GENETIC TESTING

Understanding how genetic testing relates to dental disorders

BACKGROUND

Direct-to-consumer gene-testing kits allow in-depth genetic testing from samples of saliva. Consumers receive personalized reports on many aspects of their health and development. The genetic control of tooth development is also contained in the 23 chromosomes of the human genome. Eventually the public will come to expect their dental practitioners to be able to help interpret the results of genetic testing and apply them in oral health maintenance situations. In addition, the dentist may suspect a patient has a dental problem that is actually a manifestation of an underlying genetic syndrome and refer the patient for genetic testing. There are, however, some highly sensitive issues that must be addressed before offering such a referral (Box 1).

GENETIC DENTAL DISORDERS

Several dental conditions have a genetic component and can be detected through saliva DNA tests. Among these are oral human papillomavirus infection, periodontal susceptibility, and a 'sweet tooth' gene that may be related to diabetes, obesity, and caries. More than 1000 genes are already known to be associated with tooth development, and the 'human dentome' is not yet completed.

Dentists may be the first to diagnose genetic conditions from their dental presentation alone. These disorders include hypophosphatasia, X-linked hypophosphatemic rickets, and ectodermal dysplasia. Syndromes where the mildest form or carrier status in manifests through dental appearance will require further investigation.

In many cases, finding single-gene disorders that are purely dental will not alter the management of the patient. In cases where patients have genetic disorders that first manifest in the dentition but are actually related to systemic diseases, the dentist must understand how the implications of findings could significantly alter a patient's or even a family's medical and/or dental care. Often it's not the dental problems that are most affected by curative interventions, but the non-dental features.

WHOLE GENOME SEQUENCING

Sequencing a person's entire genome to help diagnose a disease is rapidly becoming the preferred approach over traditional targeted sequencing of candidate genes. Whole genome sequencing (WGS) decodes the entire string of nucleotides, including sequences that are genes and the intervening sequences, which used to be termed 'junk DNA.' Many genetics diagnostic services just look at the gene-coding sections, which is termed whole exome sequencing (WES).

WGS and WES produce more than just findings related to the condition being investigated, which are considered pertinent findings (PFs). They also uncover information other than that initially being searched for, or incidental findings (IFs). The question then arises regarding what should be done with the IFs. Who should decide whether to look at the other findings? Who actually owns the data? Can an individual who asks for a compact disk (CD) containing their own genome sequence do whatever he or she wishes with that information?

HANDLING GENETIC INFORMATION

Genetic Screening Approaches

Clear guidance is needed for both patients and clinicians regarding genomic screening results. The medical geneticists currently don't agree, with those in the United States and those in Europe taking very different positions. The American College of Medical Genetics and Genomics recommends actively seeking certain IFs and have made the screening of a panel of 57 selected genes mandatory regardless of the disease being investigated. Among these genes are several cancer-causing gene variants, hypercholesterolemia, and cardiac arrhythmia conditions. Mutations found in this screening must be reported to the clinician. In contrast, the European Society of Human Genetics recommends actively not searching genomic regions other than those likely to be relevant to the disorder being investigated. Furthermore, the UK Association of Genetics Nurses and Counsellors recommends that children should not be opportunistically tested for conditions with an adult onset and believes patients should be allowed to opt out of receiving IFs.

Generally, WGS facilities are prioritized to search for more serious and life-threatening diseases than dental anomalies. Centers that offer dental genetic testing must consider aspects of probity and information sharing, especially in regard to PFs and IFs.

Pertinent dental genetic results should be made available to the patient's dentist and kept as part of the patient's clinical record. In this case, these results would also be available to the rest of the dental care team. Personal genetic information protection

Box 1. Questions a Dentist Should Consider Before Offering Referral for Dental Genetic Testing

- Is a genetic test available for this dental disorder?
- How accurate is testing and where is it offered?
- How would a diagnosis affect dental or medical treatment?
- Could a diagnosis affect dental or medical insurance?
- Who would inform other at-risk relatives?
- How will the patient and family react to knowing they carry a genetic condition?
- Do you have a duty to inform other at-risk relatives?
- Could the diagnosis affect family planning?
- How can you protect patient privacy and confidentiality?

(Courtesy of Harrison M, Bushell C-J, Irving M: 32 and you—genetic testing for dental disorders. *Br Dent J* 224:829-832, 2018.)

is an extremely sensitive area, and all practitioners should recognize the need for confidentiality. Still lacking is a determination of how much of the information obtained in a dental diagnostic investigation should be given to the family dentist and how the information must be kept.

Disclosure to Other Parties

The disclosure of genomic disease information to insurance companies has been a topic engendering considerable fear and distrust regarding the possibility of its use to discriminate against the patient. The ownership of personal genomic data remains problematic. It's likely that such issues will be detailed in medical and dental insurance policies at some point.

Commercial companies currently can reserve the right to use personal genomic data to sell personally relevant products and services. The wholesale sharing of anonymized data could potentially be extremely lucrative. Therefore caution must be exercised regarding how much will be disclosed. In addition, assurances should be in place to dictate how the patient's privacy will be protected.

Implications for Dental Training

Dental genomic education is designed to equip dental team members to be able to provide accurate diagnosis of a dental condition, to identify what is abnormal, and to take good family histories and perform pedigree analyses. Patients can then be selected for genetic investigation. Dental professionals will require training to be able to explain the implications of the tests, but could potentially offer a more relevant dental explanation than a medically trained genetic counsellor could.

For the dental team members to be able to provide a clinically relevant interpretation of genetic dental diagnoses, they will require training in human genetics and genomics. These courses have been proposed for inclusion in the dental curriculum. However, to date, the offer of genetic education has been limited to just a few institutions.

Clinical Significance

It's easy to become enthusiastic about the possibilities related to having genetic testing done for dental developmental disorders. This enthusiasm must be tempered by a clear understanding of the profound implications related to what is actually uncovered in genetic testing. Both dentists and the dental research community must work with and learn from medical genetics services, especially in the areas of genetic counselling, disclosure of findings, and confidentiality of the results. Further research is needed in the areas of how dental genetic information is generated, interpreted, and communicated.

Harrison M, Bushell C-J, Irving M: 32 and you—genetic testing for dental disorders. *Br Dent J* 224:829-832, 2018

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ORAL MICROBIOME

Manipulating the oral microbiome

BACKGROUND

The oral microbiome consists of microorganisms that interact dynamically with the host in an intimate relationship. In health, the oral microbiome is made of dental biofilms that positively affect one's health, with many of the bacteria delivering important benefits. The interdependency that exists contributes to maintaining stability and resistance to change. Should the conditions of the environment change, the intimate relationship can be disrupted and lead to deleterious consequences for the host and result in disease (dysbiosis). A review of the changes that can disrupt the healthy symbiotic relationship and possible ways to manipulate the conditions in the oral biofilm was offered.