

TECHNICAL BULLETIN: Exanthem and Eruptive Skin Rash

Eurofins Diatherix is expanding diagnostic offerings to include testing for exanthems and eruptive vesiculopustular skin rashes. Exanthems are rashes caused by infections and/or drug interactions. These widespread rashes may be accompanied by fever, headache, or malaise, sometimes prior to the appearance of skin inflammation. Exanthems are often caused by a body's immune response to infection and accordingly, a pathogen cannot be isolated from the rash. Eruptive vesiculopustular rashes in contrast, are caused by direct infection of the inflamed area, and have detectable levels of the pathogen present in vesiculopustular fluid that can be identified by PCR. Some of these rashes are common in children and are often diagnosed visually based on characteristic appearances of the rash. However, mimicry of other infectious agents or inflammatory conditions creates the need for a multiplex PCR test to aid in the clinical evaluation and diagnosis of such rashes.

A number of causative agents belong to the Herpesviridae family (Table 1), which establish latent infections that can be detected by PCR assays after the primary infection subsides. As a result, it is always necessary to correlate a test result with the overall clinical picture and symptoms, the details of which are described below:

Table 1. Human herpesviruses in the exanthem and/or eruptive skin rash testing options

Name	Common Name
HHV-1	Herpes simplex virus type 1 (HSV-1)
HHV-2	Herpes simplex virus type 2 (HSV-2)
HHV-3	Varicella zoster virus (VZV)
HHV-4	Epstein-Barr virus (EBV)
HHV-5	Cytomegalovirus (CMV)
HHV-6	Roseolavirus
HHV-7	Roseolavirus

- 1.) Herpes simplex virus 1 and 2:** A swab of a suspected herpetic lesion is optimal and recommended for testing. However, throat swabs are accepted as a specimen source for the additional Eurofins Diatherix HSV Test when HSV pharyngitis is suspected.
- 2.) Varicella zoster virus:** Varicella zoster virus can be detected from a throat swab or a swab of an unroofed vesicle. Due to its pattern of latency, VZV is not frequently detected in the absence of active chickenpox or zoster (shingles).
- 3.) Epstein-Barr virus:** Epstein-Barr virus, the primary causative agent of infectious mononucleosis, causes a maculopapular rash in some cases of primary infection and/or when an aminopenicillin is administered during an active EBV infection.⁴ While EBV can be detected via throat swab during an active infection, B-cells and salivary glands shed viral particles in saliva during latent infection. Seroprevalence for EBV infection increases with age from 54% at ages 6-8 to 82% by ages 18-19.² As such, correlation of results to clinical picture and symptoms is necessary for accurate diagnosis.
- 4.) Cytomegalovirus:** Cytomegalovirus can cause infectious mononucleosis in a minority of cases of primary infection. Like EBV, CMV can be detected in throat swabs and saliva in asymptomatic individuals, though less prevalently than Epstein-Barr virus.

5.) HHV-6 and HHV-7: The viruses that cause roseola in infancy and early childhood persist and are shed in the saliva throughout life during latent infection. In immunocompetent individuals, replication is controlled by the immune system, so detection of HHV-6 and/or HHV-7 in a throat swab should be interpreted in light of the clinical appearance. Primary infection with HHV-6 and/or HHV-7 often occurs within the first 24 months of life. Roseolavirus seroprevalence is near ubiquitous in adults, exceeding 95%.¹ Therefore, it is not recommended to test for confirmation of roseola by PCR in patients over the age of two, as HHV-6 and HHV-7 can be detected at a particularly high rate after childhood.^{1, 3}

Ordering options:

Eurofins Diatherix offers testing for exanthems or eruptive skin rashes according to optimal specimen sources as indicated in Table 2 for accurate pathogen detection.

Table 2. Eurofins Diatherix testing options for exanthems or eruptive skin rashes

Oropharyngeal, Throat		Lesion, Rash, Unroofed Vesicle Swab	
Exanthem	Exanthem + Roseola	Eruptive Skin Rash	Eruptive Skin Rash + HSV1/HSV2
<i>S. pyogenes</i> Parvovirus B19 Cytomegalovirus Epstein-Barr virus Enterovirus group Parechovirus Measles virus Varicella zoster virus	<i>S. pyogenes</i> Parvovirus B19 Cytomegalovirus Epstein-Barr virus Enterovirus group Parechovirus Measles virus Varicella zoster virus HHV-6 HHV-7	<i>S. pyogenes</i> Enterovirus group Varicella zoster virus <i>S. aureus</i> MRSA	<i>S. pyogenes</i> Enterovirus group Varicella zoster virus <i>S. aureus</i> MRSA HSV-1 HSV-2

Eurofins Diatherix has configured these testing options based on the localization of the pathogen during an active infection (see Figure 1). The exanthem testing options identify pathogens that either produce a rash within which a pathogen is not detectable, such as parvovirus B19, or are easily detectable from a throat swab, like enterovirus. The enterovirus group target is inclusive of coxsackievirus A16 and enterovirus 71, viruses that cause hand, foot, and mouth disease. Roseola viruses are included in a separate testing option which is only recommended for children under two years of age. The eruptive skin rash testing options are configured for pathogens present in vesiculopustular fluid. Varicella zoster virus and enterovirus group are included in both the exanthem and eruptive skin rash testing options due to presence of the viruses in the oropharynx and vesiculopustular fluid during chicken pox or hand, foot, and mouth disease. *Streptococcus pyogenes* is included in the exanthem and eruptive skin rash testing options to confirm scarlet fever or impetigo respectively.

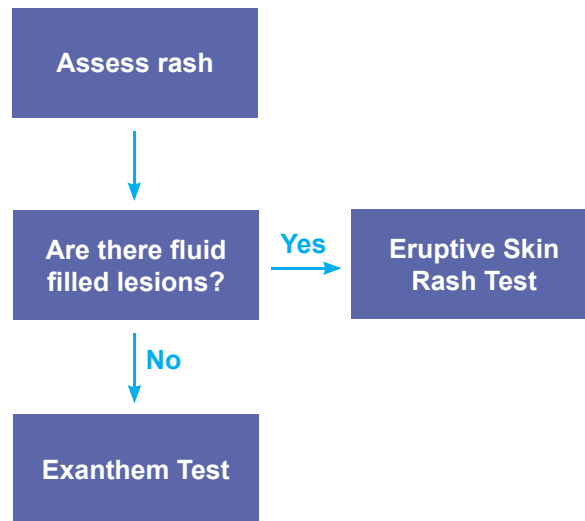


Figure 1. Decision tree for skin rash testing options.

References:

1. DeBolle, L. et al. Update on Human Herpesvirus 6 Biology, Clinical Features, and Therapy. *Clinical Microbiology Reviews* **18:1**, (2005).
2. Dowd, J. B. et al. Seroprevalence of Epstein-Barr Virus Infection in U.S. Children Ages 6-19, 2003-2010. *PLOS One* **8:5**, (2013).
3. Grinde, B. et al. Herpesviruses: Latency and Reactivation – Viral Strategies and Host Response. *Journal of Oral Microbiology* **5**, (2013).
4. Ónodi-Nagy, K. et al. Amoxicillin rash in patients with infectious mononucleosis: Evidence of true drug sensitization. *Allergy, Asthma & Clinical Immunology* **11**, (2015).