careful counselling the parents decided to proceed with prenatal diagnosis and a chorion villus biopsy was performed. A high risk result was obtained and the pregnancy terminated. This case represents the first prenatal diagnosis for VHL disease. Although prenatal diagnosis for VHL disease is now available, the likely demand is uncertain.

Molecular genetic analysis of spinal muscular atrophy
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The spinal muscular atrophies (SMA) are a group of inherited disorders characterised by degeneration of the anterior horn cells of the spinal cord, resulting in muscle wasting and death. Common etiological factors include flanking chromosome aberrations, which may be deletions, duplications, inversions, or translocations. In addition, there is considerable variation in the phenotypes of the deleted segment. Some SMA subgroups are transmitted as an autosomal dominant or recessive trait, whereas the majority of SMA cases are sporadic, unbalanced translocations of variable size.

A comparison of three cytogenetic measures of chromosome instability in ataxia telangiectasia
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Seven families with ataxia telangiectasia were examined. In one case of Nijmegen breakage syndrome patients were investigated to compare three different cytogenetic methods of assessing chromosome instability. Original diagnosis was based on clinical phenotype and immunoreaction sensitivity as assessed by a reference laboratory. Cytogenetic preparations were made from peripheral lymphocyte cultures set up from 10 controls and 19 family members. The preparations were scored for the following: (1) spontaneous rearrangements, particularly involving chromosomes 7 and 14, (2) chromosome aberrations following X irradiation in G2 phase of the cell cycle, (3) chromosome aberrations induced by the chemical mutagen adriamycin in G1/S phase of the cell cycle. All methods were found useful, with no overlap between controls and AT patients. However, the range of values suggests that each test might not always provide clear diagnosis on its own. Spontaneous rearrangements were detected at a mean level of 12% in AT patients (range 6 to 32) compared with 0-3% in the controls (range 0 to 2). X irradiated AT cases (100 Gy) had a number of aberrations per cell of 1-03 (range 0-6 to 1-65) compared with control levels of 0-19 (range 0-15 to 0-45). Adriamycin treated AT patients (0-01 µg/ml) gave a mean number of 2-52 aberrations per cell (range 1-1 to 4-15) as compared with a mean of 0-35 in controls (range 0-25 to 0-65). These results suggest that sensitivity to adriamycin might be a useful additional diagnostic test for AT, especially if X irradiation is difficult to arrange. Scoring of chromosomal aberrations is a valuable and available screening test for ataxia telangiectasia, but at least two methodologies should be used for definite diagnosis.

Eight cases of 7p deletion: clinical features, cytogenetic findings, and molecular studies
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Craniosynostosis or premature closure of the cranial sutures is a common malformation occurring in approximately 1 in 2000 children. To date more than 70 different types of 7p monosomies have been described, approximately half of which have been associated with craniosynostosis. There is considerable variation in the phenotype associated with deletion of the 7p11.2-12 site. Analysis of a panel of eight 7p deletion cases (three with craniosynostosis) was undertaken using informative DNA probes, in order to characterise and define the extent of the deletions at the molecular level. In six of these, unbalanced translocations, t(7p;2p), resulting in an interstitial 7p deletion, and one 7p deletion resulting from the unbalanced product of a paternal unbalanced insertion. Parental DNA was available for analysis in four out of six of these deletions; these cases of 7p deletion was found to be of maternal origin, and in two parental origin could not be determined.

The results of the DNA studies, together with a summary of the relevant clinical and cytogenetic findings, are presented. Our findings have enabled us to further refine the localisation and relative position of five probes and two loci. (1) p57-11, previously mapped to 7p14-ppter, does not extend proximally to p14 as case 4 is heterozygous for this probe. (2) TM102L, previously mapped to 7p14-ppter, does not extend proximally to p14 or terminally to pter, as case 7 (del 7p15-p22) is deleted for this probe and heterozygous for MS31 (pter). (3) CR1-R944 and CR1-P137, assigned to 7pter-q22, have previously been shown to be tightly linked and to flank the Greig-cephalopolysyndactyly (GCP) translocation breakpoint. However, cases 3 (del 7p13) is deleted for CR1-R944, but heterozygous for CR1-P137, indicating that these two probes are not co-located apart that CR1-R944 is restricted to 7p13 only, whereas CR1-P137 maps more distally. (4) TCRG, previously mapped to 7p15, maps more proximally, as case 2 (del 7p12.2-p14.2) is deleted for this probe, but case 3 (del 7p13) is heterozygous. This suggests that the TCRG gene is located at 7p14.1-14.2. (5) As craniosynostosis is an occasional feature in GCP, it has been considered possible that the CR2S and GCPS loci were one and the same, but the results of case 4 (del 7p13-p15) suggest that they are distinct. Cases 6 (del 7p15-p21.2) and 8 (del 7p22.1-pter) do not have craniosynostosis and therefore the
CRS1 locus is most likely to be in 7p21.2 or 7p21.3. Case 8 is also heterozygous for the probe but no evidence of the 5 (del 7p15-p21.2) and 7 (del 7p15-p22).

Trisomy 22: in situ hybridisation and molecular studies

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We present a case of a baby girl with the following clinical features: micrognathia, cleft lip, broad nasal bridge, ocular ptosis, epicantthic folds, preauricular pit, posteriorly rotated ears, short neck, widely spaced nipples, hypoplastic nails, and joint contractures. Birth weight and length were below the 3rd centile. The baby died at 8 months of age. Cyto genetic studies using GTG banding of lymphocytes and skin fibroblasts showed a chromosome complement of 47,XX,+22. This finding was confirmed using in situ hybridisation with a chromosome 22 library (pBS-22). DNA samples from both parents and the affected baby were analysed with a minisatellite probe pMS619, which recognises a VNTR polymorphism. The baby inherited three alleles, two identical to the two maternal alleles and one identical to that of the father. We therefore surmise that non-disjunction occurred during maternal meiosis. Trisomy 22 is the second most frequent autosomal trisomy detected in spontaneous abortions but only a handful of cases of liveborn infants have been described.

Assessing the utility of fibroblast karyotyping

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A request for a fibroblast karyotype represents a significant and expensive cytogenetic investigation. In the light of an increasing demand for this investigation over the last several years an analysis of the previous five years of skin chromosomal analysis was undertaken in an attempt to evaluate its success in the clinical setting. Each request was classified with respect to the blood and skin karyotype into one of six classifications: blood normal/normal/equivocal versus skin normal/normal. A total of 54 requests from live (non-moribund) subjects was received over this time period. Of these 10 were reported as abnormal (18-5%) when a previous blood karyotype had been normal. This compared favourably, for a second line investigation, to the mean over a similar time period of 13-7% abnormality rate for blood samples processed in the laboratory. This audit also suggested whether to proceed with a skin biopsy in order to exclude a chromosomal aetiology.

Behavioural Science and Genetics Group

JOSEPINE M GREEN AND OTHER MEMBERS OF THE BEHAVIOURAL SCIENCE AND GENETICS GROUP

UK — nationwide.

Since January a group of social scientists including psychologists, sociologists, and health economists with interests in genetics, as well as a clinical geneticist, has been meeting informally, approximately three times a year. The group exists primarily to allow its members to keep up to date with each other’s research and to exchange ideas and information. A secondary aim is to inform non-social scientists of research on social and psychological aspects of genetic screening and related issues. Aside from meetings we have organised joint workshops, written some joint papers, and conducted some research together. Some members of the Group were invited to give presentations at the recent MRC Workshop on cystic fibrosis carrier screening. Future plans are to hold a symposium for geneticists and behavioural scientists to consider both the structure and content of future collaborative work.

Patient satisfaction: a pilot study

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A postal questionnaire was sent to a sample of families attending the Genetic Counselling Clinic in late 1990. Forty families responded (77%); 90% were very satisfied while the remaining 10% were satisfied most of the time. Many respondents commented on the professional, courteous, and friendly attitude of the staff. Preclinical visits, in particular, were said to be very helpful (to 94% of families) as well as the time and care taken in explanations. However, 25% of families found the length of time before a clinic appointment to be too long. This study endorses previous findings which identify affective aspects as key determinants of general satisfaction with genetic services.

An autosomal dominant muscular dystrophy characterised by early onset of contractures

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We describe two brothers born to healthy, unrelated parents with similar abnormalities affecting predominantly the brain and skeletal systems. Both boys were noted to have relatively large heads with poorly calcified skulls and very large fontanelles. The eyes appeared prominent (with congenital glaucoma in the second) and there were contractures of hands, feet, and knees, with expanded, flattened tips to the digits. Skeletal surveys showed osteo dysplastic changes including delayed maturation, slender, poorly modelled long bones and, in one boy, widespread punctate calcification in epiphyses. CT scan of the brain showed marked cerebellar hypoplasia and cerebral atrophy. Both boys were profoundly handicapped. The older boy died at the age of 17 months having had recurrent infections and infantile spasms. His brother is still alive at 10 months.

PKU in south west England: a new mutation in the leader sequence of the phenylalanine hydroxylase gene and more similarity with the French Canadians

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To date, about 40 mutations have been defined at the phenylalanine hydroxylase (PAH) locus which give rise to phenylketonuria (PKU). Some are unique to individual races or ethnic groups and are in linkage disequilibrium with specific haplotypes. Others are more widespread and several have been found on a variety of haplotype back- grounds. We report a CAC to CCC transition in the leader sequence of the PAH gene,