systematically separated into different pools. The panel was also intended to work for all HPV DNA detection systems known today (and as far as possible also for conceivable improvements).

The recommendation for a laboratory performing HPV testing is that sensitivity and specificity should be evaluated at least annually using a blinded proficiency panel issued by the WHO HPV LabNet. Results should at least conform to what is considered useful for the intended purpose (HPV surveillance). Mis-typing and false positives should not occur and there should be sensitivity at an acceptable level [50 genome equivalents (GE)]. GE will be replaced with the corresponding amount of international units of HPV DNA, which is expected to be defined during 2008 (2).

THE WHO HPV LabNet

Sharing of experiences is very useful in the QA system. The HPV LabNet aims to define and agree on quality indicators for HPV testing and how they should be measured and share experiences and documents (Standard Operating Procedures) in the quality work. The mission of the WHO Global HPV LabNet is to improving quality of laboratory services for effective surveillance and monitoring of HPV vaccination impact, through enhanced, state-of-the-art laboratory support as well as to support the introduction of HPV vaccines and surveillance of disease and infection. Although the activities of the HPV LabNet may be of use for HPV-based screening programs, the mission of the LabNet does not include improved screening but is focussed on the need of HPV testing for the furthering of HPV vaccination (2).

Progress so far is that a proficiency panel for HPV DNA testing and typing has been prepared and a first proficiency study has been completed.

A reference standard for unitage of HPV-16 antibodies has been prepared and assigned a WHO unitage of 5 units. The reference standard can be ordered from the National Institute for Biological Standards & Controls in the UK.

Guidelines Standard and Quality Indicators, examples of SOPs etc “The WHO HPV laboratory Manual” is in progress. At the GRL Sweden, we have as part of our WHO assignment performed several pilot projects on how to design HPV vaccination surveillance systems. A pilot project on HPV typing of condylomas at sentinel STD clinics has been implemented. A national HPV Vaccination Registry has been implemented and we have received ethical permission for nationwide linkages with pathol-ogy/cytology biobanks to retrieve specimens for HPV typing and to determine if the HPV-type-specific burden of disease changes after vaccination. We also have permission to link with the population-based serum biobanking system to allow for a random sample to assess if titers wane (population coverage of immunity) and to find serum samples taken before breakthrough cases, to assist in determining a serological correlate of protection.

REFERENCES


LIQUID COMPARED WITH CONVENTIONAL CERVICAL CYTOLOGY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Marc Arbyn1, Christine Bergeron2, Paul Klinkhamer3, Pierre Martin-Hirsch4, Albertus G. Siebers5, Johan Bulten5

1Unit of Cancer Epidemiology, Scientific Institute of Public Health, Brussels, Belgium
2Laboratoire Pasteur-Cerba, Cergy Pontoise, France
3Laboratory of Pathology, PAMM Laboratories, Eindhoven, The Netherlands
4Central Lancashire Teaching Hospitals, Preston, UK
5Department of Pathology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Address for correspondence: M. Arbyn, Scientific Institute of Public Health, Unit of Cancer Epidemiology, J Wytsmanstreet 14, B1050 Brussels, Belgium. E-mail: marc.arbyn@iph.fgov.be
Key words: liquid-based, conventional, cytology, meta-analyses, lesions

OBJECTIVE

To compare test performance characteristics of conventional Pap smears and liquid-based cervical cytology samples.

DATA SOURCES

Eligible studies, published between 1991 and 2007 were retrieved through Pubmed/EmBase searching, completed by consultation of other sources.

METHODS OF STUDY SELECTION

Studies were selected if a conventional and a liquid-based sample were prepared from the same woman or when one or the other type of sample was taken from separate but similar cohorts. The current systematic review is restricted to studies where all subjects where submitted to gold standard verification, based on colposcopy and histology of colposcopy-targeted biopsies allowing computation of absolute and relative test validity for cervical intraepithelial neoplasia grade-II or worse. Randomized trials were selected as well, if all test positive cases were verified with the same gold standard, allowing computation of the relative sensitivity. Impact of study characteristics on accuracy was assessed by sub-group meta-analyses, meta-regression and summary ROC (receiver operating characteristic) curve regression.

TABULATION, INTEGRATION, AND RESULTS

The relative sensitivity, pooled from 8 studies, with complete gold standard verification, and from one randomized clinical trial, did not differ significantly from unity. Also the specificity, considering high-grade and low-grade squamous intraepithelial lesions as cut-off, was similar in conventional and liquid cytology. However, a lower pooled specificity was found for liquid-based cytology when presence of atypical squamous cells of undetermined significance was the cut-off (ratio=0.91; 95% CI: 0.84-0.98). Differences in study characteristics did not explain inter-study heterogeneity.

CONCLUSIONS

There is no evidence available indicating that liquid-based cytology improves detection of cervical intraepithelial neoplasia grade-II or worse.

Note: Published in Obstet Gynecol 2008, 111, 167-77

CERVICAL SCREENING IN ENGLAND:
LIQUID-BASED CYTOLOGY IN THE CONTEXT
OF MODERNIZATION OF THE NHS CERVICAL SCREENING PROGRAMME

Amanda Herbert
Guy’s & St Thomas’ NHS Foundation Trust, London, UK

Address for correspondence: A. Herbert, Histopathology Department, Second Floor, North Wing, St Thomas’ Hospital, London, SE1 7EH, London, UK. E-mail: amanda.herbert@kcl.ac.uk

Summary
The article will briefly explain the processes of organized screening in the NHS Cervical Screening Programme (NHSCP). Quality control is well established and monitored by regional quality assurance reference centres. The final outcome of screening is also monitored by national cervical cancer mortality and incidence rates: data will be presented for rates of in situ and invasive cervical carcinoma before and after the introduction of organized screening. The NHSCP is using the introduction of liquid-based cytology as a platform for modernization, which is planned to include high-risk human papillomavirus (HR HPV) testing for low-grade cytology triage as well as a test of cure after treatment. Trials of computer-assisted screening are also in progress. High standards of quality control will be needed in the era of vaccination, when prevalence of preinvasive and invasive cervical cancer will decline. The NHSCP is well placed to take on these challenges, if necessary by introducing primary HR HPV testing so that cytology screening can be concentrated on women who are genuinely at risk.

Key words: screening, cervical cancer, liquid-based cytology, England