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PRENATAL DIAGNOSIS: CYTOGENETIC PROBLEMS AND FUTURE DEVELOPMENTS[1]

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Summary. A short account of prenatal diagnosis services in Great Britain is given with reference to the estimated demand for these investigations. The following diagnostic problems are discussed in detail: unsuspected structural anomalies, diagnosis of fragile *X* chromosome, distinction between pseudo and true mosaicism and maternal cell admixture. Current problems involved in the use of trophoblast biopsy in prenatal diagnosis are also discussed.

Prenatal diagnosis, or the examination of the fetal status for developmental, biochemical and cytogenetic information is now a commonly accepted procedure and is most frequently achieved by the examination of the amniotic fluid cells and the supernatant. In Britain, prenatal diagnostic services are available on regional basis within the National Health Service, to all pregnant women who are at risk of having a severely handicapped fetus and where the abnormality can be detected. Approximately 14 000 or 2% of all pregnancies are tested each year by amniocentesis. This, however, represents only 25% of pregnancies identifiable as being at risk for a genetic defect and is responsible for the disappointingly small overall reduction of births with severe chromosome aberrations (Ferguson-Smith 1983).

The Duncan Guthrie Institute for Medical Genetics in Glasgow serves the population of the West of Scotland of 4 million people with 36,000 births and 1,450 genetic amniocenteses per year. In the West of Scotland 4% of all pregnancies are tested. This is twice the national average (Ferguson-Smith, Ferguson-Smith 1983). Since 1967, when the prenatal diagnosis service was introduced, Glasgow tested over 8,500 pregnancies for specific indications (Table 1). Like the national experience, in the West of Scotland the reduction in actual births with chromosome aberrations is small. This is in great contrast to the reduction of births with neural tube defects since the introduction of maternal serum screening programme in 1975 (Ferguson-Smith 1983). Without a doubt, a substantial reduction in births with chromosome aberrations could be achieved if a determined effort was made to inform and educate

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the entire community about genetic risks and make facilities for prenatal diagnosis more readily available. Nevertheless, despite the disappointing overall reductions in abnormalities, prenatal diagnosis has allowed women who otherwise would not contemplate a pregnancy, to have healthy children.

Table 1. Indications for prenatal chromosome analysis: results of West of Scotland series, 1969-82 inclusive. Prevalence of unbalanced chromosome abnormality in newborn = 0.44%

Indication	Number of pregnancies tested	Chromosome abnormality		Tris-21	Tris-13 tris-18	Sex chrom. abnorm.	Others
		number	%				
Maternal age ≥40	1188	39	3.3	25	7	6	1
Maternal age 35-39	2479	29	1.2	14	8	5	2
Previous trisomy-21	319	1	0.3	1	–	–	–
Parental translocation	65	5	7.8	–	–	–	5
Parental mosaicism	6	0	0	–	–	–	–
Previous aneuploidy (ex. 21)	76	0	0	–	–	–	–
Family history Downs	294	1	0.3	–	–	–	1
Maternal anxiety	301	2	0.7	1	–	1	–
Raised serum afp	1400	11	0.8	1	8	–	2
Amniotic fluids drawn for other indications	2365	6	0.3	3	0	2	1
Fetal sexing for *X*-linked disorders	55	(19*)	34.5	–	–	–	–
Totals	8543	94	1.1	45	23	14	12

* Male infants

To provide a good prenatal diagnostic service, a very close working collaboration between the clinical geneticist, obstetrician and experienced genetic laboratory personnel trained in biochemistry and cytogenetics is essential.

The main object of this paper is to discuss some of the sources of errors in fetal chromosome analysis. Excluding the possibility of clerical or technical errors — failure to interpret fetal karyotype correctly, mosaicism in culture and growth of maternal cells are the three common sources of mistakes. When added together, the number of mistakes are, in fact, small, but since they can result in the birth of an abnormal baby or termination of a normal fetus, each such problem must be dealt with individually, but in the light of previous experience.

The problems can be divided into 4 major groups and will be dealt with individually.

1. Unsuspected structural anomalies.
2. Diagnosis of fragile-X.
3. Distinction between pseudo and true mosaicism, and —
4. Maternal cell admixture.

1. Unsuspected Structural Anomalies. When the indication for amniocentesis is not parental translocation, and a structural rearrangement is found in the fetal cells, a number of questions in the interpretation of fetal karyotype must be answered.

1. Is this inherited or not?
2. Is it balanced or not? and —
3. Is the fetus going to be normal?

The parental karyotype must be studied and any number of banding techniques employed to determine if the fetal rearrangement is balanced or not. If the karyotype is balanced and inherited, then the decision is simple (Fig. 1). The difficulty arises when the rearrangement occurs *de novo*. A number of investigators have reported the association of congenital malformations and mental retardation with an apparently normal balanced structural rearrangement (Ayne et al. 1979, Fryns, Van den Berghe, 1979, Tharapel et al. 1977) Consequently, when the structural balanced rearrangements were diagnosed in the fetus, some centers recommended terminations. The decisions were made on the grounds that the deficiency of the breakpoints could not be excluded. There appears to be no risk of fetal abnormality in the *de novo* Robertsonian translocations, or fetal abnormality in reciprocal balanced translocations (Boué et al. 1983), and since present banding techniques make the definition of the breakpoints much more accurate, the drastic decision to terminate such a pregnancy is not justified.

It is our policy in Glasgow and also of the group in Paris (Boué et al. 1982), to advise terminations only when the karyotype is shown to be unbalanced. To the end of February, 1983, in the 8619 cases studied in Glasgow for a variety of indications, excluding parental translocations, 33 unsuspected structural rearrangements were found in the fetal karyotype (Table 2). 22 were inherited, 9 were *de novo* and 2 of unknown origin. 27 were balanced and 6 unbalanced. Of the 6, 3 were inherited and 3 were *de novo*. In all the 6 cases the pregnancy was terminated and the findings confirmed on fetal or placental tissue. The remaining 27 pregnancies continued and apparently normal infants were born. The same policy of not recommending termination included one case of *de novo* extra marker chromosome (Fig. 2). This baby is also developing normally. The findings of unexpected structural rearrangements in prenatal diagnosis are more frequent than expected from the results of studies in the new born. It is also important to follow these children and assess their development to ensure that our policy in not terminating these pregnancies is justified.

Table 2. Frequency of structural chromosome rearrangements

Prenatal diagnosis

		*Paris	*Los Angeles	Glasgow to March, 1983.	*Newborn survey
Number of cases		5315	2296	8619	59.452
Number unexpected		29	9	33	144
Balanced Structural Rearrangements	%	23	9	27	113
	%	0.43	0.39	0.31	0.19
	Frequency	1/230	1/255	1/319	1/526
Unbalanced Structural Rearrangements		6	—	6	31
	%	0.1		0.06	0.05
De Novo		14/29	—	9/33	—
Inherited		15/29	—	22/33	—
Unknown		—	—	2/33	—

* From Boué, 1982.

2. Diagnosis of fragile-*X*. It is estimated that 1 in 5 males with nonspecific mental retardation (IQ 30 - 55) have an *X*-linked recessive disorder (Turner, Turner 1974). Female carriers have a variable degree of mental retardation or normal intelligence (Turner et al. 1980). Physical factors of the affected male include macroorchidism, unusual facial features with large ears, large hands and feet. Recent cytogenetic studies have shown that the site is at a distal end of chromosome *X* at q27 - 28. Affected males may have fragile *X*'s in 2 - 50% of their cells, obligate female carriers show the defect in a lower frequency. It has been noted that in blood cultures the frequency of fragile *X* decreases with the age of the individual. The microscopic identification of the fragile site is very difficult since it requires the use of folate deficient media and additions of folate antagonists such as methotrexate or fluoroadeoxyuridine. A very large number of mitosis must be counted to establish the diagnosis. The antagonists increase the proportion of cells with fragile *X* but drastically reduce the yield of mitosis. The analysis is particularly difficult in fibroblasts and amniotic fluid cells. In prenatal diagnosis fetoscopy and fetal blood sampling after 21 week gestation and subsequent chromosome analysis of fetal lymphocytes are regarded as the only reliable procedures. So far only few cases have been diagnosed in time to allow for selective termination (Webb et al. 1983). Tissue culture techniques are being established to make the diagnosis possible at 16 to 19 weeks gestation. Since the medium used must be folate deficient and low on fetal bovine serum, there is a considerable art involved in obtaining suitable cells for analysis. Recently, we have been successful in diagnosing an affected male pregnancy with amniotic fluid cultures. This has been confirmed by fetal lymphocytes obtained at fetoscopy by Mr. Charles Rodeck, FRCS, King's College Hospital, London, and cytogenetic studies of these lympocytes by Dr. Tessa Webb. Before termination of this pregnancy in Glasgow, a further sample of amniotic fluid was obtained and a tissue culture technique established by one of our technicians, Mrs. Anne Theriault. The amniotic fluid cells have been set up in Ham's F-10 media with the usual fetal calf serum supplement. After establishing, the cells were subsequently fed with folic acid deficient T.C.199 with only 10% fetal calf serum. 24 hours before harvesting methotrexate (2×10^{-5} M) was added. The results are shown in Table 3 and Fig. 4.

Table 3. Comparison of fragile-*X* in fetal blood and tissue culture

Fetal blood cultured with foliate antagonists by Dr. T. Webb	1st amniotic fluid sample-antagonists	2nd amniotic fluid sample-antagonists	2nd amniotic fluid Sample + Methotrexate
	No cells = 24	No cells = 41	No cells = 51
	No positive = 2	Positive = 6	Positive = 16
19% positive	8.3% positive	14.6% positive	31.4% positive

It has recently been appreciated that the fragile-*X* syndrome is second only to Down's syndrome as a cause of severe mental retardation (Herbst, Miller, 1980). Since the carrier mothers can be easily identified and since the risk of producing an affected pregnancy is 25%, the opportunity for selective termination of affected male pregnancies is far greater, for example, than in cases of Down's syndrome. Here prenatal diagnosis has a great potential in reducing the number of affected births.

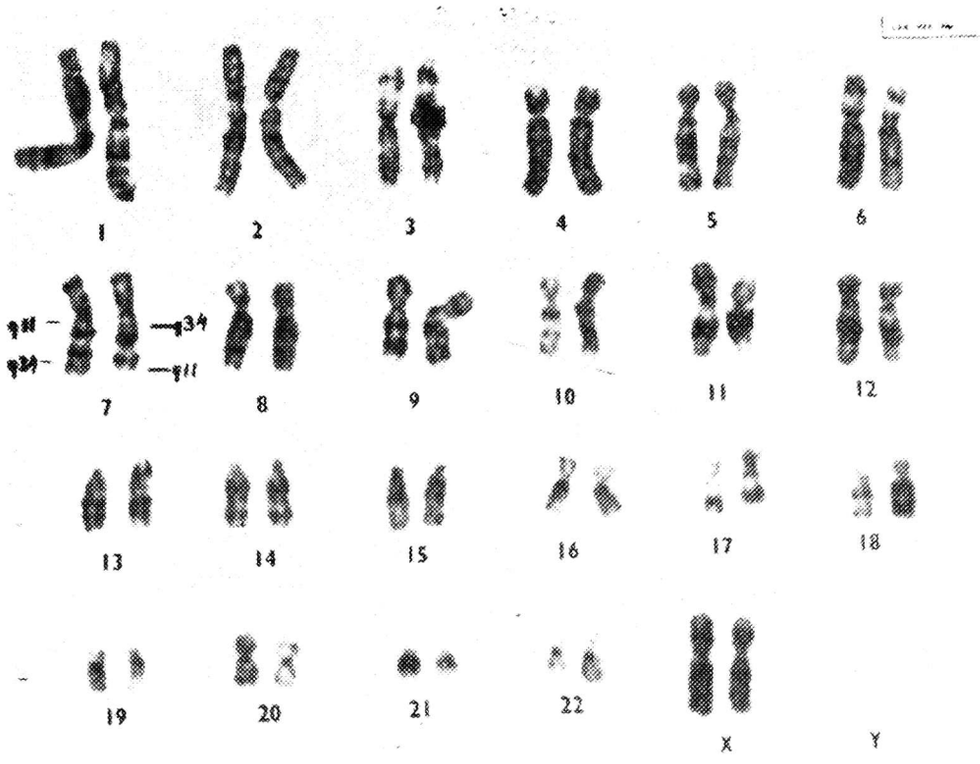

Fig. 1. Inverted 7 – 46, XX, inv. 7 (q 11; q 34). Paracentric inversion in the long arm of one homologue of chromosome 7 also present in mother. Normal female infant born

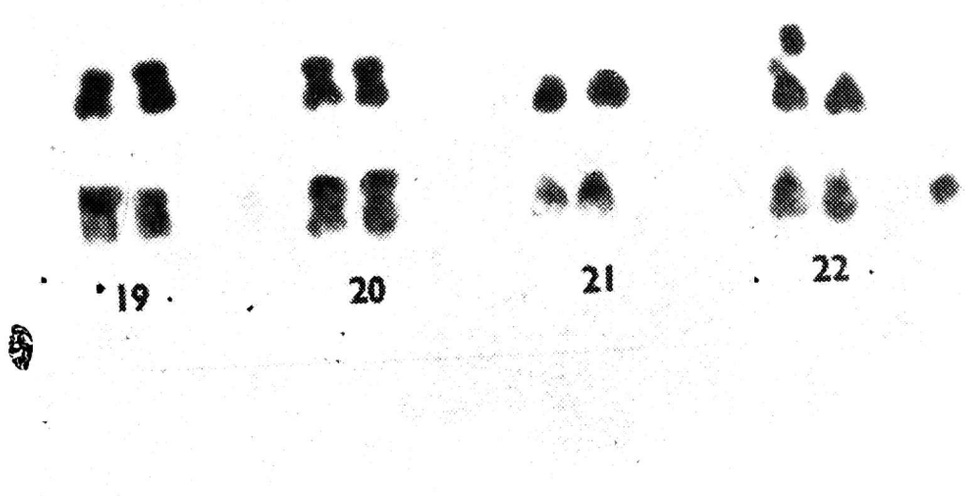

Fig. 2. Bisatellited marker chromosome found in amniotic fluid cells at 17 weeks gestation. A *de novo* occurrence. Infant normal

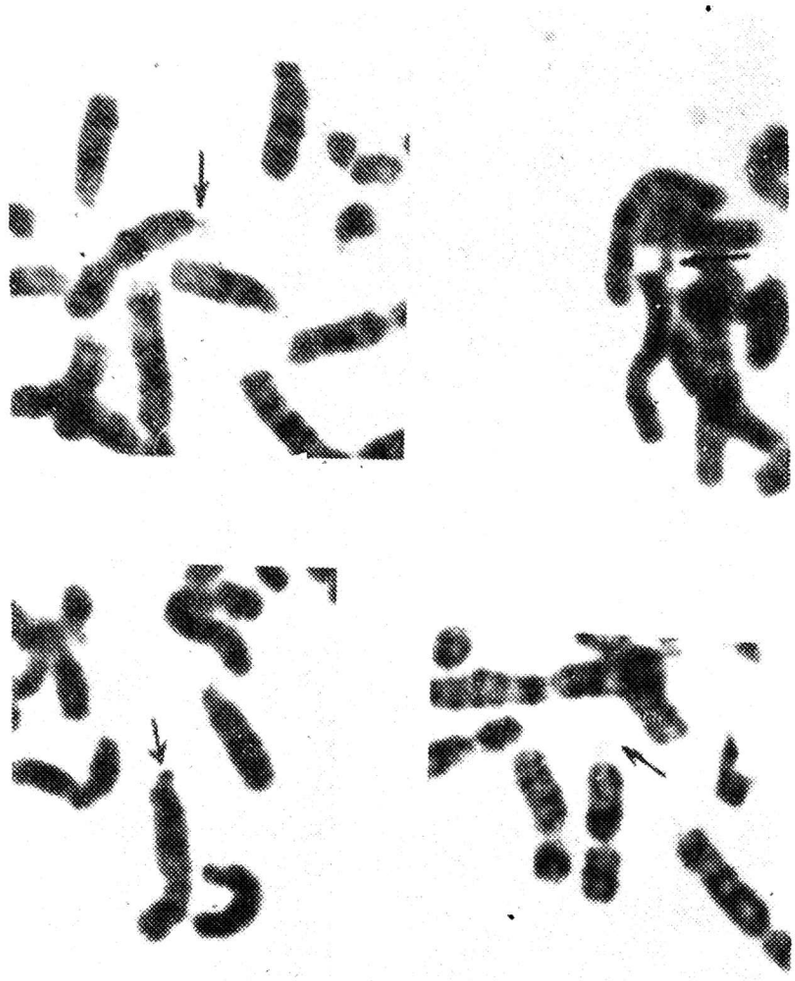

Fig. 3. Fragile X's from amniotic fluid cultures with metotrexate. Fetus terminated

Fig. 4. DAPI/Distomycin stain confirming that chromosome is derived from 2 short arms of chromosome 15. Fetus terminated

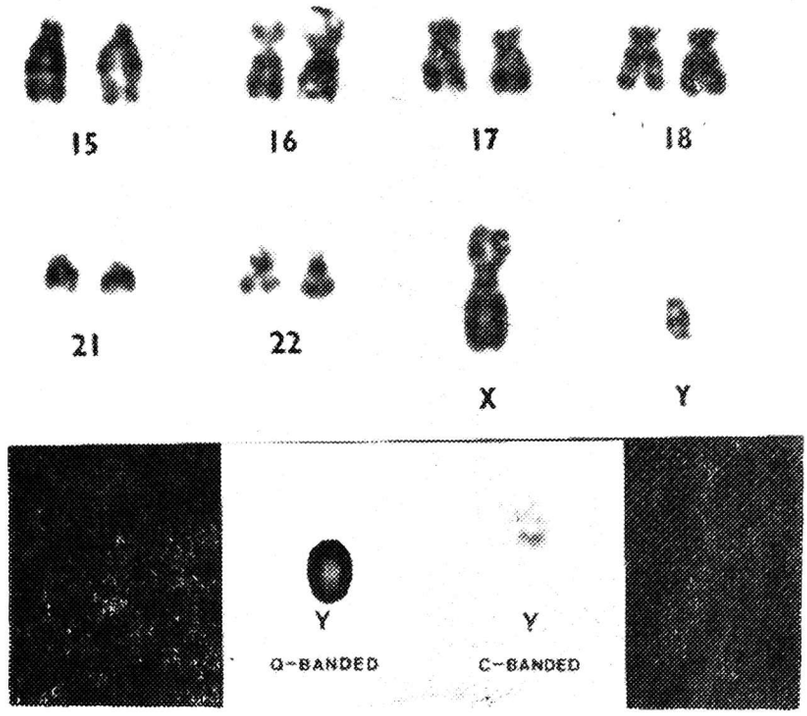

Fig. 5. Dicentric isochromosome for short arm and euchromatic region of long arm of Y. Fetus terminated

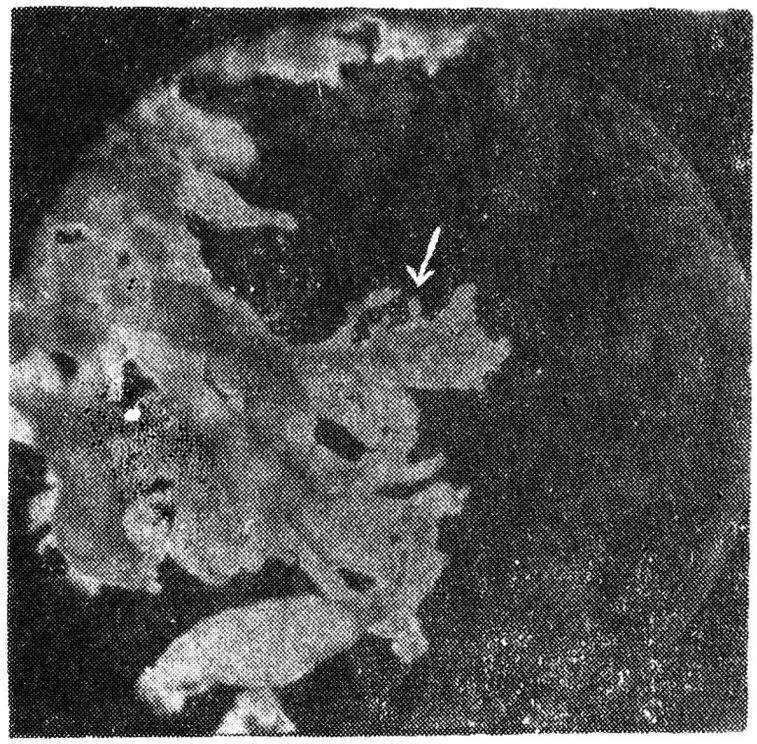

Fig. 6. Positive sample of villi with sprout like structures

3. Mosaicism. Mosaics are individuals where two or more different cell lines are derived from the same fertilised ovum. In amniotic fluid cultures, mosaicism can be divided into 3 groups —

1. True mosaic where more than one abnormal cell is found in more than one culture.

2. Pseudo-mosaic, where more than one abnormal cell is found in one colony, or culture, and

— 3. One cell mosaic, where one cell is found in only one colony or culture.

Recent reviews show that in prenatal diagnosis true mosaicism is found in. 2 to. 8% of all cases (Table 4). If more than one abnormal cell is found in more than one culture the karyotype can be described as "true mosaic." Not all true mosaic

Table 4. Mosaicism

Investigator	No of samples	Total no of mosaics	True mosaics	Pseudomosaics
Rudd	2000	18 (0.9%)	2 (0.1%)	16 (0.8%)
Hsu	1401	24 (1.75%)	5 (0.35%)	19 (1.35%)*
Peakman et al.	1100	31 (2.78%)	2 (0.18%)	29 (2.6%)**
Dill	531	59 (11.07%)	2 (0.37%)	57 (10.7%)***
Mikkelsen	1650	3 (0.18%)	3 (0.18%)	0
King et al.	975	9 (0.9%)	2 (0.2%)	7 (0.7%)
Najafzadeh et al.	522	9 (1.7%)	4 (0.8%)	5 (0.9%)
Simpson et al.	1000	59 (5.9%)	0	59 (5.9%)
Glasgow	8283	46 (0.55%)	9 (0.10%)	37 (0.45%)

* 46/47+2 in 5 cases ** 46/47+2 in 12 cases *** 46/47+A in 5 cases

cultures represent the true fetal karyotype. It seems that trisomy 20 mosaicis where 12 cases have been reported and 8 pregnancies terminated only 2 fetuses showed the same mosaicism and possibly abnormal features (for review see Bosze et al. 1982). The other 6 aborted fetuses and the 4 liveborn infants showed normal karyotype. In our own 2 cases, both pregnancies resulted in normal infants, with normal chromosomes. Since repeat amniocentesis only confirms the original karyotype, it may be important to confirm cases of mosaicism on fetal lymphocytes obtained by fetoscopy. This rationale was recently used in Glasgow, when mosaicism for a comparatively large extra dicentric chromosome (which was not present in either parents), was diagnosed, fetal blood sampling was undertaken by Mr. Charles Rodeck, FRCS, at the King's College Hospital, London, and within five days the diagnosis of mosaicism was confirmed and the dicentric chromosome by special staining was identified as a product derived from two chromosomes 15.

In the 9 cases of true mosaic cultures in Glasgow, only 2 fetuses were in fact true mosaics (Table 5). Different tissues show different degrees of mosaicism. It is possible that mosaicism is confined to specific fetal membranes, the urinary tract, for example, so the infant itself does not always show specific disability. When an abnormal cell line is confined only to one culture or colony it can be termed as pseudomosaic. The frequency of pseudomosaicism in cultures can be as high as 10% and depends largely on the laboratory methods and conditions. In these cases, in order to distinguish this type of mosaicism from the true mosaics, a large number of cells

from primary and sub-cultures must be counted. If the abnormal cell line is confined to only one colony or culture we may assume that it is an effect which has arisen in vitro. Very often, only one abnormal cell is found in only one culture. This is described as one cell mosaic and can lead to a mistaken diagnosis. In our

Table 5. Results of true mosaic cultures

Karyotype	Number of cases	Details of analysis	Outcome of pregnancy
46, XY/46, XX	3	2 on 2 cultures 1 on 4 cultures	All normal males
46, XY/45, XY-D	1	4 cultures	Normal male
46, XY/47, XY + Frag.	1	3 cultures	Normal male
46, XY/47, XY 20^3	2	1 Amniocentesis 4 cultures 2 Amniocenteses 8 cultures	Normal males
46, XX/47, XX T15	1	2 Amniocenteses 8 cultures Fetal blood	Fetus terminated Cordiac blood and tissue Confirmed T15/15 mosaic
46, XY/47, XY 18^3	1	2 Amniocenteses 8 cultures	Fetus terminated Cordiac blood and tissue Confirmed 18^3 mosaic

own series, 2 cases of 37 pseudo and once-cell mosaics (Table 6), proved to be true mosaic fetuses. The first case was a 15^3 in one cell out of 14 counted. The pregnancy resulted in a stillbirth and the placental tissue showed true trisomy 15 karyotype. The second case was a *46, X* dic *Y* with 1 cell out of 30 showing *45, X* karyotype. The parents elected termination and the fetal tissue showed 25% of cells to be *45, X* (Fig. 5).

Table 6. Results of one cell/pseudomosaics

Karyotype	Number of cases	Outcome of pregnancy
46, XX or XY/45, X	6	All normal *XX* or *XY*
46, XX/XY	10	All normal males
46 + fragments	2	All normal
Structural	7	All normal
Ring 2	1	Normal
12^3	1	Normal
15^3	1-1 cell in $14\text{-}15^3$	Stillborn, macerated $\frac{28}{52}$ placenta 15^3
16^3	2	Normal
18^3	2	Normal
G^3	4	Normal
46, Xdic Y	1-1 cell in 30 45X	Terminated — tissue 25% *42, X*

Mosaicism presents the investigator with the most difficult problems of interpretation and when deciding on the fate of the pregnancy it is essential to draw on the knowledge of the phenotype observed in affected live births, and the karyotypes of spontaneous abortions. Mosaics will be missed and mistakes in interpretation are bound to be made. It is, however, important to be quite honest about our own limitations. So, in cases where a clear answer cannot be given, the parents must be given all the facts available and can have the option of terminating the pregnancy.

4. Maternal Cell Admixture. One of the hazards of fetal chromosome analysis is the contamination of amniotic fluid sample with the maternal cells, so that maternal instead of the fetal karyotype is reported. Contamination of fluid with maternal cells occurs more frequently when there has been more than one attempt at amniocentesis, when the sample is very small, when the fluid is contaminated with maternal blood, or when the samples have taken longer than usual to grow. Maternal cell contamination can be avoided if at amniocentesis a stillette is used in the needle and if the first few drops of amniotic fluid withdrawn are discarded. In our own experience (See Table 7), 14 cases of maternal cell admixture have been

Table 7. Maternal cell admixture results

Number of cases	14	*46, XX/46, XY*	
Number of cases Confirmed at birth	13	12 – *46, XY*	1 – *47, XXG+*
Number of cases Confirmed by pathology	1	Male stillbirth at $\frac{28}{52}$, macerated	

Possible reasons		
Number of samples		Counts
Bloody/Brown threatened abortion	8	3 × 2 stabs with needle 1 × 2 amniocenteses Includes case of mistaken diagnosis
Fluid/Urine	2	2 × very small amount of fluid
No other apparent reason	4	2 × details not known

identified. One resulted in a mistaken diagnosis. This sample of amniotic fluid was heavily bloodstained and took over 4 weeks to grow. The cells were all fibroblast in morphology. A normal female karyotype was reported, but at birth the infant was a girl with Down's syndrome.

Ultrasound plays an essential part in prenatal diagnosis, it establishes the fetal heart beat and the correct gestation. It localises the placenta and shows the best area of entry avoiding the placenta and the bladder. It also provides much extra information about abnormalities not detected by amniotic fluid. In cases of anencephaly, it avoids unnecessary amniocentesis. Under expert ultrasound, amniotic fluid samples, even in cases of anterior placenta, can be clear of blood contamination.

Sexing of amniotic fluid cells by direct preparation can also eliminate some of the mistakes in reporting of wrong fetal sex, though in our own case of mistaken diagnosis it would have been useless. The presence of fibroblast cell line in culture rather than the variety of epithelial cells, is another sign of possible maternal cell admixture.

When a mosaic or pseudomosaic admixture of *46, XX/46, XY* cells is found, the chromosomes of both cell lines should be compared with the parental karyotypes for polymorphic variants. If the parental karyotypes are not informative, a repeat amniocentesis might be necessary.

In the cases where admixture of normal female and normal male cells is found, and where all possibility of cross-contamination of cells from another culture is ex-

cluded, the cytogeneticist's report should state clearly that there is the possibility of maternal cell contamination on otherwise normal male karyotype.

True *46, XX/46, XY* mosaics, though rare, can only be confirmed by repeat amniocentesis or fetal lymphocytes.

FUTURE DEVELOPMENTS IN PRENATAL DIAGNOSIS

Termination of pregnancy after 18 weeks gestation is very distressing for the mother, and can lead to complications. Since prenatal diagnosis was introduced, a variety of methods and supplements have been used to stimulate cell growth to obtain quicker results. All attempts, however, have still made amniocentesis at 15 to 16 weeks gestation necessary. The development of techniques of trophoblast sampling at 8 to 11 weeks gestation led to completely new concepts in prenatal diagnosis and has great promise. The sampling of villi by the transcervical route was attempted as early as 1973 (Kullander et al. 1973). It is in the last two years, however, that greatest progress has been made.

A method for trophoblast biopsy fetal sexing has been reported from the U.S.S.R. and Scotland, with few obstetric complications (Kazy et al. 1982, Gosden et al. 1982). In 1982, methods for diagnosing haemoglobin diseases by restrictive endonucleases analysis of fetal DNA obtained by chorion biopsy were successful (Williamson et al. 1982, Old et al. 1982). Also, in 1982, activity in 8 enzymes was measured directly in the villi to diagnose related metabolic diseases and compared with cultured amniotic fluid cells (Kazy et al. 1982, Simoni, et al. 1983).

Chromosome analysis from cultured trophoblasts was successfully completed in 1981 (Niazi et al. (1981), Simoni et al. (1983)). However, the most promising method for chromosome analysis was reported by Simoni and his colleagues this year (Brombeti, Simoni, 1983). By modifying Evans's direct method of obtaining metaphases from mouse embryos (Evans et al. 1972), Simoni could obtain suitable mitoses for analysis on chorionic villi within 5 hours following the biopsy. Consequently, a trisomy-21 pregnancy was diagnosed by them at 11 weeks gestation. In Glasgow, for the past 8 months, concentrated efforts have been made by our team, Dr. David Gilmour, Obstetrician and Registrar in Genetics, Mrs. Catherine Frew, Senior Technician in Prenatal Diagnosis Unit, and myself, to establish —

1. A safe method for chorion biopsy
2. A method for suitable direct mitotic preparations, and —
3. Reliable tissue culture techniques to be used on a routine basis in chorion biopsy material.

In all, 53 biopsies have been attempted. 14 others had to be excluded because of various technical instrument failures. Consent was asked of 51 patients prior to therapeutic abortion for social reasons, and two patients were for prenatal diagnosis. A number of patients consented to have the biopsy done without anaesthetic and 24 hours prior to the terminations. None felt discomfort, and none had any further complications.

The biopsy is performed under ultrasound guidance by the vaginal route using

an endoscope with 6 French gauge suction catheter attached to it. 20ml syringe is attached to the other end. The catheter is attached to the villi and a piece of villi is sucked up, placed in media and examined under the microscope in the operating theatre. Any maternal tissue is removed from the villi and the sample is then classified as positive, small, or degenerate. The positive sample or tissue suitable for analysis is villous in morphology with plenty of sprout-like structures (Fig. 7). The sample for direct preparation is placed in media with colchicine; the rest is set aside for culture. Evans's method is used to obtain direct preparations and our routine tissue culture method for *in situ* culture analysis. Sample of the abortus material is also set-up in culture for confirmation (Table 8). 63% of direct preparations on villi with sprouts had successful chromosome analysis and all results were checked against karyotype from abortus an all were correct. In cultured preparation the success rate is 72%, but in two cases of positive villi and one case of degenerate villia ma-

Table 8. Table of results from Glasgow

	Biopsies completed = 53		Samples obtained = 51	Failed = 2
DIRECT METHOD	Type of sample:	Positive	Small	Degenerate
	Number	28	10	13
	Attempted	27	4	2
	Obtained result	17	2	0
	%	63%	50%	0
	Fails	9	2	2
	Mistaken karyotype	0		
CULTURED METHOD	Number	28	10	11
	Attempted	11	6	5
	Obtained result	8	2	5
	%	72%	33%	50%
	Fails	2	0	5
	Mistaken karyotype	2	0	1
	Results to come	1	4	1

All cases confirmed on abortus material, except one case of prenatal diagnosis.

ternal tissue was grown. One chromosome abnormality was diagnosed in pre-termination sample — a *45, X* karyotype was found both in direct and cultured mitosis. Both cases for prenatal diagnosis were carriers for *X*-linked disease. The first patient is a haemophilia carrier and at biopsy no suitable sample was obtained. The second patient is an obligate carrier for Duchenne muscular dystrophy and found diagnosis at 16 weeks gestation and possible subsequent termination two weeks later unacceptable. Her biopsy was performed without anaesthetic and was successful — a *46, XX*

female fetus was diagnosed 3½ hours after biopsy on direct preparations and on cultured cells two weeks later. Both pregnancies continue uneventfully.

This new and exciting approach still remains a very delicate method, and the safety of the ultrasound guided aspiration will have to be carefully assessed before widespread use is recommended. Since we are diagnosing pregnancies in the first trimester (and many of them would abort spontaneously in any case), the pick-up rate of chromosome abnormalities is bound to be higher than in the present gestations.

The first trimester prenatal diagnosis will change the obstetric approach to pregnancies at risk of genetic defect. In these cases, prenatal diagnosis might be planned prior to conception, and patients will have to present themselves immediately after missing their first menstrual period. The laboratory cost will definitely be lower — but, most of all, terminations can be carried out quickly and efficiently reducing the drawn-out prostaglandin-induced labour which, without exception, is most distressing to the pregnant mother. The next few years will determine whether our excitement and the present promise are, in fact, justified.

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DIAGNOSTYKA PRENATALNA — PROBLEMY Z ZAKRESU CYTOGENETYKI I KIERUNKI BADAŃ W TYM ZAKRESIE

Streszczenie

Przedstawiono zakres stosowania diagnostyki prenatalnej w Wielkiej Brytanii wraz z oceną zapotrzebowania na te badania. Szczegółowo omówiono następujące problemy diagnostyki prenatalnej: stwierdzenie nieoczekiwanych anomalii strukturowych chromosomów, rozpoznawanie zespołu zwiększonej łamliwości chromosomu *X*, różnicowanie pomiędzy rzekomym a prawdziwym mozaicyzmem oraz obecność komórek matczynych w badanym materiale. Omówiono również aktualny stan badań nad zastosowaniem biopsji trofoblastu w diagnostyce prenatalnej.

ПРЕНАТАЛЬНАЯ ДИАГНОСТИКА — ПРОБЛЕМЫ ЦИТОГЕНЕТИКИ И НАПРАВЛЕНИЯ ИССЛЕДОВАНИЙ В ЭТОЙ ОБЛАСТИ

Резюме

В работе представлена сфера применения пренатальной диагностики в Великобритании, а также оценивается потребность на этого типа исследования. Подробно рассмотрены следующие проблемы пренатальной диагностики: обнаружение неожиданных структурных аномалий хромосом, распознавание синдрома повышенной ломкости хромосома *X*, дифференциация между ложным и истинным мозаицизмом, а также наличие материнских клеток в исследуемом материале. Рассматривается также актуальное состояние исследований о применении биопсии трофобласта в пренатальной диагностике.