

**NEOPLASIA II: Benign and malignant neoplasms in squamous epithelium
(and other tumours)**

AIMS

1. To study the multistep development of cervical neoplasms
2. To develop an understanding of metaplasia: what it is and where it occurs.
3. To recognise Cervical Intraepithelial Neoplasia (CIN) as a pre-malignant neoplasm in the CIN-carcinoma sequence.
4. To identify invasion as evidence of malignancy in a squamous carcinoma of the cervix uteri.
5. To see an important example of cytopathological screening for neoplasia
6. To examine an example of a neoplasm caused by virus infection
7. To see other examples of tumours from skin, breast, stomach and meninges

CERVICAL NEOPLASIA

Cervical cancer is one of most prevalent cancers worldwide and it is socially and economically important. It illustrates several aspects of neoplasia well:

- The multistage development of neoplasms
- Metaplasia and the progression to neoplasia
- The role of infectious agents in some neoplasms
- Screening by cytopathological detection of pre-cancerous neoplastic cells

Squamous epithelial neoplasms and metaplasia

Both benign and malignant neoplasms can arise from any area of SQUAMOUS EPITHELIUM. This includes not only the epidermis of the skin, but also the internal surfaces which are normally lined by squamous epithelium. **Q1: Can you think of some?** (Think about the Gastro-Intestinal Tract).

There are also other important sites where SQUAMOUS CELL CARCINOMAS can arise, perhaps unexpectedly at first sight as these sites are not initially lined by squamous epithelium. This is because it follows a change in the epithelial differentiation programme, known as METAPLASIA, which usually occurs as a response to injury. In such circumstances, tough, multilayered squamous epithelium is particularly suited to replace more delicate, specialised single-layered epithelium and does so quite frequently. Metaplastic change to squamous epithelium is a response to chronic injury and as such has an increased turnover rate, quite apart from other molecular differences which may be present.

| Term | Meaning | Normal or abnormal? | Example |
|--------------------|---|---|--|
| Hyperplasia | increased cell number | either | normal in breast in pregnancy; abnormal hyperplasia can be an early precursor of neoplasia |
| Metaplasia | change of differentiated cell type | either: often a normal response to injury | squamous metaplasia of endocervix (from glandular epithelium); squamous metaplasia of bronchus (from respiratory pseudostratified epithelium); intestinal metaplasia in stomach (from gastric glandular epithelium to intestinal goblet cell epithelium) |
| Dysplasia | abnormal growth pattern with features of benign neoplasia (no invasion) | abnormal | CIN 3 in cervix (see below) – pleomorphic & hyperchromatic nuclei with mitoses above the basal layer (no invasion); squamous dysplasia in the bronchus; glandular dysplasia in colorectal adenomas |

We shall look at an example of squamous metaplasia in the uterine cervix, and follow a possible course of evolution through a premalignant dysplastic stage called Cervical Intraepithelial Neoplasia (or CIN) to an invasive squamous cell carcinoma (this is the CIN-carcinoma sequence).

NORMAL ADULT CERVIX

UG7 Adult uterine cervix: normal
Scanned example 82.74. Glass Slide provided 82.74 or 87.1081
 (which shows one side of the endo cervical canal only).

| Catalogue Number | Small Image | Image Map | Large Image |
|------------------|--------------------------------------|---------------------------|--------------------------------------|
| N_UR_CX_11.jpg | Adult uterine cervix | Image map | Adult uterine cervix |
| N_UR_CX_14.jpg | Adult uterine cervix | | Adult uterine cervix |
| N_UR_CX_07.jpg | Adult uterine cervix | | Adult uterine cervix |
| N_UR_CX_02.jpg | Adult uterine cervix | Image map | Adult uterine cervix |
| N_UR_CX_01.jpg | Adult uterine cervix | | Adult uterine cervix |

Find the **squamo-columnar junction**, which is where the single-layered, **columnar** glandular **epithelium** that lines the endocervical canal of the uterus meets the squamous epithelium of the ectocervix (the part that projects into the vagina). Note how sharp and distinct the boundary can be. The region of the cervix where the squamo-columnar junction occurs is often known as the **transformation zone**.

SQUAMOUS METAPLASIA

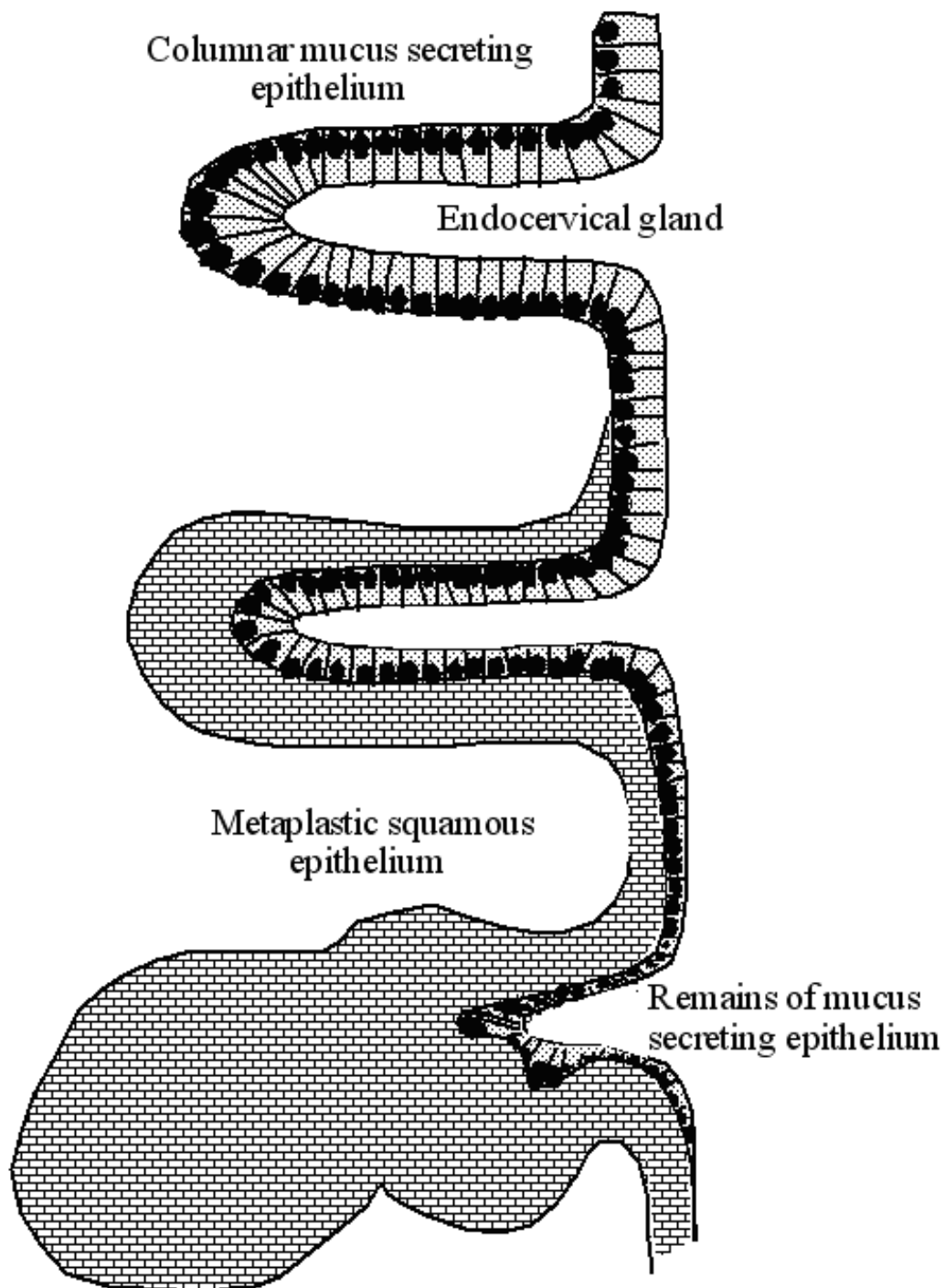
24.1 Endocervix: squamous metaplasia, H&E
87.1210 (diagram follows)

You are given both an H&E stained slide and a scan of a duplicate stained with Alcian Blue to show mucin.

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|-----------|--|
| A_NP_ME_CX_18.jpg | Endocervix – squamous metaplasia | | Endocervix – squamous metaplasia |
| A_NP_ME_CX_19.jpg | Endocervix – squamous metaplasia | | Endocervix – squamous metaplasia |
| A_NP_ME_CX_01.jpg | Endocervix – squamous metaplasia | | Endocervix – squamous metaplasia |
| A_NP_ME_CX_06.jpg | Endocervix – squamous metaplasia | | Endocervix – squamous metaplasia |

24.2 Endocervix: squamous metaplasia - Alcian Blue stain
87.1210

| Catalogue Number | Scanned Image |
|---|---|
| Endocervix – squamous metaplasia- Alcian Blue stain - 87.1210 | Endocervix – squamous metaplasia- Alcian Blue stain |



This tissue represents the lining of the cervix uteri at the transformation zone. As the uterus grows in size around and after puberty, the cervix expands outwards bringing some columnar glandular epithelium (originally from the endocervical canal) onto the ectocervical surface (around the os) and here it is exposed to the low pH vaginal environment. This zone is therefore subject to chronic irritation. As a result, there is often a change from the normal mucus-secreting glandular epithelium, which consists of a single layer of regular tall columnar cells with basal nuclei, to multilayered squamous epithelium. This has happened in this example; over the surface there is extensive squamous metaplasia at the transformation zone.

The Alcian Blue stain helps to distinguish the columnar epithelium (stained blue for mucin) from the metaplastic epithelium (no mucin). In places you can see where the metaplastic epithelium has spread under the columnar epithelium.

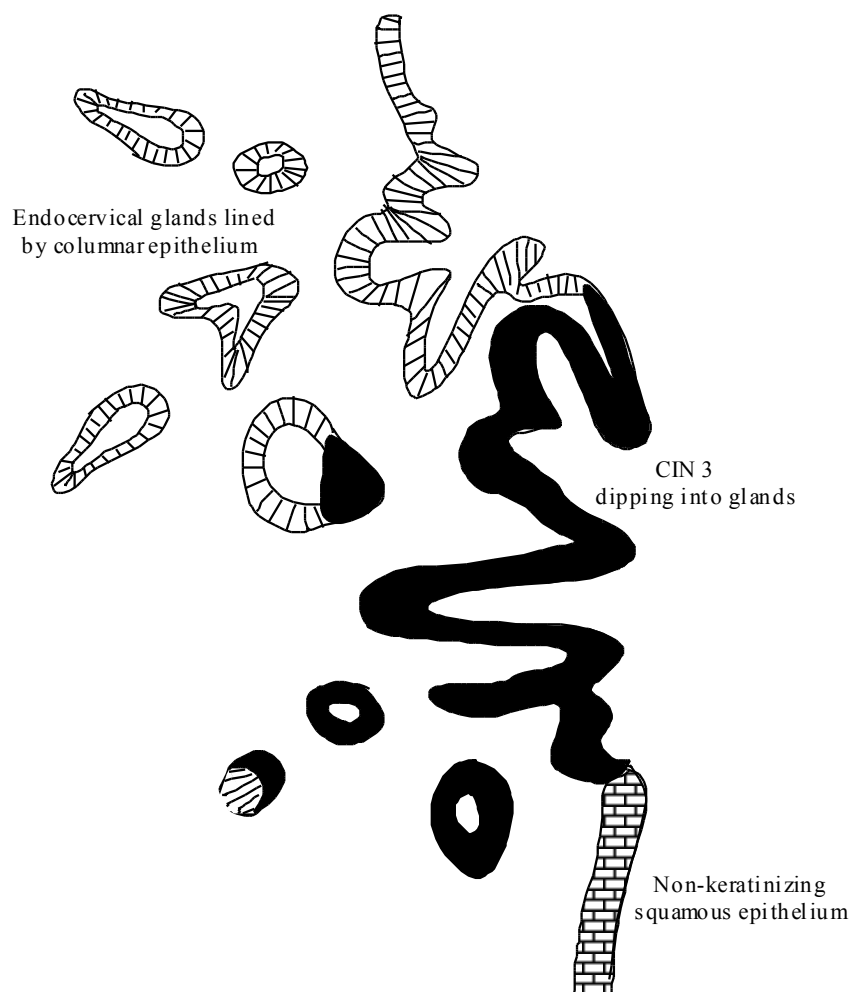
Q2: Squamous metaplasia is common in the cervix uteri and in the respiratory tract. What is the most likely irritative cause in the bronchial tree?

CERVICAL INTRAEPITHELIAL NEOPLASIA [CIN] CAN DEVELOP FROM METAPLASIA

The commonest form of cervical cancer is squamous carcinoma of the cervix which arises within metaplastic squamous epithelium. It often passes through premalignant stages before invasion occurs. These premalignant (or pre-invasive) stages are termed CERVICAL INTRAEPITHELIAL NEOPLASIA, often shortened to CIN. CIN can vary in severity of the neoplastic change, from low grade or CIN 1 (where the neoplastic cells occupy the lower one third of the squamous epithelium, nearest to the basement membrane), through CIN 2 (two thirds occupation by neoplastic cells) to high grade or CIN 3 (full or 3/3 occupation by neoplastic cells). In older textbooks, you may see these changes referred to as dysplasia (for CIN 1 & 2) and carcinoma-in-situ (for CIN 3); these terms are no longer used for neoplasms of the cervix, although they are still used for similar lesions elsewhere, such as in the bronchus. In the USA, the term Squamous Intraepithelial Lesion (SIL) is used and is split into Low Grade SIL (LSIL) and High Grade SIL (HSIL). However, as this term has only 2 subcategories and refers to a "lesion"—and thus does not specify that the abnormality is a neoplasm—it is considered less informative compared to CIN (with 3 subcategories), and thus use of CIN is preferred in the UK (although both systems of nomenclature may be used).

See **DIAGRAM of CINI-III** added to slide folder as an image file.

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|-----------|--|
| A_NP_CU_CX_22.jpg | Uterine cervix-CIN I-III | | Uterine cervix-CIN I-III |



**24.3 Uterine cervix: CIN 3
80.224**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|---------------------------|--|
| A_NP_CU_CX_17.jpg | Uterine cervix – CIN 3 | | Uterine cervix – CIN 3 |
| A_NP_CU_CX_10.jpg | Uterine cervix – CIN 3 | | Uterine cervix – CIN 3 |
| A_NP_CU_CX_04.jpg | Uterine cervix – CIN 3 | Image map | Uterine cervix – CIN 3 |
| A_NP_CU_CX_08.jpg | Uterine cervix – CIN 3 | | Uterine cervix – CIN 3 |

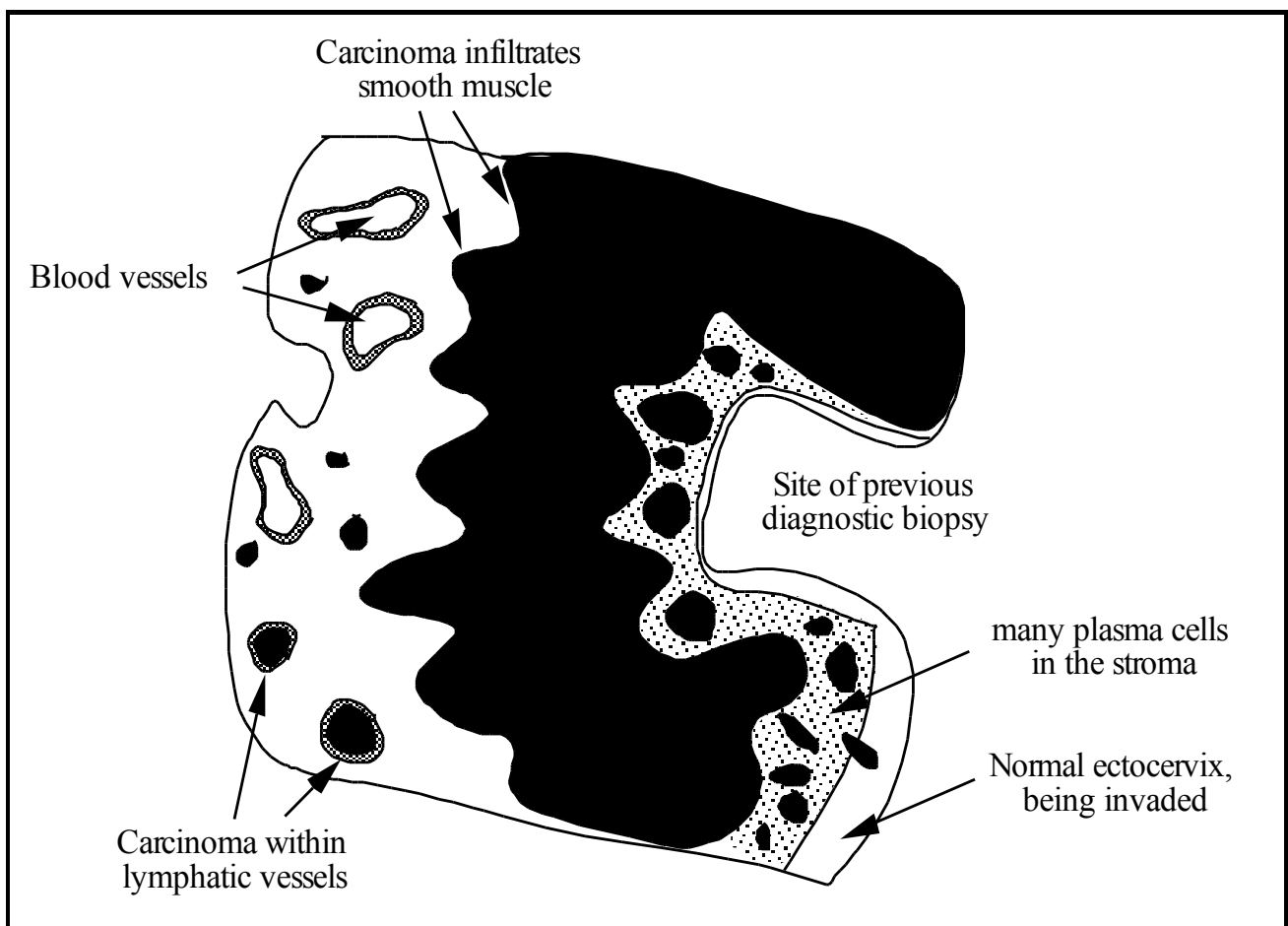
This section of cervix includes an area of **CIN 3** which is confined **within the epithelium** (no invasion through the basement membrane under the epithelium), even though you can see that it extends downwards into the endocervical glands. (Note that this is the same distribution as the squamous metaplasia in the previous sections).

The CIN 3 looks much darker than the normal non-keratinised ectocervical epithelium which is present at one end of the tissue section. This is because there is full-thickness occupation of the epithelium by far more nuclei (which are often larger and more darkly staining than normal); the cells are abnormally orientated, often appearing to stream towards the surface; and there are mitotic figures at all levels of the epithelium (in normal squamous epithelium only the basal layer contains mitotic figures). After the discovery of abnormal cells in the cervical smear of a 39 year old woman, her uterus was removed and these changes were found.

Q3. Can you see evidence of loss of normal proliferative controls in CIN 3?

INVASIVE SQUAMOUS CELL CARCINOMA (CERVIX)

**24.4 Uterine cervix: Invasive squamous cell carcinoma
82.194**



| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|---------------------------|--|
| A_NP_CA_CX_13.jpg | Uterine cervix – Invasive squamous carcinoma | Image map | Uterine cervix – Invasive squamous carcinoma |
| A_NP_CA_CX_17.jpg | Uterine cervix – Invasive squamous carcinoma | | Uterine cervix – Invasive squamous carcinoma |
| A_NP_CA_CX_18.jpg | Uterine cervix – Invasive squamous carcinoma | | Uterine cervix – Invasive squamous carcinoma |
| A_NP_CA_CX_19.jpg | Uterine cervix – Invasive squamous carcinoma | | Uterine cervix – Invasive squamous carcinoma |
| A_NP_CA_CX_20.jpg | Uterine cervix – Invasive squamous carcinoma | | Uterine cervix – Invasive squamous carcinoma |

The features of this section are indicated in the diagram. Notice in particular that the carcinoma has invaded down from the epithelium deeply into the connective tissue stroma of the cervix, forming islands and tongues of cancer cells and some solid sheets of cancer cells. Around the deepest invasive edge, the carcinoma has invaded into some **lymphatic vessels**.

This slide was prepared from the resected uterus of a 47 year old woman who had never had a cervical smear screening examination, but already **had invasive carcinoma** by the time she presented to her doctor, having noticed some irregular vaginal blood loss.

- Q4. Can you see evidence of invasion into the cervical stroma? Is there a host response to invasion? Why does this host response occur?
- Q5. What features can you recognise to determine the pattern of differentiation of this neoplasm (and therefore its histogenesis)?
- Q6. What are some possible sites of origin of squamous cell carcinomas?
- Q7. What is meant by CIN? Is it non-invasive or invasive? How would you recognize it histologically?
- Q8. How do you define metaplasia?
- Q9. What type of vessel do (a) carcinomas usually invade earliest? (b) sarcomas usually invade earliest?

CERVICAL SCREENING

The cervix presents an ideal opportunity for cancer screening, because the precursors of cancer, CIN 1 to 3, are accessible, detectable and removable. Thus, it is possible to identify and remove many precursors before they become malignant—the most effective kind of screening. Cells are scraped from the surface of the cervix with a wooden/plastic spatula and put on a glass slide (either by smearing the cells directly on to the slide to make a “cervical smear” or by washing the cells off the spatula and spinning them on to a slide [liquid-based cytology or LBC preparation], and examined cytologically. The abnormal neoplastic cells from pre-invasive CIN lesions can be recognized (as “dyskaryotic” cells with abnormal nuclei) and subsequently eradicated by treatment (surgical removal often with a hot wire loop). To be effective this screening procedure must be carried out as a regular, routine examination (usually every 3-5 years).

24.5, 24.6A&B Cervical Cytology Specimens (Scans only, no glass slides)

The scanned image of LBC slide 24.5 shows normal squamous cells scraped from the cervix; whereas LBC slides 24.6A & 24.6B show neoplastic cells from CIN, illustrating the abnormal nuclear appearances seen in cervical liquid-based cytology of CIN 1 (24.6A showing mild dyskaryosis) and CIN 3 (24.6B showing severe dyskaryosis) cells. (Hint: look at the cells or cell clusters between the coloured dots.)

| Catalogue Number | Scanned Image |
|--|--|
| CERVICAL CYTOLOGY - Normal | CERVICAL CYTOLOGY - Normal |
| CERVICAL CYTOLOGY – Mild Dyskaryosis | CERVICAL CYTOLOGY – Mild Dyskaryosis |
| CERVICAL CYTOLOGY – Severe Dyskaryosis | CERVICAL CYTOLOGY – Severe Dyskaryosis |

Human Papillomaviruses (HPV) & neoplasms of the cervix

Cancer of the cervix is one of the human cancers strongly associated with an infectious agent, and an important example in the developed world. Almost all cervical carcinomas contain a high-risk Human Papillomavirus such as HPV16 or HPV18. The virus infects the metaplastic epithelium and following persistent infection with high risk HPV there may be development of CIN. HPV can be detected in sections of cervical neoplasms by in-situ hybridisation, i.e. hybridisation of labelled DNA probes to HPV DNA in the section, as illustrated in the next slide.

24.7 In-situ hybridisation for Human Papillomavirus HPV16 DNA in a CIN I lesion. (Scan only, no glass slide)

| Catalogue Number | Scanned Image |
|---|---|
| Human Papillomavirus HPV16 DNA in CIN I | Human Papillomavirus HPV16 DNA in CIN I |

Slide in which the presence of human papillomavirus nucleic acid has been detected by hybridising to a DNA probe (brown signal in the nuclei = hybridisation by labelled probe). Transient genital HPV infections are very common in young sexually active women. Most are subclinical and resolve, with many lesions appearing as low grade CIN 1. A minority of women develop persistent infections, and if they are infected with high risk HPVs, the infected epithelium may gradually progress to CIN2/3 and in time to invasive carcinoma. The virus brings with it certain viral genes that stimulate cell proliferation, immortalization, reduced apoptosis and probably genetic instability, which provide some components of loss of growth control, and facilitate the acquisition of additional mutations that complete the process of progression.

OTHER TUMOURS

24.8 Skin: invasive squamous cell carcinoma 59.574

This section of skin shows an invasive squamous cell carcinoma. Islands of tumour cells infiltrate through the dermis of the skin. The appearances of many of the islands shows keratinisation with formation of central keratin – bright pink protein, in a pattern roughly similar to that seen in normal squamous epithelium of the skin, sometimes forming ovoid shapes with layers of keratin termed “keratin pearls”. This is clear evidence of squamous differentiation in the tumour, indicating its squamous histogenesis.

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|---------------------------|--|
| A_NP_CA_SK_31.jpg | Skin – Invasive squamous carcinoma | Image map | Skin – Invasive squamous carcinoma |
| A_NP_CA_SK_32.jpg | Skin – Invasive squamous carcinoma | | Skin – Invasive squamous carcinoma |
| A_NP_CA_SK_33.jpg | Skin – Invasive squamous carcinoma | Image map | Skin – Invasive squamous carcinoma |

This is a cross section of skin, from a 71-year-old man who developed a firm, crusty plaque on his ear.

**24.9 Lymph node: metastatic squamous cell carcinoma
87.1120**

| Catalogue Number | Small Image | Large Image |
|-------------------|--------------------------------------|--------------------------------------|
| A_NP_MT_LN_34.jpg | Lymph node - Unknown | Lymph node - Unknown |
| A_NP_MT_LN_01.jpg | Lymph node - Unknown | Lymph node - Unknown |
| A_NP_MT_LN_04.jpg | Lymph node - Unknown | Lymph node - Unknown |
| A_NP_MT_LN_05.jpg | Lymph node - Unknown | Lymph node - Unknown |
| A_NP_MT_LN_06.jpg | Lymph node - Unknown | Lymph node - Unknown |
| A_NP_MT_LN_12.jpg | Lymph node - Unknown | Lymph node - Unknown |

The two larger lymph nodes are extensively replaced by abnormal tissue in which there is deep pink laminated material, often arranged as whorls; this is **keratin** and it is immediately surrounded by large cells with features of neoplastic squamous cells. Some contain kerato-hyaline granules. At the edges of the epithelial areas, the cells resemble the basal cells of the skin but have nuclei that are quite pleomorphic and contain frequent mitotic figures. The appearance is that of metastases of well differentiated or **keratinising squamous carcinoma**. The primary tumour was present in the area drained by these nodes, for example in the neck where nodes drain the region including the ear and this might represent spread from the ear skin squamous cell carcinoma of the previous case.

**24.10 Breast: invasive adenocarcinoma
96.359 and 11.1948**

This section of breast tissue is composed of fatty tissue and contains an invasive adenocarcinoma. Centrally, there are variably sized clusters and irregular cords and islands of cancer cells within a fibrous (desmoplastic) stroma. More peripherally, the islands and tongues of tumour cells infiltrate outwards into the fibrous and fatty connective tissue of the breast. The appearances of some of the tumour islands show gland lumen formation with variable sizes and shapes of glandular lumen. Much of the tumour is formed of more solid-appearing sheets of cancer cells and small clusters of cancer cells. This gland formation represents clear evidence of glandular differentiation in the tumour, indicating its glandular (adeno-) histogenesis.

SOME BENIGN TUMOURS MAY BE LIFE-THREATENING

Pathologists define a tumour as 'benign' if it does not show invasion and therefore is incapable of metastasis. However, there are certain 'benign' tumours that are potentially life-threatening and not what we would usually think of as 'benign', such as in the brain.

**24.11 Photograph of a brain with a benign tumour at the surface - a meningioma
Museum specimen 55.315**

This brain tumour, a meningioma, arising from the meninges (membranes overlying the brain), was an incidental finding at post mortem, and the pathologist was able to peel the tumour cleanly away from the rest of the brain, illustrating that it was not invasive. However, as the benign tumour expanded it pressed on (and damaged the function of) the underlying brain structures. If allowed to grow unchecked to a large size, depending on its location on the surface of the brain, it could potentially become life-threatening.

Q10: Do you think it could metastasise? Do you think it could damage or kill the patient?

Q11: Do you know of other tumours that are incapable of metastasis but life-threatening (think physiologically)?

MANY BENIGN TUMOURS ARE NOT LIFE-THREATENING

**24.12 Photograph of a skin lipoma
Museum specimen 26.225**

| Catalogue Number | Small Image | Image map | Large image |
|------------------|---------------------------------------|-----------|---------------------------------------|
| A_NP_TU_SK_04 | Skin: Lipoma (26.225) | | Skin: Lipoma (26.225) |
| A_NP_TU_SK_05 | Skin: Lipoma (26.225) | | Skin: Lipoma (26.225) |

This lipoma is a relatively common tumour in subcutaneous adipose tissue of skin. An example of a benign tumour of mesenchymal origin (fat cells). Note how the pathologist was able to easily separate the tumour from surrounding tissue.

UNKNOWN SLIDE

**24.13 Stomach
80.0863**

| Catalogue Number | Scanned Image |
|------------------|----------------------------------|
| Stomach: 80.0863 | Stomach: 80.0863 |

This section is from the stomach of a patient complaining of upper abdominal discomfort and weight loss of 2 stones.

Sketch the appearances and describe the main features present in this section, then identify the pathological process and give a diagnosis.

Q12. Why might this disease often be fatal?

***Please remember to collect an answer sheet at the end of the practical.
Before you leave, please dim and turn off the light. Cover the microscope.***

DEMONSTRATIONS: CARCINOGENESIS

**A MOUSE: PAPILOMA (induced by carcinogen and promoter)
87.1133**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|-------------------------------|-----------|-------------------------------|
| A_NP_TU_SK_02.jpg | Skin - Tumour | | Skin - Tumour |
| A_NP_TU_SK_03.jpg | Skin - Tumour | | Skin - Tumour |

One of the most informative models of carcinogenesis is the mouse skin system. Application of a single dose of a chemical carcinogen such as DMBA or NMU—the 'initiator'—followed by multiple applications of a 'tumour promoter' such as the phorbol ester TPA, gives skin papillomas as shown here. The initiator has to be applied before the promoter and its effect is irreversible and dose dependent.

It has been shown that in most mouse skin papillomas, initiation involves the mutation of a RAS PROTO-ONCOGENE to a (mutated) RAS ONCOGENE.

Thus, a classical **carcinogen** effect is **activation of an oncogene** (such as RAS).

CLASS 24 MUSEUM SPECIMENS

I **CERVIX: SQUAMOUS CELL CARCINOMA** **24.67**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|------------------------------------|-----------|------------------------------------|
| A_NP_CA_CX_22.jpg | Cervix - Carcinoma | | Cervix - Carcinoma |

The cervix is replaced and expanded by carcinoma which is itself eroded.
From a woman of 48 years who had a blood stained discharge for eight months.

II **BRONCHUS: SQUAMOUS CELL CARCINOMA** **43.339**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--------------------------------------|-----------|--------------------------------------|
| A_NP_CA_BH_57.jpg | Bronchus - Carcinoma | | Bronchus - Carcinoma |

A squamous cell carcinoma that, as in the cervix, arises from a columnar epithelium that has converted by metaplasia to squamous epithelium. The bronchial mucosa is nodular; much of the wall is destroyed by squamous cell carcinoma, which has spread to lymph nodes; the large node below the carina is necrotic. There are distended bronchi distal to the obstruction; some containing inspissated secretion and organising pleurisy is seen over the collapsed and consolidated lower lobe.

Persistent infection may draw attention to underlying carcinoma of the lung.
A 45 year old man with a 5 month history of cough, breathlessness and chest pain.

III **OESOPHAGUS: SQUAMOUS CELL CARCINOMA** **37.162**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--|-----------|--|
| A_NP_CA_OG_01.jpg | Oesophagus - Carcinoma | | Oesophagus - Carcinoma |

An example of a squamous cell carcinoma that arises from a normally squamous epithelium, without metaplasia. A large carcinoma of the lower oesophagus with metastasis to a lymph node.

IV **SKIN: SQUAMOUS CELL CARCINOMA** **26.124**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|----------------------------------|-----------|----------------------------------|
| A_NP_CA_SK_40.jpg | Skin - Carcinoma | | Skin - Carcinoma |

A carcinoma behind the ear, which is undergoing central ulceration.

V **CERVIX : SQUAMOUS CELL CARCINOMA** **26.129**

| Catalogue Number | Small Image | Image map | Large image |
|-------------------|------------------------------------|-----------|------------------------------------|
| A_NP_CA_CX_23.jpg | Cervix - Carcinoma | | Cervix - Carcinoma |

The tumour has spread from the cervix into the body of the uterus. From a 56 year old woman.

**VI BREAST: ADENOCARCINOMA
22.23**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|---|-----------|---|
| A_NP_CA_BE_50.jpg | Breast - Adenocarcinoma | | Breast - Adenocarcinoma |

This is an old specimen and the adipose tissue has become rather dark. However it shows well an ill-defined greyish tumour in the breast, through which run yellow streaks of necrosis. The effect of the fibrous stroma is to draw in the nipple and pull on the underlying pectoral muscle where the carcinoma reaches it. From a 49 year old woman.

**VII BREAST: ADENOCARCINOMA
S61.2405**

| Catalogue Number | Small Image | Image map | Large image |
|------------------|--|-----------|--|
| A_NP_CA_BE_51 | Breast -Adenocarcinoma | | Breast -Adenocarcinoma |

The breast contains an irregular pale tumour with yellowish streaks of necrosis on the surface. The slightly enlarged lymph nodes to which the carcinoma has spread, are included. From a 66 year old woman who had noticed a little blood-stained discharge from the nipple.

**VIII BRONCHUS: SQUAMOUS CELL CARCINOMA
P80.869**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|--------------------------------------|-----------|--------------------------------------|
| A_NP_CA_BH_56.jpg | Bronchus - Carcinoma | | Bronchus - Carcinoma |

The site of origin of the squamous cell carcinoma can not be seen but it is wrapped around the main bronchi and has spread to the lymph nodes, (look at the back of the pot). The enlarged nodes compress the innominate artery and veins are thrombosed. From a 69 year old man who had been coughing and breathless for a few months.

**IX OVARIAN CYST: TERATOMA
27.67**

| Catalogue Number | Small Image | Image Map | Large Image |
|-------------------|---------------------------------------|-----------|---------------------------------------|
| A_NP_TM_OV_14.jpg | Ovarian Cyst-Teratoma | | Ovarian Cyst-Teratoma |
| A_NP_TM_OV_15.jpg | Ovarian Cyst-Teratoma | | Ovarian Cyst-Teratoma |

Teratomas are tumours of germ cells and some, particularly the benign ones, are remarkable for their ability to differentiate into all kinds of tissues (those tissues normally derived from the endoderm, mesoderm and ectoderm in the embryo), emulating embryonic development. This specimen is a large cyst formed by a benign teratoma, which has developed many different tissue types including skin, hair and

teeth. Note that it remains enclosed without invasion — it is benign. A scan of a section through such as teratoma, case 58.0318, is provided for the curious.

**X SKIN: LIPOMA
26.225**

| Catalogue Number | Small Image | Image map | Large image |
|-------------------|---------------------------------------|-----------|---------------------------------------|
| A_NP_TU_SK_04.jpg | Skin: Lipoma (26.225) | | Skin: Lipoma (26.225) |

An example of a benign tumour of mesenchymal origin. Note how the pathologist was able to easily separate the tumour from surrounding tissue. A relatively common tumour in subcutaneous adipose tissue.

**XI BRAIN: MENINGIOMA
55.315**

| Catalogue Number | Small Image | Image map | Large image |
|-------------------|--|-----------|--|
| A_NP_TU_BR_08.jpg | Brain: Meningioma (55.315) | | Brain: Meningioma (55.315) |

This is the brain tumour, arising from the meninges, mentioned above. It was an incidental finding at post mortem, and the pathologist was able to peel the tumour cleanly away from the rest of the brain, illustrating that it was not invasive. However, if it had grown larger, it could have been life-threatening.