CARCINOMA OF THE CERVIX

BIOLOGY AND DIAGNOSIS

edited by

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4. CERVICAL CARCINOMA IN PANAMA

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I. CANCER AS A HEALTH PROBLEM IN PANAMA

I. A. Mortality

Tropical countries have historically devoted most of their health resources to infectious diseases. In countries such as Panama with rapidly improving environmental and health standards, infectious diseases remain the principal cause of morbidity but not mortality. Along with the population's increasing life span, non-infectious chronic diseases have emerged as major public health problems. Panama's published cause-specific mortality rates show this (Table 1); cancer has been among the three principal causes of death since 1968 (Dirección de Estadística y Censo 1979). These crude death rates contradict the fact that more than half of Panama's population is younger than 15 years. A

Table 1. Leading causes of certificated deaths in Panama, 1974-1978.

	Cause of death	% Total deaths	Rate per 100,000
1.	Ischaemic		
	heart disease	12.7	-15.1
2.	Accidents –	12,7	45.1
~.	suicide		
	homicide	12.2	43.4
3.	Cancer	12.2	43.1
3. 5.	Cerebro- vascular		
	disease	8.6	30.3
5.	Pneumonia	5.8	20.5
5.	Enteritis		
	diarrhea	3.8	13.9
	Infant mortality per 1,000	leenin.	
	live births	31.5	

similar mortality pattern appears to be evolving in other tropical countries.

1. B. Incidence

The National Oncology Institute of Panama initiated a National Cancer Register in 1974 to document cancer incidence (Valdés et al. 1979). The Panama National Cancer Register actively ascertains all histologically diagnosed cancers by annually reviewing every certified pathologist's histology reports. Registration includes each cancer_ patient's name, age, sex, hospital/clinic/chart numbers, date of diagnosis, anatomic site, and town where the tissue specimen was obtained (this allows a crude estimation of residence). Registry information is coded (cancer site according to the Ninth Revision of the International Classification of Diseases), and all data is maintained on interactive disc files on the Gorgas Memorial Laboratory computer. Duplicate registration is monitored by checking the patient's name and hospital/clinical/ chart number; when necessary specific charts are retrieved to verify information.

The National Cancer Register records only histopathologically diagnosed cancers. No attempt has been made to search hospital or clinic records for clinically diagnosed malignancy nor to include death certificate data. Limiting registration to histopathologically diagnosed malignancy eliminates local variation in clinical criteria and defines cases by objective histologic criteria. Pathologic criteria were constant between 1974–1978 because only three of Panama's nine Provinces (Panama, Colon, Chiriqui) had pathologists. Tissue specimens from all other provinces were sent to Panama City and evaluated by the Pathology Department of either Santo Tomas or Seguro Social Hospital. Both have

Table 2. Most commonly diagnosed cancers in Panama, 1974-1978.

1	Male	Female	
Site	Rate*	Site	Rate
		Uterine	West land
Skin	16.9	cervix	37.8
Prostate	14.4	Skin	14.7
Stomach	10.4	Breast	14.4
Trachea,			
Bronchus,			
Lung	5.0	Stomach	6.1
Rectum	3.2	Corpus.	4.1
		uteri	
Mouth	3.2	Ovary	3.1
Larynx	2.7	Mouth	3.7
Connective			
issue	2.3	Rectum	3.1
Bladder	2.4	Colon	2.4
Liver	2.1	Other fem.	2.4
		genital	
Penis	1.9	Connective	1.8
		tissue	

Incidence per 100,000 population adjusted to standard world population.

*Includes only invasive cervical cancer.

active Pathology Resident training programs and maintain frequent interchange with pathologists from major U.S., South American, and European Medical Schools.

Although the National Cancer Register underestimates true cancer incidence, it has high specificity. Table 2 summarizes the age standardized rates of the most common registered cancers between 1974–1978. Cancer of the uterine cervix was overwhelmingly the most frequent, accounting for 33% of all female cancers. This age-adjusted cervical cancer incidence was among the highest reported in the world.

11. CERVICAL CANCER IN PANAMA

II. A. Epidemiology

In order to investigate this high cervical cancer incidence, Standardized Cervical Cancer Register was established. Registry personnel visited every hospital and regional health center and enumerated all patients diagnosed as having, or certified as dying with, cervical cancer since 1974. The Standardized Register includes all data recommended by

the IARC (World Health Organization 1976). It abstracts each patient's entire medical record and frequently includes data from several clinic and hospital charts. All data is maintained on computer files using the Conversational Statistical System for Medical Records (Kronmal et al. 1970).

The Standardized Cervical Cancer Register includes all patients seen between 1974-1978 at Panama City's three Medical Center teaching hospitals (The National Oncology Institute, Santo Tomas Hospital, and Social Security Medical Center). There have been 1,013 cervical cancers registered, 685 invasive and 328 intraepithelial. There were 708 cases detected by the National Cancer Register, and we discovered 305 previously unknown cases. These registered cases represent approximately 60% of all cervical cancers known to occur between 1974-1978. There were only three hospitals in Panama where invasive cervical cancer could be properly evaluated and treated; residents from anywhere in Panama had unrestricted access to their facilities; and physicians from every province were well-indoctrinated to the importance of rapidly referring cancer patients. Thus, these registered cases comprised a representative country-wide sample of invasive cervical cancer.

This sample revealed an invasive cervical cancer incidence of 28.2 per 100,000 women older than 15 years of age (the population at risk). Age-adjusted to the standard world population (Doll 1976) comprises 23.9 cases per 100,000. Six of seven provinces (including the capital) had a uniform age-adjusted invasive cervical cancer incidence of 20.7, while women from Herrera Province, with an age-adjusted rate of 66.3, had a 3.2 fold greater risk.

In addition to presenting a higher invasive cervical cancer incidence, 39/90 cases (43%) registered from Herrera involved women younger than 40 years. The age specific Herrera invasive cervical cancer incidence was significantly different from that seen in the remainder of Panama or in other countries (Henderson 1977; Waterhouse et al. 1976; Persaud 1977). This geographic clustering of unusually young cases was reported based on previous data from the National Cancer Register (Reeves et al. 1979; Valdés et al. 1979).

Confounding factors did not account for this clustering. Errors in denominator enumeration would cause an excessive rate. However, Panama maintained an extremely accurate census and the rural population was not affected by large-scale immigration. Biased case ascertainment did not occur; most Herrera cervical cancers (93%) were confirmed by biopsy (evaluated at the capital). Lastly, Herrera resembled other rural provinces with respect to physician; population ratio, availability of primary health care facilities and patient utilization of such facilities.

Other factors were similar among all provinces. Essentially all women were sexually active with an average of 2.0 life-time sex partners and multiple pregnancies. Most of them were from lower socioeconomic strata. Overall, 661 of 685 (96%) invasive cervical cancers were confirmed by biopsy; 629/661 (95%) were classified as epidermoid carcinoma, the remainder were adenocarcinoma. The ratio was similar in all provinces.

II. B. Clinical parameters

The National Oncology Institute is the only place in Panama with the capability to administer radiation therapy. Therefore virtually all invasive cervical cancer patients were referred, classified and treated there (592 of 685, 86%). Most women presented with advanced disease. However, between 1974–1978, in situ and lower staged cancers showed a relative increase in frequency (Figure 1). This may reflect an increased awareness of cervical cancer

and implementation of cancer detection programs in rural areas.

III. CONCLUDING REMARKS

Chronic non-infectious diseases are the most important contributors to mortality in Panama. Cancer has been among the first three causes of death since 1968, and invasive cervical cancer accounted for 33% of all female malignancies. In addition, Panama's age-adjusted invasive cervical cancer incidence ranked among the highest reported in the world. This is consistent with published data showing that cervical cancer mortality rates have steadily increased in developing countries of Asia, Africa and Latin America (Hill 1975), while concurrently decreasing in industrialized countries (Persaud 1977). The Latin America-Caribbean area supports the highest documented cervical cancer incidence (Caorsi et al. 1976; Hendersen 1977; Madrigal et al. 1976). The three areas reporting cervical cancer incidences comparable to Panama's (Cali, Colombia, Recife, Brazil; Kingston, Jamaica) have many cultural and ethnic similarities.

In addition to an overall high country-wide cervical cancer incidence, Herrera had an incidence three times greater than the rest of the country. Herrera Province also demonstrated a unique age profile with almost half the cases occurring before

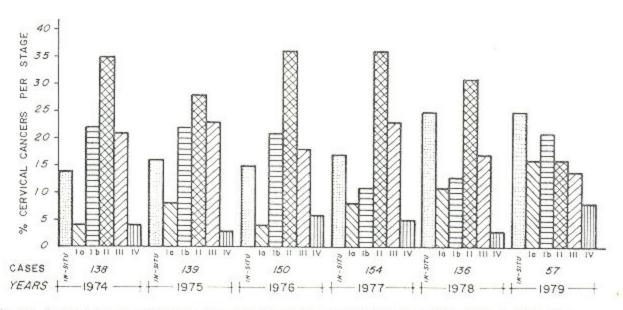


Figure 1. Percent cervical cancers in each chinical stage who were treated at the National Oncology Institute, 1974-1979,

40 years of age. Young women from Herrera were evidently exposed to unique risk factors (Alexander 1973; Kessler and Aurelian 1975). An understanding of these risk factors would not only contribute to the basic epidemiology of cervical cancer but would also allow development of effective local cancer prevention programs.

A cervical cancer situation similar to Panama's also exists in other Central American countries but has not as yet been well documented. It is possible to implement an accurate population-based cancer register in a developing country in spite of limited resources devoted to chronic diseases. Accurate documentation of disease occurrence is necessary to convince and enable individual governments to initiate and support well-planned, effective, cervical cancer detection and treatment programs.

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REFERENCES

Alexander ER: Possible etiologies of cancer of the cervix other than herpes virus. Cancer Res 33: 1485-1496, 1973.

Caorsi I, Norambuena ML; El câncer cervicouterino en el sur de Chile. Bol Ofic Sanit Panamericana 80: 68–77, 1976.

Dirección de Estadística y Censo: Panamá en Chifras, Años 1972 a 1976. Panama. Contraloría General de la República, 1977.

Doll R: Comparison between registries, age standardized rates. In Waterhouse J, Muir C, Correa P, Powell J (eds): Cancer incidence in five continents Vol III. Geneva: JARC, 1976: 453-459

Henderson BE (ed): Epidemiology and cancer registries of Pacific basin. National Cancer Institute Monograph 47, 1977.

Hill GB: Mortality from malignant neoplasm of the uterus since 1950. WHO Statistical Report 28: 323–338, 1975.

Kessler IL, Aurelian L: Uterine-Cervix. In: Schottenfeld (ed): Cancer Epidemiology and Prevention, Current Concepts. Springfield, 111: Thomas, 1975: 262-317.

Kronmal RA, Bender L, Mortenasen J: A conversational Statistical System for Medical Records, J Roy Stat Soc Series C 19: 82–92, 1970.

Madrigal LM, Assal NE. Anderson PS: Cáncer de los organos de la reproducción en Costa Rica. Bol Ofic Sant Panamericana 81: 345–354, 1976.

Persaud V: Geographical pathology of cancer of the uterine cervix. Trop Geogr Med 29: 335–345, 1977.

Reeves WC, Britton R, Valdés PL, Benenson AS: Cervical cancer in Panama. Am J Epidemiol 110: 369, 1979.

Valdés PF, Britton R, Reeves WC, Benenson AS: Câncer del cuello uterino en Panamá. Rev Med Panama 4: 236–245, 1979.

Waterhouse J, Muir C, Correa P, Powell J (eds): Cancer Incidence in Five Continents Vol III. Geneva: IARC, 1976: 486–535.

World Health Organization: WHO Handbook for Standardized Cancer Registries. Geneva: World Health Organization, 1976.