- 4 Sowers JR, Herschmann JM, Carlson HE, *et al.* Effect of human chorionic gonadotrophin on thyroid function in euthyroid man. *J Clin Endocrinol Metab* 1978;47:895-8.
- 5 Norman RJ, Lowrings C, Oliver T, *et al.* Doubts about human chorionic gonadotrophin as a thyroid stimulator. *Lancet* 1985;i:1096.

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Importance of negative result of cervical biopsy directed by colposcopy

Treatment is not recommended for patients with cervical intraepithelial neoplasia unless the lesion has been assessed colposcopically. The aim of our study was to examine the accuracy of cervical punch biopsy directed by colposcopy in excluding disease.

Patients, methods, and results

We reviewed the records of all patients referred to the colposcopy clinic at Birmingham and Midland Hospital for Women from March 1984 to October 1985 for investigation of persistent cytological abnormalities of the cervix. At the initial visit patients were assessed by colposcopy and a cervical smear and punch biopsy specimen were taken. In 132 patients the initial biopsy did not confirm the presence of disease. These patients were reviewed at intervals of four months and further smears and biopsies performed as necessary. Four groups with the following characteristics were identified.

Group 1 (n=51)—A histological abnormality was seen in a subsequent punch biopsy specimen.

Group 2 (n=65)—Subsequent cervical smears showed no abnormality; the median follow up period was 14 months and the median number of follow up smears per patient was two. Initial smears showed no abnormality in 31 patients.

Group 3 (n=8)—The cytological abnormality continued. A further punch biopsy yielded negative results in five cases.

Group 4 (n=8)—These patients underwent cone biopsy because of persistent unexplained cytological abnormality (six) or a predicted glandular lesion of the cervix (two). In the patients with an unexplained abnormality histological

Comparison of cytological findings on day of initial punch biopsy in patients who did and did not have abnormality at subsequent examinations

Outcome	Cytological findings*					Total
	No abnormality	Atypical	IIa	IIb	IV	
Subsequent positive histological findings	12	5	12	12	14	55
Negative findings at follow up smear	31	6	17	9	2	65
Total	43	11	29	21	16	120

*Atypical=Cellular atypia not amounting to mild dyskaryosis. IIa=Mildly dyskaryotic cells suggesting cervical intraepithelial neoplasia Grade 1. IIb=Moderately dyskaryotic cells suggesting cervical intraepithelial neoplasia Grade 2. IV=Severely dyskaryotic cells or cells that appear malignant, suggesting cervical intraepithelial neoplasia Grade 3.

examination of the biopsy specimen showed cervical intraepithelial neoplasia grade III (one patient), adenocarcinoma in situ (one), adenocarcinoma in situ with cervical intraepithelial neoplasia grade III (one), and no abnormalities (three). In the two further patients histological examination showed mild cervical glandular atypia in one and no abnormalities in the other.

Comment

We found that 55 of 132 women in whom an initial punch biopsy gave a negative result had a cervical lesion on repeat biopsy. Absence of histological abnormalities at the initial screening may be due to a false positive result for the referral smear, a false negative result for the initial biopsy, or spontaneous regression of a cytological abnormality. A false positive result was unlikely as only patients with a history of persistent cytological abnormality were seen. False negative results of biopsy may result from inaccurate sampling of a small lesion or one located in the lower part of the endocervical canal or from the pathologist overlooking a lesion if the tissue has not been completely sectioned after initial histological assessment has given a negative result. A true negative biopsy result would occur if the lesion had regressed spontaneously before colposcopy.

Spontaneous regression of cytological abnormalities is well recognised^{2,3} and seems to have occurred in the 31 patients in group 2 in whom cytological and histological examination on the day of the initial assessment and subsequent cytological review did not show any abnormality. In these cases the colposcopist probably misinterpreted inflammation or immature metaplasia as intraepithelial neoplasia when selecting the area for biopsy. The 34 cases in group 2 in which cytological examination showed abnormalities on the day of the initial punch biopsy but subsequently yielded negative results are difficult to explain. This might occur if the biopsy removed the whole lesion but the pathologist did not detect it or if the colposcopist failed to obtain a specimen of the lesion, which then regressed spontaneously before the next smear was taken. The rate of false negative results would decrease if the colposcopist took multiple specimens, but we disagree with this policy because it would lead to an increase in morbidity and laboratory workload and almost certainly to a less critical colposcopic assessment.

The cervical smear taken on the day of initial colposcopy was of limited value in predicting the final outcome (table). We emphasise, therefore, the importance of follow up examinations in patients referred because of cytological abnormality in whom the initial biopsy directed by colposcopy does not confirm the presence of disease.

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- Jordan JA, Sharp F, Singer A, eds. *Pre-clinical neoplasia of the cervix. Proceedings of the ninth study group of the Royal College of Obstetricians and Gynaecologists*. London: Royal College of Obstetricians and Gynaecologists 1982:299.
- Nasiell K, Nasiell M, Vaclavinkova V. Behavior of moderate cervical dysplasia during long term follow-up. *Obstet Gynecol* 1983;61:609-14.
- Nasiell K, Roger V, Nasiell M. Behavior of mild cervical dysplasia during long term follow-up. *Obstet Gynecol* 1986;67:665-9.

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