Clinical Algorithms

The abnormal cervical smear

ALBERT SINGER

Squamous cervical cancer (which comprises 95% of all cervical cancers) is completely preventable if its precancerous stages of dysplasia, carcinoma in situ (now called cervical intraepithelial neoplasia), or microinvasive cancer are detected and treated. Detection is relatively simple and entails analysis of a sample of cells exfoliated within the ectocervix and endocervix. Exfoliative cytology, which is performed on nearly three million women in the United Kingdom each year, has unfortunately not reduced the number of deaths from cervical cancer as it has in other countries.[1] The relative ineffectiveness of the screening programme in the United Kingdom seems to be related to two factors: the lack of an initial call system coupled with inadequacy of record and recall systems for women with abnormal findings and the fact that most smears are performed on relatively low risk young women. There has been a dramatic increase in the number of the precancerous lesions found, especially in young women, with an associated increase in deaths in this group, and this is imposing a great strain on the cytology screening system.[2]

What does an abnormal smear mean?

Abnormal conditions of the cervix identified in a smear can be divided into those which are definitely benign and those which are believed to have neoplastic potential. Benign abnormalities are relevant to the smear only if they prejudice its reliability as a test for the precancerous stages or if they are known to be associated with cervical intraepithelial neoplasia, as in the case of the human papillomavirus.

BENIGN ABNORMALITIES

Inflammatory changes

Inflammatory changes are associated with cervicitis caused by *Trichomonas vaginalis*, candida, or other micro-organisms. They cause degenerative and regenerative changes in the epithelial cells, and some of the more severe changes approach the borderline with cervical intraepithelial neoplasia. Indeed, recent studies have shown that up to one fifth of recurrent inflammatory smears are associated with an underlying cervical intraepithelial neoplasia. Atrophic postmenopausal epithelium often shows severe inflammatory changes.

The cytopathic effects of the two main genital viruses—that is, herpes genitalis and human papillomavirus—are easily identified, the first by its multinucleate cell appearance and the second by the characteristic large perinuclear cavity or koilocyte and binucleation and hyperchromatism associated with keratinisation of the squamous cells. It is sometimes difficult for the cytologist to distinguish morphologically between cervical intraepithelial neoplasia and the effect of human papillomavirus with nuclear atypia. Indeed, about 83% of important squamous lesions have cytological evidence of infection with human papillomavirus.[3]

Unsatisfactory smear

In an unsatisfactory smear a diagnosis cannot usually be made because of too few cells, air drying of the cellular specimen, excess blood, the presence of large amounts of inflammatory debris, or the absence of endocervical cells. The absence of endocervical cells, sometimes in more than half of routine cervical smears, may result from the physiological condition of the cervix or inadequate sampling. Theoretically, their absence should indicate the inability to comment objectively on the state of the endocervix.

NEOPLASTIC ABNORMALITIES

Glandular cells

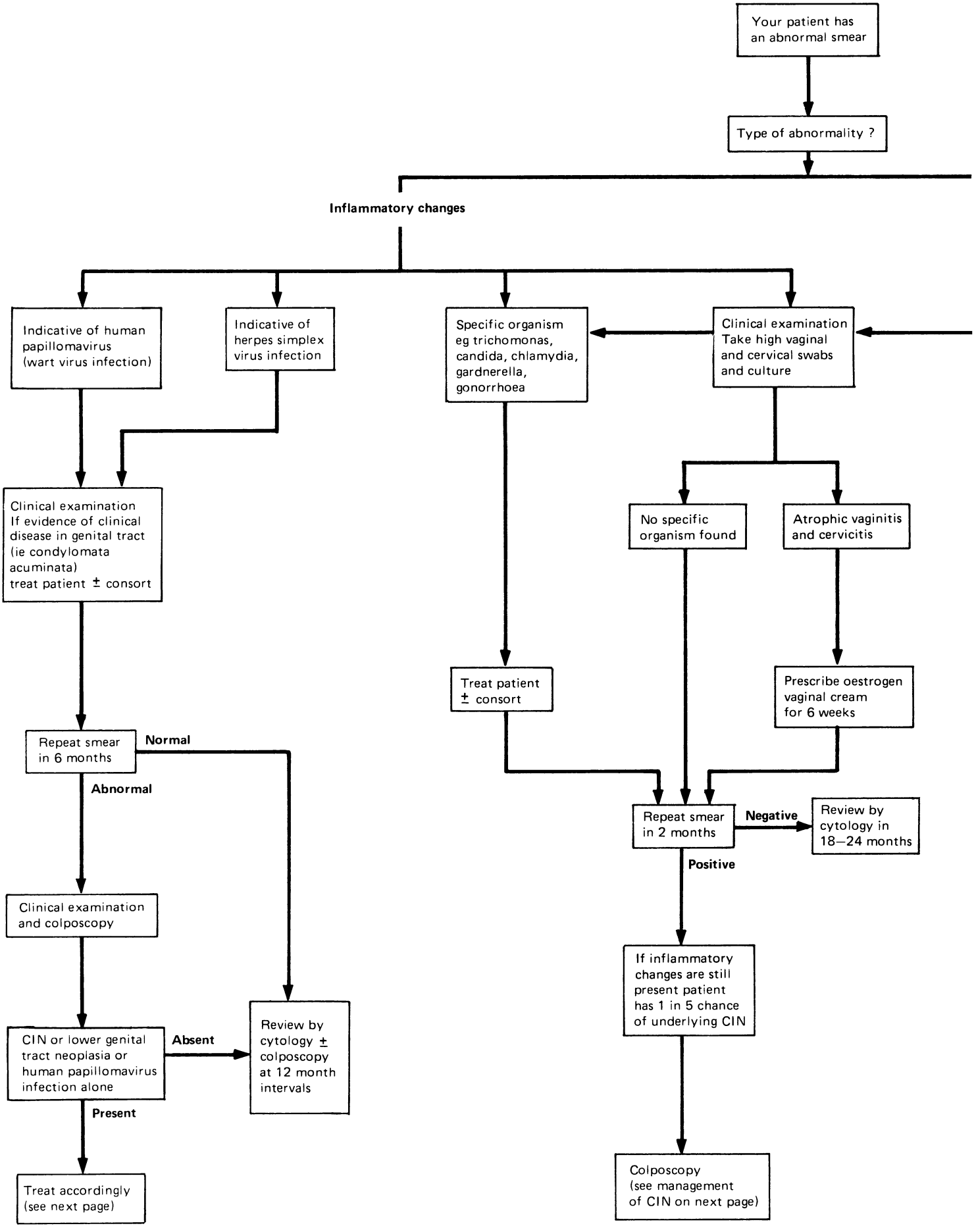
Inappropriate endometrial cells sometimes persist in a smear for up to three days after menstruation, and their presence may interfere with the analysis of cervical epithelial abnormalities, either squamous or columnar. Their presence at other times of the cycle, however, may indicate endometrial neoplasia.

Abnormal glandular cells—Characteristic changes of endocervical adenocarcinoma or even a combination of squamous carcinoma and adenocarcinoma may be seen in abnormal glandular cells. Lesser degrees of atypicality, again of a squamous or glandular nature, may coexist.

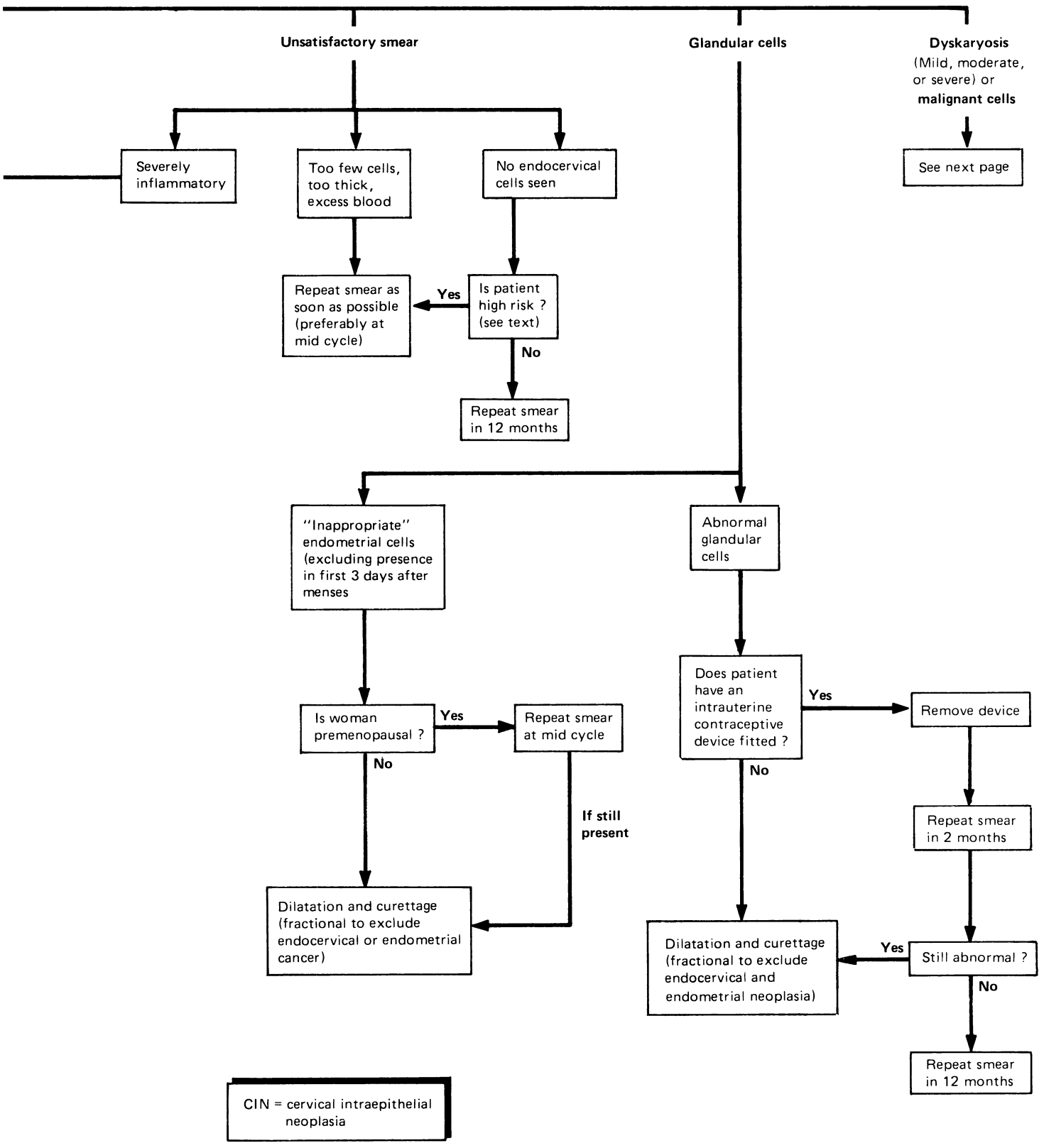
Cervical intraepithelial neoplasia

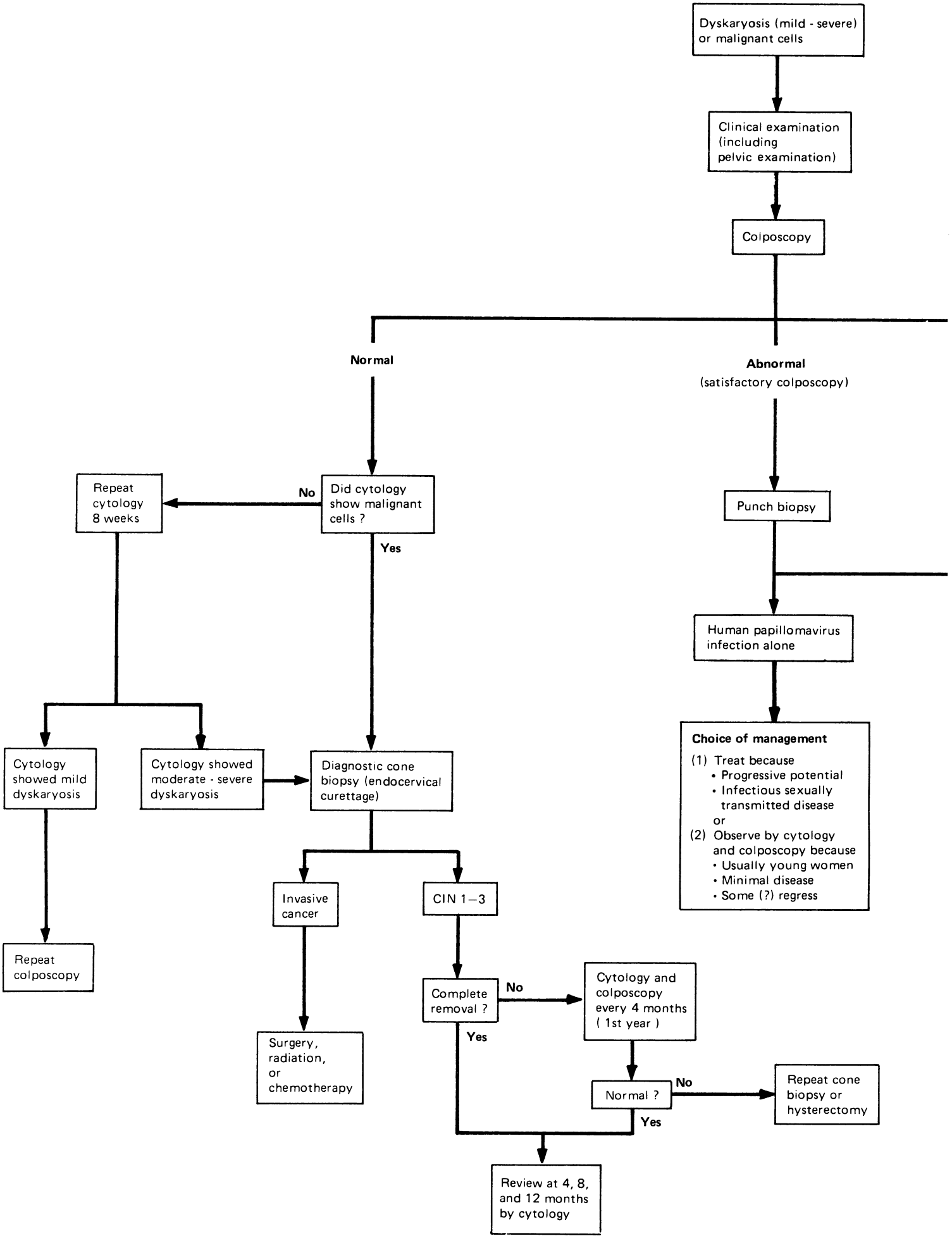
Cervical intraepithelial neoplasia may be identified cytologically because the abnormal epithelial cells show: abnormal nuclei, an increased nuclear to cytoplasmic ratio, and immature cytoplasmic differentiation. These cells are called dyskaryotic (occasionally the term atypia is also used). Dyskaryosis means an abnormal nucleus and describes cells with nuclear features of neoplasia rather than inflammation or hyperplasia. They are derived from the cervical surface epithelium showing cervical intraepithelial neoplasia or invasive cancer. Dyskaryotic cells described as mild, moderate, or severe are derived from epithelium containing cervical intraepithelial neoplasia grade 1, 2, or 3 respectively (or mild, moderate, or severe dysplasia/carcinoma in situ). An alternative cytological terminology exists which depends more on the cytoplasmic differentiation of the dyskaryotic cells. The table compares the cytological and histological terminology. Some cytologists use the term "malignant cells" to describe the presence of severe dyskaryosis or a more advanced lesion, either microinvasive or

Royal Northern and Whittington Hospitals, London N19
ALBERT SINGER, DPHIL, FRCOG, consultant gynaecologist

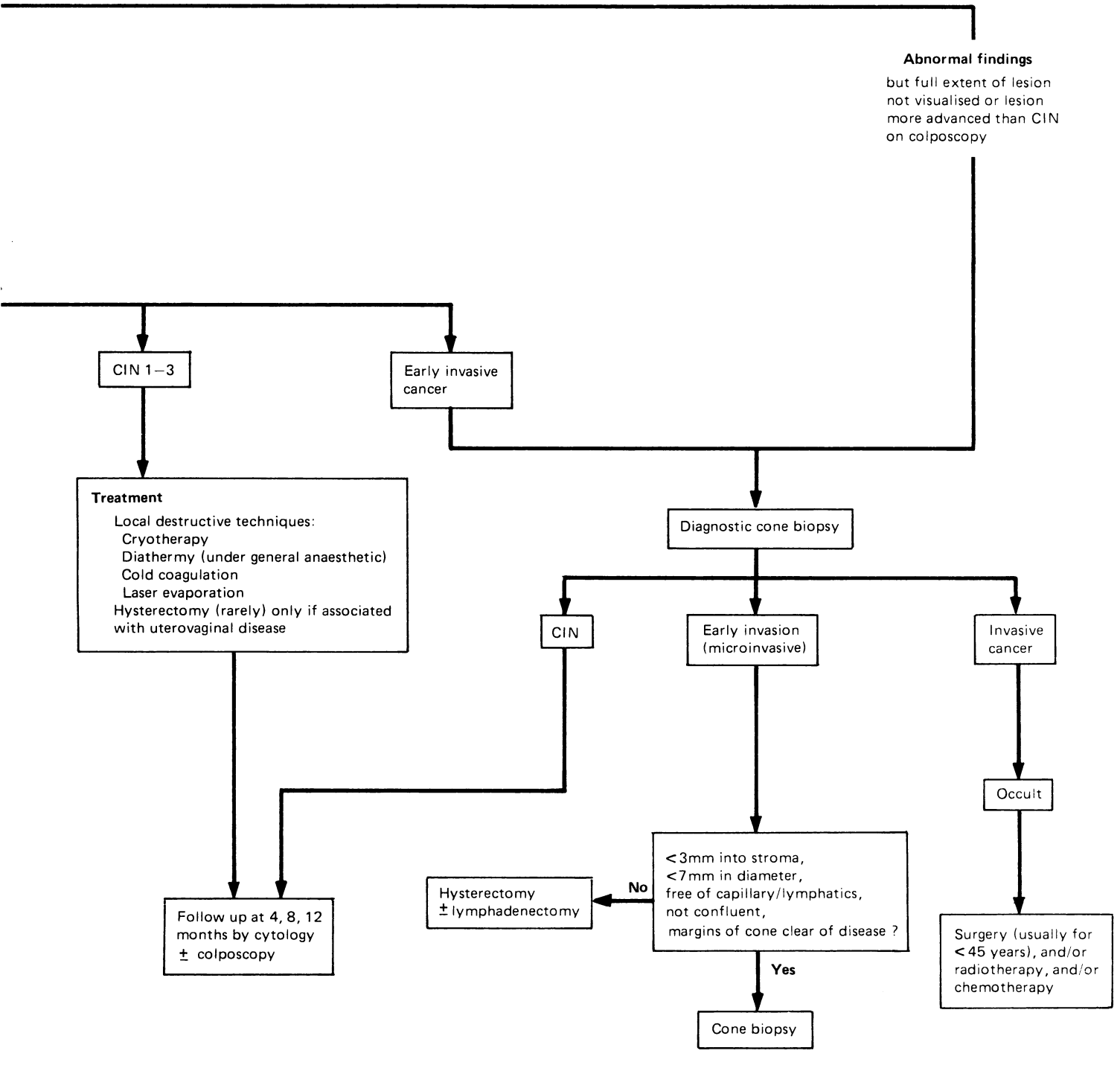

Your patient has an abnormal smear
Type of abnormality ?
Inflammatory changes
Indicative of human papillomavirus (wart virus infection)
Indicative of herpes simplex virus infection
Specific organism eg trichomonas, candida, chlamydia, gardnerella, gonorrhoea
Clinical examination Take high vaginal and cervical swabs and culture
Clinical examination If evidence of clinical disease in genital tract (ie condylomata acuminata) treat patient ± consort
No specific organism found
Atrophic vaginitis and cervicitis
Treat patient ± consort
Prescribe oestrogen vaginal cream for 6 weeks
Repeat smear in 6 months
Normal
Abnormal
Repeat smear in 2 months
Negative
Review by cytology in 18–24 months
Positive
Clinical examination and colposcopy
If inflammatory changes are still present patient has 1 in 5 chance of underlying CIN
CIN or lower genital tract neoplasia or human papillomavirus infection alone
Absent
Review by cytology ± colposcopy at 12 month intervals
Present
Treat accordingly (see next page)
Colposcopy (see management of CIN on next page)

Abnormal cervical smear 1




Dyskaryosis (mild - severe) or malignant cells
Clinical examination (including pelvic examination)
Colposcopy
Normal
Abnormal (satisfactory colposcopy)
Did cytology show malignant cells ?
No
Yes
Repeat cytology 8 weeks
Punch biopsy
Human papillomavirus infection alone
Choice of management
(1) Treat because
• Progressive potential
• Infectious sexually transmitted disease
or
(2) Observe by cytology and colposcopy because
• Usually young women
• Minimal disease
• Some (?) regress
Cytology showed mild dyskaryosis
Cytology showed moderate - severe dyskaryosis
Diagnostic cone biopsy (endocervical curettage)
Repeat colposcopy
Invasive cancer
CIN 1–3
Surgery, radiation, or chemotherapy
Complete removal ?
No
Yes
Cytology and colposcopy every 4 months (1st year)
Normal ?
No
Yes
Repeat cone biopsy or hysterectomy
Review at 4, 8, and 12 months by cytology

Abnormal cervical smear 2



Comparison of cytological and histological terminology[10]

Cytological terminology		Histological equivalent
Preferred terms	Alternative terms	
Mild dyskaryosis	Superficial cell dyskaryosis Mild atypia	CIN 1 (mild dysplasia)
Moderate dyskaryosis	Intermediate cell dyskaryosis Moderate atypia	CIN 2 (moderate dysplasia)
Severe dyskaryosis	Parabasal cell dyskaryosis Severe atypia	CIN 3 (severe dysplasia or carcinoma in situ)
Malignant cell		Invasive cancer (some cytologists also include CIN 3 or microinvasive cancer)

CIN = Cervical intraepithelial neoplasia.

invasive cervical cancer, but this is not acceptable and the term neoplasia should be used for all preinvasive and invasive lesions and "malignancy" reserved for invasive disease.

Who should be screened?

Controversy surrounds the question of who should be screened, which is particularly relevant in view of the dramatic increase in precancerous lesions in women under the age of 35. With limited resources the aim is to give efficient coverage to all women of all ages. With this in mind the Department of Health and Social Security has recommended that "five year interval screening be performed on: women over 35 years of age (in whom 94% of deaths from cervical cancer occur) [and] women who have been pregnant on three or more occasions."[4] The emphasis must be on recruiting women over 35 years of age who have never been screened; indeed, 92% of all women presenting with cancer fall into this group.

Screening younger women—that is, under the age of 35—also poses a problem. At present, 55% of all cytological tests originate from this age group. The DHSS has therefore suggested that "all women who have been sexually active should be screened at five yearly intervals but that unnecessary repeat smears in intervening years should not be taken. Also any women when first presenting for contraceptive advice should be smeared and thereafter at ages of 20, 25, and 30."

Women who have been subjected to regular screening up to the age of 70 need not have smears after this age. Women presenting for the first time after the age of 70 or those who have symptoms of postmenopausal bleeding or a bloodstained discharge should, however, be clinically examined and have a smear taken; if necessary, referral should be arranged for dilatation and curettage.

Women at high risk of developing cervical carcinoma are: those who had their first pregnancy at an early age; those who have had three or more pregnancies; those with a history of sexually transmitted diseases, particularly genital warts, or multiple sexual partners; those whose male partner has genital warts; heavy smokers (more than 25 cigarettes a day); and women born around 1951, in whom there is a cohort group effect.

How often should women be screened?

Although the policy of five year screening seems rational considering present financial restraints, there are certain facts that may require it to be changed. Firstly, if, as seems likely, the present increase in the incidence of cervical dysplasia among young women continues throughout their lives, and if succeeding cohorts of young women show similar increases, it will become imperative to increase the level of screening. Secondly, the presence of human papillomavirus in a cytological specimen indicates the need for surveillance at possibly yearly intervals because the virus is associated with the development of neoplasia in the lower genital tract.[5] Thirdly, and probably most important, evidence shows that the degree of protection against cervical cancer given by a negative smear falls steadily after only three years.[6] This last fact and data from other clinical studies suggest that the intervals between smears may need to be reduced below five years.[7]

Treatment

Cone biopsy, the removal of a segment of cervix under general anaesthesia, is both diagnostic and therapeutic. There are, however, both short term and long term complications, which invalidate its use in treating all precancerous lesions.[8] Local destructive techniques using cryotherapy, electrodiathermy under general anaesthesia, cold coagulation, or laser evaporation (probably the most versatile and effective) all give acceptable cure rates of 85-95% after one treatment. These methods are used to treat 80-85% of women presenting with abnormal smears in the United Kingdom; cone biopsy or hysterectomy (rarely) is used in the remainder.

Follow up of an abnormal smear

Many centres report that only up to 60% of women have satisfactory follow up and management after the first abnormal smear. Whatever the treatment given for an abnormal smear, the risk of developing subsequent invasive cancer still exists. A recently published study conducted over nearly 30 years found that women who continued to have abnormal smears after treatment had a risk of developing invasive cancer 25 times greater than normal; even those women who had normal smears after treatment had a risk 3·2 times greater than normal.[9]

These data indicate the need for lifelong cytological follow up.

References

1 Draper GJ, Cook GA. Changing patterns of cervical cancer rates. *Br Med J* 1983;**287**:510-2.
2 Chamberlain J. Failures of the cervical cytology screening programme. *Br Med J* 1984;**289**:853-5.
3 Meisels A, Roy M, Fortier M, *et al.* Human papillomavirus infection of the cervix: the atypical condyloma. *Acta Cytol* 1981;**25**:7-16.
4 Department of Health and Social Security. *Screening for cervical cancer.* London: DHSS, 1984. (HC (84) 17.)
5 Singer A, Walker P, McCance DJ. Genital wart virus infections: nuisance or potentially lethal? *Br Med J* 1984;**288**:735-7.
6 MacGregor EJ, Moss SM, Parkin DM, Day NE. A case control study of cervical cancer screening in north east Scotland. *Br Med J* 1985;**290**:1543-6.
7 IARC Working Group on Evaluation of Cervical Cancer Screening Programmes. Screening for squamous cervical cancer: duration of low risk after negative results of cervical cytology and its implication for screening policies. *Br Med J* 1986;**293**:659-64.
8 Singer A, Walker P. What is the optimum treatment of cervical premalignancy? *Br J Obstet Gynaecol* 1982;**89**:335-7.
9 McIndoe WA, McLean MR, Jones RW, Mullins PR. The invasive potential of carcinoma in situ of the cervix. *Obstet Gynecol* 1984;**64**:451-8.
10 Evans DM, Hudson E, Brown C, *et al.* Terminology in gynaecological cytopathology: report of the working party of the British Society for Clinical Cytology. *J Clin Pathol* 1986;**39**:933-44.

Does the level of atmospheric pressure affect the incidence of thromboembolism?

The level of atmospheric pressure per se does not affect the incidence of thromboembolism. The incidence of venous thrombosis, however, is increased in patients with hyperviscosity syndromes such as polycythemia rubra vera. In a study from the central Andes of Peru at an altitude of 14 200 feet above sea level the mean haemoglobin value was 21·1 g/100 ml with a PCV of 59% and in patients with chronic mountain sickness the figures were 24·8 g/100 ml and 79% respectively.[1] An increase of thromboembolism in individuals living under conditions of reduced atmospheric oxygen pressure might therefore be expected. Hurtado, however, spent three decades in an Andean town at 12 000 feet.[2] In describing his personal experience of the clinical aspects of life at high altitudes he commented that coronary thrombosis was rare though he did not comment specifically on thromboembolism. Another report from Yukon territory found that retinal haemorrhage is more common than retinal thrombosis.[3]—C W H HAVARD, consultant physician and endocrinologist, London.

1 Penaloza D, Sime F. Chronic cor pulmonalae due to loss of altitude acclimatization (chronic mountain sickness). *Am J Med* 1971;**50**:728-43.
2 Hurtado A. Some clinical aspects of life at high altitudes. *Ann Intern Med* 1960;**53**:247-58.
3 Frayser R, Houston CS, Bryan AC, *et al.* Retinal haemorrhage at high altitude. *New Engl J Med* 1970;**282**:1183-4.