

EXFOLIATIVE CYTOLOGY IN THE EARLY DETECTION OF CERVICAL CARCINOMA IN GENERAL PRACTICE

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TWENTY years have passed since the Royal College of Obstetricians and Gynaecologists set up the subcommittee under Mr Malcolm Donaldson to enquire into the efficiency of exfoliative cytology in clinical practice. In this time the object of eliminating cervical cancer has grown from an idea interesting small groups of research workers and clinicians to a subject which has fired the imagination of varying groups of medical and lay people. It has been a hotly debated point in local and national politics, women's organizations and women's magazines.

It is a field in which the general practitioner can play a vital part. He is in close contact with the population at risk and "once the signal of a 'positive smear' is given, a team is essential for the care of the patient and the key man is the family doctor." (*Brit. med. J.* 1964). This point of view being supported by many others (Spenser 1967).

Large numbers of 'at risk' women consult their family doctor. Many vaginal examinations are carried out and I subscribe to the view that a gynaecological examination which does not include vaginal cytology should be regarded as incomplete (Wachtel 1964).

The following groups were considered as providing a representative cross section of the women 'at risk' in the practice.

1. Postnatal examinations (including post-abortion examinations). As a general rule antenatal patients were not screened as there are a number of disadvantages if it is done during this time, although some authorities do not agree with this (Rad *et al.* 1966).
2. Women attending with gynaecological complaints.
3. Examination prior to the fitting of contraceptive diaphragms and caps, prescribing oral contraceptives and the periodic examinations on all women taking the oral contraceptive.
4. Screening of 'at risk' age groups who requested it, and by propaganda amongst this group.
5. Women with miscellaneous conditions where a pelvic examination is

incidental to a general examination.

6. A small group who were found to be pregnant when examined.

It was decided therefore to screen groups 1, 2, 3, 5 and 6 routinely at the same time as a pelvic examination was done.

With regard to group 4, propaganda was carried out by personal approach and by displaying in the waiting room posters worded as follows:

A test for the early detection of women who are likely to develop cancer of the cervix (neck of the womb) is available.

This applies to all married women up to the age of 60 years and single women between the ages of 20-60 years, if they wish.

If you would like to have this done, please ask me for an appointment.

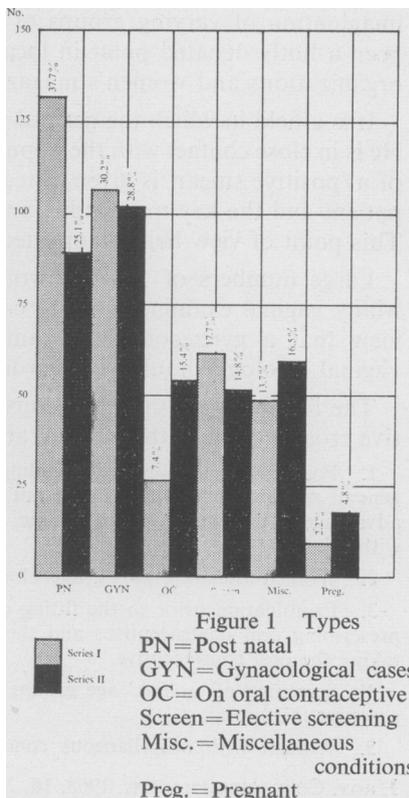
Using this grouping as a 'net' which would 'catch' the majority of the women at risk in the practice was considered better than two other methods which have been described by Spenser *et al.* (1967) viz.

(a) Offering the test to women in the risk group only when they attended the surgery for other reasons, either for themselves or with children. (b) A personal letter offering the test to the women at risk.

By doing this (i.e. grouping as in 1-6) normal general practice is combined with at least one aspect of preventive medicine and there is much less chance of a screening programme being seen out of perspective. That the 'net' was effective is shown by the fact that the majority of the women at risk were screened (*see* under 'Findings' for details).

A graph illustrating the numbers in each group is shown in figure 1.

The patients screened were divided into Series I and II. Series I were those seen from 19 July 1963 to 19 October 1965, 350 in number and Ayre



scrapes alone were done.

The following 350 cases from 20 October 1965 to 3 March 1967 constitute Series II and on these both Ayre scrapes and Papanicolaou smears were done.

It was decided to do the additional Papanicolaou smear in series II with the object of comparing the diagnostic 'pick-up' rate as compared with using the Ayre scrape alone as in series I and also with the object of investigating the greater likelihood of detecting carcinoma of the body of the uterus by using this technique.

Method

A history including parity and any gynaecological symptoms is taken.

With the patient in the dorsal position, the abdomen is palpated and the external genitalia inspected. Then with a good light the cervix is exposed with a bivalve speculum.

Using a bulb and sterile pipette, material is then aspirated from the posterior forniceal pool and transferred to a labelled slide, spread thinly and immediately immersed in fixative. (Slides are marked with the patient's name and P.S. indicating Papanicolaou smear or A.S. indicating Ayre scrape—using a diamond pointed stylus).

Excess mucus or discharge is then removed with a sterile swab and using an Ayre spatula a 360 deg sweep is made round the external os. A slide is made and also immersed in fixative.

Any erosions present are cauterized with silver nitrate stick and then a digital bimanual vaginal examination is done.

All information is then recorded on the following card and the patient instructed to return in two weeks for the result.

NAME	AGE	CERVICAL CYTOLOGY	CODE LETTER
History			
Abdomen:			
P.V.: Anteverted/retroverted uterus:			
Speculum:			
Ayre scrape, Papanicolaou smear:			
CYTOLOGY			

Figure 2

Repeat Ayre scrapes were done if requested by the laboratory. In series I, Ayre scrapes reported as being positive for carcinoma cells were repeated with the addition of a Papanicolaou smear and then referred to a consultant gynaecologist for cone biopsy. In series II, following a report of "carcinoma cells present" repeat Ayre scrapes and Papanicolaou smears were done and then referred for cone biopsy.

Record cards are filed and a master analysis card for quick reference is kept (table I).

TABLE I
THE RECORD CARD USED FOR ANALYSIS

	50	100	150	200	250	300	350
Carcinoma cells							
Atypical or suspicious cells							
Trichomonas							
Oral contraceptive							
Total patients							
Total scrapes and smears							

At the top right hand corner of each card is recorded a code letter as follows:

- PN=Postnatal examination
- POC=Pre-oral contraceptive examination
- Ca=Carcinoma cells seen
- Sc=Atypical or suspicious cells seen
- TV=*Trichomonas vaginalis*
- R=Repeat requested by laboratory
- Misc=Miscellaneous
- S=Screening of 'at risk' age group
- GYN=Gynaecological complaints as presenting symptoms
- CAN ALB=*Candida albicans*
- PREG=Pregnant

Analysis of information

An analysis of the information gained is illustrated graphically in figures 4-8.

Parity (figure 3). The majority of cases screened in both series had borne one or two children, these together being over twice the number of nulliparous and mothers of three children examined.

In both series the maximum number examined were in the 20-30 year age group with the 30-40 year and 40-50 year groups in succession (figure 4).

In both series as shown in figure 1 the number of cases classified as postnatal and gynaecological was roughly twice the number who were screened at their own request or as a result of propaganda in the practice. These and the figures shown in figure 4 show that in

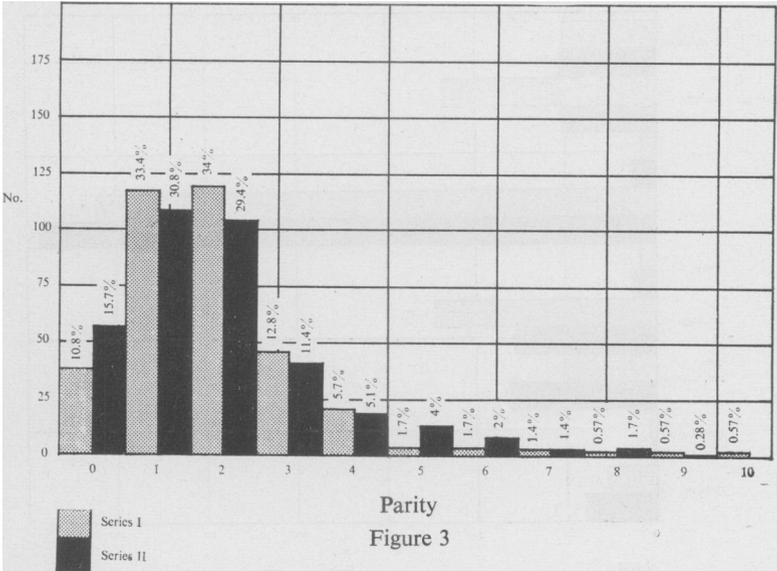


Figure 3

general practice at least, the age groups screened are more likely to be younger than those envisaged by the Ministry of Health (i.e. 35-60 years). In series I and II, 70.1 per cent were in the age group 15-40 and in the under-35-year groups, the latter therefore not qualifying for the Ministry criterion for the women at risk. Had this group been excluded in the survey six cases which were positive for carcinoma cells (i.e. 0.85 per cent of the total and 42.8 per cent of the positive smears) would have been missed.

Figure 5 shows the other abnormalities which were found at examination, many of which bore no relation to the reason for examination. Two interesting findings were the incidence of *Trichomonas vaginalis* infections (nearly 7.2 per cent in both series) and cervical erosions (34.1 per cent in both series).

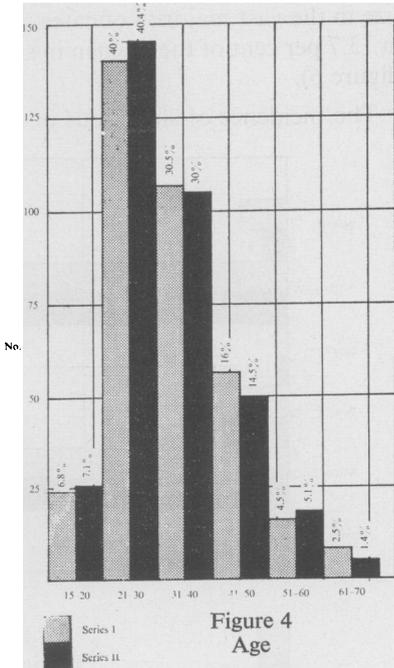


Figure 4 Age

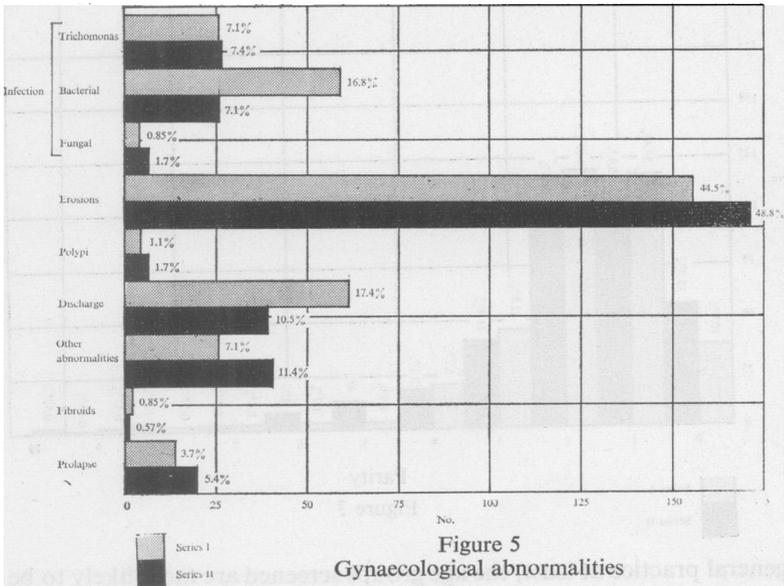


Figure 5
Gynaecological abnormalities

As was to be expected, the uterus was anteverted and of normal size in the vast majority of cases, but a retroverted uterus was found in 13.7 per cent of the women in series I and 29.4 per cent in series II (figure 6).

The incidence of suspicious or atypical cells where the laboratory

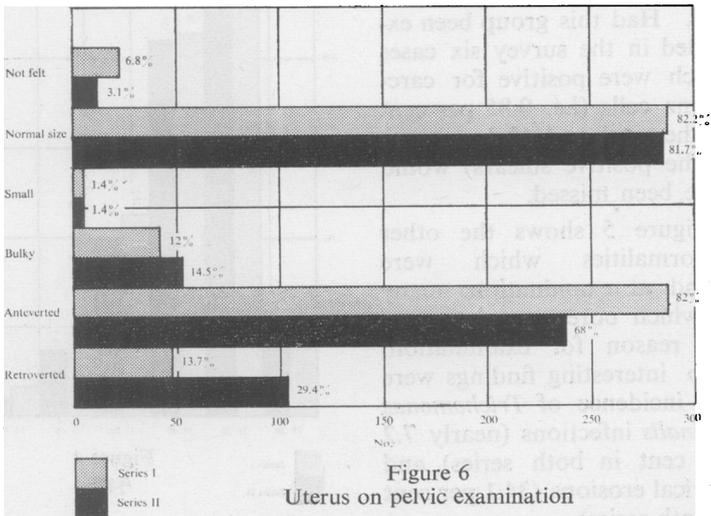


Figure 6
Uterus on pelvic examination

requested a repeat was 9.7 per cent in series I and 18.0 per cent in series II (figure 7).

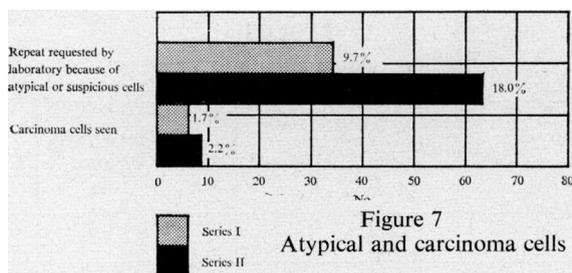


Figure 7
Atypical and carcinoma cells

The percentage of cases which were positive for carcinoma cells was 1.7 per cent in series I and 2.2 per cent in series II. The combined incidence was 14 cases in 700, i.e. two per cent, which is much higher than some figures quoted, e.g. 0.42 per cent by Kirkland in South Australia (Kirkland 1966), 0.73 per cent at a local authority clinic in Derby, but slightly lower than the 2.65 per cent in a domiciliary testing series in Derby (Osborn *et al.* 1966).

In series II using the Papanicolaou smear as an additional screening test, the percentage of atypical or suspicious cells seen was nearly twice that of series I, and carcinoma cells were seen in 2.2 per cent of cases in series II as against 1.7 per cent in series I.

The high incidence in this series may be explained by the fact that they all occurred in social classes IV and V which are the predominant classes in the practice. These figures confirm the findings of Osborn *et al.* (1966).

Technique of making the smears might be considered as a factor in the incidence of false negatives in studies done in other centres. In both series of this exercise a deliberate policy of producing the best possible smear was pursued so that the cytologists would have as ideal a slide as possible to examine. Centres examining large numbers of smears from widely varying sources have commented on the variable standard of the smears submitted, and this factor must be borne in mind by all who are concerned with cytodagnosis. (In the series described by Osborn *et al.* (1966) the home nurses taking the smears were taken to the local pathological laboratory where they were shown good and poor smears).

A total of 807 Ayre scrapes and Papanicolaou smears were done on the 700 women in both series.

Findings

Of the 20–60 year age group in the practice, 700 out of a possible 774 were examined in the period 19 July 1963 to 3 March 1967

(i.e. three years eight months).

Table II shows the age groups with positive smears (series I and II).

TABLE II
THE AGE GROUPS WITH POSITIVE SMEARS

<i>Age groups</i>	<i>No.</i>	<i>Percentage of total cases</i>	<i>Percentage of positive smears</i>
15-20	3	0.42	21.4
21-25	2	0.28	14.2
26-30	1	0.14	7.14
31-35			
36-40	4	0.57	28.5
41-45			
46-50	1	0.14	7.14
51-55			
56-60	1	0.14	7.14
61-65	2	0.28	14.2
Percentage of total number in both series under 35			0.85
Percentage of total number in both series over 35			1.14
<i>Percentage of positive cases in both series</i>			
Percentage under 35			42.85
Percentage over 35			57.14

These figures, like those of Dunn (1966) show a steep rise from age 17-22 years to a peak at 30-45 years after which there is a second but lower peak at and after 60 years. They also serve to emphasize that a high percentage of women at risk are well under the age of 35, thus giving added point to Dunn's comment that carcinoma *in situ* is a disease of young women.

Table III shows the age, parity, marital state, social class and 'type' of case of those with positive smears.

Table IV shows the relationship between cytological and histological diagnosis in those cases with positive smears.

TABLE III

AGE, PARITY, 'TYPE' OF CASE, MARITAL STATE AND SOCIAL CLASS OF THOSE WITH POSITIVE SMEARS

No.	Age	Parity	"Type"	Marital state	Social class
1	60	3	Gynae	Married	IV
2	38	3	„	„	IV
3	29	2	„	„	IV
4	17	0	„	Single	IV
5	63	2	„	Married	IV
6	38	3	„	„	IV
7	20	1	„	Single	IV
8	37	6	Misc.	Married	V
9	47	4	Gynae	„	IV
10	36	7	Misc.	„	V
11	22	3	„	„	V
12	17	0	Gynae	Single	IV
13	26	1	Postnatal	Married	IV
14	65	0	Gynae	Widow	IV

Thus it is noted that the cytological diagnosis was proved histologically in 11 cases.

In case 2 of series I, the pathologist is in no doubt about the cytological diagnosis and he says:

The smears in this case are positive though some cytologists would call the condition 'dyskaryotic'. I have very little use for this term, it only means wrong nuclei and the question is with which family of disorders the lesion belongs. These 'dyskaryotic' lesions keep company with carcinoma *in situ* and invasive carcinoma, the more I see of it the more convinced I am that it is a precursor of carcinoma *in situ*.

The cone biopsy shows a large erosion. Some of the surface epithelium has been rubbed off mechanically. This is one of the serious problems in diagnosing carcinoma *in situ* because the attachment of a carcinoma *in situ* to the underlying tissues is exceedingly loose, quite unlike the normal epithelium, it is therefore very easy for the gynaecologist cleaning the cervix before operation to wipe it all off. Should we not have the good fortune to find parts which have penetrated glands we are unable to make the diagnosis histologically. Because of the size of the erosion there is not a great deal of squamous epithelium present, some of

TABLE IV
THE RELATIONSHIP BETWEEN CYTOLOGICAL AND HISTOLOGICAL DIAGNOSIS

<i>Cytological diagnosis</i>	<i>Histological diagnosis</i>
1. Atypical squames	Cone biopsy: Carcinoma <i>in situ</i> or its precursor. (Hysterectomy)
2. Probable carcinoma cells	Variation in cell size and mitotic figures. No proof of carcinoma <i>in situ</i> . (<i>Vide infra</i>)
3. Carcinoma cells present	Carcinoma <i>in situ</i> cervix. Endometriosis
4. Probable carcinoma cells present	Dyskariosis anaplasia or commencement of carcinoma <i>in situ</i>
5. No tumour cells seen. Carcinoma cells present 6/52 later	Papillary adenocarcinoma of corpus uteri
6. Carcinoma cells present	Carcinoma <i>in situ</i>
7. Atypical squames. Carcinoma cells 5/12 later	„ „ „
8. Carcinoma cells present	„ „ „
9. „ „ „	„ „ „
10. „ „ „	„ „ „
11. „ „ „	Mainly dysplastic, one area of carcinoma <i>in situ</i>
12. Probable carcinoma cells present	Metaplasia. No sign of malignancy. (<i>Vide infra</i>)
13. Carcinoma cells present	Carcinoma <i>in situ</i>
14. Probable carcinoma cells present	Carcinoma <i>in situ</i>

this shows 'basal hyperplasia' which again is an alternative term for 'dyskaryiosis' and I regard it as an early stage of carcinoma *in situ*. Complete removal appears improbable.

Unfortunately only routine sections were taken from the hysterectomy specimen because we were not supplied with any notes and because of the large amount of work involved we cannot undertake complete histological examination of the cervix from every uterus removed.

In case 12 (series II) it is possible that the area of carcinoma *in situ* was not included in the sections examined.

In a further communication the pathologist reports:

The first smear from this case had atypical cells which may or may not be a

consequence of the *Trichomonas vaginalis* infection she had at that time. The later smears were positive.

Various epithelial abnormalities are present in the cone biopsy, one is multiple foci of 'dyskaryosis' where the surface cells have not differentiated normally. I believe this lesion to be an early precursor of carcinoma *in situ*. A patch only a few cell layers thick is probably carcinoma *in situ* but it would be given various interpretations by different pathologists. Removal is probably complete. I believe this is a case of carcinoma *in situ* in the first stage of simple replacement.

The pathologist also says:

A problem in interpretation frequently arises in this work, some think that a carcinoma *in situ* can be given an exact definition and if the appearances do not fall into this they call it another name. Because no two malignant tumours are ever exactly alike we *have* to be prepared for a wide range of appearances in conditions given the same diagnosis.

Case 14 (series II) on admission for D & C and cone biopsy after treatment for the trichomonas infection was proved carcinoma *in situ*.

A period of five minutes was found to be the average time taken to do an abdominal palpation, inspection of the genitalia, take the smears and do a bimanual examination. To this must be added the time taken to complete the details on the current M.O.H. cytology screening form, some of which can be done by a secretary. Clinical details are always done by the doctor. Spenser (1967) found that 4.4 per cent of total professional time was involved (this did not include smears taken during a pelvic examination done for other reasons).

Therefore one can say that in this survey a higher percentage of time was involved.

The exercise confirms that the family doctor is most favourably placed to obtain the smears for cytodiagnosis.

Two criticisms of the present system are valid.

1. The M.O.H. policy that only the 35-60 year old group should qualify for a fee when done by general practitioners. This series shows the incidence to be high in a much lower age group and Osborn and also Kirkland confirm this (table V).

2. In terms of professional time the fee is unrealistic and unlikely to encourage family doctors to participate in screening schemes. A random enquiry of 17 family doctors in an area where good facilities were available revealed that only eight took their own smears.

The intention of the Minister of Health (1964) to rely upon general practitioners to carry out the screening of their patients will not be realized unless radical changes are introduced in both these aspects. of the 70 patients taking oral contraceptives (Ortho-novin in all cases), none had positive smears. One showing atypical squames initially showed no abnormality after 3½ years. A repeat after one

TABLE V
 POSITIVE SMEARS FOR THE YEAR 1966. (DERBYSHIRE ROYAL INFIRMARY)
 (This shows the age distribution and source of positive smears at the pathology department of the Derbyshire Royal Infirmary. General practitioners are an important source of those occurring in the 16-20 year group).

	16-20	21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	76-80	81-85	Total
Local authority clinics (including domiciliary nurses)	2	3	3	8	19	15	3	4	—	—	—	—	—	—	57
Hospital cases	3	6	2	7	5	9	4	6	6	5	2	1	2	1	59
Antenatal and postnatal cases	1	2	4	1	—	1	—	—	—	—	—	—	—	—	9
General practitioner	3	—	2	1	7	2	3	—	—	—	—	—	—	—	19
TOTAL											+ 1	87-year-old			144

year was requested in one case and a further repeat in one year when this was done.

Fungal infections (monilia and *Candida albicans*) were found in nine cases. Of these, two were taking the oral contraceptive but one of these already had candidiasis before she started taking the contraceptive. Catterall (1966) reports the incidence of candidiasis in women taking oral contraceptives, but this was not a feature seen in the 70 cases in this series. In fact, the most persistent case was one who used a diaphragm.

Summary

A cervical cytology screening programme in general practice is described. 700 out of a possible 774 women at risk were screened in two series of 350—the first using Ayre scrapes alone, the second using Papanicolaou smears in addition. The programme covered a period of three years eight months, and a total of 807 Ayre scrapes and Papanicolaou smears were done. Fourteen positive smears were found, all except three of which were proven on histology.

Suspicious or atypical cells were seen in a further 97 cases and these are being followed up.

All the positive smears were found in cases where the screening was incidental to a clinical examination and all occurred in social classes IV and V.

The family doctor is considered to be an essential part of any national screening programme but administrative changes are urgently necessary if this is to be realized.

Acknowledgements

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REFERENCES

- Brit. med. J.* (1964). **2**, 1410.
 Catterall, R. D. (1966). *Lancet*. **2**, 830.
 Dunn, J. E. Jnr (1966). *Proc. roy. Soc. Med.* **2**, 1198.
 Kirkland, J. A. (1966). *Aust. N.Z. J. Obstet. Gynec.* **6**, 15.
 Osborn, G. R. *et al.* (1966). *Lancet*. **1**, 256.
 Rad, M. *et al.* (1966). *Amer. J. Obstet. Gynec.* **94**, 465.
 Report of Ministry of Health for 1963 (1964). London. Her Majesty's Stationery Office, cmdn. 2389. Health & Welfare Services.
 Spenser, J. T. (1967). *Practitioner*. **198**, 274.
 Wachtel, E. G. (1964). *Exfoliative cytology in gynaecological practice*. London. Butterworths.