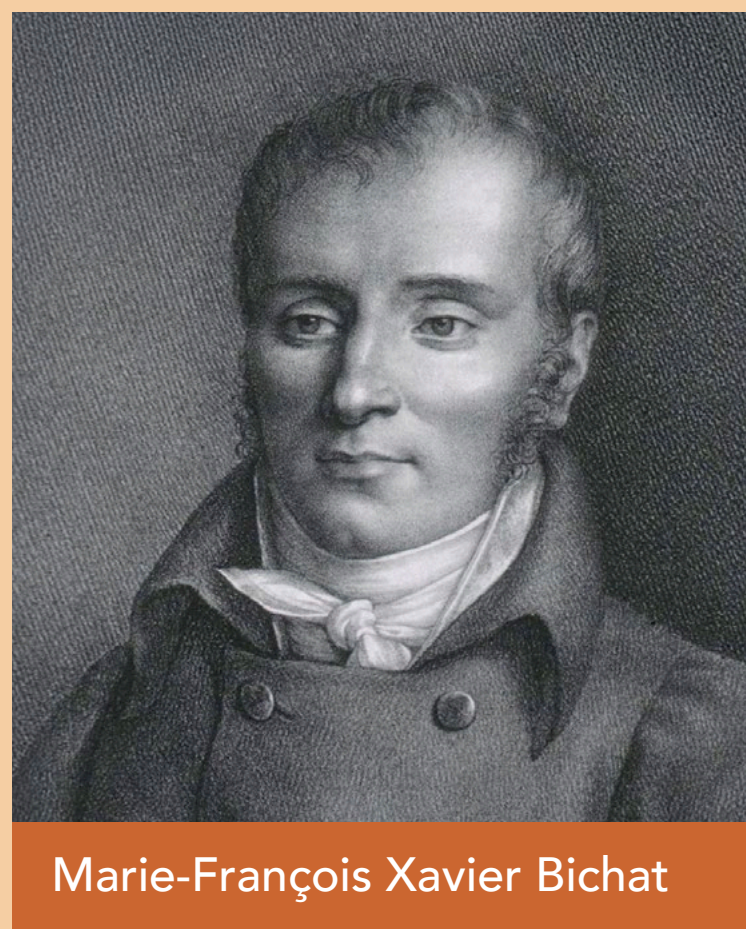


# Cytology: some developments in cancer diagnosis and screening

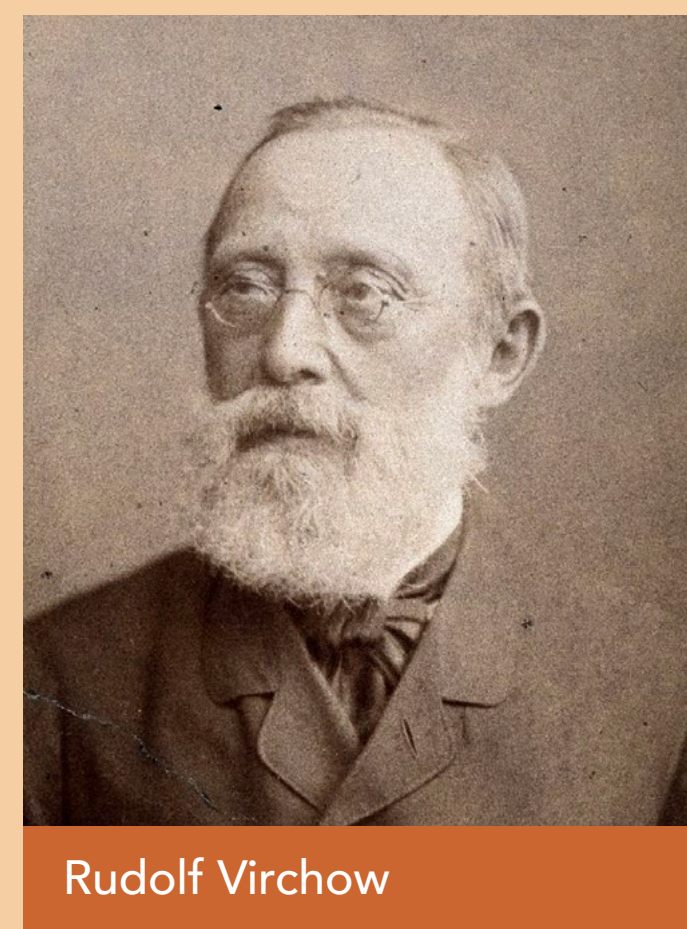
Since the dawn of the age of microscopy in the 17th century and the birth of cell theory in the 18th century, the art of cytology has progressed to become an integral part of laboratory medicine and the screening and diagnosis of malignant disease.

## Cellular Theory: A Brief History

- Marcello Malpighi (1628–1694) was the first scientist to observe capillaries, and thus was considered to be the 'Father of Histology'.
- Marie-François Xavier Bichat (1771-1802), a French pathologist and anatomist known as the 'Father of Modern Histology', was the first to propose that tissue is a central element in human anatomy.
- Bichat considered organs as collections of often disparate tissues, rather than as entities in themselves. He first described the concept of tissues in 1794, and surmised that disease began at the cellular level. He introduced the term 'tissue' in 1801, a year before his death.
- August Franz Josef Karl Mayer (1787–1865), a German anatomist and physiologist, coined the term 'Histology' in 1819, combining the two Greek root words *histos* (tissues) and *logos* (study).
- In 1855, at the age of 34, Rudolf Ludwig Carl Virchow (1821–1902) published his famous aphorism '*omnis cellula e cellula*' (every cell stems from another cell). He stated that all diseases involve changes in normal cells; hence, all pathology ultimately is cellular pathology.



Marie-François Xavier Bichat

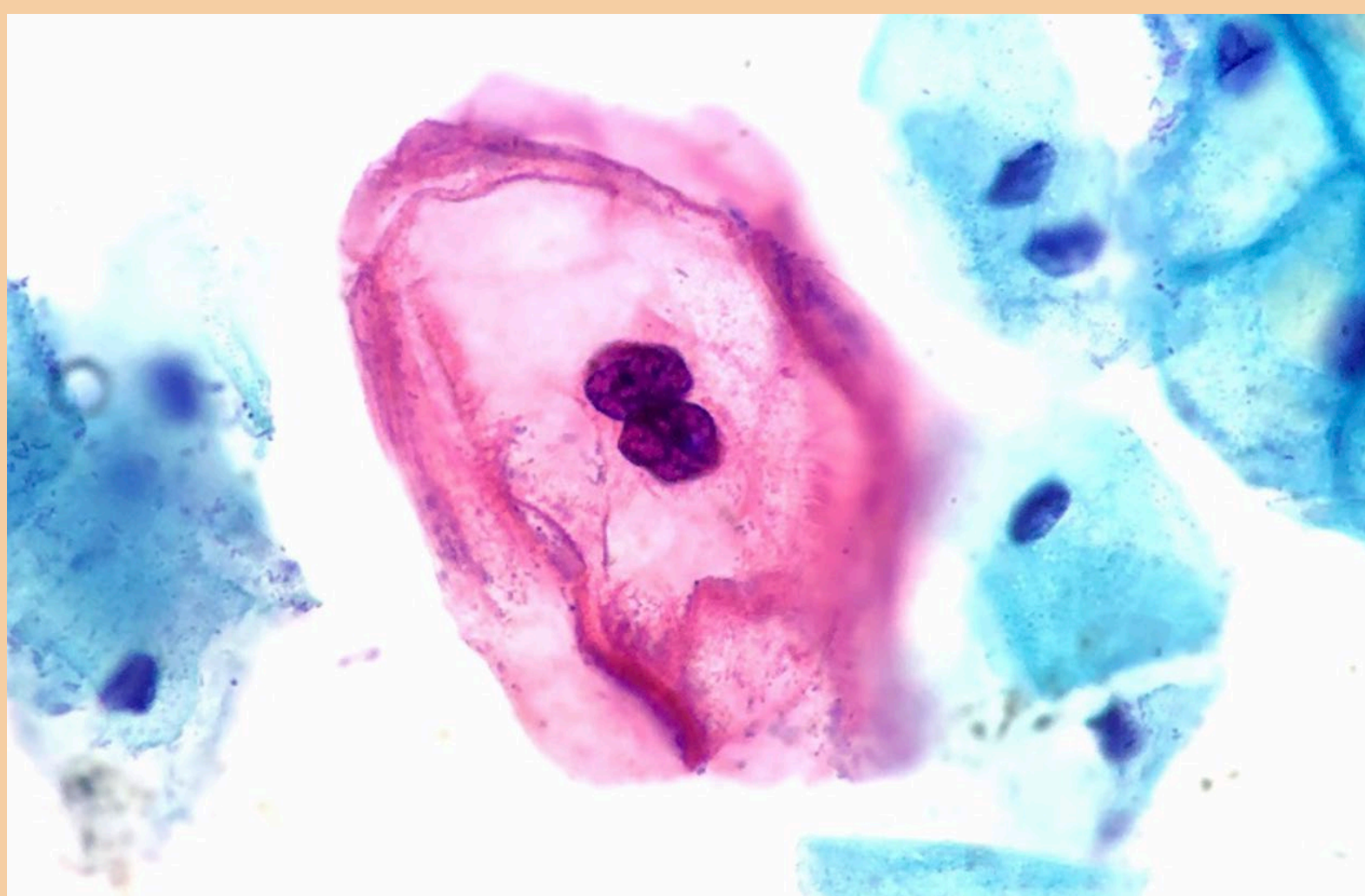


Rudolf Virchow

## The NHSCSP and Support for Cytoscreeners

While cervical screening started in England in the 1964, it was not until 1988 that the NHS Cervical Screening Programme was introduced. This had a significant positive impact on the detection of cancer of the cervix, thanks to the introduction of the cytoscreener grade as part of the UK-wide programme. Cervical cancer prevention based on cervical cytology screening over the past 50 years has proved a major success in the UK. However, recent rapid advances in understanding of human papillomavirus (HPV), its role in carcinogenesis, the clinical applications of primary prevention by HPV immunisation and secondary prevention by HR-HPV testing, the approach to cervical cancer prevention in the UK is undergoing significant change.

In 1989, Jan Gauntlett, Dennis Williams, Russell Smith, Nick Dudding and other interested parties held discussions which finally led to the formation of the National Association of Cytologists (NAC) in the United Kingdom. In the early 2000s, the NAC began to work more closely with the British Society for Clinical Cytology (BSCC), and the two organisations merged in 2011 to form the British Association for Cytopathology (BAC).



Squamous cell showing koilocytotic atypia caused by human papillomavirus.

## Cytology and a Royal Connection

During the 1930s and '40s, the identification of malignant cells in sputum or bronchial aspirates found slowly increasing application. In the early 1950s the link between tobacco smoking and lungs disease had yet to be recognised. Against this background, in September 1951 HM King George VI was diagnosed with lung cancer, and one, perhaps apocryphal, story suggests that sputum/bronchial aspirate cytology played a role in the diagnosis, the confidence in which was challenged in light of the source of the specimen. The King subsequently underwent a left pneumonectomy, performed by Westminster Hospital thoracic surgeon Clement (later Sir Clement) Price Thomas in the Buhl Room at Buckingham Palace.



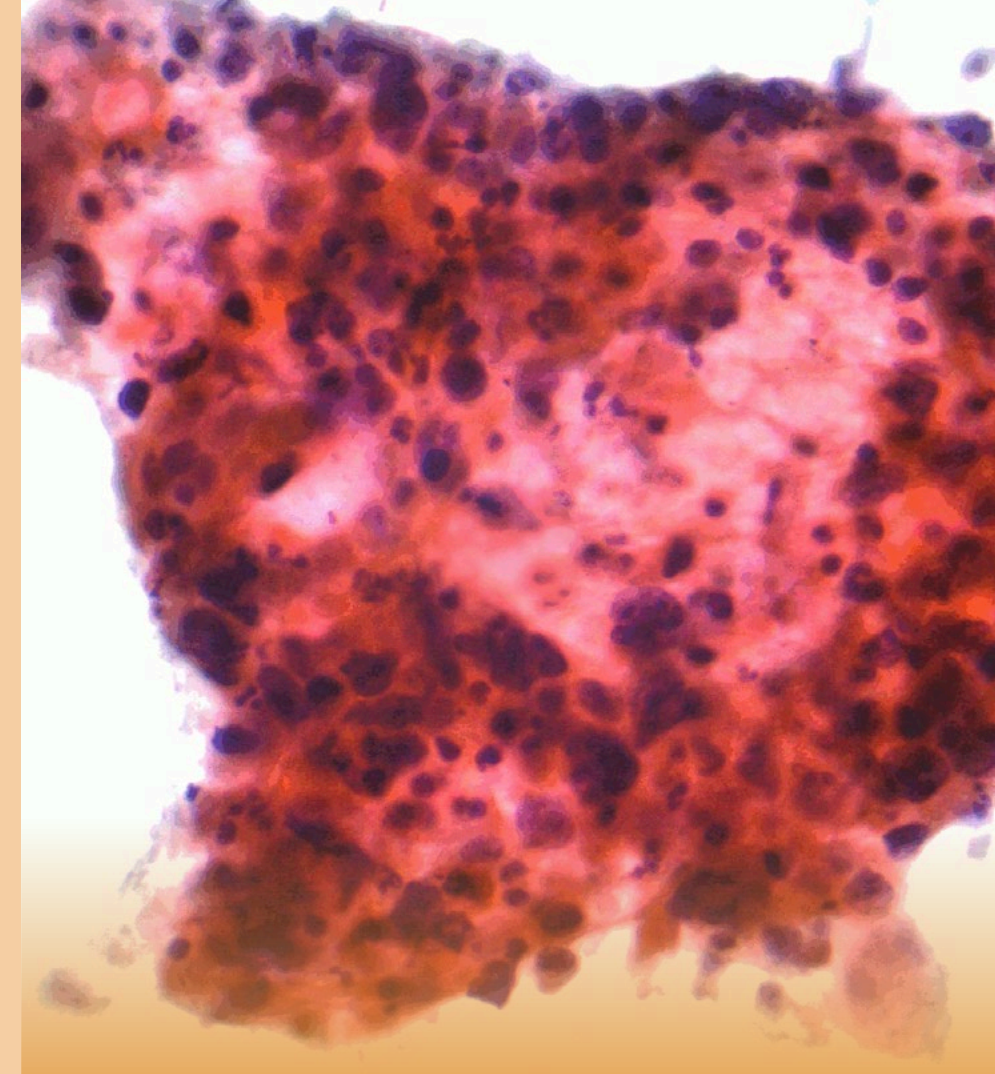
HM King George VI



Dr Papanicolaou on a commemorative stamp issued in the US to promote early cancer detection

## From M&S to HPV Testing

Cervical smear screening was introduced in England in 1964. In 1965, Marks and Spencer offered free cervical screening for female staff. The system was somewhat ad hoc with no organised follow up of abnormal findings. It took until 1988 for the introduction of an NHS centralised system with call and recall for women between 20 and 64. Liquid-based preparation of slides was introduced in 2003 and this allowed the automated standardisation of slide production. By 2014, the use of liquid-based samples for HPV testing superseded microscopy as the primary screening tool for cervical cancer detection, as it was recognised that this approach had a high negative predictive value for the disease. These samples may also be used for the detection of other sexually transmitted diseases.



Fine-needle aspiration showing squamous carcinoma of the lung.

## Cancer Detection and Screening

The following are significant milestones in cytological practice and its detection of malignancy.

- **1927** Leonard S Dudgeon and C V Patrick described a new technique for examining fresh tissues removed during surgery.
- **1927/1928** Aurel Babeş (1886–1961), along with Constantin Daniel, conducted the first studies – subsequently published – demonstrating that cervical cancer could be diagnosed via smears
- **1928** Georgios Nikolaou Papanicolaou (1883–1962), a Greek physician, zoologist and microscopist, and pioneer in cytopathology and early cancer detection, first published his work on recognising cancer in cervical/vaginal aspirates from posterior fornix washings
- **1934** Dudgeon and N R Barrett had published in the *British Journal of Surgery* a paper on the examination of fresh tissue using a wet-film method
- **1935** Dudgeon and C H Wrigley reported on the examination of a large numbers of specimens of sputum from patients with different kinds of pulmonary disease.
- **1938** Barrett reported on the examination of sputum for malignant cells.
- **1941** Papanicolaou developed the 'Pap' smear for cervical cancer.
- **1955** In the journal *Cancer*, Leopold G Koss and Grace R Durfee focused on the cellular appearances preceding the appearance of *in situ* carcinoma of the uterine cervix.
- **1956** In the *Annals of the New York Academy of Sciences*, Koss and Durfee published on koilocytotic atypia in the squamous epithelium of the uterine cervix.
- **1970s** Several series of lung cancer screening trials with sputum cytology were conducted in the USA. The National Cancer Institute funded the Cooperative Early Lung Cancer Detection Programme designed to assess the screening of sputum cytology and chest radiographs to reduce lung cancer mortality in male smokers. One study was conducted at the Mayo Clinic, one at Johns Hopkins University, and one at Memorial Sloan-Kettering. The results of these studies were interpreted as showing that sputum cytology offered no addition benefit.