CORR Insights

CORR Insights®: Osteochondritis Dissecans Lesions in Family Members: Does a Positive Family History Impact Phenotypic Potency?**Kent A. Reinker MD****Where Are We Now?**

The etiology and pathophysiology of osteochondritis dissecans (OCD) remains unknown. While we suspect that trauma may have a role in the development of OCD, we also know that many patients with OCD do not have a definable traumatic event, and many of those who do report trauma have a

contralateral lesion that cannot be linked to trauma and is frequently asymptomatic [2, 3]. Overuse is also suspected to play a role, but studies examining this role are lacking [1].

The authors note that other studies, particularly those involving twins, support a genetic etiology of OCD. In addition, they note that several syndromes, including some with known genetic linkage, have a higher incidence of OCD as part of their pattern. The authors have provided strong evidence that OCD is a familial disease. Since most familial diseases prove to have a genetic component to their etiology, showing that OCD is familial adds to the evidence that genetics plays a role in the etiology. The authors were unable, however, to show that patients who had a family history

had a more severe disease. Such a result would have suggested that the familial incidence was due to genetic causation, as opposed to shared environmental influences. Since their results were negative, we are unable to tell from their data whether the familial incidence they detected is due to environmental influences or is the result of shared genes.

Where Do We Need to Go?

We cannot effectively prevent or treat diseases without understanding their pathophysiology. This study indicates that OCD is likely to be familial. The next obvious question is whether the familial incidence is due to genetics or a shared environment. In answering this question, the role of genetics should certainly be investigated further. However, genetics is not likely to be the only causative factor of OCD. The role of overuse, the effects of training patterns, the influence of athletic equipment and shoes, and a search for specific trauma patterns leading to OCD all warrant further study.

This CORR Insights® is a commentary on the article “Osteochondritis Dissecans Lesions in Family Members: Does a Positive Family History Impact Phenotypic Potency” by Gornitzky and colleagues available at: DOI: 10.1007/s11999-016-5059-x.

The author certifies that he, or a member of his immediate family, has no funding or commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

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This CORR Insights® comment refers to the article available at DOI: [10.1007/s11999-016-5059-x](https://doi.org/10.1007/s11999-016-5059-x).

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How Do We Get There?

In their discussion, the authors outlined two powerful mechanisms for clarifying the genetic role in this disease, namely a genome-wide association study using single nucleotide polymorphisms (which they have already undertaken) and the possibility of whole exome studies in families with a large number of members having OCD. Both of these methods are appropriate, and they tend to complement each other leading to different forms of information. Studies of large families tend to focus on single-gene mutations that are important in that specific family, but may not be widely shared in the general population, while genome-wide association studies often reveal multiple genes that may be associated with the disease, but these genes may not be important in

the individual patient seen by the practitioner.

Bench-to-laboratory studies can also yield important information. Knockout mice, in which a strain of mice is created that manifests a high incidence of the disease being investigated, are prime investigative tools in genetic disease. Since there are known syndromes involving OCD, a knockout mouse model is feasible. In addition, the pathophysiology of OCD should be prospectively evaluated in patients with known syndromes involving OCD. Early identification of OCD lesions in these patients, even before they are symptomatic, might yield important insights into the natural history of the disease. Studies aimed at identifying factors that lead up to the onset of OCD are, therefore, appropriate and potentially offer

benefits for the greater community of patients with OCD. The identification of a gene that plays a role in a disease is a key requirement for understanding its pathophysiology, but it is the beginning of the process, not the end. The researcher must then understand how the gene leads to the disease.

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