Caused by a rare genetic mutation found almost exclusively in those of Ashkenazi Jewish descent, Familial Dysautonomia (FD), also known as Riley-Day syndrome, is a disease that affects the autonomic and sensory portions of the Central Nervous System. With approximately 600 cases diagnosed worldwide, FD is caused by a mutation of the IKBKAP gene on chromosome 9, a mutation occurring once in 3,700 births. A newborn diagnosed with FD has only a 50% chance of living until the age of 30[3].

Common symptoms of the disease include respiratory and cardiovascular dysfunction, diminished sensitivity to pain, lack of motorcoordination, incoordination of the gastrointestinal tract, absence of emotional tears, and spinal curvature. Patients experience what is known as a dysautonomic crisis brought about by physical or emotional stress. During a crisis, patients show symptoms such as elevated blood pressure, skin blotching, and violent vomiting [5,6].

Although the oral and dental manifestations of FD are less prominent than the systemic characteristics of the disease and, unlike the systemic symptoms, are not life-threatening, the oral and dental symptoms are, nonetheless, an important aspect of the disease. Some distinctive orofacial characteristics, such as small jaws and dental crowding, are unique to those with FD [1,3]. In addition, patients with FD lack fungiform papillae (structures that house taste buds) on the tongue, often a diagnostic symptom of FD [5]. As a result of their poor appetites, as well as difficulties with sucking and swallowing, FD patients often suffer from inadequate nutrition. To increase their intake of nutrients, many patients undergo gastrostomy (a surgical insertion of a feeding tube), so that the nutrients enter directly into the stomach without passing through the mouth. FD patients also experience chronic gingivitis, at least partly attributable to plaque accumulation and to poor oral hygiene. Finally, due to the patients’ low sensitivity to pain, many injuries, such as fractures and burns, go unnoticed, patients also undergoing dental trauma and orodental self-mutilation. [1].This, dental problems among FD sufferers result directly from intrinsic complications within an FD patient’s system, and indirectly from non-dental effects of the disease such as the limited ability of FD individuals to feel pain.

FD is a genetic, congenital disorder, and, like many genetic disorders, it stems from a splicing error caused, in this case, by a nucleotide mutation on the IKBKAP gene. The splicing error removes a portion of the transcript which is normally translated into a protein, while introducing an early stop codon into the transcript, thereby terminating translation prematurely. The human elongator complex, of which the IKAP protein is a part, is thereby compromised, bringing about many of the observed neurological dysfunctions in FD patients. The neurological problems of FD are caused by a failure of sensory and autonomic neurons to develop and survive, likely explaining their diminished sensitivity to pain as well as their unsteady gait [5].

Many FD sufferers have serious dental problems, but it is not clear to what extent these dental problems result from genetic disorders associated with FD or from non-genetic factors associated with the disease.

Genetic disorders may also affect tooth development, which occurs from the 6th to 8th week in utero until an individual is a year old. An embryo is made up of three primary germ-cell layers, the mesoderm, endoderm, and ectoderm. The ectoderm cells go on to differentiate into cells of the nervous system, the epidermis, and tooth enamel. Dysfunction of the neural crest, which is part of the ectoderm, is thought to lead to the dysautonomic problems in FD patients. Because the neural crest also plays a role in tooth formation, FD tends to be associated with dental abnormalities [3].

In fact, many FD sufferers have serious dental problems, but it is not clear to what extent these dental problems result from genetic disorders associated with FD or from non-genetic factors associated with the disease. As noted above, dental problems can occur because of the patient’s impaired sensitivity to pain, often resulting in oro-dental self-mutilation. Self-mutilation in-
volves behavior that results in self-inflicted tissue damage. Such behavior, for example tongue biting and self-extraction of teeth, frequently occurs in the oral cavity. But in a 2004 study, Gadoth and Mass observed that self-mutilation is not just the result of insensitivity to pain, it may also be due to feelings of depression or self-destructive urges [2].

A 2010 study by Zilberman et al. examined the primary molars of FD patients to gain insight into the trauma experienced in their first year of life. The study utilized the fact that subjecting teeth to great enough stress, actually leaves an imprint on the tooth enamel. Indications of trauma were found in the enamel of 100% of the molars of the FD children and in only one of the healthy children. This finding supports the hypothesis that infants with FD experience frequent episodes of traumatic stress in the first year of life and that much of their dental problems are non-genetic [6].

To obtain information about the actual treatment of the dental pathologies of an FD patient, Dr. Edward A. Stein, an endodontist in the Atlanta Georgia area, was interviewed. Dr. Stein has treated a 15-year-old patient with FD, who presented a unique situation in which the dentin of the upper central tooth had begun to wear away. This process is known as internal resorption. This case of resorption was diagnosed by a pedodontist during a general exam, the patient being unaware of the condition, because of impaired sensitivity to pain. If left untreated, the tooth would have broken down from the inside out. Even if treated, resorption may only be slowed down, not permanently stopped. The treatment of choice for the patient was endodontic and restorative therapy, involving a root canal and inserting filling material where the tooth had broken down from the inside. While local anesthesia is not absolutely indicated in dental procedures with patients with FD due to their inability to feel discomfort, local anesthesia was performed as a precaution. One year later, the patient still has the tooth.

There is no cure for FD. While genetic testing is now available to prevent future cases of FD, the question remains as to how those suffering with FD should be treated. Researchers in the Laboratory for FD Research at Fordham University, led by Dr. B. Rubin and Dr. S. Anderson, discovered that while the patients are producing the mutated form of the transcript, they are also producing, to a small extent, the full-length transcript, leading to the production of the full-length, functional IKAP protein. Research has led to the use of nutritional supplements that promote the production of the full-length protein. In 2003, Dr. Anderson and co-workers discovered that tocotrienol, a form of vitamin E, can help increase the production of the correctly spliced transcript. In addition, a component of green tea, known as epigallocatechin gallate (EGCG), was found to alter the splicing process, thereby producing the correctly spliced transcript and increasing the full length IKAP protein in FD individuals [5].

Aside from taking tocotrienol and green tea, which has improved the lives of many FD individuals, increased attention to dental health can also enhance the quality of life of FD sufferers, especially because their overwhelming medical needs often result in the neglect of their dental health. Not only does poor dental health cause great discomfort, which can have immediate adverse consequences on overall health, neglecting dental health can also damage a person’s self-image, which is already poor among many FD sufferers. As mentioned earlier, FD patients often suffer from oro-dental self-mutilation, likely resulting from depression and low self-esteem, and not only from impaired pain perception.

When treating any patient, one must try to understand him or her as a whole person made up of interrelated sides and challenges that cannot be treated in isolation. The dental aspects of FD are important not only because they add to the physical distress of the patient, but because dental treatment may address not just a single symptom but may provide a vehicle for improving the patient’s overall well being and health.

ACKNOWLEDGMENTS
My parents’ support for my education is just one of the ways in which they show their love for me. Special thanks to my father for reading and commenting on all the earlier drafts of this article.

Thank you, Dr. Babich, for directing me in my research, and for referring me to Dr. Berish Rubin, Director of the Laboratory for FD Research at Fordham University. I thank Dr. Rubin for speaking to me about his important research on FD.

I am very grateful to Dr. Edward Stein and his staff for providing me with valuable information concerning the treatment of patients with FD.

A warm thank you is reserved to my orthodontist, Dr. Daniel Farber, for reading and commenting on this article, doing so in the clear and kind manner he used when explaining to me how braces work.

This article is dedicated to my dear friend Melanie Cohen, whose sweet smile is just one of many endearing qualities, and to her parents, Dana and Gary Cohen, good friends to me and my family.
REFERENCES


