Lecture 15.
Genetic monitoring of human populaton

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HUMAN GENETIC MONITORING

Genetic monitoring of human populations is the last step in identifying possible genetic hazards and is a system of long-term population studies on the control of the mutation process in humans. It is carried out to assess the dynamics of changes in the parameters of genetic load and other adaptive-significant features in a population in time and space by the levels of environmental pollution.

Mutations, to some extent reducing the viability of their carriers, belong to the ***genetic load*** of the population.

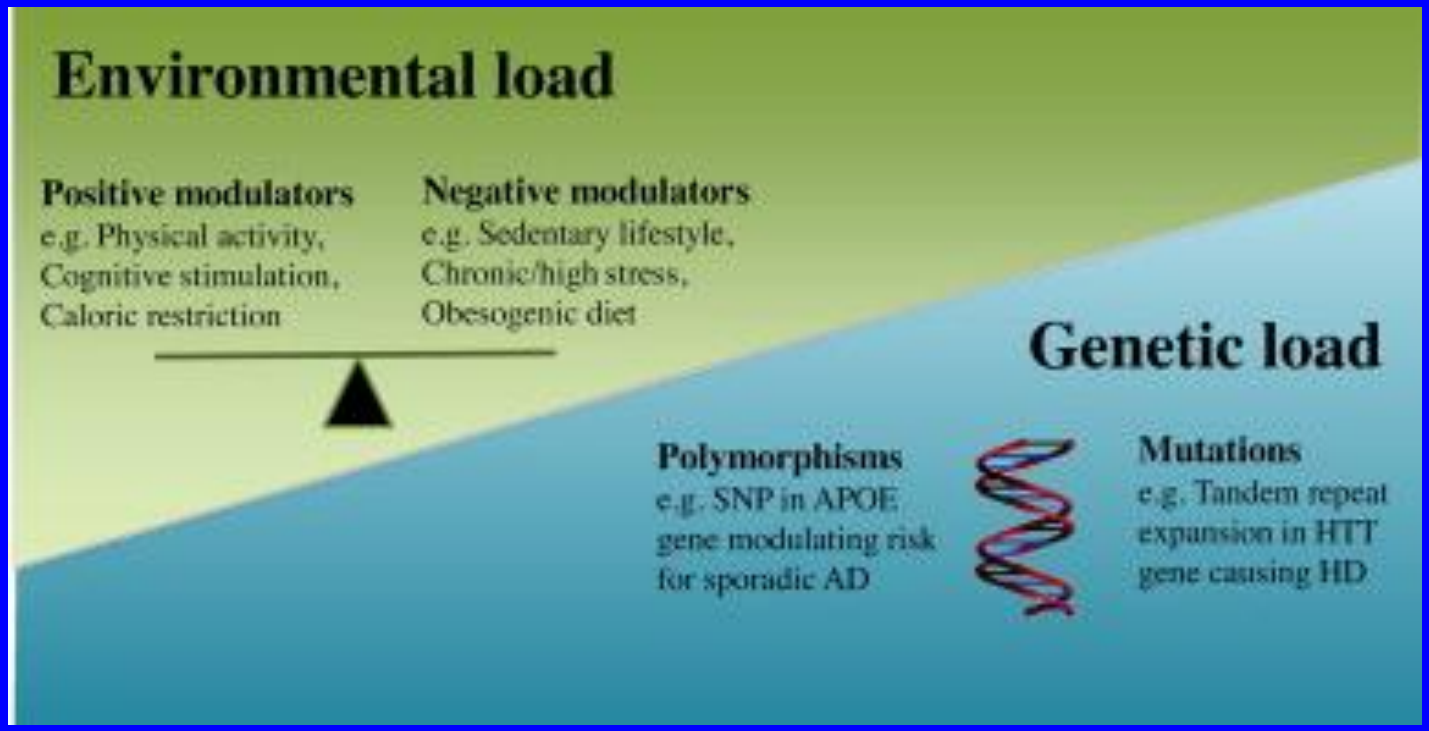
The following data of medical statistics can be used as parameters of genetic load:

1) individual hereditary diseases or diseases with hereditary predisposition;
2) congenital malformations - all or indicator phenotypes;
3) spontaneous miscarriages;
4) perinatal and infant mortality;
5) oncological morbidity or mortality.

HUMAN GENETIC MONITORING

The size of the genetic load of a population is determined by the size:

- ✓ mutational load - newly arising mutations
- ✓ segregation load - the presence in the population of heterozygous genotypes of polymorphic (segregating) loci that produce less adapted homozygous genotypes;
- ✓ substitute load - is detected when the adaptive value of the genotype changes (for example, when moving to other conditions).



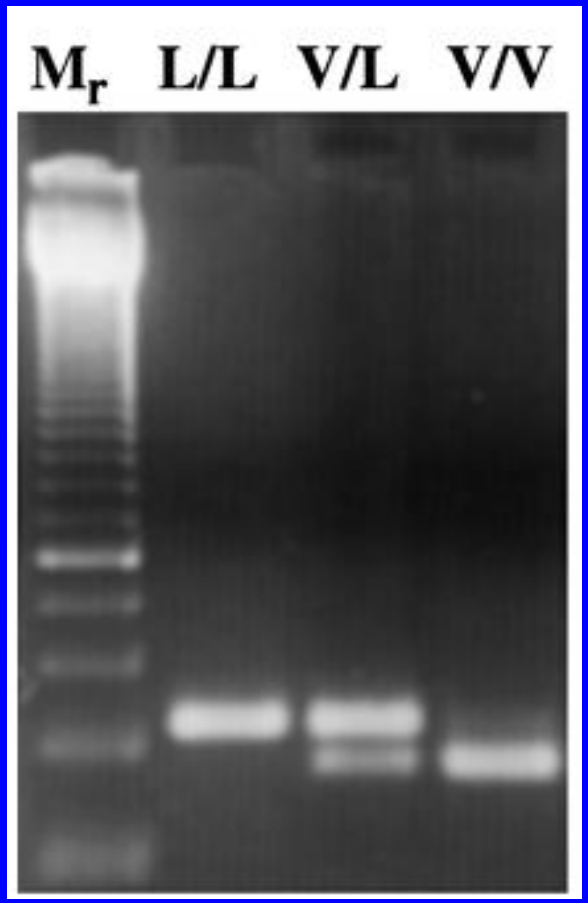
METHODS OF HUMAN GENETIC MONITORING

Biochemical methods.

Biochemical monitoring involves monitoring the frequency of newly occurring mutations based on the results of a study of the polymorphism of human blood proteins. It is based on the analysis of electrophoretic variants of proteins as markers of the corresponding structural genes.

Accounting for ''specific phenotypes".

By "specific phenotype" is meant a sporadic disease that is the result of a single gene mutation (autosomal dominant or X-linked to the inheritance type, which occurs at relatively high frequency and is easily recognized in the neonatal period): neurofibromatosis, achondroplasia, imperfect ontogenesis, polycystic kidney disease, etc.



METHODS OF HUMAN GENETIC MONITORING

Accounting for spontaneous miscarriages and congenital malformations.

This method has several advantages:

1) in the origin of spontaneous miscarriages and congenital malformations a significant place is occupied by the mutation component;

2) the population prevalence of spontaneous miscarriages and congenital malformations is large enough, therefore, requires a smaller sample size;

3) the studied parameters are recorded in medical institutions, which makes them easily accessible for analysis and provides the opportunity to study the dynamics of their frequency by year.

study	year	Trisomy	monosomy X	Triploidy	Tetraploidy	Double trisomies	Structural anomalies	Autosomal monosomy	Masaic	47.XXY	Polyploidy
Plachot	1989	66.67%	14.29%	4.76%	4.76%	4.76%	4.76%				
Causio	2002	62.07%	24.14%	6.90%	6.90%						
Lathi	2004	84.38%	3.13%	6.25%			6.25%				
Ma	2006	58.00%	10.00%		4.00%	14.00%	14.00%				
Bettio	2008	71.35%	7.57%	8.11%	3.78%	5.95%	3.24%				
Massie	2008	86.91%	3.74%	9.35%							
Kushnir	2009	78.09%	3.37%							6.74%	
Kim	2010	72.94%	6.88%	6.88%		6.42%					6.88%
Martinez	2010	59.47%	8.28%			5.62%	5.62%	0.59%	8.58%	0.30%	11.54%
Kroon	2011	68.11%	8.70%	11.59%	1.45%		5.07%		5.07%		
Bingol	2012	56.00%	17.33%	17.33%						6.67%	
Werner	2012	90.91%	4.55%				4.55%				
Li	2012	62.50%	3.57%	5.36%			21.43%	1.79%	5.36%		

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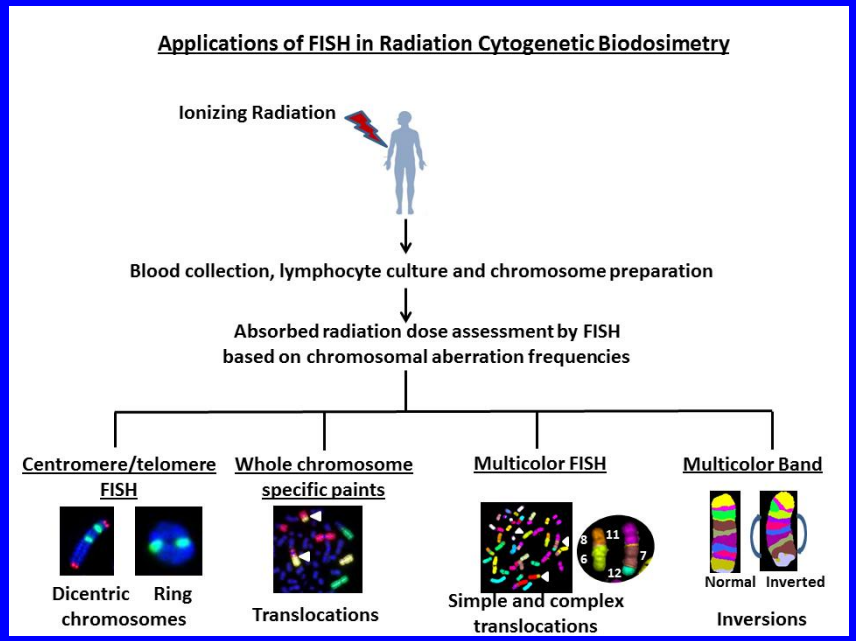
METHODS OF HUMAN GENETIC MONITORING

Cytogenetic methods

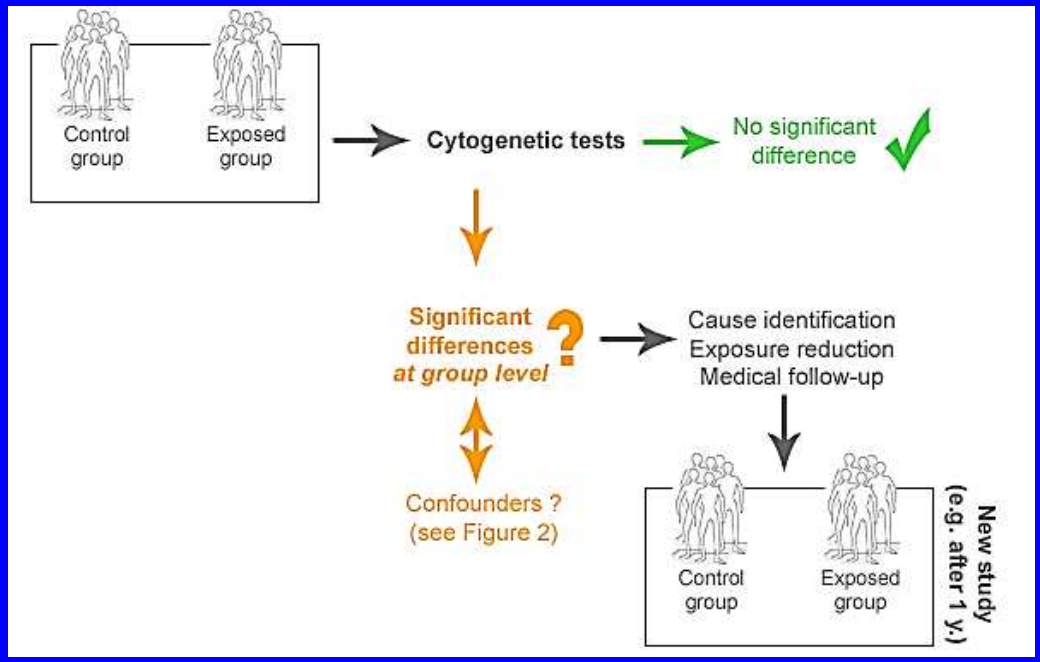
Cytogenetic monitoring is the accounting of cytogenetic abnormalities in human somatic cells in order to assess mutagenesis in somatic cells. Standard methods are used to account for the frequencies of chromosomal aberrations, micronuclei, and sister chromatid exchanges in human peripheral blood lymphocytes. In recent years, methods for recording micronuclei and other karyological changes in human exfoliative cells have become widespread.



RESULTS INTERPRETATION

Interpreting such trials is tricky and requires comparison with a matched control group. Results are mainly interpretable at the group level and not at the individual level, as no limit decision values for cancers or other diseases are defined. However some further analysis should be conducted to apprehend the origin of unexpectedly high level of genetic damages in a particular individual.

In case effects are observed at group level some measures should be envisaged to lower the exposure level. In occupational exposure, the aim will be to create better working conditions through implementation of measures to reduce exposure to mutagens/carcinogens in the work environment.



Thank you for attention!