disorders and which has on occasion been associated with the progressive development of one or other malignancy. Further investigation of patients may well show the occurrence of common pathogenetic mechanisms.

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Accepted 7 Jun 1993.

The value of abrasive cytology in the early detection of oesophageal carcinoma

A pilot survey in Ciskei

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The use of abrasive cytology as a screening procedure in the diagnosis of early cancer of the oesophagus among asymptomatic rural Ciskeians was assessed. An inexpensive, locally manufactured brush biopsy capsule was used to obtain cytological material from 1 336 subjects. The technique gives a high yield, has a high predictive value and identifies a high prevalence of sufferers at the detectable preclinical phase of the disease.

S Afr Med J 1994; **84:** 488-490.

Squamous cancer of the oesophagus is the commonest cancer among black men in southern Africa. Only cancer of the cervix among black women is more prevalent.[1] It was especially common among rural Transkeians,[2] but is now also found increasingly in urban populations of the region.[2-6]

As a rule, patients with oesophageal cancer present at an advanced stage of relentless progression. While patients' symptoms are usually of recent origin, their period of survival is short.[7,8] This cancer therefore seems to fulfil many of the criteria necessary for it to be suitable for screening. These include: *(i)* a high prevalence in a susceptible population; *(ii)* its recognition as a serious disease in the community; *(iii)* effectiveness of cancer therapy, either by means of surgery or radiotherapy; and *(iv)* a well-documented, prolonged 'detectable pre-clinical phase' (DPCP) when effective therapy could lead to a cure.[9]

Abrasive brush cytology as a screening technique for oesophageal cancer has been used for many years in high-incidence areas of China. Early diagnosis and many long-term survivors have been reported.[10,11] In southern Africa,

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brush cytology has also been used as a diagnostic aid and research tool.[12-15] In one study 15 asymptomatic oesophageal cancer patients were identified by means of brush cytology with an inflatable balloon catheter.[16] However, brush cytology has not been used in mass screening.

This pilot study was undertaken to determine the feasibility of brush cytology with a simple, inexpensive brush biopsy capsule as a screening programme for oesophageal cancer in asymptomatic rural subjects from Ciskei.

Subjects and methods

Villages in the Keiskammahoek district of Ciskei were visited between 1986 and 1990. In most cases the villages selected were those with high oesophageal cancer prevalence rates, as estimated from case records at Cecilia Makiwane Hospital (unpublished data). The co-operation of local chiefs, headmen and community leaders was sought, and adult villagers were invited to participate in the study.

The brush biopsy capsule used is an inexpensive, locally manufactured capsule similar to that described by Nabeya.[17] It consists of a sponge within a capsule attached to a long thread. The subjects swallow the capsule with some water. The capsular covering of the sponge dissolves within 10 minutes and the sponge expands within the stomach; this allows it to obtain cytological material when it is withdrawn through the oesophagus. The material thus obtained is smeared onto a glass slide, fixed, stained and examined cytologically.

Subjects who were experiencing difficulty with swallowing or in whom the capsule failed to reach the stomach (as assessed by the length of thread remaining outside the mouth) were excluded from the study and referred for other investigations. The few subjects from whom no suitable material for cytological examination was obtained were excluded from the study.

All subjects with cytological reports of severe dysplasia or carcinoma underwent endoscopy with Lugol staining of the oesophagus.[18,19] Those whose diagnosis of carcinoma was confirmed histologically were counselled and referred for further investigation and treatment. In order to evaluate the predictive value, the detected prevalence of the DPCP and the yield of the test, the following definitions were used: **true positive** — subjects whose results were cytologically positive for cancer with the result confirmed by means of endoscopy and biopsy; **false positive** — subjects whose results were cytologically positive for oesophageal cancer but which were not confirmed by endoscopy and biopsy; **predictive value** — among subjects positive on the screening test, the proportion found by subsequent diagnostic evaluation actually to have the disease. This was calculated as follows:

$$\frac{\text{True positives}}{\text{True positives + false positives}} \times \frac{100}{1}$$

The detected prevalence of the DPCP among all subjects screened, was the proportion found on the screening test and subsequent diagnostic evaluation to have the disease. **The yield** entailed the number of tests that had to be done in order to identify 1 person whose prognosis would be improved as a result of the screening programme.

The study was approved by the Committee for Research at Cecilia Makiwane Hospital and by the Department of Health of the Ciskei.

Results

One thousand three hundred and thirty-six subjects (926 women and 410 men) underwent the procedure. They were representative of the usual week-day resident population of the villages, with large numbers of older subjects present. Of the 1 336 subjects, 9 true-positive cases were detected.

A further subject reported as positive by the pathologist revealed a diffuse, granular oesophagus at endoscopy but histology of the biopsy specimens revealed acanthotic, dysplastic epithelium without invasion. This subject has been regarded as a false positive.

The predictive value of the programme as determined in this study is therefore:

$$\frac{9}{9+1} \times \frac{100}{1} = 90\%.$$

The detected prevalence of the DPCP was 9 out of 1 336 subjects brushed.

The 9 subjects whose carcinoma was confirmed histologically were counselled and referred for further investigations and treatment. In 7 cases the carcinoma was at an early stage while in 3 it was advanced. Two of the subjects with early carcinoma were old and infirm and so received no further treatment. Three other subjects declined intervention despite counselling. Only 2 of the 9 subjects underwent the recommended treatment.

The yield of this study is therefore strictly 2 cases (668 screens per case treated) but the programme yield could potentially increase to 9/1 336 (148 screens per case).

Discussion

The aim of screening for cancer is to detect and treat the disease at a stage when it is still curable. In practice this implies the detection of the cancer before it is clinically evident. While the idea that detection of a disease in a pre-clinical phase will be beneficial has a strong intuitive appeal, the value of screening as a means of cancer control remains controversial.

While the major benefit would appear to be an improved prognosis, the disadvantages are significant. These include the expense of the screening programme, diagnostic investigations and treatment, the time and discomfort of those screened, a longer period of morbidity for those found to have the disease and the overtreatment of borderline cases. In addition, inappropriate reassurance will be given to 'false-negative' subjects and unnecessary anxiety engendered among 'false-positive' subjects.

Hence, any effective screening programme needs to be inexpensive, easy to implement and well tolerated by those tested. In addition, the screening technique itself needs to be reliable and the results readily reproducible.

The procedure of obtaining cytological material by brush biopsy capsule was reasonably well tolerated by most subjects. Little difficulty was experienced when the capsule

was swallowed, although subjects usually 'gag' when the sponge is retrieved and a few subjects vomited at the same time. Apart from a mild sore throat in some, no pain was experienced.

While the brush biopsy capsule has been known to lodge in the oesophagus above an advanced carcinoma and so fail to obtain malignant cells when withdrawn,[20] our study suggests that the technique can establish the diagnosis in asymptomatic patients. Although some field-workers responsible for performing the survey had relatively little training, material suitable for cytological assessment was obtained in almost all cases.

Although the brush biopsy capsule itself is inexpensive (R1/capsule approx.), the hidden costs (field workers, transport, preparation of slides and cytological assessment), while difficult to evaluate, are considerable. The high detected prevalence (9/1 336 subjects) may in part be explained by the large number of older individuals assessed, in whom the disease would be more likely to be present. However, it is possible that the specific villages chosen for the survey because of their apparent high mortality rates for oesophageal cancer did, in fact, have an unusually high prevalence of the disease.

The validity of brush cytology as a screening test may be assessed in terms of its sensitivity and specificity.[21,22] In this study, it was not possible to make the distinction between true- and false-negative subjects necessary for this assessment. To administer the confirmatory test to apparently healthy subjects whose screening test was negative is ethically unacceptable and economically impractical.[21] Predictive value among those subjects positive for the screening test is the proportion confirmed as having the disease in question. For a disease such as oesophageal cancer the major determinants of predictive value are the prevalence of the DPCP, the specificity of the test and, to a lesser extent, its sensitivity.[21] A high predictive value indicates that the programme appears to be satisfactory.

The high predictive value of 90% obtained in this survey suggests that the programme is satisfactory; the test has a high specificity and confirms a sufficiently high prevalence in the population screened.

The yield is the number of tests which must be performed to identify 1 case[22] and is useful in justifying (or not) the cost of the screening programme in relation to the value of the cases successfully treated.

This pilot survey suggests that brush cytology as a means of screening for oesophageal cancer in southern Africa may be as valuable a tool in the control of this disease as it has been in China, provided that screening is accompanied by an intensive community-based health education programme. In this study, 5 subjects whose general health was good were assessed as having 'early carcinoma' and were encouraged to undergo appropriate therapy. Despite adequate counselling, 3 of the 5 declined any further treatment. This is due to the community's observation that most patients undergoing surgery or radiotherapy for cancer eventually die and that treatment aggravates the condition. Thus to treat a cancer which is, as yet, not producing any symptoms is unacceptable. Community acceptance of subsequent treatment is therefore an essential prerequisite of any screening programme.

Results of studies conducted in high-risk patients in Chicago[23] suggest limited use of brush cytology as a screening method for the early detection of oesophageal carcinoma. On the other hand, the efficacy of oesophageal cancer screening has been adequately documented in China. This survey suggests that this could be true for southern Africa. We recommend that economic and educational implications of mass screening for this disease be investigated by health authorities with the enthusiasm that we believe would be present if a disease of such prevalence was to affect the First-World population of the region.

We would like to thank the D. G. Murray Trust, the Pharmaceutical Manufacturers' Foundation, South African Druggists Ltd, Warner Lambert and Oxfam for their generous financial assistance; the Department of Community Health of the S. S. Gida Hospital, Mrs M. Hassall of the South African Medical Research Council and Mrs V. N. Majola for assistance with the field work; Ian Corr Medical Manufacturers, Cape Town, for the production of the capsules; and the Department of Health of the Ciskei for permission to publish.

Some material from an 'in press' publication in *Cytopathology* was used. Permission of *Cytopathology* is greatly appreciated.

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Accepted 12 Aug 1992.