

# The Role of Varicella Zoster Virus in the Development of Periapical Pathoses and Root Resorption: A Systematic Review

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## Abstract

**Introduction:** Varicella zoster virus (VZV) and subsequent herpes zoster (HZ) infection have been proposed as a causative agent of periapical pathoses and root resorption. This review aimed to identify, synthesize, and present a critical analysis of the available data on the association among VZV, subsequent HZ infection, and the development of periapical pathoses and root resorption and to analyze the level of evidence of available studies. **Methods:** The literature search covered MEDLINE, Science Citation Index Expanded, and Scopus. A qualitative critical appraisal of the included articles was performed. **Results:** The electronic database search yielded 66 hits from PubMed, 73 hits from Web of Science, and 107 from Scopus. Seven case reports and 3 cross-sectional studies were included in the final review. When summarized, in 7 patients with a history of a previous HZ attack and with no other apparent cause, 23 teeth were diagnosed with apical periodontitis, 8 teeth with internal and 1 tooth with external root resorption. The cross-sectional studies investigated the presence of VZV DNA in samples of acute apical abscess. The VZV DNA was found only in 2 of 65 samples. **Conclusions:** All studies included in this systematic review had a low level of evidence (4 and 5). Still, the potential role of VZV in the etiopathogenesis of periapical pathoses and root resorption cannot be ruled out. Future investigations should be directed toward the analysis of VZV pathologic effects on pulp blood vessels, which might cause local ischemia and tissue necrosis. (*J Endod* 2017; ■ :1–7)

## Key Words

Apical periodontitis, chickenpox, herpesvirus 3, herpes zoster, periapical abscess, root resorption

Chronic inflammation and destruction of tooth-supporting tissues in periapical pathoses are mainly caused by microorganisms derived from the infected root canal. Apical

periodontitis and periapical abscess are essentially polymicrobial infections caused by opportunistic and anaerobic bacteria (1, 2). Inflammation caused by bacterial infection and/or mechanical stimuli are also recognized as major factors contributing to the development of root resorption (3–5).

In previous reports, different herpesviruses have been implicated as putative pathogens in apical periodontitis and acute periapical abscess (6–10). Being the most frequently detected species, epidemiologic studies have associated Epstein-Barr virus and human cytomegalovirus with the development of periapical lesions (6–10).

Apart from Epstein-Barr virus and human cytomegalovirus, varicella-zoster virus (VZV) and subsequent herpes zoster (HZ) infection were also implicated in the development of periapical pathoses and root resorption (11–20). VZV, or human herpesvirus 3, is a large, double-stranded DNA-containing virus enclosed in a protein capsid and envelope. It represents a human neurotropic virus that causes 2 distinct diseases, varicella or chickenpox and herpes zoster infection or shingles (21). Primary VZV infection results in chickenpox, a childhood skin disease characterized by eruptive vesicles with the highest incidence between 1 and 9 years of age. After primary infection, VZV remains latent in the cranial nerve ganglia, dorsal root ganglia, and autonomic ganglia along the entire neuraxis. During the latent infection, VZV can be reactivated, leading to HZ infection. VZV reactivation is caused by the decline of VZV-specific cell-mediated immunity, which decreases with age or by immunosuppression. HZ represents a secondary neurodermic viral infection that involves the dermatome supplied by the sensory nerve that arises from the specific ganglion. It is characterized by severe pain and painful vesicles on the skin and mucosa around the affected sensory nerve (21–23).

Previous studies investigated the association of VZV and subsequent HZ infection with osteonecrosis of the jaw, exfoliation of teeth, odontogenic pain, skin scars, and so

## Significance

Follow-up of patients suffering from herpes zoster attack might be considered in order to establish a timely diagnosis and treatment of the affected teeth.

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## Review Article

on (24–26). In addition, several studies correlated the presence of VZV or HZ infection and the development of periapical pathoses and root resorption (11–20).

Evidence-based dentistry represents an approach to oral health care that requires the judicious integration of systematic assessments of clinically relevant scientific evidence, relating to the patient's oral and medical condition and history, with the dentist's clinical expertise and the patient's treatment needs and preferences (27). Systematic reviews and meta-analysis of randomized clinical trials have the highest level of evidence (LOE). These are followed by cohort studies, cross-sectional studies, case-control studies, case series, case report studies, and expert opinions (28). However, there are no registered or published systematic reviews related to the association of VZV and the development of periapical pathoses and root resorption.

Hence, the aim of this systematic review was to identify, synthesize, and present a critical analysis of available data on the association among VZV, subsequent HZ infection, and the development of periapical pathoses and root resorption. Additionally, we aimed to analyze the LOE of the available studies according to established criteria (28). Therefore, we addressed the following focused question: What is the LOE that VZV contributes to the development of apical periodontitis, acute apical abscess, and root resorption?

### Materials and Methods

This systematic review was based on the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist and followed the 4-phase flow diagram (29). The LOE was assessed using the guidelines provided by the Oxford Centre of Evidence-Based Medicine (28).

### Inclusion and Exclusion Criteria

The following article types were considered:

1. Original scientific articles, case series, case reports, and short communications published in the English language in peer-reviewed scientific journals AND
2. Documented data on the identification of VZV in samples obtained from apical periodontitis, acute apical abscesses, and root resorption OR

3. Documented data on clinical and radiographic signs and symptoms of apical periodontitis, acute apical abscesses, and root resorption in areas previously affected by HZ attack

Exclusion criteria included the following: cell culture laboratory studies or animal studies.

### Search Strategy and Study Selection

The systematic search, evaluation of relevant articles, and their critical appraisal were performed by 2 independent reviewers (AJ and JKP) who were blinded to each other. The following electronic databases were searched: MEDLINE using the PubMed search engine, Science Citation Index Expanded using Web of Science, and Scopus. Additional manual searches involved reference lists from all articles retrieved for possible inclusion. Full-text publications and English language were set as limits. The search key words used included the following Medical Subject Heading terms: (periapical disease OR apical periodontitis OR periapical lesion OR periapical abscess OR root resorption) AND (viruses OR herpesvir\*). Electronic and manual searches were last conducted on June 10, 2016. The literature search is available in Table 1.

Literature search results were deduplicated in EndNote X7 software (Thomson Reuters, New York, NY). Initially, the titles and abstracts of the retrieved articles were screened. Full texts were obtained for studies that appeared to be relevant or had insufficient data in the title or abstract to make a clear decision. After the full-text assessment, articles were submitted to a final eligibility evaluation by the same 2 reviewers. Different findings in each round were settled by discussion between the 2 reviewers, and disagreements were managed by consultation with a third party (MA).

### Data Extraction and Data Analysis

The reviewers used standardized, predefined extraction sheets to obtain relevant information from the included studies. Extracted data included the publication details (author, year of publication, and language); study design and sample size; sex and age of the included patients; oral-related clinical and/or radiographic sign and symptoms of apical periodontitis, acute apical abscess, and root resorption; report

**TABLE 1.** Electronic Search Strategy for the PubMed Database with the Following Medical Subject Heading Key Words: (periapical disease OR apical periodontitis OR periapical lesion OR periapical abscess OR root resorption) AND (viruses OR herpesvir\*)

((“periapical diseases”[MeSH Terms] OR (“periapical”[All Fields] AND “diseases”[All Fields]) OR “periapical diseases”[All Fields] OR (“periapical”[All Fields] AND “disease”[All Fields]) OR “periapical disease”[All Fields]) OR (“periapical periodontitis”[MeSH Terms] OR (“periapical”[All Fields] AND “periodontitis”[All Fields]) OR “periapical periodontitis”[All Fields] OR (“apical”[All Fields] AND “periodontitis”[All Fields]) OR “apical periodontitis”[All Fields]) OR (periapical[All Fields] AND lesion[All Fields]) OR (“periapical abscess”[MeSH Terms] OR (“periapical”[All Fields] AND “abscess”[All Fields]) OR “periapical abscess”[All Fields]) OR (“root resorption”[MeSH Terms] OR (“root”[All Fields] AND “resorption”[All Fields]) OR “root resorption”[All Fields])) AND (“virology”[Subheading] OR “virology”[All Fields] OR “viruses”[All Fields] OR “viruses”[MeSH Terms]) OR (herpesvir[All Fields] OR herpesviral[All Fields] OR herpesvirales[All Fields] OR herpesviridae[All Fields] OR herpesviremia[All Fields] OR herpesviren[All Fields] OR herpesvirida[All Fields] OR herpesviridae[All Fields] OR herpesviridea[All Fields] OR herpesviridae[All Fields] OR herpesvirinae[All Fields] OR herpesvirinea[All Fields] OR herpesvirion[All Fields] OR herpesvirioni[All Fields] OR herpesvirions[All Fields] OR herpesviriridae[All Fields] OR herpesvirologist[All Fields] OR herpesvirologists[All Fields] OR herpesvirology[All Fields] OR herpesvirosis[All Fields] OR herpesvirove[All Fields] OR herpesvires[All Fields] OR herpesviruses[All Fields] OR herpesvirus[All Fields] OR herpesviru[All Fields] OR herpesvirua[All Fields] OR herpesvirukset[All Fields] OR herpesvirum[All Fields] OR herpesvirus[All Fields] OR herpesvirus’[All Fields] OR herpesvirus1[All Fields] OR herpesvirus6[All Fields] OR herpesvirus68[All Fields] OR herpesvirus8[All Fields] OR herpesvirusabort[All Fields] OR herpesvirusabortes[All Fields] OR herpesvirusarten[All Fields] OR herpesviruscs[All Fields] OR herpesvirusenkefalitiin[All Fields] OR herpesviruserkrankungen[All Fields] OR herpesviruses[All Fields] OR herpesviruses’[All Fields] OR herpesviruseses[All Fields] OR herpesvirusexanthem[All Fields] OR herpesvirusinfecties[All Fields] OR herpesvirusinfeksjon[All Fields] OR herpesvirusinfeksjoner[All Fields] OR herpesvirusinfekte[All Fields] OR herpesvirusinfektioihin[All Fields] OR herpesvirusinfektion[All Fields] OR herpesvirusinfektionen[All Fields] OR herpesvirusinfektioner[All Fields] OR herpesvirusisolate[All Fields] OR herpesviruslaakkeita[All Fields] OR herpesviruslatens[All Fields] OR herpesviruslike[All Fields] OR herpesvirusmyeloencephalopathy[All Fields] OR herpesvirusna[All Fields] OR herpesvirusnachweis[All Fields] OR herpesvirusok[All Fields] OR herpesvirussen[All Fields] OR herpesvirusspecific[All Fields] OR herpesvirustatien[All Fields] OR herpesvirusu[All Fields]))).

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