Medical genetics in China

LUO HUI-YUAN (WILSON HWEI-YUEN LO)
From the Department of Medical Genetics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, China.

Medical genetics blossomed in Western Europe and North America in the years after the second world war. The momentum of this development has remained strong and is felt in every branch of medicine.

In China, Russian influence held sway in the early days after the liberation. In genetics, the so-called Michurin-Lysenko school dominated the field and classical Mendelian genetics was criticised as capitalist and idealistic. The break with the Russians in the mid 1950s brought new vitality to the Mendel-Morgan school. Medical genetics from the western world thus gained a foothold in China. In 1962, the first cytogenetics group in China was started by Wu Min in the pathology department of the former Institute of Experimental Medicine in Beijing. In 1963, the first medical genetics division, headed by the author, was set up in the Department of Medicine of the Peking Union Medical College (PUMC) Hospital by Professor Zhang Shiao-quian, then head of the department. Work in this field also began in Shanghai in the Department of Biology of the Fudan University and the Department of Pediatrics of the Sixth People’s Hospital in Shanghai. Unfortunately, the political turmoil in the mid 1960s interrupted scientific activities throughout the country. It was not until the end of this disaster that medical genetics regained its ground. It has since developed rapidly, especially after the founding of the Chinese Genetics Society and its Human and Medical Genetics Section in 1978 and 1979 respectively. In what follows, a concise description will be given of the historical development and the present state of affairs of several of the subspecialties of medical genetics in this country.

Cytogenetics

The first cytogenetic report from this country was that of Wu Min, published in 1961. It dealt with the cloning of normal and malignant human cells and studies on their chromosome complement. The normal karyotype of Chinese was described in articles published in 1962 and 1966. After this, investigations on chromosomal aberration syndromes, chromosomal anomalies in cancer and leukaemia, and cytogenetic effects of radiation followed, only to be interrupted by the political chaos that started in 1966. Work was resumed with vigour when order was re-established. Because of the relative simplicity of the procedures for karyotype analysis, cytogenetics groups mushroomed in many parts of the country in a relatively short period of time.

Surveys among newborns for incidence of chromosomal aberrations have been carried out. In a typical series of 3415 newborns, the incidence was found to be 0·73%, which is similar to that reported elsewhere. Screening was also carried out among the mentally retarded in different populations for the fragile X syndrome. This revealed, after correcting for those refusing to be examined, a population incidence of 5·8/10 000 males, which is somewhat lower than that reported from other parts of the world. Among 1260 patients diagnosed as having genetic diseases seen in a six year period at the Pediatric Genetics Clinic at PUMC Hospital, 8·5% were found to have chromosomal abnormalities.

At the top of the list are Down’s syndrome, Turner’s syndrome, and Klinefelter’s syndrome. This is in accord with findings in other clinics.

In the wake of developments in the west, various banding techniques, prenatal diagnosis of chromosomal disorders, sister chromatid exchange, cytogenetic effects of chemicals and radiations, fragile sites, and high resolution banding became topics of interest. Worthy of note are the construction of the ideogram of high resolution banded human chromosomes in the Chinese, work on fragile sites, chromosomal instability in relation to
cancer and cancer susceptibility, a case of homologous 14q14q Robertsonian translocation, and a marker chromosome in patients with nasopharyngeal carcinoma. In particular, chorionic biopsy for fetal sexing was first introduced by Han in this country. It is now being used the world over for prenatal diagnosis in the first trimester. Recently, the mechanism of expression of the common fragile site at 3p14 was studied. The results support the conclusion that DNA repair inhibition plays an important role in the expression of FRA3B.

Recently, molecular techniques have been applied in combination with chromosomal banding to the mapping of genes directly onto chromosomes. Cheng et al. have used the in situ hybridisation method to map the interferon gene and the yellow mutation gene of the mouse to chromosome 4C3→C6 and chromosome 2H1 respectively. This will certainly be the precursor of microcytogenetics in this country.

Biochemical genetics

Biochemical genetics is more sophisticated and difficult to grasp. Progress in this area was also hampered by the difficulty in obtaining the necessary reagents and equipment, most of which have to be imported. As a consequence, only institutions in the larger cities, such as Beijing, Shanghai, and Guangzhou, have been able to carry out work in this area. Genetic services with regard to inborn errors of metabolism are, therefore, limited to a few large institutions in these cities.

For obvious reasons, work in this area started with the haemoglobinopathies and glucose 6-phosphate dehydrogenase deficiency. Mass screenings for the haemoglobinopathies were started in 1980. Abnormal haemoglobins were found to be widely distributed throughout the country and in various ethnic groups, though more prevalent in the south. Simultaneously, studies at the molecular level to determine the amino acid substitution in Hb variants were begun by Liang and Lo at the Institute of Basic Medical Sciences (IBMS) in Beijing and Zeng and Huang in Shanghai. About 65 types of abnormal haemoglobins were identified, 16 of which are new. Hb S was not detected and Hb E was the most prevalent. The thalassaemias are more or less confined to provinces in south and south-western China and are rare to the north of the Yangtze River; this is also the case for glucose 6-phosphate dehydrogenase deficiency. Several new variants of G6PD have been identified by Du in Guangzhou, based on their electrophoretic mobility, KmG6P, percentage utilisation of 2-deoxy-G6P and deamino-NADP, heat stability, and optimum pH.

Surveys of phenylketonuria among newborns revealed an incidence of about 1/15,000 which is similar to that in Caucasians. It is a pity that China is still unable to produce a low phenylalanine diet in large enough quantities for adequate therapy for most affected babies.

Studies on the lysosomal storage diseases have been in progress at the IBMS since 1982 and also in Shanghai. The number of patients with this group of diseases seen at PUMC Hospital was second only to those with aminoacidopathies among the inborn errors of metabolism. Assays for the lysosomal enzymes in serum, skin fibroblasts, amnioncytes, and chorionic villi have established the normal values for Chinese. Cases with GM1 and GM2 gangliosidoses, mucolipidosis III, the various mucopolysaccharidoses, Niemann-Pick disease, and Gaucher disease have been diagnosed and the prenatal diagnosis of some of them accomplished. Cases with methylmalonic aciduria and maple syrup urine disease have also been reported, the diagnosis being confirmed by gas chromatographic analysis for the abnormal organic acids involved.

Large scale population studies of the various polymorphic systems in different ethnic groups showed several interesting features. The Rh(−) rate was very low, less than 1%. with the exception of the minority races in Xinjiang Province in north-west China. As for α1 antitrypsin, no deficient alleles, PiZ or PiS, have been found. Only recently, an infant with the genotype M1S who died of hepatitis was reported from Shanghai. Lactase deficiency was widespread with the exception of the Kazakhs and Uyghurs who are traditional herders in Xinjiang. The deficient type of aldehyde dehydrogenase was quite prevalent among the Han race (the majority race in China), a fact that may be related to the relatively low incidence of alcoholism among Chinese.

Molecular genetics

The success of DNA analysis in prenatal diagnosis and its great potential in medical genetics has had a major impact on Chinese researchers. Work on gene diagnosis started in 1982 both at the IBMS in Beijing and in Shanghai. It started with the thalassaemias and has extended to other genetic diseases, such as phenylketonuria, haemophilia, etc.

The α thalassaemias were studied first. Workers at the IBMS investigated the α gene organisation in 54 cases of Hb H disease. Nearly 50% of them were found to be of the non-deletion type. A similar study was done in Shanghai with comparable results. It is evident that, in contrast to the α thalassaemias seen in south-east Asia where α gene

Luo Hui-yuan (Wilson Hwei-yuen Lo)
deletion plays a major role, both α gene deletion
doing gene defect and α gene are important in the patho-
genesis of α thalassaemia in China. Bart’s hydrops
dehisence has been successfully diagnosed both in
Beijing and Shanghai.44 45

Using seven gene or DNA probes and 11 restriction
sites, the RFLP haplotypes in the β globin gene
cluster in 15 families with β thalassaemia from
Guangdong Province were determined.46 Thirty
βT chromosomes were found to be associated with
seven haplotypes, three of which were new, suggest-
ing that the βT genes they carry are probably new.
About 55% of the haplotypes were of the β gene
framework III Asian. A similar study was done in
Shanghai and 10 new haplotypes were found among
50 βT chromosomes.46a In order to discover the
common βT genes in south China, it is necessary to
close and sequence βT genes. Two βT genes from
Guangdong were cloned and sequenced,47 48 one of
which was due to a point mutation in the TATA box
and was a new one in the Chinese. Such data will
undoubtedly contribute to the successful use of the
oligonucleotide probe method and to the improve-
ment of the success rate of prenatal gene diagnosis of
the β thalassaemias, which has already been
accomplished by the indirect linkage analysis
method.49 50 Recently, investigators in Shanghai
have succeeded in using the oligonucleotide probe
diagnostic to β thalassaemia prenatally.51a 50b
Work is in progress to develop new methods of gene
diagnosis, such as biotin labelling of gene probes
and the amplification of target DNA sequences by
polymerase chain reaction.

Recently, successful prenatal gene diagnoses of
haemophilia A51 and B52 and phenylketonuria53
have been reported. It is to be expected that with
the acquisition of more gene probes more and more
genetic diseases will be amenable to prenatal diag-
nosis and carrier detection. However, because of the
difficulty and expense in obtaining 32P labelled
dNTPs and restriction enzymes, such work will
probably be limited to a few institutions in the larger
cities.

Clinical genetics

In the past, genetic diseases were seen by paediatric-
cians and internists. With the surge of enthusiasm in
medical genetics after the cultural revolution,
clinical genetics departments or divisions were set
up in many of the large hospitals over the country,
especially those affiliated to major medical schools.
However, only a limited number of medical schools
are offering courses in medical genetics and clinical
genetics has not yet reached the status of a medical
specialty. Dysmorphology became a distinct branch
of clinical genetics years ago in the advanced
countries, yet it remains to be initiated in China.

Even though many hospitals in the larger cities
have genetics clinics, the level of expertise varies a
great deal. Qualified and experienced genetic
counsellors are relatively few. Only a few hospitals
in Beijing, Shanghai, and Guangzhou can do
enzyme assays, though many are able to perform
karyotype analysis. Gene diagnosis is limited to one
or two institutions in Beijing and Shanghai. It is
evident that much needs to be done to upgrade
clinical genetics in this country. However, it will not
be long before this situation changes because of the
increased emphasis placed on the prevention of
genetic diseases by the Ministry of Public Health.

Research in clinical genetics has not received
enough attention. Worthy of note is a group in
Shanghai which has collected a large amount of data
on inherited eye diseases from reports throughout
the country, providing comprehensive coverage of
this topic.53a A classical genetic study on congenital
deficit of a district of Shanghai was carried out
by the same group.53b Relatively few centres are
engaged in the study of multifactorial disorders.
A mass survey of 11 congenital malformations, as
recommended by the International Clearing House
for Congenital Malformations of Newborns, was
carried out between 1984 and 1986 in Sichuan
Province.54 Among the more serious malformations,
the incidence of hydrocephalus is high compared
with figures from other parts of the world. The
incidence of neural tube defects was much higher in
north China than in the south55 and a nationwide
survey is presently under way. A group in Shanghai
has been studying the recurrence risk of a series of
multifactorial diseases.56 However, no report on the
pathogenetic mechanism of any of the multifactorial
disorders has appeared.

The future

With the serious population situation in China,
prevention of genetic diseases has become an urgent
problem. The seventh five year plan, starting from
1986, of the Ministry of Public Health has included
genetic medicine on the top priority list. More and
more funds will be allocated to genetic services and
 genetic research in the years ahead. Plans to
organise a genetic counselling network are being
drawn up and steps have been taken to set up
several national centres for referrals in different
regions of the country. These centres will also be
responsible for the supervision of activities of this
network as well as the training of personnel. It is
expected that these measures will substantially
reduce the incidence of many genetic diseases in the
long run. The founding of the Chinese Society of Medical Genetics last year will also contribute to the furtherance of efforts to control genetic diseases in China as well as to academic exchange and international collaboration. The future of medical genetics in China has never been so bright.

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Correspondence and requests for reprints to Dr Luo Hui-yuan, Department of Medical Genetics, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing, China.
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L Hui-Yuan

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