EDITORIAL

Recent Advances in Genetics

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A number of surveys have indicated that at least one in fifty newborn children have a major congenital abnormality, one in a hundred has a unifactorial disorder and approximately one in two hundred has major chromosomal abnormalities. If we consider the situation before birth, it was found that in early spontaneous abortions over 60% have a chromosomal abnormality. Therefore, the vast majority of chromosomal abnormalities present at conception are lethal, either in early pregnancy or later. The principle approach to the control of genetic disease is prevention through genetic counselling, where prenatal diagnosis is possible.

During the last fifteen years there has been tremendous development in the field of investigation of genetic disorders, in establishing the diagnosis prenatally and confirming the carrier status of the parent.

The following list of diseases are amenable to prenatal diagnosis (until June 1984).

I. Currently available

1. Sickle Cell
2. Thalassaemia
3. Christmas Disease
4. Neural Tube Defects
5. Mongolism

II. Gene specific probe (current use limited)

1. Alpha I anti trypsin deficiency
2. Phenyl Ketonuria
3. Certain causes of osteogenesis imperfecta congenita
4. Certain causes of growth hormone deficiency
5. Certain causes of Lesch - Nyhan syndrome
6. Certain causes of ornithine carbomyl transferase deficiency

III. Linked DNA probes (current use limited)

1. Duchenne muscular dystrophy
2. Huntington's Chorea
3. X linked retinitis pigmentosa
4. Haemophilia A.

The following are some of the methods used:

1. Restricting endo nuclease analysis.

   To recognise the specific sequence of bases in double stranded DNA molecules and cut the DNA wherever this restriction site occurs. Each specific gene will be present within a DNA fragment with a characteristic size.

2. Southern hybridisation.

   To identify the fragments of DNA containing any particular gene.

3. Recombinent DNA cloning technology.

   Can be used to insert and replicate the gene in bacterial cells and thus provide a large amount of the specific DNA fragments required for a detailed analysis of gene structure. Once a specific DNA fragment containing a gene has been cloned, it is a straightforward method to know the entire sequence of the cloned DNA. This assists in the detailed study of gene structure and in gene mapping.

4. DNA hybridisation.

   To detect disorders which result from gene deletion, e.g. Alpha Thalassaemia. The specific messenger RNA for the Alpha globin chain may be isolated from reticulocytes and a complementary strand of radio-active DNA (cDNA) synthesised using a viral reverse transcriplase and radio labelled bases. This is used to detect the presence or absence of Alpha globin gene.

5. Linkage analysis.

   If two genes are linked, it is possible to determine the nature of linkage (attraction or repulsion). The presence or absence of one gene may be determined by the presence or absence of the other, although the first gene is not expressed in the tissue under study. This method is used in the prenatal diagnosis of haemoglobinopathies e.g. sickle cell disease by using amniotic fluid cells (amniocytes) and therefore, there is no need to carry out foetal blood sampling.

The other field in which there are tremendous developments, is the field of oncogene or the gene which causes cancer.
A number of papers containing highly significant data regarding transformation inducing retroviral and cellular genes (the so called oncogene) have been published recently. The localisation of the position of some of these genes on human chromosomes provide support for the hypothesis regarding the role of chromosomal changes in the aetiology of cancer.

Methods used for the localisation of oncogenes.

1. Somatic cell hybridisation.

   In which human cells are fused with rodent cells.

2. In situ hybridisation.

   The oncogene DNA is amplified in an appropriate vector, radiolabelled with 3H or I135 and hybridised in situ to chromosomal preparations on a slide.

The following table shows the specific translocations (oncogene) associated with human neoplasms.

Specific Translocations Associated
With Human Neoplasms

Translocation	Neoplasm
t(9;22) (q34;q11)	CML, AML. ALL
t (8;21) (q22;q22)	M2-ANLL
t (15;17) (q22;q21)	APL
t (9;1) p21;q23)	AMoL
t(4;11) (p21;q23)	ALL
t(8;14) (q24;q32)	BL
t(2;8))p12;q24)	BL-variant
t(8;22) (q24;q11)	BL-variant
t(6;14) (q21;q24)	SCCO
t(3;8) (p25;q21)	SGT

'p' and 'q' refer to short and long arms of chromosomes, respectively. Translocations described in the Paris nomenclature. CML chronic myelogenous leukemia; AML acute myelogenous leukemia; M2-ANLL acute non-lymphatic leukemia of the M2 subset; APL acute promyelocytic leukemia; AMol acute monoblastic leukemia; ALL acute lymphoblastic leukemia; BL Burkitt's lymphoma; SCCO serous cystadeno-carcinoma of ovary; SGT salivary gland tumour.