

Cervical Cancer Screening- Are the Days of the Pap Smear Numbered?

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The Pap Smear

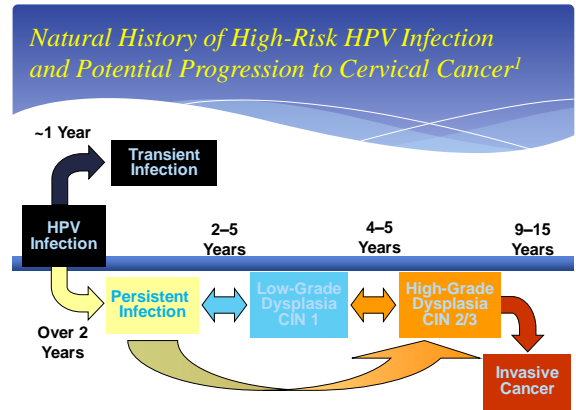
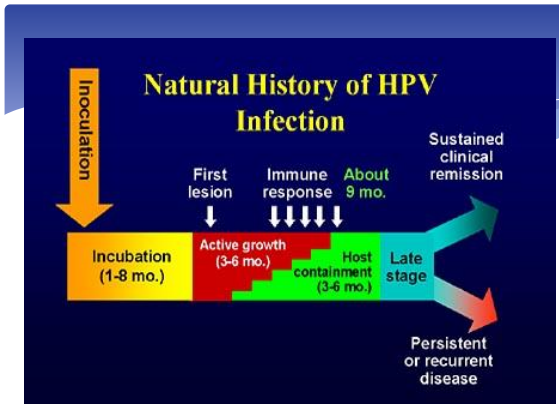
George N. Papanicolaou, Zoologist
(1883 – 1962)

- Examination of vaginal debris in guinea pigs;
- *"The diagnostic value of vaginal smears in carcinoma of the uterus."* Am J Obstet Gynecol. 1941;42:193
- Introduced into the USA in 1941
- Cervical screening program – BC '45

Screening for Cervical Cancer

Oncogenic HPV types are a Necessary Cause of Cervical Cancer

- * Infection with oncogenic HPV types is the most significant risk factor in cervical cancer
- * Analysis of 932 specimens from women in 22 countries indicated prevalence of HPV DNA in cervical cancers worldwide = 99.7%.¹
- * Specific oncogenic HPV types (16, 18, 45, 31, 33, 52, 58 and 35) are responsible for 95% of cervical cancers and HPV 16 and 18 for 70% of cancers.



Cervical Cancer Cases Canada, 2014 (Estimates)

- * Number of new cases 1,450
- * **Incidence rates** * 7.0 ('77 - 15.4)
- * Number of deaths 380
- * **Mortality rates** * 1.6 ('77 - 4.8)

*rate per

100,000

Canadian Cancer Statistics 2014

Cancer of the Cervix Canada

- * Lifetime probability of:
 - * Developing cancer of the cervix - 0.7% (1:153)
 - * Dying from cancer of the cervix - 0.2% (1:444)
- * Incidence rates declining 1.4% / year
- * Mortality rates declining 3.4% / year

The current system of Cervical Cancer Prevention in Canada is based on a secondary prevention strategy – detection of cancer or precancerous abnormalities after they develop.

Cervical Cancer Screening in Canada

“The majority of deaths from cervical cancer are avoidable...”

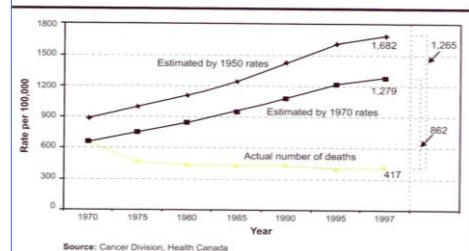
Cervical Cancer Screening in Canada: 1998 Surveillance Report, Health Canada.

Screening Reduces Mortality

- * High screening rates for Cervical Cancer are associated with a decline in disease mortality;
- * Mortality is stable in places with proper screening, suggesting that limits of screening effectiveness have been reached;
- * Because screening does not identify all abnormalities, it does not always ensure early intervention;
- * Some women with cancer have had a recent normal Pap smear prior to diagnosis;
- * Some women are non adherent to Cervical Cancer Screening

Cervical Cancer – Actual / Expected Number of Deaths (Canada)

Figure 5: Actual and Expected Number of Deaths from Cervical Cancer, Canada (1970 to 1997). Estimated by 1950 and 1970 Mortality Rates



Cervical Cancer Prevention

Cervical Cancer Prevention

- *Primary Prevention
 - *Vaccines
- *Secondary Prevention
 - *Screening

HPV Vaccines

Human Papillomavirus (HPV) VLP Vaccines

	Quadrivalent (Merck)	Bivalent (GSK)
Licensed in Canada	2006	2009
VLPs types	HPV 6/11/16/18	HPV 16/18
Producer cells	<i>Saccharomyces cerevisiae</i> (yeast) – expressing L1	<i>Trichoplusia ni</i> insect cell line infected with L1 recombinant baculovirus
Composition	20 µg HPV 6 40 µg HPV11 40 µg HPV 16 20 µg HPV 18	20 µg HPV 16 20 µg HPV 18
Adjuvant	Alum: 225 µg aluminum hydroxyphosphate sulfate	AS04: 500 µg aluminum hydroxide 50 µg 3-O-deacyl-4'-Monophosphoryl lipid A
Schedule	0,2,6 months	0,1,6 months

New Vaccines

- * The duration of protection provided by a new vaccine cannot be determined when the vaccine is introduced
- * Only true way to tell if immunity is waning is by vaccine failures, or breakthrough disease

HPV Vaccines

- There is no immune correlate of protection, no antibody threshold or other immune measurement defined that correlates with protection
- Prophylactic administration of quadrivalent or bivalent HPV vaccines to young women results in some cross-protection efficacy against disease
- However, while cross-protection efficacy has been demonstrated, the true impact and duration of this cross-protection is unknown

Secondary Prevention Screening

Secondary Prevention - Screening

- * Pap Smear (cytology)
- * HPV Testing
- * Co-testing (combination of cytology & HPV testing)
- * VIA (Visual Inspection with Acetic Acid)
- * Self-collected HPV testing

Pap Smear

- * Model for cancer screening
- * Effectiveness – no randomized trials
 - * Exclusively from observational studies
- * Less sensitive for detecting endocervical glandular abnormalities (50-72% vs. 30 to 87% for squamous)
- * Direct correspondence between cytology (Pap) and histology only ~ 50%
- * Liquid-based cytology – no difference in detection rates, but increased specimen adequacy

Is Pap screening enough to prevent cervical cancer?

- ❖ Pap testing is secondary prevention; it only detects abnormalities
- ❖ Cervical cancer incidence and mortality rates have steadily declined over the past 30 years, but rates have reached a plateau
- ❖ 40% of Canadian women who develop carcinoma of the cervix had frequent Pap screening

Screening – HPV Testing

- * Possible 2 roles:
 - * Primary Screening – as adjunct to or instead of cytology
 - * Triage of Pap smears – equivocal or low-grade abnormalities

Screening – Primary HPV Testing

- * More sensitivity than cytology for detection of high-grade lesions
- * Primary HPV testing in women < 30 years f age results in substantial detection of transient HPV infections and unnecessary colposcopy;
- * One trial suggested a decrease in incidence of cancer with HPV testing, but no change in mortality rates;
- * Concerns... HPV testing, will increase the number of positive results and hence increase number colposcopy which can result in overdiagnosis and overtreatment.

HPV- Prevention

Strategies for the reduction in HPV diseases:

- Prevention of acquisition
 - Safer sex practices
 - Prophylactic vaccination
- Improved detection & treatment of HPV pre-cancerous lesions (Cervical Dysplasia)

Summary

- * The Pap smear remains the model for Cancer Screening;
- * No difference between the conventional smear or liquid-based cytology;
- * The role of HPV testing continues to evolve – either as adjunct to cytology or as the primary screening modality especially for the woman >30 years of age;
- * Cervical Cancer Screening should continue to be part of a Cervical Cancer Prevention Strategy which includes the HPV vaccine;
- * In Canada, over 50% of women with Cancer of the Cervix did not participate in the Screening Program.

*Thank You
Questions?*