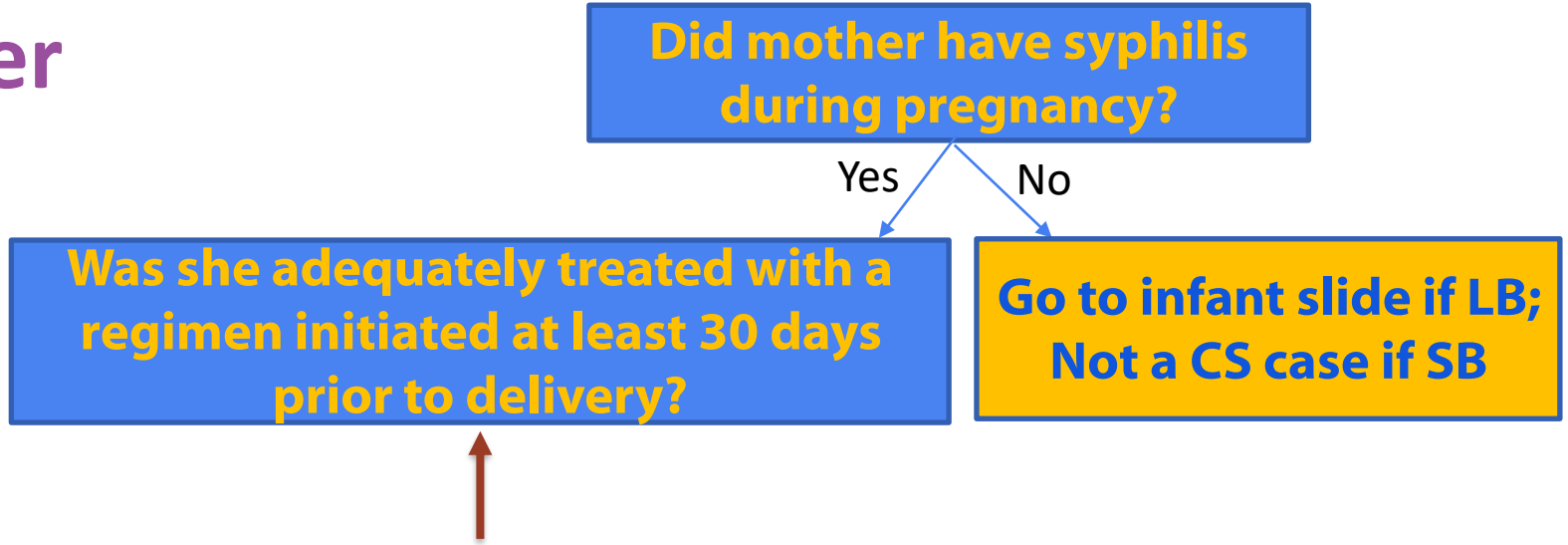
What do the 2015 STD Treatment Guidelines say about bicillin spacing and pregnant women?

Recommended Regimen
Pregnant women should be treated with the penicillin regimen appropriate for their stage of infection.

Recommended Regimens for Adults—Unknown Duration or Late Syphilis
Benzathine penicillin G 7.2mu total, administered as 3 doses of 2.4mu IM, each at 1-week intervals

- **"If a person misses a dose of penicillin in a course of weekly therapy for latent syphilis, the appropriate course of action is unclear. Clinical experience suggests that an interval of 10–14 days between doses of benzathine penicillin for latent syphilis might be acceptable before restarting the sequence of injections… Pharmacologic considerations suggest that an interval of 7–9 days between doses, if feasible, might be more optimal (*420-422*). Missed doses are not acceptable for pregnant women receiving therapy for latent syphilis (*423*). Pregnant women who miss any dose of therapy must repeat the full course of therapy."**

Mother



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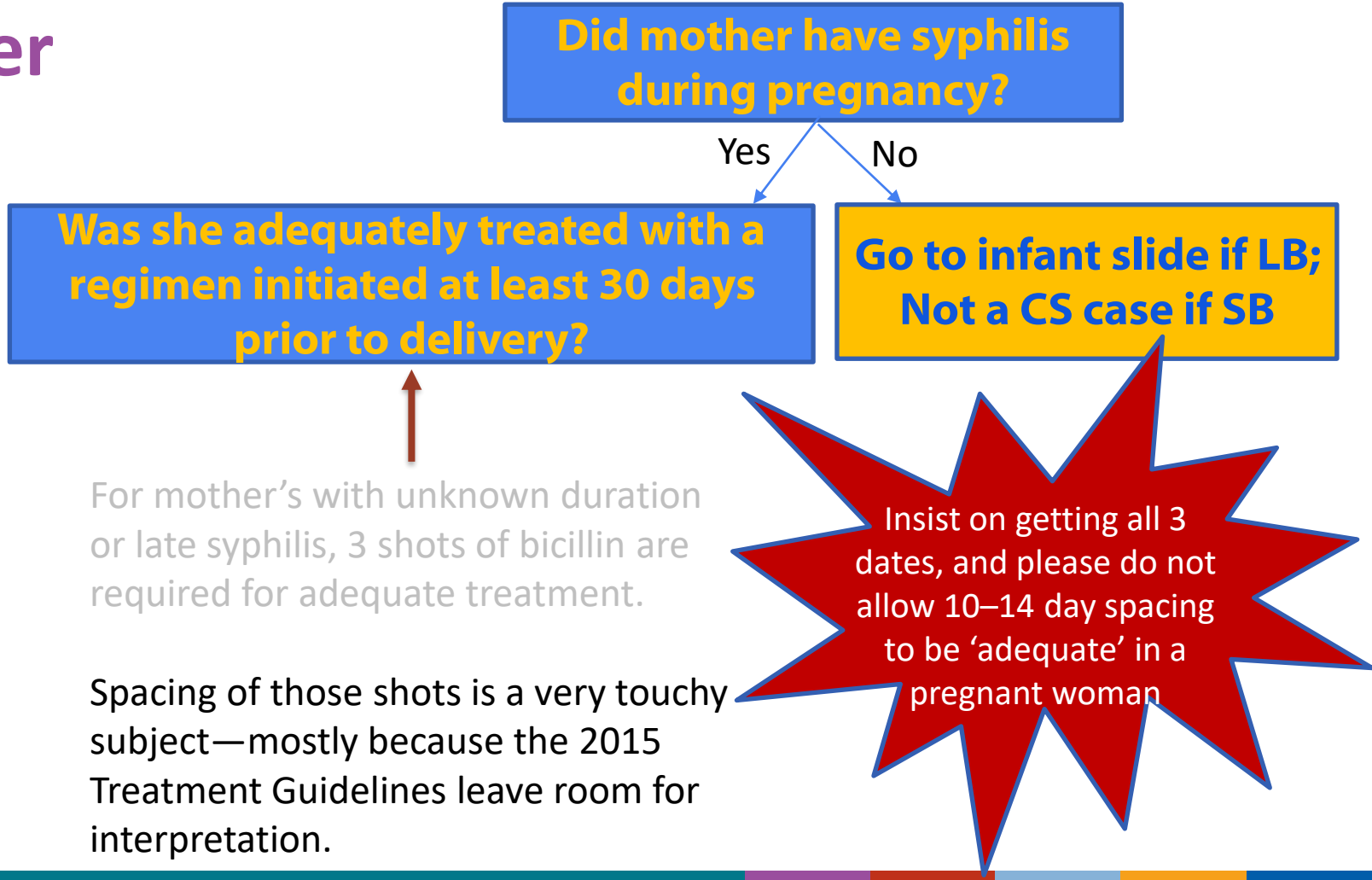

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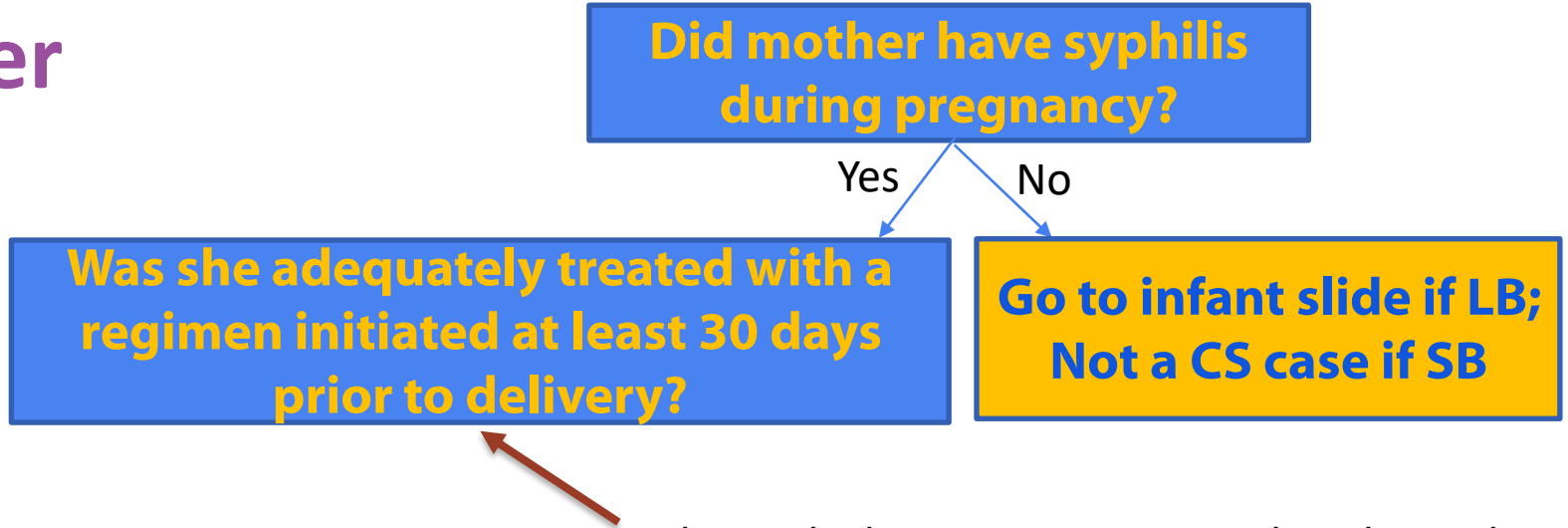
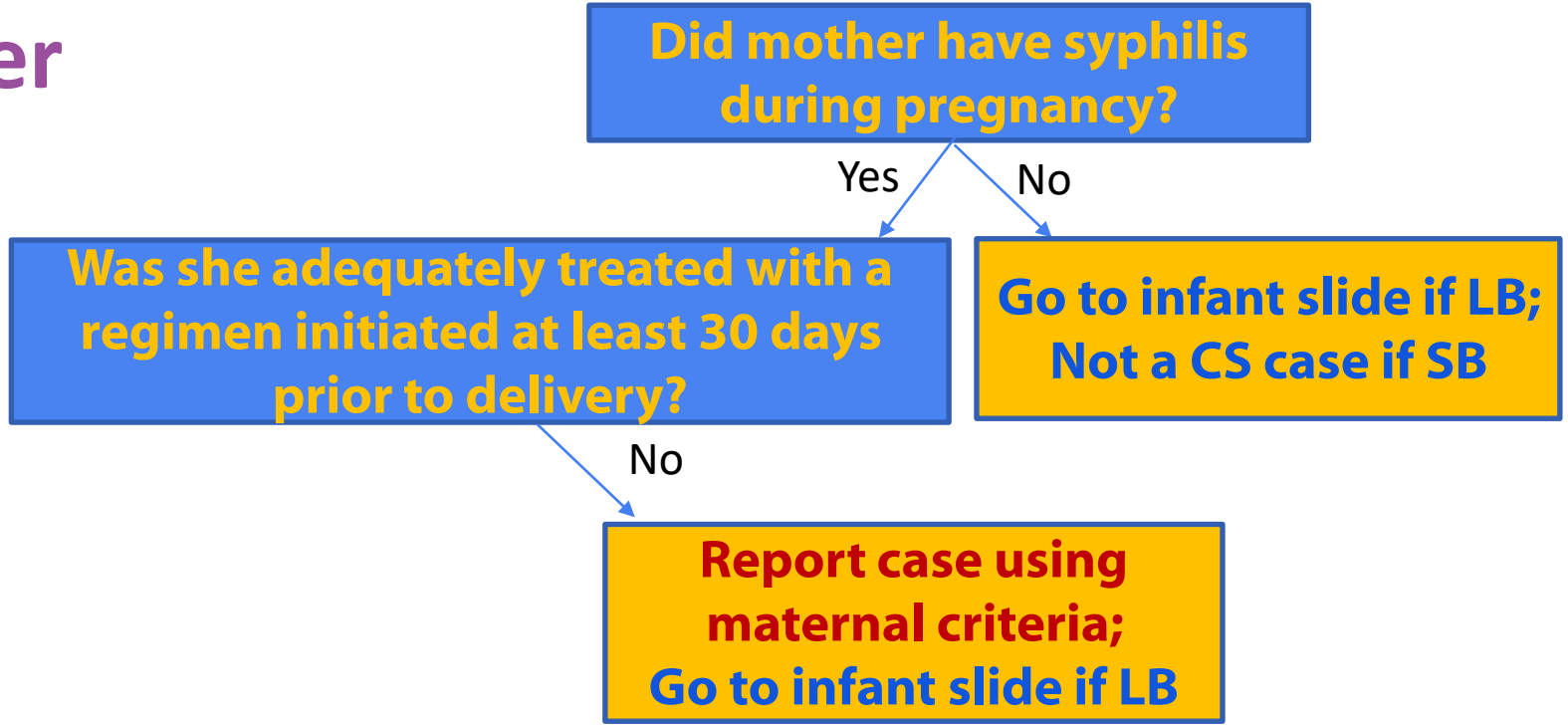


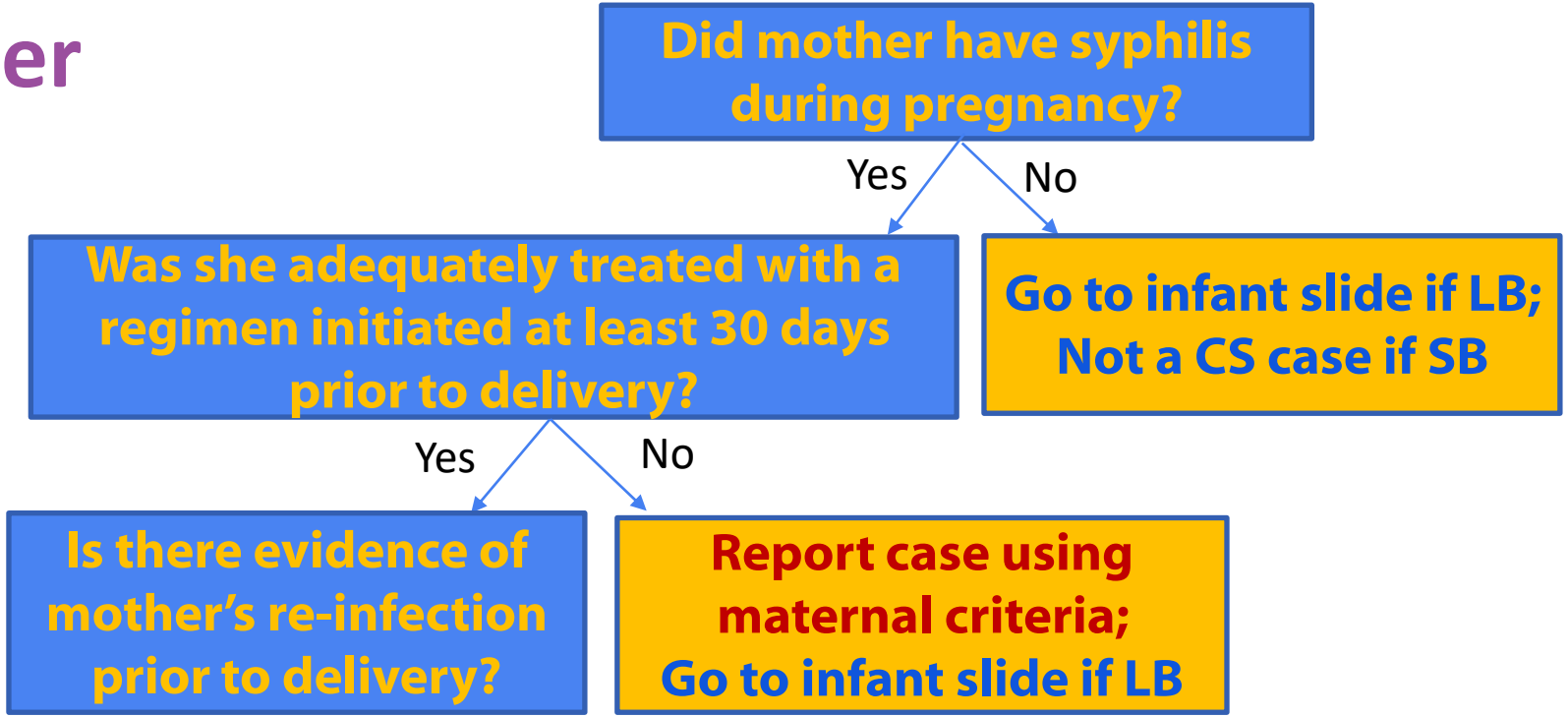
When calculating timing, remember that only the *first* shot of the 'adequate regimen' needs to be administered ≥30 days prior to delivery.

It is a common misconception that the entire *series* must be completed ≥30 days prior to delivery.

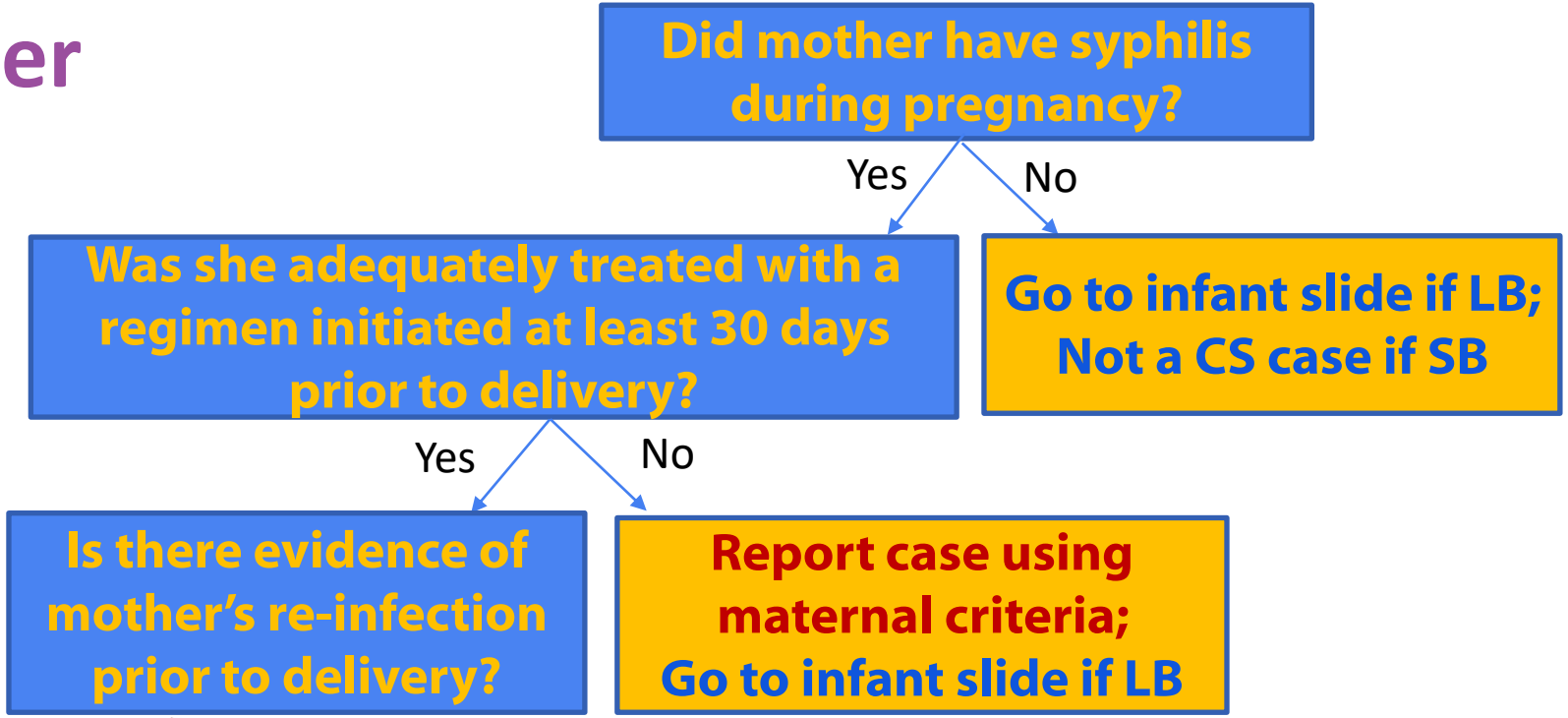
Mother


Did mother have syphilis during pregnancy?
Yes
No
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Go to infant slide if LB; Not a CS case if SB
No
Report case using maternal criteria; Go to infant slide if LB

Mother

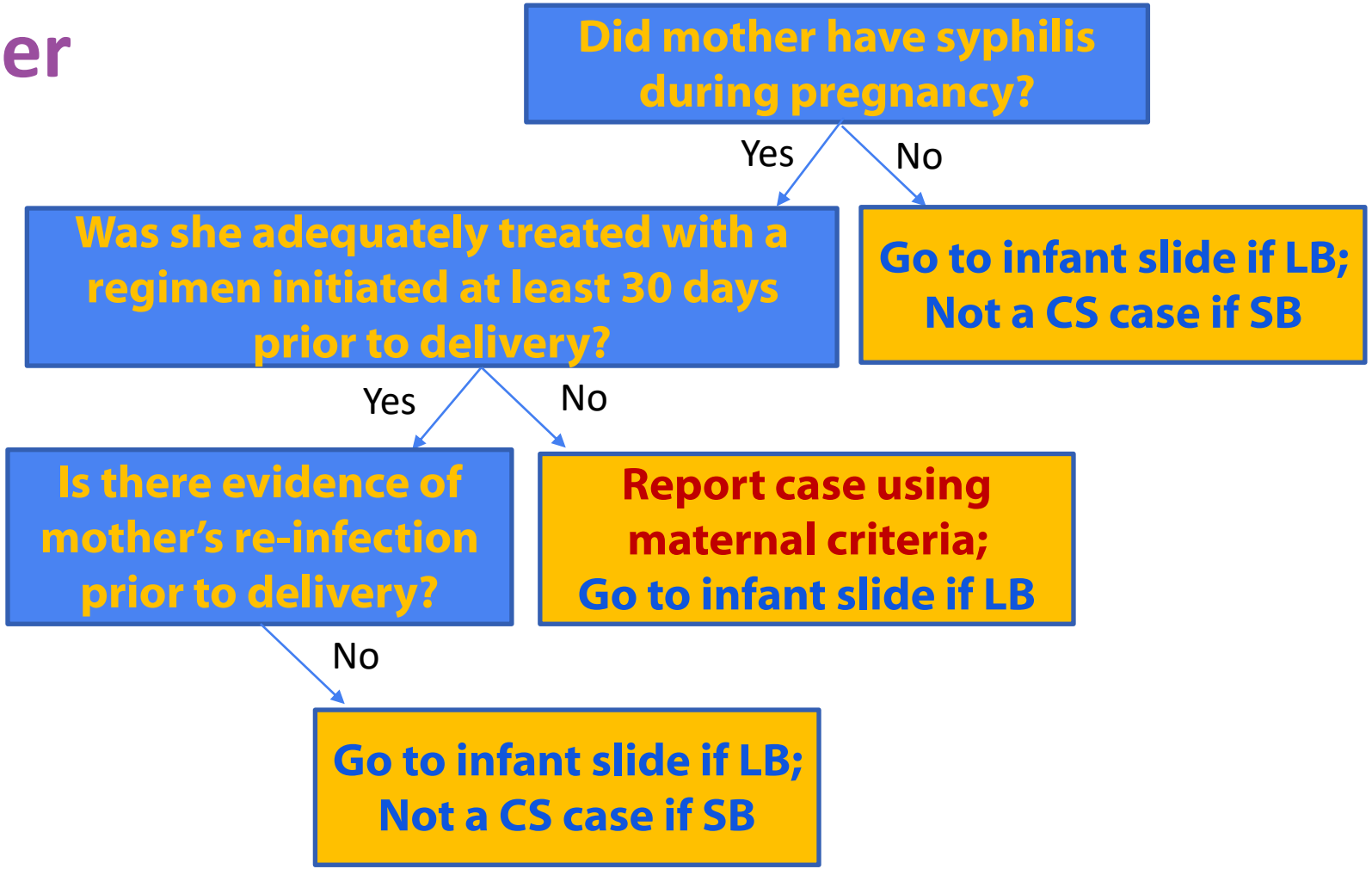

Did mother have syphilis during pregnancy?
Yes
No
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Go to infant slide if LB; Not a CS case if SB
Yes
No
Is there evidence of mother's re-infection prior to delivery?
Report case using maternal criteria; Go to infant slide if LB

Mother



You're looking for test results that suggest a 4-fold increase in mom's titer following treatment during pregnancy. Day of delivery testing is key!

Mother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Yes
No
Is there evidence of mother's re-infection prior to delivery?
Report case using maternal criteria; Go to infant slide if LB
No
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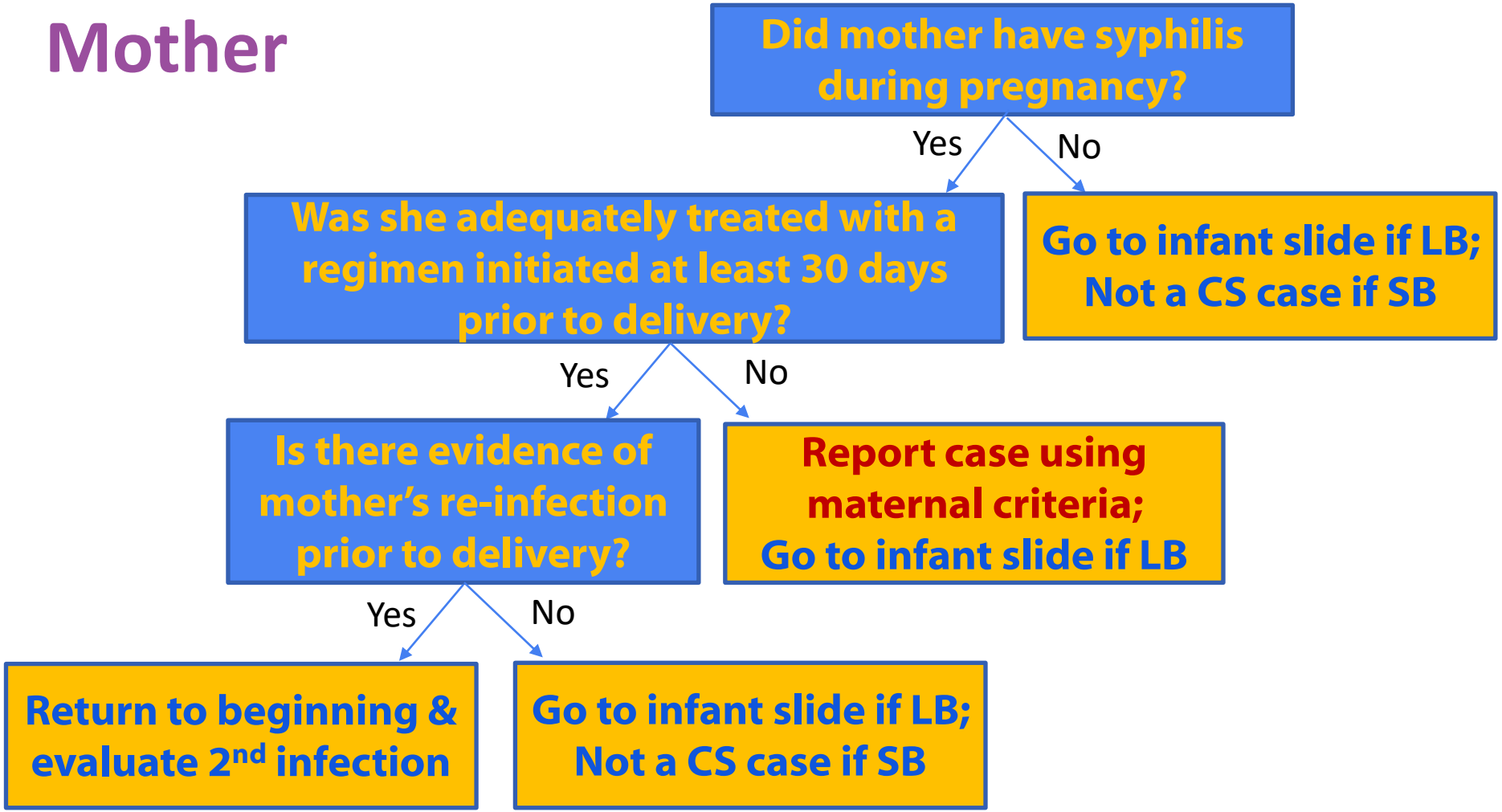
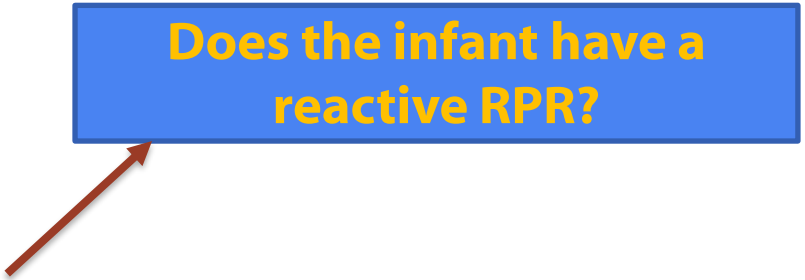

Did mother have syphilis during pregnancy?
Yes
No
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Go to infant slide if LB; Not a CS case if SB
Yes
No
Is there evidence of mother's re-infection prior to delivery?
Report case using maternal criteria; Go to infant slide if LB
Yes
No
Return to beginning & evaluate 2nd infection
Go to infant slide if LB; Not a CS case if SB

Infant

Does the infant have a reactive RPR?

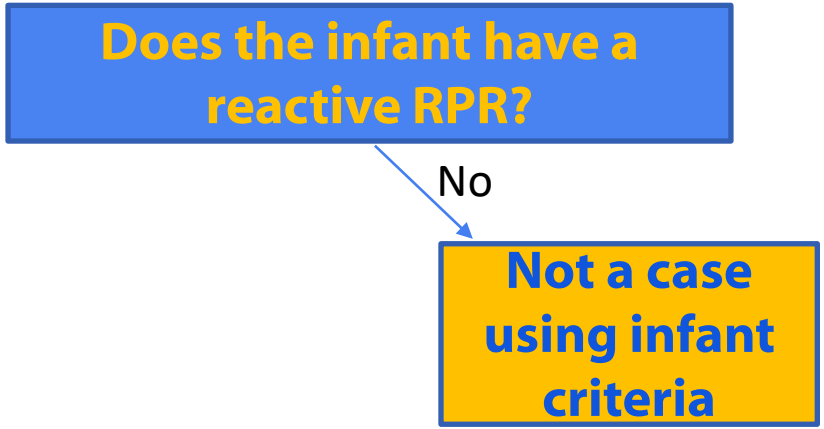
Infant



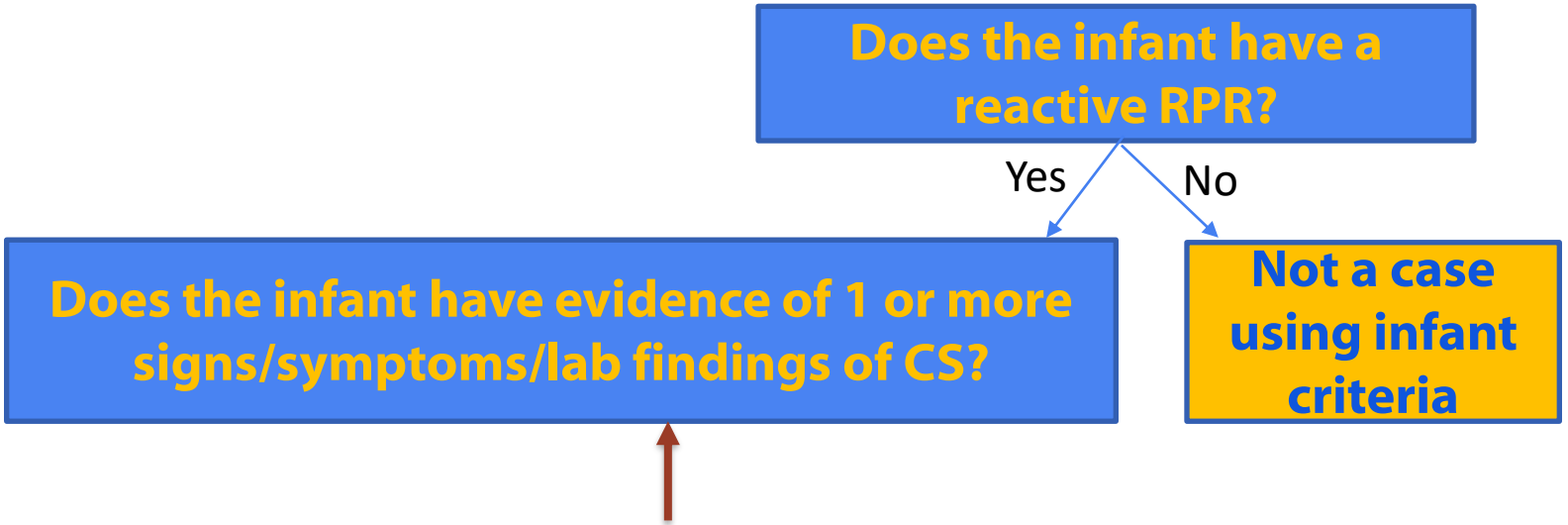
This is a yes/no question. Note that the question is *not*: “What is the infant’s RPR and how does it compare to mom’s RPR?”

It is a common misconception that case classification involves comparing maternal and infant titers. This is important for infant *treatment* and *evaluation* purposes but not CS case classification!

Infant

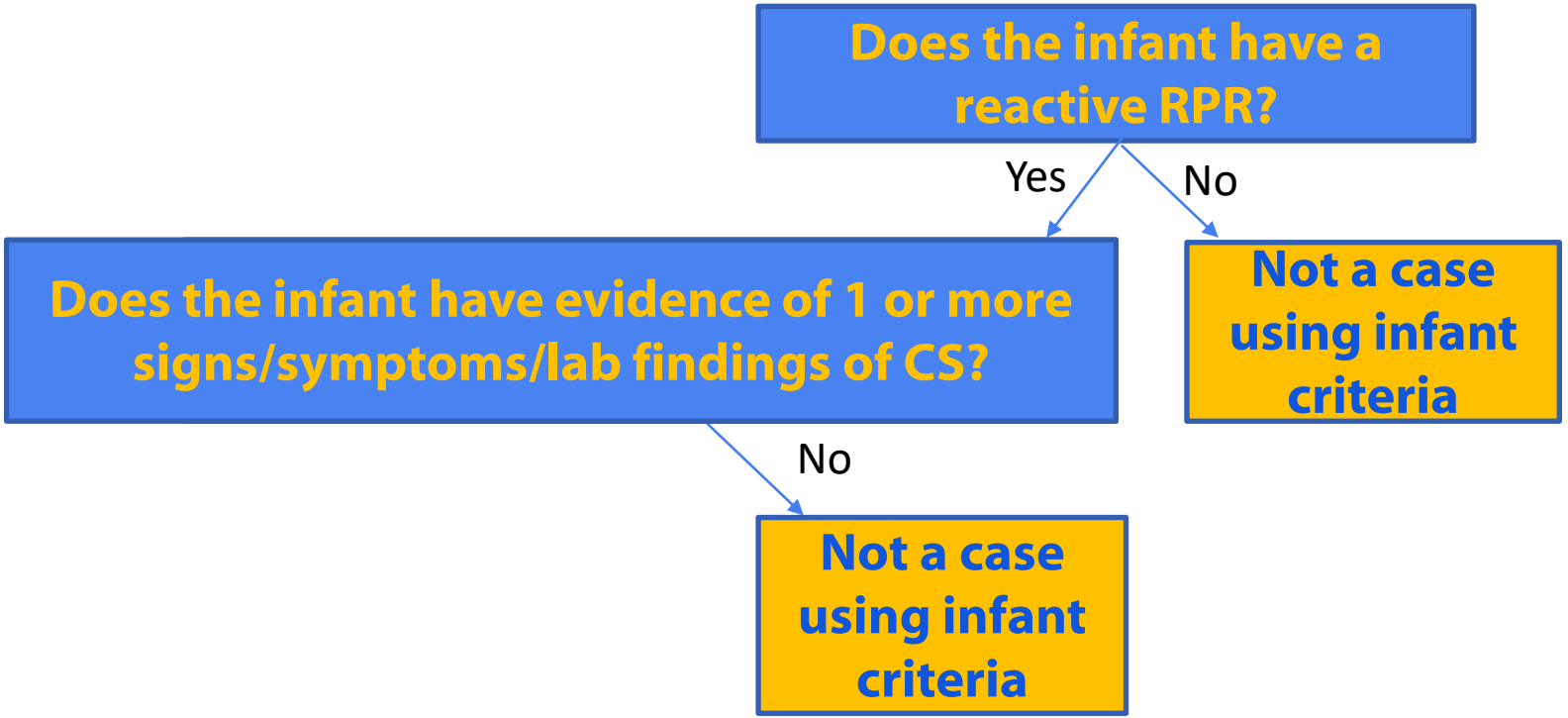

Does the infant have a reactive RPR?
No
Not a case using infant criteria

Infant

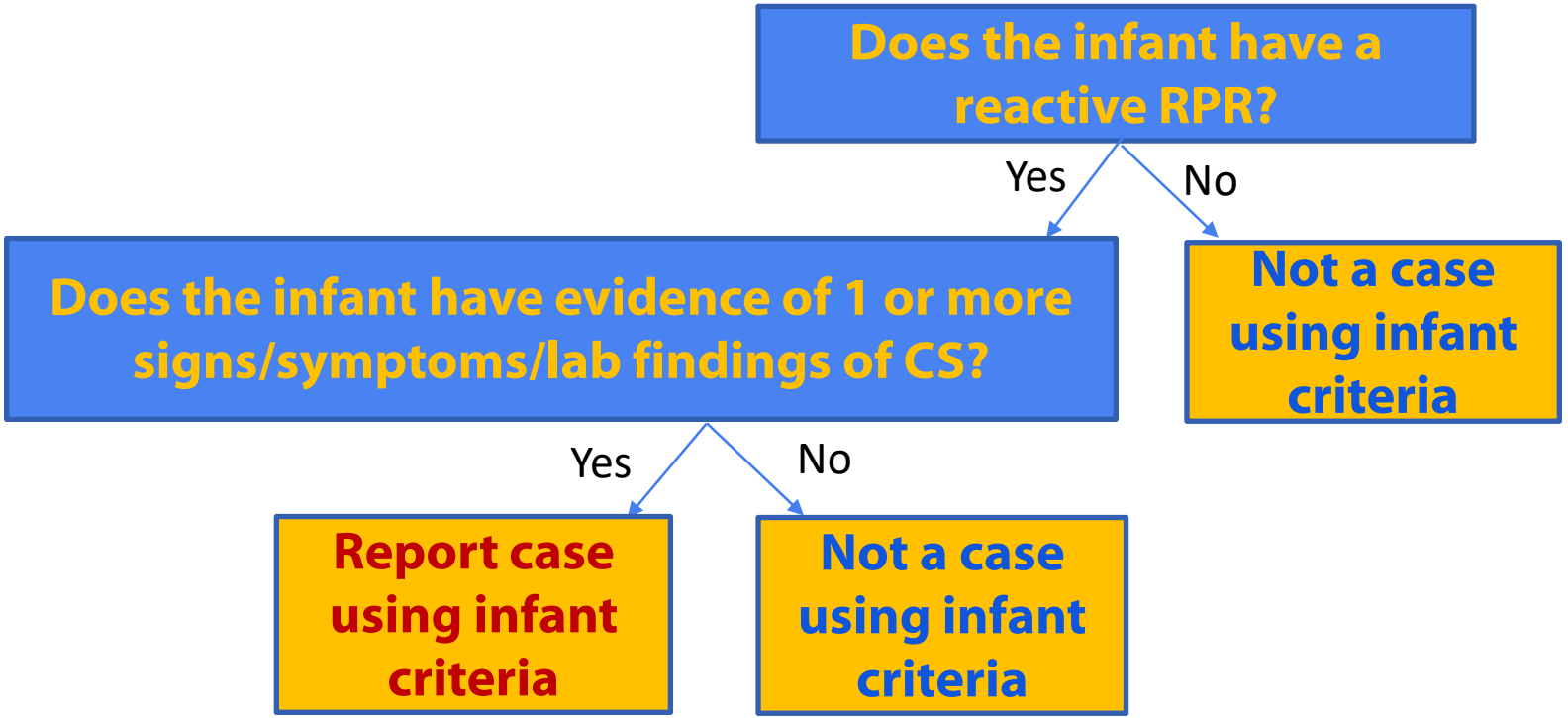


It only takes one! There is no hierarchy of importance here. Snuffles are as meaningful as a reactive CSF-VDRL for CS classification purposes.

Infant


Does the infant have a reactive RPR?
Yes
No
Not a case using infant criteria
Does the infant have evidence of 1 or more signs/symptoms/lab findings of CS?
No
Not a case using infant criteria

Infant


Does the infant have a reactive RPR?
Yes
No
Not a case using infant criteria
Does the infant have evidence of 1 or more signs/symptoms/lab findings of CS?
Yes
No
Report case using infant criteria
Not a case using infant criteria

Infant

Does the infant have a

Direct detection of *T. pallidum* in the infant overrides this flowchart!

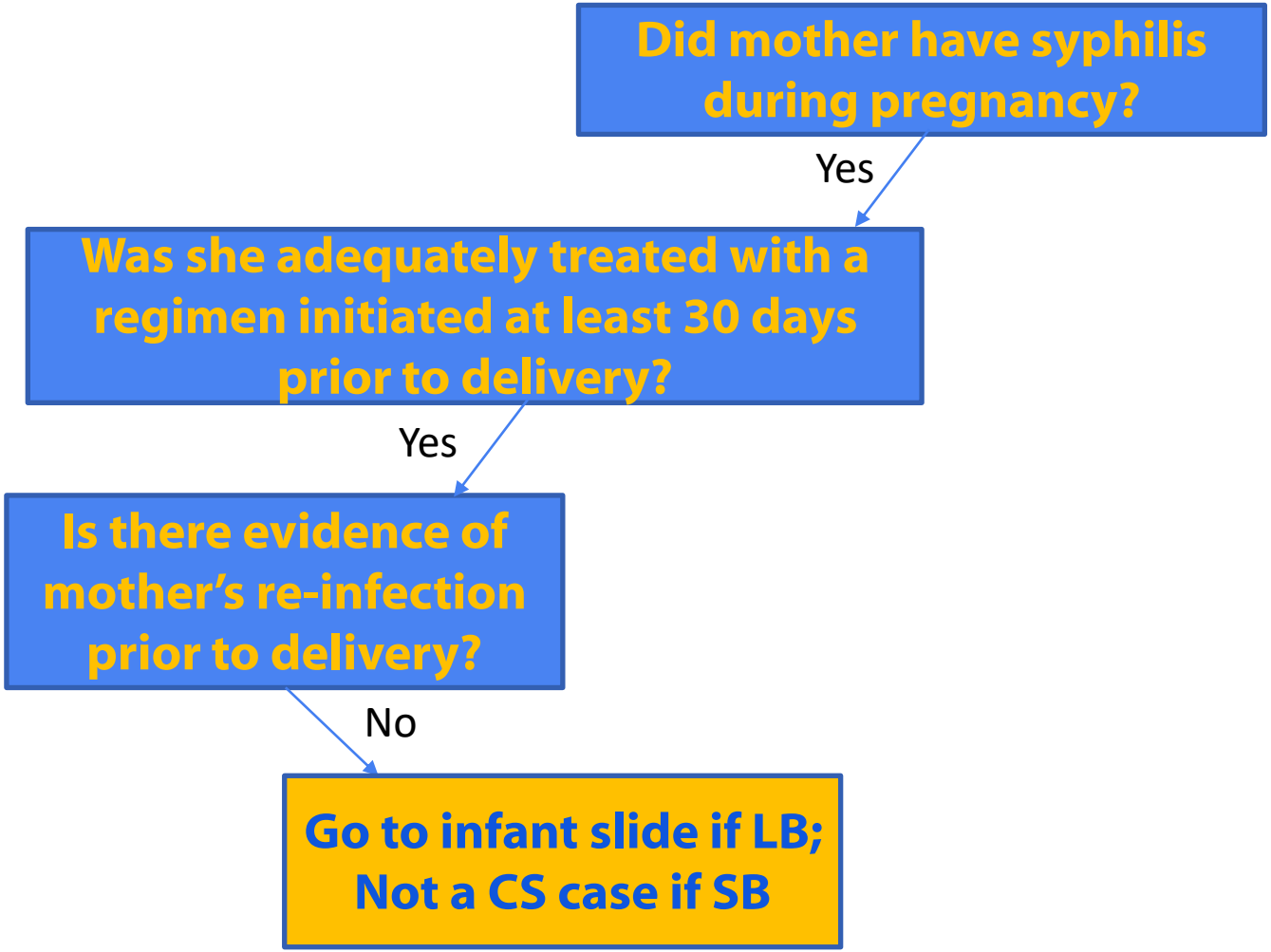
If *T. pallidum* is detected in the infant using PCR, darkfield, direct fluorescent antibody (DFA), or immunohistochemistry (IHC) staining, the infant is a reportable ‘confirmed case.’ They do not need any clinical signs or RPR testing to meet the case definition.

Advanced:
Making CS Case Classifications

Frequently Asked Questions: Serofast Syphilis

- **What do we do with serofast maternal syphilis during CS case classification?**
  - By definition, serofast cases of syphilis are *previously treated* episodes of syphilis with a stable titer
  - Serofast moms CAN deliver CS infants, but only if mom shows signs of reinfection at delivery or if the infant meets infant criteria

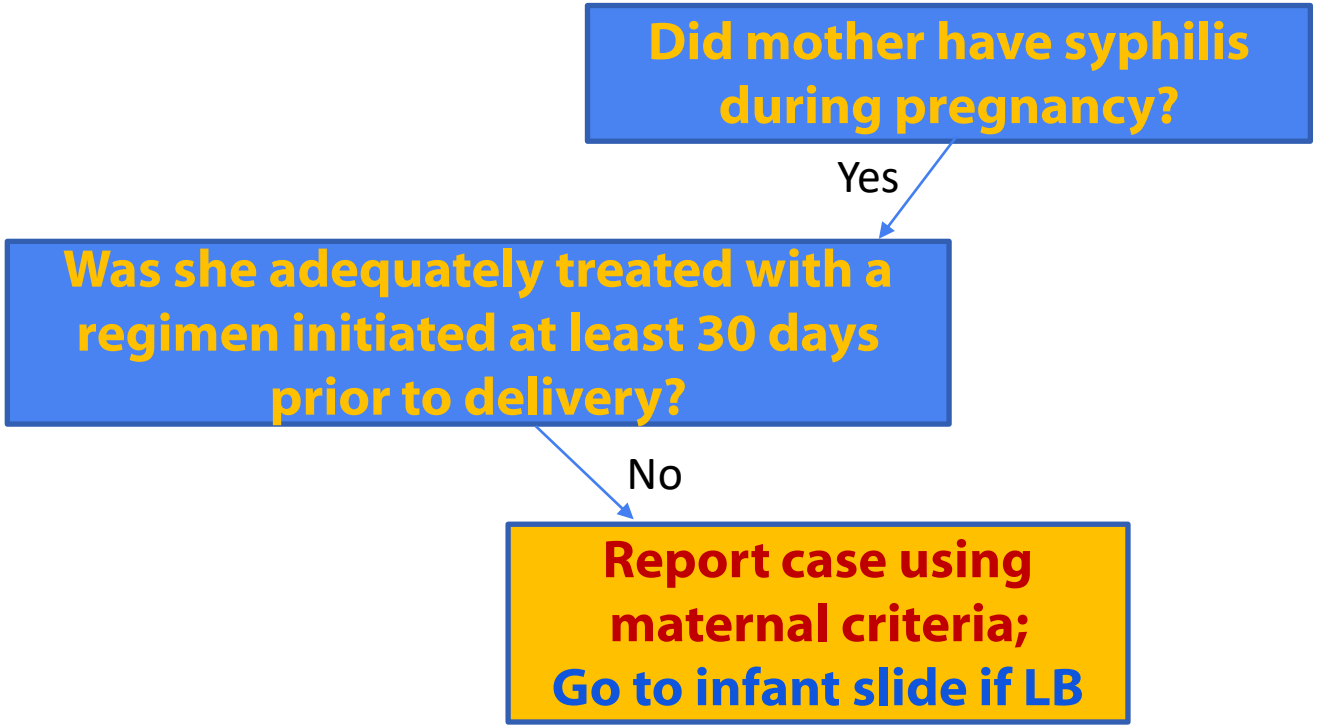
Serofast


Did mother have syphilis during pregnancy?
Yes
Was she adequately treated with a regimen initiated at least 30 days prior to delivery?
Yes
Is there evidence of mother's re-infection prior to delivery?
No
Go to infant slide if LB; Not a CS case if SB

Frequently Asked Questions: Old Syphilis

- **What do we do with previously reported (old) maternal syphilis during CS case classification?**
  - Look for evidence of treatment
    - Finding none, aim to treat her during pregnancy using a regimen appropriate for her *current* stage of syphilis
    - If unable to treat her during pregnancy, proceed as ‘not adequately treated’

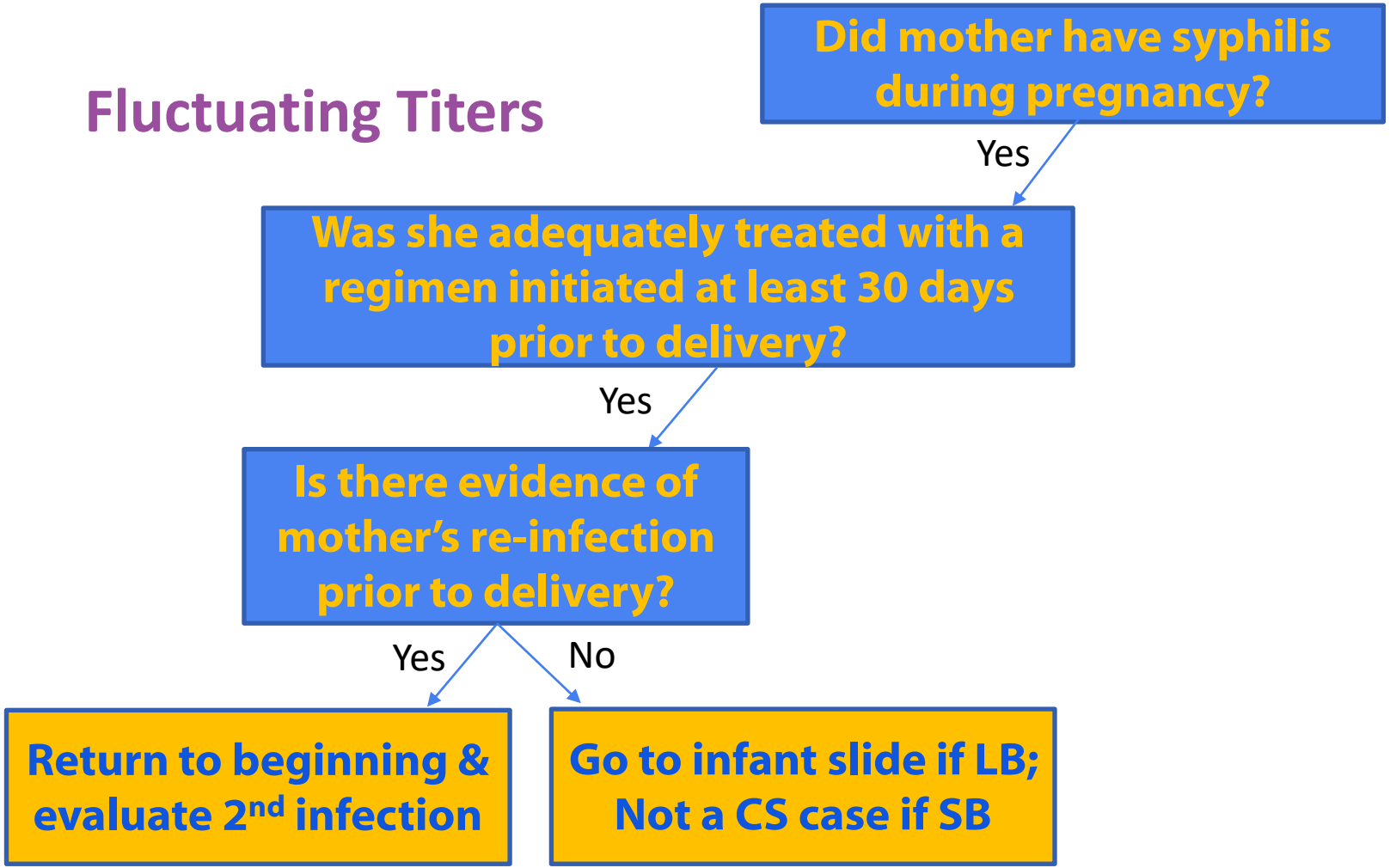
Old, untreated syphilis



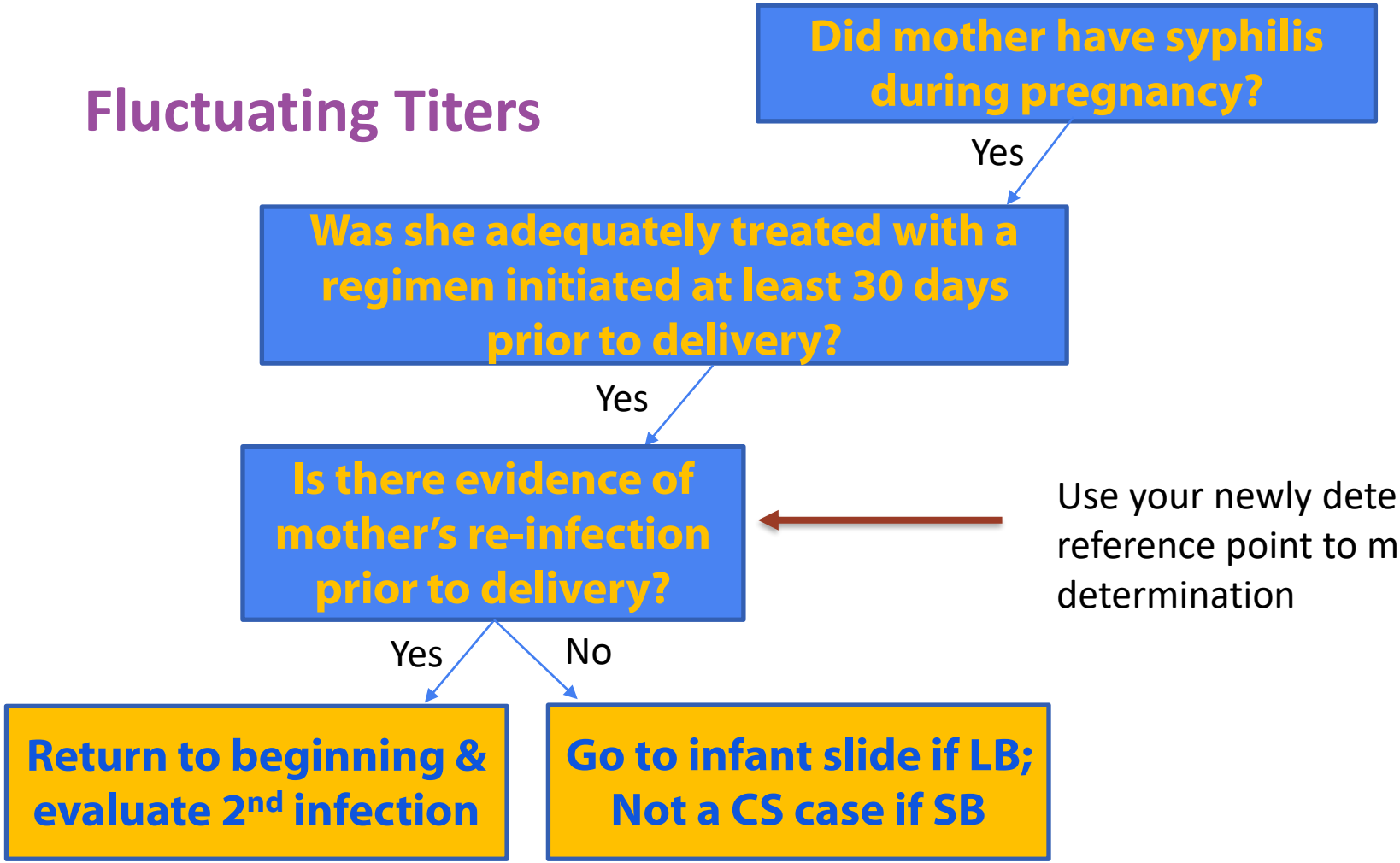
Frequently Asked Questions: Fluctuating Titers

- **What do we do with fluctuating titers during CS case classification?**
  - Fluctuating titers become important when assessing re-infection
  - Aim to identify the point ‘around which they are fluctuating’
    - Use this reference-point when assessing re-infection
  - *Do not* liberally apply the term ‘fluctuating titers’ to someone with a short history of syphilis to avoid classifying an infant as a CS case

Fluctuating Titers



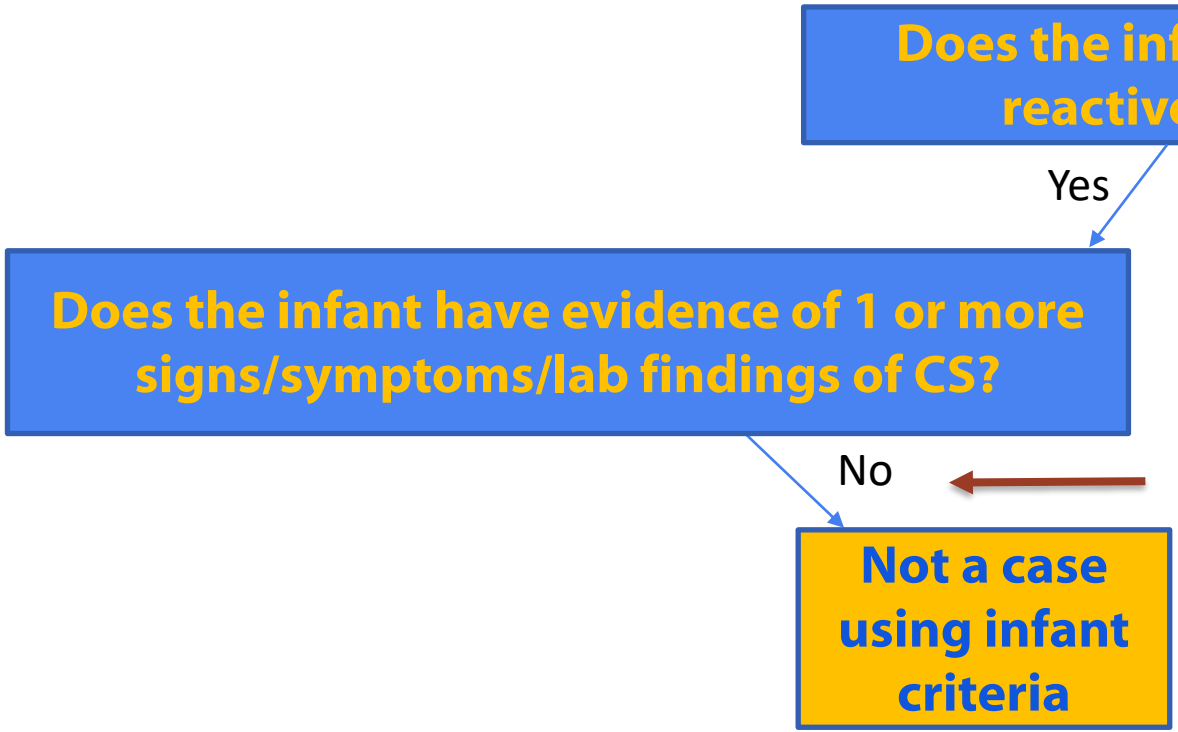
Fluctuating Titers



Frequently Asked Questions: Elevated CSF values

- **What do we do when the only sign/symptom of CS in the infant is an elevated CSF protein or WBC *with other cause*?**
  - One of the only signs/symptoms where 'other cause' may negate reporting
  - If the infant's lumbar puncture is traumatic, clinicians will often try again
    - Use results from the second lumbar puncture if interpretable
    - If no re-draw, consult a clinician about whether the CSF results are interpretable based on CSF red blood cell count
  - *Do not* go out of your way seeking alternate explanations for elevated CSF values, but you're free to use them if the clinician provides one in the chart

Elevated CSF WBC or protein with other cause



Choose ‘No’ if the elevated CSF values are the *only* sign/symptom *and* they were reported with another attributed cause

Practice:
Making CS Case Classifications

Conclusion

Conclusion:
Key take-aways

- **Making a CS case classification can be as straightforward as asking a set of formulaic questions**
  - This doesn't mean it's easy
  - You may encounter unique situations requiring decision-making along each step of the flowchart

Conclusion:
Key take-aways

- **Making a CS case classification can be as straightforward as asking a set of formulaic questions**
  - This doesn't mean it's easy
  - You may encounter unique situations requiring decision-making along each step of the flowchart
- **Surveillance and clinical classifications are not the same**
  - A reasonable clinician may choose to treat an infant aggressively even if you are not calling the infant a CS case
  - Case classification decisions for surveillance purposes belong to the health department, not the diagnosing provider

Conclusion:
Ask if you are confused!

- **Help is only an email away**
  - Ginny Bowen and clinical colleagues tackle most questions together
  - Email **vbowen@cdc.gov** with pertinent details of the case

Poll Question #2: Post-workshop Comfort

- **After this workshop, my level of comfort with making CS case classifications is best described as:**

1) **Very comfortable**
   - I've got this. I could likely handle 95-100% of case classifications on my own.
2) **Somewhat comfortable**
   - I'm feeling better than I was before. I could likely handle 80% of case classifications on my own.
3) **Somewhat uncomfortable**
   - I'm getting there but still need a fair bit of coaching or assistance.
4) **Very uncomfortable**
   - I'm going to need to sit with these notes for a while!

Special Thanks To:

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Mark Stenger (CDC)
Lizzi Torrone (CDC)
Hillard Weinstock (CDC)
India Bowman (CSTE)
Lynn Sosa (CT)
Mary McNeil (OH)
Amber Rose (OK)
Ryan Murphy (CA)
Nicole Burghardt (CA)
The Noun Project (decris & Weltenraser)

For more information, contact CDC
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