

This Week's Citation Classic

Fitzgerald R J & Keyes P H. Demonstration of the etiologic role of streptococci in experimental caries in the hamster. *J. Amer. Dent. Ass.* 61:9-19, 1960.

[National Institute of Dental Research, National Institutes of Health, Bethesda, MD]

Dental caries was induced in 'caries-inactive' albino hamsters by oral inoculation of pure cultures of a streptococcus isolated from a caries lesion of a caries active hamster. A streptomycin-resistant mutant of this organism was used to demonstrate its presence in caries lesions and to trace the transmission of the labeled organisms between animals. [The SCJ[®] indicates that this paper has been cited over 265 times since 1961.]

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"It was surprising to learn how popular this paper has been since it was aimed primarily at dental researchers. The frequency with which it has been cited is probably due to several 'firsts' which it reported. It was the first demonstration of caries induction by the organism we now know as *Streptococcus mutans* and which is now highly suspect as a cause of caries in humans; it was the first report of caries induction by a single organism in an animal harboring a 'conventional' microflora, as distinguished from the germfree animal model; and it was the first time antibiotic-resistant labeled organisms had been utilized to trace the transmission of an oral disease.

"As in the case of a number of studies which have become 'Citation Classics' serendipity played a prominent part in this research. Paul Keyes had obtained a strain of albino hamsters from the National Institutes of

Health's Animal Production Unit which appeared to be virtually immune to caries when fed the high sucrose diet that resulted in high caries activity in golden hamsters. At first, thinking that this was a genetically mediated phenomenon, he soon discovered that when albino and golden hamsters were caged together both strains developed caries.¹ This indicated that the albinos did not harbor a cariogenic microflora but could acquire the infection on contact with the golden hamsters.

"At the time, I had been using germ free rats to test the potential cariogenicity of pure cultures of microorganisms isolated from caries in rats and humans. Recognizing that the albino hamster would be simpler and more convenient as a test animal for these studies, Keyes and I joined forces. I isolated a series of organisms from caries lesions in golden hamsters and we began to infect the albinos with them. Within a few months we showed that only a single type of streptococcus was cariogenic. By making this organism resistant to streptomycin and using selective media containing streptomycin to re-isolate it, we had a convenient way to show that it fulfilled Koch's postulates as the cause of caries in these animals.

"It was not until several years later that we learned that a similar organism had been isolated from human caries by Clarke² in 1924 and named *Streptococcus mutans*. Unfortunately, Clarke had no way to demonstrate that his organism actually caused caries. Ironically, the success of our study depended on the advent of antibiotics, for it turned out that the albino hamster breeding colony had been treated with a number of antibiotics to eliminate intercurrent infections. This treatment apparently also eliminated any cariogenic organisms they may have harbored."

1. Keyes P H. Infections and transmissible nature of experimental dental caries.

Arch. Oral Bio! 1:304-20, 1960.

2. Clarke J K. On the bacterial factor in the etiology of dental caries. *Brit. J. Exp. Pathol.* 5:141-7, 1924.