

Cervical Cancer in Brazil: State of the Art

The history of cervical cancer control (CC) began to be written little longer than 100 years ago. The first three decades of last century concentrated big breakthroughs in this area. Between 1899 and 1911, Schauta and Wertin demonstrated the curability of cervical cancer by surgery (radical hysterectomy)¹. Almost simultaneously, Dominici (1911) discovered the principle of radium infiltration, which would later be successfully used to cure cancer¹, which brought forth, from 1920 onwards, a period marked by the gradual removal of surgery in favor of radiation therapy². At this same time in 1925 Hinselmann innovated by inspecting the cervix with a telescope, which resulted in the advent of colposcopy¹. Shortly after, in 1928, Papanicolaou³ and Babes⁴ presented the initial description of the cytological changes at the cervix to the scientific community but cytology as a diagnostic tool would be introduced only in 1941 by Papanicolaou and Traut after having overcome the initial indifference to the method.

It didn't take long for the news to reach Brazil. In 1934, Arnaldo de Moraes, upon learning of colposcopy, becomes the first to use it in the country. Just a year after the launch of Papanicolaou and Traut's monograph⁵, exfoliative cytology was advocated as a method for diagnosis of cervical cancer by Antonio Vespasiano Ramos, assistant of Dr. Moraes at Universidade do Brazil (currently Universidade Federal do Rio de Janeiro) in a teaching thesis entitled "New method for early diagnosis of cervix cancer"⁶. There is also a record that Arnaldo de Moraes was the first in the world to use both colposcopy and cytology⁷. Nevertheless, the method was poorly recognized internationally, to the point that, in 1952, Ralston Paterson, one of the world's foremost authorities in treating cancer with radiotherapy, in an article published in the Brazilian Journal of Oncology (RBC)⁸, acknowledge his little experience with the technique developed by Papanicolaou, commenting on the rise of "preventive clinics" in other countries, and highlighting, mistakenly, that "since cervical cancers grow very quickly, the best prevention was immediate therapy... and not periodic examinations at one or two years intervals."

In 1956 the first cytopathology Service in Brazil was founded at Santa Casa de Belo Horizonte and in that same year, the Brazilian Society of Cytology was created⁹. The acquisition of knowledge caused that, in 1957, in an article also published in RBC¹, Professor Alberto Henrique Rocha alerted the scientific community that "between 30 and 50, phase of increased incidence of cervix cancer, every woman should undergo a gynecological examination at least once a year, aimed at discovering early cervical cancer." Thus began a paradigm shift, wherewith, in addition to surgery and radiotherapy, important for the treatment of patients with cervical cancer, the disease's early detection was valued by encouraging what would become one of the most effective secondary prevention strategies known today: CC's screening by Pap smear. That same year (1956), then President Juscelino Kubitschek sponsored the construction of the Luiza Gomes de Lemos Research Center, the Foundation of Social Pioneers, in Rio de Janeiro (now Cancer Hospital III / INCA) to care for breast cancer and female genital organs cases. It is believed that this was the first initiative of institutional dimension aimed to control CC in our country¹⁰. It was a biologist from the Foundation of Social Pioneers, Sérgio Ré de Paiva who, in 1973, conceived the use of a brush - that would be later known as "Campos da Paz" brush - to collect endocervix material. Responding to a request from his teacher, Dr. Artur Campos da Paz, Paiva he devised the instrument after watching his wife applying mascara with a brush on her eyelashes. Currently public domain, the brush is used universally¹¹. In this issue of RBC, an article of historical feature, authored by **Temperini**, highlights the pioneering spirit and innovative nature of the work of the Foundation of Social Pioneers in the use of the Pap smear as a mass prevention strategy.

The first nationally structured responses of the Federal Government emerged only in 1980, when the Ministry of Health launched in partnership with the Pan American Health Organization (PAHO), a first "Handbook of standards and procedures for the control of cervical cancer". Shortly after (1983/1984), the National Division of Maternal and Child Health of the Ministry of Health has set the foundations for the Integral Women Healthcare, including, recommendations, and actions to control the CC and breast cancer¹².

With regard to the target population for preventive examinations for the detection of cervical cancer and its frequency, according to Faerstein¹³, the manual released in 1980 proposed that the actions should be integrated with other public health activities; examination should be collected on an annual basis, focusing attention on high-risk populations: women 20 to 49 years, with early onset of sexual activity, multiparity, pregnancy at an early age and low socioeconomic status. In 1986, an update of the manual proposed that in case of two or more negative cytology, the controls could be spaced for 2 or 3 years, which had already been proposed since 1972 by PAHO, through the Scientific Publication number 248: "Manual de normas y procedimientos para el control del cancer del cuello uterino" (Manual of Standards and procedures for cervix cancer control). But it was in 1988, after a consensus meeting, that the Ministry

of Health, with the support of related scientific societies, proposed that, in women from 25 to 60 years, the preventive screening for cervical cancer were conducted every three years after obtaining two negative results with an interval of one year. Recommendations remain almost untouched these days: screening is indicated for women from 25 to 64 years with three years interval between examinations after two negative tests with one year time between them¹⁰.

To these first actions was coupled, in 1986, the proposal of development of decentralized actions in the areas of prevention of cervical cancer through the National Campaign Against Cancer / Health Ministry. However, in the following year (1987), when it was realized that, "for lack of a broader executive structure, the basic purposes of the National Campaign Against Cancer had been carried out on a limited way nationwide," the Oncology Program (PRO-ONCO) was created, which established, among other projects, the expansion of prevention and control of cervical cancer in the country¹⁶. In 1990, the Organic Health Law defined the National Cancer Institute (INCA) and the Foundation of Social Pioneers as benchmarks for the Unified Health System (SUS) in service delivery, human resources training and technology transfer, although, since the 1960s, INCA has developed national initiatives in the fields of health care, science and education.

Despite the available scientific knowledge, government investment and normalization in force, the country lived for many years with unacceptable CC mortality rates, lacking structured, comprehensive and continuing actions to correct them. It was in this scenario that the Brazilian government in 1995, during the VI World Conference on Women, held in China, committed itself to develop a program aimed at controlling the CC in Brazil. In response, in 1996, INCA launched a pilot project called "Programa Viva Mulher" (Viva Woman Program) in five capital cities and in a state, having as a goal to reduce by 50% the incidence of cervical cancer in the country. Two years later, based on the experience of INCA, the Ministry of Health established the National Program to Fight Cervical Cancer (PNCCCU)¹⁸ and launched a national campaign (August 18 to September 30, 1998) that hit all States and 98% of municipalities in Brazil. For the first time in the country, the early detection of cervical cancer was addressed uniformly following the same technical recommendations of the Ministry of Health. In 2002, a second campaign, of even greater proportions, was conducted in March and April. These initiatives are highlighted in the article of **Freitas, Silva and Thuler**.

The following years brought the recognition of cancer as a public health problem and strengthen INCA as executor, normalizer and coordinator of national policy for cancer control in Brazil. The Ministry of Health published in 2005 the National Oncological Care Policy, which included among its key components the control of CC¹⁹. Given the importance of the problem, in 2010 the President of the Republic launched the "Program for Strengthening the Network for Prevention, Diagnosis and Treatment of Cervical and Breast Cancer."

Although in 1983, zur Hausen's team had established HPV 16 as the main element in the pathogenesis of invasive and pre-invasive cervical cancers, it was only in 2002 that in the editorial of *New England Journal of Medicine*²⁰, Christopher Crum announced the firsts clinical trial results on HPV vaccine questioning whether this would be the "beginning of the end of cervical cancer". Since then, many advances have been reported in the diagnosis and prevention of HPV infection. In a significant opinion article, Corrêa and Russomano highlight the undeniable success of cytological screening of cervical cancer precursor lesions, and argue why the prevention model that has been adopted in recent years in developed countries, based on testing for HPV and the use of the HPV vaccine, should not be generalized and imported without prior assessment of their viability, sustainability and cost-effectiveness and show the reader the basis for current recommendations.

One of the main goals of PNCCCU²¹, in recent years, has been increased coverage of Pap smear. The article by Murata, Gabrielloni and Schirmer shows that in Maringá, Paraná, coverage of Pap smear in the previous three years was 87.6% in women between 25 and 59 years, and that no significant association between sociodemographic data and submission to screening was observed. In another article, Freitas, Silva and Thuler analyzed secondary data from the State of Mato Grosso do Sul and obtained, for 2003 and 2008, results slightly lower on the coverage: 82.0% and 82.9%, respectively.

Besides guaranteeing coverage, there is a growing concern in the country about the quality and performance of the tests, which was expressed in several articles in this issue. **Bortolon and colleagues**, after evaluating the quality of cervix cytopathology laboratories in Brazil, highlighted, among other aspects, the low laboratorial network capacity for identifying high grade intraepithelial lesions and the need for quality control programs for cytopathologic examination. **Bastos and colleagues**, in turn, based on data from SISCOLO of State of Rio de Janeiro, concluded that the presence of cellular elements representative of the transformation zone of the cervix in blade collected for Pap screening increased by five times the chance of detecting atypical cells. On the other hand, **Etlinger and colleagues** analyzed the diagnostic discrepancies of cytopathologic tests from the external quality monitoring program in the State of São Paulo, between 2000 and 2010, and established that there was diagnostic disagreement in 16,581 (13.48%) of the 123,002 samples reviewed, although the correlation between the original and review diagnoses was considered good (Kappa = 0.77).

Still on the subject, **Collaço and colleagues** presented their findings on the quality control of products and biopsies of high-frequency surgery in cervical cancer prevention program in the state of Paraná. The more common diagnostic discrepancies were between low-grade intraepithelial lesion and diagnosis of benign lesions (super diagnosis) and between low-grade intraepithelial lesion and high-grade intraepithelial lesion (underdiagnosis). Excellent agreement rates were found ($Kappa = 0.99$). By its turn, **Fernandes and colleagues**, in Rio de Janeiro, studied the atypical squamous cells of undetermined significance in the Integrated Cytology Technology Service (SITEC) / INCA and found that their frequency was below 5%. ASC-US was most commonly diagnosed in younger age groups, while ASC-H had little variation between the different age groups. In another study, **Prado and colleagues** characterized the profile of women with abnormal cytology in Rio Branco, Acre, and concluded for the need for improvements in the cervical cancer prevention program in the state. The study showed that 54.0% of women with ASCUS / AGC, LSIL and HSIL Pap smear results received no treatment after the alterations were detected and that 45.7% of the cytologic diagnosis of alterations with undetermined significance showed themselves as high-grade lesions or cancer at the histopathology test. **Solé Pla and colleagues** compared the cytopathologic profile of the cervix in Indian women to that of non-indigenous women in the country, and revealed that the ratio of high-grade lesion / invasive cervix cancer dropped from 11.5 in 2009 to 16.1 in 2011 among the non-indigenous and from 1.7 to 5.0 among Indians, respectively.

Beside the concern with the performance of the examination, there are efforts to have a reliable information system. The creation of an application for computerization of results of cervical screening, the Information System of Cervical Cancer (SISCOLO), in late 1990²², represented an important advance for the monitoring and evaluation of activities in Brazil. In this issue of CBR, **Almeida and colleagues**, by assessing the quality of SISCOLO data from Vitória, concluded by its accessibility and opportunity, even though its completeness problems, mainly from epidemiological data.

Studies of the clinic and epidemiologic profile of patients with cervical cancer and precursor lesions have become increasingly common in the country. **Silva and colleagues** present the natural history of precursor lesions of cervical cancer in a cohort of 227 women of Rio de Janeiro and point to a greater propensity to regression of low-grade lesions in women younger than 30 years and persistence or progression of high degree lesions in women aged 50 years or more. In another article, **Thuler, Bergmann and Casado** are based on data from hospital records of 77,317 cervical cancer cases diagnosed in Brazil between 2000 and 2009, to present the demographic and clinical profile of women with the disease: young, brown color, with low education and with advanced disease at diagnosis. In Vitória, Espírito Santo, **Mascarello and colleagues**, in a study which also was based cancer hospital records, showed that age, education, type of cancer, recurrence and metastases were associated with disease staging. In another article, **Vilaça and colleagues** analyzed differences in treatment patterns and the epidemiological characteristics of adult and elderly patients with CC and have observed a higher incidence of advanced tumors in elderly women; they also reported that, for the same staging, adult women were more often subjected to surgical procedures, radiotherapy and chemotherapy, while for the elderly the most common treatment was radiotherapy alone. In an attempt to change this scenario, by proposing new approaches to disease, **Nogueira-Rodrigues and Melo**, in an opinion article, spoke about how the molecular changes that influence the pathophysiologic and clinical behavior of CC may constitute therapeutic targets in the future, bringing promising perspectives for the treatment of cancer.

Concern about the strategies to face the disease and quality of life of survivors has also been targeted. **Panobianco and colleagues**, in order to understand how women diagnosed with advanced cervical cancer face the disease and treatment, undertook a qualitative study and concluded the importance of individual beliefs based on experiences previous to the disease. On the other hand, the quality of life of patients with cervical cancer undergoing radiotherapy was depicted on article by **Santos et al.** After analyzing women with cervical cancer treated with adjuvant radiotherapy, exclusive or concurrent to chemotherapy, they concluded that radiotherapy did not alter the health-related quality of life of these women.

The role of the nurse in the prevention of cervical cancer in primary care was addressed in a qualitative study presented by **Melo and colleagues**, demonstrating the importance of this professional, of their integration with the team and the community, of knowledge of local realities, of the establishment of a connection and of the constant evaluation of results. Another article dealt with the interface of CC care in the health economic and industrial complex. In it, **Gomes, Lima and Kuschnir** highlighted the productive and technological dependence of the expansion of attention to CC and its power to leverage the National Innovation Strategy of the Ministry of Science, Technology and Innovation as well as industrial development.

Decreasing the incidence and mortality from cervical cancer is among the goals of the current PNCCCU²⁰. In the study presented by **Freitas, Silva and Thuler**, it is observed an increase of 33.8% in specific rates of cervical cancer mortality, adjusted by age, in the state of Mato Grosso do Sul, in the last 30 years. Fortunately, this reality is not

replicated in the country as a whole. Recently, when correcting the mortality rates between 1981 and 2006, based on the proportional redistribution of deaths from “unspecified part” cervical cancer, **Silva and colleagues**²³ showed a downward trend in rates for the country as a whole, decreasing in capitals in all regions, while for the country side municipalities there was an increase in the North and Northeast, decline in the Southeast and stability in South and Midwest. In an article published in this issue, **Guimarães and colleagues** used three different statistical techniques to show the decrease in these rates in Brazil between 1980 and 2009. According to the authors, the reduction can be linked to the actions of screening for precursor lesions of cervical cancer and to control of HPV transmission.

We dare qualify this editorial as “state of the art” as it synthesizes academic production on CC, from different areas of knowledge, mapped in this thematic issue of RBC. When complete it, we highlight the importance of this initiative to bring together multiple perspectives and plurality of approaches, allowing the organization of the set of information and results obtained by Brazilian researchers. Your reading should not be linear or follow a simple chain. Each text, more than connected those that precede and follow it, brings in its interior important statements. The image that can best summarize this compilation is the “network” and not a chain. Network of wires that are joined, that rupture, that intersect, that produce...

Thank!

Good reading.

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