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REVIEW

It's 'back to school' for genetic screening

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Implementation of population genetic screening programmes requires consideration of strategies for reaching the greatest proportion of the target population in order to achieve maximum awareness. This article reviews the current strategy of school-based population genetic screening programmes. The school environment is an ideal setting for offering relevant genetic screening programmes as it provides an opportunity to engage people at a time when they are exposed to a range of educational experiences and are sufficiently mature to be involved in decision-making processes. Such programmes allow all students, not only those studying biology, an opportunity to be educated and experience genetic screening in a supportive environment, ultimately increasing understanding and empowering students. While the major form of genetic screening in schools has been for reproductive health information (eg carrier screening for TaySachs disease and cystic fibrosis), genetic screening in schools for other conditions may be a timely proposition.
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Background

In recent times, genetic research has made a substantial impact on health improvement and disease prevention.[1,2] Screening of populations is one such application for these research advances. Principles of population screening, developed in 1968,[3] have evolved and have been modified in light of recent knowledge to encompass genomic medicine.[4–7] As our understanding of the genetic contribution to conditions increases, so will the number of candidates for population genetic screening programmes. After establishing that a genetic condition meets the population screening criteria, a careful planning process is required for successful implementation. Human Genetic Societies have developed policies and guidelines for the effective implementation of genetic screening programmes within communities.[8–10] These guidelines state the need for population genetic screening programmes to be voluntary, to have defined health goals and target populations, laboratory controls, measures ensuring confidentiality and provision of education. Pilot screening programmes assessing the test validity and acceptability, uptake rates, how results are used in decision making, the psychosocial consequences and costs should precede their implementation within populations.[9]

The aim of population medical screening is 'to identify individuals at sufficient risk of a specific disorder to benefit from further investigation or direct preventive action, among persons who have not sought medical attention on account of symptoms of that disorder'.[11] Genetic screening differs because in addition, 'its aim is not necessarily to prevent or treat disease in the person screened; it may be used for health related reproductive or lifestyle choices' and has familial implications.[9]

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Box 1 Summary of types of genetic screening

Screening for reproductive health information

- *To identify carriers of a condition*
  Where the condition does not affect that person (ie they are most often a 'healthy carrier') but the information has implications for reproduction. For example Tay-Sachs disease, cystic fibrosis and thalassaemia.

Screening for personal health information

- *To identify increased risk for a condition*
  Screening for conditions that will affect a person's health, for example, newborn screening for phenylketonuria.
- *To identify increased risk for susceptibility to a condition*
  Asymptomatic individuals may be offered screening throughout their lifetime, which may either predict or determine their susceptibility to adult-onset conditions with a possible genetic component. For example HFE screening for susceptibility to hereditary haemochromatosis, or Factor V Leiden screening for susceptibility to blood clotting disorders.
- *For information regarding drug, food or toxin metabolism*
  Screening for variants which may be pharmacologically significant, for example screening for cytochrome variants to predict metabolism of particular drugs.

For the purposes of this review, genetic screening will be broadly divided into two categories: (1) genetic carrier screening to provide reproductive information and (2) screening for personal health reasons (ie for intervention or health information). These categories are outlined in Box 1. It is important to note that these categories are not comprehensive, nor mutually exclusive, as some genetic conditions will fall into both categories eg. Fragile X syndrome.

Screening may occur in the clinical or nonclinical setting, although due to the nature of screening, where asymptomatic individuals have not sought medical attention, the nonclinical setting is likely to have a greater impact. Community gatherings,[12] the workplace[13] and schools[14,15] are nonclinical settings where screening programmes have been offered.

Genetic carrier screening programmes in schools

The school setting has been adopted for population genetic screening programmes worldwide. The original Montreal programme[14] offered screening for carrier status of Tay Sachs disease (TSD), a neurodegenerative condition, fatal usually by 5 years of age. The programme was initiated by the community itself and has existed since 1972.[14,16–18] Pilot studies were performed and school boards, principals, teachers, parents and community leaders approved the idea of a school-based screening programme. Schools were selected from areas within Montreal in which the majority of the Ashkenazi Jewish community are located. The carrier frequency for TSD in this community is one in 28.[14] Students in their senior years of schooling were offered education, carrier screening (by enzymatic analysis) and genetic counselling at the receipt of results. After two decades of screening an outcome evaluation found the average uptake of voluntary testing in the school-based programme to be 67%.[14] The study also showed that all couples in Montreal using prenatal diagnosis for TSD acquired their knowledge during the school screening programme. The incidence of TSD in Quebec has, consequently, fallen by 95%.

To date, school-based programmes offer voluntary testing for carrier status for various conditions. Some examples include α- and β-thalassaemia in Hong Kong,[19] haemoglobinopathies in Marseille,[20] cystic fibrosis (CF) in Israel[21] and TSD and CF in Australia[15,22] and Canada.[14] In addition, it has been demonstrated in the programme in Sydney, Australia, that carrier screening is comparable in cost to prenatal carrier screening for CF.[23]

The experiences described here reinforce the importance of the social structures and values of the community. The success of school-based carrier screening programmes in both Australia[22] and Canada[14] have been largely attributed to the initial and ongoing support from the communities involved.

Here, we have reviewed the case for school-based genetic *carrier* screening. A positive result from a carrier test does not affect the individual, rather it may affect the reproductive choices made by the individual. Therefore, it is important to consider the screened community's religious and cultural beliefs towards termination of pregnancy. Certainly, within the Jewish communities screened worldwide,[14,15,22] the high levels of acceptance and testing uptake suggests that screening and the consequences of a possible termination of pregnancy are acceptable. Indeed, the screening information is remembered and used effectively in their reproductive choices by individuals up to 20 years following the event.[14] However, carrier screening programmes for other conditions have been introduced more recently and as yet there is no information regarding their long-term follow-up and whether the participants have indeed acted on their testing result.

Genetic screening for personal health information in schools

Genetic screening for personal health has several different implications to consider. Information about the individual's future health and well being (not reproductive health) is being provided. Although school-based genetic screening for personal health has not yet been offered, research into community attitudes suggests that such programmes within the Australian school community may be acceptable.[24]

Health programmes in the school setting

Health programmes currently operating in schools have a specific focus such as HIV/AIDS, sex education, nutrition, exercise, oral hygiene, drugs and alcohol, suicide awareness and general health. It is suggested that successful programmes utilise a team approach with the contribution from students, school staff, parents, local community members and expert technical organisations.[25]

Internationally, the health-promoting schools model[25–28] is touted as being a comprehensive approach with foundations on a holistic view of health including physical, social, mental, emotional and environmental. However, a fundamental aspect of health has been overlooked in their 'comprehensive' model, and that is the contribution of genetics to health. This is remarkable given the recent emphasis on 'health promoting schools' in a time of greater understanding of both genetic and environmental influences on the aetiology of disease.

It has been suggested that school education may help to create a public well informed about the influence of genetic factors on human health.[29–31] Learning genetics in a real-life or contextualised environment such as within a genetic screening programme in schools empowers students to promote their decision-making, analytical and coping skills which are fundamental objectives of the learning experience. Moreover, the teaching of genetics is not necessarily restricted to the scientific discipline as the related issues cover other areas of study such as ethical, health, legal and economic issues.

Genetic testing of adolescents

This empowerment for individual decision making is often central to the ethical debate of genetic testing of adolescents. The debate surrounds the issue of the competence of the individual to make an autonomous, informed decision.

Guidelines for genetic testing of children and adolescents have been developed by Human Genetics Societies around the world. The guidelines state that predictive and susceptibility testing for genetic predisposition is generally not recommended unless a treatment or preventive strategy is available and the implementation of which is immediately required to benefit the health of that individual.[32]

Debate in this area is centred on a number of issues such as the potential impacts and psychosocial consequences, compromising of future autonomy, parental authority and the competence of the individual in the decision-making process and coping with testing consequences.[32]

Adolescents and consent to screening

The principles of a mature minor are relevant here. Based on common law, the definition of mature minor varies between countries, and indeed, between states. In Australia, it is generally considered that individuals over the age of 16 years are competent to make their own medical decisions, however the law is complex.[33,34] In the United Kingdom (UK) 16 years is also considered the appropriate age,[35] however, 14 years of age is considered appropriate in Canada for consent to sexual activity,[36] while at 16 years a person is considered an adult and has all the rights of the adult without the need for parental consent.[37] In the United States of America (USA), a mature minor has constitutional rights to make medical decisions without parental consent, however, the laws vary from state to state.[38] Hence the situation in the USA is much less clear cut than Australia, Canada and the UK.

With the successful implementation of carrier screening programmes within schools and the above-mentioned evidence, the foundation appears to be laid for introduction of other genetic screening programmes in schools. However, further studies are essential prior to widespread school-based genetic screening.

Other concerns and debate

The vulnerability of a young person is often used as an argument against offering testing. However, we offer tests to adults even though we know adults are also vulnerable. A certain level of adverse events is generally accepted when adults receive a genetic test result if the overall benefits outweigh the harms. Under this premise, to conclude that genetic testing of young people should not be offered, it would have to be shown that the rate of adverse events is higher than that which we already accept in adults. Little empirical evidence exists in this context, however, a study describing the psychological consequences in the context of predictive genetic testing for the nonpreventable Huntington's disease in adults showed that 21.8% of individuals testing positive experience an adverse event such as diagnosis of clinical depression, psychiatric hospitalisation or attempted suicide.[39] Further studies are required to compare psychological consequences of adults and young people for other (preventable) genetic conditions. Young people are also considered to be subject to family influence, with one study showing 14 and 15-year olds' hypothetical medical decisions were reflective of their parents' wishes.[40] Further, social learning theory suggests

the influence of many factors, for everyone, in decision-making processes.[41]

The concerns expressed about psychosocial impacts of genetic testing in general are heightened with respect to testing of young people. Again, there is minimal empirical evidence addressing these concerns. One study on emotional impact of predictive genetic testing for familial bowel cancer found children's results did not cause greater anxiety or depression than adults,[42] while another study actually suggests adults were more anxious than young people.[43]

Some argue that when a young person is tested he or she loses the chance to make a decision about testing as an autonomous adult and therefore future autonomy is threatened.[43–45] However, students tested for their TSD carrier status as adolescents, in the Montreal school-based programme, appreciated the experience and used the knowledge to their advantage up to 20 years after screening. Indeed, being considered a mature minor indicates that an informed decision was made and, therefore, future autonomy is not compromised.

Clearly, separate issues arise with genetic screening for personal health, compared with those for carrier screening. Despite the existence and knowledge of the guidelines recommending against predictive genetic testing in children and adolescents, a recent international study suggests that predictive genetic testing of individuals under the age of 18 years is occurring more frequently than expected.[46] The debate concerning testing and screening for personal health will continue to be played out with increasing pressure on the need for empirical evidence of the impact of genetic testing and screening on children and adolescents.

A summary of the essentials for a successful school-based genetic screening programme

The school setting may provide an appropriate addition or alternative to other settings, as the results of the Human Genome Project are realised and new tests become available. However, as success of a genetic screening programme has been attributed to having the support of the community, it is important to assess the acceptability of new programmes to the school community including students, the parents and school authorities, prior to their implementation. We have recently reported on community attitudes towards offering a hypothetical genetic susceptibility screening programme for hereditary haemochromatosis in Australian schools, with favourable results.[24] As a result, a pilot study is underway to determine uptake, acceptability and psychosocial sequelae of offering such a programme.

Many researchers agree with the notion that concerns about the possible misuse of genetic information should not impede 'the careful development of responsible programmes aimed at educating and testing adolescents'.[47] For screening to have the greatest impact, it is necessary to consider initial strategies for gaining access to the maximum number of individuals within the target population that is realistically achievable. Certainly, in the case of genetic screening for carrier status, schools provide an opportunity to reach large numbers of young people before they reproduce, which is ideal in this context.[48] Gaining access to a population will enable raised awareness, and in turn facilitate increased access to other populations. From a practical perspective, there are benefits for school-based population genetic screening. In 2001, the Australian Census showed 3 301 776 of 3.4 million (97.1%) eligible individuals were in school attendance.[49] Furthermore, schools provide valuable links with parents and the wider community; thus the potential to raise awareness is unparalleled.

Acceptability not only relates to the purpose of the genetic screening programme but also to the genetic testing process employed. Education plays a critical role in this process as it has a significant impact on knowledge, beliefs, attitudes and consequently, the decision to be tested.[24] As schools are an educational setting, promotion of informed choice may be maximised through comprehensive education, which is less often the case in adult medical screening programmes where limited knowledge has been shown.[50,51]

After access, awareness and education, the next step in the process of genetic screening programmes is to offer genetic testing. High testing uptake is often considered to indicate a successful programme. We have shown that offering cheek swab testing rather than blood testing maximises the uptake of testing and is acceptable to the school community.[52] Furthermore, the convenience of offering testing in a school-based setting shows a high uptake rate.[14,15,22] Our study of community attitudes showed that given the opportunity and education, students have increased confidence in their ability to make decisions and feel less affected by peer pressure.[24] Also, students are able to decline testing in the school setting, with the majority citing that knowledge of their TSD carrier status was not relevant at this life stage.[15] The safe and supportive environment of schools is ideally suited to provide the first experience of genetic screening, empowering students to be prepared to make independent decisions in the future.

The importance and benefits of evaluation of population genetic screening programmes is evident. Furthermore, rigorous evaluation of the educational intervention and its impact on the success/test uptake of the programme require that measurements are ideally taken (with validated measurement tools) pre- and postintervention, or in a randomised control design. This process is required to adequately minimise adverse psychosocial events, which will in turn build trust and acceptability. This acceptability

Box 2 The essential components for offering a school-based genetic screening programme

1 The school setting is an effective place to offer screening to the majority of a population.
2 Acceptance for the programme must be established within the school community prior to implementation.
3 Efficient and comprehensive education empowering participants to make decisions about their own and their children's future health.
4 Consideration must be given to the time required for deliberation about individual decisions.
5 A convenient, easy, noninvasive and acceptable test should be offered with minimal anxiety to the participants.
6 Evaluation of the impact on the school community is essential to the success, acceptance by the community and ultimately the continuation of the programme.

will ultimately contribute to the success of the programme and benefits for the community. In summary, there are several points to consider when planning a school-based genetic screening programme, these are highlighted in Box 2.

Conclusions

School-based genetic screening programmes provide a vast range of possibilities by empowering students through education and experience, which will be invaluable to their future health, as well as the future health of the community at large. We have reviewed the process of school-based genetic screening, which can be applied to other communities and different genetic screening programmes. School-based genetic screening programmes may be the way forward for a variety of conditions and populations. To realise this potential, communities and governments must be prepared for change.

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