

Gynemed LLC

## PAP COMBINATION CELL COLLECTION DEVICE

~ Endocervix and Ectocervix ~

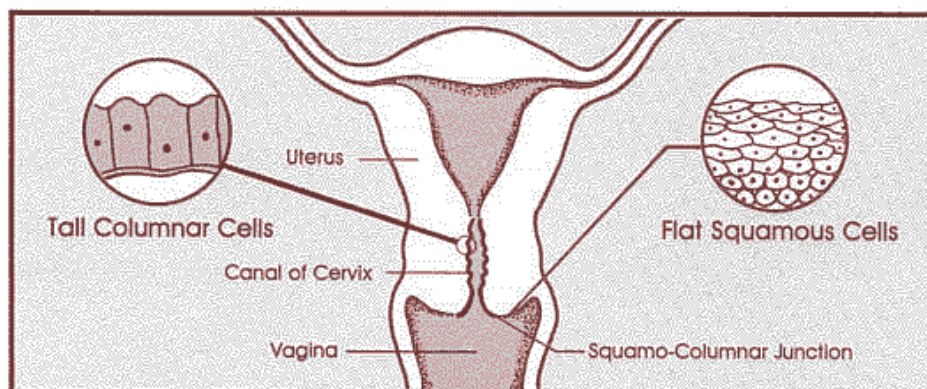
Gary W. Gill, CT(ASCP)CFIAC  
Cytotechnological Consultant

December 2004

### BACKGROUND

Successfully harvesting cells from the area of the uterine cervix known as the transformation zone (T-zone) is a necessary, but not sufficient, first step in ensuring detection of early cervical cancer using the Pap test. The cervical transformation zone is of particular significance as it is the location where cervical dysplasia most often occurs. Why squamous cervical cancer develops specifically along the T-zone still lacks a satisfactory theoretical explanation.<sup>1</sup>

The cervix is made up of two histologically unique parts: 1) the endocervix, which is predominantly comprised of columnar cells, and 2) the exocervix, which is made up of squamous cells. The transformation zone, also called the squamocolumnar junction (see figure), is the area of the cervix where the exocervix and endocervix meet. Starting during puberty, the columnar cells of the endocervix slowly transform into squamous cells by a normal process known as metaplasia,<sup>^</sup> thus it is said that the exocervix “moves in” towards the cervical os throughout a woman’s life.<sup>2</sup>



---

<sup>^</sup> Greek *metaplasia*, transformation

As successful as the Pap test has been in reducing the mortality rate, it still depends on adequate cell collection at the T-zone. The absence of abnormal cells in a Pap test results in clinically-based false negative results, which can result ultimately in fatal patient outcomes.

Cell collection devices should be designed to optimize the yield of cells from these lesion-prone anatomic areas, maximize transfer of cells from the collection device into either a vial of preservative solution or onto a conventional micro glass slide—all the while minimizing potentially deleterious differences in technique among smear takers. Hutchinson *et al.*, for example, “showed that only a fraction of the available epithelial cells on the sampling devices (medians, 6.5% to 62.5%) was actually deposited on the slides... This demonstrates a new source of error, preparation error, in conventional smears.”<sup>3</sup>

## MATERIALS AND METHODS

The “Pap Collection Device” by Gynemed LLC, an early prototype of which is described in the attached 1-page Pap Collection Device,<sup>\*</sup> is designed to overcome these limitations—especially preparation error:

- Sheathing the brush within the distal end of the canula maintains the structural integrity of the bristles during storage and transport, and ensures one-to-one correspondence between the location of the cells *in situ* and along the length of the brush.
- The cervical canal sounding ring ensures correct placement in the endocervical canal, without extending the tip into the lower uterine segment that is lined with unfamiliar cells that cytoprofessionals may misinterpret, either undercalling (i.e., false negatives) or overcalling (i.e., false positives) in terms of biologic behavior (i.e., normal or abnormal).
- Pulling back on the canula—using the finger grip<sup>♦</sup>—exposes the bristles to the sampling area.

---

<sup>\*</sup> The “ball” at the tip of the brush will be absent in future models. Patients report the balls cause discomfort.

<sup>♦</sup> Note in the drawing that the “finger grip” resembles the vamplate, or funnel shaped hand guard, that was added to the jousting lance during the 14<sup>th</sup> century.

- The white bristles are softer and better suited for sampling the endocervical canal—along which the transformation zone is located—while the blue-colored bristles are stiffer and splay to sample the ectocervical surface.
- Rotating the brush ½ turn samples the circumferential epithelium 360° along the length without inducing obscuring blood, which can result from over-rotating the brush.
- After the device is removed from the cervix and the brush end immersed in liquid preservative up to the sounding ring, moving the canula back-and-forth along the length of the brush ensures transferring cells from the length of the bristles to the preservative. *This is a key difference between this device and the conventional endocervical brush as FDA-approved for use with the ThinPrep Pap test vial.*
- Alternatively, the same back-and-forth movement can be applied to transfer cells to the surface of glass micro slides that are used for conventional Pap smears.

## RESULTS

Used as intended—and as demonstrated in pilot studies, the Gynemed LLC Pap collection device can be expected to enhance the usefulness of cervical cytology specimens as follows:

1. Minimizes differences in smear taking technique among professionals.
2. Displaces cervical plug, reducing the amount of non-cellular material collected.
3. Patients experience less discomfort and hemorrhage, and thus producing fewer limited/unsatisfactory samples due to obscuring blood.
4. The controlled sampling length reduces the likelihood of sampling the lower uterine segment, which contains unfamiliar cells that may confound morphologic interpretation.
5. Endocervical cell sampling is improved as evidenced by the presence of numerous recognizable groups of endocervical cells in all specimens from women with a cervix. While the absence of endocervical cells is less significant in the 2001 Bethesda System terminology for reporting results of cervical cytology than it was in the 1991 version, clinicians do not want to see such “no EC” results reported to them. Clinicians associate the absence of endocervical cells as evidence of poor smear

taking and the potential risk of increased risk of a false negative result for which they might be held accountable. Some clinicians will recall patients whose Pap tests did not include endocervical cells for repeat Pap tests.<sup>^</sup>

6. Higher yield of atypical cells by better sampling as S/C Junction, reducing sampling error non-correlations.
7. Higher cellularity and better removal of cellular material from the collection device, which should produce fewer sampling-based false negative Pap test results.

## CONCLUSION

Numerous cervical cytology sampling devices have been patented since 1949, when Ayre patented his wooden dog-bone style scraper. A representative sample of these patents is shown in the attached table: Ectocervical Spatulas, Endocervical Brushes, and Combination Devices. Few of these devices remain in current use, which suggests those that are not did not satisfy the needs of the market place. Gynemed LLC's Pap combination cell collection device appears to do so.

## REFERENCES

1. Tewari KS, Taylor JA, Liao SY, DiSaia PJ, Burger RA, Monk BJ, Hughes CC, Villarreal LP. Development and assessment of a general theory of cervical carcinogenesis utilizing a severe combined immunodeficiency murine-human xenograft model. *Gynecol Oncol* 2000;77(1):137-48.
2. Jastreboff AM, T Cymet. Role of the human papilloma virus in the development of cervical intraepithelial neoplasia and malignancy. *Postgrad Med J* 2002;78:225–8. Review. Free full text article available at: <http://pmj.bmjournals.com/cgi/reprint/78/918/225>. Accessed 12/24/2004.
3. Hutchinson ML, Isenstein LM, Goodman A, Hurley AA, Douglass KL, Mui KK, Patten FW, Zahniser DJ. Homogeneous sampling accounts for the increased diagnostic accuracy using the ThinPrep Processor. *Am J Clin Pathol* 1994;101(2):215-9.

---

<sup>^</sup> "I submit to you that any Pap test which lacks endocervical cells, is no Pap test at all."—Carol Ann Armenti, Director of Cervical Health and cervical cancer survivor despite misread Pap tests, testifying at Open Meeting of the Hematology and Pathology Devices Panel, FDA Medical Devices Advisory Committee, January 28, 1998.