THE PREVENTION OF INVASIVE CANCER OF THE UTERINE CERVIX

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THE PROBLEM IN SINGAPORE

Cancer is the chief cause of death among women in Singapore today. The commonest site is the uterine cervix, accounting for 75 per cent of gynaecological malignancies (excluding choriocarcinoma) seen at the Kandang Kerbau Hospital for Women (Cancer Committee Report, 1965). During the three years 1962-4, 460 cases of cervical cancers were diagnosed at the Kandang Kerbau Hospital, Singapore, an average of some 150 cases each year. Of these, 95 per cent were in the invasive stages 1-4 and only 5 per cent were in the in situ or pre-invasive 0. Of 157 cases diagnosed in 1962, 75 are known to have died, 33 are alive while the fate of 49 could not be determined. Based on these figures, the known 5-year survival rate is 21 per cent. At best, assuming that the untraced 49 cases were all alive, the 5-year survival rate would not be more than 52 per cent. If the pattern of disease and methods of therapy remain unchanged, it may be deduced that between 75 to 120 women die from cervical cancer in Singapore each year. According to a World Health Organisation Expert Committee report on the Prevention of Cancer (1964) 75 per cent of all cancers are preventable. Mass screening utilizing the Papanicolaou cytological technique represents the most effective and specific method of preventing and eradicating invasive cervical cancer (Day, 1963).

THE PAPANICOLAOU METHOD

Briefly stated, Papanicolaou's method of cancer detection is based on these principles:

1. Exfoliated cells accurately reflect the state of the tissue of origin.
2. Invasive cervical cancer is preceded by a pre-invasive or in situ stage.
3. Pre-invasive cervical cancers exfoliate malignant cells long before the appearance of the frank invasive growth.

In 1965 the Papanicolaou cytological technique was established in the University Unit at the Kandang Kerbau Hospital with the help of the Cancer Detection Centre in Perth, Western Australia. In the three years up to the end of 1967, 10,693 patients have been screened for cervical cancer. These comprised 5,451 smears of women attending the postpartum Intra-uterine Device Family Planning Clinic, with the detection of 12 pre-invasive cervical cancers (2·2 per 1000) and 5,242 smears on women attending the Gynaecological Outpatient Clinic, with the detection of 25 pre-invasive lesions (4·7 per 1000). The overall "pick-up rate" was 3·5 per 1000 patients screened. A number of patients with abnormal smears are still under observation. The pick-up rate of 3·5 per 1000 must therefore be regarded as a minimum rate which will have to be revised when more cases come to light. In addition 8 cases of early invasive cervical cancer and 4 cases of endometrial cancer were detected.

METHOD OF DIAGNOSIS

All cases with "positive" or "highly suspicious" cytological reports were subjected to cervical biopsy. The standard procedure was a cone or ring biopsy. In a few cases multiple punch or wedge biopsies only were taken. All specimens were sent to the Government Pathology Laboratory for report.

TREATMENT AND RESULT

The treatment employed was total hysterectomy in 28, cone/ring excision biopsy in seven, while two are awaiting definitive treatment. In determining the method of treatment, the patients' age, parity and need for further childbearing were taken into account. Follow-up consists of 6-12 monthly visits for clinical and cytological examination.

No deaths have occurred in the present series of cases, either from treatment or during the follow-up period. At the present time 25 per cent of cervical cancers diagnosed in the University Unit at Kandang Kerbau Hospital are in situ growths. This is a five-fold increase since 1962-4.

DISCUSSION

Whereas in Western populations, cancer of the breast outnumbers that of the uterine cervix by about 2:1 the position in Singapore is quite the opposite. Investigations have shown that cervical cancer is the commonest malignancy diagnosed in Singapore women, its frequency being almost double that of the breast. The elimination of cervical cancer is therefore an important public health problem.

Cytological screening has been widely used in the detection of carcinoma in situ of the cervix since its introduction by Papanicolaou and Traut in 1943. Despite trials with newer techniques such as fluorescence microscopy and biochemical analyses (6-GPD), cytology remains the only effective practical diagnostic tool for mass employment.

Invasive cervical cancer does not develop directly from normal epithelium but evolves in a series of steps, each assuming recognizable morphological features with a life span measurable in years. These evolutionary steps may be depicted thus:

Normal epithelium
↓
Dysplasia
↓
Carcinoma in situ
↓
Micro-invasive carcinoma
↓
Clinical invasive carcinoma

This concept clearly recognizes carcinoma in situ as the precursor of invasive carcinoma. it is based on cummulative knowledge of the natural history of carcinoma in situ acquired over many years by many different investigators, involving clinical, histological and cytological studies. The histological progression of one stage to another has never and can never be observed to take place in a particular case for the simple reason that a biopsy specimen cannot be grafted back into its tissue of origin for further study.

What, then, is the evidence in support of the above concept? Even as early as 1912, Schottlander and Kermauner drew attention to the common occurrence of a zone of in situ carcinoma on the borders of an invasive lesion. Such a zone may be regarded as a growing edge of the tumour. The chief credit for emphasizing the importance of carcinoma in situ as a forerunner of the invasive lesion goes to Schiller (1927) who is best remembered for describing the iodine staining technique to aid early diagnosis.

Many studies have shown that a long latent interval exists between the original diagnosis of in situ carcinoma and the eventual discovery of invasion. This is reflected in the fact that the average age of patients with carcinoma in situ is 10 years less than that of patients with invasive carcinoma. (Galvin, Jones and TeLinde, 1955; McKay, Hertig and Younge, 1954).

Morphologically, there are significant similarities between carcinoma in situ and invasive carcinoma (Friedell, Hertig, and Younge, 1960). The cells comprising the epithelium of carcinoma in situ fulfil all the criteria for the diagnosis of malignancy and when exfoliated are indistinguishable from those derived from invasive carcinoma. The appearance of carcinoma in situ is identical with that of the epithelial changes adjacent to invasive carcinomas. The results of ultraviolet absorption, histochemical and biochemical studies, and tissue culture in situ are similar to those in invasive carcinoma.

Further support, from an epidemological viewpoint, is provided by the British Columbia study in which the elimination of carcinoma in situ has led to a fall in the incidence of invasive carcinoma. (Boyes, Fidler and Lock, 1962). Over a period of 14 years, more than half the adult female population were screened resulting in a drop in the incidence of invasive carcinoma from 28·4 per 100,000 in 1955, to 15·5 in 1962. Even more striking was the incidence of invasive carcinoma in the previously screened population which was 3·5 per 100,000 in 1962, compared with 24·1 in the unscreened population (Bryans, Boyes and Fidler, 1964). In a similar study in Louisville, Kentucky, invasive carcinoma was eradicated after three years of mass cytological screening. (Christopherson et al, 1962).

Most authorities agree that not all cases of carcinoma in situ will invariably develop into invasive carcinoma. Peterson's work in Denmark (1956) indicates that within a period of 5-10 years about 25 per cent will become invasive, the figure rising to 35 per cent by the 14th year (Peterson, 1959). The British Columbia study put the "ceiling" of invasive change at 60 per cent (Boyes, Fidler and Lock, 1962).

One of the objections raised against the mass cytological screening in British Columbia is that there has been no appreciable fall in the morta-

lity from cervical cancer. (Green, 1966). Two reasons may be given to explain this apparent deficiency. Firstly, a number of cancers may not go through a prolonged in situ phase and thus would likely escape detection by cytological screening methods. Dunn (1958) and Ashley (1966) indeed believe that certain cancers are rapidly growing and become invasive right from the start. Secondly, many "high-risk" cancer patients may be among those who fail to attend for screening as demonstrated in one survey (Macgregor and Baird, 1963).

Although the British Columbia results have not fully satisfied the critics, the value of cytology is by no means nullified. A more distinct fall in mortality may be confidently expected in the near future.

ACTION PLAN FOR SINGAPORE

Singapore has a young, highly literate and largely urban population, with a good doctor-population ratio. The solution of its No. 1 female cancer problem is, therefore, something well within the realm of possibility. An "Action Plan" aimed at eradicating cervical cancer within 5-10 years is outlined hereunder.

1. Training of personnel.
2. Education of medical and allied personnel.
3. Education of the public.
4. Organization of clinic, laboratory and hospital facilities.

1. Training of Personnel

Systematic courses of instruction in cytopathology and cytotechnology extending over 10-12 weeks should be initiated, followed by further practical training over 6-12 months. In this way a functional team of cytologists and cytotechnicians may be established.

Ancillary personnel such as clerks, follow-up and recall staff, and clinic nurses will require training in the mechanics of running a cancer detection clinic, the management of positive smears, tracing of defaulters, correspondence, filing and indexing—important supporting functions of a cancer detection outfit.

2. Education of Medical and Allied Personnel

The success of the Action Plan will depend to a large extent on the active co-operation and participation of the profession and allied personnel such as nurses, midwives, health workers, hospital assistants, radiographers, technicians, social workers and clerical staff. It is vital that all medical and health personnel appreciate the problem and give their active support. Emphasis should be placed especially on the fact that the cervix with carcinoma in situ gives no warning symptoms or typical appearance: it behaves like any other cervix. A perfectly benign cervix may look "suspicious" while a "normal-looking" cervix may well harbour an in situ cancer. One cannot rely on appearances. To pass a cervix as "clinically healthy" and free from malignancy without cytological evidence should no longer be acceptable practice in this present age.

Lecture courses on the natural history of the disease, the principles and practice of cancer detection and its place in the adult female population should be conducted. Doctors should be trained in the method of cancer detection *i.e.* the history, physical examination and taking of Papanicolaou smears. Family physicians occupy a key position for influencing women under their care and the enlisting of their help is of greatest importance.

3. Education of the Public

This should commence on a small scale, gradually extending to reach the whole adult population as facilities become available to cope with the demand for screening. The public should be told the facts about cancer of the cervix and other cancers, the curability, methods of detection and facilities available. The giving out of information pamphlets could begin initially in all Government Clinics and Hospitals, and Private Practitioners' consulting rooms. At a later stage, other institutions and meeting places may be utilised. Finally, when all is set for mass response, then mass information media of newspapers, radio and television may be employed.

4. Organization of Clinics, Laboratory and Hospital Facilities

All Government Clinics where women attend should be organized for the taking, fixing and handling of smears. The Co-operation of Private Practitioners would be most valuable. The setting up of "Well-women" Clinics for cancer detection may come at a later stage of development. A cytological laboratory with adequate technical, clerical and follow-up staff would form the central hub of the organization.

A gynaecological service to cope with the diagnosis and treatment of "pick-ups" must be available for definitive diagnosis and treatment.

Physical Examination and Taking of Papanicolaou Smears

When facilities are ready all women attending Gynaecological, Antenatal, Postnatal and Family Planning Clinics should have smears taken from the posterior vaginal pool, exocervix and endocervix, according to the method of Wied and Bahr (1959).

The examination should include breast palpation, taking of Papanicolaou smears and bimanual examination of the pelvis. In the process, breast lumps, uterine and ovarian tumours will be detected, as a "bonus" to the harvest of cervical lesions.

YIELD TO BE EXPECTED

Our experiences suggest that an average yield of four in situ lesions per 1000 women screened may be expected. With the addition of early invasive cervical cancers, endometrial and ovarian cancers, the overall yield may exceed 5-6 per 1000 women examined.

What response may be expected if a mass screening campaign should be launched? From experience elsewhere (Boyes, Fidler and Lock, 1962; MacGregor and Baird, 1963) response is likely to be under 50 per cent. Singapore has, in round numbers, a target population of about 400,000 adult females. A 25 per cent response in the first year, would mean 100,000 smears to be screened. The expected yield would be 400 in situ carcinomas and a smaller number of invasive cervical cancers, breast, ovarian and endometrial growths.

LABORATORY COSTING

Working on a supposition of 25 per cent response, we will need a team of 15 cytotechnicians, 4 cytologists, and 5 clerical and follow-up staff. Excluding initial capital expenditure, the recurrent laboratory expenditure and staff salaries would be well under $200.000 per year. This would work out to less than two dollars per smear or less than $500 per cervical cancer detected. This seems a not unreasonable price to pay for the eradication of a disease which is difficult to treat, carries a high post-therapy morbidity, long months of suffering and misery, and generally a poor prognosis in terms of 5-year survival.

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SUMMARY

1. Cervical cancer is the chief malignancy and a major cause of death among women in Singapore.
2. Using the Papanicolaou cytological screening technique between 1965 and 1967, the in situ carcinoma "pick-up" rate was 2·2 per 1000 puerperal women and 4·7 per 1000 gynaecological patients in the University Unit, Kandang Kerbau Hospital, Singapore.
3. The rationale for the mass use of the Papanicolaou smear method to prevent invasive cervical cancer is discussed in the light of the natural history of the in situ lesion.
4. Despite the introduction of newer techniques, the Papanicolaou smear method remains the only certain means of detecting preinvasive cervical cancer.
5. An Action Plan for Singapore is outlined.

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