What the science tells us … Propensity Test Panel Sources

The most common Gram-negative bacterial genera in the oral cavity include: Treponema, *Bacteroides*, Porphyromonas, Prevotella, Capnocytophaga, Peptostreptococcus, Fusobacterium, Actinobacillus, and *Eikenella*. Early studies identified *Porphyromonas gingivalis*, *Actinobacillus actinomycetemcomitans* and *Tannerella forsythia* as causative agents in periodontal disease, and much of the research on periodontal disease continues to focus on these microorganisms. (SOURCE)

The red complex, which includes *Porphyromonas gingivalis*, *Treponema denticola*, and *Tannerella forsythia* (formerly *Bacteroides forsythus*), are recognized as the most important pathogens in adult periodontal disease. These bacteria are usually found together in periodontal pockets, suggesting that they may cause destruction of the periodontal tissue in a cooperative manner. (SOURCE)

Evidence indicates that chronic infections and inflammation are associated with increased risk of cancer development. There has also been considerable evidence that proves the interrelationship between bacterial and viral infections and carcinogenesis. Periodontitis is a chronic oral infection thought to be caused by gram-negative anaerobic bacteria in the dental biofilm. Periodontal bacteria and viruses may act synergistically to cause periodontitis. Many studies have shown that periodontal pockets may act as reservoirs for human papilloma virus, cytomegalovirus, Epstein Barr virus, and suspected agents associated with oral cancer. Periodontitis, characterized by epithelial proliferation and migration, results in a chronic release of inflammatory cytokines, chemokines, growth factors, prostaglandins, and enzymes, all of which are associated with cancer development. (SOURCE)

Nowadays cancer is the second main cause of death in the world. The most known bacterial carcinogen is *Helicobacter pylori*. Pathogens that can have an impact on cancer development in the gastrointestinal tract are also found in the oral cavity.

Some specific species have been identified that correlate strongly with oral cancer, such as *Streptococcus* sp., *Peptostreptococcus* sp., *Prevotella* sp., Fusobacterium sp., *Porphyromonas gingivalis*, and *Capnocytophaga gingivalis*.

Many works have also shown that the oral peripathogens *Fusobacterium nucleatum* and *Porphyromonas gingivalis* play an important role in the development of colorectal and pancreatic cancer. Three mechanisms of action have been suggested in regard to the role of oral microbiota in the pathogenesis of cancer. The first is bacterial stimulation of chronic inflammation.

Inflammatory mediators produced in this process cause or facilitate cell proliferation, mutagenesis, oncogene activation, and angiogenesis. The second mechanism attributed to bacteria that may influence the pathogenesis of cancers by affecting cell proliferation is the activation of NF-κB and inhibition of cellular apoptosis.

In the third mechanism, bacteria produce some substances that act in a carcinogenic manner. This review presents potentially oncogenic oral bacteria and possible mechanisms of their action on the carcinogenesis of human cells. (SOURCE)

Periodontal disease, a complex polymicrobial inflammatory disease, is a public health burden and is partially responsible for tooth loss. Existing epidemiological studies have linked periodontal disease to numerous systemic conditions, such as cardiovascular disease, preterm birth, osteoporosis, and diabetes mellitus, all of which may be attributed to systemic infection and inflammation. In recent years, there is increased interests in exploring the relationship between periodontal disease and cancer risk, particularly for cancers in the head and neck, upper gastrointestinal system, lung, and pancreas.

Periodontal disease may be a potential risk factor for the development of breast cancer among women, and thus effective periodontal therapy may present as a valuable preventive measure against breast cancer. (SOURCE)

Guven et al, evaluated the risk of cancer in patients with periodontal diseases and found that periodontal diseases were associated with increased risk of several cancers. In this study, they showed that the presence of any periodontal disease increased the risk of cancer by 17% in patients from a comprehensive dentistry hospital. The association was particularly significant for breast and head and neck cancer in women and prostate, head and neck, and hematological cancers in men.

These findings are in accordance with the findings obtained in their previous study and showed that in a population of patients with milder forms of periodontal disease, cancer risk is still increased, but the magnitude of the risk is lower than the risk for those with moderate to severe periodontitis. Besides other well-known benefits for health, the provision of oral/dental health should be considered and employed as a cancer prevention measure. (SOURCE)

According to Michaud et al, periodontitis may influence cancer risk through changes in immune response, or alternatively, through dissemination of harmful bacteria. Given that half of US adults have periodontal disease, the public health impact of periodontal disease on chronic diseases, including cancer, needs to be addressed. This study provides additional evidence that cancer risk, especially for lung and colorectal cancer, is elevated in individuals with periodontitis. Additional research is needed to understand cancer site–specific and racial differences in findings. (SOURCE)

Oral microbiota may play an important role in different gastrointestinal cancers. Validating the association of the oral microbiota with gastrointestinal cancers may lead to significant advances in understanding the etiology of gastrointestinal cancers. Some species of oral microbiota or the shift of the oral ecosystem may also serve as readily accessible, noninvasive biomarkers for the identification of high risk for gastrointestinal cancers. Therefore, a comprehensive understanding of the underlying mechanisms will be necessary for the prevention and/or treatment of gastrointestinal cancers. (SOURCE)

A study by Mascitti et al. investigated the relationship between oral microbiota and tumour development in distant organs and found that Overall, the results presented here showed a significant shift in oral microbiota composition between cancer patients and healthy controls. For example, *Firmicutes* and *Actinobacteria* were the most predominant phyla in cancer patients, while *Proteobacteria, Fusobacteria*, and *Bacteroides* were significantly more abundant in healthy controls. (SOURCE)

Emerging evidence has shown the potential of oral microbiota as a noninvasive diagnostic tool in gastrointestinal (GI) cancer. Pathogens involved in periodontal disease, such as *Porphyromonas gingivalis* and *Tannerella forsythia*, were linked to various kinds of GI cancer. Besides, more

oral bacteria significantly differed between cases with upper digestive cancer and healthy controls when compared to colorectal cancer (the most common form of lower digestive cancer), probably indicating a different mechanism due to anatomical and physiological differences in the digestive tract.

Oral microbiota changes were associated with risk of various kinds of GI cancer, which could be considered as a potential tool for early prediction and prevention of GI cancer, but validation based on a large population, reproducible protocols for oral microbiota research and oral-gut microbiota transmission patterns are required to be resolved in further studies. (SOURCE)

Lee et al, investigated the link between periodontal disease and prostate cancer. This study is the first to investigate the association of PC with PD using a retrospective analysis of a nationwide population-based NHIS-HEC. In contrast to some previous studies, the present cohort study has shown that patients with PD have a significantly but slightly positive in patients with PC. Further studies are required to strengthen this hypothesis and focus on identifying the mechanisms underlying the links between PD and PC. If confirmed, this observation could have clinical and public health implications given the increasing prevalence of PD worldwide. (SOURCE)

The relationship between dental diseases and the prevalence of digestive system cancers remains unclear. The present results showed that digestive system cancers were closely associated with multi-tooth loss and/or a low denture-wearing rate. The prevalence of severe periodontitis was also found to be higher in cancer patients. These results suggest that periodontitis and associated multi-tooth loss play a potential role in digestive system cancers. (SOURCE)

To date, *Helicobacter pylori* is the only bacterial species demonstrated to be a causative agent of cancer. It is involved in the etiology of gastric carcinomas and gastric lymphomas originating in mucosa-associated lymphoid tissue, and is the most important infectious cause of cancer in countries with a high human development index. Yet, it has become apparent that some bacteria commonly found among the human oral and gastrointestinal microbiota may have the tumor-promoting capacity. Thus, an association with cancer has been shown for other bacteria, such as *Chlamydia trachomatis* with cervical squamous cell carcinomas and ovarian cancer

and *Fusobacterium nucleatum, Bacteroides fragilis, Streptococcus gallolyticus, Enterococcus faecalis, and Streptococcus bovis* with Colorectal carcinoma (CRC).

In support of this, epidemiological studies have established a clear relationship between some bacterial species that normally inhabit the oral cavity, such as *Streptococcus sp., Prevotella melaninogenica, Porphyromonas gingivalis*, and *Capnocytophaga gingivalis* and oral squamous cell carcinoma (OSCC) as well as CRC and pancreatic cancers. (SOURCE)

Co-infection between Helicobacter pylori (Hp) and groups of periodontal pathogens may alter the onset of Alzheimer's disease (AD) and all-cause dementia. We examined the interactive associations among Hp sero-positivity, periodontal disease (Pd), and infections with incident AD and all-cause dementia, among older adults (≥65 years at baseline). Up to 1431 participants from phase 1 of the National Health and Nutrition Survey III (1988–1991) had complete data till January 1st, 2014 on Hp sero-positivity with a mean follow-up of 10–11 years for AD and all-cause dementia incidence. Exposures consisted of 19 periodontal pathogens, constructed factors and clusters, and two Pd markers- probing depth and clinical attachment loss (CAL). Cox proportional hazards models were performed. Around 55% of the selected sample was Hp. We found that Prevotella intermedia, Campylobacter Rectus, Factor 2 (Pi/Prevotella nigrescens/Prevotella melaninogenica), and the Orange-Red cluster interacted synergistically with Hp sero-positivity, particularly with respect to AD incidence.

The presence of higher levels of Actinomyces Naeslundii (An) enhanced the effect of being Hp+ on both AD and all-cause dementia incidence. In contrast, Fusobacterim nucleatum (Fn), and Factor 1 (which included Fn), exhibited an antagonistic interaction with Hp in relation to all-cause dementia. Both probing depth and CAL had direct associations with all-cause dementia among Hp+ individuals, despite nonsignificant interaction. Selected periodontal pathogen titers, factors, and clusters interacted mostly synergistically, with Hp sero-positivity, to alter the risk of AD and all-cause dementia. Ultimately, a randomized controlled trial is needed, examining effects of co-eradication of Hp and select periodontal pathogens on neurodegenerative disease. (SOURCE)