Diagnosis of genetic disease using recombinant DNA. Third edition

The potential to analyze over 300 conditions using molecular genetic methods is now available. In this third edition, these authors summarise the exponential rise in reports dealing with such analysis up to the end of 1990. For a given condition, McKusick number, available probes, distance between probes and disease locus, method of detection, mutation type, and references are listed. Of 304 conditions, 152 are dominant, 82 recessive, and 70 X linked. For single gene defects the vast majority of lesions are point mutations or deletions; gene insertions, duplications, and rearrangements are so far relatively minor components. For 80 conditions, direct analysis is not available and linkage analysis by RFLPs cannot be avoided. Like previous editions, this article provides a valuable quick reference to the relevant reports on a given disease and thereby to the groups who might be able to assist in the analysis of a genetic condition. A quarterly update by computer printout or floppy disk is available on request.

JOHN C K BARBER

Couple screening for cystic fibrosis

The precise mechanics by which advantages of cystic fibrosis mutation detection might be applied to the benefit of the wider population in a humane and non-directive manner are the subject of scrutiny in a number of ongoing regional trials. In this article Wald suggests a couple based approach to population screening for cystic fibrosis. Mouthwash samples are obtained simultaneously from both partners. Either sample is tested for two of the most common mutations, identifying 80% of all mutations. If a mutation is present, the second (partner's) sample is then tested. In the authors' sample of 21 mutations, the couple are notified of a 'positive' result. This 'no news is good news' form of screening is justified mathematically by the hypothetical figures calculated for a mythical population. Clearly this approach has much to recommend it, especially in minimising anxieties which 'stepwise' screening inevitably arouses. My main concern stems not from the method of screening, but the overriding theme of the article that the aim of screening is handicap prevention with minimum side effect for minimum cost. Humane, non-directive screening must surely reflect the modern permissive society, with choices and not cross the boundary of repressive thinking which regards a 'positive' birth as a failure of screening. Is the eugenic pendulum on the upswing, Professor Wald?

W REARDON

Minisatellite repeat coding as a digital approach to DNA typing

Among the sources of human polymorphic DNA variation, the tandemly repeated hypervariable minisatellites (HVMs) are particularly useful; because of their high heterozygosity, they have been applied widely in genetic mapping and forensic work. Alec Jeffreys has always been at the cutting edge of this field, and in another technical tour de force has now advanced matters a step further. In 1990 Jeffreys et al showed that the repeat units of MS32 (one of the earliest known HVMs) comprised two types interspersed in a semirandom fashion, and distinguishable by restriction enzyme digestion. His group has extended this analysis using the polymerase chain reaction to identify and genotype variant repeats or MVRs. The order for any allele can be expressed as a simple binary code which turns out to be remarkably variable: all 334 unrelated subjects tested could be distinguished by their diploid MVR code. This method should avoid the subjectivity of band length techniques and has tagged the forensic use of HVMs, and will reawaken the debate about HVM function. Of 7/572 new mutant MVRs detected in progeny, two appeared interallelic than intra-allelic in origin, giving renewed credence to the theory (recently out of fashion) that HVMs serve as recombination hotspots.

ANDREW WILKIE

Standards for selected anthropometric measurements in Prader-Willi syndrome

In this report, Butler and Meaney have collected data over a six year period on linear growth of two sets of 72 twin partners discordant for Prader-Willi syndrome (PWS). The patients (42 males and 29 females) were all Caucasian and the diagnosis of PWS was based on infantile hypotonia, hypogonadism, delayed puberty and growth, obesity, and hyperphagia. The PWS patients showed significant differences in anthropometric measures compared with their non-deleted male and female counterparts. Of particular interest was the lack of difference between our PWS patients and the non-deleted females. These findings are consistent with the theory that the deletion of the paternal chromosome 15q13-q15 results in the phenotype of PWS. Our study, on a large sample of PWS patients, extends the observations of previous studies and provides a method for determining if this is a step forward in the clinical management of PWS.

T R P COLE

Diagnosis of susceptibility to malignant hyperthermia with flanking DNA markers

Malignant hyperthermia is one of the major causes of death owing to anaesthesia. It is a metabolic disorder of skeletal muscle and it can be triggered in susceptible people by certain anaesthetics and depolarising muscle relaxants. Early clinical diagnosis is often difficult and the European Malignant Hyperthermia Group test, based on in vitro studies of caffeine and halothane induced contractions in muscle, is sometimes equivocal. Susceptibility to malignant hyperthermia is inherited as an autosomal dominant trait with complete penetrance in most families. DNA linkage analysis of a large Irish malignant hyperthermia family with 27 members confirmed linkage with markers from 19q13.1-13.2 (multipoint D19S9-CYP2A-MSH-D19S16-APOC2, D19S10, D19S2) and with these markers the probability that five members of the pedigree who had not been investigated with the MHS gene was estimated to be greater than 99.7% for three of them and less than 0.3% for the remaining two. Both the rydane receptor (RYR1) and the caesium sensitive lipase gene (LIPE) also map to the interval between D19S9 and D19S16 and are possible MHS candidate genes.

ANDREW NORMAN