Identifying Cancer Cells

(Slide 1 - Introduction) Cytology is the fascinating world of the cell. You are about to see a series of slides that are typical of what a cytotechnologist can see when screening patient samples. You will learn how we identify normal cells and also the cellular changes that occur in disease. There are three "unknown" slides at the end, so you may try your hand at making your own diagnosis.

(Slide 2) Here is the cytotechnologist who examines cells under the microscope to detect signs of cancer in its earliest stages. Cytotechnologists must hold baccalaureate degrees and have special training to search out the smallest abnormalities in the color, shape and size of cells. In the 1940's, Dr. George Papanicolaou published a paper that outlined the procedure now commonly called a Pap smear. This test focuses on early cancer detection by examining cells that are being shed, or exfoliated, from a woman's uterine cervix. New techniques, particularly fine needle aspiration, allow us to obtain cells from deep organs, the lungs and other sites.

Types of Cells Seen on the Pap Smear

(Slide 3) The squamous epithelium diagrammed here is the outermost layer of cells on body and organ surfaces such as the skin and the uterine cervix. Note that the cells are layered on top of a basement membrane. The first layers of cells, immediately atop the basement membrane appear very round and have large nuclei. By comparison, the cells at the top, or surface, are more polygonal or "square" shaped, and have much smaller nuclei. The flat surface cells provide protection for the soft tissue beneath the basement membrane. The surface cells are the oldest and most differentiated of the cells in the epithelium. They will exfoliate naturally and be replaced by cells beneath them, which grow upward from the basement membrane.

(Slide 4) These are normal squamous epithelial cells commonly seen in a Pap smear. A Pap smear is a scraping from the cervical area of the uterus. The cells are spread on a glass slide, stained with the Papanicolaou stain and examined under the microscope. Usually, the cytoplasm of the superficial cells stain pink while the intermediate cell cytoplasm stains blue. Other differences are seen in the nucleus. The superficial cell has a "pyknotic" nucleus which is smaller and darker than the intermediate cell nucleus. In contrast the intermediate cell nucleus is larger and not as dark. The very small cells on the slide are white blood cells. These often have lobed or kidney shaped nuclei with scant amounts of cytoplasm. The entire cell is about the size of the nucleus of an intermediate cell. White blood cells respond to infection and foreign bodies.
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(Slide 5) Glandular cells line a gland and are different than the cells that are layered in squamous epithelium. Glandular cells are tall, with cytoplasm shaped like a column. The nucleus is located at one end of the column. They may have cilia attached to the cytoplasm at one end of the cell. The role of a glandular cell is secretion so the cytoplasm often looks filled like a balloon. When glandular cells are smeared on a glass slide, they are often arranged in a picket fence or honeycomb grouping as seen here.

(Slide 6) The three cells in the center of this slide are koilocytes which show cellular changes that are characteristic of infection by the human papilloma virus (HPV). The nuclei are slightly enlarged, and the area of cytoplasm around the nuclei is “cleared out,” with the appearance of a cavity in the cell. Compare these atypical cells to the neighboring intermediate and superficial cells and note the differences in the cytoplasm. The human papilloma virus is strongly associated with squamous carcinoma in both the female and male genital tracts.

(Slide 7) Herpes is another viral infection. In the center of this slide are several atypical cells showing changes characteristic of herpes infection. The nuclei are molded to one another. Notice that the interior of the nuclei have lost all chromatin detail — an appearance described as “ground glass” nuclei. Some nuclei have dark masses inside called inclusion bodies, another characteristic of cells infected by the herpes virus. In the background there are a large number of white blood cells which have responded to the infection.

(Slide 8) This is a diagram of cancer development. On the left, the epithelium is benign or normal. Dysplasia is the atypical growth pattern in cells that often precedes cancer. Dysplastic or atypical cells are confined to the epithelium above the basement membrane and the degree of severity depends upon how much of the epithelium is involved. When all of the epithelium is involved, carcinoma in situ is diagnosed, indicating that the risk of developing cancer is high. Treatment for the patient is minor surgery to remove the atypical cells which results in a total cure in most cases. However, if the abnormal cells break through the basement membrane, they are considered invasive carcinoma and are capable of traveling to different sites in the body. Cancer that is growing in one site but originated in and traveled from another site is termed “metastatic” and the cancer is said to have “metastasized.”

(Slide 9) These cells exhibit the changes characteristic of mild dysplasia. Compare the two atypical cells (right) with the neighboring normal superficial and intermediate cells. Notice that the size of the whole cells are the same in both the normal and atypical cells, but the nuclei are quite different. The dysplastic cells have enlarged nuclei and the ratio between the size of the nucleus and the amount of cytoplasm has increased. The chromatin pattern in the dysplastic nuclei is granular, with obvious dark spots. There are also scattered white blood cells present.

(Slide 10) These cells show severe dysplasia. Focus your attention on the small dark cells that are grouped in a line. The dysplastic cells have very dark nuclei and small amounts of cytoplasm compared to the normal superficial and intermediate cells in the background. The nuclei also have very irregular shapes. Inside the nucleus of each cell, the chromatin is very hyperchromatic or dark and is coarsely clumped. These cells represent the most severe degree of dysplasia, but still can be treated successfully with minor surgery.
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(Slide 11) These are the major criteria which cytotechnologists use to diagnose a malignancy. Keep these characteristics of malignant and benign cells in mind as you see different types of cancer cells in the following slides.

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Types of Cancer Cells

(Slide 12) These two cells are very characteristic of invasive squamous carcinoma. The telltale features of the nuclei are irregular borders, hyperchromasia and areas of chromatin clumping and clearing. One cell has only a small amount of cytoplasm while the other cell has a long tail-like protrusion of cytoplasm. This “pleomorphism,” or extreme variation in shape, can be characteristic of squamous carcinoma.

(Slide 13) These are the cells of adenocarcinoma, or cancer of glandular origin typified by cells in a three dimensional arrangement. Notice that the cytoplasm looks bubbly. The nuclei are showing features similar to other abnormal cells — irregular shape, chromatin clumping and clearing, and nucleoli within individual cells. Another clue that these cells are malignant is the irregular arrangement within the group. There is no regular orientation or spacing as we saw in the earlier slide having normal glandular cells. In addition, some nuclei overlap and run into each other.

(Slide 14) The bronchoscope is used by physicians to look into the bronchi of the lungs. The long black tubing contains a fiberoptic cable. The tube is passed down a patient’s throat into the trachea and bronchi and a light source allows clear visibility though the eyepiece. Cells can be obtained through the tube by suctioning or brushing the epithelium. The recovered cells are sent to the cytology laboratory to be stained and examined for cancer. A similar instrument can be used to take cells from the esophagus or the stomach.

(Slide 15) Cytotechnologists use many special stains to identify particular organisms. We have discussed the Pap smear stain. Here, silver stain is used to treat a specimen containing pneumocystis carinii. This organism is a common cause of pneumonia in patients with suppressed immune systems, so patients with HIV or recent organ transplants are at risk for this disease. The organism is encased in a cyst which stains very darkly and sometimes has a bullseye or target appearance. The pneumocystis organism is commonly present in most people but does not cause disease unless the patient’s immune system cannot keep the organism in check. Infections like these are known as opportunistic infections.
Identifying Cancer Cells - 4

(Slide 16) Small cell carcinoma is characterized by small cells lined up in a single file arrangement and can be seen in several types of malignancies. They are a classic feature of lobular breast cancer and small cell or oat cell carcinoma of the lung (shown here). The cells are quite small with very little cytoplasm. The chromatin pattern is dark and uneven, and the nuclei often mold to one another. Accurate diagnosis as to the type of cancer is very important because treatment can vary greatly. Small cell carcinoma of the lung is a very aggressive cancer that is strongly associated with smoking.

(Slide 17) Fine needle aspiration, or FNA, is a relatively new procedure in which a physician inserts a needle directly into a tumor, withdraws a sample of cells, and smears them on a glass slide to be stained and examined under the microscope. If the tumor is located in a deep organ such as the lungs, liver or pancreas, the procedure is performed under x-ray guidance. Often a cytotechnologist is present during the procedure and assists in making the slides. A diagnosis can be made shortly after the procedure. FNA actually is less traumatic for the patient and less costly than a biopsy obtained through surgery. The procedure is generally painless and the patient is awake and does not need hospitalization.

(Slide 18) These cells were obtained through fine needle aspiration of the lung. This is an example of large cell carcinoma of the lung. There is great variation in the size and shape of the cells and no uniform arrangement. Malignant characteristics of the nuclei include the irregular membranes, hyperchromasia or dark staining, coarse chromatin with clearing and clumping, and multiple nucleoli.

Making a Diagnosis

Sides 19, 20 and 21, are "unknowns." It's your turn to make a diagnosis. Each case provides the site from which the specimen is taken and an abbreviated patient history. Refer to the Student Worksheet which charts the characteristics of malignant and benign cells. Consider these key points:

- types of cells present
- characteristics that are consistent with normal vs. atypical cells
- features that make diagnosis easy or difficult

(Slide # 19) Unknown Number 1

Site: Lung
History: 38 year old man who is HIV positive with lung infiltrates

Diagnosis: Pneumocystis carinii pneumonia
Criteria for this diagnosis are:
- Dark staining organism
- Bullseye appearance
- Encased in a cyst.
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(Slide # 20) Unknown Number 2
Site: cervix of the female genital tract
History: 36 year old woman with a previous negative Pap smear

Diagnosis: Negative - normal squamous cells
Criteria for this diagnosis are:
• Small nuclei with even chromatin pattern
• Consistent shape and size from cell to cell
• Low nuclear/cytoplasmic ratio
• Pronounced lack of malignant criteria

(Slide # 21) Unknown Number 3
Site: cervix of the female genital tract. Note the white blood cells in the background.
History: 41 year old woman with a history of dysplasia

Diagnosis: squamous carcinoma
Criteria for this diagnosis are:
• Irregular size and shape of nuclei
• Irregular chromatin
• Scant and ill-defined cytoplasm
• Nucleoli
To The Teacher:

This slide/script program was created for use in the high school or junior college science classroom. The goal is to introduce students to the role of cytotechnology and cytotechnologists in the diagnosis of cancer and other diseases. We hope that this material will enhance the curriculum and provide avenues for developing related topics. We also hope that exposure to this material will encourage students to learn more about health related professions.

Please read the script and view the slides prior to showing the material to your students. The evaluations, additional topics and glossary which follow are intended to supplement the slides and script. You may consult your local hospital, laboratory or the American Society of Clinical Pathologists for further information and material.

Objectives

After seeing the presentation students should:
- have an understanding of cytotechnology and the role of a cytotechnologist
- recognize squamous and glandular epithelium
- recognize individual cell types
- recognize the characteristic features of normal epithelial cells
- have an understanding of cancer and pre-cancerous processes in epithelium
- recognize cellular features of atypical and malignant cells
- recognize white blood cells when seen with epithelial cells
- recognize the terms found in the glossary

Vocabulary

Students should be familiar with these words prior to the presentation:
  Cytoplasm
  Female genital tract
  Nucleus
  Nucleoli
  Secretion
  Virus

Additional terms are listed in the Glossary, which can be reproduced as a student worksheet.
Teaching Tips

Following are some tips for using this presentation:

- Provide copies of the glossary prior to viewing so students will be prepared, or have students read the definitions as each word arises in the presentation.
- As slides are shown, discuss situations. Have students attempt to diagnose the three unknown cases at the end of the presentation in discussion or as a writing assignment. Use the "Identifying Cancer Cells" worksheet provided.
- Have students draw cell parts and features of benign and malignant cancers.
- Have students do research on topics related to cytology and cancer diagnosis and present their findings in interesting ways including oral reports, a videotaped "science news" interview, computer demonstration, or poster presentation. Possible topics include:
  - Latest findings on the causes of cancer including genetic predisposition, environmental factors, and sexual transmission.
  - Cancer treatment methods
  - Specific types of cancer such as breast, skin, or lung cancer — what are the risks? symptoms? treatments? prognosis?
  - What does cancer do to the individual cell?
- Have students interview an oncologist, pathologist, or cytotechnologist about the nature of their work.
- Have students interview professionals associated with cancer research, education or support. These include scientists, volunteers with local branches of the American Cancer Society or the American Lung Association, and hospice personnel.
- Arrange a tour of a laboratory where cells are identified.
- Invite a cytotechnologist to present "Identifying Cancer Cells," and to bring sample glass slides which students can view under the microscope. Create additional "unknown" cases with sample slides and worksheet.

The ASCP Career Recruitment Network can help you identify a resource person from a local hospital or independent laboratory. Currently, there is a shortage of cytotechnologists and most professionals are eager to introduce students to the profession, offer laboratory tours and provide one-on-one counseling for seriously interested students. For more information, call 312-738-1336 ext. 364.

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Identifying Cancer Cells

Glossary

- Basement membrane — separates the epithelium from the connective tissue
- Benign — normal or nonmalignant
- Biopsy — removal of cells or tissue for the purpose of making a microscopic diagnosis
- Carcinoma — malignancy or cancer in epithelial cells
- Cervix — lower portion or neck of the uterus which extends into the vagina, "birth canal"
- Chromatin — nuclear material composed of DNA, RNA and protein
- Cytology — the study of cells
- Differentiated — changed or specialized to perform a particular function
- Dysplasia/dysplastic — faulty growth of cells, abnormal tissue development
- Epithelium — layer of cells covering internal and external surfaces of organs and the body
- Exfoliate — to shed or fall off
- Glandular — belonging to a structure that is secretory
- Hyperchromatic — staining darkly, literally "excess color"
- Malignant — abnormal growth that tends to spread, cancerous.
- Metastatic — disease that has spread from its site of origin
- Pleomorphism — unusual and irregular cytoplasmic shapes often associated with squamous carcinoma
- Pyknotic — a nucleus that is opaque, showing no nuclear detail resulting from degeneration or aging of the cell
- Pap smear — a sampling of cells from cervix of the female genital tract which is stained for microscopic examination to allow early cancer detection
- Squamous — layered epithelium with flat pavement-like cells, scaly
- Uterus — hollow, muscular, pear-shaped organ where the fetus develops, "womb"
- White blood cell — leukocytes, blood cells that serve as defense against foreign objects, bacteria, viruses
Identifying Cancer Cells

Student Worksheet

Here is the list of the major criteria a cytotechnologist uses to diagnose malignancy. Use these characteristics to decide which slides you think are cancer. For each case, make a diagnosis of malignant or benign, and explain the criteria you used to make your decision.

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