GeNeDit

Privilege to be a Clinician for Six Thousand Genetic Disorders!

Editorial

Yes, you got it right; I am talking about a clinical geneticist who cares for rare disorders. We are just on the verge of a new paradigm in the treatment of genetic disorders. Success of gene therapy trials is what the first-generation clinical geneticists were dreaming of. The GenExpress in this issue lists some success stories of gene therapy. We expect similar results for more monogenic disorders. Other than direct modification of the defective gene, strategies based on the understanding of molecular pathology, modification of gene transcription and translation, and use of recombinant products are on the way. The treatments of genetic disorders may now be prenatal infusions of deficient protein as in X-linked anhidrotic ectodermal dysplasia or gene therapy after newborn screening/presymptomatic testing. Prenatal gene therapy may make survival of fetuses with alpha thalassemia possible. Gene therapy trials for Sanfilippo disease are a prototype for storage disorders with central nervous system involvement. With many options of treatment strategies, accurate diagnosis of genetic disorders, currently estimated to be more than 6000, is vital. As shown for neuronal ceroid lipofuscinosis, the drug may be specific for each patient. For some disorders like spinal muscular atrophy, currently three separate therapies have been approved. The supervision of these patients with novel treatments needs clinical experience and documentation of how the clinical course gets modified by the treatment, is of paramount importance. The development of these novel genetic treatments stresses the need for more clinicians with expertise in rare genetic disorders, in our vast and populous country.

Thanks to the Doctorate of Medicine (DM) program in medical genetics started in India three decades ago we have competent medical geneticists providing care to patients with genetic disorders and their families. Envisioned by late Dr S S Agarwal, the objective of the course was to train clinicians in the specialized area of medical genetics. Hence, the training was offered to postgraduate degree holders in pediatrics, obstetrics and gynecology or internal medicine. Over the years, 43 clinicians have completed DM training in medical genetics from the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow. They have contributed to ushering in the new era of molecular medicine in India. Similar DM and Diplomate of National Board (DNB) courses have now started in six more medical institutes in India. World over, clinical experience in one of the above three areas is considered essential to pursue a career in medical genetics for patient care.

The Society for Indian Academy of Medical Genetics (SIAMG) reiterates the need to continue the same eligibility for DM / DNB (medical genetics) programs to maintain the international standards achieved by the degree holders in India. Correct and timely diagnosis, using novel molecular technology, counseling for prenatal diagnosis, prenatal treatment, newborn screening and counseling for complex issues need a highly specialized set of knowledge and clinical skills for taking on the challenge of twenty-first century medical genetics. Availability of next generation sequencing has made diagnosis possible for many disorders. At the same time, there is a fear of incorrect diagnostic labels if the clinical geneticist is not involved in clinical evaluation. The clinical geneticist also has to collaborate with the laboratory with the language of Human Phenotype Ontology (HPO) terms after deep phenotyping. Knowledge and use of databases [that are exponentially growing], understanding of developmental and metabolic pathways and their correlation with clinical findings to navigate the jungle of overlapping phenotypes and genetically heterogeneous disorders are the various functions a medical geneticist needs to perform simultaneously and expertly, to help the patients. It may superficially appear that NGS has made diagnosis easy. But ask the medical geneticist who has got a novel sequence variation in a known gene for a disorder the phenotype of

which is not similar to that of the patient or who has to deal with the array of variants of unknown significance. Expanding phenotypes, blended phenotypes, modifier genetic variations, novel phenotypes for known genes, novel phenotypes without identified causative gene variants are regular scenarios in genetic clinics. This needs an astute clinician with vast clinical experience and knowledge of genomic medicine.

Though this discussion is about clinicians taking care of genetic disorders, mention is needed for the contributions of scientists deciphering genes, proteins and pathways, developing animal models, and combing the treasure of molecules with bioinformatics tools to look for suitable targets for development of therapies. These highly scientific activities need another kind of bright minds with scientific and medical background for molecular diagnostics in the laboratory. All pathology departments need up-gradation and there is a need of short-term courses to empower the pathologists and microbiologists with genomic techniques and functional assays. The expertise in laboratory genetics in medical colleges needs to grow parallel to that of clinical geneticists. Hence, there is an urgent need of DM / Fellowship / short term programs in molecular genetics / genetic diagnostics to fill in the vacuum of trained laboratory geneticists. More training programs and research projects in the area of genetic disorders by pre- and para-clinical departments will be beneficial to the patients. Laboratory diagnostics, basic research and clinical care of patients with genetic disorders are different specialized areas requiring different expertise but close interaction. They need to grow together.

The McKusick course on human genetics and genomics is an example of congregation of seekers of the latest knowledge of different aspects of genetics. The team of medical geneticists of Sir Gangaram Hospital, New Delhi has shared their excitement of attending the 61st course this year. Attending this course at least once in their lifetime was the dream of geneticists. Now with the course becoming virtual, we can attend this academic feast once in a few years. Listening to the stalwarts talk about their work and experiences takes learning to a different level.

With a better future for patients with 6000 plus genetic disorders on the horizon, many young internists, pediatricians and obstetricians need to take up a career in medical genetics. When genetic disorders were considered untreatable, incorrect diagnosis might have done less harm. But now if the diagnosis of a treatable disorder is missed, it will be unfortunate for the patient, family and may be for the clinician as well!

Dr. Shubha Phadke
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