Sultan Qaboos University Medical Journal
July 2008, Volume 8, Issue 2, p. 129-135
Sultan Qaboos University©
Submitted - 27th April 2008
Accepted - 20th May 2008

EDITORIAL

Genetic Services in the Sultanate of Oman and other Gulf Countries

Progress is needed now!

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الخدمات الجينية (الوراثية) في سلطنة عمان وبقية دول الخليج

التقدم مطلوب الآن!

ساندي ريبورن

During the past decade there has been an explosion of new genetic information, with a greater understanding of gene functions and more powerful DNA-based technologies.[1] The challenge is to apply such knowledge to the greatest benefit of patients and their families.[2] In Oman and neighbouring countries, genetic services have been developed, both within the health care system and in universities. [3, 4] Such genetic services have been prompted by local needs as well as by prevention agendas, often initiated internationally. [4 – 9] Given the different origins of these services, they may have been established piecemeal, without a unifying vision of the community objectives. Dependent on whether a service originates from a research laboratory setting or from clinical needs, there may be a laboratory or clinical focus.

This editorial emphasises that, in Oman and in neighbouring Gulf States, high quality integrated genetic services are needed now. Genetic consultations and tests must be professionally designed, as well as made accessible, cost-effective and equitable. Simple low-cost strategies, applied in the community health services could improve access to genetic resources, facilitating the effective use of laboratory services. Patient and family needs are the priority.

A GLOBAL VIEW

In most developed countries, genetic counselling services have been in place for many years.[10-11] Clinical services were usually established first, often within departments of paediatrics, but some cytogenetic services date from the early 1960s. The organisation of such services, in each country, reflects the common genetic diseases, the type of health care provision and the culture.[10-12] Thus European Community genetic services address disorders such as cystic fibrosis, Duchenne muscular dystrophy, Huntington's disease and the fragile X syndrome.[11.] Countries with citizens of Mediterranean, Bedouin, African or Asian origins will focus first on haemoglobinopathies such as thalassaemias or sickle cell disease. [3, 13, 14]

Rare genetic disorders are seen in all countries and are always difficult to diagnose and to manage. Investigation of such disorders often involves international cooperation and sharing of clinical information, of blood and DNA samples and of specialised technology, to the benefit of the patient, the family and the global community. But differences must be acknowledged; they will influence the design of any nationally planned genetic service.

In Europe and North America, rare disorders usually occur in small families with a single affected person. There may be doubts about the mode of in-

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heritance; therefore, investigations (to clarify both the diagnosis and the mode of inheritance) will focus more on affected persons and less on the family tree.[12] The emphasis is on the rare disorders of *that* community.

In contrast, affected Arab families in the Middle East region often have disorders causing several people to be affected, either in a sibship or in the wider family,[3,14] usually the mode of inheritance is Mendelian and is not in doubt. Informative family trees here can confirm the single gene inheritance and focus investigation using tests which should have high predictive values. For example, whole genome genetic marker studies (e.g. using single nucleotide polymorphisms (SNPs) or microsatellite markers) in affected and unaffected people in the family may now be more logical as a first step in a multiplex Omani family than the protocols used in the West. Even if a country like Oman can call on much collaboration from international genetic centres (and will frequently need this for specialised techniques in some families), their primary and secondary genetic services must reflect what is common in the Omani community. Strategies in 'Old World' countries are necessarily different and should not be applied 'off the shelf'.

GENETIC DISORDERS IN THE GULF COOPERATION COUNCIL COUNTRIES

Lihadh Al Gazali has pointed out the high proportion of unique disorders in the UAE; [7] similar data come from other Arab countries[3, 5, 14-16] including Oman. In summary, there are regions with a high prevalence of sickle cell disease and β thalassaemia, as well as moderate numbers of worldwide disorders. Rajab and her colleagues have reported the approximate birth incidences of some key conditions in Oman.[5] Some approximate incidence figures from that report are summarized in Table 1.[5]

In most of these countries there are also many families with other progressive single gene disorders which lead to early death in affected people. Here, in addition to the health effects, severe social and financial difficulties can occur in sibships with several affected people. Also, discrimination against healthy members of the family can happen, for example when they consider marriage. Individually, such disorders may be uncommon but their cumulative effect in the population can be major.

SERVICES AVAILABLE NOW IN GCC COUNTRIES

Most Gulf countries have established genetic services, but there are urgent calls for greater integrated service provision.[3, 4] Genetic departments comprising clinical, molecular and cytogenetic sections (and often biochemical genetics, immunogenetics and/or HLA and tissue typing too), work best as an integrated team. [3,17] Health services in Kuwait, the United Arab Emirates (UAE), the Kingdom of Saudi Arabia, Qatar, Oman and Kingdom of Bahrain all have genetic centres and departments that meet some of the needs of families with genetic disorders. In addition, there have been excellent pan-Arab initiatives to pool important genetic information, backed up by international conferences (e.g. the Centre for Arabic Genomic Studies based in the UAE).

These existing services can delineate the clinical features of a disease in affected individuals, exclude or confirm chromosomal abnormalities and initiate molecular investigation towards identifying causative gene mutations. Sometimes they also access centres abroad for specialised molecular studies, but access to fully integrated services may be patchy; other affected people in an identified family may not receive the support they need and genetic counselling facilities for the 'cascade' of genetic information to relevant family members may be limited. We note that simple feedback to a family after successful gene mapping may empower the family,[17] by clarifying future genetic risks. For example, even if the causative mutation is unknown, carrier testing in an undiagnosed autosomal recessive disorder could be based on linkage if the gene has been mapped. The predictive value in such families would be less than 100%, but is better than no information at all. Genetic centres need to establish family counselling urgently, with follow-up to record the natural history of the disorder and to offer further counselling as the family extends and ages. These elements would be essential in future genetic services. Beyond the genetic investigation and counselling needs, there may also be requirements for financial support or for aids towards normalisation of the affected people. Genetic centres should therefore interact with the support services of the Ministries of Social Affairs as well as with charitable organisations.

Table 1: ***Incidence of some autosomal recessive genetic disorders in Oman (based on a total of 420,000 live births in the period 1993-2002)***

Condition	Total affected	Birth incidence
Bardet-Biedl syndrome	14	1/30,000
Congenital adrenal hyperplasia	55	1/10,000
Cystic fibrosis	32	1/10,000
Ellis van Creveld syndrome	18	1/25,000
Meckel-Gruber syndrome	9	1/50,000
Metachromatic leukodystrophy	18	1/25,000
Microcephaly (primary)	31	1/15,000
Spinal muscular atrophy	56	1/10,000

Taken from Rajab et al[5]

MINISTRY OF HEALTH: HEALTHCARE IN OMAN

Healthcare Services in Oman are administered centrally in Muscat by the Ministry of Health (MoH) which coordinates healthcare provision in semi-autonomous regions. Each region has resources to provide health care through purpose-built family clinics and regional hospitals. Nationally, there are also tertiary referral centres for specialised services, mostly located in or near to the capital. The main MoH genetic centre is in the Royal Hospital, backed up by a cytogenetics laboratory and a molecular laboratory in another part of the city. Plans are well advanced for there to be a national Genetic Centre, funded by the MoH, which would draw together these elements of the genetic service. However, there may not yet be provision for university input, which would coordinate the teaching of the new generation of medical undergraduates as well as assimilating new research findings into future services of the MoH Centre.

The College of Medicine and Health Sciences of Sultan Qaboos University (SQU) has a Genetics Department with 4 sections: clinical genetics, cytogenetics, immunogenetics and molecular genetics**.** The mission of this team is: 'to seek greater understanding of serious genetic disorders in the Sultanate of Oman, to apply new knowledge to the investigation, diagnosis and genetic counselling of affected families and to teach present and future doctors and scientists how to use genetic principles in their work'.

This means that the traditional academic roles of a university department, teaching and research, are intended to be augmented by some service provision.

Currently, five doctors are training to be consultant clinical geneticists, there are three holders of PhDs leading cytogenetic, immunogenetic and molecular genetic sections respectively, a scientist is abroad for PhD training and several others are planning to study, or already taking part in, relevant master's programmes. All sections of the Department perform service work for patients attending the Sultan Qaboos University Hospital (SQUH), usually as tertiary referrals. Space both for genetic clinics and laboratories is very limited.

SERVICES THAT COULD BE AVAILABLE SOON IN GCC COUNTRIES

The genetic literature is awash with studies of disorders in which causative gene mutations have been identified by the new methodologies.[18,19] Often these have included Arab families with informative structures. In particular, whole genome scanning in single Arab families has sometimes provided opportunities for rapid mapping of new disease genes.[19] A caveat to this optimism is that the complex nature of some families, including consanguineous marriage, may on the one hand simplify a whole genome search whilst making fine mapping more difficult.

The urgent need in Oman and other GCC countries now is to design services which utilise Arabian family structures (and genetic disease patterns), as well as available global genetic expertise. These services must address the questions asked by Arab families, within the context of their culture and existing health service provision.

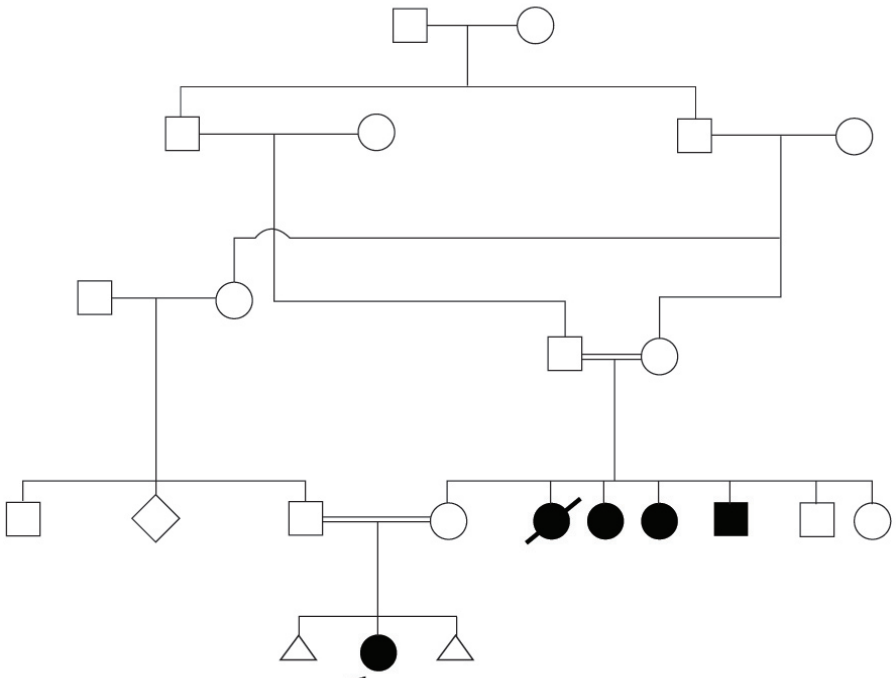

Figure 1: ***A typical family tree of an autosomal recessive disorder in an Omani family***

Facilitation of this pro-active approach needs three simple elements: (i) Strong collaboration between the MOH and the Universities; (ii) Access points in the community for the primary recognition of genetic disease in families and (iii) A positive role for disease-centred parent and patient organisations.

Patient organisations could play a part in the identification of needs and also in the coordination with agencies outside health which are required. The model of the Genetic Interest Group (GIG) in the UK could be applied in the GCC countries, but with a special focus on autosomal recessive disorders.

A VISION FOR GENETIC SERVICES IN THE ARABIAN PENINSULA

In all GCC countries, collaboration between the Ministries of Health and the universities could now be strengthened and built into robust partnerships. Co-ordinating committees and conferences are valuable, but must be seen as steps towards improving genetic health, not the final outcome.

Some pilot initiatives from the Genetics Department of Sultan Qaboos University are relevant here. These have shown the acceptability of university-led outreach genetic clinics in regional MoH hospitals (Sultan Qaboos Hospital in Salalah and Nizwa and Sohar Hospitals). The enthusiasm and support from families, who have much shorter distances to travel with their affected offspring could have been expected. But there has been support too from the specialists and medical directors in those regional hospitals.[20] The paradigm is to work together to provide holistic genetic health care for the many, not to make research forays into the community to gain publications for the few.

A spin-off of the specialised genetic outreach clinics has been experiences gained when visiting Omani families at their home, usually when there are several affected people. A glance at one family tree shows why it is better for the genetic team to visit the home [Figure 1]. After a home visit the team was able to confirm that the proband in generation 5 (arrow) had the same disorder as the 3 living affected people in generation 4, who were siblings of the proband's mother.

A valuable outcome of home visiting in village communities has been the opportunity to meet non-medical professionals in the health centres. These professionals take great pride in their work but often feel isolated; they are willing to contribute to genetic health care if they are taught how to do so.[20] This raises the issue of the degree of genetic competence

Table 2: ***Three questions which non-medical health centre staff could answer***

1. Do all 'affected' people have the same condition?
2. Are 'unaffected' people in the family definitely free from the disorder?
3. Does the family tree suggest a need for specialist referral?

needed in such health centres. A provocative answer might be that the genetic package may be extremely simple, involving just the ability to answer 3 questions [Table 2].

GENETIC KNOWLEDGE IN THE OMANI COMMUNITIES

A substantial proportion of Omani families touched by a genetic disease are aware that the disorder in their family is inherited and can lead to increased risk of the disease in relatives. As in any country, they may deny the diagnosis, or shop around for second opinions. Also unrelated families may be (excessively) concerned about future risks if they marry into an affected family. They may choose to avoid such marriages, often based on inaccurate information.

Omani families also know that marriages between close relatives may increase the risk of having affected children. They face the dilemma of choosing whether to abandon traditional practices or to consider procedures which are ethically sensitive (such as prenatal diagnosis) or expensive and less likely to result in much-wanted pregnancies (such as pre-implantation genetic diagnosis).[21, 22] These families may wish to consider other ways to utilise genetic tests. For example, carrier tests might assist family decisions if several cousins were tested before engagement or marriage; genetic counselling approaches might then be used to identify the low and high risk partnerships.[20]

Omani families at the SQU genetic clinics have welcomed simple biological information about the mode of inheritance of the disease in their family. As in the UK, this information-giving element of counselling can ease psychological traumas, probably by reducing uncertainty.[22-23] In any case, such information is required by families before they decide to embark on carrier testing, prenatal diagnosis, pre-implantation genetic diagnosis or presymptomatic detection. They also need to understand why genetic testing is only required or helpful in certain family members.

Table 3: ***Elements of an integrated genetic service***

- Accessible clinics with trained staff, nationally and in the regions
- Genetic Service laboratories with trained staff:
* *Cytogenetics covering both constitutional chromosome disorders and cancer cytogenetics*
* *Molecular genetic staff trained in service provision in preference to research training*
* *Immunogenetic staff experienced in general tissue typing and in transplant donor matching*

This preparatory work has shown us that a greater attention to the family tree and less emphasis initially on laboratory tests is more appropriate for genetic counselling in the Gulf setting [Table 3].

WHAT ARE THE CONSTRAINTS IN OMAN?

INADEQUATE FUNDING

Oman, the United Arab Emirates and the Kingdom of Saudi Arabia face greater numbers of autosomal recessive conditions[5,7] than Europe and double the European prevalence of genetic malformations and handicaps.[4] Logically, they should need higher staffing levels than recommended in, for example, the UK;[12] however, this wish is unrealistic in Oman, both at present and in the near future. We recommend measures to tackle the major needs of families with genetic disadvantages which are realistic, in terms of resources.[20]

WIDE GEOGRAPHICAL DISTRIBUTION OF FAMILIES WITH SPECIALISED GENETIC SERVICE NEEDS

The distance travelled to attend specialist genetic centres creates problems for many families, especially for those with limited resources.

INADEQUATE GENETIC UNDERSTANDING BY CLINICAL STAFF AND FAMILIES

This may be exacerbated by an excessive enthusiasm of doctors to initiate DNA-based genetic investigations without first assessing the family tree and the prior risks of the family or their psychosocial, informational or financial needs.

ARE STUDIES OF OTHER GENETIC SERVICES RELEVANT?

There are extensive publications on genetic counselling and other genetic services published from well-established genetic institutes in the West.[10,12, 21] Caution should be exercised before planning genetic services

Table 4: ***Action points***

1.	More integrated departments of genetics are needed, so that clinical needs set the agenda in the laboratories as well as for management.
2.	Closer collaboration between the MOH and University Departments dealing with genetic disorders is essential.
3.	Outreach clinics are needed in main regional hospitals: - Consultants with a genetic interest in each region, backed by a genetic counsellor or specialist nurse and a part-time coordinator. - Resources to facilitate the interaction between staff in the Genetic Centre in Muscat and in regions. Travel expenses and short-term accommodation costs for staff from the National Genetic Centre and the reverse for Regional teams.
4.	Facilitation of home visits to families in which multiple affected individuals are identified. Transport availability, occasional overnight accommodation etc.
5.	Genetic database resources in the genetic centre, compatible with local computing facilities and laptops for outreach work and home visiting.
6.	Adequate resources for other specialties that see genetic disorders frequently, e.g. electroretinogram equipment may be needed for the tertiary referral departments of Ophthalmology.
7.	Development of a simple community teaching package for health centre staff. The aim will be to have one or two staff members in each health centre with skills in family tree preparation and simple interpretation.

in Oman, based on such models. The options available might not be acceptable in Omani communities; more importantly, the spectrum of genetic diseases differs considerably from the West. Health care providers and practitioners in Oman may need to adopt a more pragmatic and family-focused approach.

EVOLVING SOLUTIONS

There must be universal support for the MoH initiatives towards offering genetic counselling for all families with people affected by genetic disorders. However, families with multiply affected members need to be ascertained too and prioritised. In such families, with several affected people already, there should be opportunities for pre-marital counselling and relevant carrier testing. An accurate family tree, as well as considerable practical molecular genetic expertise is crucial to success here.

Simple genetic counselling needs to be provided regionally and should be organised in consultations separate from clinical management of affected patients. This is because either the impact of the genetic risks or concerns about progression disease will limit understanding. The patient needs time to absorb information on genetic risks and separate allocations of time. The progress and treatment of disease is a clinical issue which needs to be distinct from genetic counselling.

In the long term, each region requires a consultant, trained in clinical genetics, to lead and coordinate the local programme. The consultant fulfilling this role regionally may have joint accreditation, e.g. as a clinical geneticist and a paediatrician (or physician). Each regional team requires a genetic nurse specialist, who can prepare family trees, collect blood samples and give counselling support. This nurse will see high risk couples with the geneticist and provide follow-up. Each team also requires a part-time coordinator, who will organise genetic clinics. Later, regional teams will include trained genetic counsellors. Regional genetic teams do not need laboratory facilities locally except those for DNA separation; specialist genetic laboratory services will be provided by laboratories in the new MoH Genetic Centre, complemented by the genetic laboratories at SQU.

The model for genetic service development described here may be of interest to neighbouring Arab nations; services designed for the Middle East region could be piloted jointly by Oman and by neighbours with larger populations. The 'action list' (Table 4) summarises what could be completed with some speed.

CONCLUSION

This editorial is based on real experience and figures from Oman, backed up with data from neighbouring countries. The action points are therefore not hypothetical, nor are they based on a blind willingness to copy genetic services of the Western developed countries. It is hoped that the issues raised will stimulate actions as well as discussions, along with the confidence to go in a different direction from established (Western) genetic services. Solutions for genetic services in the Middle East need to be designed for their purpose, not translocated from other less relevant structures in the 'First World'!

ACKNOWLEDGEMENTS

It is a pleasure to acknowledge the many discussions with my colleagues in the Genetics Department of the College of Medicine and Health Sciences at the Sultan Qaboos University, particularly Dr. Aisha Al Shehi, Rayhanah Al-Mjeni, Dr Almundher Al-Maawali and my wife, Arlene Raeburn. Rahma Al-Jashmi kindly prepared the family tree.

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