

# CERVICAL CANCER SCREENING IN BALI: A PUBLIC HEALTH ISSUE

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**Abstract.** Cervical cancer is the most common cancer in women in developing countries. Regarding cervical cancer in Bali, we sought to determine the incidence, to evaluate existing preventive and screening programs, to identify the population being screened, and to examine the methods of testing. The records of the Udayana Teaching Hospital pathology laboratory and Cancer Registry were reviewed, retrospectively.

The incidence of cervical cancer in Bali is 7/100,000. There has already been a substantial increase in the number of Papanicolaou tests (PT) from 767 in 1990 to 1,355 in 1992. In 63% of these tests the results were Class II, indicating a need for attention to infection. Cervical intraepithelial neoplasia has a statistically significant increase with age. The number of PT performed peaks in the 35-44 year age group, with a sharp decline thereafter. Fifty-four percent of PT are performed in the capital city, which has only 20% of the female population. Bali Hindu women make up 94% of the female population, but receive only 81% of PT, while Muslim women make up 5% of the population and receive 12% of PT. Seventy-eight percent of PT contain no endocervical cells.

There has already been a promising increase in the number of PT performed in Bali. Public health promotion efforts as well as outreach programs should be expanded, perhaps using the Banjar system, to reach older and rural women. Collectors of Pap smears should be instructed on the importance of endocervical sampling.

## INTRODUCTION

Cervical cancer is the most common cancer in women in developing countries (Anonymous, 1986; Coppleson, 1992). As countries such as Indonesia, with aggressive preventive medicine programs, and increased of life expectancy, cancer becomes an important issue. Cervical cancer is a preventable disease, with a course that may take from months to decades to develop into cancer (Berek and Hacker, 1989). In a well-screened population in Canada with 40% of all women over 15 years of age receiving Pap tests, a decrease occurred in the incidence of cervical cancer from 28.4/100,000 in 1955 to 4.2/100,000 in 1988 (Benedet *et al*, 1992).

The primary issue in women's health in the developing world has been maternal mortality. In 1969, Indonesia began a series of 5-year development plans that have focused on maternal and child health. Indonesia was successful in instituting family planning programs and increasing the education of labor attendants. For the Bali region, the total fertility rate has fallen from 5.96 in 1971 to 2.2 for 1991 (Central Bureau of Statistics Jakarta, 1991). The overall life expectancy also increased from 41 years in 1969 to 52 years in 1982. However, cancer

as a cause of death has risen from 14th in 1972 to 9th in 1980 (Sutnick and Gunawan, 1982). With the success of family planning programs and the increased education of labor attendants, attention can now be given to issues affecting later life, such as cancer.

Among cancers, cervical cancer stands out as a major problem in the Indonesian province of Bali. In a population-based mortality study in Bali from 1980-1982, malignant neoplasms accounted for 9.2% of deaths of women age 14-49 (Fortney *et al*, 1986). Data from Bali indicate a high rate of cervical cancer; from 1977-1979, 34% of cancers were designated as cervical (Pringgoutomo, 1985) and from 1980-1982, 42% of cancers were defined as from the female genital tract (Mangunkusumo *et al*, 1985).

Previous articles have suggested that women in Bali are at particularly high risk for cervical cancer, which may be due to the high rate of penile cancer. In Bali, studies over several decades indicated an unusually high rate of penile cancer, which is the second most frequent carcinoma in Balinese men, and begins to occur in the 20-39 year age group (Pringgoutomo, 1985; Boon *et al*, 1989). The male factor in human papillomavirus (HPV) infections

and cervical cancer is well-documented (Graham *et al*, 1979; Barrasso, 1987).

The objectives of this study were to determine the incidence of cervical cancer in the Province of Bali; to examine the preventive programs already in place; to identify the demographics of the population being serviced; to identify any ethnic or geographic group at increased risk; and to identify improvements in methods of collection of Pap tests (PT).

## MATERIALS AND METHODS

The Internal Review Board for the University of North Carolina granted exemption from review by the Committee on the Protection of the Rights of Human Subjects based on the criteria for exemption in 45 CFR Part 46, Section 101, numbers 2 and 4. The study is a retrospective review of the cancer registry and the cytology records of the Department of Pathology of the Udayana Teaching Hospital in Denpasar. All cancer specimens and all PT taken throughout the province of Bali are sent to the pathology laboratory at Udayana Teaching Hospital. Not only are all PT sent to this laboratory, but women with complaints requiring a PT who present to a primary health center (Pus Kes Mas) are referred to the cancer center at the teaching hospital in the capital city to have the Pap smear taken. Most Pap smears are taken with only a wooden spatula and cotton-tipped swab, without benefit of a cytology brush. The Pap smears are then fixed in alcohol. They are stained with hematoxylin and eosin at the Udayana Pathology Department.

Each entry was reviewed and assigned to a classification based on the microscopic description. Normal smears were assigned to Class I. A normal smear would have fewer than 30 polymorphonuclear cells (PMN) per high power field. More than thirty PMNs would make the smear Class II. The reading of acute infection was given if only PMNs were present. The slide was read as chronic infection if lymphocytes, plasma cells, or giant cells were present. Dysplasia was assigned to classification of cervical intraepithelial neoplasia CIN I, CIN II, or CIN III. Carcinoma-in-situ (CIS) and cancer were recorded as such. Pap smears showing radiation effect from a previous treatment of cancer were recorded in a separate category. If a Pap smear was

deemed inadequate or inconclusive, it was recorded as inadequate.

Place of origin of the patient was deemed important to determine the existing structure for preventive care, which is based on politically determined geographic divisions called regencies. If the PT was from a screening program, this was recorded in a separate category, with note made of the regency.

The patient's ethnic-religious background was assigned by identification of the name with the respective ethnic-religious group. If the name was missing, ambiguous, or not identifiable as one of the common groups, it was assigned to the "unknown" category.

Incidence was determined from the cancer registry of Udayana University Hospital. All cervical biopsies from the province of Bali are sent to this hospital's laboratory. The population was based on the government census from 1990. The religious-ethnic configuration of the population was provided by the Indonesian Embassy.

SAS Proc was used for analysis of statistical significance. Row Mean Scores Differ test was applied to analyze the relationship between cytology and age. Wilcoxon signed rank test was used to evaluate the effect of screening programs. Poisson regression analysis was used to analyze geographic testing. Chi-square test was used to analyze the relationship between religion and cytology. Although records from 1990-1992 were reviewed, only patient data from 1992 was used because the raw data set did not allow for adequate control for patients receiving repeat PT.

## RESULTS

There were 93 new cases of cervical cancer in 1990, 103 in 1991, and 97 in 1992, for an average of 97.6 new cases per year. The population census for 1990 reported a female population of 1,392,408. The incidence was 7/100,000.

A striking aspect of the cytology study is the rapidly increasing number of PT, shown in Fig 1. In 1990, for the entire province of Bali, there were only 767 Pap smears. By 1992, this number had almost doubled to 1,355.

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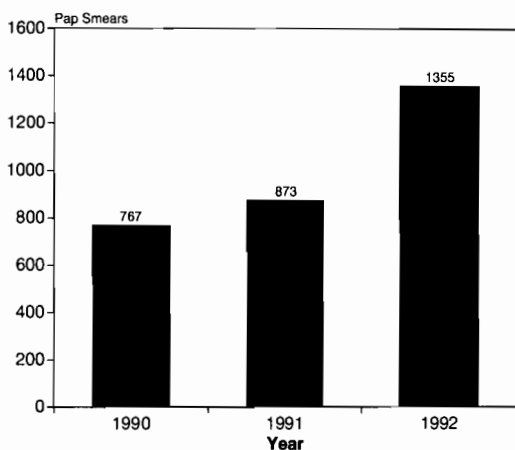


Fig 1—Increase in Pap tests 1990 to 1992 N = 2995.

A PT program needs to be targeted at the correct age groups. Ninety-eight percent (1,329/1,355) of the Pap smears for 1992 had the age of the recipient recorded. Fig 2 indicates a large increase in the number of PT beginning in the 25-34-year age group. There is a sharp drop as women move into the later decades.

Fig 3 shows the cytologic findings. Two Pap smears had descriptions that did not fit into the classification system and were not counted. Of these remaining, 95% were deemed adequate for interpretation. Twenty-seven percent were normal (Class I); 63% Class II, 3% were CIN I and CIN II, and only 5 were read as CIN III or cancer. Three percent of the PT are done for patients already treated with radiation. Of the 855 Class II PT, the most common reading was chronic infection, accounting for 74% (528/717). Only 1% of the PT suggested HPV.

The relationship between the age of the patients and the cytology can be seen in Fig 4. There were 27 cases for which the age was not recorded. In 1992, CIN did not appear until the 25-34-year age group. In 1990 and 1991, there were 4 cases of CIN I and II in the 15-25-year age group. In the 15-24-year age group, 7 were inadequate. Of the 81 adequate tests, 22 (27%) were Class I, and 59 (73%) were Class II. Of the 297 adequate smears in the 25-34-year age group, 91 (31%) were Class I, 195 (66%) were Class II, and 11 (3.7%) were CIN. Of 602 adequate PT in the 35-44-year age group, 165 (27%) were Class I, 422 (70%) were Class II, and 15

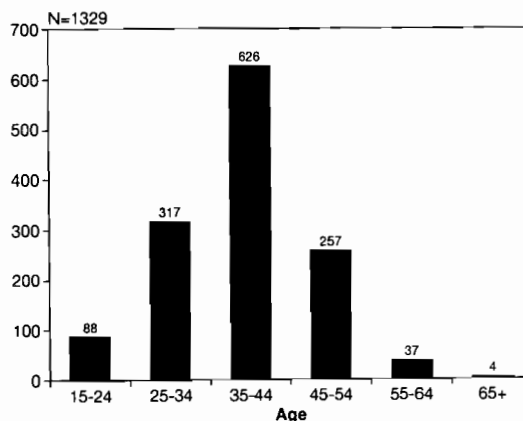


Fig 2—Age of Pap recipients by ten year age group.

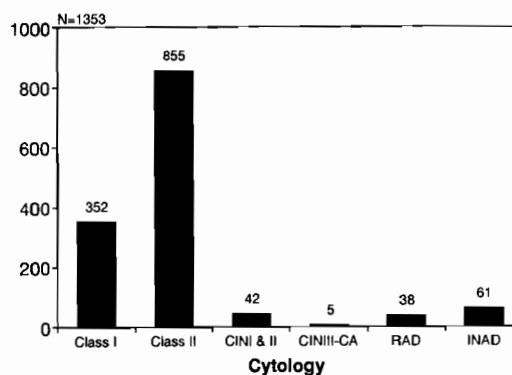


Fig 3—Cytology findings 1992.

CIN = Cervical intraepithelial neoplasia; RAD = Radiation changes; INAD = Inadequate

(2.5%) were CIN. The first PT with radiation changes occurred in this age group. The 45-54-year age group, with 229 adequate screening PT's, had 18 cases of radiation changes. The 45-54-year age group had 65 (28%) Pap smears that were Class I, 149 (65%) Class II, 13 (5.7%) CIN, and 2 (0.9%) showing CIS-CA. The 55+ age group, with only 23 adequate Pap smears, had 17 with radiation changes, 3 with CIS/CA, and 4 with CIN. In the group over 55, of the 40 PT's done, 42% were done for patients already treated with radiation. With cytology divided into two categories, benign and CIN I through cancer, there was a statistically significant association between increasing age and cytology ( $p < 0.001$ ).

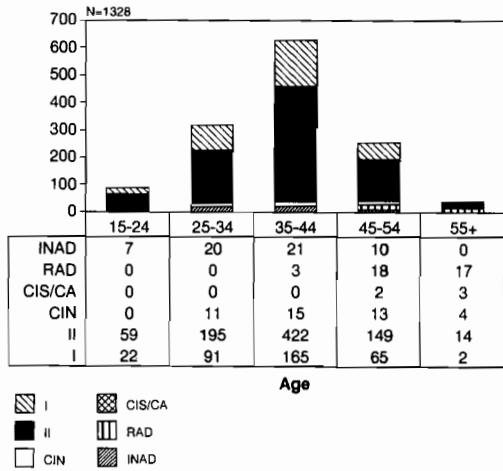


Fig 4—Age and cytology 1992.

I = Class I; II = Class II; CIN = Cervical intraepithelial neoplasia; CIS/CA = Carcinoma-in-situ Cancer; RAD = Radiation changes; INAD = Inadequate

Table 1

Pap tests by regency Pap tests per 1,000 women.

	Population	Total No. paps	Paps per 1,000
BAD	294,775	732	2.5
BAN	88,738	109	1.2
BUL	274,801	91	0.3
GIA	164,118	44	0.3
JEM	110,291	48	0.4
KAR	172,263	106	0.6
KLU	80,992	92	1.1
TAB	177,042	131	0.7
TOT	1,363,020	1,353	1.0

1991 Census/1992 Pap tests

BAD = Badung; BAN = Bangli; BUL = Buleleng; GIA = Gianyar; JEM = Jembranan; KAR = Karangasem; KLU = Klungkung; TAB = Tabanan; TOT = Total

With such a small percentage of the population receiving Pap smears, it is not surprising that the 35-45-year age group had only 15 cases of dysplasia and in the next age group had 18 PT's which indicated treatment for advanced cervical cancer. The prevalence of cervical cancer among the older women belies the low incidence of dysplasia in the younger age groups.

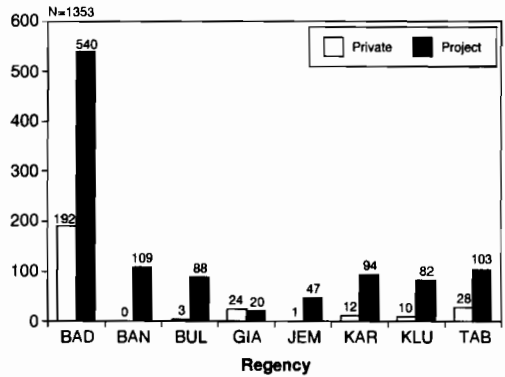


Fig 5—Effect of screening programs 1992.

BAD = Badung; BAN = Bangli; BUL = Buleleng; GIA = Gianyar; JEM = Jembranan; KAR = Karangasem; KLU = Klungkung; TAB = Tabanan

The total female population of each regency, the number of PT's, and the number of PT's per 1,000 women are displayed in Table 1. Badung, the regency which includes the capital city, has 54% of the Pap smears, but has only 22% of the female population. Buleleng, the second most populated regency, has 20% of the female population, but had only 7% of the PT's, for a screening rate of 0.3/1,000 women. Poisson regression analysis was used to compare the rate of Pap smears per 1,000 women in Badung with the other regencies. In all cases, there was a statistically significant higher rate of Pap tests in Badung ( $p < 0.001$ ). Nonetheless, even in Badung, only 2.5 per 1,000 women obtained a Pap test.

Data from the place of origin of the PT's indicate that the organized screening programs (SP) have greatly contributed to the increased numbers of women receiving PT's. A large percentage of the PT's in each regency come from SP's (Fig 5). The regency of the capital is again the primary beneficiary of SP's, most of which originate from the workplace. In 1990, there were 767 PT's. Seven-hundred and ten of these came from Badung, with 421 from SP. In 1992, of 1,355 PT's, 621 came from outside Badung with 543 from SP. Of the total 1,355 PT's taken in 1992, 1,186 were obtained through SP. The p-value was 0.0156, suggesting that significantly more PT's were done through SP's.

In Bali, 94% of the population is Bali Hindu (BH). Bali Chinese, Christian and Muslim (M) make up the remaining 6%. The BH group is believed to be at particularly high risk for cervical cancer associated with the high incidence of penile cancer (Boone *et al*, 1989). Bali Hindu women were the recipients of only 81% of the PT's. The M population makes up 5% of the population and received 12% of the PT's. Muslim women benefit by living in the capital and being affiliated with the workplace programs.

Bali Hindu women may be at an increased risk for cervical cancer. Of the Pap smears from BH women, 25% are Class I, 64% class II, 2.6% CIN, 0.3% CIS-CA, 3.2% with radiation changes, and 4.8% inadequate. For the M women's Pap smears, 27% are Class I, 64% Class II, 5.3% CIN, 0.5% CIS/CA, 0.6% with radiation changes and 2.3% inadequate. A possible association between the BH and M religions and cytology was found using cytology classifications of benign and CIN through cancer ( $p = 0.07$ ).

Specimen quality is a problem. Method of collection is a probable cause of inadequate samples as well as missed dysplasia. Endocervical swabs are collected with a cotton-tipped swab rather than an endocervical brush. Seventy-eight percent of PT's had no endocervical cells; tests with changes indicating radiation therapy were not included in this group.

## DISCUSSION

These data constitute a pilot investigation of the cervical cancer screening program currently in place in the province of Bali, Indonesia. The conclusions of this research suggest directions for the expansion of Pap smear collection, and can guide future research and data collection.

Ideally, a population based data set assesses the cervical cancer prevalence and cervical cytology. The incidence of 7 cases of cervical cancer per 100,000 women is based on the entire female population of Bali, however, the data are from patients who presented for biopsy. An age-weighted census is not currently available, but one can assume that a substantial percent of the population is quite young, making the actual age-weighted incidence higher.

All PT's taken in the province of Bali are referred to the pathology laboratory at Udayana hospital. Therefore, the authors believe that the data are complete and accurately reflect all PT's obtained on the island of Bali from 1990-1992. The dramatic increase in the number of PT's reflects an increase in the number of special programs dedicated to this aspect of women's health. Still, even in the most highly served area, only 2.5 women per 1,000 are obtaining PT's.

There are several policy implications that can be made from the age of the women obtaining PT's. The age of women receiving Pap smears peaks in the 35-45-year age group. This corresponds with recommendations of the World Health Organization that Pap screening begin by at least age 35. However, in Bali, the sharp fall after age 45 indicates that an older, higher risk population is being missed.

Women in the 35-45-year age group may be successfully targeted in cities through workplace-based screening programs. Women not in the work force will be accessing the health care system for contraceptive and reproductive needs. The intrauterine device (IUD) is the most popular method of contraception in Bali and brings women into contact with a health professional. A PT could be obtained at the time of IUD insertion, if supplies are available. Women accessing the health system in the reproductive age group must be informed of the importance of continued surveillance in the post-reproductive years. Workplace and clinic based programs can only be expected to reach the 35-45-year age group in the cities.

In the rural areas, contraception has been successfully promoted through the "Banjar" or local village system. This social system has been expanded to incorporate public health for the purpose of contraception. The Banjar system reaches women of all ages and may be particularly effective in reaching older women.

Many countries are seeing an increase in cervical cancer among younger women (Coppleson, 1992). This group should also be targeted for a screening program.

In Bali, dysplasia first appears in the youngest age group. By the 35-44 year age group, there are already patients being treated with radiation. Although the numbers are small, the implication re-

mains strong that the 25-34 year age group should be strongly targeted in a screening program. This is a group in which PT's obtained as part of maternal health programs might be successful.

Again, although the number of PT's obtained decreases as women enter the older age groups, a trend can be seen of an increase in the severity of dysplasia, culminating in the over-55-year age group having 17 of 40 Pap smears done showing radiation changes and 3 of 40 with CIS-CA.

The resulting cytology of the Pap tests does not indicate the gravity of the situation. Five percent of PT's were deemed to be of insufficient quality to be read by the pathologist, while 78% had no endocervical cells. Endocervical cells are considered important to assure that the transformation zone has been sampled. A higher rate of atypia has been demonstrated in PT's with endocervical cells (Elias *et al*, 1983), and endocervical brushes have been shown to improve the collection of endocervical cells (Dotters *et al*, 1988; Lai-Goldman *et al*, 1990). Cytobrushes are not easily available on Bali. The vast majority of Pap tests were done with a spatula and cotton-tipped swab only. Not surprisingly, only 22% of the tests showed endocervical cells present. As screening programs become more prevalent, improvements in training and equipment must be made.

The high number of Class II readings indicates first that there is a high rate of cervical or vaginal infection. In a regency where IUDs are the most common form of birth control, this is certainly a health issue to be addressed. Due to cost, cultures are not routinely taken at the time of Pap tests. Although expensive, more specific screening for infectious organisms could be carried out simultaneously with the Pap smear collection. A second concern with the number of Class II PT is that inflammation may actually be cancer.

In Bali, one group should not be singled out for Pap screening; however, BH make up 94% of the population and only 81% of the Pap smears. This is most likely a reflection of the concentration of the Muslim community around the capital where screening programs are in place. This finding further emphasizes the need for Pap testing in rural areas. The numbers of PT obtained from groups other than the BH and M are too small to make meaningful comparisons as to whether one group is at an increased risk for cervical dysplasia or cancer.

From 1990-1992 there has been a tremendous increase in the number of Pap smears being done in the province of Bali. However, for the most part, PT's are available only to residents with access to the capital city. People who present in the outlying regencies with complaints indicating the necessity of a PT are often referred to the central hospital in Badung. The large majority of Pap smears from Badung indicate that the programs in place in Badung should be encouraged and expanded and that programs should be designed for the outlying areas.

Implications for future research would begin with a data collection method that would allow patients to be tracked, and their cytology followed over time. A study of the causes of inflammatory changes to the cervix with diagnosis by culture would also provide guidelines for improved health care. Few cytologic diagnosis specific for HPV were made. Investigating which HPV strains are prevalent in Bali would be fascinating, although quite expensive.

At this time, the policy recommendations of this study are that the Banjar system should be used for education of women as to the need for PT's. If funding is available, endocervical brushes should be used for all PT's. All persons obtaining PT's should be educated regarding the importance of endocervical sampling. Pap tests can be successfully obtained through work-based programs, but special outreach programs will be needed to reach the majority of the female population, which is in the more rural regencies.

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#### REFERENCES

- Anonymous. Control of Cancer of the Cervix Uteri. *Bull WHO* 1986; 64 : 607.
- Barrasso R, De Brux J, Croissant O, Orth G. High prevalence of papillomavirus-associated penile intraepithelial neoplasia in sexual partners of women with cervical intraepithelial neoplasia. *N Engl J Med* 1987; 317 : 916-23.

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- Benedet JL, Anderson GH, Matisic JP. A Comprehensive Program for Cervical Cancer Detection and Management. *Am J Obstet Gynecol* 1992; 166 : 1254-9.
- Berek JS, Hacker NF. Practical gynecologic oncology. Baltimore: Williams and Wilkins 1989: p 207.
- Boon ME, Susanti I, Tasche MJ, Kok LP. Human papillomavirus (HPV) - associated male and female genital carcinoma in a Hindu population: The male as vector and victim. *Cancer* 1989; 64 : 559-65.
- Central Bureau of Statistics Jakarta. Indonesia Demographic and Health Survey 1991. Columbia MD: Indonesia and Macro International, 1991 : p 30.
- Coppleson, M. Gynecologic Oncology Fundamental Principles and Clinical Practice. New York: Churchill Livingstone, 1992: pp 11, 16.
- Dotters DJ, Carney CN, Droegemueller W. Nylon brush improves collection of cervical cytologic specimens. *Am J Obstet Gynecol* 1988; 159 : 814-9.
- Elias A, Linthorst G, Bekker B, Vooijs PG. The significance of endocervical cells in the diagnosis of cervical epithelial changes. *Acta Cytol* 1983; 27 : 225-9.
- Fortney JA, Susanti I, Gadalla S, Saleh S, Rogers SM, Potts. Reproductive mortality in two developing countries. *Am J Public Health* 1986; 76 : 134-8.
- Graham S, Priore R, Graham M, Browne R, Burnett W, West D. Genital cancer in wives of penile cancer patients. *Cancer* 1979; 44 : 1870-4.
- Lai-Goldman M, Nieberg RK, Mulcahy D, Wiesmeier E. The cytobrush for evaluating routine cervicovaginal-endocervical smears. *J Reprod Med* 1990; 35 : 959-63.
- Mangunkusumo R, Taufik E, Setyawan S. Relative frequency of cancer in the female genital tract in Indonesia. *Southeast Asian J Trop Med Public Health* 1985; 16 : 651-5.
- Pringgoutomo S. Epidemiologic aspects of some malignant neoplasms in Indonesia. *Southeast Asian J Trop Med Public Health* 1985; 16 : 594-7.
- Sutnick AI, Gunawan S. Cancer in Indonesia. *JAMA* 1982; 247 : 3087-8.