

# The Six Decades of *Acta Cytologica*

Dear Readers,

Our 60-Year Anniversary Issue with the title “The Six Decades of *Acta Cytologica*” is now complete. The enthusiasm and support of the senior editors and some of our regular reviewers meant we were able to publish this special issue in the format that was originally planned [1]. The past 60 years have coincided with the emergence of clinical cytology as an independent discipline, so this Jubilee issue is a tribute to the monumental work of the pioneering generation of cytologists and heirs, and does not forget to acknowledge some of the most notable developments of the more recent past.

According to the original idea, a group of senior editors was asked to identify the single most influential study to represent each of the six decades of the life span of *Acta Cytologica*. When this selection was complete, we invited a foremost expert in each particular field to write a commentary on the selected article. The idea of these commentaries is to give a summary of the original article and its significance at the time of its publication as well as to describe its impact (i) on the development of our discipline and/or (ii) in increasing our scientific understanding. As always, the selected articles represent the preferences of our editors, but in most cases the selections were unanimously agreed upon by all, which I consider to have decreased the selection bias. No distinction was made between original studies and reviews, if the latter were considered influential enough to merit recognition in this Jubilee issue. No detailed instructions were given to the invited experts as to the writing of their commentary and, importantly, none of the authors invited declined the request.

In the final compilation of this issue, the selected articles have been reproduced in their original format, each accompanied by the commentary. In addition to these invited commentaries, we have included a couple of proffered articles [2] considered to be of special interest to the readers and perfectly matched to the theme of this issue. For the first time, the publishers, too, wanted to contribute a short editorial [3] and give their expert view on the journal-related items that were discussed in the most recent editorials by our Editor-in-Chief [1, 4].

The series of commentaries starts with the contribution of Dr. Marshall Austin [5], who was invited to comment on the only paper by Dr. Papanicolaou to be published in *Acta Cytologica* [6]. Towards the end of Dr. Papanicolaou's career, he became interested in human endometrial explants placed into tissue culture. The initial focus of his studies was the phagocytic cells emanating from endometrial explants, and their role in cleansing the uterine cavity after each menstrual cycle and sterilizing the uterine cavity in the face of infection. Dr. Papanicolaou observed that explants of endometrial malignancies exhibited not only increased growth rates but also a visible proliferation of cells with readily identifiable cytological features of malignancy. Acknowledging that cytological screening for intrauterine malignancies had not been proven to be as reliable as screening for cervical cancer [7], he hoped that this tissue culture explant technique might emerge as a new adjunctive method for the diagnosis of endometrial malignancies not readily detectable by other diagnostic procedures. Unfortunately, Dr. Papanicolaou's untimely death in 1962 cut short his progress in this area.

While viewing the contents of *Acta Cytologica* in the 1960s, it is difficult to pass over the landmark study of Dr. Kazumasa Masubuchi and his associates that appeared in 1967 [8]. Being one of these colleagues, Dr. Robert Osamura is the right candidate to comment on this important report [9]. In his commentary, Dr. Osamura discusses the impact of this milestone article on the accuracy of cervical smears for detecting cancer, back in the developmental and transforming era of the cytological detection of atypical and malignant cells. Clearly, this study served in the establishment of cancer screening in Japan, subsequently shown to have contributed greatly in decreasing the mortality from cervical cancers in this country.

Yet another pioneering study appeared in 1967 [10]. Dr. Tani was invited to write a commentary (coauthored by Drs. Fuentes-Martinez and Skoog) [11]. The original article was composed of two separate parts, as indicated by its title. Both are of great historical interest. The first describes the early days of the fine-needle aspiration cytology diagnosis of breast lesions, particularly carcinomas. The results are still impressive today, with a diagnostic accuracy close to 90%. The second part deals with the effect of negative pressure on cell viability during the aspiration procedure. These studies were aimed at evaluating the usefulness of aspirated tumor cells to analyze the effects of therapy and the origin of tumor cells.

In our last issue of 1976 and the first of 1977, two revolutionary reports were published, independently of one another, by two research groups, one in Canada and one in Finland [12, 13]. These are the first reports to link human papillomavirus (HPV) with the development of cervical cancer and its precursor (CIN) lesions. As Editor-in-Chief, it is a great pleasure for me to comment on the global impact of this finding in this Jubilee issue [14]. Today, 40 years later, it is not an overstatement to conclude that these two studies are the most influential ever to be published in this journal. To fully appreciate the significance of their novel discovery, it is essential to align them in the right context, both retrospectively and prospectively. The commentary hopefully orients the reader by (1) summarizing the existing knowledge on HPV before the two reports appeared, and (2) describing the incredibly rapid progress that the reports evoked during the subsequent decades, which led to recognition of HPV as the single most important human tumor virus. As final proof of HPV and cancer causality, prophylactic HPV vaccines have been effective in preventing (a) virus transmission and HPV infection, (b) benign HPV-induced tumors (genital warts), and (c) CIN. Formal evidence of the prevention of cervical cancer by these HPV vaccines still

awaits confirmation, and the same applies to the possible prevention of human cancers at other anatomic sites, as part of the global burden of oncogenic HPVs.

An important landmark in the next decade was covered by an editorial by Dr. L.G. Koss [15] that appeared in our January 1980 issue. Dr. Volker Schneider [16] agreed to write a commentary on this groundbreaking contribution. The editorial addressed the recently emerged critical opinions in the general media on cervical screening and its associated costs. It marked the beginning of a more critical approach to cytology by the lay press, health care providers, and epidemiologists. It was also the first in a series of highly thoughtful editorials by Dr. Koss that discussed the critical issues of cytology during the 1980s. The elegance and clarity of his articles reflect the high standard of editorial writing in *Acta Cytologica* at this time. In his insightful commentary, Dr. Schneider also reviews these other articles by Dr. Koss, including some carefully selected excerpts.

A few years later, in 1983, Dr. Marluce Bibbo gave the Presidential Address at the Annual Meeting of the American Society of Cytology in Denver, CO, USA, entitled “Analytic and Quantitative Cytology,” published in *Acta Cytologica* the next year [17] and commented on in this Jubilee Issue by her colleague and friend, Dr. David Wilbur [18]. In her presentation, Dr. Bibbo included a summary of 30 years of work already accomplished, the present state of the art, and her musings about the issues encountered, potential resolutions, progress that needs to be made, and her perception of how the field needs to evolve in order to ultimately become successful as a clinical service. Dr. Wilbur’s commentary looks back 34 years, with observations about Dr. Bibbo’s predictions and how the field of cytology automation did actually evolve in the decades following this address. New challenges are identified and possible paths forward are discussed.

Dr. Ritu Nayar, together with Dr. David Wilbur, was invited to write a commentary [19] on a contribution by Dr. Diane Solomon’s group that introduced The Bethesda System (TBS) for reporting cervical cytology (a 1989 publication) [20]. The aims of TBS were to (1) provide effective communication from the laboratory to the clinical provider; (2) facilitate the correlation of cytology and histology and also research into the epidemiology, biology, and pathology of cervical disease; and (3) provide reproducible and reliable data for national and international statistical analysis comparisons. The significance of TBS for the further development and implementation of standardized terminology in pathology and the research/

management of cervical cancer have continued to evolve over the past three decades. TBS has always been a multidisciplinary effort, and acknowledgement needs to be given to several stakeholders, who, over the years, have contributed to its success, with molecular methods ultimately being closely integrated into cervical cancer screening, triage, and prevention.

Finally, a more recent contribution, dating back to 2007, was also selected as the target of a commentary [21]. The article was another contribution by Dr. Bibbo, a former Editor-in-Chief of *Acta Cytologica* (2004–2013). The article reports the results of a survey, moderated by Dr. Bibbo, where 17 participants from countries throughout the world were asked to give their opinion on how new technologies were being applied in their respective laboratories, and whether future advances and challenges could be predicted. Today, 10 years later, two participants from this Golden Anniversary Cytology Symposium, Dr.

Fernando Schmitt and Dr. Philippe Vielh, agreed to write a commentary [22], making an outstanding reappraisal of all those predictions made back in 2007. Details can be found in their comprehensive commentary, in which they state that after 10 years, they can conclude exactly as Dr. Bibbo concluded that discussion: “Since molecular biology results are meaningful only when interpreted with proper morphologic correlation, it is important to standardize molecular techniques ...” [22].

Perusal of these original texts should give you, the reader, an impression of clinical cytology during the past decades as well as clues as to the major impact that these studies we have selected have had on the discipline today. Ideally, a careful reading of this Jubilee issue will also inspire innovative thoughts and ideas on how to develop *Acta Cytologica* as a journal and clinical cytology as a discipline during the decades to come.

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## References

- 1 Syrjänen KJ: *Acta Cytologica* 60 years. *Acta Cytol* 2017;61:1–2.
- 2 Chantziantoniou N: Two fortuitous papers in 1917 that conceived diagnostic cytopathology. *Acta Cytol* 2017;61:262–265.
- 3 Karger G, Lavender P: Publisher’s note. *Acta Cytol* 2017;61:257–258.
- 4 Syrjänen K, Vielh P, Schmitt F, Nold T: Editorial. *Acta Cytol* 2015;59:1.
- 5 Austin RM: George Papanicolaou’s efforts to develop novel cytologic methods for the early diagnosis of endometrial carcinoma. *Acta Cytol* 2017;61:281–298.
- 6 Papanicolaou GN, Maddi FV: Diagnostic value of cells of endometrial and ovarian origin in human tissue cultures. *Acta Cytol* 1961;5: 1–16.
- 7 Chantziantoniou N, Donnelly AD, Mukherjee M, Boon ME, Austin RM: Inception and development of the Papanicolaou stain method. *Acta Cytol* 2017;61:266–280.
- 8 Masubuchi K, Tenjin Y, Fujii J: The detection of cervical cancer at Cancer Institute Hospital in Tokyo from 1952 to 1963. *Acta Cytol* 1967; 11:32–34.
- 9 Osamura RY: A groundbreaking work which laid the foundation for mass screening in cervical cytology in Japan. *Acta Cytol* 2017;61: 299–304.
- 10 Zajicek J, Franzén S, Jakobsson P, Rubio C, Unsgaard B: Aspiration biopsy of mammary tumors in diagnosis and research – a critical review of 2,200 cases. *Acta Cytol* 1967;11: 169–175.
- 11 Tani E, Fuentes-Martinez N, Skoog L: A review of the use of fine-needle aspiration biopsy of mammary tumors for diagnosis and research. *Acta Cytol* 2017;61:305–315.
- 12 Meisels A, Fortin R: Condylomatous lesions of the cervix and vagina. 1. Cytologic patterns. *Acta Cytol* 1976;20:505–509.
- 13 Purola E, Savia E: Cytology of gynecologic condyloma acuminatum. *Acta Cytol* 1977;21: 26–31.
- 14 Syrjänen KJ: Two landmark studies published in 1976/1977 paved the way for the recognition of human papillomavirus as the major cause of the global cancer burden. *Acta Cytol* 2017;61:316–337.
- 15 Koss LG: The attack on the annual “Pap smear.” *Acta Cytol* 1980;24:181–183.
- 16 Schneider V: Criticism of the Pap smear as a diagnostic tool in cervical cancer screening. *Acta Cytol* 2017;61:338–344.
- 17 Bibbo M: Presidential address. *Acta Cytol* 1984;28:519–526.
- 18 Wilbur DC: Dr. Bibbo’s presidential address on automation in cytology: were her predictions right, wrong, or somewhere in the middle? *Acta Cytol* 2017;61:345–358.
- 19 Nayar R, Wilbur DC: The Bethesda System for reporting cervical cytology: an historical perspective. *Acta Cytol* 2017;61:359–372.
- 20 Solomon D, et al: The 1988 Bethesda System for reporting cervical/vaginal cytologic diagnoses. Developed and approved at the National Cancer Institute Workshop, Bethesda, Maryland, USA, December 12–13, 1988. *Acta Cytol* 1989;33:567–574.
- 21 Bibbo M: How technology is reshaping the practice of nongynecologic cytology: frontiers of cytology symposium. *Acta Cytol* 2007;51: 123–152.
- 22 Schmitt FC, Vielh P: Expectations and projections for the future of nongynecological cytology 10 years ago: did they materialize and how did we do? *Acta Cytol* 2017;61:373–407.