

Organisation of Cervical Cytology Screening in Croatia: Past, Present and Future

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ABSTRACT

This presentation highlights strengths and weaknesses of cervical cytology screening in Croatia, with particular reference to the opportunistic screening, the use of conventional Papanicolaou (Pap) test and the analysis of some organizational, educational and performance issues that are associated with it. Its aim is to propose measures to improve the efficiency of cervical cytology screening in order to reduce cervical cancer mortality. Currently, in excess of 450,000 Pap tests/year are examined at 35 laboratories scattered throughout the country. All of these laboratories use standard operating procedures including internal and external quality control. They employ a total of 68 cytologists and 91 cytotechnologists. The sensitivity of cervical screening in Croatia is 90.0%, specificity 98.6%, positive predictive value 92.3%, negative predictive value 98.1% and overall diagnostic accuracy 97.2%. The high diagnostic accuracy of cervical cytology is attributed to the long-standing tradition of education and training of cytologists (postgraduate MSc course since 1967, independent residency since 1974) and cytotechnologists (since 1968). This tradition spanning more than half a century means that today in Croatia there is a developed network of cytology laboratories staffed by highly competent cytologists and trained cytotechnologists. The high accuracy of cancer detection through Pap tests provides strong evidence in support of cervical cytology screening remaining the basic method of prevention for cervical carcinoma. However, some modifications to the current situation are needed. These relate primarily to opportunistic screening. The current screening coverage rate is 68%, although there is capacity, which would allow for all women at risk, i.e. those aged 25–64, to be screened once in three years. The screening coverage relates mainly to those women visiting gynecological out patient clinics for unrelated conditions. A properly organized and controlled national screening programme should replace this. This should be accompanied by the introduction of alternative, highly sensitive methods of sample collection and preparation, such as are available through the introduction of new technologies, e.g. liquid based cytology.

Key words: Pap test, cervical carcinoma, cervical screening programme, Croatia

Introduction

Cytological diagnosis of conventional cervicovaginal smear or Pap test is one of the most efficient screening tests known to date, which has been credited with the significant decline in the incidence and mortality of uterine carcinoma all over the world. In Croatia, it has been used as the main method of secondary prevention of uterine carcinoma for more than half a century now, being at the same time employed as a classic screening test

for lesion detection and as a differential diagnosis method predicting histological diagnosis. The rate of cervical carcinoma in Croatia, directly resulting from the large-scale use of Pap test, reflects the indisputable value of the method, while also pointing to some shortcomings.

The current state of cervical cytology in Croatia is presented. In addition to its achievement, the aim was to identify the weaknesses, such as opportunistic screening,

the use of conventional Pap test and analysis of the organizational, educational and performance issues with the aim to propose measures to upgrade the efficacy of cervical screening.

The History of Gynecological Cytology in Croatia

In Croatia, as in the rest of Europe, gynecologists were the first to perform microscopic analysis of cervical cytological specimens. The first laboratory headed by E. Baršić, a gynecologist, was established in 1953 at University Department of Gynecology, School of Medicine, University of Zagreb, now University Department of Gynecology and Obstetrics, Zagreb University Hospital Center. Jasna Ivić, MD was the first to devote exclusively to gynecological cytology since 1959. In 1968, she was appointed Head of the Laboratory of Cytology, which developed into Institute of Gynecological Cytology in 1984; Jasna Ivić organized cytology service in line with the principles adopted worldwide, and is most credited for the progress of cervical cytology in Croatia¹⁻³. During the past fifty years, Institute of Gynecological Cytology in collaboration with other institutions, Department of Cytology and Clinical Genetics, University Department of Gynecology and Obstetrics, Merkur University Hospital in particular, has stimulated continuous development of gynecological cytology in the professional, scientific and educational aspects in Croatia, while promoting due recognition of the Croatian gynecological cytology abroad. At the beginning of the third millennium, these efforts have also been intensified at Department of Gynecological Cytology, University Department of Gynecology and Obstetrics, Rijeka University Hospital Center and Department of Clinical Cytology, Osijek University Hospital, which also became the leading laboratories in the field in Croatia.

The key events in the development of clinical cytology in Croatia are mentioned in Table 1, for which merit goes to many professionals¹, amongst others: Professor Ante

Zimolo, Professor Erik Hauptmann, Professor Inga Črepinko, and already mentioned Professor Jasna Ivić.

Specialist Education of Cytologists and Cytotechnologists

The 1967–1974 period characterized by the establishment of organized education of cytotechnologists (continuing education course for cytotechnologists in 1968) and cytologists (Postgraduate Study in Medical Cytology in 1967 and respective residency in 1974, both subsequently renamed as Clinical Cytology). Both played a key role in the development of diagnostic as well as gynecologic cytology in Croatia.

The Postgraduate Study in Medical Cytology was established at the Zagreb University School of Medicine in 1967, with 31 courses attended by 397 postgraduate students held until 2006. The study underwent two revisions, first in 1996 with the introduction of professional studies, and second in 2005 as residency study.

In 1974, independent residency in Medical Cytology, subsequently renamed as Clinical Cytology, was introduced. Initially, residency took three years (pathology one year and cytology two years, with postgraduate study as a form of organized education). Twenty years later, it grew into four-year residency (pathology one year and cytology three years, also with two terms of postgraduate study), within the frame of general revision of residency *curricula* in Croatia. The introduction of independent residency resulted in appropriate education of these professionals, qualified to meet the very demanding challenges posed by the profession.

In the process of approaching the European Union, the phase of adjustment of education in clinical morphology professions of cytology, pathology and forensic medicine has begun, resulting in a new proposal of residency in all three until now independent professions.

The education of cytotechnologists is an important part of education in cytology. Professor Inga Črepinko organized the first course of additional education of medical technicians for cytology technicians. During the 1968–

TABLE 1
KEY POINTS IN THE DEVELOPMENT OF CLINICAL CYTOLOGY IN CROATIA¹

Year	Event
1967	Postgraduate Study in Medical Cytology, later Clinical Cytology at the School of Medicine of the University of Zagreb
1968	Continuing education course for cytotechnologists at the Medical College of Zagreb
1970	Section of Cytology and Cytological Diagnosis established at the Croatian Medical Association (CMA), to be later renamed as the Croatian Society of Clinical Cytology of the CMA
1970	Later, continuing education courses for the cytologists, cytology technicians, gynecologists, etc., organized by the Croatian Society of Clinical Cytology of the CMA and Zagreb University School of Medicine
1974	Residency in Medical Cytology, later Clinical Cytology, as independent residency regulated by the Ministry of Health and Social Welfare of the Republic of Croatia
1981	Fifth grade qualification – laboratory technician at the Medical College, Zagreb
2000	Continuing education for cytotechnologists at the Ministry of Health and Social Welfare of the Republic of Croatia

1977 period, the education of cytotechnologists was performed in the form of six-month course upon completion of medical technician high school education at Medical College in Zagreb. One-year programme in the form of fifth grade education was offered from 1981 to 1992 at the same College; however, the status of thus trained professionals was not properly solved. The pursuit for continuing, complete and officially recognized education led to the development of two-year programme, initially delivered at the Medical College. The program was verified by the Medical College and the School of Medicine (at the time, College was part of the School of Medicine); however, it has not yet been performed in practice.

Since 2000, sixty cytotechnologists have received education at three courses organized by the Ministry of Health and Social Welfare of the Republic of Croatia, in collaboration with the Croatian Society of Clinical Cytology of the Croatian Medical Association (CMA), and held by Assist. Professor Željka Znidarčić, having thus at least in part mitigated the worrying shortage of these extremely important team members.

The one-year course consisted of 630 periods of practical and theoretical education in all fields of cytology diagnosis with 200 periods of education in particular cytology services. Adjustment to the Bologna Process has opened new options for cytotechnologists at the Medical College; harmonization of the new form and *curriculum* of their education has just been under way.

Current Organization, Medical Staff and Number of Cytological Analyses

Presentation of the current structure in terms of organization, staff profile and number of Pap tests performed

is based on a survey performed by the Croatian Society of Clinical Cytology of the CMA in 2003 and 2005.

According to the above survey, gynecological cytology is performed at 35 of 48 (73%) organizational units. Twenty-seven of these are at state-owned health institutions (25 at hospitals and 2 at health centres) and eight in private offices (6 specialist practices and 2 at private polyclinics). Of the twenty-five hospital units, eight are organized as independent departments and seventeen are combined with other professions, i.e. fourteen within pathology, two at the University Departments of Gynecology and Obstetrics, and one at the Department of Laboratory Diagnosis. Eight cytology laboratories are predominantly engaged in gynecological cytology, whereas the remaining 27 laboratories are equally dealing with general diagnostic by cytology and gynecologic cytology.

Two private cytology laboratories were excluded from analysis because their heads failed to submit current data, and one hospital laboratory was excluded due to the very low proportion of Pap tests in their overall performance; thus, data on 32 units are presented (Figure 1).

Sixty-two professionals with university education (not including residents), i.e. 58 clinical cytologists, two pathologists, one anaesthesiologist and one graduated biologist, along with 91 cytotechnologists, and 43 technical, administrative and auxiliary staff members are employed in 32 cytology laboratories. The cytologists to cytotechnologist to other personnel ratio is 1:1.4:0.6. An ideal screening team would consist of one cytologist, two cytotechnologists and one laboratory technician; accordingly, the majority of cytology teams in Croatia are in part incomplete.

A total of 574,290 cervical smears were taken in 2005 in a whole country, of which 452,809 (79%) Pap tests were successfully performed. The proportion of Pap tests

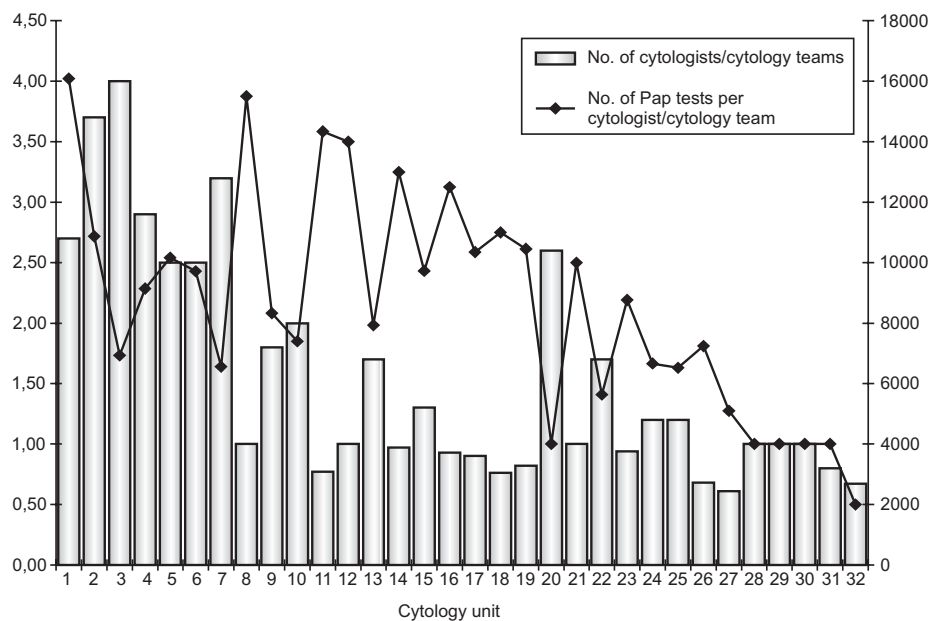


Fig. 1. Number of Pap tests per cytologists/cytology team at 32 cytology units in Croatia in 2005.

out of the total number of tests varied from 59% to 100% in different counties. Forty-nine cytologists and seventy-one cytotechnologists performed these Pap tests. Comparison of the number of Pap tests and number of cytologists and cytotechnologists engaged in their performance showed that one cytologist with the respective team have performed a mean of 9,241 Pap tests, whereas one cytotechnologist examined a mean of 6,378 Pap smears (approximately 28 *per day*!). The laboratories included in the analysis varied greatly according to the number of tests performed, Pap test in particular (Figure 1). The number of Pap tests *per* cytologists/cytology team ranged from 2000 to 16,000, and *per* cytotechnologist from 3300 to 10,000.

The highly uneven pattern of performance recorded in the cytology service across Croatia according to organizational unit and localization, number and profile of professional staff, and number of tests *per* team performed imposes the need of developing distinct legal regulations to standardize the mode of organization, location, staff structure and performance standards in the field of cytological diagnosis, consistent with the respective catchments population. Taking into account more than 30 years of residency in clinical cytology, it is not justifiable that cytology testing is performed by anyone but physicians-cytologists.

Overall, the high number of specialists in cytology and properly educated cytotechnologists, and the number of Pap tests performed (n=452,809) offer a capacity adequate to cover the female population at risk aged 25–64, if screened once in three years. According to the 2001 census, there were 1,178,052 women of these age groups in Croatia⁴; thus, screening per year should cover 392,684 women.

»Zagreb 2002« Uniform Classification of Uterine Cervix Cytological Findings in Croatia

In Croatia, a uniform classification named »Zagreb 2002«⁵, a modification of »Zagreb 1990«⁶ and »NCI Bethesda System 2001«⁷, has been used in cytological analysis of cervical smears. Two groups of »satisfactory« and »unsatisfactory« (explaining the reason for the latter) are used on assessment of specimen adequacy. According to general classification, findings are categorized as »negative for intraepithelial or invasive lesion« (normal finding, changes with reactive and reparatory reactions, a finding suggesting certain risk) and »abnormal cells« (cellular changes that are morphologically consistent with intraepithelial or invasive malignant lesions).

Descriptive diagnosis includes the items »microorganisms« (listing the microorganisms that can be identified directly or based on the specific cytopathic effect), »other non-neoplastic findings«, and »abnormal cells« (squamous, glandular, of undetermined significance, and other malignant neoplasms). The group of »other non-neoplastic findings« that may be found with or without abnormal

cells includes reactive cell changes, reparatory epithelium, spare cells, parakeratosis, dyskeratosis, hyperkeratosis, a post-hysterectomy finding of cylindrical cells, a finding of endometrial cells beyond the cycle or in menopause, and a conclusion that the cytohormonal status does not correspond to the patient's age and/or history.

Squamous lesions are divided into three groups, as follows: »atypical squamous cells« (ASC), »squamous intraepithelial lesion« (SIL), and »squamous cell carcinoma«. The ASC group is further subdivided into »undetermined significance« (ASC-US), »high-grade SIL cannot be excluded« (ASC-H), and »invasion cannot be excluded«. Considering SIL group, all three terms currently in use have been retained, with the addition of »invasion cannot be excluded«. This parallel terminology (*dysplasia* – CIS, cervical intraepithelial neoplasia – CIN and SIL) has been retained to avoid diagnostic-therapeutic identification of moderate *dysplasia* (CIN 2) with severe *dysplasia* and carcinoma *in situ* (CIN 3), thus leaving an opportunity for cytological and colposcopic follow-up of the lesion up to its regression or progression.

Glandular lesions are also classified into three groups, as follows: »atypical glandular cells« (three subgroups: probably reactive, probably intraepithelial, and probably invasive), »adenocarcinoma *in situ*« (AIS), and »adenocarcinoma«, with a note on its origin.

The groups of »abnormal cells of undetermined significance« and of »other malignant neoplasms« refer to abnormalities where differential cytological diagnosis cannot be established.

This uniform classification enables both internal and external quality control of the laboratory performance, along with appropriate reproducibility of cervical cytology relative to the terminology adopted in the world.

Methods of Quality Assurance in Cervical Cytology

All laboratories have been structured in line with the standard work protocols, to include internal and external quality control^{8–11}.

Internal quality control of laboratory performance includes the following:

- a) control of material sampling,
- b) control of technical processing (preparation) and smear staining,
- c) primary screening using the following methodology^{8,10}:
 - *selected pre-screening* – refers to pre-screening of cervical smears in patients with particular clinical entities such as abnormal bleeding, clinically suspect cervix, etc. In this case, all slides should be observed as having evidence for abnormality, i.e. they should be examined twice by a cytotechnologist and also by a cytologist if some abnormality has been demonstrated;

- *double screening* – it is a reliable method of internal control, ensuring continuous caution on test performance. It is used in all diagnostic specimens;
 - *proportional re-screening* – so-called random screening of some 10% of negative specimens;
 - *rapid screening* – it includes re-screening of all negative and inadequate smears by use of the known rapid screening technique, performed by cytotechnologists that have not previously analyzed the respective specimens¹²;
 - *previous cytology review* – it is performed when high-grade dyskaryosis/dysplasia is found in cytological specimen, and previous cytology was negative or has been inadequate for 5-years back, when carcinoma or high-grade CIN is histopathologically diagnosed following negative cytology, and when cytological finding is negative following previous cytological abnormalities;
- d) slides and findings are stored for at least 10 years;
- e) result analysis by daily cyto-histological correlation of findings; and
- f) continuing education.

External quality control implies control of performance of a number of cytology laboratories by a commission consisting of the representative profession and national health authorities. The commission controls the work of a cytological laboratory and tests skill of the cytotechnologists and/or cytologists either by mail or by testing organized at a previously agreed location¹³. *Preparation exchange* includes several (e.g., four or five) laboratories, each submitting up to 10 slides sent from one to another laboratory for screening. Eventually, they all meet together to discuss their results. *Verification tests* make an alternative method of external quality control, where 10 slides are analyzed within 2 hours; all slides included in cervical carcinoma screening can be analyzed^{8,10}.

The Value of Opportunistic Screening by Conventional Pap Test

The efficacy of conventional Pap test in opportunistic screening is assessed on the basis of its detection and differential diagnostic value, and population coverage. In addition to accurate Pap test may also produce inaccurate diagnosis, i.e. false negative or false positive results. A false negative finding may be due to insufficient sampling, inappropriate laboratory processing, screening failure, or erroneous evaluation of the cells present in the respective smear. A false positive cytology finding is by definition a positive cytology finding in a woman free from cervical lesion. It also includes erroneous interpretation as well as so-called falsely false positive findings, referring to a positive cytology finding in a patient with cervical lesion but negative biopsy finding. The proportion of cytological screening error can be defined as the number of false negative findings in the total number of cytology smears analyzed over a period of observation,

yielding a very low error rate, or as the number of false negative findings in the total number of women with cervical lesion, which yields a much greater error percentage. As about 95% of smears negative for CIN lesions, the value of cytological screening lies in the possibility of detecting those 5% of specimens that are abnormal; thus, the error proportion may be expressed also as the number of false negative findings out of the total number of women with cervical lesion. When thus expressed, the rate of false negative findings varies from nil to 29.7%^{14–27}.

The measures of cervical cytology appropriateness as a screening test are its sensitivity, specificity, predictive values, and diagnostic accuracy. In case of cervical cytology, sensitivity is the rate of positive cytology findings in a group of women with intraepithelial or invasive cervical lesion, ranging from 30 to 87%²⁸. Specificity is the rate of negative cytology findings in a group of women free from intraepithelial or invasive cervical lesion, varying from 86 to 100%²⁸. Sensitivity and specificity are not independent measures. An increase in sensitivity with a seemingly decreased rate of false negative findings may be accompanied by an increase in the number of false positive findings, and *vice versa*. The relationship between sensitivity and specificity is best illustrated by predictive values.

Positive predictive value (PPV) is a measure of probability that an individual with positive finding is ill. In cervical cytology, it is a useful measure of finding accuracy in case of lesions that require additional diagnostic procedures. On determining PPV, the time to histologic verification should be limited to a maximum of six months. In case of a longer period, the inconsistency between histological and cytological diagnoses resulting in a low PPV may be due to lesion regression rather than inaccurate cytological finding. Negative predictive value (NPV) is a measure of probability that an individual with negative finding is healthy.

In a study conducted in Croatia to estimate the reliability of conventional Pap smear in the screening for both low and high grade intraepithelial cervical lesions and early invasive cervical cancer^{29,30}, the rate of false negative findings was 10%, of which screening error accounted for 3.1% and sampling error for the rest of 6.9%. The rate of false positive findings was 1.4%, of which erroneous smear interpretation accounted for 0.6%, and SIL detected on follow-up and/or repeat biopsy for the rest of 0.8%, switching the categorization of these cases from »cytologically false positive« to »histologically false negative« due to error on collecting biopsy specimens. The sensitivity was 90.0%, specificity 98.6%, PPV 92.3%, NPV 98.1%, and overall diagnostic accuracy 97.2%.

The main objection to conventional cytology as a screening test refers to its low sensitivity. However, the rate of false negative findings can be considerably reduced by strictly following professional rules, primarily careful sampling and smear preparation, fixation and processing through thorough screening and professional interpretation, thus upgrading the test sensitivity.

TABLE 2
NUMBER OF WOMEN AGED 25–64 IN OSIJEK-BARANJA COUNTY (2001 CENSUS) AND NUMBER OF WOMEN COVERED BY CYTOLOGY SCREENING DURING A THREE-YEAR PERIOD (2003–2005)

Number of women	Age (years)								Total
	25–29	30–34	35–39	40–44	45–49	50–54	55–59	60–64	
Osijek-Baranja County	10,378	11,188	12,396	12,635	12,045	10,730	9,195	10,655	89,222
With Pap test	10,081	9,180	8,922	9,124	8,761	6,908	4,288	3,110	60,374
% of tested	97	82	72	72	75	64	47	29	68

Conventional Pap test is not only used as a classical screening test for lesion detection but also as a differential diagnostic method predicting histological diagnosis. It is of great importance because the type and severity of the lesion detected will dictate further diagnostic and therapeutic procedure. Differential cytology of squamous intraepithelial lesions, distinguishing three grades of dysplasia and carcinoma *in situ*, has a total sensitivity of 67%, specificity of 87%, PPV of 59%, NPV of 90%, and overall diagnostic accuracy of 75%; diagnostic accuracy increases with lesion severity and is directly proportional to reproducibility of each cytological diagnosis^{29,31–33}.

The small number of glandular intraepithelial lesions neoplasia relative to squamous ones, and the fact that their morphological properties have only been intensively investigated and characterized in the last two decades, have resulted in the lack of experience and attention in the search for these lesions in cytological smears. Consequentially, diagnostic accuracy in recognizing abnormal columnar cells in cytological smears, alone or in combination with a squamous component, is only 55%³³.

The Osijek-Baranja County was taken as a representative sample to assess the risk population coverage by opportunistic screening⁴. Pap smears collected at gynecology clinics and hospital departments in the County were analyzed at Department of Clinical Cytology, Osijek University Hospital in Osijek, Croatia. During a three-year period (2003–2005), 104,062 conventional Pap smears, 77,692 (74.7%) of these primary cases and 26,370 (25.3%) duplicate cases, were examined. The number of primary cases corresponded to the total number of women examined. The target population of women aged 25–64, that should be examined once in three years, accounted for 60,374 (68%) Pap smears (Table 2).

Opportunistic screening covered 68% of the target population, i.e. those spontaneously visiting gynecological offices for reproductive age physiology/pathology, while the total number of tests performed should have included the entire population at risk. Study results explained the unfavourable pattern observed in the incidence and mortality of cervical carcinoma in Croatia as compared with other west and south European countries, pointing to the need of implementing the national programme of cancer prevention and early detection, which should include the entire population at risk³⁴.

Liquid-Based Cytology: Alternative Cytology Method of Higher Sensitivity

New techniques of cervical-endocervical cytology sampling and processing have been developed in the last few decades, with the introduction of liquid-based cytology (LBC) as one of the most important achievements in the field. In contrast to conventional Pap test, in LBC technique the specimen obtained from uterine cervix is not applied onto the slide but the instrument is immersed in a glass containing transport fixation liquid, where it is thoroughly vortexed for optimal utilization of the entire cell material³⁵. Using conventional method, up to 80% of the specimen is lost with the discarded instrument^{36–38}; it is considered to be one of the main reasons for false negative Pap tests (6–50%)^{39–42} and false negative findings in women with HGSIL and invasive carcinoma (20–50%)^{42–44}.

Cell suspension in fixation liquid is stable at room temperature for up to several weeks^{38,45}, and is laboratory processed by use of semi-automated or automated commercial devices. Currently, a number of such devices are available, with those approved by the United States Food and Drug Administration (FDA) for cervical screening being best known: ThinPrep[®] processors (Cytic Corporation, Massachusetts, USA) and AutoCyte-Prep[®] system (ThiPath Imaging, Inc., North Carolina, USA). Excess blood and inflammatory exudate is mechanically removed from suspension specimen, and a small representative specimen is transferred and uniformly applied in thin layer onto the slide, in a circle of 13 mm (AutoCyte-Prep[®]) or 19 mm (ThinPrep[®]) in diameter.

Most authors point to the advantages of LBC over conventional smear, which include a reduced rate of inadequate samples^{35,46–48} (by even up to 97%)⁴⁷ and of false negative findings^{49–51}, higher rate of abnormal cytology findings detected^{52,53}, and significantly shorter time (by up to 60%) needed for analysis of a specimen prepared by the new method⁴⁸. Another advantage of the LBC method, also admitted by those who found no difference when evaluating these two methods of cervical cytology sample preparation⁵⁴, refers to the fact that the remaining cell suspension can be used for more sophisticated diagnostic methods such as Human papillomavirus (HPV) analysis (so-called reflex testing), thus upgrading the screening test sensitivity and specificity, in order to prevent unnecessary overtreatment of lesions that would otherwise undergo spontaneous regression. In addition, cell suspension can also be used for the diag-

nosis of other sexually transmitted diseases (*Chlamydia trachomatis*, gonorrhoea, etc.), or molecular and cytogenetical methods can be employed, thus making »the impossible possible« in the future⁵⁵. The more so, the rest of material can be used for additional preparations for education and external quality control.

The major hindrance to the introduction of LBC technique is the high cost of its utilization in organized screening actions. Yet, according to the report issued by the Sheffield School of Health and Related Research (SchHARR)⁴⁸, the initially high price of the instrumentation will pay off, primarily through a reduced number of inadequate specimens, avoiding unnecessary retesting, and centralization of material processing at only a few laboratories. Furthermore, the implementation of LBC requires additional training of cytologists and cytotechnologists. Cytological analysis of thick layers may frequently prove quite demanding, along with a lower specificity as compared with conventional Pap test⁵⁶.

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Conclusion

The tradition of more than half a century, the network of cytology laboratories staffed with cytologists and properly trained cytotechnologists of enviable skill and competence, and more than 450,000 Pap tests performed per year provide strong basis for the success of cytological screening as the basic method of secondary prevention for cervical carcinoma in Croatia. Opportunistic screening in Croatia reflected in the substantial decrease of cervical cancer incidence from 26 to 15 per 100,000 women-years between 1970 and 1990 remaining almost constant till then⁵⁷. However, some modifications appear to be necessary, which primarily refers to the substitution of opportunistic screening by a properly designed, organized and controlled national screening, as all preconditions for it have been fulfilled. In addition, alternative, high sensitivity methods of sample preparation should be introduced in the cytology service at the national level.

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CITOLOŠKI PROBIR RAKA VRATA MATERNICE U HRVATSKOJ – PROŠLOST, SADAŠNJOST I BUDUĆNOST

SAŽETAK

Prikazan je segment kliničke citologije u Hrvatskoj koji se bavi cervikalnom citologijom, kako bi se analizom organizacije, izobrazbe i učinjena rada, uz objektivnu vrijednost identificirale i slabe točke oportunističkog probira konvencionalnim Papa-testom, te predložile mjere za postizanje njegove najveće moguće učinkovitosti u cilju smanjenja smrtnosti od raka vrata maternice. U 35 laboratorija koji su ustrojeni u skladu sa standardnim protokolom rada uz kontinuiranu unutarnju i vanjsku kontrolu kvalitete, u kojima je uposljeno 68 specijalista citologa i 91 educirani citoskriner, pregleda se na godinu preko 450.000 Papa testova. Iako je tim brojem moguće jednom u tri godine obuhvatiti sve žene u rizičnoj dobi od 25–64 godine, obuhvati se tek 68% onih koje se spontano javljaju ginekologu zbog fiziologije/patologije reproduktivne dobi. U Hrvatskoj je pouzdanost citološkog probira na zavidnoj razini, što se može pripisati dugoj tradiciji sustavne izobrazbe citologa (poslijediplomski studij od 1967. i samostalna specijalizacija od 1974.) i citoskrinera (od 1968.). Osjetljivost Papa-testa je 90,0%, specifičnost 98,6%, pozitivna prediktivna vrijednost 92,3%, negativna prediktivna vrijednost 98,1%, a ukupna dijagnostička točnost 97,2%. Glavna zamjerka se odnosi na nisku osjetljivost. Tradicija duža od pola stoljeća, razvijena mreža citoloških laboratorija sa zavidnim fondom specijalista citologa i educiranih citotehnologa, te broj pregledanih Papa-testova na godinu snažan su argument mišljenju da citološki probir u Hrvatskoj treba ostati temeljnom metodom sekundarne prevencije raka vrata maternice. Nužne su pritom određene promjene, u prvom redu zamjena oportunističkog probira dobro osmišljenim, organiziranim i kontroliranim nacionalnim probirom za koji su ispunjeni svi preduvjeti, te uvođenje alternativnih metoda pripreme uzorka više osjetljivosti.