

Short Communication

Opportunities and Challenges in Molecular Genetic Testing in China: The Experience of an Academic Center for Clinical Molecular Medicine

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Molecular genetic testing and molecular pathology are relatively new but rapidly growing fields in China. This article reports on the experience of providing molecular genetic testing at the Center for Clinical Molecular Medicine (CCMM) of Chongqing Medical University in China. This center is the first of such centers in the southwestern region of China and implements a spectrum of genetic tests on constitutional cytogenetics, oncology cytogenetics, molecular cytogenetics, molecular genetics, molecular oncology, metabolic genetics, and newborn screening. The annual test volume had a 78-fold increase in the past five years and reached approximately 380,000 tests in 2012. This tremendous growth reflects both great opportunities and challenges for China's healthcare system. Some of the challenges such as the lack of a medical genetics professionals and qualified training programs for clinical geneticists, laboratory specialists and genetic counselors are discussed.

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INTRODUCTION

The Center for Clinical Molecular Medicine (CCMM) of the Children's Hospital of Chongqing Medical University is located in Chongqing, a city of 33 million in southwestern China. Chongqing Children's Hospital is a leading pediatric medical center in China. CCMM was established in 2008 and is the first of a few such centers in southwestern China that is specialized in molecular genetics and molecular pathology testing. Increased demand of genetic services and rapid growth of molecular genetic testing have been noted in the past five years. The opportunities for a better transition toward molecular and personalized medicine and the challenges adding onto the medical genetics training and practice system are discussed.

RAPID GROWTH OF MOLECULAR GENETIC TESTING IN CCMM

In the past five years, the center has grown from five staff members and fewer than 10 tests to 25 laboratory personnel (four with doctoral degrees, nine masters, and eight undergraduates) and offers over 60 different tests. The technical capacities include constitutional cytogenetics, oncology cytogenetics, molecular cytogenetics (fluorescence *in situ* hybridization, FISH), molecular genetics, molecular

oncology, and cytogenomic array. In 2012, the center started to offer newborn screen tests and established liquid chromatography tandem mass spectrometry (LC-MS/MS) for metabolic disorders. Now the center offers genetic testing for conditions related to hereditary disorders, infectious diseases, hematological and solid tumors, and newborn screening. It is accredited by the National Center for Clinical Laboratory (NCCL) of the Chinese Ministry of Health, and designated by the Chongqing Municipal Government as the Chongqing Diagnostics Center for Clinical Molecular Medicine. It is also one of two newborn screen centers in Chongqing. CCMM serves patients referred from clinics including neonatology, infectious diseases, hematology, oncology, gastroenterology, neurology, child development, urology, nephrology, and cardiology. The annual test numbers grew from 5,000 in 2008 to 380,000 in 2012. The annual test revenue increased 100-fold in the same period to approximately 20 million Chinese Yuan (equivalent to US \$3.2 million) in 2012. Although the growth has been in all test categories, the most were in molecular genetics, molecular pathology, metabolic genetic testing and newborn testing.

CCMM is active in translational research and has participated in several national and regional research projects. CCMM also functions as a training site for the undergraduate and graduate laboratory medicine programs and has trained 15 graduate students. Additionally CCMM has provided training for genetic testing professionals from other parts of China.

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The success of CCMM is attributed in part to continued improvement in health care in China which results in increased demand for high quality care including molecular and genomic medicine. Our rapid growth in molecular genetic testing reflects tremendous opportunities for molecular genetics and molecular pathology testing in China. It is expected that the needs for such service will continue to grow as the middle class in China expands and the demand for better medical care including personalized medicine rises. The center has also been benefitted from the strong institutional supports from the Chongqing Children's Hospital, Chongqing Medical University and the local government.

CHALLENGES AND OPPORTUNITIES

Molecular genetic testing and molecular pathology are still at an early development stage in China. Here we discuss some of the challenges we experienced and the approaches we adopted in the last five years. First, although China is one of the first countries to introduce genetics testing in clinical services, modern molecular genetics and molecular pathology remain new to the medical community.¹ China has yet to develop national standards and guidelines for clinical genetics laboratories like the ones set by the American College of Medical Genetics and Genomics (ACMG). Absence of such standards and guidelines has posed difficulties in achieving uniform standard practices among genetic testing centers across the country. Variations in practices are common between laboratories. From its inception, our center in Chongqing not only followed the relevant Chinese guidelines and regulations for clinical laboratories, we also adopted many practices outlined in the ACMG guidelines for genetic testing.²⁻³ Although some of the practices require more resources including additional personnel training and quality control and quality assurance measures, the payoff is high quality testing results. Our quality control parameters exceed many of those from our domestic and overseas counterparts.

Second, there are no formal education programs in China to train clinical genetics professionals including clinical geneticists, clinical laboratory geneticists, and molecular pathologists. Many current topics on clinical molecular genetics are not well covered in the medical school curriculum. There are few training opportunities in clinical molecular genetics and molecular pathology for medical residents and fellows. Medical genetics has not been recognized as a clinical specialty in the country. An unclear career path in medical genetics may also contribute to considerable shortage of qualified clinical genetics professionals. It is not uncommon that a genetic testing laboratory is directed by a physician or medical technologist with limited formal training in clinical molecular genetics and molecular pathology. CCMM in Chongqing has been under direction of medical geneticists with extensive working experience in international clinical genetics laboratories. Its founding members were trained in an international clinical molecular genetics laboratory following international standards for clinical genetic testing. The center has its own training programs. Completion of relevant training is

required for each technical person at the center prior performing clinical testing.

Third, pricing for genetic tests in China is strictly regulated by governments. Some test prices are not adequately adjusted to reflect cost increases and technology advances. As a result, many test prices are set at levels lower than the cost for doing testing. Although such regulation on pricing is intended to constrain health care expenses and to make the services accessible to the general population, it may provide few incentives for laboratories to either offer tests that cost more than they are charged or improve quality that require additional resources. Many medical insurance policies still do not cover some genetic tests that are deemed medically necessary. Some of genetic tests are provided in research settings supplemented with research funds. In the past five years, we have been consistently working with relevant government agencies as we developed new tests and technologies. We have been able to receive supports from local governments for introducing new tests and price adjustment. We are encouraged by new government policies that we think would promote molecular genetic testing. We think that communication between the government and medical professionals should be an ongoing process to ensure government's support to the field.

Forth, inter-laboratory proficiency testing (PT) survey for genetic tests at the national level is limited, particular those for hereditary diseases and molecular oncology. Insufficient inter-laboratory PT survey programs present challenges in standardizing practices among laboratories. We consider inter-laboratory PT as a critical part of our overall quality assurance program. In addition to participating in the inter-laboratory PT offered by the Chinese NCCL, the center is enrolled in several international inter laboratory PT survey programs for the tests with no PT available from Chinese NCCL. These include PT programs provided by the College of American Pathologists (CAP)⁴ and the US Center for Disease Control and Prevention (CDC). The center routinely exchanges samples with other Chinese laboratories which perform the same tests. The center has excelled in all international PT surveys it is enrolled.

Fifth, genetic counseling is not commonly available to patients receiving genetics testing in China. This is likely attributed to the fact that many physicians at major medical centers in which genetic testing is offered lack either time or appropriate knowledge to provide the service. This is often left to laboratory technical personnel who are usually not prepared for the task. Genetic test reports from many clinical laboratories in China only list analytic data with no or limited clinical correlation and interpretation, a practice that is meant to minimize liability in the environment in which relationship between the general public and medical communities is tense and trust is low in many places. Our center has designated senior staff members who have been trained in assisting patients and clinicians to understand test results. The center maintains ongoing communications with physicians on the tests it provides and to help providers understand test utilization. We also incorporate relevant clinical significance

and recommendations in our reports to the extent possible considering the health care environment unique to China.

Last but not least, although significant strides have been made in the past decade in protecting patient privacy, much remains to be done to improve relevant legal and ethical regulations to better safeguard population from discrimination based on personal genetic information.

CONCLUSION

Our experience in providing molecular genetic and molecular pathology testing is a testament to the tremendous opportunities for medical genetics in general and molecular genetic testing and molecular pathology in particular in China. Although the challenges remain, we are optimistic that as the middle class in China continues to expand, the demand for high quality of medical care including personalized medicine will grow. Several national initiatives on molecular medicine and personalized medicine are in progress that we hope will move the field forward. As more China-developed technologies and reagents become available, costs of molecular genetic testing and molecular pathology are expected to go down significantly and the services will be more accessible to the general population. Professional

societies like Association of Chinese Geneticists in America (ACGA) are going to continue to play invaluable role in facilitating the progresses.

CONFLICT OF INTEREST

None.

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