Adenocarcinoma of the cervix has become more common over the years, while squamous cell carcinoma has become less common. (Smith, Tiffany et al. 2000; Sasieni and Adams 2001; Wang, Sherman et al. 2004) This is mainly due to the effectiveness of cervical screening programs. Squamous cell carcinoma precursors are frequently detected in Pap smears, and can generally be readily visualized by colposcopy and eradicated. On the other hand, adenocarcinoma precursors are often difficult to identify, and invasive adenocarcinoma is often present by the time the tumor is detected. Thus, there has been a relative increase in invasive adenocarcinoma compared to invasive squamous cell carcinoma. In addition, there is evidence that there has also been an absolute increase in adenocarcinoma cases over the years. In the 1950’s adenocarcinoma accounted for only about 5% of cases of cervical cancer. Currently, adenocarcinoma accounts for 10-25% of cases of invasive cervical cancer.

Most cervical adenocarcinomas are HPV related cancers. HPV 16 is the most common HPV type, with HPV 18 nearly as common and HPV 45 occurring less often. (An, Kim et al. 2005; Quint, de Koning et al. 2010) There does not appear to be a correlation between the HPV type and the clinical behavior of the carcinoma. As discussed below, some types of adenocarcinoma, such as minimal deviation carcinoma, do not appear to be HPV related.

The average age at presentation is in the 45-55 year range, but it is not uncommon to see adenocarcinoma in situ and invasive adenocarcinoma in younger women. The clinical presentation can be with an abnormal Pap smear, especially in patients with adenocarcinoma in situ and microinvasive adenocarcinoma, but most patients have abnormal bleeding. About 2/3 of patients have stage I tumors at diagnosis and most of the rest have stage II tumors. Only 8-9% of women have stage III or IV adenocarcinomas at presentation. Survival is 70-80% in stage I and 32-37% in stage II. (Baalbergen, Ewing-Graham et al. 2004; Gien, Beauchemin et al. 2010) Staging of cervical cancer is based on clinical parameters. It is not a clinicopathologic staging system as is used in endometrial or ovarian cancer (therefore, patients with stage Ib cancers can be found to have pelvic lymph node metastases). An abbreviated version of the current staging system is given below.

<table>
<thead>
<tr>
<th>Staging of Cervical Cancer (Abbreviated Version)</th>
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<tbody>
<tr>
<td>Ia</td>
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<tr>
<td>Ib</td>
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<tr>
<td>II</td>
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<tr>
<td>III</td>
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<tr>
<td>Class</td>
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<td>-------</td>
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<tr>
<td>IV</td>
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The pathology report should include comments on the grade, the tumor type, the depth of invasion, the presence or absence of lymphovascular space invasion and the status of the resection margins, which should be inked for accurate assessment. Some tumors are exophytic or polypoid, while others are ulcerated or endophytic. A visible or palpable mass is generally present. Lymph node status is a significant prognostic indicator, along with stage. A copy of our synoptic comment for cervical cancer is included with this handout.

**Early Invasive Adenocarcinoma**

Early invasive adenocarcinoma can be difficult to differentiate from adenocarcinoma in situ. (Young and Clement 2002) In some cases there are cytoplasmic and nuclear changes like those seen in early invasive squamous cell carcinoma. These include more abundant cytoplasm in cells at the site of invasion, cytoplasmic eosinophilia, and large nuclei with nucleoli. Most cases of early invasive adenocarcinoma are difficult to recognize, as the tumor cells are identical to those in adenocarcinoma in situ (ACIS). Microscopic findings that suggest invasion include: too many atypical glands per unit area; haphazard distribution of glands; crowded to confluent glands; growth of glands around vessels or nerves; an infiltrative appearance of the glands; and external complexity of glands – large branching glands, pushing lobules, lobules on a stem. Internal complexity of glands can be seen in ACIS but the presence of a cribriform pattern or prominent papillary growth is thought by some to indicate invasion. Other findings that suggest invasion include a fibrous reaction or desmoplastic stroma around the glands or a prominent inflammatory infiltrate around the glands. Generally, the diagnosis of early invasion is based on a combination of findings, rather than on the presence of a single one of the above findings. Many of these criteria are subjective and it is difficult to get agreement in every case.

Microinvasive adenocarcinoma can be recognized by pathologists, (Ostor, Duncan et al. 2000; Ceballos, Shaw et al. 2006) but gynecologic oncologists in our area, who readily accept and conservatively treat for a diagnosis of microinvasive squamous cell carcinoma tend to be skeptical of microinvasive adenocarcinoma. They often treat it as they would an early but grossly visible adenocarcinoma (stage Ib1), usually with radical hysterectomy. There are two systems by which early invasive adenocarcinoma can be classified. In the SGO system, a microinvasive adenocarcinoma is one with a depth of invasion \( \leq 3 \) mm and no lymphovascular space invasion. In the FIGO system FIGO stage I is divided into two categories:

- **Ia** – depth of invasion \( \leq 3 \) mm and horizontal spread \( \leq 7 \) mm; no consideration of lymphovascular space invasion.
- **Ib** – depth of invasion \( > 3 \) mm and \( \leq 5 \) mm and horizontal spread \( \leq 7 \) mm.

There are a number of clinicopathologic studies of microinvasive adenocarcinoma, mainly published by pathologists. In a review of the literature, Ostor found that of 436
women with adenocarcinomas with ≤ 5 mm depth of invasion, 2% had lymph node metastases, 3.4% developed recurrences and 1.4% died of tumor. (Ostor 2000) It is important to accurately microstage early adenocarcinomas, with the idea that microinvasive adenocarcinoma may be treated conservatively by conization or simple hysterectomy. In general, when a glandular abnormality is suspected, a cold knife cone is a better way of evaluating the process than a LEEP excision. This is because it tends to be easier for the pathologist to orient, and assessment of margins can be critical. Also, it is more likely to encompass the lesion. However, with the increasing popularity of LEEP excisions for dysplasia, we are finding that younger gynecologists no longer know how to perform cold knife conizations.

**Classification of Adenocarcinoma**

A number of histologic subtypes of adenocarcinoma have been described. Adenocarcinoma of “endocervical” or “NOS” type is the most common, but the pathologist is likely to see examples of the less common types from time to time. A modification of the current WHO classification that we use at UCSF is given in the table below.

<table>
<thead>
<tr>
<th>Adenocarcinoma of the Cervix</th>
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<tbody>
<tr>
<td>Endocervical (NOS) type adenocarcinoma</td>
</tr>
<tr>
<td>Villoglandular adenocarcinoma</td>
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<tr>
<td>Mucinous adenocarcinoma</td>
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<tr>
<td>Minimal deviation adenocarcinoma (mucinous and endometrioid types)</td>
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<tr>
<td>Enteric/GI type adenocarcinoma</td>
</tr>
<tr>
<td>Endometrioid type adenocarcinoma</td>
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<tr>
<td>Clear cell adenocarcinoma</td>
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<tr>
<td>Serous adenocarcinoma</td>
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<tr>
<td>Mesonephric adenocarcinoma</td>
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<tr>
<td>Adenosquamous carcinoma</td>
</tr>
<tr>
<td>Adenoid basal carcinoma</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
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</tbody>
</table>

**Adenocarcinoma, NOS**

This is the most common type of cervical adenocarcinoma, accounting for about 90% of all cases. Cervical adenocarcinoma is often referred to as being a mucinous type adenocarcinoma, but the amount of mucin in the cytoplasm is variable and sometimes inconspicuous, resulting in an overlap in histologic appearance with endometrioid adenocarcinoma. The glands are often large with complex outlines and they can be branching or angulated, and vary greatly in size. The amount of stroma between the glands varies, as does the type of stromal reaction present, if any. Some tumors contain lobular arrangements of glands, and higher-grade tumors can contain solid areas. The tumor cells are columnar with the nuclei usually being located at the base. Compared with endometrial endometrioid adenocarcinoma, the tumor cell nuclei in endocervical adenocarcinoma tend to be more hyperchromatic and thinner and more elongated. Some cell stratification is usually present in malignant glands. Mitotic figures and apoptotic bodies are usually easy to identify. Mitotic figures are often in the supranuclear cytoplasm, so called “floating” mitoses. The cytoplasm ranges from basophilic and mucinous to dense and eosinophilic. Not all tumors have
obviously mucinous cytoplasm. The grade is based on a combination of architecture and nuclear features. The architecture is assessed as with endometrial adenocarcinoma: grade 1, less than 5% solid areas, grade 2, 5-50% solid, and grade 3, > 50% solid growth. The architecture is typically predominantly glandular, but the nuclei are often too atypical for the tumor to be viewed as grade 1. As with endometrial adenocarcinoma, when there is nuclear atypia out of proportion to the glandular differentiation, the grade is increased by 1.

**Villoglandular Adenocarcinoma**

This type of adenocarcinoma grows in a villoglandular pattern, similar to villoglandular adenocarcinoma of the endometrium. A well-differentiated group has been described in young women, with an average age in the mid-30s, who often have a history of oral contraceptive use. The authors of the first reports on this tumor type viewed it as having a highly favorable prognosis, and proposed that it might be amenable to conservative therapy. (Young and Scully 1989; Jones, Silverberg et al. 1993)

Microscopically, the growth pattern is characterized by surface villi and glands. The villi range from long and thin with a scant amount of stroma to short and fat with abundant stroma in their cores. The villi and glands are lined by one or several layers of columnar cells. No tufting or solid growth should be present. Mucin is absent or scanty. Mitotic figures are present but not numerous. For a diagnosis of well-differentiated villoglandular adenocarcinoma the nuclei should be low grade (grade 1) throughout. These tumors tend to be exophytic with no or minimal invasion of the underlying stroma. Lymph node metastases are rare.

Conservative management is possible in some cases. Superficial well-differentiated villoglandular adenocarcinomas have a favorable prognosis. However, I tend to be cautious in making this diagnosis. It is necessary to see the entire tumor before making a diagnosis of well-differentiated villoglandular adenocarcinoma, and no higher grade patterns should be present. Nuclei must be grade 1 throughout. Tumors with a villoglandular pattern but with higher-grade areas, areas of deep stromal invasion, or even with other types of differentiation have been described. Such tumors can behave aggressively. (Fadare and Zheng 2005; Macdonald, Kirwan et al. 2006) Thus, it does not seem prudent to make this diagnosis based on a small biopsy specimen. As Heatley found on reviewing the literature, there seems to be a problem with reproducibility of this diagnosis. (Heatley 2007)

**Mucinous, Enteric and Gastric Types of Adenocarcinoma**

I have grouped these three types of adenocarcinoma together for convenience in discussing them.

Mucinous adenocarcinoma resembles typical endocervical adenocarcinoma, except that the cytoplasm of a majority of tumor cells contains abundant mucin. This contrasts with the mucin poor appearance of the tumor cells in most endocervical adenocarcinomas.

In some cervical adenocarcinomas the tumor cells have abundant clear or pale cytoplasm and distinct cell borders resulting in a resemblance to gastric cells of pyloric gland type. These stain with immunostains for a type of gastric mucin (HIK 1083). (Kojima, Mikami et al. 2007) As far as I know, this antibody is not available in the US. Tumors in which gastric type cells account for > 10% of the tumor have been designated as “gastric” type adenocarcinomas; in one study about a quarter of endocervical adenocarcinomas fell into this category. Most studies of cervical adenocarcinomas showing “gastric” differentiation have come from Japan. Clinicopathologic studies of have demonstrated a
worse prognosis for adenocarcinomas of gastric type, (Kojima, Mikami et al. 2007) so it may be important to specifically recognize this type of adenocarcinoma. So far, no studies from the United States have reported on this type of adenocarcinoma, and confirmed the significance of the histologic type. Patients with mucinous adenocarcinoma, particularly of gastric type, may have multifocal mucinous lesions involving the female genital tract, including mucinous metaplasia and mucinous adenocarcinoma. (Mikami, Kiyokawa et al. 2009)

Intestinal type adenocarcinomas contain goblet cells, and may also occasionally contain Paneth cells or endocrine cells. Occasional tumors have abundant extracellular mucin, as seen in “colloid” carcinoma. (Shintaku, Kushima et al. 2010) Such tumors can be immunoreactive with such markers as CDX2 and CK20, (McCluggage, Shah et al. 2008; Park, Bramlage et al. 2009) but they are also strongly positive for CK7. Rarely, a signet ring cell adenocarcinoma arises in the cervix. In most cases, the signet ring cell pattern is mixed with other more typical patterns of cervical adenocarcinoma, but a few pure signet ring cell adenocarcinomas of the cervix have been reported.

**Minimal Deviation Adenocarcinoma**

Pathologists are often concerned about this tumor but it is quite rare, accounting for less than 1% of cervical adenocarcinomas. It occurs at a slightly younger age than adenocarcinoma, nos. Two varieties have been described, the mucinous type minimal deviation adenocarcinoma, sometimes called “adenoma malignum,” and an endometrioid variant, which is discussed in the section on endometrioid adenocarcinoma. The average patient is in her mid-40s. The clinical presentation is with abnormal bleeding or a mucoid vaginal discharge. Some minimal deviation adenocarcinomas of the mucinous type occur in women with the Peutz-Jeghers syndrome or with mucinous adenocarcinomas elsewhere in the female genital tract. (Mikami, Kiyokawa et al. 2009) In the sporadic form a putative tumor suppressor gene involved in the pathogenesis of MDA has been localized to chromosome 19p13.3 and mutation of the STK11 gene was documented in 6 of 11 minimal deviation adenocarcinomas in women who did not have the Peutz-Jeghers syndrome. (Kuragaki, Enomoto et al. 2003) Patients with the mutation had a worse prognosis than those who did not have it. Minimal deviation adenocarcinoma does not appear to be associated with HPV infection. Japanese workers have speculated that lobular endocervical glandular hyperplasia is a precursor of minimal deviation adenocarcinoma. (Kawauchi, Kusuda et al. 2008)

Clinically and grossly, the cervix tends to be enlarged and firm. Cysts are often visible on the cut surface. Microscopically, the tumor is predominantly composed of glands lined by well-differentiated cells with mucinous cytoplasm and bland, basal nuclei. The endometrioid variant is lined by cells similar to those in endometrial adenocarcinoma, with basal rounded nuclei and eosinophilic cytoplasm lacking mucin. Mitotic figures are rare to absent. The invasive glands vary considerably in size and shape. Some are cystic. Glands sometimes grow around vessels and nerves, which helps establish the diagnosis. The malignant glands extend deep into the cervical wall, usually to a depth of > 8 mm, and they are usually below the level of residual benign glands. A superficial biopsy or even a cone may be insufficient to establish the diagnosis. A subtle or obvious periglandular stromal reaction is seen around some glands. Careful search usually reveals some glands lined by more atypical cells with mitotic activity, which helps confirm the diagnosis.
Special stains are often not helpful. Stains that tend to be positive in HPV associated adenocarcinomas, such as CEA and p16 tend to be negative. Mucinous minimal deviation adenocarcinoma is reported to stain for HIK 1083, and often for MUC6, but staining for the latter is not entirely specific and as far as I know, the former is not available in the United States.

Features that favor a diagnosis of minimal deviation adenocarcinoma include the presence of symptoms, the presence of a mass, a periglandular stromal response, perivascular or perineural invasion, the focal presence of atypical cells and mitotic figures, positive cytoplasmic staining for CEA, and lack of staining for PAX2. (Rabban, McAlhany et al. 2010)

Endometrioid Adenocarcinoma

Endometrioid adenocarcinomas of the cervix resemble typical cases of endometrial adenocarcinoma, but they are located in the cervix. The percentage of cases of cervical adenocarcinoma that are designated as being of the endometrioid type varies by author, but this is probably an uncommon type. Pathologists often think of endocervical adenocarcinoma as having a mucinous phenotype, but in fact there is a range of cytologic features, including tumors with dense eosinophilic cytoplasm. Such tumors have often been classified as endometrioid adenocarcinomas of the cervix in the past, resulting in a high percentage of endometrioid adenocarcinomas of the cervix in some series. However, other factors also need to be considered when assessing cervical adenocarcinomas, such as the size and shape of the glands, the size and shape of the nuclei, the location of mitotic figures, the staining pattern with mucin stains such as PASD, and the immunophenotype. Endocervical adenocarcinoma of the usual type, with or without mucinous cytoplasm, tends to consist of large, irregular glands lined by columnar cells with stratified, hyperchromatic fusiform nuclei. Mitotic figures tend to be numerous and often appear to “float” in the supranuclear cytoplasm. Endometrioid adenocarcinoma of the endocervix consists of more simple tubular glands lined by columnar cells with less nuclear stratification and basal round to oval nuclei. Mitotic figures vary but may not be numerous, and they tend to be located in the basal cytoplasm of the cells.

It is not clear how helpful immunostains may be in distinguishing this type of cervical cancer from endometrial cancer, since the immunophenotype is similar. Kamoi et al found that staining results depended more the endometrioid phenotype than the site of origin. (Kamoi, AIJuboury et al. 2002) Thus, endometrioid carcinoma of the cervix is rarely positive for CEA, which stains more than 75% of typical endocervical adenocarcinomas. Positive staining for ER and vimentin appears to favor an endometrial origin.

A minimal deviation variant of endometrioid adenocarcinoma has been described. (Young and Scully 1993) Like the more common mucinous type of minimal deviation adenocarcinoma, this tumor is characterized by invasive but typically bland glands. The glands are tubular to cystic, and the cells lack cytoplasmic mucin. The tumor cells are columnar and have an endometrioid appearance, with basal nuclei. Nuclear atypia is minimal as is mitotic activity. Staining can overlap with endometrioid adenocarcinoma of the endometrium, so the tumor cells can express estrogen receptors. Although the glands are lined by bland cells there is glandular crowding, haphazard arrangement of glands, and deep stromal invasion.

Clear Cell Adenocarcinoma
Patients with clear cell adenocarcinoma fall into two clinical categories, those exposed to DES in utero and those with no exposure. These days most patients are postmenopausal women. A bimodal age distribution was noted in cases studied in the Netherlands, with a peak at 26 years and another at 71 years. (Hanselaar, Van Loosbroek et al. 1997) Cases unassociated with DES are currently most likely and account for about 5% of cases of cervical cancer. A review of patients treated for clear cell carcinoma of the cervix after the DES era at the Mayo Clinic, Washington University and Memorial Sloan Kettering Cancer Center (34 cases 1982-2004) revealed that only 2 had a history of DES exposure. (Thomas, Wright et al. 2008) The median age was 53 years, and only 18% had an abnormal Pap smear. Three patients were less than 30, and rare cases of clear cell carcinoma have been reported in children with no history of DES exposure. (Ahrens, Barron-Rodriguez et al. 2005) The usual presenting symptom is abnormal vaginal bleeding, present in 85% of cases. The stage at diagnosis was 71% stage I, 6% stage II, 17% stage III, and 6% stage IV. The prognosis is similar to that of other cervical adenocarcinomas. Patients with stage I or IIa tumors had a 91% 3 year survival. The presence of lymph node metastases had a significant negative impact on survival.

DES related cases, which were formerly more common, occurred in young women with an average age of 19 years. Tumors in this group were located more towards ectocervix, tended to be detected early, and had a favorable prognosis. (Herbst, Ulfelder et al. 1971; Herbst, Norusis et al. 1979)

The microscopic pattern is similar to clear cell carcinomas elsewhere in the female genital tract. Clear cell carcinoma often has an endophytic growth pattern. (Reich, Tamussino et al. 2000) The tubulocystic pattern is the most common. The tubules are lined by cuboidal or flat cells with clear cytoplasm. Some hobnail cells may be present. Other characteristic patterns are growth in solid sheets of clear cells and papillary growth. Some tumors exhibit variable differentiation, with high grade areas that would be difficult to recognize as clear cell carcinoma were it not for the presence of more characteristic areas of growth elsewhere in the tumor. Hyaline material is often present in the stroma and in the cores of the papillae. Mitotic figures are often inconspicuous, but the nuclei are usually high grade. The immunophenotype is similar to that of clear cell carcinoma at other female genital tract sites: positive for CK7, negative for ER, and negative for p53. The cases we have tested have shown positive nuclear staining for HNF-1beta. Since clear cell carcinoma does not appear to be associated with HPV infection (Pirog, Kleter et al. 2000) the diffuse strong staining for p16 that is seen in other types of cervical adenocarcinoma is not likely to be present.

Serous Adenocarcinoma

Serous carcinoma is a rare type of endocervical adenocarcinoma. (Gilks and Clement 1992) Serous carcinoma of the cervix occurs much less frequently than serous carcinoma of the endometrium. Only one series with a significant number of patients has been reported and it contained only 17 cases. (Zhou, Gilks et al. 1998) In one study, serous carcinoma did not appear to be associated with HPV infection. (Pirog, Kleter et al. 2000)

Serous carcinoma of the cervix occurs over a wide age range, but there appears to be a bimodal distribution, with a peak <40 years and another >65 years. (Zhou, Gilks et al. 1998) The typical clinical presentation is with abnormal vaginal bleeding or an abnormal Pap smear. Treatment has been the same as for other types of cervical carcinoma. In the largest series 6 of 15 patients died of carcinoma, an outcome similar to that observed in adenocarcinoma of the cervix overall. (Zhou, Gilks et al. 1998) Most patients have visible
tumors but a few stage Ia tumors have been reported. The gross appearance is similar to that of other types of cervical carcinoma. An exophytic pattern of growth is reported to be most common. Microscopically, the appearance is similar to serous carcinoma of the endometrium. The tumor grows in a papillary or glandular pattern with a variable amount of solid growth. The tumor cells are low columnar with large hyperchromatic nuclei. Nucleoli are variable, but can be large and conspicuous. Mitotic figures are numerous and there are generally more than 10/10 hpf. Psammoma bodies may be present. Lymphovascular space invasion is frequently identified. Serous carcinoma can occur as a pure type or a second type of cervical adenocarcinoma can be admixed. This can be villoglandular adenocarcinoma, and the villoglandular pattern can predominate. Tumors with a villoglandular component are most likely to occur in young patients.

Immunohistochemical studies of serous carcinoma of the cervix are limited. It appears to show positive staining for p53, like serous carcinomas elsewhere in the female genital tract, but in contrast with other types of cervical adenocarcinoma, it is unlikely to stain for CEA. (Nofech-Mozes, Rasty et al. 2006)

Since serous carcinoma of the endometrium is much more common than serous carcinoma of the cervix, endocervical spread of an endometrial serous carcinoma must be excluded before a diagnosis of serous carcinoma of the cervix is made.

**Mesonephric Adenocarcinoma**

Mesonephric adenocarcinoma is a very rare type of cervical adenocarcinoma that occurs over a wide age range. (Clement, Young et al. 1995; Silver, Devouassoux-Shisheboran et al. 2001; Bague, Rodriguez et al. 2004) Most patients present with abnormal bleeding and about 80% have stage IB tumors.

A variety of microscopic patterns have been reported, and multiple patterns are often present in the same tumor. These include crowded small tubules lined by cuboidal cells and containing eosinophilic material, reminiscent of mesonephric tubules, a retiform pattern, with branching slit like glands, a sieve like pattern, a solid pattern, and a sex cord like pattern. The three cases I have seen have all had glandular endometrioid like areas as a conspicuous finding. An admixed sarcomatous component has been reported in some cases – a carcinosarcoma pattern. (Clement, Young et al. 1995; Bague, Rodriguez et al. 2004) Mesonephric adenocarcinoma can extend into the lower uterine segment. Based on limited experience, mesonephric adenocarcinoma appears to be negative for ER, PR, and CEA. (Silver, Devouassoux-Shisheboran et al. 2001) The most helpful stain is CD10, which shows apical and luminal staining for CD10. (Silver, Devouassoux-Shisheboran et al. 2001) Some cases also show focal nuclear and cytoplasmic staining for calretinin. (Silver, Devouassoux-Shisheboran et al. 2001; McCluggage, Oliva et al. 2003)

Most cases are associated with mesonephric hyperplasia, which is often florid and of the diffuse type. (Ferry and Scully 1990; Seidman and Tavassoli 1995) Based on my experience, it can be difficult to differentiate between diffuse mesonephric hyperplasia and mesonephric adenocarcinoma. In one case, a cone biopsy showed numerous mesonephric tubules with low proliferative activity as shown by minimal nuclear staining for MIB-1. However, the hysterectomy contained mesonephric adenocarcinoma with more typical patterns of growth and areas where the mesonephric tubules exhibited a greater degree of proliferative activity. Diffuse mesonephric hyperplasia is said to differ from mesonephric adenocarcinoma due to absence of a back to back pattern, malignant nuclear features, other

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patterns of mesonephric adenocarcinoma, or vascular or perineural invasion, but a small biopsy or a cone biopsy may not be sufficient to reveal this difference and in my opinion patients with what appears to be diffuse mesonephric hyperplasia should have a hysterectomy.

**Adenoid Basal Carcinoma**

Adenoid basal carcinoma is an uncommon tumor that most often arises in elderly women. (Brainard and Hart 1998; Grayson, Taylor et al. 1999) It is usually detected when the patient is evaluated for an abnormal Pap smear. (Parwani, Smith Sehdev et al. 2005) The cervix generally appears clinically normal and the tumor is detected when the patient is treated for high grade SIL. (Ferry and Scully 1988) In some cases the adenoid basal carcinoma is detected in a cervical biopsy or a cone biopsy, while in others it is an unexpected finding in a hysterectomy.

A gross tumor is generally not seen. Or, if one is present, it proves to be squamous cell carcinoma or adenocarcinoma. Microscopically, adenoid basal carcinoma consists of round to irregular small to medium sized nests of basaloid cells with peripheral palisading. The tumor cells have bland nuclei and mitotic figures are usually infrequent. Gland lumens and squamous metaplasia can be present within the nests and if they are sufficiently prominent they can obscure the diagnosis. (Cviko, Briem et al. 2000) Despite the invasive pattern of growth there is generally no stromal reaction. The depth of invasion is variable, but it is not uncommon for it to be > 3 mm.

The diagnosis is made based on the H&E appearance of the tumor. Immunostains typically show a thin peripheral rim of cells that show positive staining for low molecular weight keratins such as Cam5.2 and for p63. Adenoid basal carcinoma is an HPV associated tumor as demonstrated by in situ hybridization and PCR testing; (Jones, Kounelis et al. 1997) it shows diffuse positive staining for p16. (Parwani, Smith Sehdev et al. 2005)

Adenoid basal carcinoma is usually an incidental finding, discovered when the patient is evaluated for an abnormal Pap smear. It is typically associated with high grade SIL, but invasive or microinvasive squamous cell carcinoma or in situ or invasive adenocarcinoma can be present. Adenoid basal carcinoma does not appear to give rise to metastases and no tumor related deaths have been reported. The prognosis is determined by whatever type of in situ or invasive carcinoma is associated with it.

**Adenoid Cystic Carcinoma**

Adenoid cystic carcinoma of the cervix is an uncommon type of cervical carcinoma that occurs mainly in postmenopausal women. (Ferry and Scully 1988) It is an aggressive form of cervical cancer and it is important to differentiate it from adenoid basal carcinoma. In my experience, adenoid basal carcinoma is the more common of the two. The clinical presentation is generally with abnormal bleeding. A visible cervical mass is almost always present. These are aggressive tumors with a propensity for hematogenous spread and about two thirds of patients die of tumor.

A tumor is generally visible at gross examination. Microscopically, the tumor cells have high nucleus to cytoplasm ratios resulting in a basaloid appearance. The cells grow in a cribriform pattern, and in nests, sheets, and cords. A mixture of patterns is typically present, but one can predominate and a solid variant of adenoid cystic carcinoma has been described. (Albores-Saavedra, Manivel et al. 1992) Variable amounts of hyaline basement membrane
like material are present in the cribriform spaces and in the stroma. In cases I have seen the biphasic tubular and basaloid pattern seen in salivary gland adenoid cystic carcinoma has not been present. The degree of nuclear atypia and mitotic activity is greater than is seen in adenoid basal carcinoma and necrosis and a stromal response are present. A point of controversy in reports on this type of cervical cancer has been whether it is a form of aggressive carcinoma with an adenoid cystic phenotype, or a true adenoid cystic carcinoma with patterns of differentiation similar to those present in salivary gland adenoid cystic carcinomas, including the presence of myoepithelial cells. (Ferry and Scully 1988; Grayson, Taylor et al. 1999)

### Synoptic Comment for Cervix Cancer Used at UCSF

**Type of tumor:**

- [ ] Keratinizing squamous cell carcinoma
- [ ] Nonkeratinizing squamous cell carcinoma
- [ ] Verrucous squamous cell carcinoma
- [ ] Warty (condylomatous) squamous cell carcinoma
- [ ] Papillary squamous/transitional cell carcinoma
- [ ] Lymphoepithelioma-like squamous cell carcinoma
- [ ] Small cell nonkeratinizing squamous cell carcinoma
- [ ] Adenocarcinoma
- [ ] Mucinous adenocarcinoma
- [ ] Clear cell adenocarcinoma
- [ ] Minimal deviation adenocarcinoma
- [ ] Villoglandular adenocarcinoma
- [ ] Adenosquamous carcinoma
- [ ] Glassy cell carcinoma
- [ ] Adenoid basal cell carcinoma
- [ ] Adenoid cystic carcinoma
- [ ] Carcinoid tumor (typical or atypical)
- [ ] Large cell neuroendocrine carcinoma
- [ ] Small cell carcinoma
- [ ] Mesonephric adenocarcinoma
- [ ] Other __________________________

**Grade of tumor:**  
- [ ] I  
- [ ] II  
- [ ] III

**Depth of invasion:**
Tumor invades to a depth of _______ cm.  
Cervical wall is _____ cm. thick.  
Tumor invades through _______% of the cervical wall.

**Maximum tumor length:** _______ cm.
Estimated volume: ________ ml.
This can be calculated in various ways, depending on what measurements you can make. 1) Measure all 3 dimensions, \( v = \text{length} \times \text{width} \times \text{depth} \); 2) Measure length and depth, calculate width as number of involved blocks x 2.5mm; 3) Estimate as \( v = \text{length} \times \text{width} \times \text{width} \times 1.5 \)

Width=___________; length=___________; depth=__________

Location in cervix:
- [ ] Anterior cervix
- [ ] Posterior cervix
- [ ] Entire cervix
- [ ] Exocervix
- [ ] Transformation zone
- [ ] Endocervix
- [ ] Confined to polyp
**Lymphatic/vascular invasion:**
- None
- Present in:
  - Lymphatics
  - Blood vessels

**Tumor in parametrium:**
- None
- Microscopic tumor present
- Gross tumor present
- No parametrial tissue present

**Margins:**
- Negative
  - Vaginal cuff margin is ______ cm away from tumor.
  - Deep paracervical (radial) margin is ______ cm away from tumor.
- Positive (list slides _____________)

**Involvement of uterus:**
- None
- Tumor present in endometrium
- Tumor present in myometrium
- Tumor present in endometrium and myometrium

**Lymph node status:**
- None present
- Negative. Total number of nodes examined ______
- Positive. Total number of positive nodes ______
  Total number of nodes examined______

**Other pathology:**
- High grade SIL
- Low grade SIL
- Adenocarcinoma in situ
- None / other ____________________________

*Staging Note: Cervical cancer is staged clinically. This is because some cases are treated surgically and some by radiotherapy. In order to permit comparison between these groups, a clinical stage is assigned. Pathologists should not report a stage for cervical cancer as this might get picked up by a tumor registry or some other agency, and bias treatment statistics.*
References


