#### Key messages

- Patients' satisfaction rates with outpatient hysteroscopy and day case hysteroscopy were similar
- The outpatient group recovered preoperative fitness more quickly than the day case group
- Requirements for postoperative analgesia were similar in both groups
- 78% of patients considered that the pain from outpatient hysteroscopy was less than that usually experienced during menstruation
- Postmenopausal women may benefit less from outpatient hysteroscopy than premenopausal women

#### Conclusion

Patients are not disadvantaged by the introduction of outpatient hysteroscopy. Several advantages may prove attractive to patients and healthcare providers: return to mobility, full fitness, and work occur more quickly after outpatient hysteroscopy than after day case hysteroscopy. Increased attention should be paid during counselling of patients at higher risk of dissatisfaction with hysteroscopy, such as postmenopausal patients. The development of outpatient hysteroscopy is a potentially significant advance in gynaecological investigation. It lends itself to a greater accessibility for general practitioners and patients, especially if a direct referral service from a general practitioner is contemplated.

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# Prenatal ultrasound examinations and risk of childhood leukaemia: case-control study

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Obstetric ultrasound examination is part of routine antenatal care and is regarded as safe for both the fetus and the mother. In vitro, however, ultrasound has been shown to cause membrane changes that could affect embryogenesis and late prenatal and postnatal development. Studies have also shown an association between exposure to ultrasound and an increased frequency of non-righthandness, indicating that fetal development may be affected by the ultrasonic waves.<sup>2</sup>

Concerns over a possible association between exposure to ultrasound in utero and an increased risk of childhood malignancies have not been substantiated, but previous studies have been hampered by low statistical power or based on interviews with the parents done retrospectively, or both.<sup>3–5</sup>

To assess the impact of ultrasound and the risks of childhood lymphatic and myeloid leukaemia, we performed a nationwide population based casecontrol study using prospectively assembled data on prenatal exposure to ultrasound.

#### Subjects, methods, and results

The cases in this study comprised all children born and diagnosed as having leukaemia between 1973 and

1989 and reported to the nationwide Swedish registers of birth, cancer, and causes of death—in all, 752 cases. One control was randomly selected for each child with leukaemia from the Swedish Birth Registry and matched by sex and year and month of birth. The study was restricted to cases and controls without Down's syndrome (n=731), and medical records of 652 (89%) matched case-control pairs could be retrieved (578 cases with lymphatic leukaemia and 74 with myeloid leukaemia).

Altogether, 361 (48%) of the children with leukaemia had developed it before the age of 4, and 21 children were born in twin pregnancies. Information on exposure was extracted from antenatal, obstetric, and other standardised medical records by one of us (EN), who was blind to whether the child was a case or control. Conditional logistic regression was performed to study the association between prenatal exposure to ultrasound and childhood leukaemia (lymphatic and myeloid leukaemia). Maximum likelihood methods were used to estimate the odds ratio and 95% confidence intervals.

In all, 200 children with lymphatic leukaemia and 214 controls had been exposed prenatally to ultrasound (odds ratio 0.85; 95% confidence interval 0.62 to 1.17) (table). The risk of lymphatic leukaemia was not influenced by either the number of ultrasound

examinations or when the examination was performed (data not shown). Twenty nine of the children with myeloid leukaemia and 27 of the controls had been exposed to ultrasound prenatally (odds ratio 1.0; 0.42 to 2.40) (table). The risk of myeloid leukemia was not influenced by the number of ultrasound examinations (table). A slightly higher, but not significant, risk was seen for those examined during the second trimester (odds ratio 1.42; 0.88 to 2.29). Adjustments for potential confounding, such as maternal age, high birth weight, and twin pregnancies, did not alter the results (data not shown).

#### Comment

We could not detect any association between exposure to ultrasound during pregnancy and lymphatic or myeloid leukaemia, and the results of the study are therefore reassuring. The strengths of the study are its size, the exclusion of children with Down's syndrome, and the use of prospectively assembled exposure data. Ultrasound examination was gradually introduced in Sweden during the study period, and the proportion of exposed fetuses (36%) is therefore appropriate; any possible underestimation of exposure should be similar in both cases and controls.

We conclude that single or repeated intrauterine exposure to ultrasound, early or late in the pregnancy, does not influence the risk of subsequent development of lymphatic or myeloid childhood leukaemia.

Contributors: EN coordinated the study and assembled the data. SC and AE were responsible for initiating the study and the original study design. RB was responsible for the statistical work. PH contributed to the interpretation of the data. The paper was written jointly by all authors, with EN as lead author. AE is guarantor for the paper.

Risk of childhood leukaemia in relation to ultrasound examinations and number of examinations: results of Swedish population based nationwide case-control study

	Myeloid leukaemia			Lymphatic leukaemia		
	No of cases	No of controls	Odds ratio* (95% CI)	No of cases	No of controls	Odds ratio* (95% CI)
All pregnancies						
Not exposed to ultrasound	334	318	1.00	42	39	1.00
Exposed	200	214	0.85 (0.62 to 1.16)	29	27	1.00 (0.42 to 2.40)
Missing information†	44	46	NA	3	8	NA
No of ultrasound exam	inations					
None	334	318	1.00	42	39	1.00
1 or 2	161	159	0.93 (0.67 to 1.23)	22	20	1.00 (0.40 to 2.50)
≥3	39	55	0.64 (0.40 to 1.04)	7	7	1.00 (0.30 to 3.33)
Missing information†	44	46	NA	3	8	NA
Odds ratio (linear trend)‡	NA	NA	0.95 (0.85 to 1.06)	NA	NA	1.01 (0.74 to 1.38)

NA=Not applicable. \*Calculated by means of conditional logistic regression. †Missing information on exposure. ‡Calculated by means of conditional logistic regression, assuming linear effect for number of ultrasound examinations.

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### Drug points

## Lichenoid drug eruption with proton pump inhibitors

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We report a patient who developed a recurrent lichenoid eruption after treatment with omeprazole, lansoprazole, and pantoprazole.

An 81 year old man presented with a three month history of a widespread pruritic rash. He suffered from oesophagitis and had been taking omeprazole 20 mg/day for nine months. Examination revealed an annular scaly erythematous rash on the dorsal aspects of his forearms and, to a lesser extent, on his trunk and thighs (figure). A clinical diagnosis of adverse drug eruption was made and omeprazole stopped. The rash cleared in a month, but his dyspepsia recurred and he was prescribed lansoprazole 30 mg/day. Three weeks later, the eruption recurred, and a skin biopsy showed features of a lichenoid drug reaction. Lansoprazole was stopped, and the rash resolved. He suffered a second recurrence several months later after inadvertent challenge with pantoprazole 40 mg daily.

The most common adverse effects of omeprazole are diarrhoea, headache, and rashes, of which urticaria and toxic erythema are the most common.<sup>12</sup> Premarketing



Lichenoid eruption in reaction to proton pump inhibitors

trials on lansoprazole showed a similar adverse reaction profile to omeprazole.<sup>3</sup> The Committee on Safety of Medicines has received one report of lichen planus associated with omeprazole and two reports associated with lansoprazole but no reports associated with pantoprazole (personal communication). The identical lichenoid eruption induced by all three proton pump inhibitors suggests a "class effect, possibly" related to their similar substituted benzimidazole structure.

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