HIGH GRADE SQUAMOUS INTRAEPITHELIAL LESIONS

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- Cells are smaller and immature than LSIL. Single cells, sheets or syncytial aggregate. Variable size. Same size as LSIL or smaller as basal cell type.

- Hyperchromatic nucleus; variable size and shape
- Variable nuclear enlargement.
- Some HSIL nuclei are similar size as LSIL but cytoplasm is scant. High nuclear/cytoplasmic ratio.

- HSIL may have smaller nuclei than LSIL but high N/C ratio.
- Homogenous granular or coarse chromatin.
- Irregular nuclear membranes, often contain indentation or groove.

- Inconspicuous nucleolus but prominent in HSIL with endocervical glandular involvement
- Variable cytoplasm. Immature, Immatür, lacelike or dense metaplastic, infrequently dense and mature keratinized (keratinized HSIL).

LIQUID BASED PREPERATION

- LBP are composed of sparsely single cell pattern, sheets and syncytial aggregates.
- Isolated cells are between clusters of cells.
- Isolated cells are inconspicuous on conventional smears.
- Relatively, normal cells are less than in conventional smears rather than in LBP.
Hyperchromasia may be subtle rather than LSIL.

Other cytologic findings of HSIL (High N/C ratio, irregular nuclear membranes).

Detection of 3D nuclear abnormality is essential to distinguish simple nuclear irregularity in benign cells. Not every HSIL cells comprise that abnormality.

High N/C ratio, isolated cells and 3D abnormality and:
- Hyperchromatic small crowded molding groups
- Irregular nuclear polarity. Chaotic groups with different size and shape
- Naked nuclei. Atrophic smears may have naked nuclei but it is also a feature of HSIL.

- LSIL dominancy with HSIL. Progression concept..

- Irregular nuclear size (large cells) is singly the less important feature of dysplasia.
- Nuclear irregularity associated with 3D nuclear abnormalities are more crucial.

- Hyperchromasia is significant

- Granular chromatin clumping is occasionally indicative for HSIL. But it is associated with 3D abnormalities and high N/C ratio.

- Inconspicuous nucleoli. Attention to nuclear features may help because the chromatin pattern in HSIL is not as coarsely granular as in AIS.
- Nucleoli are conspicuous at inflammatory conditions, reactive changes or glandular involvement
Glandular involvement of HSIL

Endometrial cells

HSIL

Squamous cell carcinoma (SCC)
- Most common cancer of cervix uteri.
- Bethesda system does not subdivide SCC.
- Cells are larger and more squamoid appearance than carcinoma in situ (HSIL) cells.
- Nuclear features indicate malignancy, cytoplasmic features are helpful for subtypes.
### Non-keratinizing Squamous cell carcinoma

- Most common carcinoma of cervix uteri
- Medium to large cells, sheets or syncytial groups.
- Basophilic cytoplasm, dense and mildly vacuolated
- Vacuolization resembles glandular cells but cellular findings are squamous.

### Non-keratinizing Squamous cell carcinoma

- Cells occur singly or in syncytial aggregates with poorly defined cell borders.
- They lack true glandular features such as; rosette forming, acini, round borders, columnar differentiation, elongation and nuclear crowding
- Cells are frequently somewhat smaller than those of many HSIL, but display most of the features of HSIL.
- Nuclei demonstrate markedly irregular distribution of coarsely clumped chromatin

### Non-keratinizing Squamous cell carcinoma

- Chromatin pattern when discernible, is coarsely granular and irregularly distributed with parachromatin clearing.
- Macronucleoli may be seen but are less common than in nonkeratinizing squamous cell carcinoma.

### Non-keratinizing Squamous cell carcinoma

- Tumor diathesis is important for invasive neoplasms and it is seen at 50-80% of invasive carcinomas.
- Tumor diathesis and necrosis are usually identifiable in LBS but can be subtle compared to conventional smears.
- Necrotic material often collects at the periphery of the cell groups, referred to as clinging diathesis as opposed to being distributed in the background as in conventional smears.

### Non-keratinizing Squamous cell carcinoma

- Cytolitic smears, infection or atrophic smears may have tumor diathesis like material
- Only tumor diathesis like background is not sufficient for diagnosis
- But it is warning when tumor diathesis is the single criteria for a neoplasm.

### Nuclear features are the key for malignancy.
Keratinizing Squamous cell carcinoma

- Relatively few cells may be present, often as isolated single cells and less commonly in aggregates
- Marked variation in cellular size and shape, bizarre, spindled, tadpole, etc.
- Caudate and spindle cells that frequently contain dense orangeophilic cytoplasm
- This marked pleomorphism resembles smear artefact
- Nuclei also vary markedly in size, nuclear membranes may be irregular
- Associated keratotic changes (hyperkeratosis or pleomorphic parakeratosis) may be present but are not sufficient for the interpretation of carcinoma in the absence of nuclear abnormalities
- Abundant keratinization cause ghost cell

Keratinizing Squamous cell carcinoma

- Cytoplasmic keratin blebs
- These findings are helpful to differentiate SCC from atypical parakeratosis and keratinizing LSIL.

Small Squamous Cell Carcinoma

- Small cell carcinoma could be diagnosed at LBP.
- These lesions are composed of uniformly small, poorly differentiated cells.
- High nucleus/cytoplasm ratio is definitive.