Antimicrobial Stewardship Guidelines

Neonatal HSV Guidance Document

This guideline was developed by the following multidisciplinary group:

Infectious Diseases: Patrick Reich, MD; Gregory Storch, MD
Emergency Medicine: Kimberly Quayle, MD; Tara Copper, MD
Hospital Medicine: Chrissy Hrach, MD
Neonatal Intensive Care: Melissa Riley, MD
Dermatology: Carrie Coughlin, MD

This clinical practice guideline includes a review of the background, evaluation, and management of herpes simplex virus (HSV) in patients ≤6 weeks of age for use at St. Louis Children's Hospital. This serves as a guide and may need to be adapted based on clinical judgement as well as the individual patient and family situation.

A. Neonatal HSV Background:

1. Neonatal Herpes Simplex Virus (HSV) disease occurs in infants less than 6 weeks of age; approximately 90% present in the first 21 days of life days of life (Brower, 2020).
2. Clinical manifestations can be non-specific and approximately 80% are born to mothers with no known history of genital HSV during pregnancy nor lesions at delivery (Kimberlin, 2004). Presentation varies, with the clinical subtypes (skin-eye-mucosal, disseminated, and central nervous system) described below.
    a. Skin-Eye-Mucosal (SEM): >80% have vesicular skin lesions (others with only ocular or oral manifestations).
    b. Disseminated: Hepatitis, pneumonitis, sepsis, coagulopathy, >60% have skin lesions.
    c. Central Nervous System (CNS): Lethargy, seizures, fever, irritability, >60% have skin lesions.
3. Early initiation of therapy with IV acyclovir is associated with decreased mortality (Shah, 2011).

B. When to Consider Neonatal HSV: Infants ≤6 weeks of age who present with one or more of the following:

1. Vesicular or pustular skin lesions that are not characteristic of normal newborn skin findings (e.g., erythema toxicum neonatorum, transient neonatal pustular melanosis, etc.) and/or sequelae of these lesions (punched out ulcers, eschars or crusts). These lesions can be individual, grouped, and/or coalescing. See Appendix for photo examples of HSV and common mimics.
2. Critical illness (e.g, hypotension, respiratory failure, poor perfusion, lethargy, obtunded) without another known explanation (similar findings to those of bacterial sepsis).
3. Other clinical findings such as hepatitis, coagulopathy, CSF pleocytosis in the absence of a positive gram stain, seizures, focal neurologic signs, encephalopathy, or irritability without another known explanation.
4. Fever in an otherwise well appearing infant without HSV risk factors: Refer to SLCH Clinical Practice Guideline "Fever – Patients 8-60 Days of Age" for guidance regarding HSV evaluation in this group of patients.

C. Evaluation & Treatment: In patients meeting any of the criteria in B.1 - B.3 above, initiate management as described below. For patients meeting only criteria B.4, follow recommendations as outlined in the Clinical Practice Guideline "Fever – Patients 8-60 Days of Age."

1. Initiate acyclovir*
    - 20 mg/kg/dose IV, first dose in ED. Subsequent dosing Q8 hours.
    - Of note, initiation of acyclovir should not be delayed and can be started before specimens are obtained.
2. Obtain the following studies at the time of presentation:
    - HSV PCR testing from the following sites:
        - Blood
        - CSF

        - Skin/eye/mucosal lesions
        - Surface specimens (conjunctivae, nasopharynx, mouth, anus) using a separate swab for each location.
    - ALT
    - Additional studies as clinically indicated based on the patient's presentation. Of note, there is clinical overlap between some HSV infections and febrile neonate evaluations. Additional testing for bacterial infections may be warranted and is outside the scope of this clinical practice guideline.
3. Obtain the following studies when feasible:
    - Eye exam (see 4 below)
    - Neuroimaging (head ultrasound for all patients, brain MRI based on the clinical presentation)
4. Specialist consultations
    - Recommend Pediatric Infectious Diseases consultation
    - In the presence of CNS disease/symptoms, recommend Pediatric Neurology consultation
    - Recommend Pediatric Ophthalmology consultation for ocular exam during admission
    - Consider Dermatology consultation if diagnostic uncertainty
5. Disposition: patients being evaluated for HSV should be admitted to the hospital with empiric therapy, pending results of PCR-based testing. Admission to floor versus ICU depends on their clinical condition.*
6. Discontinuation of therapy: Acyclovir can be discontinued after HSV PCR results negative or if an alternative diagnosis is established (Ex positive parechovirus/enterovirus PCR).

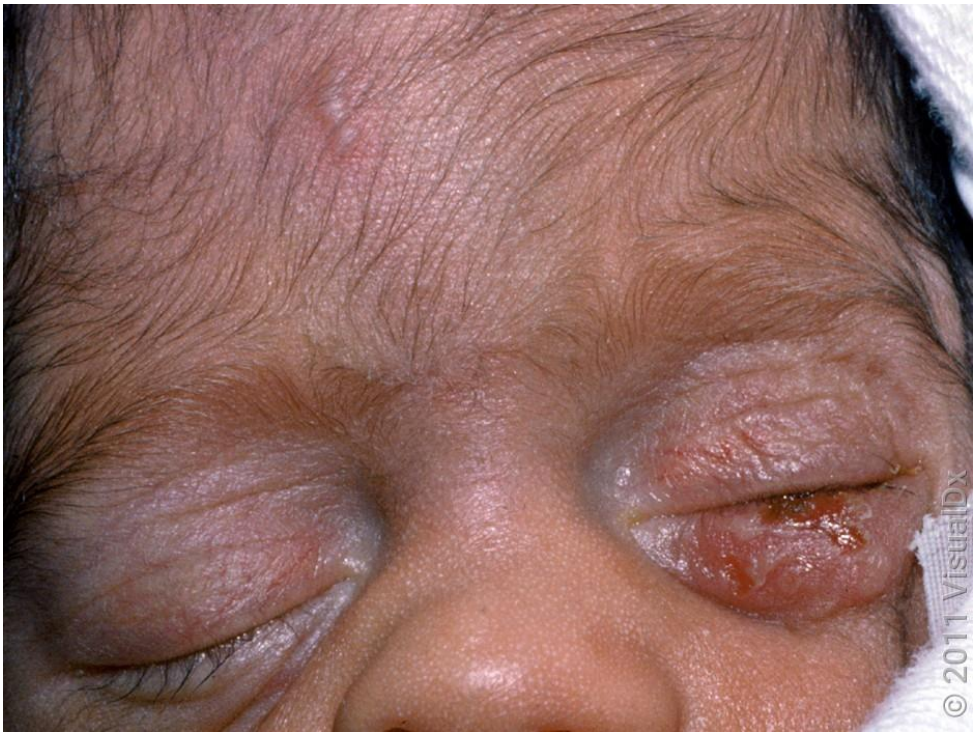
*If the clinical suspicion for HSV is low in a well-appearing infant with a plausible alternative diagnosis and for whom close follow up is assured, the provider may have a risks/benefits discussion with the parent(s) regarding discharge while testing is pending versus admission with early initiation of IV acyclovir. It is vital to ensure any patients discharged home have an appropriate follow plan in place, have a reliable contact phone number, and can return to care.

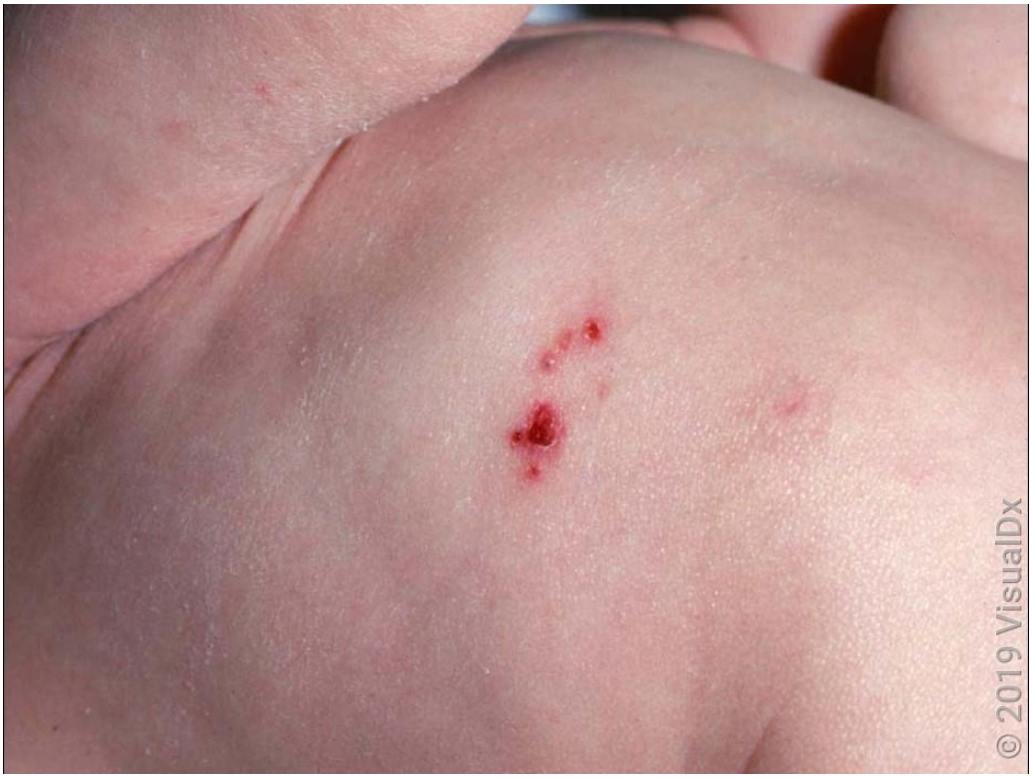
References:

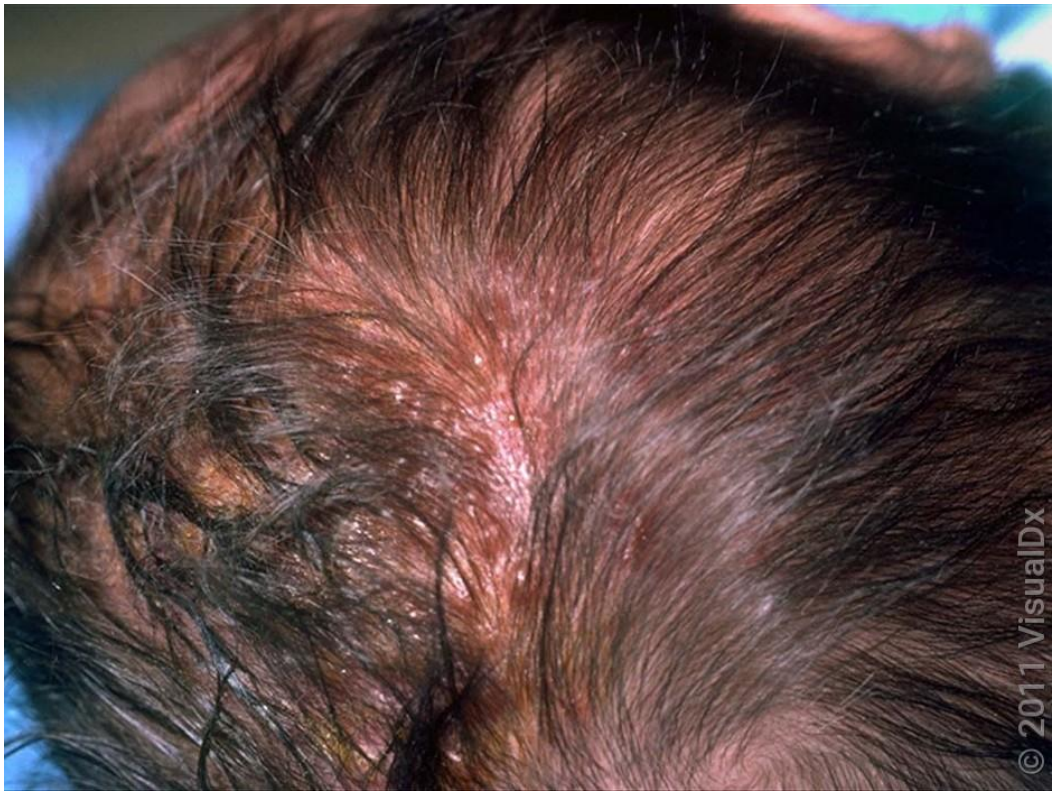
1. Brower LH et al. Evaluation for Neonatal HSV in Infants Undergoing Workup for Serious Bacterial Infection: A 5-Year Retrospective Review. *Hosp Pediatr*. 2020.
2. Kimberlin DW. Neonatal Herpes Simplex Infection. *Clin Microb Rev*. 2004.
3. Long SS et al. HSV Infection in Young Infants in Two Decades of Empiric Acyclovir Therapy. *PIDJ*. 2011
4. Red Book: 2021 Report of the Committee on Infectious Diseases, American Academy of Pediatrics; Thirty-second edition.
5. Shah SS et al. Delayed Acyclovir Therapy and Death Among Neonates With Herpes Simplex Virus Infection. *Pediatrics*. 2011.
6. Herpes Simplex Virus Infection | Consultant360
7. Neonatal Herpes Simplex Virus (HSV) Infection - Pediatrics - Merck Manuals Professional Edition

Appendix

HSV Photos (Credit: VisualDx)



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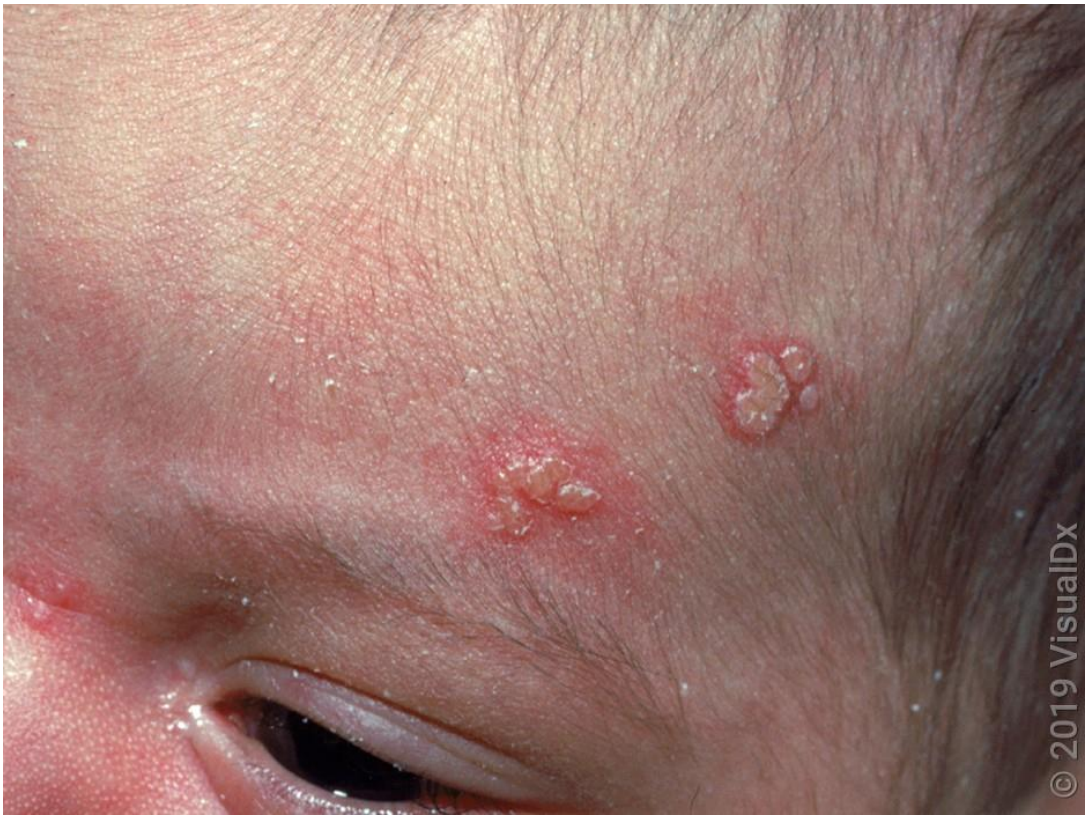
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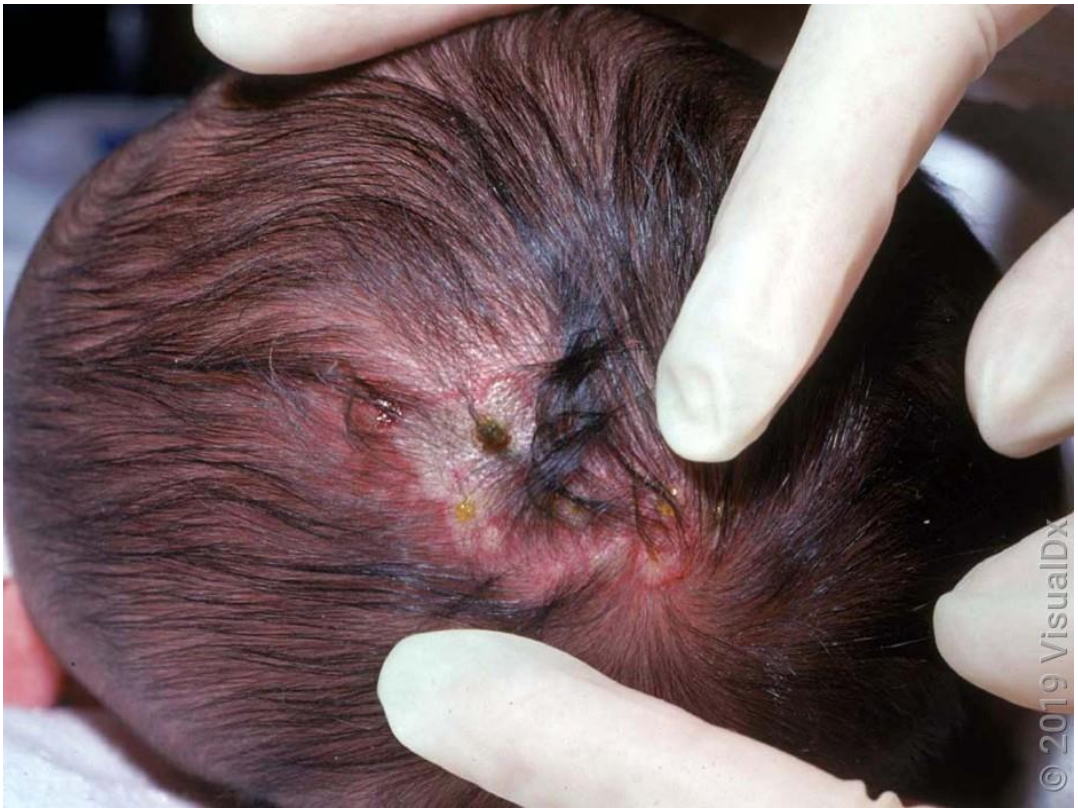
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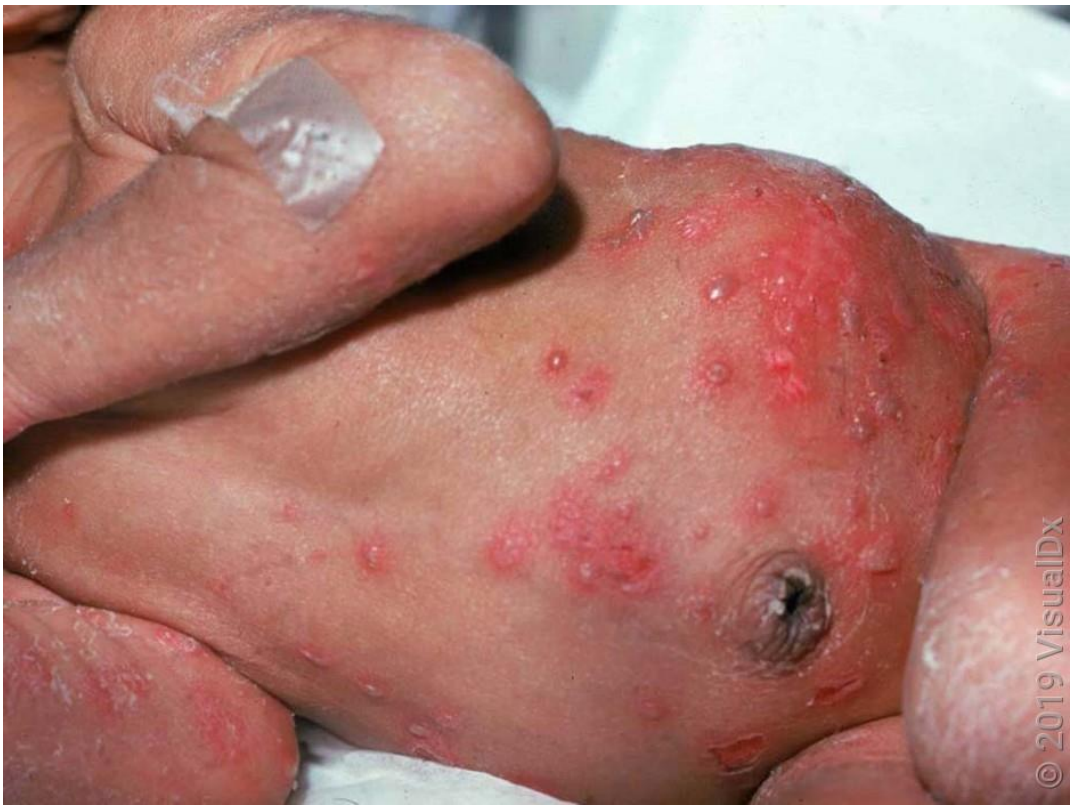
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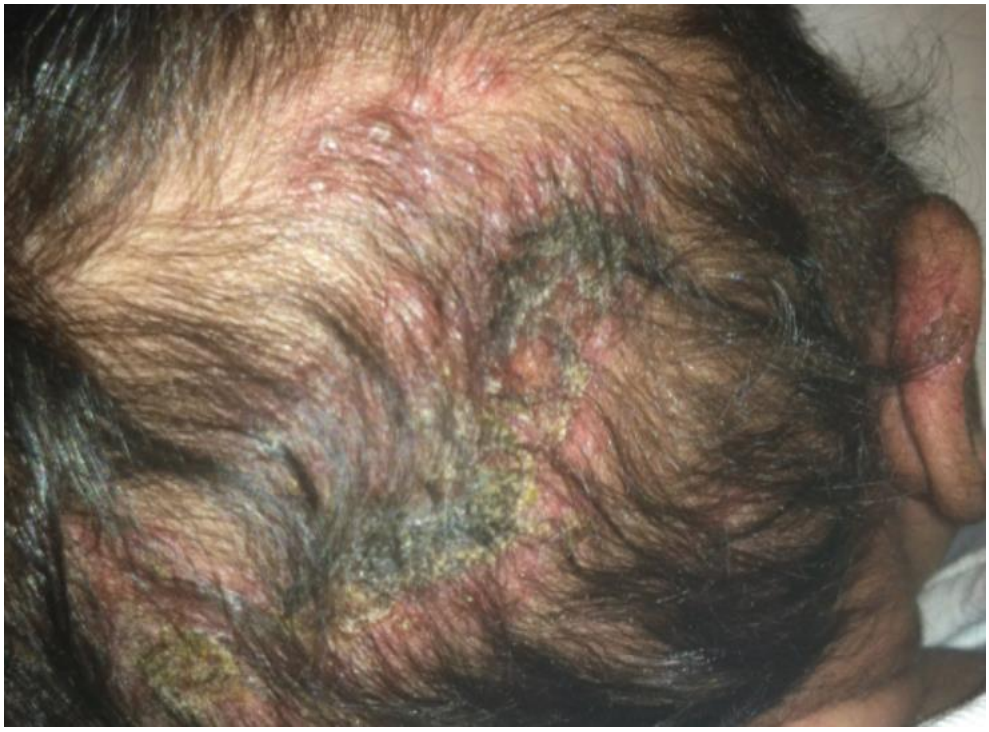


Image credit: Consultant 360

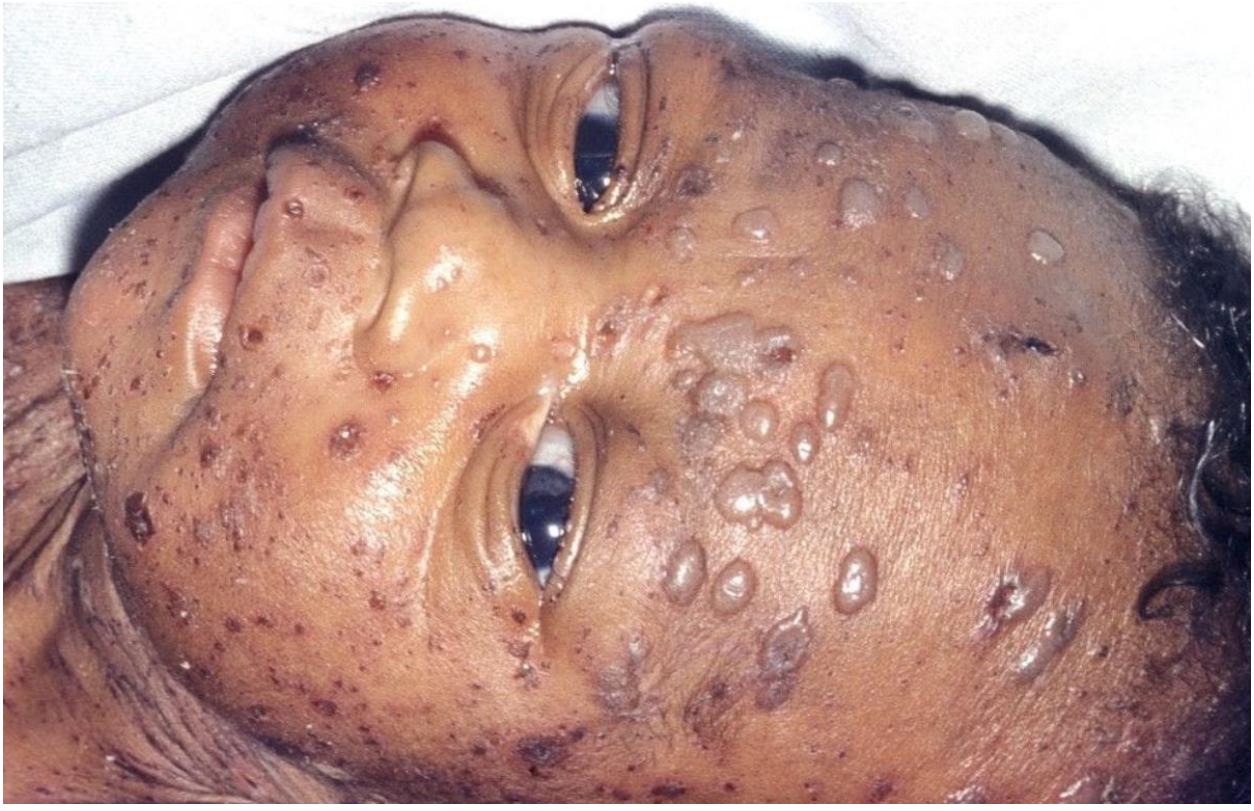
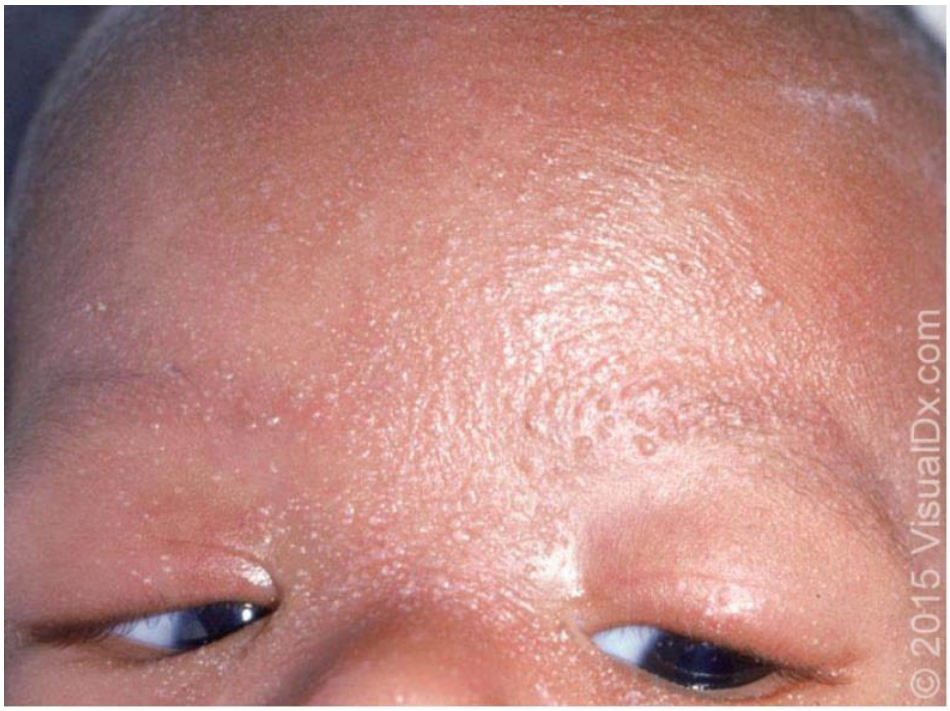
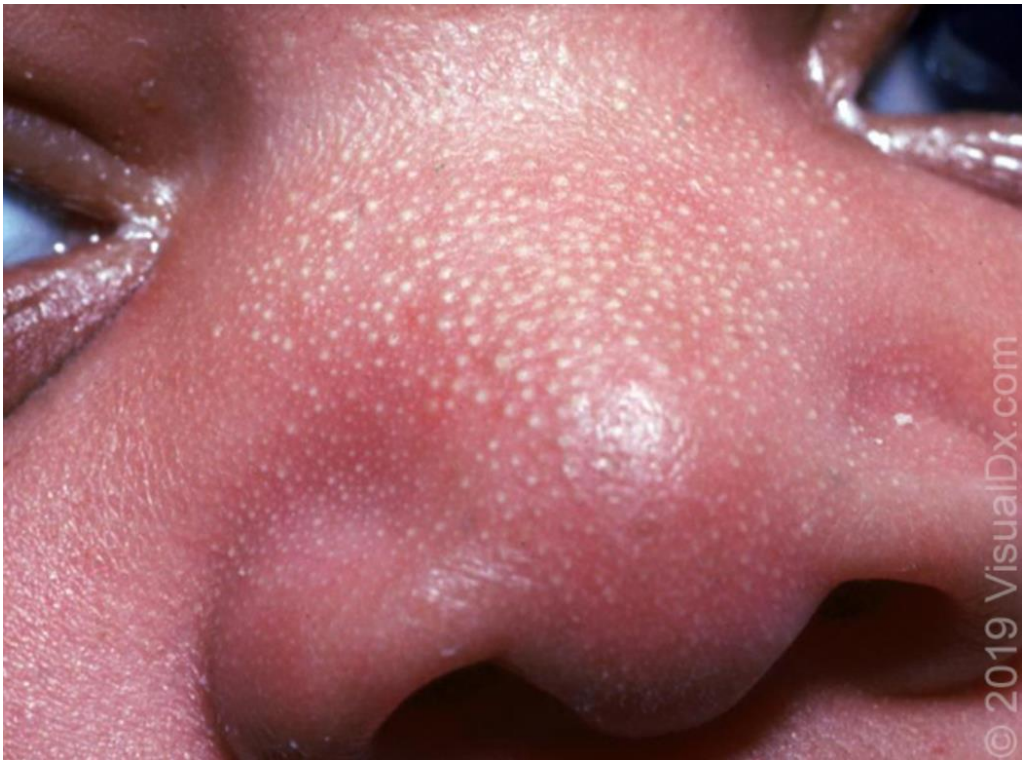


Image credit: Merck Manual. Infant co-infected with HIV.

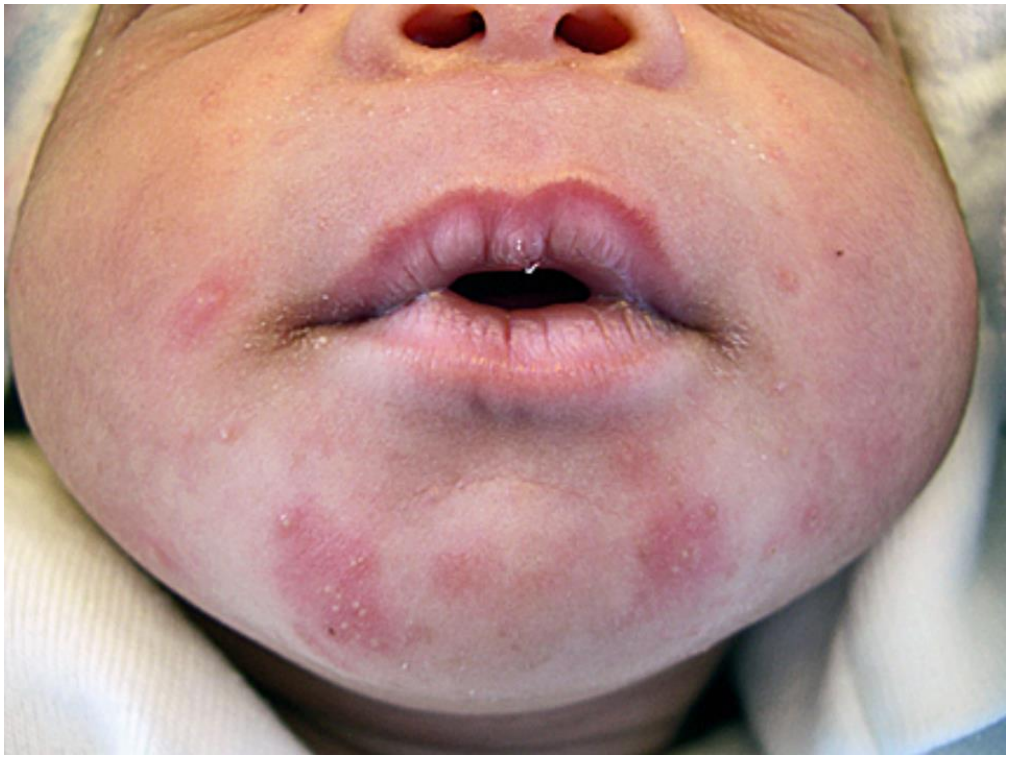
HSV Mimics



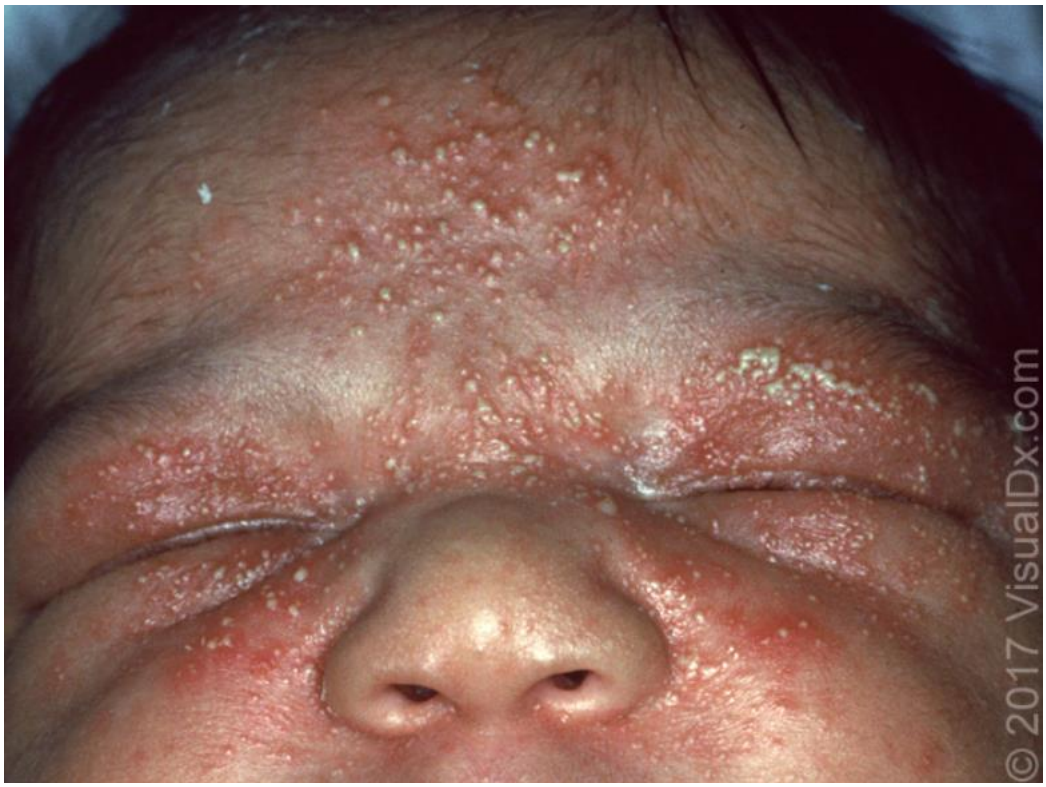
Miliaria crystallina. VisualDx.com



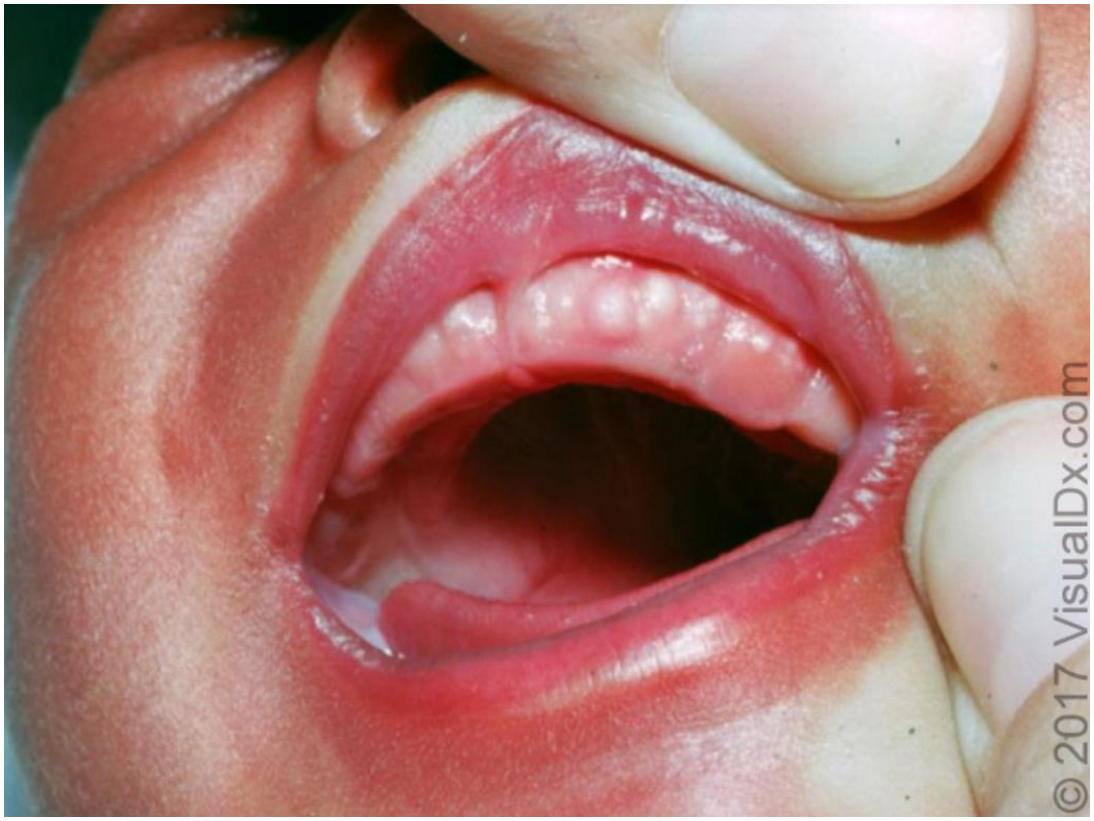
Sebaceous hyperplasia. VisualDx.com



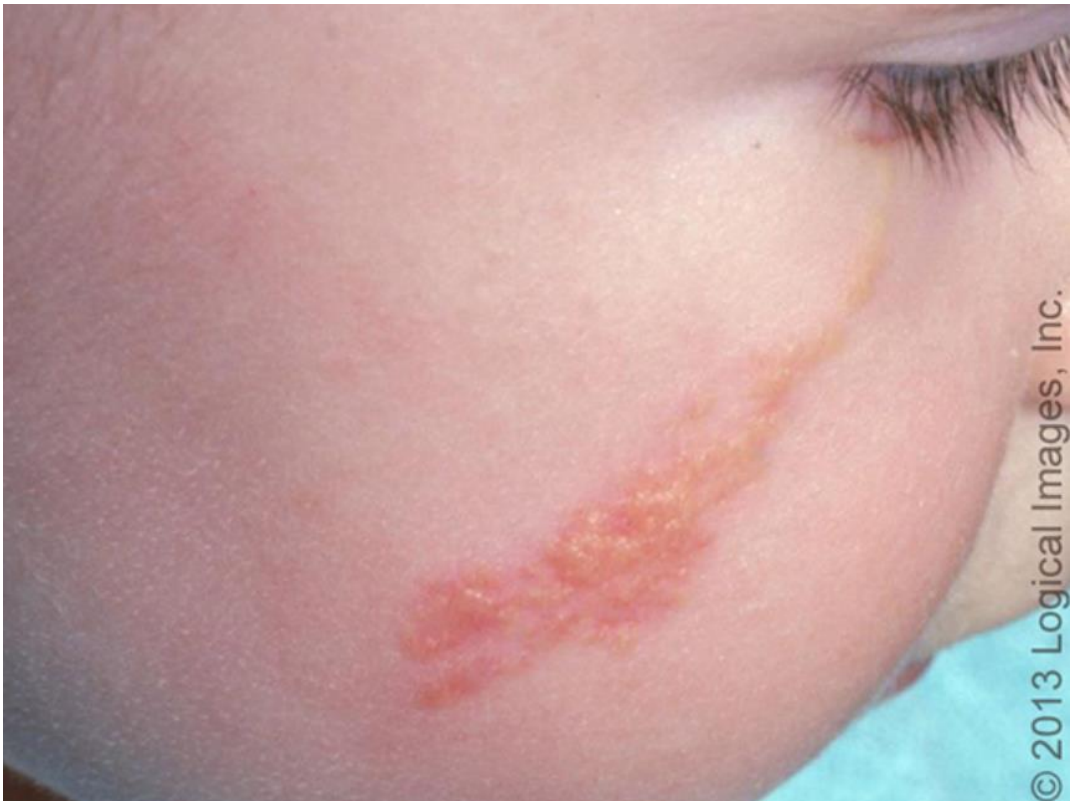
Erythema toxicum neonatorum. Douglas Hoffman, MD, Dermatlas.



Neonatal cephalic pustulosis. VisualDx.com



Bohn nodules (gingival inclusion cysts). VisualDx.com.



Nevus sebaceous. Logical images, inc.