06.01
Maternal serum screening for Down’s syndrome: a survey of midwives’ views
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The Northern Genetic Service is currently responsible for the maternal serum screening services offered by 16 units across the region. A system for each unit to have a coordinator was introduced. A previous survey of midwives by questionnaire, in one health authority was reported in 1996, from which it was suggested that other unit coordinators could repeat the survey in their locality. To date, 7/14 remaining units have completed the survey. Although the response rate varied around 50%, responses to each question showed little inter unit variation. The majority of midwives support the principle of maternal serum screening and consider it should be available as a NHS provision for all pregnant women regardless of age. Not all midwives were found to be confident with key aspects of counselling, even when regularly involved with service delivery, reflecting the need for additional training. Most welcomed regular updating. The role of the unit co-ordinator was not always recognised. National coordination of maternal serum screening is now under review. This study demonstrates the potential benefits of a co-ordinated approach but highlights the difficulties in achieving appropriate recognition of the co-ordinator by the midwives.

06.06
A Web site for Public Health Genetics
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A Web site (http://www.medinfo.cam.ac.uk/pgu), managed by the Public Health Genetics Unit, has been set up to provide a source of news and information about the public health aspects of genetics. The site contains regularly updated information about the genetics and epidemiology of common diseases, and about progress in genetic testing and screening for susceptibility to these diseases, together with news and discussion about the ethical, legal and social and insurance implications of genetic testing and screening. Links are included to further sources of information including reports of the Government’s Advisory Committees, genetics journals and newsletters, and other organisations concerned with the public health aspects of genetics.

06.08
Ethical and psycho-social issues encountered in a linkage study of a family with CADASIL (Cerebral autosomal dominant arteriopathy with sub-cortical infarcts and leukoencephalopathy)
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We were referred a gentleman who was a member of a large pedigree with several people affected by CVA at an early age. CADASIL seemed a likely diagnosis. The proband, 4 siblings and his eldest daughter were clinically affected so we proposed linkage analysis to the CADASIL locus on chromosome 19q12. Our study comprised DNA analysis; MRI scan; neurological examination and a psychometric questionnaire. Following positive linkage to 19q12 the clinically affected family members were found to have the CADASIL mutation. 3 other family members had changes on their MRI scan consistent with early stages of CADASIL despite being asymptomatic. DNA analysis confirmed the presence of the mutation in these individuals. A full explanation of the study and the implications of both a negative or positive result had been given before individuals decided to participate in the study. All participants chose to be given their results personally. Two asymptomatic individuals shown to have the mutation have required follow-up by the Genetic Nurse. One has specifically requested that we do not inform his GP of our findings. What started as a ‘linkage study’ has provided a ‘predictive test’ for these asymptomatic individuals, the implications of which have been far reaching.
06.23
Neonates with transient hypertrypsinaemia and heterozygous for delta F508 are at risk of a second mild mutation
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Routine screening of neonates for cystic fibrosis (CF) from this and other centres has identified an excess of deltaF508 heterozygosity in babies with transient hypertrypsinaemia. Moreover, on retesting initially hypertrectic babies at 27 days age, deltaF508 heterozygotes were found to have higher blood concentration than those without deltaF508, leading us to suspect that the former may be at increased risk of a second, possibly mild, CF mutation. To investigate this hypothesis, a cohort of 91 anonymous samples was screened for further mutations. Screening of 17 exons, intron 12 and intron 19 has shown 19 compound heterozygotes (R117H x8, R117H x3, 3849+10kb x2, P67L, R75X x2, F693L, F1052V, R1066H, R851X, S987T) and included both mild and severe mutations. Thus the risk of a second mutation in this cohort was 21% overall. However, examination of the day 27 IRT's showed a second IRT >25ng/ml conferred a risk of 41% of a second mutation; conversely a second IRT of <25ng/ml was associated with a risk of <6%, suggesting that the second IRT may be a good biochemical marker for a second mutation. Screening of the remainder of the CFTR gene in this cohort will be completed by the summer.

06.25
A ready-reckoner for rapid genetic analysis of complex traits.
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The theoretical relationship between penetrance (P) of incompletely penetrant traits and their concordance rates in twin pairs has already been described. Concordance in MZ twins equals P/2-P, irrespective of the mode of inheritance or number of genes involved. If disease occurs only in the presence of a single dominant allele, concordance in DZ twins equals P(1-P). If due to the joint presence of two dominant alleles, DZ concordance equals P(P-1-P); for three dominants, P(1-P), or for four dominants, P(3-P), etc. The same expressions define the theoretical DZ concordance when disease has a recessive or partially recessive basis. This presentation illustrates the relationship between MZ and DZ concordances as a two-dimensional plot, with different zones of the graph corresponding to different numbers of genes. The purpose of this presentation is to enable the rapid genetic analysis of complex hereditary conditions without recourse to difficult mathematics. A point defined by the MZ and DZ probandwise concordance rates for that disease is entered on the graph, its position immediately indicating the penetrance of the disease in MZ twins, as well as the most probable number of major genes involved in causation. Distinction between dominant and recessive modes is made by cross-generation comparison of empirical risks in first and second degree relatives. The device should enable researchers and counsellors who are not skilled in mathematics to make rapid assessment of the most probable g... [Abstract truncated at 1500 characters]
06.27
The status of genetics education on diploma-level training courses for nurses in the United Kingdom

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A survey has been carried out of genetics education provided on all diploma level training programmes for nurses in the UK. A questionnaire was devised that aimed to establish the current status of genetics education and the attitudes and opinions of those with responsibility for the provision and development of curricula. All nursing branch programmes were contacted; the response rate was 84% (n=142). Whilst genetics is taught on all but two training courses, the teaching varies widely in respect of content, delivery and time allocated. The majority (72%) of nursing courses incorporate 10 hours or less of genetics. Clinical exposure is used infrequently to facilitate learning. Most courses do not have compulsory assessment for genetics. The majority of respondents (81%) agreed that genetics will have a major impact on health care, and become an increasingly important issue in education. Only a small majority (58%) agreed that genetics should have a higher profile in professional training and many respondents (68%) felt that the teaching they were already offering was appropriate to meet patient needs. We question whether current training can provide nurses with the basic genetic literacy needed to respond to developments in genetics as they impact on health care.

06.31
Intermediate zone alleles in Fragile X syndrome

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Fragile X syndrome is the most common cause of inherited mental retardation and is the most frequent referral reason for samples received in our laboratory. Since the introduction of PCR-based repeat sizing in 1996 we have been able to differentiate alleles in the 45-55 CCG repeat 'intermediate' zone which lies between the normal and premutation size ranges. The clinical significance of carrying an allele in this size range is unclear but there may be an increased risk of allele expansion in future generations. Of 1441 samples tested, 24 were found to lie within this intermediate range, compared with 17 full mutation expansions identified in the same period of 29 months. Comparison of the clinical information provided showed a wider variation of phenotypes in individuals with intermediate sized alleles than in those with full mutations. However unspecified developmental delay was the most common feature in both groups. Analysis of the mothers of 4 individuals with intermediate alleles showed that these alleles had been inherited without any intergenerational increase in repeat number. We feel that the possible clinical implications of finding an allele in the intermediate size range needs further clarification.