

## **Prenatal screening and genetics**

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Although the term 'genetic screening' has been used for decades, this paper discusses how, in its most precise meaning, genetic screening has not yet been widely introduced. 'Prenatal screening' is often confused with 'genetic screening'. As we show, these terms have different meanings, and we examine definitions of the relevant concepts in order to illustrate this point. The concepts are (i) prenatal (ii) genetic screening (iii) screening, scanning and testing (iv) maternal and foetal tests (v) test techniques and (vi) genetic conditions. So far, prenatal screening has little connection with precisely defined genetics. There are benefits but also disadvantages in overstating current links between them in the term genetic screening. Policy making and professional and public understandings about screening could be clarified if the distinct meanings of prenatal screening and genetic screening were more precisely observed.

Key words: genetic screening, maternal and foetal tests, prenatal screening, scanning

2094 words

## **Introduction**

The phrase 'genetic screening' has been used for approximately 20 years.(1-4) This paper argues that genetic screening, in its most precise definition, has not yet begun to be used widely, although it is often discussed as if it is already in common use. The language has long preceded the practice and one reason for this is confusion between prenatal screening and genetics screening. Yet, so far, prenatal screening in many European countries has little to do with the new genetics. During our European research project, we discussed the use of key terms across different cultures, languages and disciplines. The concepts are (I) prenatal (ii) genetic screening (iii) screening, scanning and testing (iv) maternal and foetal tests (v) test techniques and (vi) genetic conditions. Our discussions are summarised in this paper in order to clarify differences between genetic and prenatal screening. We conclude that premature use of the term genetic screening opens the way for prenatal screening to become genetic without debate about whether societies, practitioners and prospective parents wish to make this step

### *Prenatal*

Prenatal generally means 'pregnancy up to birth'. Yet it can include the pre-conceptual period in relation, for example, to advice about smoking, alcohol and folic acid. The '>couple forming' stage involves prenatal considerations, such as when testing for thalassaemia or Tay Sachs among certain ethnic groups. Prenatal can be stretched to cover any stage of life when people are tested for their genetic carrier status in order to inform future family planning by themselves or their relatives.(3-6)

### *Genetic conditions*

Genetic conditions include the following.

- (I) A heritable condition determined by a single gene that is recessive (for example, cystic fibrosis or aspartylglucosaminuria (AGU) in Finland) or dominant (Huntington's chorea) or is linked to sex chromosome genes (haemophilia).
- (Ii) A congenital condition due to prenatal environmental effects on genes or chromosomes, but not showing clear Mendelian inheritance and so not genetic in a narrow sense, such as, chromosomal disorders (Down's syndrome) or neural tube, organ and limb disorders.
- (Iii) A condition which develops postnatally when a polygenic predisposition interacts with the environment (diabetes, cancer and, possibly, some behaviours) and which is also not strictly genetic.

### *Genetic screening*

The Nuffield Report (3) divides genetic screening into tests for single gene disorders, polygenic disorders, and chromosomal conditions. Yet these conditions are either not commonly screened for prenatally or are not precisely genetic.

### *Prenatal screening*

Screening is the systematic search for a specific condition among a large, asymptomatic subpopulation selected by demographic characteristics such as age, sex or ethnicity. Screening typically identifies at-risk groups for further diagnostic testing. Routine maternal screening, for age, weight, blood pressure, rhesus factor, syphilis, HIV and diabetes can be used to promote maternal, and thereby foetal, health. Screening for foetal conditions does not exactly fit the World Health Organisation (WHO) principles (7) and, so far, collects only partial and indirect evidence of probabilities through the parents' carrier status or through

maternal blood samples. As the screening does not directly access the fetus, the tests are not highly reliable. The main available 'treatment' and methods of 'improving' the natural history are through termination of pregnancy.

Mass screening overlaps with diagnostic testing when tests such as amniocentesis or chorionic villus sampling (CVS) are routinely offered as initial rather than follow-up checks, and offered to asymptomatic subpopulations such as women aged over 35 years.

### *Prenatal testing*

More precise diagnostic testing is possible when material associated with the fetus is obtained through amniocentesis or CVS. Because the tests are invasive and expensive and incur high maternal anxiety and the risk of miscarriage (8-11) they are generally offered to selected individuals after initial screening (such as of maternal serum) shows them to be a higher risk.

Tests can be classified by the evidence examined and the techniques used. The evidence is either the genotype (DNA) or the phenotype (how the condition expresses itself in anatomy, biochemistry, bodily functions or behaviours) which include the following.

(I) Molecular chromosomal tests (cytogenetics).

(ii) Single gene disorder tests which, because genes are invisible, test for proteins which the gene produces, or else genetic markers which indicate the position of the gene on the chromosome.

(iii) Biochemical tests, such as of hormonal changes in maternal serum possibly in response to a foetal condition.

(iv) Ultrasound scanning of the fetus.

To our knowledge, at present in Europe, no prenatal mass screening is strictly genetic in the sense of examining genotypes in a genetic laboratory. Single gene conditions subjected to carrier screening such as thalassaemia are tested for phenotypes in haematology laboratories. Serum screening for Down's syndrome and neural tube defects, which are not strictly genetic conditions, involves biochemical markers not DNA or DNA tests. Single gene conditions, which are investigated by DNA tests, are so far not routinely screened for, although this is likely to change if researchers succeed in isolating foetal blood from maternal blood samples.

### *Prenatal scanning*

Prenatal scanning, ultrasound, blurs differences between screening of large asymptomatic groups and diagnostic testing of individuals. As unfocused screening, scanning detects hundreds of anomalies. Scanning fits few of the WHO screening criteria,(7) which are clearer than more recently proposed criteria.(12-13) So far, the more common, serious and single gene disorders such as cystic fibrosis and haemoglobinopathies have not been clearly linked to features that can be detected by scans and may not have such features.

Scanning is too routinely used with large asymptomatic groups to count as individual testing, but the investigations are often too varied, individual, specifically diagnostic or linked to rare conditions to count as mass screening. The process of scanning would classify it as screening, but the outcomes of scanning would often classify it as testing (see table 1).

## **Discussion**

So far, prenatal genetic screening, in the precise sense of mass screening of asymptomatic groups for heritable genetic conditions confirmed by DNA analysis during pregnancy, does not yet occur in Europe. So why have prenatal and genetic screening been linked for two decades? (Refs 1-4) The advantages of such associations for prenatal screening and scanning

are that 'genetics' attracts public interest and respect, funding and prestigious associations with scientific progress and precise diagnosis.

The disadvantages are that overuse of the word genetics could be alarmist and often inaccurate.(12, 14) It can divert attention from the way social, psychological and economic conditions increase or reduce congenital disabilities and how 'the notion that health or illness can be predicted on the basis of DNA patterns becomes highly questionable' . (15) To present choices in terms of genetics can inadvertently make prospective parents feel ignorant and dependent on experts for guiding their decision making. (16, 17) Scanning further complicates consent because of the great range of possible conditions the scan may unexpectedly reveal. (18) Assumptions that genetics means Mendelian inheritance patterns can increase fears misleadingly (i) into worries about a kind of family infection or inadequacy (ii) into guilt when parents feel they should somehow predict and prevent affected births and (iii) into an implied or explicit overemphasis on biological determinism which can undermine confidence in human agency and social opportunities.(19) These trends are likely to encourage people to reduce their thinking about prenatal questions to terms of medical problems and solutions, the most immediate solution being termination of pregnancy.

Except for thalassaemia and sickle cell in some areas, the big step of introducing routine single gene prenatal screening has not yet been made. Attempts to screen for AGU in Finland were interrupted as impractical and unethical.(20) Talk of prenatal screening as if it is already genetic opens the way for it to become so without debate about whether society wishes to make this step. Discussion which links genetics to prenatal screening and scanning could misinform people who receive, plan and provide these services instead of clarifying their informed, unpressured decision making.

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**Table 1. Types of prenatal conditions, screening and tests**

<u>Types of tests</u>	<u>of genotypes</u>		<u>of phenotypes</u>			
	DNA		biochemistry	anatomy/function	history	
from:	amnio	blood	amnio	blood	scan	observation/ interview
subject:	foetal	parental	foetal	parental	foetalparental	family
<u>Examples of prenatal conditions/ maternal health</u>						
<u>Environment and maternal health</u>						
age, diet, weight					s	s
smoking alcohol					s	
infection			s			
hypertension					s	
diabetes (urine)			s			
<u>Environment and polygenic effects</u>						
neural tube,			t	s	u	s
organ and limb disorders			t	s	u	s
<u>Chromosomal</u>						
Trisomy 13, 21			t	s	u	s
<u>Single gene</u>						
cystic fibrosis	t	t				s
thalassaemia.		t	t			s
sickle cell,		t	t			s
fragile X	t	t				s
AGU	t	t				s

s - screening, t - testing, u - ultrasound scanning

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