Early amniocentesis: a cytogenetic evaluation

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We investigated the use of amniocentesis performed at eight to 14 weeks' gestation as a possible alternative to chorionic villus sampling.

Patients, methods, and results

Samples of amniotic fluid were taken from 40 women undergoing termination of pregnancy. Informed consent was obtained from each patient by the counselling clinician. Thirty samples were obtained at the Chelsea Hospital for Women and 10 from the Samaritan Hospital for Women. The study was approved by the ethics committees of both hospitals. The procedure was done under the guidance of an ultrasound scanner (Technicare) with a 5 MHz probe. When appropriate the gestational age was confirmed by measuring the crown-rump length and biparietal diameter. Only pregnancies in which the fetal heartbeat was identified were included in the study. A 20 gauge spinal needle was used for the amniocentesis, the placenta being avoided when possible. Fetal material was obtained at termination for confirmation of the karyotype. The samples of amniotic fluid were divided into 5 ml aliquots and cultured by routine methods.[1]

The table shows the cytogenetic results from the 40 samples of amniotic fluid. A success rate of 100% was obtained with 15 samples taken at 12-14 week's gestation, and the mean time to the cells being harvested was 12·6 days. In contrast only 17 (68%) of the 25 samples taken at eight to 11 weeks yielded a result. One sample taken at 13 weeks' gestation yielded a female karyotype, whereas the fetal parts revealed a male karyotype; the sample was subsequently identified as maternal urine. The mean volume of amniotic fluid obtained was 13·9 ml (range 1-40 ml).

Results of karyotyping amniotic fluid samples taken at eight to 11 and 12-14 weeks gestation

Gestation (weeks)	No of cases	Karyotyping successful	Karyotyping unsuccessful	Success rate (%)	Mean (range) time to cells being harvested (days)	Karyotype 46XX	Karyotype 46XY
8	1	1		60	10·0		1
9	9	5	4	60	12·0 (10-17)	3	2
10	8	6	2	75	14·3 (10-24)	4	2
11	7	5	2	71	13·3 (10-17)	3	2
Total	25	17	8	68	12·3 (10-24)	10	7
12	7	7		100	11·2 (6-14)	4	3
13	6	6		100	14·6 (10-20)	4	2
14	2	2		100	11·0*	1	1
Total	15	15		100	12·6 (6-20)	9	6

*Eleven days in both cases.

Comment

All 15 samples taken at 12-14 weeks' gestation yielded a result. The mean time to cells being harvested in this group (12·6 days) compared favourably with the current mean of 11 days for the samples obtained routinely at 16-19 weeks that are processed by our laboratory. Culture of all the 5 ml aliquots obtained at 12-14 weeks was successful. Thus a 10 ml sample would provide two cultures, which are necessary for the interpretation of equivocal results and in case of microbial infection.

In one case, a urine sample was obtained at 13 weeks' gestation from an obese patient in whom imaging was poor. In a clinical environment sampling would not have been attempted, and this patient would have been recalled later.

Our results show that amniocentesis from as early as 12 weeks' gestation can provide sufficient material for cytogenetic diagnosis and could be offered as an alternative to current methods of prenatal diagnosis. Furthermore, the procedure could be carried out by doctors already familiar with the technique, using existing resources. Patients must, however, be advised that the risks of this procedure are unknown. Preliminary reports from the United States suggest that early amniocentesis is safer than chorionic villus sampling.[2-4] Further evaluation, preferably by means of a randomised trial, is urgently needed. We are continuing our investigation of amniocentesis before 12 weeks with the aim of bringing the procedure forward into the first trimester of pregnancy.

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Geriatric rehabilitative care after fractures of the proximal femur: one year follow up of a randomised clinical trial

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Proximal femoral fractures in the elderly often lead to permanent disability and dependency. A controlled trial of postoperative rehabilitation by a team led by a physician in geriatric medicine showed immediate benefits in earlier discharge from hospital and greater personal independence at the time of discharge,[1] but no studies show whether such rehabilitation confers longer term benefit. We report the impact on quality of life, strain on carers, and survival in the year after operation for fracture of the proximal femur.

Patients, methods, and results

One year after entry into a randomised clinical trial the following evaluations were made in all survivors: the Katz index of independence in the activities of daily living, the Pfeiffer short portable mental status questionnaire, a carer strain questionnaire (for women looked after at home by a member of the family),[2] and a life satisfaction index[3] slightly modified for use in a Scottish population. The evaluations were carried out

Change in physical dependence, change in residence, strain on caregiver, and life satisfaction in elderly women with femoral fractures

		Treatment group	Controls
Katz index of independence in the activities of daily living:			
Before fracture *v* at discharge from orthopaedic inpatient care*	Better or no change	15	6
χ^2 (with continuity correction)=3·88, df=1, p=0·048	Worse	34	43
Before fracture *v* 1 year after fracture†	Better or no change	21	7
χ^2 (with continuity correction)=5·78, df=1, p=0·016	Worse	22	28
Residence:			
Before fracture *v* at discharge from orthopaedic inpatient care	Better or no change	40	26
χ^2 (with continuity correction)=8·49, df=1, p=0·004	Worse	9	24
Before fracture *v* 1 year after fracture	Better or no change	38	21
χ^2 (with continuity correction)=6·65, df=1, p=0·010	Worse	6	15
Caregiver strain index[2] 1 year after fracture (n=30; no family carer=50)	Median	1	1
Wilcoxon rank sum test (correction for tied ranks) T=206·5, p=0·83	Range	0-11	0-9
Life satisfaction index[3] 1 year after fracture (n=65; not testable‡=15)	Median	17	18
Wilcoxon rank sum test (correction for tied ranks) T=976, p=0·85	Range	6-22	6-21

*N=98; data missing=1. †N=78; data missing=2. ‡Subjects with severe communication problems.

at each patient's current residence. Records were kept of all periods of institutional care during the year and, where appropriate, the date of death.

Postoperative randomisation yielded two study groups of 54 patients after 36 others had been excluded.[1] Five patients in the treatment group and four in the control group died between entry into the trial and discharge from orthopaedic inpatient care. One year after the fracture 67% (95% confidence interval 60% to 75%) of the control group, 81% (71% to 92%) of the treatment group, and 67% (54% to 79%) of all 144 patients survived. One patient in the treatment group was alive but was otherwise lost to follow up.

Significantly more women were less independent in the control group than in the treatment group after one year compared with their prefracture state (table). Even with walking aids only 37% of the 79 patients assessed at one year had achieved their prefracture mobility. At the follow up 69% of the treatment group and 39% of the control group were living in the same place as before the fracture; 6% and 13%, respectively, had moved into institutional nursing care. The survivors in the group given rehabilitative care spent more of the follow up year living at home than the control group (median difference 20 days, 95% confidence interval 0 to 48 days). No differences were found between the groups in life satisfaction or strain on carers.

Comment

Survival rates of 75-81% one year after proximal femoral fractures have recently been reported.[4] We found 74% of subjects alive at one year; this proportion is 67% if the patients excluded from the study are also taken into account. The higher rate of survival after discharge in the group cared for by the rehabilitation team is consistent with other reports of improvements in both quality and length of life after similar interventions in elderly patients.[5]

Few studies relate the functional outcomes after hip fracture to the patient's circumstances before the fracture. Although comparison with outcomes achieved in other health care systems is complex, our findings are broadly consistent with previous studies. The better outcomes in the treatment group could not be explained satisfactorily by age, cognitive function, or any other variable that we measured. The earlier and greater numbers of hospital discharges in this group were not detrimental to either the patients' quality of life or the stress perceived by family members who cared for them; as we assessed subjective attitudes, however, these results may merely reflect the ability of most elderly people to adapt to chronic disability.

These outcomes challenge the conventional practice of keeping elderly patients with femoral fractures in orthopaedic wards for their postoperative rehabilitation. For optimal long term results more detailed attention needs to be paid to the ward environment, the enabling role of the nurse, the treatment provided, and the leadership of the rehabilitation team.

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Plasma cholesterol concentration and primary brain tumours

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Two previous studies have shown a relation between raised blood cholesterol concentration and primary brain malignancies in men.[1,2] In both studies the selection of controls was seriously flawed. Furthermore, in such retrospective studies the disease itself may have produced behavioural or physiological changes that resulted in raised cholesterol concentrations. We therefore examined the association between plasma cholesterol concentration and mortality from brain cancer in a large cohort study.

Subjects, methods, and results

In the Whitehall study of London civil servants[3] plasma cholesterol concentrations were measured in 17718 men aged 40-64 from 1967 to 1969. During follow up until 31 January 1985, 33 deaths due to malignant neoplasms of the brain (International Classification of Disease (eighth revision) code 191) occurred; 21 of these occurred more than five years after screening. Death certificates were reviewed, and one case was excluded because of inadequate diagnostic information.

The table shows mortality from brain cancer standardised for age by fifths of cholesterol concentration. The analyses were repeated after excluding the deaths from brain cancers that occurred within five years after screening. As most brain cancers prove fatal within five

Mortality from brain cancer per million person years by fifths of plasma cholesterol concentration. Figures in parentheses are actual numbers of deaths

	Plasma cholesterol (mmol/l)				
	≤4·11	−4·73	−5·27	−6·05	>6·05
Total mortality	42 (2)	73 (4)	156 (8)	183 (10)	145 (8)
Mortality excluding deaths in first five years	30 (1)	84 (3)	115 (4)	219 (8)	127 (5)