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Emerging Issues on HPV Infections

From Science to Practice

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From Science to Practice

Editor

Joseph Monsonogo Paris

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Foreword

All of us working in the field of cervical cancer obviously feel privileged among medical professionals, because during the past 20 years, we have had the opportunity of witnessing such an incredible breakthrough in our understanding of a major human disease, with significant impact on women's health on a global scale. Indeed, looking back at the history of medicine, it is rare that such a major progress has been made in such a relatively short time period as has elapsed since the early 1980s, when the basic concepts on cervical cancer and its causes were elaborated.

Despite this tremendous progress made along several different lines of research, it does not mean that cervical cancer has been overcome. Instead, the contrary is true. The disease continues to be the leading cause of cancer mortality among women worldwide and responsible for a significant annual morbidity, despite the increased knowledge and the substantial efforts made to prevent the disease by early detection and other measures pursued by national health authorities and international organizations like the World Health Organization, the International Agency for Research on Cancer and the European Research Organization on Genital Infection and Neoplasia (EUROGIN).

Indeed, the unsatisfactory state of affairs was the single most important reason why EUROGIN was established in the early 1990s. In alignment with its core mission, EUROGIN continues to pursue a wide variety of educational and training activities, all aiming at the widespread distribution of accurate and state-of-art information in the field of cervical cancer prevention, in the widest sense of the word. The latest outcome of these activities is presented in this new book.

This book is a concise update of the current knowledge on HPV infections and their intimate links to cervical cancer, provided by the basic, epidemiological and clinical research, and provides valuable implications in therapy and, most importantly, in the prevention of cervical cancer by prophylactic HPV vaccination. Thus, the book represents an important contribution to continuing medical education, and as such, aimed to be both convenient and educational in its very nature.

It is written by foremost international authorities who share their experience and summarize the current state-of-art knowledge on the highly specialized topics in research, diagnosis and management of these conditions, aiming to reach a multidisciplinary readership consisting of health care professionals and representing divergent specialities coping with HPV-associated diseases at genital and extragenital sites. The main focus of the text is on five different but interrelated topics: (1) high-risk and low-risk HPV infections, (2) methods for HPV detection and use of molecular markers, (3) HPV testing in primary screening and patient management, (4) morphological diagnosis and treatment, as well as (5) prevention of cervical cancer by vaccines: current status, impact and prospects.

In the era of HPV vaccine development, a lot of confusion still exists among physicians and patients in regard to HPV infections in general. One of the aims of this book is to help elucidate these controversies by emphasizing the importance of distinguishing the two types of diseases, i.e. those induced by low-risk HPV and those due to high-risk (oncogenic) HPV types. Throughout the book, the authors highlight these differences, while describing the HPV biology and carcinogenesis, as well as issues related to infection, epidemiology, natural history, clinical features, treatment and prevention of the infections.

Cervical cancer is caused by infections with a range of high-risk (oncogenic) HPV types which differ from the low-risk HPV types in many of their key biological characteristics. Indeed, molecular markers targeted at specific intracellular pathways hold great promise to become important tools not only in dissecting the molecular pathways involved in HPV-induced carcinogenesis, but also in increasing our understanding of the fundamental differences between the low-risk and high-risk HPV types in causing the human disease.

Similarly, infections due to oncogenic HPV types demonstrate a different epidemiology and natural history from those of the low-risk HPV genotypes. Some of the differences between these two categories of viruses are likely to be due to their different immunological recognition by the infected host. Because of the huge morbidity and potential risk of cancer associated with oncogenic HPV infections, it is essential to make a distinction between the low- and high-risk viruses in the communication between the practitioners and their patients. In the same way, proper attention should be paid to providing adequate diagnostic and

management services to populations at particularly high risk of contracting oncogenic HPV infections and prone to disease progression towards invasive cancer.

The principles of the different HPV detection techniques and the recent developments in the field of HPV diagnosis are addressed by several authors. The Hybrid Capture technique has an established position as a cornerstone diagnostic tool, subjected to extensive testing in different settings (both screening and diagnosis) during the past several years. Also PCR-based technology has undergone major technical development towards more user-friendly applications that currently compete with Hybrid Capture 2 assay as routine diagnostic tools in HPV detection and typing. The past few years have witnessed a remarkable explosion of research focused on molecular markers that would accurately predict the outcome of HPV infections and their associated clinical disease at the level of individual patients. Apart from methods based on HPV DNA detection, assays analyzing HPV RNA expression in clinical lesions have become commercially available as well and are currently under vigorous testing in different diagnostic and screening settings.

Cervical cancer has an unequal geographic distribution, with the highest global disease burden confined to the developing countries, where the facilities to combat the disease are clearly insufficient. On the other hand, the declining trends in incidence and mortality rates witnessed in many of the developed countries during the past 4 decades are mainly attributable to the implementation of organized screening programs based on the use of cervical Pap smear, e.g., in the Nordic Countries, where an organized screening has resulted in up to 80% reduction in cervical cancer incidence since the early 1960s. Unfortunately, these highly effective organized screening programs exist in few countries only, and the prospects for effective cervical cancer screening based on the Pap test in the majority of the developing countries seem gloomy, if not entirely pessimistic, even in the foreseeable future. This fact has been well appreciated among the scientific community and has led to an extensive search for optional screening tools, currently under testing in different countries.

One of these optional screening tools is HPV testing, that enables to target the screening directly to the key etiological agent of cervical cancer, instead of the clinical precursor (CIN) lesions detected by the Pap test. Adequate early detection by screening is the prerequisite for effective management of the cervical lesions, which follow different algorithms for low-grade and high-grade abnormalities. On the other hand, no screening is meaningful unless adequate facilities for proper treatment are available, which is not the case in many of the poorest developing countries.

One of the main focuses in the future research is the development of effective prophylactic HPV vaccines and their testing for applicability in general use

in populations at high risk of cervical cancer. The current status, impact and prospects for cervical cancer prevention by vaccines are addressed by several authors in this section. The texts following an in-depth review on this subject by the editor are dealing with different aspects, including the discussion about the rationale of HPV vaccines, their immunogenicity and safety, as well as the efficacy and its assessment and follow-up.

Cost-effectiveness of the vaccination programs plays an important role, particularly in the developing countries. In addition, HPV vaccination holds great promise to further reduce the disease burden of cervical cancer, even in countries where organized screening programs are effectively implemented. In these countries, the vaccination strategies will most probably be different and have important implications on the execution of the existing screening programs, with a great potential to reach substantial cost savings, e.g., by extending the screening intervals and changing the target age groups. However, there are still several issues to be solved before such programs are ready to be implemented. This applies differently to high- and low-resource settings. These include important public health issues related to HPV vaccines, and several more specific unsolved issues that need to be addressed before the measures for implementation can be undertaken.

By compiling this book, EUROGIN intended to bring these topics into general awareness of colleagues who are not able to attend the regular EUROGIN educational and training events. Cervical cancer is our common target, and the global control of this major disease burden necessitates a joint effort of a wide spectrum of medical and paramedical expertise. We sincerely hope that you will find this information helpful in your daily practice and other activities aiming at this goal. According to its mission, EUROGIN continues pursuing these efforts by distributing timely information and by active training of various groups of health professionals in these traditional educational events and scientific meetings, of which more information is available at our website (www.eurogin.com).

J. Monsonogo
Paris