

monogenic dominant (OMIM 127000¹) and recessive (OMIM 244460¹) forms.

In addition to the previously reported family,² we recently ascertained some more patients in unrelated Bedouin families, who met the criteria for the diagnosis of KCS and had the same traits (microcephaly and psychomotor retardation) that distinguish the phenotype in Arab children from the classical profile of KCS.³ In one particular new, non-consanguineous, Bedouin family,³ a brother, who died at the age of 6 months, had the manifestations of DiGeorge syndrome (DGS) with major cardiovascular involvement, while his older sister had the Arab phenotype of KCS, without any cardiovascular manifestations. Cardiovascular involvement represents a consistent part of the DGS spectrum, but has not been emphasised as a major component of the KCS profile. Thus, within this particular family, a clinical link between Kenny-Caffey syndrome and DiGeorge syndrome was established by the coexistence of the two phenotypes in the same sibship. Moreover, a paternally inherited 22q11 microdeletion was also identified in this new family, a finding that adds further support, in addition to the clinical link, for a molecular link between KCS and DGS.^{2,3}

The identification of 22q11 microdeletion in only a fraction of patients with KCS is not surprising. The lack of 22q11 microdeletion in some Bedouin patients with the Arab phenotype of KCS has been previously reported⁴ and has also been our experience in some of our recently ascertained families.³ Genetic heterogeneity seems to be evident in KCS, as it is in DGS, certainly with room for other possibilities in addition to monosomy 22q11. Because of the clinical overlap between KCS and DGS, it would be reasonable to explore the possibility that, like DGS, some patients with KCS might have some abnormality of chromosome 10p. There is also potential for the possibility of monogenic inheritance, although it is our opinion that the comparison between KCS and Bernard Soulier syndrome is probably less valid than one may think. It seems more likely that KCS is a contiguous gene syndrome, as is probably the case for DGS, rather than being the result of one gene which happens to be located within 22q11, as in the case of Bernard Soulier syndrome. Also, one additional mechanism that could account for the inter-/intrafamilial phenotypic heterogeneity in KCS is the role of interactions with individual background genes that would be expected to modify the phenotype.

Although the report by Khan *et al.*,⁵ also from Kuwait, promotes the notion of autosomal recessive inheritance for the Arab variant of KCS, none of the families mentioned in this report was investigated for potential 22q11 hemizyosity. In that report, the presence of parental consanguinity and several affected family members of both sexes, has been used to point to autosomal recessive inheritance as the mode of inheritance in Bedouins with KCS. It is recognised that the presence of consanguinity and multiple affected members in the same sibship would "suggest" autosomal recessive inheritance. On the other hand, the same criteria should not be seen as evidence that "confirms" autosomal recessive inheritance, as the paper by Khan *et al.*⁵ emphatically stated, even in the title. In Kuwait, with consanguinity occurring in more than 50% of marriages, one would expect an excess of recessively transmitted diseases. By the same token, the widespread

parental consanguinity among Bedouins tends to reduce the importance of this parameter in the analysis of the mode of inheritance.

Presumably, the presence of some peculiar traits in Arab patients, microcephaly and psychomotor retardation, has caused some confusion in the diagnosis of such cases. To that effect, reports¹ of some Arab children with the phenotype described above^{2,3} have been lumped into an isolated category (OMIM 241410¹) that has been designated "Sanjad-Sakati syndrome" in the McKusick catalogue, after the authors who first reported this phenotype in Saudi Arabia. Surprisingly, the Bedouin patients recently reported by Khan *et al.*⁵ have been listed in OMIM as part of the presumed autosomal recessive entry of Kenny-Caffey syndrome, despite the fact that they have the same "Arab phenotype".

We have been prompted to review medical publications for cases with the phenotype mentioned above in an attempt to determine whether they represent a separate syndrome or an Arab variant of KCS. The details of this review are described elsewhere.³ Our results indicate that the main features of the Arab phenotype are very similar, if not identical, to the KCS phenotype. At least in part, the presence of microcephaly in Arab patients is probably apparent, considering the global reduction of their anthropometric indices consequent upon their severe pre-/postnatal developmental retardation. While medullary stenosis of the long bones seems to be the most consistent finding in KCS, it is only seen in a smaller fraction of Arab cases. However, this number may be an underestimate since in some of the reports describing this Arab phenotype, there was no mention of any radiological assessment to verify the presence or absence of medullary stenosis. Finally, there are some different possible alternative mechanisms to explain the association of the Arab variant of KCS with some peculiar traits. One attractive possibility, for example, is the interaction with certain background ethnic specific mutations.

Again, we would like to re-emphasise the coexistence of both DGS and Kenny-Caffey syndrome (or its Arab variant) in the same sibship, as described previously,³ which indicates that these syndromes should be seen as a spectrum of a host of traits rather than being rigidly classified into separate entities.

In conclusion, for the evaluation of the genotypic/phenotypic heterogeneity encountered in KCS and its Arab variant, more thorough effort is needed through a world wide collaboration between different centres.

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Tricuspid atresia in sibs

Tricuspid atresia is a rare cardiovascular malformation (CVM) and familial recurrence is uncommon. In the Baltimore-Washington Infant Study (BWIS),¹ one girl (of 93 probands) with tricuspid atresia had a sister with an unspecified CVM. Weigel *et al.*² reviewed the occurrence of heart defects in 210 sibs of 96 probands with tricuspid atresia. One boy had an older sister with atrial septal defect (not specified whether secundum or primum type) and another older sister had mitral valve prolapse. Grant³ described a boy with tricuspid atresia with pulmonary stenosis whose younger sister had Ebstein anomaly. We report the first instance of tricuspid atresia in sibs.

The proband, an Italian boy, was diagnosed at birth by echocardiography and catheterisation with classical tricuspid atresia. He had levocardia with situs solitus of the atria and viscera, right atrioventricular valve atresia, D ventricular loop, and normally related great arteries. At the age of 5, he had surgery for a right atrial-pulmonary artery Fontan anastomosis, but died shortly afterwards of heart failure.

The younger brother, now 7 years old, was born eight years later to the same parents. He had the same cardiac anatomy as his brother and was treated with a Glenn superior vena cava-pulmonary artery shunt. He is currently a candidate for a Fontan-type anastomosis.

Neither boy had dysmorphic facial features or non-cardiac malformations. High resolution prometaphase (1250 bands) chromosome analysis was normal in both (46,XY). Fluorescent in situ hybridisation was negative for chromosome 22q11 microdeletion. The family history is negative for cardiovascular malformations. The parents are not related. Auscultation of them was normal; echocardiogram and electrocardiogram were refused. The maternal prenatal history was negative for exposures.

The recurrence risk for sibs with tricuspid atresia is low, about 1.0%.^{1,2,4} The family in this report typifies the challenge of providing accurate genetic counselling for many families with non-syndromic CVMs. Assuming the parents are not affected, the suggested risk of recurrence after two affected sibs triples to 3%.⁴

The occurrence of tricuspid atresia in two brothers may tempt one to speculate that autosomal or X linked recessive inheritance is present, implying a much higher risk of recurrence. Further evidence for an X linked gene is suggested by the significant odds ratio for males with tricuspid atresia (1.93) in the BWIS, which follows in frequency the more familiar male predominance of d-transposition of the great arteries (2.57) and aortic stenosis (2.52).⁵ The parents have not had echocardiography to determine if they have a clinically asymptomatic microform of tricuspid atresia, which would implicate autosomal dominant inheritance. As our understanding of the genetic factors causing CVMs increases, so may our ability to counsel specifically rather than using empirical data only.

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The Science behind Jeans for Genes Day: Teaching Packs for Primary (Key Stage 2) and Secondary (Key Stage 4) Schools. M Pembrey. The Progress Educational Trust.

It is often suggested that if genetics teaching within the national curriculum could be focused on practical issues that could affect students themselves (such as genetic diagnosis and screening), this change in emphasis could help them to learn by involving their natural interest, and also prepare them for the impact of current genetic advances on their adult lives. However, teachers need help from expert geneticists if this is to come about.

Professor Marcus Pembrey has an unusual ability to communicate genetic concepts in imaginative ways, and has put his ability to work in creating these two teachers' packs, adapted to specific stages of the national curriculum. The packs are intended to support teachers in teaching genetics in a realistic way that will be useful for students in later life as well as supporting educational objectives. Each pack consists of (1) a resource book for teachers, the "Progress Guide to Genetics", and (2) a file of four case studies, which can be photocopied for the children: these are the same in both the primary and the secondary packs. There are also (3) teachers' notes, and (4) four worksheets, also to be photocopied: these differ between packs.

The materials are imaginative and attractive. For example, the worksheet for primary schools shows a picture of Professor Pembrey's own family, with clues for drawing up a family tree, the common symbols used, and hints to help young children learn the principles of pedigree drawing. One worksheet

explains the structure of DNA, the way it is packed into chromosomes, and the location of the chromosomes in the nucleus of the cell. Another shows some organs of the human body, challenges the students to place them in a body outline, and explains which of the organs can be affected by the genetic disorders outlined in the case histories. The teachers' notes include suggestions for games that can be used to illustrate, for example, the pairing principle that permits faithful replication of DNA. The secondary school pack uses the same basic resources to develop the basic concepts of genetics further. Subjects tackled include Mendelian inheritance and inheritance of sex, replication of DNA and the function of genes, inheritance of genetic disease, and genetic testing in the family and its uses. The teachers' pack includes information to assist teachers in discussing complex issues, such as prenatal diagnosis and other difficult choices.

The progress guide to genetics also illustrates Professor Pembrey's flair for simple, benign, and graphic illustration, and includes the images used on the worksheets. However, the text is not as clear and simple as the diagrams. It uses a conversational tone, which may be helpful for people who have no previous understanding of genetics, but does not quite match the simplicity and clarity of the worksheets.

This is an excellent resource, not only for teachers, but for nurses, genetic counsellors, and others who sometimes go into schools to help teach pupils about genetic issues.

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