PREVENTION OF CRANIOFACIAL MALFORMATIONS

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It is often said that the ultimate objective of any of the health professions is the elimination of the disease or diseases for which it was created. A little reflection brings to mind numerous preventive measures, for example immunization for poliomyelitis, that have brought about major changes within a few years. The fact that such breakthroughs were unthinkable before their introduction gives hopes for disease such as cancer and birth defects where preventive measures have been, for the most part, unsuccessful. This opinion paper is an attempt to briefly summarize the state of the art in prevention of birth defects, especially craniofacial malformations. Let us examine procedures that are currently employed, procedures currently at the experimental level and our hopes for the future.

The only widely used preventive measure for birth defects at the present time is risk counselling where there is a family history of the particular defect. Risk figures have been slowly improved over the years, but so far can be credited with prevention of only a small number of craniofacial malformations.

Prenatal detection of facial malformations and elective abortion is, in a sense, prevention. Procedures for early detection of relatively common malformations such as anencephaly and cleft lip are currently available. As with the counselling procedures, however, it is difficult to identify pregnancies with sufficiently high risk, while religious and moral considerations become a major limitation to significant utilization of these procedures.

Considerable hope for the near future is offered by preventive measures now at the experimental level. Recently conducted studies on neural tube defects (NTD; anencephaly and spina bifida) provide an example. Selective vitamin and other nutritional supplements for pregnant women following the birth of a child with an NTD have lowered the recurrence rate from the expected rate of 6% to as low as 0.06%. Similar studies on pregnancies subsequent to the birth of a child with cleft lip (with or without cleft palate) appear to reduce the recurrence rate to about one third of that expected. The numbers for the cleft lip studies were not large and the reductions in the recurrence rates were of borderline statistical significance.

Experimental studies conducted on animal models offer a more controlled approach and provide different sorts of information such as the developmental alterations leading to the malformations. Although the human relevance of the results must be interpreted with a great deal of caution, they provide further information on which to base human studies. For example, a mouse model for the fetal alcohol syndrome suggests that the major alterations in craniofacial development result from very early anterior neural plate damage subsequent to the administration of “binge” doses of alcohol (ethanol) administered over a very short period. The mouse studies suggest that the critical exposure time would cover approximately the 17th and 18th days of human pregnancy.

Also in mice, elevated levels of maternal respiratory oxygen dramatically reduce the incidence of both spontaneous and environmentally-induced cleft lip. It is of considerable interest that a dietary supplement used in one of the studies on cleft lip recurrence in man stimulates oxidative metabolism.

Many problems remain such as the identification of high-risk pregnancies where the family history is negative. This is the case for most pregnancies which result in the birth of an infant with a craniofacial malformation. However, our understanding of the mechanisms involved in normal craniofacial development is increasing rapidly as is also our understanding of the interactions of genetic and environmental factors leading toward or away from developmental abnormalities. While major reductions in craniofacial malformations are currently unthinkable, hope for more rapid progress in the future is becoming brighter.