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CELLULAR PREPARATIONS

Case No. 1

For orientation purposes several normal cell types are depicted. The three large polygonal forms with delicate transparent cytoplasm originate in a stratified squamous mucosa. The cytoplasm appears wrinkled and there are distinct perinuclear clear zones. In two of the cells the nuclei are centrally placed while in the lowermost cell the nucleus is displaced. The nuclei are relatively small in relation to the amount of cytoplasm. They appear opaque or translucent indicating pyknosis. The smaller cells are of endometrial origin. Some forms are isolated while others are arranged in groups. Many of the cells have little discernible cytoplasm. Where cytoplasm can be visualized the nuclei are eccentric. For the most part the nuclei are round or oval with a dense compact chromatin. In some round forms there is a more abundant vacuolated cytoplasm while in other cells the nuclear mass is somewhat larger and has a finely granular chromatin. The latter forms may have originated in the endometrial stroma.

NORMAL SUPERFICIAL SQUAMOUS CELLS AND ENDOMETRIAL CELLS

Case No. 2

Some of the cells are isolated while most are arranged in a sycytium. The cells are much smaller than squamous cells and larger than those of endometrial origin. Where isolated they are oval in shape. Their cytoplasm is finely reticulated and in some instances vacuolated. Cell borders are indistinct. The nuclei are relatively large in relation to the cytoplasmic masses and are round or oval. There is variation in nuclear size but little variation in nuclear shape. The nuclear membrane is wrinkled in some forms and appears indistinct in others. The nuclear chromatin is basically coarsely granular and hyperchromatic. There are larger aggregates of chromatin in some nuclei. These are basophilic in staining and are chromocenters. The nuclear patterns suggest an impending prophase in some cells.

CELLS FROM CARCINOMA IN SITU
Case No. 3

Some of the cells are isolated while others have a syncytial-like arrangement. The cells have a polymorphous shape and in some instances approach the size of the smallest squamous cell of Case No. 1. Cell borders are not distinct. The cytoplasm is somewhat granular. The nuclei are relatively large in relation to the cytoplasmic masses and are predominantly oval. The nuclear forms vary more in size than in shape and have a hyperchromatic granular chromatin. The chromatin is much more coarsely granular than in the normal interphase nucleus. Many of the nuclei contain one or several discrete masses some of which are irregular in their configuration. Some of these stain intensely acidophilic and represent nucleoli while others are basophilic. It is of interest that many of the nuclei have a small chromatin mass in apposition to the nuclear membrane. These masses probably represent the so-called female "sex chromatin". Overlying and about the cells there is exudate and bacteria.

CELLS FROM A LARGE CELL (NON-KERATINIZING) SQUAMOUS CELL CANCER

Case No. 4

The cells occur isolated and also in a rather large grouping. The cells are about twice the size of the normal endometrial cells in Case No. 1. The isolated forms are distinctly oval in shape. In many cells the cytoplasm is disintegrated by lysis. In other forms it is vacuolated. Where orientation is possible the nuclei are eccentric. They are round or oval. The nuclear membrane is distinct and several nuclei have small dense chromatin masses in apposition to the clearly defined nuclear membrane. The chromatin is finely granular. In many of the nuclei there are one or several large discrete and sometimes irregular masses. In most instances, these stain acidophilic and are nucleoli. There is exudate surrounding the cells.

CELLS FROM ADENOCARCINOMA OF THE UTERINE CERVIX
Case No. 5

Most of the cells are relatively large approaching the size of the normal squamous cell. The cells are polygonal in form with distinct cell borders. The cytoplasm is abundant and transparent. Most of the cells are mononucleate although one and possibly two of the cells are binucleated. The nuclei are relatively large in relation to the cytoplasmic mass and are round or oval. The nuclear membrane is distinct and often wrinkled. Small chromatin masses lie in apposition to the nuclear membrane. The chromatin is finely granular and small chromocenters are present. Also present are several smaller round cells with centrally placed small pyknotic nuclei. One of these cells has an acidophilic cytoplasm. Two cells have a rather bizarre shape nuclear mass which is opaque. One of these has a nucleus which is indented by a vacuole. A few neutrophiles are present.

CELLS FROM MARKED DYSPLASIA OCCURRING IN PREGNANCY (Slide No. 1)

Case No. 6

Some of the cells are isolated while others occur in a syncytial-like arrangement. The cells are relatively large and are polymorphous. The cytoplasmic border is indistinct in most cells. Cytoplasmic phagocytosis is evident in one cell. The nuclei are relatively large in relation to the cytoplasmic masses. Round, oval, and irregular nuclear forms are present. The nuclear membranes are indistinct in some cells. The nuclear chromatin is arranged in large aggregates in some cells and is more finely granular in other forms. Within some of the nuclei there are large discrete and sometimes irregular bodies which stain acidophilic. There are also basophilic masses as well. There are small circumscribed inclusions in some nuclei. In addition to the large forms there are smaller cells with limited cytoplasm and relatively large nuclei having hyperchromatic finely granular chromatin. There is abundant exudate overlying and surrounding the cells. These cells are characterized by changes which are observed in cancer cells and by changes which are often seen in irradiated cells.

CELLS FROM RESIDUAL CANCER WITH IRRADIATION CHANGES (Slide No. 2)
HISTOLOGICAL PREPARATIONS

Case No. 1 (81627)

There are significant abnormalities in the surface mucosa and in a transected cell mass lying within 1 mm. of the surface. The latter may represent a transected gland space or a tangential transection of a rete peg. In the altered epithelium there is evidence of cellular proliferation and a disturbance in the maturation process. As a result there are numerous primitive cells in the deeper layers of the epithelium and abnormally large nuclear masses lie at relatively high levels in the epithelium. In the deeper layers of the epithelium corresponding to the deep spinous layer of normal squamous mucosa mitoses range from 1-5 per high power field. In this site there is a moderate variation in the nuclear size and shape. As the surface is approached there is a progressive increase in the size of the cells and in their degree of acidophilia. This is indicative of maturation. There is little evidence of altered cellular polarity in this site. Some of the cells at this level are prematurely keratinized and many are undergoing degenerative changes. In some sites the epithelial cells are vacuolated. The epithelium is infiltrated by leukocytes as is the underlying stroma. The stroma contains many Nabothian cysts. In response to pregnancy, the uninvolved stratified squamous epithelium covering the portio vaginalis is hypertrophic as are the stromal cells.

MARKED DYSPLASIA OF THE UTERINE CERVIX IN PREGNANCY

Case No. 2 (75242)

There is considerable distortion of the tissue which is made up of a connective tissue stroma whose cells are atrophic. At one site in the tissue there are bands of smooth muscle lying in a loose connective tissue stroma. Throughout the stroma there are numerous vascular spaces with small slit-like lumens and thick hyalinized walls. At some sites within the vascular walls there is a fibrinoid-like material. The intervening stroma is infiltrated by small round cells. Along one margin there is a somewhat looser connective tissue stroma which contains numerous small endothelial lined spaces. There is no intact epithelium overlying this loose stroma which is badly distorted. There are small epithelial masses which lie in relation to this surface and which may have been detached from the stroma. The component cells are polygonal with an acidophilic cytoplasm and large nuclei which are varied in size and shape. The nuclear mass appears translucent or opaque indicating a degenerative change. The stromal changes are compatible with previous irradiation. The specimen does not represent a satisfactory sampling of the uterine cervix since the surface mucosa has been dislodged.

IRRADIATION EFFECT IN CERVICAL STROMA. NOTE: THE SURFACE EPITHELIUM IS NOT PRESENT
Case No. 3 (87486)

There is an alteration involving the surface mucosa overlying gland bearing stroma and the neck of a transected endocervical gland. The altered mucosa varies in thickness from one site to another. Well formed rete pegs are not observed in relation to the mucosa. In the deeper levels of the mucosa there is evidence of increased cellular proliferation. Mitoses range from 0-5 per high power field. All mitoses are normal forms. As the surface is approached there is progressive enlargement of the cells and prominent cytoplasmic acidophilia. Nuclear masses at higher levels in the epithelium are abnormally large but have a finely granular chromatin pattern. Cells near the surface do not have an altered polarity. In some sites there is prominent perinuclear vacuolization. Over the surface there are several layers of small cells with acidophilic cytoplasm and small pyknotic nuclei. This is analogous to the parakeratosis which may be observed in epidermis. The underlying stroma is densely infiltrated by lymphocytes, plasma cells, and neutrophiles. Similar cells are observed in the mucosa.

SLIGHT DYSPLASIA OF UTERINE CERVIX

Case No. 4 (86312)

There is a pronounced abnormality of the surface mucosa of the uterine cervix. A similar change involves the underlying gland spaces to a depth which does not exceed 3 mm. The stratified squamous mucosa covering the portio vaginalis has broad elongated rete pegs. In the deeper levels of the epithelium there is an increase in the number of primitive cells without evidence of differentiation. At higher levels in the mucosa there is evidence of cellular differentiation and a pronounced vacuolization of the cells. Beneath the surface there is a granular cell layer. The surface at this site is covered by keratin.

Overlying the gland bearing stroma of the uterine cervix there is a multilayered epithelium whose component cells are relatively small and have no appreciable increase in their spatial dimensions as the surface is approached. These cells are polygonal or spindle shaped with poorly defined cell borders. Spindle shaped cells are often arranged with their long cell axis at right angles to the surface. The nuclear masses are relatively large in relation to the cytoplasmic mass and have a coarsely granular hyperchromatic chromatin. Mitoses range from 2-24 per high power field and are present throughout the entire thickness of the epithelium. There is evidence of degeneration in the surface cells. The underlying dilated gland spaces are replaced by similar epithelium. Many gland spaces have
Case No. 4 (86312) cont.

...a central cavity which contains desquamated primitive cells. The underlying stroma is infiltrated with small mononuclear cells and several lymphoid aggregates are present. In studying a case of this type it is necessary to make a systematic study of the cervix in order to establish that the described changes represent the fullest extend of the process. Invasion is not present.

CARCINOMA IN SITU INVOLVING SURFACE EPITHELIUM AND GLAND SPACES ASSOCIATED WITH DYSPLASIA

Case No. 5 (79392)

There is polypoid mass made up of numerous gland spaces and transected solid cell masses lying in close apposition with little or no intervening stroma. A multilayered disorganized cylindrical secretory epithelium lines the glands. Within the epithelium there are numerous goblet cells, and collections of neutrophiles. Mitoses range from 2-8 per high power field. The transected cell masses in some instances represent tangential sections of glands, however, in other sites they are made up of polygonal cells in a syncytial arrangement. These primitive cells have round or oval nuclei with prominent nucleoli. The mitoses in this site are normal and range from 3-10 per high power field. The stroma is densely infiltrated by lymphocytes and neutrophiles. There is equivocal evidence of vascular invasion. There is hypertrophy of the deeper stromal cells and focal edema.

Elsewhere there is an abnormality involving the surface mucosa and the underlying gland spaces. The component cells have poorly defined cell borders and round or oval nuclei. The long cell axis is more or less perpendicular to the surface. Mitoses range from 2-7 per high power field. There is relatively little evidence of maturation as the surface is approached. Similar epithelial changes involve the underlying gland spaces.

ADENOCARCINOMA OF THE UTERINE CERVIX

(79547)

There is a polypoid mass covered in part by an altered surface mucosa although in some sites there is normal cylindrical epithelium. Transected gland spaces lying within 1 mm. of the surface are replaced by an altered epithelium.

The altered mucosa has well defined expanded rete pegs in some areas. In the lower two-thirds of the epithelium there are numerous small cells whose...
Case No. 5. cont.

long axis is often arranged at right angles to the surface. The nuclei are oval with a finely granular chromatin pattern. From 3-11 mitoses are seen in a high power field. These include normal and abnormal forms. In the upper one-third of the epithelium there is focal evidence of cellular maturation. Cell borders are indistinct and the long cell axis is more or less parallel to the surface. While there is active cellular proliferation in the epithelium there is little disorganization of the cells. Elsewhere there is an immature type of metaplasia underlying an intact columnar epithelium. The epithelial changes in the gland spaces are similar to those observed in the surface. There is a pronounced vascularization of the stroma and a decidual reaction.

MARKED DYSPLASIA OF UTERINE CERVIX IN PREGNANCY

Case No. 6 (86636)

The tissue is composed of transected glands, cell cords, and papilliferous processes throughout which there is focal necrosis. The glands are variable in their size and shape and in their relationship to one another. The lining epithelium varies from a simple cuboidal type to a pseudostratified cylindrical epithelium. Although in some sites ciliated, secretory, and intercalated cells can be demonstrated, elsewhere the epithelium is more primitive with 1-16 mitoses per high power field. The transected cell cords are made up of polygonal cells with vacuolated cytoplasm in some areas and granular basophilic cytoplasm in other sites. The nuclei are round or oval and often indented by the vacuoles. The nuclear chromatin is coarsely granular with scattered macronucleoli. The papilliferous processes are composed of a central vascularized connective tissue core covered by epithelium. The latter is of pseudostratified columnar type. The nuclei are round or oval and many forms are degenerated. The stroma is relatively sparse and in some sites includes considerable collagenous connective tissue. Vascular invasion is not evident. On purely morphological grounds this neoplasm could involve the corpus or the cervix of the uterus.

ADENOCARCINOMA OF UTERUS
Deep within the myometrium there is a circumscribed hemorrhagic zone containing scattered hyalinized masses. At the periphery of the hemorrhagic zone there is a rim of viable trophoblast which lies within 1 mm. of the surface of the uterus.

The transected structures lying within the hemorrhagic zone may represent either hyalinized villi or hyalinized islands of the myometrium which persists because of their relationship to small vascular spaces. While the former explanation seems more likely there is no viable trophoblast at the periphery of the masses in the sections studied. Although some masses contain cells which are reminiscent of Hofbauer cells this in itself does not establish the structures as being villi. The trophoblast which lies at the periphery of the hemorrhagic zone compresses the surrounding stroma. This suggests that these cells have a rather limited growth potential in their present environment. Both syncytiotrophoblast and cytotrophoblast are represented. The cytotrophoblast is only moderately pleomorphic with scattered mitoses which do not exceed 3 per high power field. In the sections examined there is no evidence of vascular invasion.

Although it is difficult to predict the ultimate outcome of this lesion the evidence suggests that it has only a limited growth potential. The presence of a radiodensity in the lung is not necessarily indicative of a fatal outcome since this may diminish in size and disappear following the removal of the uterus. Since the majority of choriocarcinomas are fatal within one or two years the chance of a favorable outcome increases in this patient with each year of survival.

CHORIOCARCINOMA WITH LIMITED GROWTH POTENTIAL

Underlying the stratified squamous mucosa there are ill-defined accumulations of round or spindle shaped cells, multinucleated giant cells and an embryonic mesenchyme with abundant matrix and sparse cells. Round or spindle shaped cells have scant amounts of cytoplasm and relatively large oval or round nuclei with granular hyperchromatic chromatin. Some cells have a more abundant acidophilic granular cytoplasm and pyknotic nuclei. The giant cells have a large granular acidophilic cytoplasmic mass. There are many nuclei scattered throughout or at the periphery of the cytoplasmic mass. These nuclei are round or oval and uniform in size and shape for the most part although in some sites they are more variable in their form. The intervening stroma has an abundant matrix and a paucity
Case No. 8 cont.

of cells. The latter are bipolar for the most part and stellate forms cannot be identified with certainty. There are numerous endothelial-lined spaces throughout the stroma. Neither cartilage nor osteoid is demonstrated.

MIXED MESODERMAL TUMOR (SARCOMA BOTRYOIDES) INVOLVING UTERINE CERVIX

Case No. 9 (64327)

Throughout the tissue there are interlacing bundles of cells enclosing epithelial lined spaces. The cellular bundles are variable in their arrangement. The component cells are spindle shaped when transected parallel to their long axis and polygonal on cross section. Some of the cells are compressed bipolar forms, which are uniform and have elongated wrinkled nuclei with blunt ends. In other sites, the cells have more abundant deeply acidophilic cytoplasm and are varied in size and configuration. Such components have one or several large nuclei which are pleomorphic. The nuclei are hyperchromatic, coarsely granular, and in many instances opaque masses. Scattered cells have one or several large acidophilic nucleoli. Tumor giant cells are prominent in some sites. The mitoses range from 2-18 per high power field and include both normal and abnormal forms. With the P.T.A.H. stain longitudinal fibrils can be demonstrated, however, cross striations are not detected.

Surrounding the epithelial lined spaces the stromal cells are more loosely arranged and in this site there are cells with multiple processes in addition to the bipolar forms. The epithelial cells lining the gland spaces are disorganized. They are varied in their size and shape and have a granular acidophilic cytoplasm. The nuclei are pleomorphic, hyperchromatic, and in many instances pyknotic. Mitoses range from 1-4 per high power field in the epithelium. Some of the gland spaces contain desquamated necrotic epithelial cells.

MALIGNANT MIXED MULLERIAN TUMOR OF UTERUS

Case No. 10 (S-57-3238)

The tissue is rather poorly preserved. Where identified, the surface mucosa is of simple columnar type without evidence of secretory activity. Throughout the underlying stroma there are sparsely scattered tubular glands. These for the most part are straight with small lumens although elsewhere there are larger glands with infolding of the lining epithelium. The intact glandular epithelium which can be studied is of simple columnar.
Case No. 10 cont.

or cuboidal type without evidence of secretion. There are broad expanses of hypertrophied stroma cells with a decidual-like appearance. The vascular spaces throughout the stroma are small and there are no venous lakes. The stroma is edematous in some sites and is infiltrated by scattered lymphocytes and neutrophiles. Autolysis is evident in some areas.

The changes indicate a marked progestational effect with some evidence of an estrogenic effect. The endometrium is not divided into a compacta, spongiosa, and basalis as is usually observed in a decidual cast in pregnancy. Similarly, venous lakes are not seen. These changes have been observed following the use of norethynodrel as in Enovid.

ENDOMETRIUM WITH MARKED PROGESTERONE EFFECT

Case No. 11 (L-1612)

Throughout the stroma there are numerous glands. These have an abnormal relationship to the muscular portion of the uterine cervix. For the most part the glands are tubular in type with small lumens although in other sites they are branching with dilated lumens. The lining epithelium is of simple columnar type although it varies in height depending on the phase of cellular activity. The nuclear masses have a variable position in the cells and most have a normal interphasic structure. Mitoses range from 0-4 high power field. There is degeneration and necrosis in the stroma. There is no prominent papillary configuration and vascular invasion is not evident.

ADENOCARCINOMA OF UTERINE CERVIX