

Introducing Reveille™

E6/E7 Cell Transformation Alert Assay

OVERVIEW OF HPV AND CERVICAL CANCER

Cervical cancer ranks as the third most common cancer among women in the U.S.¹ HPV is now well established as the cause of cervical cancer and has been implicated in 99.7% of the cases of cervical squamous cell carcinoma worldwide.¹

About 30 HPV types are spread through sexual contact and infect the genitals, anus, and cervix.¹ Of these, types 16, 18, 31, and 45 account for about 75-80% of cases in the U.S. and Europe.

Mechanism of Transformation

HPV infection is usually transient, and self-resolving in most women under 30. However, persistent infection is more common with the high-risk types of HPV, and is a significant factor in the development of cervical cancer.¹

Infection with high-risk HPV types interferes with the normal cell function and expression of cellular gene products. In benign lesions, viral DNA is located extrachromosomally in the nucleus; in high-grade intraepithelial neoplasia, HPV becomes integrated into the host genome.¹

CYTOLOGY & HPV TESTING

Traditional methods of screening include Pap testing which has high specificity (>90%)²⁻⁵, but low sensitivity particularly if there has not been regular testing.

HPV testing increases sensitivity, but with only a marginal increase in specificity and positive predictive value.

Only about 5% of HPV positive patients actually progress to cervical cancer if left untreated.⁷ Determining which 5%, however, has proved elusive.

Reveille™ E6/E7 CELL TRANSFORMATION ALERT ASSAY

A new assay, **Reveille™**, helps increase the specificity and positive predictive value in identifying patients who are at risk of progressing to cervical cancer. This new flow cytometry-based test identifies over-expression of the HPV E6/E7 oncogenes in individual cells.⁸ Over-expression of these oncogenes has been demonstrated to be a trigger for the beginning of the cellular transformation cycle, and plays a significant role in cervical carcinogenesis.⁸

Measuring E6/E7 can detect progression up to 2 years prior to the appearance of a high-grade lesion with a sensitivity of 96% for progression to a high-grade lesion.⁹

By measuring over-expression, clinicians can identify which patients are at risk of progressing and need to be more closely followed.

CLINICAL UTILITY

- Detects **over-expression of E6/E7** HPV oncogenes, a trigger for transforming normal cells to cervical cancer⁸
- Over-expression of E6/E7 **precedes development of cancer** in HPV infected cells **independent of specific high-risk genotype**¹⁰
- **78% positive predictive value** for CIN2+ (compared to 43% by HPV DNA alone)⁸

Pap Result	HPV Result	Recommendation	E6/E7 Result	Recommendation
Negative (≥30yrs)	Negative	Normal protocol	N/A	N/A
Negative (≥30yrs)	Positive	Reflex to E6/E7	Negative	Repeat Pap, HPV, & E6/E7 at 12 mos
			Positive	Consider Colposcopy

METHODOLOGY

Pap specimens (ThinPrep® or SurePath™) are processed and analyzed by flow cytometry for the rapid measurement of over-expression of the E6/E7 HPV oncogenes in individual cells. These oncogenes are associated with the transformation of cervical cells to cervical intraepithelial neoplasia (CIN) and ultimately carcinoma.

ORDERING INFORMATION

Test Code	Specimen/Stability	Setup Schedule & TAT
642	ThinPrep or SurePath Liquid-based Pap	Tuesday-Saturday; 24-48 hours

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9. Alameda F, Palao B. HPV E6, E7 mRNA expression in ectocervical cells (HPV 370 Oncotect) predicts disease progression in women with low grade intraepithelial 371 neoplasia (LSIL). Nice France, Eurogin 2008.
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