experts. Some knowledge of dysmorphology is clearly an advantage in this difficult area and the system must be contrasted with a much larger specialist database at the Institute of Child Health, London*.

In addition to those on the X chromosome (see report by A P Read, *J Med Genet* 1987;24:187-8) microdeletions have now been described for some seven autosomal diseases such as Wilms'-aniridia (11p13) and Langer-Giedion (8q23) syndromes. The high resolution banding and in situ hybridisation necessary to identify such microdeletions and duplications are costly and, unless the site is already suspected, difficult for routine use in undiagnosed syndromes.

The fragile X syndrome received considerable attention. Not every patient had the classic phenotype and not every subject with the phenotype could be shown to have the cytogenetic abnormality. The clinical features require further definition. The differential diagnosis includes Sotos, the 'happy puppet', and Rett's syndromes. Some 20% of males with fragile X appear to be non-penetrant and perhaps as many as one third of females with it are retarded. Cytogenetic studies in young women are reliable in some laboratories, but DNA markers when validated should prove much more satisfactory.

Rett's syndrome may be the second commonest cause of mental retardation in females (perhaps comparable with fragile X in males). These girls are normal at birth and then regress, with the appearance of wringing of the hands and later loss of use. There is ataxia with the development of secondary microcephaly and also hyperventilation. No diagnostic test has yet been confirmed.

The syndromes of abnormal sexual differentiation attracted much attention. Correlation of the different segments of the X and Y chromosomes had proved difficult because of conflicting evidence. There is perhaps greater variation at the molecular level in these chromosomes than had been expected, but also more homology. As Dr J L Simpson pointed out, there are multiple biases in published reports, bias of ascertainment (the reason for referral for investigation) as well as bias of reporting. The testicular determining factor appears to be on Yp11-2-3 and that for ovarian function on Xp11-2, though there probably are some relevant genes on Xq and possibly Yq (for example, conferring fertility) as well as on the autosomes. Re-appraisal of these subjects at clinical, cytogenetic, and molecular levels should clarify the function and position of the genes involved in normal sexual differentiation.

*There are plans to combine these and other databases.

Finally, we were all given a world wide listing of genetic centres. Unfortunately, this ambitious project was not very successful in its presentation, at least as far as the United Kingdom was concerned being too inaccurate to be of value. One wonders to whom the detailed information provided would, in any case, be useful, as it will be very difficult to keep it up to date

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'Spontaneous and induced chromosome aberrations in germ cells of mammals and man'

Several satellite meetings were held on Saturday 27 September 1986 following the Seventh International Congress of Human Genetics in Berlin, and this was one of them. Held in the Technical University, Berlin, and organised by Professor Dr Gunter Röhrborn, Institut für Humangenetik und Anthropologie, Universität Düsseldorf, the meeting aimed to look at the current state of the art with regard to the use of mammalian germ cells in mutagenicity testing.

In a brief introduction, Röhrborn pointed out that, since the Ames test had become available, most mutagenicity testing had involved the use of somatic cells and germ cells were less in favour. There was, nevertheless, still a real need to investigate the possible inheritance of genetic and chromosomal anomalies that might arise through exposure of the gonads to environmental substances. To date no known chemical has proved positive in germ cells while being found negative in somatic cell tests, but when a chemical is found positive in somatic cells, it is still important to test whether or not it is positive in the germ line.

The whole of the morning session was taken up with presentations of data concerning the analysis of human spermatozoa chromosome complements, by means of the human sperm-hamster egg in vitro fertilisation method, pioneered by Rudak and colleagues in 1978. R H Martin (Calgary) gave figures for 30 individual sperm donors, all men of proven fertility, analysed over a three year period. Figures for aneuploid and structurally abnormal complements were compared with an existing set of published data based on 33 previous donors. The aim was (1) to determine the distribution and variation of abnormalities between different men.

(2) to determine any possible effects of age, (3) to assess possible correlations between sperm morphology and genome content, and (4) to check variations in egg penetration rates.

A total of 1582 sperm complements was analysed from the 30 men whose mean age was 34.7 years (range 22 to 55 years). Numerical anomalies occurred in 5.0% (as found previously) and structural anomalies in 6.1%. Differences in frequency of anomalies found between various laboratories around the world employing the same techniques were noted; these could possibly be attributable to the small numbers of donors analysed by some of the groups.

No association between age and aneuploidy was found, but some increase in structural abnormalities was recorded with age. No relation between genome content and sperm morphology was seen, but morphological defects did rise with age. No relationship between genome content or morphology and fertilising ability was found.

In another laboratory, Brandriff (Livermore) reported on the frequencies of structural abnormalities found in sperm genomes compared with those found in somatic cells, the aim being to see whether somatic cells can be used as predictors for what might be expected in germ cells. Only in one donor out of the 10 analysed was a correlation found, however, the remainder all showing much higher levels of abnormality in sperm than in lymphocytes. No correlation existed between SCEs and sperm chromosome abnormalities. The question of whether conformation of chromatin in meiotic cells, or alternatively the egg environment, might play a role in producing the high numbers of structural abnormalities seen in all the sperm series from various laboratories was considered.

Comparisons between sperm abnormalities and lymphocyte chromosome anomalies in one donor given ^{137}Cs irradiation in doses from 100 to 400 rads showed similar dose dependent rises and to the same level in both cell types. Sperm chromosomes showed more breaks than exchanges, while lymphocytes gave the opposite result. From Jendermy (Dusseldorf) came information showing that chemotherapy in one patient produced increased frequencies of sperm chromosome abnormalities even 26 months later.

Analysis of the sperm chromosomes in a t(13q;14q) heterozygote (Sele, Grenoble) recorded eight unbalanced genomes in 78 complements analysed.

A second batch of papers then considered the frequencies and kinds of anomalies, both spontaneous and induced, found in various germ cell stages of male mammals from mouse to non-human

primates. The use of dominant lethal mutations for estimation of genetic risk was discussed (Ehling, Munich), and data on the x ray induced frequency of translocations in Rhesus monkey and macaque spermatogonial stem cells given (van Buhl, Leiden). In the latter study, mouse and monkey differed in response depending on whether the exposure was chronic or acute. At acute exposure levels, the Rhesus monkey was about half as sensitive, while after chronic exposure twice as sensitive as the mouse. Differential cell killing between the two types of exposure was offered as the likely explanation. Data for the mouse (Arni, Basle) showed how extremely low is the occurrence of spontaneous chromosome aberrations in spermatogonia and 1° spermatocytes, but induction by various chemicals (adriamycin, bleomycin, TEM, vincristine, etc) showed mainly exchanges in spermatogonia, but breaks and fragments in spermatocytes. For a total of 10 compounds tested, most were found positive in spermatocytes and bone marrow but fewer were positive in spermatogonia. The maxim that a negative somatic result can be taken as a negative germ line result was found not to be entirely borne out in these studies, but, in general, bone marrow did show a greater sensitivity to the chemicals under test than did the germ line cells.

Tates (Leiden) then described a micronucleus test in rat early spermatids which he used as an indicator of damage to primary spermatocytes. He also demonstrated how, in *Microtus oeconomus*, evidence of non-disjunction could be readily detectable cytologically in spermatid nuclei, owing to the large and mainly heterochromatic sex chromosomes. No increases in sex chromosome non-disjunction were, however, detected in extensive analyses following radiation treatment. Diploid spermatids were produced. A detailed explanation of the F_1 translocation test in the mouse was given by Adler (Neuherberg) and its use in the detection of chromosomal aberrations described. The test recognises carriers of reciprocal translocations among the progeny of treated animals. A range of 25 chemicals was reported on, 14 of these being found positive in various studies. In general, spermatids were the most sensitive stage to translocation induction.

The meeting concluded with presentations by Hansmann (Göttingen) and Chandley (Edinburgh) on aneuploidy studies in animals (Djungarian hamster and CBA mouse) and the aetiology and frequency of aneuploidy in man. The induction of aneuploidy in Djungarian hamsters has been achieved by gonadotrophic hormone injections, the increases being dose dependent. When prepubertal females were treated, altered rates of meiosis were also found, with prolongation of germinal vesicle

breakdown being a significant feature. Correlated with this was a rise in aneuploidy, demonstrated by chromosome analysis of MII oocytes. Large pairs of chromosomes tended to be preferentially involved in non-disjunction in this species, and when fluorescent spindle preparations were examined, these chromosome pairs could be seen to be among the last to separate at anaphase I. Spindle changes were reported by Chandley for CBA mice studied at various ages covering the entire reproductive span. Post-ovulatory overripeness also gave rise to such changes, and a correlation with aneuploidy was

suggested. Ageing also correlates with delay in germinal vesicle breakdown in CBA oocytes, cultured in vitro from the dictyate stage to MI. This too could be an important factor influencing chromosome segregation in oocytes, biological ageing of the female thus leading to a general increase in non-disjunctional errors attributable to such defects.

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