

First Trimester Fetal Diagnosis

Edited by

M. Fraccaro G. Simoni B. Brambati

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With 133 Figures

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Long-term Follow-up Results After Aspiration of Chorionic Villi During Early Pregnancy

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The influence on the health of mother and fetus of the aspiration of chorionic villi during early pregnancy for prenatal diagnosis is a matter of interest nowadays. Does the aspiration exert any harmful effects on the fetus or child before and after birth? Does the aspiration lead to abortion? This paper deals with the follow-up study of 66 children born after aspiration performed 10 years ago and with the incidence of spontaneous abortion among the 400 cases in which aspiration was performed for sex prediction in early pregnancy between 1970 and 1979.

Follow-up Study of Children Born After Aspiration Performed 10 Years Ago

We reported 100 cases of sex prediction in 1975 (Dept. of Obstetrics and Gynecology 1975). (Examples of sex chromosome staining to determine fetal sex are shown in Figs. 1, 2.) Of these, 66 babies were subsequently delivered. The follow-up study comprised 53 cases, or 80.3% of all the babies born. The earliest birthday was in No-

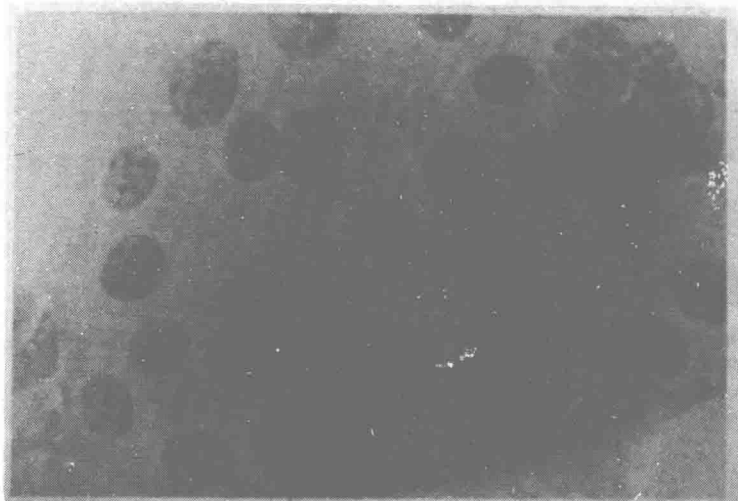


Fig. 1. X chromatin in syncytial cell groups (Pappenheim stain)

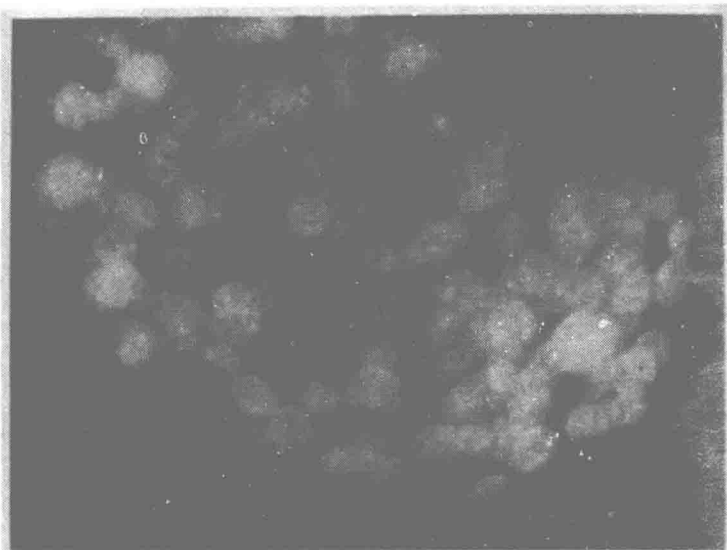


Fig. 2. Y chromatin in syncytial cell groups (Atebrin stain)



Fig. 3. Aspiration date: August 3, 1971 (91st day from LMP); number of aspirations performed: 1; contents: blood; birthday: February 3, 1972



Fig. 4. Aspiration date: August 22, 1972 (78th day from LMP); number of aspirations: 2; contents: amniotic fluid; birthday: March 10, 1973

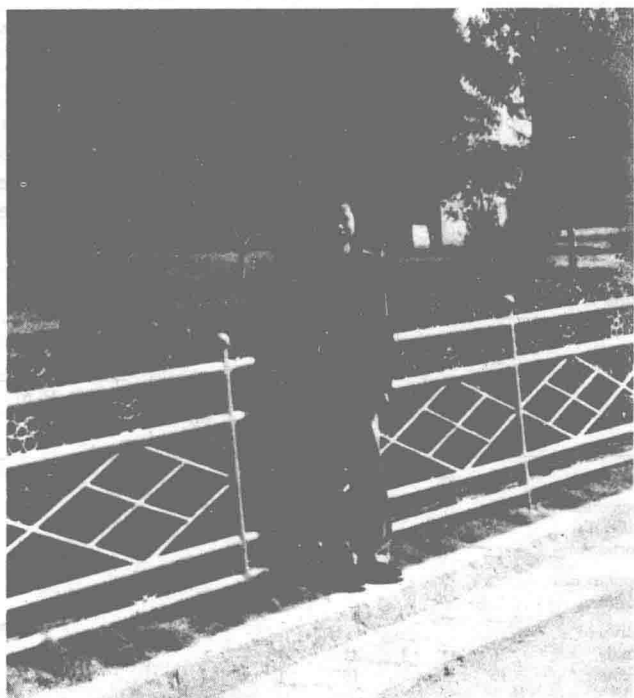


Fig. 5. Aspiration date: April 4, 1970 (54th day from LMP); number of aspirations: 1; contents: blood; birthday: November 7, 1970

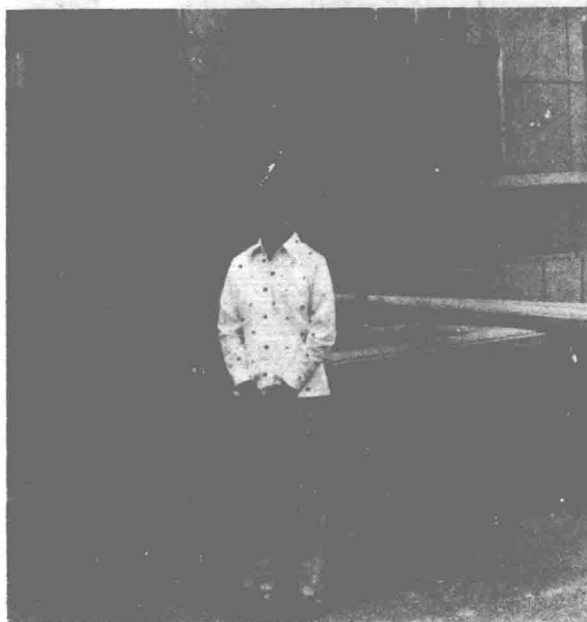


Fig. 6. Aspiration date: December 20, 1971 (55th day from LMP); number of aspiration: 1; contents: blood; birthday: July 16, 1972

vember 1970, and the latest birthday was in March 1975. These children all developed normally, are in good health, and are doing well in school (Figs. 3-6). The relation between the number of aspirations, the contents aspirated, and the day of gestation on which aspiration was performed during early pregnancy are shown in Table 1.

Table 1. Follow-up Study of Chorion Aspiration

	Number of aspirations performed			Contents			Gestational Age					Total cases
	1 (n)	2 (n)	3 (n)	Blood (n)	Bloody fluid (n)	Fluid (n)	<50	51-60	61-70	71-80	81-90	
							(n)	(n)	(n)	(n)	(n)	
Samplings	73	24	3	86	11	3	1	32	37	22	8	100
Immediate artificial abortions	20	10		27	2	1		10	11	8	1	30
Spontaneous abortions	2	2		3	1				2	1	1	4
Delivered male	36	11	3	41	7	2	1	18	20	8	3	50
female	15	1		15	1			4	4	5	3	16
Follow-up male	33	8	3	38	5	1	1	14	21	5	3	44
female	8	1		8	1			2	2	3	2	9



Fig. 4. Aspiration date: August 22, 1972 (78th day from LMP); number of aspirations: 2; contents: amniotic fluid; birthday: March 10, 1973

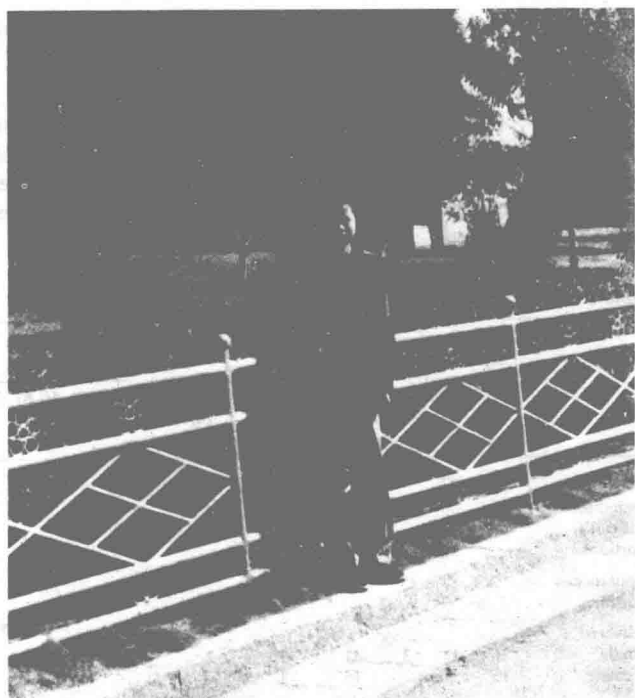


Fig. 5. Aspiration date: April 4, 1970 (54th day from LMP); number of aspirations: 1; contents: blood; birthday: November 7, 1970

the aspirated contents were bloody fluid or clear and watery), the abortion rate is 35.7% ($P < 0.01$), a very significant difference. According to our data, in 83.5% of the cases, aspiration was carried out within 70 days of the LMP. We did not find any significant difference in the perforation rate of the amniotic cavity in the various stages of early pregnancy. We knew from experience that the abortion rate is closely related to the skill of the operator. The incidence of abortion could be reduced if, chorion aspiration was carried out under the guidance of real-time ultrasound.

Second, in cases showing progestogen deficiency by cyto hormonal evaluation of the lateral wall of the vagina, the abortion rate was 19.2%, a significant difference from those with normal progestogen levels ($P < 0.05$). It must be emphasized that the period of gestation in which chorion aspiration is performed coincides with the period of the highest incidence of spontaneous abortion.

Third, the greater the number of attempts to carry out chorion aspiration, the higher the abortion rate. In the cases in which aspiration was performed three times, the abortion rate was 16.6%, although the *t* test showed no significant difference.

Fourth, the instrument and method of chorion aspiration is also related to the abortion. Originally, we thought that metal cannulae might be less safe than plastic ones. But, in practice, as shown in Table 2, the abortion rate using metal cannulae was 7.9%, while that associated with plastic cannulae was 16.6%. This finding deserves attention, even though the *t* test did not show any significant difference. Two points should be noticed when using plastic cannulae: (a) the sterile fluid in which the plastic cannula is immersed should be thoroughly removed, as it is a very important factor contributing to damage of the decidua and embryonic tissue; (b) the plastic cannula bends easily in the uterus, causing injury of the surrounding tissues.

If we can improve the four risk factors mentioned above, abortion rate after chorion aspiration will decrease further.

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Chorionic Villi Sampling: General Methodological and Clinical Approach*

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Introduction

Although chorionic villi sampling (CVS) is considered a very new area in the secondary prevention of genetic diseases, it in fact goes back more than 10 years. However, the first attempts, by two Scandinavian groups, failed to demonstrate sufficient reliability and safety for CVS to become a routine clinical technique (Hahnemann 1974; Kullander and Sandahl 1973). The advent of the modern era of first trimester fetal diagnosis can best be attributed to the research groups who proved that chorion frondosum is a reliable material for enzymatic study, DNA analysis, and fetal karyotyping and that transcervical sampling is a highly successful and relatively safe approach (Department of obstetrics and Gynecology, Tietung Hospital 1975; Goossens et al. 1983; Kazy et al. 1973; Simoni et al. 1983; Ward et al. 1983). Since then CVS has become a real alternative to second trimester diagnosis of genetic diseases (Brambati and Simoni 1983; Grebner et al. 1983; Old et al. 1982; Pergament et al. 1983).

The evident advantage of very early diagnosis frequently overcomes the disadvantage represented by the still nonquantified risk of the procedure itself, and there is thus rapidly growing demand. Moreover, the opportunity to investigate the first

Table 1. World experience in first trimester fetal diagnosis up to April 1983

Group	Country	Sampling method	No. of cases
Anshan group (1975)	China	Blind suction with a metallic cannula	100
Kazy et al. (1972)	USSR	Biopsy forceps guided by ultrasound	26
Ward et al. (1983)	UK	Plastic catheter guided by ultrasound	9
Brambati and Simoni (1983)	Italy	Plastic catheter guided by ultrasound	41
Goossens et al. (1983)	France	Biopsy forceps guided by ultrasound	5
Total			181

Modified from (1984a) World Health Organization Working Group

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Fig. 1. Geographic distribution of CVS centers as at October 1984. 1 Glasgow, 2 Edinburgh, 3 Oxford, 4, 5, 6 London, 7 Aalborg, 8, 44 Copenhagen, 9 Lund, 10 Stockholm, 11 Moskow, 12 Lübeck, 13 Rotterdam, 14 Northeim, 15 Liège, 16 Brussel, 17, 43 Paris, 18 Ulm, 19 Munich, 20 Prague, 21 Budapest, 22 Szeged, 23, 45 Milan, 24 Genoa, 25 Montecchio, 26 Rome, 27 Cagliari, 28 Athens, 29 Montreal, 30 New Haven, 31 Newark, 32 Philadelphia, 33 Washington DC, 34, 46 Chicago, 35 Detroit, 36 Richmond, 37 Kansas City, 38 San Francisco, 39 Perth, 40 Delhi, 41 Peking, 42 Anshan

trimester by means of new methodologies has stimulated several groups to start research programmes. This success is demonstrated by Table 1 and Fig. 1: in April 1983 only five centers were able to report diagnostic experience in a small number of patients (World Health Organization Working Group 1984a), while by October 1984 more than 40 centers, mostly in Europe and North America, were on the mailing list of the International CVS Collaborative Study, with about 3000 diagnoses having already been performed (Jackson 1985).

Technical Requirements

Four main methods (Table 2), and a variety of different sampling devices for each method, are used. However, more than 60% of world experience is with one procedure: transcervical aspiration by means of a plastic catheter (Portex Ltd., UK) under ultrasonic guidance (Fig. 2). This sampling approach compares favorably to the endoscopic approach, and in our experience it has proved to be highly efficient and reproducible (Simoni et al. 1983).

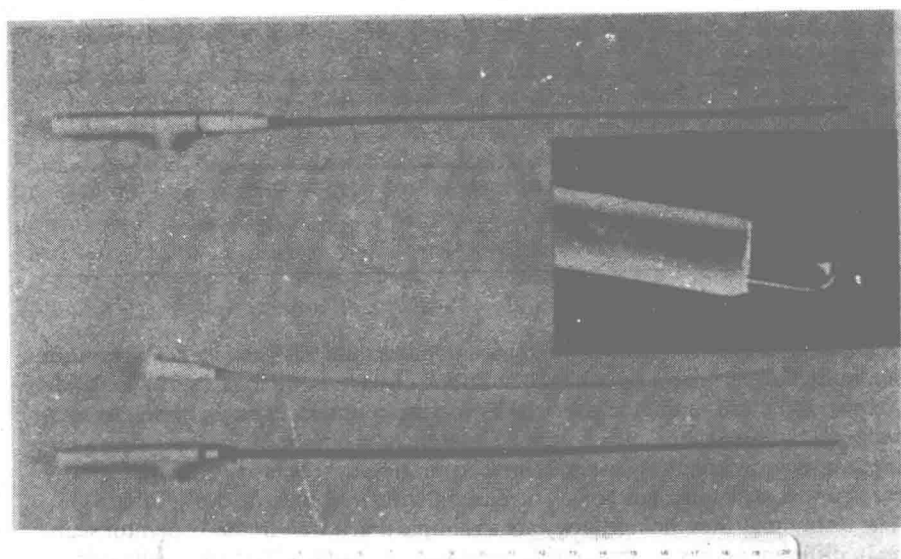


Fig. 2. The Portex sampling system, consisting of a malleable stainless steel obturator and a 1.5-mm external diameter, 18 cm long polyethylene catheter. *Above:* assembled. *Inset:* tip of obturator

Table 2. Methodological and technical characteristics of the main sampling procedures

Method	Sampling route	Sampling system
Endoscopy + aspiration	Transcervical	Operating cannula 4.0 × 4.0 mm
Endoscopy + biopsy forceps		Operating cannula 3.0 × 4.7 mm
Ultrasound + biopsy forceps	Transcervical	Biopsy forceps 1.7–2.4 mm
Ultrasound + aspiration	Transabdominal	20-gauge spinal needle, or 22-gauge needle housed in 18-gauge guide needle
	Transcervical	Plastic or malleable metallic catheter 1.5–3.0 mm in diameter

The average specimen weight was adequate for both fetal karyotyping and enzymatic or DNA analysis, although a large range of variation was observed in the sample size obtained (Table 3). The individual differences in depression produced in the syringe to aspirate chorionic tissue does not seem to be an adequate explanation for this variability. Sample weight could also be affected by other factors, such as the characteristics of the anatomical structures in contact with the extremity of the catheter at the time of aspiration. Since more than 70% of the 400 specimen obtained were between 10 and 50 mg, it would be advisable to assess techniques of reducing the scattering of sample size. Thus placental trauma could be reduced by avoiding both multiple aspiration attempts and the aspiration of excessive amounts of chorionic tissue.