Mitochondrial disease and the family physician

Dr Gordon Hutchinson

In the average family practice many patients have disease that is either genetic or has a large genetic component. Given the rapid advances in the field of genetics, family physicians may feel uncomfortable with their knowledge and with their ability to screen for genetic disease. A public database initiated by Dr Victor McKusick in the 1960s now has 2835 entries where the phenotypic description of a disorder as well as its molecular basis are known, including 2576 autosomal, 227 X-linked, 4 Y-linked, and 28 mitochondrial disorders.[1] It would not, therefore, be surprising for family physicians to feel overwhelmed by this daunting amount of information, and to simply refer any case that looked even remotely "genetic." Yet, we are all familiar with the more common genetic diseases, such as Down syndrome and cystic fibrosis. We counsel women on the interpretation of prenatal screening tests for trisomies 21, 18, and 13 as well as for neural tube defects. Although many genetic diseases are exceedingly rare, there are so many genetic diseases that any large enough practice will have several patients so afflicted. Understanding the mechanisms and modes of inheritance of genetic disease can help family physicians recognize patterns in presentation and know when there might be a benefit to referral. Knowing more about genetic disease can also help family physicians deal with the day-to-day challenges faced by affected patients.

Mitochondrial disease did not become an important topic of study until well after I attended medical school in the late seventies. That mitochondria possess their own genome apart from nuclear DNA, that they are maternally inherited, and that they appear to have a prehistoric bacterial ancestry were all facts that eluded me or were unknown in my student days. The use of mitochondrial evolution to trace human history through its matriarchal lineage, providing a genetic "fossil record" of human migration, was far in the future. Still, medicine requires us to learn constantly if we are not to become fossils ourselves, and many of us can benefit from learning more about mitochondrial disease.

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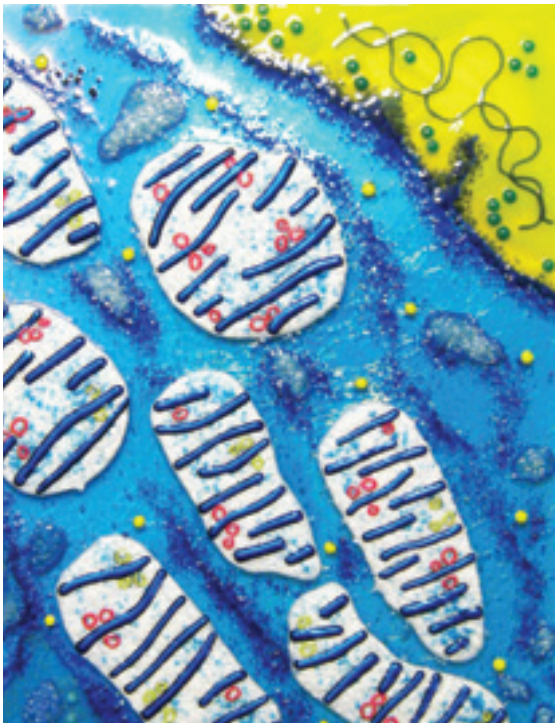

Glass art representation of mitochondria. Reproduced with permission from the artist, Teddy Devereux (www.vitreous-humor.com).

Referral and biopsy information

How to refer patients

For patients under age 18, send a referral letter along with recent lab reports, imaging, and specialty reports to the Division of Biochemical Diseases, BC Children's Hospital, Room K3-205, 4480 Oak Street, Vancouver, BC, V6H 3V4. Fax: 604 875-2349. Phone: 604 875-2880.

For patients age 18 and over, send a referral letter along with recent lab reports, imaging, and specialty reports to the Adult Metabolic Diseases Clinic, Vancouver General Hospital, Diamond Health Care Centre, 4th floor, 2775 Laurel Street, Vancouver, BC, V5Z 1M9. Fax: 604 875-5967. Phone: 604 875-5965.

Muscle biopsy

Muscle biopsy is best done at Vancouver General Hospital or BC Children's Hospital as timing of biopsies must be coordinated with the laboratory and handling of samples must be done in a specific fashion. Discuss the biopsy of skeletal muscle in advance with either the Biochemical Genetics Lab at BC Children's Hospital (604 875-2307) for patients under age 18, or the Adult Metabolic Diseases Clinic (604 875-5965) for patients age 18 and over.

In this theme issue, authors from the Adult Metabolic Diseases Clinic at Vancouver General Hospital and the Biochemical Diseases Clinic at BC Children's Hospital introduce us to the manifestations as well as the diagnostic and therapeutic approaches to mitochondrial disease.

In the first article, Dr Sirrs and colleagues provide background on the biochemistry, genetics, and epidemiology of mitochondrial disease. The second article, by Dr Mattman and colleagues, considers aspects of diagnosis and management. In the third article, Dr Mattman and another group of colleagues describe some of the clinical manifestations of mitochondrial dysfunction. Finally, in the fourth article, Drs Hameed and Hsiung discuss the role of mitochondrial dysfunction in aging and neurodegenerative disease, and look at some interventions that show promise.

As all the articles in this theme issue point out, the incidence of primary mitochondrial disease is relatively common, affecting up to 1 in 5000 people. Mitochondrial dysfunction secondary to other disease and as a side effect of drugs is even more common, and plays a role in Alzheimer disease and Parkinson disease, as well as the toxicity of some HIV antiviral medications and even the ototoxicity effects of aminoglycosides. It is possible, indeed probable, that you have or will have a patient with a mitochondrial disease in your practice. As well as remembering that presentations of mitochondrial disease are myriad and involve multiple organ systems and modes of inheritance, family physicians must remember that individuals within the same family can manifest mitochondrial disease quite differently. The presenting signs may include diabetes, hearing loss, dementia, and arrhythmia—medical concerns in a family history that would inspire few to think immediately about the possibility of mitochondrial disease.

As our recognition and knowledge of mitochondrial disease increase, we can provide better care to our patients. We can also expect new approaches to diagnosis and management to be built upon the knowledge base considered in this issue.

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Reference

1. Johns Hopkins University. Online Mendelian Inheritance of Man (OMIM) database. Accessed 6 September 2010. www.ncbi.nlm.nih.gov/Omim/mimstats.html.