

Consanguinity and inherited epilepsies

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Abstract

As a working definition, unions contracted between persons biologically related as second cousins or closer are categorized as consanguineous. The offspring of consanguineous relationships are at greater risk of certain genetic disorders. Recent studies have shown a significantly higher rate of consanguinity among parents of epilepsy patients and a significantly higher rate of epilepsy among family members with consanguineous marriages for both cryptogenic and idiopathic epilepsies. Carrier detection and genetic counseling programmes have been very successful in reducing the incidence of inherited disorders in many populations. Models for prevention of hereditary diseases due to consanguinity should be multiaxial focusing on public education on genetic diseases and also deal with applicable preventive measures. These programmes are most successful when they are sensitive to the cultural backgrounds of populations in which they are applied.

Consanguinity means the amount of shared (identical) DNA. As a working definition, unions contracted between persons biologically related as second cousins or closer are categorized as consanguineous. This arbitrary limit has been chosen because the genetic influence in marriages between couples related to a lesser degree would usually be expected to differ only slightly from that observed in the general population. Globally, the most common form of consanguineous union contracted is between first cousins, when the spouses share 1/8 of their genes inherited from a common ancestor. First cousins have four times the 'consanguinity' of second cousins.

The offspring of consanguineous relationships are at greater risk of certain genetic disorders. Autosomal recessive disorders occur in individuals who are homozygous for a particular recessive gene mutation. As relatives share a proportion of their genes, it is much more likely that related parents will be carriers of an autosomal recessive gene, and therefore their children are at a higher risk of an autosomal recessive disorder. The extent to which the risk increases depends on the degree of genetic relationship between the parents. The risk is greater in mating relationships where the parents are close relatives, but for relationships between more distant relatives, such as second cousins, the risk is lower, although still greater than the general population. Except in certain rare circumstances (new mutations or unipaternal disomy) both parents of an individual with such a disorder will be carriers of the gene. Such carriers are not affected and will not display any signs

that they are carriers, and so may be unaware that they carry the mutated gene.

Increased risk of epilepsy (at least by 2.2 folds) has been reported after familial marriages in a study from Iran. The percentage of consanguinity in parents of the epileptic patients was significantly higher in comparison to a sample of the general population which signifies the importance of consanguinity as a potential risk factor for epilepsy.¹ There is considerable overlap in arranged and consanguineous marriages with many cultures adopting both practices. A significantly higher rate of consanguinity among parents of epilepsy patients and a significantly higher rate of epilepsy among siblings (born out of parental consanguineous marriages) of patients with idiopathic and cryptogenic epilepsy has also been reported.² A recent study in Qatar showed bronchial asthma, mental retardation, epilepsy and diabetes were significantly more common in offspring of consanguineous couples.³ Progressive myoclonic epilepsies (PME), Unverricht-Lundborg disease, Lafora body disease, neuronal ceroid lipofuscinoses, Type I sialidosis, some families with Juvenile myoclonic epilepsy, cortical dysplasias/neuronal migration disorders, autosomal recessive neonatal myoclonic epilepsy are some of the human epilepsy syndromes with autosomal recessive inheritance.

Rapid industrialization and urbanization across different parts of the world has had a variable effect on consanguineous marriages. Past predictions of a rapid decline in the overall prevalence of consanguineous unions have proved to be

largely incorrect. In fact, the recorded numbers of consanguineous unions appear to have grown at least in step with increasing national and regional populations. In some economically less developed countries the proportion of marriages contracted between close biological kin has expanded. An explanation for this observation is that as greater numbers of children survive to marriageable age, the traditional social preference for consanguineous unions can be more readily accommodated. Migrant communities now permanently resident in Western countries may represent a special case, especially where they practice a religion not followed by the majority indigenous population. In such communities, the available evidence from Western Europe, North America and Australasia suggests that the prevalence of consanguineous unions is increasing. The desire to find a marital partner from within the community, the wish to maintain community traditions in a new and unfamiliar environment, and social advantages of marrying close relatives in terms of maintaining family wealth and relations between groups are the various reasons that have been advanced for this increased prevalence of consanguinity among migrant populations.

It is important to prevent hereditary diseases that are associated with consanguineous unions. Models for prevention of hereditary diseases due to consanguinity should be multi-axial focusing on public education about genetic diseases and the factors contributing to their increased frequency. Such educational programs should emphasize the effects of consanguinity and also deal with applicable preventive measures. It is important to provide for genetic screening and testing programmes for the disorders common in a population. Premarital and preconceptional testing and counseling for common and rare disorders that are present in high risk inbred families also help in reducing the societal disease burden due to consanguinity. Carrier detection and genetic counseling programmes have been very successful in reducing the incidence of inherited disorders in many populations. These programmes are most successful when they are sensitive to the cultural backgrounds of populations in which they are applied.

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